HEMISPHERIC BASES FOR EMOTION AND MEMORY

EDITED BY: Tad T. Brunye, Sarah R. Cavanagh and Ruth E. Propper
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HEMISPHERIC BASES FOR EMOTION AND MEMORY

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It has become clear that the two halves of the cortex differ in their contributions to both affective and memory processes. Still, the exact nature of the interrelationships among hemispheric function, emotion, and memory remains elusive. For example, controversy remains regarding differential hemispheric involvement in emotion, motivation, and affective style. Regarding memory, although evidence suggests differences in the manner in which the hemispheres interact may be related to memory retrieval, it is still not certain which factors involved in retrieval encourage or inhibit hemispheric communication. The goal of this Research Topic was to bring together diverse scientific perspectives on lateralized brain mechanisms underlying emotion, motivation, and memory. A range of international experts with diverse backgrounds, theoretical perspectives, and experimental methods contributed to the Topic. These contributions inform our understanding of lateralized affective and cognitive processes by providing thorough reviews of our current state of knowledge based on previous literature, by sharing intriguing new empirical findings, and by proposing theoretical models with testable frameworks to stimulate future research.

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Hemispheric bases for emotion and memory

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Keywords: emotion, brain, memory, laterality, hemispheres

The goal of this Research Topic was to bring together diverse scientific perspectives on lateralized brain mechanisms underlying emotion, motivation, and memory. The Topic resulted in eight articles, three of which report original research and five of which review and synthesize past research with the aim of developing new hypotheses and theory. A range of international experts with diverse backgrounds, theoretical perspectives, and experimental methods contributed to the Topic. Contributions strongly reflect this diversity, ranging from examining pupil dilation in response to viewing Rembrandt portraits to understanding how caffeine supplementation influences levels of spatial processing. In all cases, the authors developed strong, empirically guided insights into the lateralized brain mechanisms underlying behavioral effects. Two primary themes emerge to guide and constrain continuing research.

The first theme is related to *dynamic interhemispheric interactions* that subserve emotion, motivational states, and memory. Elizabeth Shobe's article, *Independent and Collaborative Contributions of the Cerebral Hemispheres to Emotional Processing* (Shobe, 2014) proposes a framework for understanding the interaction of lateralized brain mechanisms for identifying and understanding emotional stimuli and engaging in higher-order emotional processing. Under this framework, the right hemisphere engages subcortical structures with the goal of identifying and comprehending positive and negative emotional stimuli, whereas the left hemisphere contributes to higher-level processing such as emotion regulation and adaptation. Critically, dynamic interhemispheric interactions provide the left hemisphere with the information it needs to execute relatively strategic processes. Spielberg and colleagues emphasize the importance of lateralized approach versus avoidance networks in guiding human behavior. In their article, *Hierarchical Brain Networks Active in Approach and Avoidance Goal Pursuit* (Spielberg et al., 2013), the authors propose a hierarchical model consisting of four levels: tactical, strategic, system, and temperamental, following a neurally inspired abstraction gradient along posterior to anterior areas of the prefrontal cortex. Right hemisphere regions process and update avoidance goals, and left hemisphere regions govern approach goals. The model dictates both intrahemispheric interactions across hierarchical layers, and also interhemispheric interactions that cut across both abstraction levels and motivational states; together, these interactions guide, constrain, and update goal-directed behavior over time.

Two particular original research contributions also fit the theme related to interhemispheric interaction. The first is Parker and colleagues' *Effects of Saccadic Bilateral Eye Movements on Episodic and Semantic Autobiographical Memory Fluency* (Parker et al., 2013), demonstrating that horizontal saccadic eye movements enhance episodic but not semantic autobiographical memory retrieval. In accounting for these results, the authors point to the hemispheric encoding/retrieval asymmetry (HERA; Habib et al., 2003) model and its suggestion that episodic memory retrieval depends on efficient and dynamic interhemispheric interactions. They also suggest that saccadic eye movements may induce transient increases in executive function that serve to direct attention toward recalling specific episodic details, which is a unique proposition that will likely motivate subsequent research expanding the nature and scope of dependent measures used in these types of experiments. The second original research contribution fitting the theme of interhemispheric interaction is provided by Edlin and colleagues in their article *Memory for Hand-use Depends on Consistency of Handedness* (Edlin et al., 2013), demonstrating that inconsistent handedness enhances episodic memory for manual actions. Inconsistent-handers more frequently engage bilateral motor regions of the brain, and also have larger corpora callosa relative to consistent-handers, suggesting that increased hemispheric interaction may underlie these reported effects.

The second theme that emerged from this Research Topic is *identifying and characterizing lateralized processes* in both human beings and non-human primates. In this theme, very diverse contributions were made characterizing the universality of lateralized emotion perception and expression across primates on the one and hand, and artistically, nutritionally, and clinically altering levels of lateralized task engagement on the other. Lindell contributed a review article, *Continuities in Emotion Lateralization in Human and Non-human Primates* (Lindell, 2013), providing compelling evidence that both human beings and non-human primates, including rhesus macaques and chimpanzees, use primarily right hemisphere brain mechanisms for generating and perceiving facial emotions, suggesting some universality of lateralized emotional expression and perception. Two other reviews examined lateralized contributions to perception and memory. First, Willment and Golby (2013) support a material-specific model of how focal pathology and surgical management of temporal lobe epilepsy can result in predictable memory deficits, with left and right temporal regions mediating verbal and non-verbal memories, respectively.

Such material-specific links can inform preoperative fMRI memory mapping aimed at predicting and managing post-operative memory outcomes. This is an exciting prospect, and demonstrates a promising avenue for transitioning research on lateralized emotion and memory to high stakes clinical settings. Second, Schirillo (2013) demonstrates that viewing male Rembrandt portraits reliably produced pupil dilations when the portraits were rated as low or high in valence. The author suggests that right lateralized brain mechanisms responsible for emotion perception may explain why some artists may choose to depict the right cheek of male figures, but the left cheek of female figures, perhaps promoting perceptions of dominance in male figures. The final contribution related to identifying and characterizing lateralized processes was provided by Giles and colleagues in their article *Caffeine Promotes Global Spatial Processing in Habitual and Non-habitual Caffeine Consumers* (Giles et al., 2013). The authors found that increasing doses of caffeine promoted memory for distal but not proximal landmark relationships during a spatial memory test. They suggest that such global enhancement may be related to caffeine-induced upregulation of brain dopamine, serotonin, and norepinephrine, neurotransmitter systems that may be higher density in right versus left hemisphere brain regions.

The diverse articles published under this Research Topic advance theoretical positions related to interactive contributions of brain hemispheres toward a broad range of cognitive functions related to emotion and memory, and highlight important characteristics of lateralized mechanisms in human and non-human primates. Relatively, integrated perspectives on brain involvement across a range of cognitive tasks provide stimulating theoretical frameworks for reconciling a range of experimental findings and motivating future research. Specific outstanding questions raised by the Research Topic include:

(1) How might other individual differences modulate lateralized and bilaterally interactive brain mechanisms involved in processing specialized information types and maintaining and updating motivational states and goals?
(2) Contrasting accounts of hemispheric differences in affective and motivational processing were presented. How can we devise research paradigms to test the relative validity of these models?
(3) Much of this work infers lateralized processes from behavior, but how might functional connectivity analyses advance our understanding, for instance by exploring interhemispheric communication as a result of saccadic eye movements or inconsistent handedness?
(4) How might a wider range of nutritional influences, including psychostimulants and amino acids, bias attention, perception, and memory toward particular information types, motivational states, arousal, and mood states, or levels of focus?
(5) How can better understanding lateralized and bilateral interactive brain processes inform applied interventions for clinical or performance-based domains, including predicting surgical outcomes, and informing targeted neuromodulation (i.e., TMS, tDCS)?

REFERENCES

Edlin, J. M., Carris, E. K., and Lyle, K. B. (2013). Memory for hand-use depends on consistency of handedness. *Front. Hum. Neurosci.* 7:555. doi:10.3389/fnhum.2013.00555

Giles, G. E., Mahoney, C. R., Brunyé, T. T., Taylor, H. A., and Kanarek, R. B. (2013). Caffeine promotes global spatial processing in habitual and non-habitual caffeine consumers. *Front. Hum. Neurosci.* 7:694. doi:10.3389/fnhum.2013.00694

Habib, R., Nyberg, L., and Tulving, E. (2003). Hemispheric asymmetries of memory: the HERA model revisisted. *Trends Cogn. Sci.* 7, 241–245. doi:10.1016/S1364-6613(03)00110-4

Lindell, A. K. (2013). Continuities in emotion lateralization in human and non-human primates. *Front. Hum. Neurosci.* 7:464. doi:10.3389/fnhum.2013.00464

Parker, A., Parkin, A., and Dagnall, N. (2013). Effects of saccadic bilateral eye movements on episodic and semantic autobiographical memory fluency. *Front. Hum. Neurosci.* 7:630. doi:10.3389/fnhum.2013.00630

Schirillo, J. A. (2013). Pupil dilations reflect why Rembrandt biased female portraits leftward and males rightward. *Front. Hum. Neurosci.* 7:938. doi:10.3389/fnhum.2013.00938

Shobe, E. R. (2014). Independent and collaborative contributions of the cerebral hemispheres to emotional processing. *Front. Hum. Neurosci.* 8:230. doi:10.3389/fnhum.2014.00230

Spielberg, J. M., Heller, W., and Miller, G. A. (2013). Hierarchical brain networks active in approach and avoidance goal pursuit. *Front. Hum. Neurosci.* 7:284. doi:10.3389/fnhum.2013.00284

Willment, K. C., and Golby, A. (2013). Hemispheric lateralization interrupted: material-specific memory deficits in temporal lobe epilepsy. *Front. Hum. Neurosci.* 7:546. doi:10.3389/fnhum.2013.00546

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HYPOTHESIS AND THEORY ARTICLE
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Independent and collaborative contributions of the cerebral hemispheres to emotional processing

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Presented is a model suggesting that the right hemisphere (RH) directly mediates the identification and comprehension of positive and negative emotional stimuli, whereas the left hemisphere (LH) contributes to higher level processing of emotional information that has been shared via the corpus callosum. RH subcortical connections provide initial processing of emotional stimuli, and their innervation to cortical structures provides a secondary pathway by which the hemispheres process emotional information more fully. It is suggested that the LH contribution to emotion processing is in emotional regulation, social well-being, and adaptation, and transforming the RH emotional experience into propositional and verbal codes. Lastly, it is proposed that the LH has little ability at the level of emotion identification, having a default positive bias and no ability to identify a stimulus as negative. Instead, the LH must rely on the transfer of emotional information from the RH to engage higher-order emotional processing. As such, either hemisphere can identify positive emotions, but they must collaborate for complete processing of negative emotions. Evidence presented draws from behavioral, neurological, and clinical research, including discussions of subcortical and cortical pathways, callosal agenesis, commissurotomy, emotion regulation, mood disorders, interpersonal interaction, language, and handedness. Directions for future research are offered.

Keywords: hemisphere, emotion, brain, valence, emotion regulation, subcortical, cortical, handedness

While the debate over hemispheric asymmetries for emotion perception and identification has been ongoing for over four decades, the most recent observations are a mixture of findings such as a right hemisphere (RH) superiority for negative emotions (Kumar and Srinivasan, 2011; Önal-Hartmann et al., 2012; Sedda et al., 2013), a RH superiority for both positive and negative emotions (Hagemann et al., 2005; Killgore and Yurgelun-Todd, 2007; Alves et al., 2009; Bourne, 2010; Cheng et al., 2012; Irish et al., 2013; Najt et al., 2013; Yuvaraj et al., 2013), no asymmetries for positive emotions (Tomarken et al., 1990; Smith and Bulman-Fleming, 2005; Kumar and Srinivasan, 2011; Zhang et al., 2011; Önal-Hartmann et al., 2012; Najt et al., 2013; Sedda et al., 2013), and no left hemisphere (LH) differentiation between emotional and neutral faces (Najt et al., 2013). A recent meta-analysis concluded that the RH processes both positive and negative emotion, but the LH may only process positive emotions (Abbott et al., 2013). Given the evidence to date, it appears that the RH is integral to processing all basic emotions (positive and negative) and is the seat of subjective affect (feeling). However, inconsistent and contradictory findings make the contributions of the LH to emotional processing highly debatable. It is most interesting that regardless of the methodology and populations studied, the RH consistently demonstrates emotional competence, but the LH sometimes does and sometimes does not. Even when couched in terms of approach and avoidance/withdrawal motivations (e.g., Kinsbourne, 1978; Davidson, 1992) to account for findings that anger (a negative motion) and happy judgments have both been associated with the LH (Harmon-Jones et al., 2013), findings are still mixed with regards to the LH (e.g., Alves et al., 2009; Brüne et al., 2013; Fetterman et al., 2013; Najt et al., 2013; see Miller et al., 2013a). When LH competency is observed, it is consistent only in the identification of positive emotions. However, a broader range of evidence suggests that the LH may play a more crucial role in emotional processing at levels beyond simple identification of emotionality that have yet to be extensively explored. The current paper presents a framework that unifies evidence to date from multiple domains including neuroscience, experimental psychology, clinical psychology, and evolutionary psychobiology.

Presented here is a framework that accounts for inconsistencies of findings by suggesting that the involvement of each hemisphere is qualitatively different, occurring at different points or levels in processing of emotional stimuli, making very different contributions to emotional perception and experience, and for very different purposes. The evidence suggests that the RH directly comprehends and processes the emotional valence of stimuli and then generates the affect (feeling) that is consistent with its interpretation. However, the LH does not appear to engage indirect and genuine comprehension of emotional stimuli, nor does it seem to influence subjective affect that is consistent with the specific stimulus. Rather, being proposed is that the LH contributes an additional or secondary interpretation, based on information received from the RH. This secondary interpretation of the LH appears to be positively biased, making an important contribution to regulation of negative emotion and social interaction, both of which are important for planning, decision-making, and self-preservation. Also, being proposed is that the LH maintains a propositional understanding of RH emotional information and enables verbalization that is more informational than experiential. As such, the LH does not seem to be integral to initial perceptual and experiential stages of emotional processing, but seems more attune to the outcomes of RH interpretation and its application to executive functioning, social well-being, and knowledge representation. Thus, the LH may direct our conscious interpretation of and interaction with stimuli, but does so based on the RH direct and genuine interpretation of the stimulus. This further suggests that complex processing of and responding to emotions require a cross-hemispheric collaboration that originates in the RH, and this is particularly true for negative emotions. Suggestions for testing these hypotheses are presented in Section "Future Directions" below.

LATERAL SUBCORTICAL AND BILATERAL CORTICAL EMOTION NETWORKS

The subcortical and cortical networks provide one indication that the RH is the primary interpreter of emotional stimuli and generator of subjective affect, the outcome of which is then shared with the LH for secondary interpretation and modulation. While several recent papers on neural structures underlying emotional processing focus specifically on prefrontal cortices and the interplay between emotion, motivation, and decision making (e.g., Spielberg et al., 2013), the current framework addresses emotional processing that occurs at a more basic level that begins, appropriately, with subcortical networks and their influence on cortical activity. It appears as though the RH is critical for setting in motion one neural pathway that prepares the organism for immediate action and a second pathway that enables cross-colossal transfer, both pathways originating in subcortical structures. Subcortical connections subserve automatic or unconscious processing of emotional stimuli and subsequent activation for physiological preparation. Gainotti (2012) provided extensive evidence for the automatic and unconscious processing of emotion as being mediated by the phylogenetically old RH amygdala, pulvinar, and superior colliculus. The subcortical amygdala–pulvinar–superior colliculus pathway is considered to be a fast and coarse processor of facial stimuli (facial expressions are the most frequently used emotional stimuli) for orienting to and initiating the physiological arousal that accompanies emotion (Liddell et al., 2005, for review also see Johnson, 2005; Tamietto and de Gelder, 2010). The amygdala has long been associated with perception of emotion, specifically faces (e.g., Adolphs and Tranel, 2003), and the arousing effects of emotion (LeDoux, 1996, 2007; Wallentin et al., 2011). Pulvinar, located in the posterior thalamus, conveys salient emotional information quickly to the amygdala (Morris et al., 1999), but also receives from and influences cortical processes (Sherman and Guillery, 1996). Superior colliculus is a midbrain visual structure important for orienting head and eye movements toward a visual stimulus. Retinal fiber innervation to superior colliculus is commonly understood to enable unconscious visual abilities observed in blind-sight patients. Consistent with Gainotti's (2012) synopsis, subcortical structures of the RH seem most critical for initiating the physiological arousal associated with emotion. For example, Wittling et al. (1998) observed significantly higher myocardium activity following RH as compared to LH viewing of emotional film clips. Further, Spence et al. (1996) demonstrated that physiological responses to emotional stimuli resulted from RH, not LH presentation. As such, the RH amygdala–pulvinar–colliculus pathway automatically, and without consciousness, appears to process basic emotional stimuli and initiate the accompanying physiological responses. Troiani and Schultz (2013) recently demonstrated that unconscious processing of fearful (i.e., negative) stimuli result in a pattern of activity that includes the right amygdala, the right pulvinar, and left inferior parietal cortex, further implicating early subcortical RH involvement followed by LH involvement. Of course, the nature of LH involvement is unresolvable from that study, but it supports the notion of a second cortical–subcortical pathway for emotion processing.

The second pathway, the cortico-pulvinar–cortical pathway may provide the preliminary link between the immediate fast and coarse subcortical processing and the cortical processing of emotion. This may be the precursor for a cross-callosal transfer of emotional information from the RH to the LH. The pulvinar nucleus of the thalamus is directly connected to V4 (extrastriate cortex, part of the "what" system/ventral stream), inferior temporal cortex (TE), and the temporo-occipital area (TEO) (Baleydier and Morel, 1992; Shipp, 2003), and also to posterior parietal cortex (Raczkowski and Diamond, 1980; Webster et al., 1993; Behrens et al., 2003), medial prefrontal cortex (Romanski et al., 1998; Behrens et al., 2003), superior temporal gyrus (Eidelberg and Galaburda, 1982), and cingulate gyrus (Romanski et al., 1998). While there are no connecting fibers between the left and right pulvinar, there are numerous fibers crossing between the hemispheres via the corpus callosum (CC) from cortical areas innervating pulvinar, and several of these have been repeatedly implicated as part of an emotional processing network (Habel et al., 2005; Matsunaga et al., 2009; Park et al., 2010; Kret et al., 2011). For example, van den Heuvel et al. (2009) and Damoiseaux et al. (2006) investigated resting-state networks (RSN) to determine the synchronization of neural structures during baseline activity. The study of RSN contributes to our understanding of neural networks because the associated structures also tend to be functionally networked (Greicius et al., 2009; van den Heuvel and Hulshoff Pol, 2010). van den Heuvel et al. (2009) observed nine different, overlapping RSNs, but most relevant here is the default-mode network (DMN) that links the CC to the medial frontal cortex, the cingulum (white matter extending from cingulate cortex to medial temporal lobe) to medial frontal cortex and cingulate cortex, and the fronto-occipital fasciculi that link the medial frontal cortex, cingulate cortex, and inferior parietal lobes. Other structures belonging to the DMN include posterior parietal cortex (includes inferior parietal lobes) and superior temporal gyrus (Greicius et al., 2004; Fox and Raichle, 2007). Given these associated structures, it is not surprising that the DMN has been associated with integrating cognition and emotion (Greicius et al., 2004), regulating emotion (Grimm et al., 2008; Wiebking et al., 2011), and identifying emotional valence (Sreenivas et al., 2012).

Additionally, because the DMN consists of primarily midline structures, including the CC (the major pathway for inter-hemispheric communication) and cingulate gyrus, whose axons are the genesis of the CC (Koester and O'Leary, 1994; Rash and Richards, 2001), and is functionally associated with different aspects of emotional processing, it follows that a large amount of emotion would be communicated across the hemispheres. Indeed, a high degree of bilateral activity has been observed among DMN structures (Saenger et al., 2012). In particular, Nummenmaa et al. (2012) observed a high amount of synchrony between the structures of the DMN and other emotional processing structures (thalamus, ventral striatum, and insula) during the viewing and appraisal of negatively valenced film clips. Vecchio et al. (2013) also analyzed EEG coherence, concluding that information about negative emotions is transferred between the hemispheres, but that positive emotions were not. These findings provide additional evidence for a link between thalamic and cortical structures during emotional processing and also suggest that information about negatively valenced stimuli in particular is shared between hemispheres. For current purposes, the significance of pulvinar is its connections to both the RH unconscious processing of emotion pathway and to DMN and other emotion relevant cortical structures. Further, because pulvinar consists of association nuclei, operating in both feed-forward (to cortical) and feedback (from cortical) channels, it has been implicated as the major synchronizer of cortical areas. One function may be to synchronize the cortical structures of the DMN during processing of emotional stimuli.

Of interest then, is the type of information pulvinar shares with the cortical areas of the DMN. Pulvinar coordinates cortical function by synchronizing (strengthening communication) various and widespread cortical areas including temporal, occipital, and parietal lobes (Shipp, 2003). For example, during visual selective attention, the synchrony between pulvinar and V4 and TEO is strong, but the synchrony between the two cortical areas alone is weak (Saalmann et al., 2012). Purushothaman et al. (2012) demonstrated that pulvinar also enhances processing in V1 and that removal of pulvinar nuclei prevents visual information from V1 from spreading to other cortical areas. Although pulvinar is divided into several sections (lateral, medial, inferior, dorsal, ventral), it is generally important for synchronizing cortical areas for arousal (Shipp, 2003), selecting attention, and maintaining attentional priorities (LaBerge and Buchsbaum, 1990; Karnath et al., 2002; Ivanov et al., 2010; Li et al., 2012; Saalmann et al., 2012). Grieve et al. (2000) and Pessoa and Adolphs (2010) suggest that pulvinar is especially important in orienting individuals toward biologically important stimuli. Consistent with these findings, Padmala et al. (2010) suggest that the cortico-pulvinar–cortical pathway is important for directing attention to emotional stimuli that may have a weak signal, but are nonetheless biologically significant, such as faces. Nguyen et al. (2013) observed that pulvinar neurons do selectively respond to facial stimuli at short latencies (50 ms), and then engage in rudimentary categorization of stimuli (faces, face-like, eye-like, simple geometric) at longer latencies (100 ms) (Maior et al., 2010).

The RH amygdala–pulvinar–superior colliculus together with the cortico-pulvinar-cortico connections provide neural pathways by which emotional stimuli are subcortically processed by the RH and then cortically processed via pulvinar's widespread synchronization of cortical areas, perhaps separating biologically significant emotional stimuli from other stimuli. Johnson (2005) proposed that the subcortical route that is present in infants also serves to activate cortical structures that are important for expression and comprehension of social aspects of emotion. The pulvinar nuclei may be the key structure in the mechanism by which subcortical processing of emotional stimuli becomes cortical by elevating cortical attention to specific emotionally relevant stimuli. It is also worth mentioning that the anterior thalamus has long been associated with mood or subjective affect due to its numerous connections to limbic structures (Yakovlev et al., 1960; Taber et al., 2004). As such, the anterior thalamic nuclei's contributions to subjective affect coupled with pulvinar's contribution to processing emotional stimuli may converge in the cortical areas (particularly in cingulate cortex, Shackman et al., 2011), as these emotional aspects seem somewhat independent at the level of thalamus.

RH AND LH DISCONNECTION

The preponderance of studies on hemispheric asymmetries for processing emotions and subjective affect (feelings) have utilized presentation of facial expression stimuli, consciously perceived and labeled by participants. By recording response times, accuracies, and neural correlates to the identification of emotional expression, researchers have commonly observed RH competencies (often superiorities) for all emotional expression, and some observe LH ability to identify positive emotions, only. This methodology reveals cerebral asymmetries for perceiving and labeling emotional stimuli, but provides little information about the kind or depth of processing that is done by each hemisphere or how the hemispheres collaborate for normal emotional processing. Studies on the processing abilities and subjective affect of patients with corpus callosal abnormality (i.e., agenesis, commissurotomy) and with unilateral damage provide insight into the separate competencies of the hemispheres and evidence that normal emotional experience requires inter-hemispheric collaboration. The findings from these populations also suggest that the RH is the true seat of emotional experience, attuned to on-line processing (comprehension, identification) of specific emotional stimuli and also creating stimulus appropriate subjective affect. The LH, on the other hand, appears to be disconnected from the on-line, direct processing of emotion, relying on the RH for the transfer of such information and making abstract, propositional extractions. When the LH must process or interpret emotional stimuli in the absence of a RH contribution, the LH appears to be disconnected and lost, resulting in either confabulation or a default positive response bias. This is consistent with Gazzaniga's (1998) notion of the LH acting as interpreter and with the observations of commissurotomy patient V.P. discussed by Gazzaniga and LeDoux (1978). In V.P.'s case, his RH was able to correctly interpret a frightening scene, which resulted in a sufficient amount of physiological arousal. Interestingly, V.P.'s verbal LH appeared to have successfully interpreted the physiological arousal but was completely unaware of its origin, and therefore, confabulated a verbal reason (e.g., "the experimenters and/or room were unnerving"). V.P.'s severed CC resulted in the inability of the LH to directly interpret the emotional stimulus, forcing a reliance on other cues and the resulting confabulation. V.P. illustrates the interpretive nature of the LH or at the very least, that the LH does make interpretations of circumstantial cues in the absence of true comprehension of the causal stimulus. In their review of V.P. and several other findings, Baynes and Gazzaniga (2000) similarly (originally) conclude that the RH makes the situation-appropriate emotional contribution to the LH interpretation of events. Cleverly, they also propose that if this were true, it should be possible to "trick" the LH. This point will be returned to in the Section "Future Directions" below.

In addition to V.P., other commissurotomy studies demonstrate that the speaking LH appears to have lost access to the understanding of the emotional nature of a stimulus. For example, Bermond (1995) observed that CC dysfunction results in deficits in verbal descriptions of emotion, but intact experiencing of basic emotions. Classically, commissurotomized patients are able to use non-verbal indications that they comprehend emotion, but are unable to verbalize these feelings (Sperry et al., 1979). Commissurotomized patients also tend to use left-sided gestures to communicate emotion (i.e., shrugs, batons) (Lausberg et al., 2007), indicating a RH dominance for spontaneous emotional communication. Moreover, the deficits of CC patients do not seem to be a general inability to accurately understand or communicate emotions. For example, Benowitz et al. (1983) observed intact identification of facial emotions presented to the RH, but poor performance when presented to the LH of commissurotomized patients. As such, the problems of CC patients are in their verbal descriptions and the inability of just the LH to understand and communicate emotions.

Similarly, others have observed that a breakdown in interhemispheric communication via the CC in the absence of unilateral damage results in a LH that seems unable to effectively process emotional stimuli, understand the relationship between events and appropriate affect, and apply affect during discourse. For example, Paul et al. (2006) observed that ratings of facial-emotion valence (happy/sad) and degree of arousal (excited/calm) by patients with agenesis of the corpus callosum (AgCC) were highly inconsistent (many completely inaccurate), observing particular difficulty with negative emotions. AgCC also tended to provide lower than normal assessments of arousal. Interestingly, their GSRs (measurements of physiological arousal) were normal, suggesting that the RH subcortical pathway was normally functioning, and the absence of RH damage assumes this as well. Consistent with V.P., it appears as though the verbal LH may have been interpreting that there was some kind of emotion, perhaps based on physiological arousal, but in the absence of accurate information from the RH, it was unable to decipher the precise quality of the emotion. Additionally, O'Brien (1994) observed that AgCC older children showed normal use of language (e.g., vocabulary, sentence structure), but overuse of clichés, deficits in comprehension of jokes, social cues, or facial expressions, and speech that was frequently irrelevant or out of place. This suggests that without the RH, the LH is also impaired in the correct application of emotional language.

The disconnection between emotional experience and language is also evident in the content of AgCC speech. For example, Turk et al. (2010) observed significantly diminished use of emotional words in Thematic Apperception Test descriptions. Buchanan et al. (1980) also describe an AgCC patient as having difficulty with labeling emotional speech and prosody, and verbalizing feelings. Paul et al. (2003) also observed that AgCC patients exhibited significant impairments at matching prosody with their verbal labels, and higher frequencies of misinterpretations, use of non-emotional concrete words, and fewer words in their verbal explanations of idiomatic phrases. The deficits in idiom verbal descriptions and use during speech observed by Paul et al. (2003) and O'Brien (1994) are particularly interesting because idioms are emotionally laden, describing an emotional state or predicament of the observer or the observee (Pandian, 2012). As such, a true understanding of idioms requires accurate comprehension of situation-specific emotions. Moreover, idiom deficits do not appear to be simply a general cognitive deficit or byproduct of an abnormal brain in the AgCC population. Instead, Brown and Paul (2000) observed a preserved ability to match idioms to multiple choice meanings in conjunction with deficits in their verbal explanations (their stimuli did include some proverbs, but were not analyzed separately). This indicates that the comprehension of AgCC for verbal emotional stimuli is intact, but verbal expression is impaired. Idiom comprehension is a RH function, where RH-damaged patients show severe deficits in spoken and multiple choice descriptions (e.g., van Lancker and Kempler, 1987; Brownell et al., 1990). Brown and Paul's findings suggest that preserved idiom comprehension of AgCC was likely due to the intact processing of the RH, the outcomes of which could not transfer to the LH for verbal responding (for review of RH language abilities, see Beeman and Chiarello, 1998; and Lindell, 2006). Further, because idioms are learned by their use in context (Cain et al., 2009), they may be particularly well-suited for acquisition and semantic processing by the RH. Not only does the RH appear to have the advantage for emotional comprehension, but it also has an advantage for comprehending words in contexts (Ince and Christman, 2002), and making appropriate verbal inferences for emotional text (Tapiero and Fillon, 2007). Given these RH superiorities over the LH, it is not surprising that AgCC understand the context and emotion of idioms, but provide inaccurate verbal description. Indeed, children as young as 5 years old use context to derive meaning from idioms, and this is not dependent upon verbal skills; whereas 7-year-olds show accurate knowledge of idiom meaning and this is related to language skills (Le Sourn-Bissaoui et al., 2012). This suggests that the strong ties to language for well-learned clichés may be responsible for their spontaneous use by AgCC patients, and the inappropriateness or out of place use in spoken language appears to be due to the LH being disconnected from the RH emotional competence. In essence, the LH by itself appears to have no access to the emotional aspects of language, just the linguistic and semantic components.

However, the picture is more complex than assuming that commissurotomy or AgCC creates a RH that is simply "locked in." That is, a truly normal emotional experience appears to require some cross-hemispheric communication. Notably, commissurotomized patients are also likely to show some alexithymia (deficits with experiencing and processing emotion) (Hoppe and Bogen, 1977), suggesting that their non-verbal emotional experience is not entirely normal. Further, alexithymics show less frontal coherence between the RH and LH, indicating less information transfer from the RH to the LH (Houtveen et al., 1997). This could be due to the inverse relationship between size of the CC and severity of alexithymia (Habib et al., 2003). Lumley and Sielky (2000) observed similar findings of an association between alexithymia and poor inter-hemispheric transfer in normal participants, as did Romei et al. (2008) and Parker et al. (1999). Importantly, alexithymia does not seem to be due to hypoactivity of the RH, rather the RH shows significant activity for both positive and negative emotions (Aftanas and Varlamov, 2004, 2007). Taken together, the observations of commissurotomized, alexithymia, and AgCC patients indicate that normal emotional functioning requires cross-callosal communication. Specifically, it appears as though there is a disconnection between the RH propensity to accurately comprehend emotional stimuli and generate appropriate affect with that of the LH to verbalize and apply emotional information during social and communicative interaction, and perhaps also to add emotion to the conscious experience (as Gazzaniga and LeDoux proposed).

LH CONTRIBUTION TO EMOTIONAL EXPERIENCE

The empirical literature strongly supports the notion that the RH is integral to the processing of all basic emotions and is especially important for the processing of negative emotions (also known as the RH hypothesis) (Abbott et al., 2013). While several researchers have also observed hemispheric asymmetries for valence (RH, negative; LH, positive) (Davidson and Fox, 1982; Davidson, 1992, 1993, 2004; Davidson and Hugdahl, 1995), I could not locate a single paper published in recent years that showed clear support for this hypothesis. The closest support for the valence hypothesis is from Jansari et al. (2011), who used a fee-viewing chimeric face task. While their findings clearly indicate that positive emotions are better identified from the right side of the face, and negative from the left side, the chimeric face task is not a strong test of laterality owing to the RH ability to tap into both left and right sides of space. This is further clouded by Jansari et al.'s (2000) earlier finding that only females show the valence effect, whereas the Jansari et al. (2011) reported no gender × valence interaction for accuracy. Even though the RH hypothesis has received the most support, there is enough inconsistency to suggest that the LH plays some role in emotion processing. The nature of that role has not been systematically investigated to date nor have any clear theories been put forth, probably because most studies investigating hemispheric emotion asymmetries have been designed for detection and labeling of stimuli, not for gaining insight into how or the depth by which this is accomplished by the hemispheres. Certainly, at this point, we know that the LH can identify positive emotions, but evidence suggests that the LH comprehension of emotional stimuli is shallow, at best. That is, the previous discussion lends to the conclusion that the LH relies on the RH for early identification of the emotional nature of stimuli, and where that is not possible, the LH is inaccurate (positively biased) and confabulatory. As such, reports of LH advantages for identifying emotional stimuli are perhaps due to implementation of strategies other than initial and genuine comprehension of the emotional nature of a stimulus.

However, beyond the preliminary RH processing of emotion, the LH may be crucial for other aspects of emotion, some of which are dependent upon the RH sharing of information and some that may be independent of stimulus but dependent upon motivation. For example, the LH may be involved with regulating the emotion response of the RH or the LH may unilaterally induce a positive mood regardless of the situation. In either case, the LH may be more involved with incorporating emotions into higher cognitive functions to produce refinements or alterations to behaviors that would be otherwise driven purely by subjective affect. To use an analogy, the RH acts as the soldier in the trenches who responds to the onslaught of battleground stimuli, interpreting friend from foe, while the LH acts as higher level commanders, receiving but not directly experiencing information from the frontline, strategizing how to gain an advantage or attain peace, each of which requires keeping a level head and maybe a bluff.

One contribution made by the LH may be toward regulating emotions. Emotional regulation is the implementation of strategies to increase or decrease the intensity of emotional experience (Gross, 2002). Because emotions motivate us to approach (e.g., joy, love), avoid (e.g., sad, disgust), or attack (e.g., anger, disgust) (Stosny, 2011), their regulation lowers stress reactivity, enhances social well-being (i.e., preventing a "knee-jerk response"), and enables attainment of instrumental rewards (e.g., smile politely at a horrible boss to get a raise). The LH does appear to be much less emotionally intense than the RH. For example, participants with greater RH activity reported more intense positive and negative feelings after viewing film clips, but those with higher LH activity showed less intense feelings (Hagemann et al., 2005). Similarly, observations of two commissurotomized patients by Schiffer et al. (1998) also suggest that the LH experiences emotions much less intensely than does the RH. This attenuation of emotional intensity maybe particularly practical in the regulation of negative emotions (Eippert et al., 2007). For example, the LH shows superiority over the RH for overcoming emotional distractors (Dolcos et al., 2006), is preferentially activated during emotional regulation caused by unpleasant stimuli (Davidson, 2004; Parvaz et al., 2012), and characteristic LH activation asymmetry results in more adaptive cardiovascular responses to social threats (i.e., negative feedback) (Koslov et al., 2011) and also attenuated startle responses following offset of, but not during negative stimuli (Jackson et al., 2003). Further, LH frontal gyri abnormality (abnormal thickness) is related to deficits in emotional regulation (Wilde et al., 2012). Additionally, attenuation of an emotional response does not appear to be a general LH "numbness," but may instead be a capitalization on LH processing strategies. The most effective emotional regulation strategies are reappraisal and problem solving (Aldao et al., 2010). Reappraisal, or altering distress by reinterpreting events as positive or benign (Gross, 1998) has been associated with LH prefrontal activity (Ochsner and Gross, 2004; Kim et al., 2012). Problem-solving that requires significant planning to arrive at a solution, such as the Tower of London, has also been associated with LH frontal (Morris et al., 1993; Owen et al., 1996) or bilateral activity (Baker et al., 1996) in the medial, inferior frontal, and cingulate gyri, and the LH supramarginal and angular gyri (Lazeron et al., 2000). Reappraisal and problem-solving strategies also involve a significant amount of verbalization (e.g., self-talk), and several of the LH structures activated during these activities are related to language. Nonetheless, the LH role in emotion regulation also suggests that it is more involved with using and altering emotions than directly perceiving and identifying the emotional nature of stimuli.

Heilman and Bowers (1990) also proposed an inhibitory role for the LH that is akin to emotional regulation. They suggest that LH dysfunction results in a disinhibition of the RH, which in turn, increases physiological arousal associated with emotion. Although their proposal was conjecture at the time of their writing, these more recent findings lend additional plausibility. One additional benefit to emotional regulation may be to maintain a coherent and consistent conscious experience, for which Ramachandran (1995) has suggested the LH to also be dominant. This enables allocation of attention and other cognitive resources to tasks and goals extending beyond the immediate circumstance. Greenberg (2007) also argues that the LH mediates emotion regulation by altering conscious thoughts or interpretations of stimuli. The strategies reappraisal and problem solving most certainly involve an alteration of conscious interpretations. Interestingly, Banks et al. (2012) observed greater GSR in the left-hand (RH contralateral) to implicit presentation of positive and negative facial expressions, but greater right hand (LH) GSR to explicit presentations of negative expressions. This implicates the early role of the RH in emotion processing and the importance of LH involvement during conscious stages of emotion, but also that the LH involvement at more advanced levels may be restricted to additional cognitive processing of negative emotions.

Observations of clinical populations with affective disorders provide additional clues that the LH is important for regulation of negative emotions. Panic disorder (PD) characterized by fear, anxiety, and avoidance has been associated with hyperactivity of the RH (Drayer et al., 1989; Smeets and Merckelbach, 1997; Wiedemann et al., 1999). PD patients express fear or anxiety normally, but these emotions are invoked too frequently (such as baseline or rest phases, Gorman et al., 1988; Wilhelm et al., 2001) and show an attentional bias for threatening information (McNally et al., 1990), which is also suggestive of a hyperactive RH. Alternatively, Akiyoshi et al. (2003) using NIRS, observed LH hypoactivity, but not RH hyperactivity in PD patients. Interestingly, Prasko et al. (2004) observed that symptom reduction following pharmacological and cognitive-behavior treatment of PD coincided with reduced activity (PET/FDG uptake) in the RH and increased activity in the LH, suggesting that PD may be associated with both LH hypoactivity and RH hyperactivity. Depression has also been associated with LH hypoactivity (Henriques and Davidson, 1991). LH damage can result in reduced motivation and activity (abulia) (Förstl and Sahakian, 1991; Caeiro et al., 2013) and increased apathy (Kang and Kim, 2008; Onoda et al., 2010), each of which are symptomatic of depression. Further, these symptoms prevent attainment of goals, coinciding with a negative emotional state but are not themselves emotional states. However, a dysfunctional LH and resulting absence of emotional regulation would result in an emotional landscape dominated by negative feelings (e.g., Rottenberg, 2005; for review see Hecht, 2010). Indeed, depressed patients have a particular difficulty with emotional regulation (Pietrek et al., 2012). It is unlikely that a hypoactive LH and resulting depression indicates a lack of positive emotion and therefore, valence asymmetries because there is ample evidence demonstrating RH capability for both positive and negative emotion. Deep brain stimulation has been demonstrated to alleviate depression (Lozano et al., 2012) further implicating a pathology of neural hypoactivity. RH hyperactivity that has been observed in depressed patients appears to only be associated with stress, anxiety, and panic symptoms (Hecht, 2010). As such, it is possible that PD patients exhibit both hypoactivity of the LH and hyperactivity of the RH, where depression is associated mostly with LH hypoactivity (Iznak et al., 2011; Arnsten and Rubia, 2012). In both PD and depression, negative emotions are poorly regulated, and the added RH hyperactivity in PD patients appears to also add additional intense and negative emotions. At the least, their behaviors suggest that LH hypoactivity is a common underlying pathology. This is also suggested by the observations that PD is frequently comorbid with depression (Leckman et al., 1983; Gorman and Coplan, 1996; Kessler et al., 1998), and this comorbidity is more likely after LH stroke (Bhogal et al., 2004; Barker-Collo, 2007; for review). In keeping with the evidence suggesting that negative emotions in particular are shared between the hemispheres, the nature of each hemisphere's involvement may be that the RH mediates the subjective affect and the LH regulates it. In PD and depression, emotion cannot be regulated due to suggested hypoactivity of the LH.

Patients with RH damage (therefore, RH hypoactive) show the opposite affect problems. Specifically, patients with RH damage exhibit mania (Sackeim et al., 1982; Starkstein et al., 1989; Lee et al., 1990; Morris et al., 1996; Paradiso et al., 1999; for review see Santos et al., 2013), and this is much more bizarre and inappropriate than depression or even PD. Manic bipolar patients show decreased RH activity in response to fearful facial expressions (Harmon-Jones et al., 2002; Killgore et al., 2008; Versace et al., 2010), and cortico-vestibular stimulation of the left ear increases RH activation and reduces mania (Blumberg et al., 2000). Early uses of the Wada test (Wada, 1949) also confirm that immobilization of the RH results in mania, whereas the same for the LH results in catastrophic and depressive responses (e.g., Perria et al., 1961). Manic and euthymic bipolar patients are also relatively poor at recognizing facial emotions, as compared to healthy controls (Lembke and Ketter, 2002; Bozikas et al., 2006), further implicating RH dysfunction. If we only considered the affect disordered populations, we could assume valence asymmetries (LH, positive; RH, negative), as did the originators of the valence hypothesis. However, if this were true, then patients with dysfunction of the CC should consistently show happy speech and have no problems with happy valence discourse or facial expressions. But, as previously indicated, that is not the case.

Collectively, observations of collosal and affective clinical populations more plausibly suggest that a LH disconnected from the RH (due to callosal or unilateral damage) results in LH emotional confusion and verbal confabulation. When the two are connected, a damaged LH appears to release or fail to regulate the negative emotions of the RH and a damaged RH provides no information about negative stimuli or feelings to the LH. Pathological mania due to RH dysfunction could therefore, be an outcome of continued up-regulation of mundane non-emotional experiences in the absence of RH input or it could be due to a general positive bias of the LH. The latter suggestion seems more plausible because it is more consistent with previous literature demonstrating that the LH has at least some competence for positive emotion. Further, because the LH appears to exhibit less intense emotions under normal circumstances, a damaged or hypoactive RH forces emotional processing onto the LH, which only seems to be independently capable of positive assessments.

The behaviors of manics and depressives also indicate that the LH is poor at interpreting the emotional nature of stimuli. First, depression or catastrophic reactions would be considered normal responses to an experience of traumatic brain injury, sudden disability, and traumatic life events (a frequent trigger for clinical depression). As such, the depression observed in LH damaged patients is actually more normal and appropriate to their situation suggesting that the RH at least accurately appraises the situation. By comparison, the manic reactions of the LH are truly inappropriate to the experience of brain injury and disability, and suggest that the LH does not have the capability to comprehend and apply the appropriate emotional response. Even in non-TBI populations (unilateral hyper/hypo activity), it appears as though only the RH is in tune to the emotionality of a situation or stimulus, whereas the LH relies on a positive bias that may or may not be situation-appropriate.

Further underscoring the bizarre and out-of-touch emotional behavior of LH-reliant manics is that persistent and overly positive interpretations of stimuli are survival disadvantages. More advantageous is a negative and fearful bias, a bias that is more prominent in the natural behaviors of prey animals because it decreases the chances of being a victim of predation. As such, from an evolutionary perspective, it seems more advantageous to consistently interpret ambiguous or novel stimuli as negative and quite disadvantageous to be persistently positive. The exception to this is the advantage of interpreting kin and some familiar stimuli as positive, but this, too, appears to be a RH function. For example, infant–caregiver emotional bonding coincides with RH, not LH activity (Schore, 2005; Noriuchi et al., 2008; Minagawa-Kawai et al., 2009). Moreover, one common phylogenetical argument for asymmetry is that a dual or lateralized brain enables for greater modularity, and therefore a much wider repertoire of abilities and behaviors. As species evolved, brains evolved with the addition of mass (and hence, structure and function), and so later evolved species maintain structures of earlier species with the added benefit of additional brain. This is mirrored by observations that evolutionarily older structures appear prior to newer structures during prenatal development ("ontogeny recapitulates phylogeny") (Previc, 1991), and the RH does seem to have evolved earlier than the LH (Gupta et al., 2005; Howard and Reggia, 2007; Carmona et al., 2009). Given the advantages of avoiding predation and attaching to kin, and the earlier development of the RH, it is advantageous for the RH to possess competencies to accurately and appropriately interpret both positive and negative emotional nature of stimuli. Further, the RH may do so with a greater likelihood of negative interpretation for non-kin or non-drive stimuli which, incidentally, encompass the vast majority of stimuli used to study emotion asymmetries, such as facial expressions of complete strangers. It is also reasonable that the evolution of the LH would not add simple redundancy to this process, but would instead, add something valuable or that provides a survival advantage. As such, the LH probably did not take over positive emotion from the RH, but added new processing strategies to the information already sufficiently processed by the RH. These processing strategies may include emotional regulation, but may also be a more general positive response bias. At this point, two questions arise: (1) is the LH positively biased, without directly interpreting the emotional nature of stimuli? and (2) what possible selective advantage could this have?

There is some evidence that the LH has a general positive bias in the absence of true emotional comprehension. Nijboer and Jellema (2012) presented the case of a patient with extensive RH damage who, as expected, had difficulty recognizing most emotions but appeared normal for positive emotions. Upon closer inspection, this patient was simply biased toward providing positive responses, without any true comprehension of the positive expression. This case illustrates that the LH may not directly interpret stimulus emotionality, where observed valence asymmetries reflected a LH response bias. Note then, that typical lateralized half-field presentations of emotional faces cannot detect this bias. Rather, a LH bias would reveal accuracy to be much higher for positive and lower for negative rvf/LH stimuli, and high accuracy for both positive and negative stimuli in the lvf/RH. This is a fairly common finding where authors concede partial support for both the valence and RH hypothesis. Even where differences between emotional and neutral faces are observed in each hemisphere, it is potentially confounded because emotional faces and neutral faces differ on more than one dimension, where neutral expressions are not necessarily part of an emotion continuum because they are the absence of emotion. As such mental processes driving responses to emotional faces may be different from those driving responses to neutral faces (e.g., Bobes et al., 2000). The findings of Nijboer and Jellema (2012) warrant experimental replication, but future researchers could also utilize signal detection analyses for clarification between response bias and accuracy. To my knowledge, there have been few studies applying signal detection analysis to emotion processing tasks. One demonstrated a response bias with happy faces, but greater sensitivity to negative faces in a free-viewing task (Schulz et al., 2007), another demonstrated greater sensitivity for RH presentations of low-intensity positive stimuli (Snodgrass and Harring, 2000), and a third demonstrated greater sensitivity of the RH to emotional pictures and faces (Snodgrass and Harring, 2004). Each of these studies suggests that the LH may not be particularly accurate and maybe biased to give positive responses in the absence of true comprehension of affect. As such, a LH advantage for responding to positive stimuli used as support or partial support for the valence hypothesis is not surprising given that the LH may be consistently and inherently primed to do so.

If the LH truly has a default bias to respond positively or promote positive affect, then this should present as an advantage. One such advantage would be that interpreting events as positive and giving the impression of positive emotion is beneficial to social interaction. People tend to overemphasize positive and overreject negative descriptions of the self (Paulhus and Trapnell, 2008). Kircher et al. (2000) observed a LH dominance during PET recordings of participants making decisions about their own personality traits (replicated by Faust et al., 2004), and the LH is also more likely to endorse likable traits about ourselves (Marsolek et al., 2013). Further, patients with RH damage following stroke present an extreme positive view of their predicament, claiming fewer or outright denying physical deficits (e.g., anosognosia) (Vocat et al., 2010; Azouvi and Peskine, 2013). So, the LH appears to improve our perception of our own shortcomings. The LH may also enable us to perceive others more positively. For example, LH stimulation by rTMS results in non-hostile attributions of other's intentions (Giardina et al., 2011). Positive emotional responses are also more socially acceptable than negative responses, and people prefer to interact with those who have positive versus negative outlooks, and positive moods induce social interaction (Harker and Keltner, 2001; Lyubomirsky et al., 2005; Whelan and Zelenski, 2012; Miller et al., 2013b). As such, it is in our best social interests to actively engage in impression management by consistently promoting positive aspects of ourselves, showing positive emotional responses, and perceiving others (perhaps via facial expression) as non-hostile and approachable. Importantly, this does not suggest that the LH is the seat of "self-awareness" (Keenan and Gorman, 2007 provide a case for RH as the seat of "self"). Rather, this suggests that the LH is the seat of an idealized self, one that maintains or constructs a consistent, conscious sense of self (as suggested by Ramachandran, 1995), and enables for self-control (as suggested by Greenberg, 2007). The LH then, appears important for managing social impressions and promoting social interaction using a consistently positive frame. Pathological mania is an extreme presentation of this, and as has been previously indicated, results from a dysfunctional RH. This also suggests that while the LH may be disconnected from directly experiencing and processing the emotional nature of stimuli, in a normally functioning brain this has some very tangible benefits. Buck (1999, 2002) and Ross (1997) also advanced the idea that the LH is important for pro-social emotions, arguing in favor of a communicative gene hypothesis where fitness depends on the ability of genes to cooperate and communicate with other genes in the population pool (self or others). As such, it is perhaps advantageous for the LH to be disconnected from the direct and preliminary interpretation of the emotional nature of a stimulus, in favor of facilitating social interaction and goal attainment through regulating negative emotion and positive bias. Extending this, we could further argue that the LH cons or masks the self and others as a means toward goal attainment, making this adaptive.

In keeping with the notion that the LH is important for integrating emotional information received from the RH into higher level cognitions, it is reasonable to suggest that the LH transforms this information into propositional knowledge for categorization and verbalization. In McGilchrist's (2010) review of the literature on cerebral asymmetries, he cites several studies that demonstrate a LH propensity for categorizing and storing abstract or propositional knowledge, as compared to the RH propensity toward "real-world views" and organization of knowledge by specific exemplars. This aligns with the findings of Kensinger and Choi (2009), where the RH remembers details about emotional events, but gist information is remembered better when it is positive and presented to the LH. Further, while it is generally accepted that the RH mediates prosody, it is often observed that both RH and LH damaged patients have prosody deficits. The specific deficit in RH-damaged patients seems to be comprehension of the emotional state of the speaker (emotional prosody), whereas LH-damaged patients show deficits linking the emotional meaning to propositional speech that include differentiating interrogative, imperative, exclamatory statements (linguistic prosody) (Ross et al., 1997). Witteman et al. (2011) conducted a meta-analysis on LH- and RH-damaged patients to process prosody and concluded that RH patients show deficits in emotional prosody, but LH patients show primarily linguistic prosody deficits. In Abbassi et al. (2011), extensive review of emotional word processing, they provide evidence for LH advantage and/or activity for the initial processing of emotional words, but that a RH advantage emerges shortly thereafter. They conclude that the LH has an advantage for early semantic decoding of emotional words, but that the RH engages later. They also suggest that the RH involvement may be due to the attention-grabbing qualities of emotional stimuli. However, in light of the currently reviewed literature, it seems more likely that the LH quickly decodes the semantic meaning of the word, but the RH mediates the emotional comprehension and subsequent affect. Mirroring the findings with AgCC patients reported above, Sherratt (2007) observed that RH-damaged patients used evaluative words rather than expressions of feelings during discourse on personal topics as compared to controls, and had particularly difficulty with negative compared to positive discourse. These findings suggest that the LH dominates semantic knowledge about emotional words, but may not be able to apply those words to emotion-relevant discourse without the RH sharing its comprehension and subjective affect. The LH role in the linguistic encoding of emotional information is underscored by the observations that brain areas that are activated in the LH during emotion processing tend to be language-related structures (Killgore and Yurgelun-Todd, 2007, described in greater detail, below). This, too, suggests that only the RH is engaged in the direct processing of the emotional nature of stimuli, but also that functional neural modules (e.g., Broca's area for speech, Wernicke's for comprehension) are part of larger systems that apply general strategies to information processing. For example, LH language and categorization processing is applied not just to linguistic stimuli, but to other domains, such as emotion. Johnson-Frey et al. (2005) observed LH dominance in activity in distinct frontal, prefrontal, parietal, and temporal regions during planning and execution of tool use. Moreover, this was concurrent with activity in LH semantic regions suggesting that the LH dominance for language processing may also underlie execution and planning for the domain of tool use LH dominance for motor skills was also observed by (Janssen et al., 2011). As such, it is plausible that processing strategies of the LH would be applied to multiple domains.

INTER- AND INTRA-HEMISPHERIC PROCESSING OF EMOTION

Processing positive emotions is easier than negative, as accuracy and response time advantages to positive over negatively valenced stimuli are frequently reported (Hugdahl et al., 1993; Compton et al., 2005; Jansari et al., 2011; Najt et al., 2013). This appears to be due to additive LH and RH processes. If the RH processes all emotion and seems biased to negative emotion, then the automatic assignment of positive labels by the LH adds to the accuracy and response time of the RH for processing of positive emotions, generally. For example, Najt et al. (2013) observed a main effect for positive over negative emotions, but the interaction revealed only a RH advantage for negative and no differences between the hemispheres for positive emotions. Using a different methodology, Compton et al. (2005) presented emotionally expressive (they only used happy and angry) or neutral faces along with a third target face in either visual field. They observed an advantage for inter-hemispheric matching of the target to the samples and lvf/RH advantage for intra-hemisphere presentations. Killgore and Yurgelun-Todd (2007) presented sad and happy faces to the LH and RH, and recorded subsequent fMRI activity. They observed that unilateral presentation of happy faces resulted in activity restricted to the hemisphere of presentation. These findings suggest several points. First, either hemisphere can identify a positive face. Second, the RH is superior to the LH at perceptual matching of positive (happy) and negative (angry) even though both have been characterized as "approach." Third, when both hemispheres simultaneously contribute to the task, the advantage for identifying emotional over neutral stimuli is even greater than, but not different from just one hemisphere alone. These findings are consistent with Banich and Belger (1990), Belger and Banich (1992, 1998), and Weissman and Banich (2000) proposal that easy tasks (lower processing complexity) benefit from intra-hemisphere processing, but difficult tasks benefit from inter-hemispheric. Compton et al. also argue that their perceptual matching task has additional complexity over identification of a single stimulus. Additional evidence that both hemispheres identify positive emotions comes from observations that individuals with LH damage are not always impaired for positive emotions (Adolphs et al., 1996; Borod et al., 1998, 2002), individuals with LH temporal lobe epilepsy are not impaired at recognizing positive emotions, and intact individuals consistently show a RH/left side bias for identifying happy chimeric faces (Levy et al., 1983; Voyer et al., 2012). Because positive emotions can be identified by either hemisphere, they do not require any inter-hemispheric collaboration, and so main effects for positive over negative words are most likely due to additive, and not interactive, effects of RH and LH abilities.

Conversely, prior research suggests that only the RH can identify, comprehend, and feel negative emotions. I have also suggested, here, that for the LH to work with negative emotion (e.g., regulation, language), this information must be transferred from the RH to the LH. In addition to Killgore and Yurgelun-Todd (2007), finding that identification of positive emotions can be accomplished within either hemisphere, they observed that unilateral presentation of sad faces, resulted in bilateral activity. While the depth of processing accomplished by each hemisphere was not directly explored by Killgore and Yurgelun-Todd, it is important to note that the reported LH activity for processing of both happy and sad faces was restricted to regions that are related to language, such as left inferior and medial frontal gyri (syntax, Tyler et al., 2011), medial temporal gyrus (language and semantic memory, Tranel et al., 1997; Chao et al., 1999; Cabeza and Nyberg, 2000; Ashtari et al., 2004), insula (speech, Dronkers, 1996; verbal emotion, Ardila et al., 1997; Ackermann and Riecker, 2004), frontal cortex, fusiform gyrus (face processing in the RH, phoneme/grapheme in the LH, Démonet et al., 1994; Chance et al., 2012), and "lingual areas." These findings also support the previously mentioned hypothesis that one role of the LH in emotion processing is for verbal encoding and other language-related, higher cognitions such as planning. It is also noteworthy that some of these structures (frontal gyri) are also part of the bilateral DMN, discussed earlier as being important for processing emotion. As such, the initial involvement of the LH in inter-hemispheric processing of negative emotion appears to be restricted to linguistic contributions.

INCORPORATING VALENCE, RH, AND APPROACH/AVOIDANCE HYPOTHESES

The idea that only the RH comprehends negative valence is not original to this paper (e.g., Najt et al., 2013), but the evidence presented in this paper is consistent with a RH advantage for identification and comprehension of the emotional nature of stimuli, and also mediates a reactive affective response. This appears to be true regardless of valence and approach/avoidance motivations. Conversely, the LH does not appear to have this same ability for any emotion. The LH appears to have a default positive bias in early stages of processing emotional stimuli, suggesting that it relies on the RH for accurate interpretation of emotional stimuli. Also, consistent with the findings and proposals of others cited herein, the LH plays a major role in more advanced and different aspects of emotion processing (regulation, impression management, and verbal and propositional coding) important for social interaction, language, executive reasoning, and a coherent conscious experience. Importantly, this does not necessarily propose new functions for the LH, just an application of LH dominant processes to emotional information. Additionally, this framework incorporates elements from the three prevailing and often competing theories of emotion processing: valence, RH, and approach/avoidance theories. With regards to the valence hypothesis, the RH does seem to identify negative emotions and the LH does not. Also, the LH does seem to identify positive emotions, and so those findings are not refuted in these pages, but it does not appear to be engaged in initial identification stages to indicate true comprehension of the emotional nature of the stimulus and it too frequently appears unable to do so. However, the LH does appear to have a propensity for positive emotional assessments at higher cognitive levels. There is no evidence that the LH ever adds a negative spin or interpretation. A strict dichotomous RH/negative and LH/positive division of labor has just not been supported, and I have cited many others who have drawn that same conclusion. The RH hypothesis, however, fits very nicely with this framework during early identification and comprehension of the emotional nature of a stimulus. It does appear as though the RH readily identifies and truly comprehends emotion of all valences, where this is not possible without an intact RH, and without the RH, even LH-dominant processes, such as verbal explanations and understanding appropriate emotion in social contexts are severely disrupted. However, that the RH entirely processes all aspects of emotion is not correct. As has been cited herein, the LH is important for regulation of negative emotion, so understanding and feeling emotion seems to be RH, but its modulation and attenuation may be LH. Kinsbourne and Bemporad (1984), Root et al. (2006), and Davidson (1984) also proposed an early role for the RH emotional identification and later involvement of the LH for response preparation.

Lastly, I have not directly incorporated much work on approach/avoidance into this paper because much of the theory hinges on the emotion of anger, and there are relatively few papers that include anger as compared to just happy and sad emotions. Moreover, as has been pointed out by Carver and Harmon-Jones (2009) and Tomarken and Zald (2009), by excluding anger, many investigators of the approach/avoidance hypothesis confound the two constructs by assuming positive always leads to approach and negative always leads to avoidance. The basic theory is that approach motivations are mediated by the LH, but avoidance/withdrawal motivations are mediated by the RH. As such, typical observations of asymmetries in emotion processing actually reflect motivation, not valence, asymmetries based on evidence that anger is negative, motivates approach and is also associated with the LH (Harmon-Jones, 2004; Harmon-Jones et al., 2013). While the approach/avoidance model has come under considerable criticism, there are enough solid findings to lend credence to the notion that LH has some involvement with the emotion of anger as an approach motivation (Harmon-Jones et al., 2009, 2011; Harmon-Jones and Harmon-Jones, 2010). However, anger does not appear to be as simple of an emotion as happiness or sadness. Anger can motivate two different classes of approach: amplification with aggressive behaviors ("kill them") or attenuation and pro-social behaviors ("kill them with kindness"). Anger that motivates approach in the form of aggression [overt or covert as in leaning forward observed by Price and Harmon-Jones (2011)] has been extensively studied in humans and animals and will not be rehashed, here. Anger can also motivate avoidance, as in defensive aggression, "Your anger makes me afraid and want to run away or fight for my life," or the more subtle "I'm so angry with you, I have to walk away." Watson (2009) provided compelling evidence and reasoning indicating that anger is frequently associated with negative affect that motivates avoidance, whereas Harmon-Jones and colleagues have more thoroughly focused on approach aspects of anger. Whether anger motivates approach or withdrawal behaviors probably depends on the reward that can be attained from the resulting behaviors, even if the cause of the anger is unclear or experimentally manipulated. Reward likelihoods would be determined by contextual cues, social standing/dominance, and intensity of the stimulus. For example, an angry person may not aggress against their boss or someone of equal or higher social standing, but instead they may either approach and aggress against someone weaker or regulate the anger to create a more positive mood and responses. Conversely, an angry person may choose an avoidance strategy by running away if that is the safest path to goal attainment. For example, one may choose to avoid a spouse that caused their anger, because aggressing would jeopardize long-term and perhaps other, more important rewards. In either scenario, one could speculate approach and avoidance-motivated responses, depending on the social context, desired outcomes, and probably numerous personality tendencies. Zinner et al. (2008) also observed that social context may determine approach or avoidance motivations resulting from anger. As such, the construct of anger is more complex than other, basic emotions (also suggested by Schutter and Harmon-Jones, 2013), and simply assigning the entire construct of anger to a single hemisphere or motivational tendency is overly broad, and more importantly, not supported in the literature at this time. There are too few studies that investigate anger, its expression, interpretation, and resultant motivation in various contexts to populate an encompassing theory, but Harmon-Jones and colleagues are the only ones to have directly explored any aspect of anger associated with approach motivations in depth.

Interestingly, van Honk and Schutter (2007) have argued that anger associated with submissive/avoidant responses is associated with the RH, whereas anger associated with approach is LH. In the current framework, anger would be expected to be LH for more complex scenarios requiring a higher level thinking to incorporate emotional regulation, consideration of one's social standing (perception by others), propositional knowledge (relationships among known entities), and verbalization. Conversely, anger would be RH under conditions of ambiguous or low-intensity threat, such as identifying facial expressions of complete strangers that appear on a screen (e.g., Jansari et al., 2000; Harciarek et al., 2006; Jackson et al., 2008; Balconi and Mazza, 2010; Bourne, 2011). Consider further that when anger is experimentally induced through insults, and the opportunity exists to aggress against the insulter (anger begetting greater anger), the LH is dominant in that approach-aggression (Hortensius et al., 2012), but that this context can also be interpreted as one of social dominance or standing. Extending this, Kelley et al. (2013) observed LH association with anger that results in aggression (approach) and greater RH association with anger resulting in rumination (avoidance). Rumination is interesting because it is not regulation (which I have argued to be associated with the LH), where rumination can lead to amplified aggression, but has also been associated with depression and anxiety (Pedersen et al., 2011). In the current framework, this could be interpreted as the RH maintaining the emotional experience until such a time as it could be acted upon by the LH for regulation, impression management, verbalization, and categorization. Findings of Harmon-Jones et al. (2003) also indicate that the LH becomes engaged when there is the possibility of alleviating an anger-inducing situation.

FUTURE DIRECTIONS

First, the recent emotion literature is dominated by observations with clinical populations (neurologically intact and not) and electrophysiological techniques such as PET, fMRI, NIRS, rTMS, EEG, ERP. These studies, then, are all inherently noisy, with varying competencies and lesion locations of patients, and varying methods of interpreting and analyzing neurologic activation correlates. While neuroscientific contributions have been and will continue to be enormous, additional behavioral studies that utilize methodologies more complex than identification of laterally presented faces will enable a clearer understanding of the different competencies of the hemispheres during the normal course of emotion processing and generation of affective experience. For example, Hughes and Rutherford (2013) presented images from the International Affective Picture System (IAP, Lang et al., 2008) to the left or right visual fields as distractors while a central image was responded to by the non-distracted hemisphere. This technique could be applied to commonly used emotional stimuli, such as facial expressions. Moreover, an evolutionary approach to stimulus construction could also be utilized by varying familiarity with kinship or degree of drive reduction. The interaction between emotion and motivation is also proving to be interesting. The recent work of Spielberg, Heller and colleagues also provides interesting avenues for examining the integration of advanced emotional processing with motivation, approach, and avoidance dispositions, and have posited model of how different prefrontal areas interact to achieve goal-directed behaviors (e.g., Silton et al., 2010; Spielberg et al., 2011a,b; and Spielberg et al., 2013). Similarly, the work of Harmon-Jones and colleagues has presented some interesting and more complex methodologies by incorporating ostracism, cognitive dissonance paradigms, and experimentally inducing emotional states.

The proposed framework presents several avenues for exploration using simple emotional stimuli in non-clinical populations. For example, using signal detection analyses could help elucidate the true accuracy of the LH in judging emotions, and I have presented evidence for the prediction that the LH will show a high amount of "happy" false alarms and hits. Also, if both hemispheres independently process positive emotion, then a bilateral matching task (presenting two stimuli, one to each hemisphere) should not yield more response efficiency than unilateral presentations of the stimuli. If there is additive benefit to processing positive emotion, as suspected, then central presentation of an emotional stimulus should yield greater efficiency than left or right unilateral presentation. If the LH needs the RH to experience any negative emotion at all, then a bilateral matching task should yield greater efficiency than LH unilateral presentations, but perhaps less than RH unilateral presentations if the RH can handle it within hemisphere. The few matching tasks that have been reported warrant replication.

Further, to investigate a cross-hemispheric transfer of emotional information, one hypothesis could be that priming the RH with valenced information will bias verbal descriptions of neutral stimuli, whereas priming the LH with valenced information may have no effect at all on RH interpretation of neutral stimuli. This would be akin to "tricking" the LH, as discussed by Baynes and Gazzaniga (2000). Alternatively, unilateral emotional primes could be followed by ipsilateral or contralateral ambiguous targets. Such stimuli can be faces (as in the Emotional Hexagon Test used by Bate et al., 2013), objects and situations (as in the International Affective Picture System), complex social interactions (a breakup), or words. One could also "trick" the LH in its own territory: language. For example, sentences that have many positive words but convey a negative message ("I love the way you are so fantastically oblivious to your surroundings") or vise versa ("You make me sick with how bad you are at lying") may confuse the LH, resulting in a generally positive interpretation, especially if presented simultaneously with a congruous or incongruous context. Applying the unilateral distraction technique of Hughes and Rutherford would enable study of each hemisphere's contribution in non-clinical populations. For example, GSR for each hand could be measured under conditions of unilateral distraction. If the LH responds to negative information only after it has been shared by the RH, then distracting the LH while presenting a negative stimulus to the RH, followed by an undistracted neutral trial should result in no LH bias as compared to trials where the LH is not distracted at all. The time course of inter-hemispheric sharing can be explored by observing the activity of structures within the DMN during and after presentation of emotional stimuli at varying durations of central and lateralized exposure (e.g., from 25 through 200 ms). Response requirements can also be varied after different stimulus onsets to investigate the stage of processing for emotional information. For example, identifying emotional versus neutral faces should take place early (RH), identifying emotional words should be later (bilateral or LH), and determining if someone gave an appropriate or alternate social responses may be even later (LH). This, combined with unilateral presentations would be useful in detangling the precise contributions of each hemisphere to different aspects of emotional processing. Following the lead of Compton et al.'s (2005) matching task, one could also help determine the depth of each hemisphere's contribution by similarly presenting different emotional expressions to each hemisphere, followed by a unilateral conceptual match, rather than a perceptual match, if the target is a different person from either samples or a congruent/incongruent picture from the IAP.

One last avenue that would be promising for investigating hemispheric collaboration in emotion processing is handedness. Degree of handedness is the extent to which individuals use one hand for performing a series of tasks. Consistent-handers usually or always prefer use of the same hand (either left or right) whereas inconsistent-handers are more varied in their hand preferences, using the left for some tasks, right for others, or having no hand preference. Consistent and inconsistent-handers show reliable differences on behavioral tasks that suggest greater independence of the hemispheres in consistent-handers and greater collaboration in inconsistent-handers. As such, consistent-handers have an advantage over inconsistent-handers on tasks that require hemispheric independence, but inconsistent-handers have the advantage when tasks require a collaborative or cross-hemispheric strategy (Christman, 2001; Propper et al., 2005; Lyle and Martin, 2010). Inconsistent-handers may also have an advantage for tasks that are predominately RH, and Propper et al. (2010) observed that inconsistent-handers rate their subjective mood more negatively than consistent-handers. Consistent with the emotion literature and the hypothesis that negative emotions are distributed across the hemispheres for different kinds of processing, then inconsistent-handers are predicted to have an advantage for the identification and regulation of negative emotion. Niebauer (2004) reported that consistent-handers are more likely to ruminate and inconsistent-handers are more likely to self-reflect. He argued that inconsistent-handers are self-reflective because RH experiences update the LH fringe of consciousness (sense of rightness and general feelings). The increased inter-hemispheric communication of inconsistent-handers facilitates this process, whereas decreased inter-hemispheric communication limits this process, resulting in ruminating consistent-handers. Applying Niebauer's reasoning to emotion, it is predicted that inconsistent-handers may be better at regulating emotions than are consistent-handers, because emotional regulation may require cross-hemispheric collaboration. Relatedly, Jasper et al. (2008) observed that inconsistent-handers are better at generating alternative outcomes to stories than are consistent-handers, and the reappraisal strategy for emotional regulation requires generating alternatives to real-life events. Indeed, inconsistent-handers should show an advantage for any aspect of emotional processing that requires hemispheric collaboration, such as including more emotional content in verbal descriptions of scenes and events. Conversely, inconsistent-handers may have a disadvantage for emotional processing that is better accomplished by the LH alone or by the hemispheres, independently. For example, inconsistent-handers may have more difficulty than consistent-handers ignoring a correct emotional experience or identification in favor of a popular or socially acceptable one. Inconsistent-handers may show processing advantages for identification of negative emotions and they may also have more difficulty separating the genuine experience of the RH from the LH idealized experience.

There have been very few papers directly investigating emotion processing by degree of handedness. One paper suggests that inconsistent-handers may experience emotion more genuinely than consistent-handers. Farina et al. (2012) report that inconsistent-handers show greater emotional distress than do consistent-handers to a traumatic event (earthquake). In this instance, an earthquake truly is traumatic, and experience of associated negative emotion is expected. Because the RH appears to be the on-line information processor of real-world emotional stimuli, inconsistent-handers may have a greater understanding (ability to process, feel) of the traumatic event. Consistent-handers however, may have less of a connection to the RH emotion and so display less distress. Another study by Mikkelson et al. (2006) examined consistent and inconsistent hander differences in expressiveness and emotional control. While these authors report differences as having been observed (opposite to what is predicted, here), they do not report the statistical inferences that led to their conclusions. Certainly, more research will enable stronger speculations.

Two other papers, using different methodologies have seemingly opposing conclusions. For example, Bourne (2008), using a free vision chimeric happy-face task, observed that degree of handedness is related to degree of RH lateralization for both positive and negative emotions. This supports the RH hypothesis for consistent-handers, but may also suggest that an increased collaboration between hemispheres of inconsistent-handers results in no asymmetries for perceptual identification of happy faces. This is also predictable by the current model, where either hemisphere can identify happy emotions, consistent-handers lateralizing the task to one hemisphere and inconsistent-handers using either hemisphere. Brunyé et al. (2012) observed stronger left and right spatial biases for remembering positively and negatively valenced stimulus locations for consistent-handers. This could be used to support the valence hypothesis. While these do appear to be conflicting, their different methodologies and responses could also reflect different stages or types of emotional processing, Bourne for valence identification, and Brunyé et al. for more complex associations. Both do suggest that inconsistent-handers are less lateralized for emotional stimuli. Using degrees of handedness to research the extent to which the cerebral hemispheres interact in the processing of emotion is a largely unexplored, but promising territory. Moreover, the experimental manipulation of bilateral eye movements has been demonstrated to increase inter-hemispheric processing (Christman et al., 2003; Parker and Dagnall, 2010) particularly in consistent-handers (Lyle et al., 2008; Shobe et al., 2009). The use of degree of handedness and bilateral eye movements are two methods that can be used to explore inter-hemispheric collaboration during various types and phases of emotional processing.

SUMMARY

- The RH pulvinar–amygdala–superior colliculus pathway is a fast, coarse, and unconscious processor of emotional stimuli. The cortico-pulvinar–cortical pathway serves to orient and direct cortical attention to emotional stimuli, engaging the DMN for higher order emotional processing. Pulvinar nuclei of the thalamus may be critical for synchronizing cortical neurons with RH subcortical processing of emotion. Processing negatively valenced stimuli, in particular, results in inter-hemispheric synchrony between the structures of the DMN, suggesting sharing of negatively valenced information across the hemispheres.
- Commissurotomized and AgCC patients show deficits identifying emotions, particularly regarding negative emotions. They are also impaired at linking emotional experiences with verbal descriptions. The intact RH and LH of these patients suggests normal intra-hemispheric abilities (e.g., speech, recognizing idiom meaning, physiological arousal to emotional stimuli), and so their emotional deficits are likely due to the inability of the RH to share emotional information with the LH.
- Left hemisphere activity has been associated with regulation of negative emotions by attenuating emotional experience, avoiding emotional distractions, reinterpreting events as positive or benign, or by having an advantage at problem solving strategies used for emotional regulation. Patients with PD and depression have difficulties with emotional regulation and also may have LH hypoactivity. RH hypoactivity associated with mania may be due to the absence of RH input. Mania does not appear to be due to a LH that can only process and affect positive emotions because AgCC and commissurotomized patients do not show manic-type speech or positive content discourse. The role of the LH in emotional regulation and the exhibition of mania in the absence of RH activity suggest that the LH is detached from feeling associated with, and comprehension of emotional stimuli and situations.
- Evidence from a case study and signal detection analysis suggests that the LH has default bias to respond positively. The LH also has a tendency to identify positive traits in ourselves, generating an idealized sense of self that enables impression management. This LH tendency extends to the perception of others. A consistent positive perception of ourselves and others has evolutionary advantages by promoting social interaction.
- The LH transforms real-world, event-specific emotions of the RH into propositional knowledge and verbal codes. The LH remembers gist information about positive valence stimuli, interprets linguistic aspects of prosody, and like AgCC patients, uses evaluative and concrete words rather than feelings to describe personal emotional events. The LH appears to parse emotion stimuli and subjective affect into linguistic elements, semantic meaning, and verbal labels. LH brain structures activated during emotion processing are language-related.
- Both the LH and the RH can identify positive emotions independently, as there is within-hemisphere activity for unilateral presentations, unilateral LH damage does not always produce positive valence deficits, and there is consistent evidence for a RH/left side bias in processing positive emotions. There is ample evidence to suggest that the LH does not identify, comprehend, or experience negative affect. Instead, emotional aspects

of negative valence stimuli are processed by the RH, only. In the normal brain, where bilateral activity is observed during processing of negative valence, the LH must use information received from the RH for verbal and propositional contributions to emotion processing, and emotional regulation.

- The currently proposed theory suggests that the LH contribution to emotion is not at a basic, comprehension level. Instead, the LH receives this type of information from the RH and integrates it into higher level cognitions. As such, the LH and RH contribute to different components or levels of emotion processing. There are many methodologies that have been under-utilized in the study of hemispheric asymmetries of emotion that have been successfully utilized in other areas. As such, to date, we have little understanding of the degree to which each hemisphere processes emotional information or their relative contribution to the many aspects of the emotional experience.

REFERENCES

Abbassi, E., Kahlaoui, K., Wilson, M. A., and Joanette, Y. (2011). Processing the emotions in words: the complementary contributions of the left and right hemispheres. *Cogn. Affect. Behav. Neurosci.* 11, 372–385. doi:10.3758/s13415-011-0034-1

Abbott, J. D., Cumming, G., Fidler, F., and Lindell, A. K. (2013). The perception of positive and negative facial expressions in unilateral brain-damaged patients: a meta-analysis. *Laterality* 18, 437–459. doi:10.1080/1357650X.2012.703206

Ackermann, H., and Riecker, A. (2004). The contribution of the insula to motor aspects of speech production: a review and a hypothesis. *Brain Lang.* 89, 320–328. doi:10.1016/S0093-934X(03)00347-X

Adolphs, R., Damasio, H., Tranel, D., and Damasio, A. R. (1996). Cortical systems for the recognition of emotion in facial expressions. *J. Neurosci.* 16, 7678–7687.

Adolphs, R., and Tranel, D. (2003). Amygdala damage impairs emotion recognition from scenes only when they contain facial expressions. *Neuropsychologia* 41, 1281–1289. doi:10.1016/S0028-3932(03)00064-2

Aftanas, L., and Varlamov, A. (2004). Associations of alexithymia with anterior and posterior activation asymmetries during evoked emotions: EEG evidence of right hemisphere “electrocortical effort”. *Int. J. Neurosci.* 114, 1443–1462.

Aftanas, L. I., and Varlamov, A. A. (2007). Effects of alexithymia on the activity of the anterior and posterior areas of the cortex of the right hemisphere in positive and negative emotional activation. *Neurosci. Behav. Physiol.* 37, 67–73. doi:10.1007/s11055-007-0151-z

Akiyoshi, J., Hieda, K., Aoki, Y., and Nagayama, H. (2003). Frontal brain hypoactivity as a biological substrate of anxiety in patients with panic disorders. *Neuropsychobiology* 47, 165–170. doi:10.1159/000070587

Aldao, A., Nolen-Hoeksema, S., and Schweizer, S. (2010). Emotion-regulation strategies across psychopathology: a meta-analytic review. *Clin. Psychol. Rev.* 30, 217–237. doi:10.1016/j.cpr.2009.11.004

Alves, N. T., Aznar-Casanova, J. A., and Fukusima, S. S. (2009). Patterns of brain asymmetry in the perception of positive and negative facial expressions. *Laterality* 14, 256–272. doi:10.1080/13576500802362927

Ardila, A., Benson, D. F., and Flynn, F. G. (1997). Participation of the insula in language. *Aphasiology* 11, 1159–1169. doi:10.1080/02687039708249438

Arnsten, A. F., and Rubia, K. (2012). Neurobiological circuits regulating attention, cognitive control, motivation, and emotion: disruptions in neurodevelopmental psychiatric disorders. *J. Am. Acad. Child Adolesc. Psychiatry* 51, 356–367. doi:10.1016/j.jaac.2012.01.008

Ashtari, M., Lencz, T., Zuffante, P., Bilder, R., Clarke, T., Diamond, A., et al. (2004). Left middle temporal gyrus activation during a phonemic discrimination task. *Neuroreport* 15, 389–393. doi:10.1097/00001756-200403010-00001

Azouvi, P., and Peskine, A. (2013). “Anosognosia and denial after right hemisphere stroke,” in *The Behavioral and Cognitive Neurology of Stroke.* Section III. ed. O. Godefroy (Cambridge: Cambridge University Press), 158–169. doi:10.1017/CBO9781139058988.014

Baker, S. C., Rogers, R. D., Owen, A. M., Frith, C. D., Dolan, R. J., Frackowiak, R. S. J., et al. (1996). Neural systems engaged by planning: a PET study of the Tower of London task. *Neuropsychologia* 34, 515–526. doi:10.1016/0028-3932(95)00133-6

Balconi, M., and Mazza, G. (2010). Lateralisation effect in comprehension of emotional facial expression: a comparison between EEG alpha band power and behavioural inhibition (BIS) and activation (BAS) systems. *Laterality* 15, 361–384. doi:10.1080/13576500902886056

Baleydier, C., and Morel, A. N. N. E. (1992). Segregated thalamocortical pathways to inferior parietal and inferotemporal cortex in macaque monkey. *Vis. Neurosci.* 8, 391–405. doi:10.1017/S0952523800004922

Banich, M. T., and Belger, A. (1990). Interhemispheric interaction: how do the hemispheres divide and conquer a task? *Cortex* 26, 77–94. doi:10.1016/S0010-9452(13)80076-7

Banks, S. J., Bellerose, J., Douglas, D., and Jones-Gotman, M. (2012). Bilateral skin conductance responses to emotional faces. *Appl. Psychophysiol. Biofeedback* 37, 145–152. doi:10.1007/s10484-011-9177-7

Barker-Collo, S. L. (2007). Depression and anxiety 3 months post stroke: prevalence and correlates. *Arch. Clin. Neuropsychol.* 22, 519–531. doi:10.1016/j.acn.2007.03.002

Bate, S., Cook, S. J., Mole, J., and Cole, J. (2013). First report of generalized face processing difficulties in möbius sequence. *PLoS ONE* 8:e62656. doi:10.1371/journal.pone.0062656

Baynes, K., and Gazzaniga, M. S. (2000). “Consciousness, introspection, and the split-brain: the two minds/one body problem,” in *The New Cognitive Neurosciences*, 2nd Edn, ed. M. S. Gazzaniga (Cambridge: MIT Press), 1355–1368.

Beeman, M. J., and Chiarello, C. (eds) (1998). *Right Hemisphere Language Comprehension: Perspectives From Cognitive Neuroscience.* Mahwah: Lawrence Erlbaum Associates, Inc.

Behrens, T. E. J., Johansen-Berg, H., Woolrich, M. W., Smith, S. M., Wheeler-Kingshott, C. A. M., Boulby, P. A., et al. (2003). Non-invasive mapping of connections between human thalamus and cortex using diffusion imaging. *Nat. Neurosci.* 6, 750–757. doi:10.1038/nn1075

Belger, A., and Banich, M. T. (1992). Interhemispheric interaction affected by computational complexity. *Neuropsychologia* 30, 923–929. doi:10.1016/0028-3932(92)90036-L

Belger, A., and Banich, M. T. (1998). Costs and benefits of integrating information between the cerebral hemispheres: a computational perspective. *Neuropsychology* 12, 380–398. doi:10.1037/0894-4105.12.3.380

Benowitz, L. I., Bear, D. M., Rosenthal, R., Mesulam, M. M., Zaidel, E., and Sperry, R. W. (1983). Hemispheric specialization in nonverbal communication. *Cortex* 19, 5–11. doi:10.1016/S0010-9452(83)80046-X

Bermond, B. (1995). Alexithymie, een neuropsychologische benadering (Alexithymia, a neuropsychological method of approach). *J. Psychiatry* 37, 717–727.

Bhogal, S. K., Teasell, R., Foley, N., and Speechley, M. (2004). Lesion location and poststroke depression systematic review of the methodological limitations in the literature. *Stroke* 35, 794–802. doi:10.1161/01.STR.0000117237.98749.26

Blumberg, H. P., Stern, E., Martinez, D., Ricketts, S., de Asis, J., White, T., et al. (2000). Increased anterior cingulate and caudate activity in bipolar mania. *Biol. Psychiatry* 48, 1045–1052. doi:10.1016/S0006-3223(00)00962-8

Bobes, M. A., Martín, M., Olivares, E., and Valdés-Sosa, M. (2000). Different scalp topography of brain potentials related to expression and identity matching of faces. *Brain Res. Cogn. Brain Res.* 9, 249–260. doi:10.1016/S0926-6410(00)00003-3

Borod, J. C., Bloom, R. L., Brickman, A. M., Nakhutina, L., and Curko, E. A. (2002). Emotional processing deficits in individuals with unilateral brain damage. *Appl. Neuropsychol.* 9, 23–36.

Borod, J. C., Cicero, B. A., Obler, L. K., Welkowitz, J., Erhan, H. M., Santschi, C., et al. (1998). Right hemisphere emotional perception: evidence across multiple channels. *Neuropsychology* 12, 446–458. doi:10.1037/0894-4105.12.3.446

Bourne, V. J. (2008). Examining the relationship between degree of handedness and degree of cerebral lateralization for processing facial emotion. *Neuropsychology* 22, 350. doi:10.1037/0894-4105.22.3.350

Bourne, V. J. (2010). How are emotions lateralised in the brain? Contrasting existing hypotheses using the chimeric faces test. *Cogn. Emot.* 24, 903–911. doi:10.1080/02699930903007714

Bourne, V. J. (2011). Examining the effects of inversion on lateralisation for processing facial emotion. *Cortex* 47, 690–695. doi:10.1016/j.cortex.2010.04.003

Bozikas, V. P., Tonia, T., Fokas, K., Karavatos, A., and Kosmidis, M. H. (2006). Impaired emotion processing in remitted patients with bipolar disorder. *J. Affect. Disorders* 91, 53–56. doi:10.1016/j.jad.2005.11.013

Brown, W. S., and Paul, L. K. (2000). Cognitive and psychosocial deficits in agenesis of the corpus callosum with normal intelligence. *Cogn. Neuropsychiatry* 5, 135–157. doi:10.1080/135468000395781

Brownell, H. H., Simpson, T. L., Bihrle, A. M., Potter, H. H., and Gardner, H. (1990). Appreciation of metaphoric alternative word meanings by left and right brain-damaged patients. *Neuropsychologia* 28, 375–383. doi:10.1016/0028-3932(90)90063-T

Brüne, M., Nadolny, N., Güntürkün, O., and Wolf, O. T. (2013). Stress induces a functional asymmetry in an emotional attention task. *Cogn. Emot.* 27, 558–566. doi:10.1080/02699931.2012.726211

Brunyé, T. T., Gardony, A., Mahoney, C. R., and Taylor, H. A. (2012). Body-specific representations of spatial location. *Cognition* 123, 229–239. doi:10.1016/j.cognition.2011.07.013

Buchanan, D. C., Waterhouse, G. J., and West, S. C. (1980). A proposed neurophysiological basis of alexithymia. *Psychother. Psychosom.* 34, 248–255. doi:10.1159/000287465

Buck, R. (1999). The biological affects: a typology. *Psychol. Rev.* 106, 301–336. doi:10.1037/0033-295X.106.2.301

Buck, R. (2002). The genetics and biology of true love: prosocial biological affects and the left hemisphere. *Psychol. Rev.* 109, 739–744. doi:10.1037/0033-295X.109.4.739

Cabeza, R., and Nyberg, L. (2000). Imaging cognition, II: an empirical review of 275 PET and fMRI studies. *J. Cogn. Neurosci.* 12, 1–47. doi:10.1162/08989290051137585

Caeiro, L., Ferro, J. M., and Costa, J. (2013). Apathy secondary to stroke: a systematic review and meta-analysis. *Cerebrovasc. Dis.* 35, 23–39. doi:10.1159/000346076

Cain, K., Towse, A. S., and Knight, R. S. (2009). The development of idiom comprehension: an investigation of semantic and contextual processing skills. *J. Exp. Child Psychol.* 102, 280–298. doi:10.1016/j.jecp.2008.08.001

Carmona, J. E., Holland, A. K., and Harrison, D. W. (2009). Extending the functional cerebral systems theory of emotion to the vestibular modality: a systematic and integrative approach. *Psychol. Bull.* 135, 286. doi:10.1037/a0014825

Carver, C. S., and Harmon-Jones, E. (2009). Anger is an approach-related affect: evidence and implications. *Psychol. Bull.* 135, 183. doi:10.1037/a0013965

Chance, S. A., Sawyer, E. K., Clover, L. M., Wicinski, B., Hof, P. R., and Crow, T. J. (2012). Hemispheric asymmetry in the fusiform gyrus distinguishes *Homo sapiens* from chimpanzees. *Brain Struct. Funct.* 218, 1391–1405. doi:10.1007/s00429-012-0464-8

Chao, L. L., Haxby, J. V., and Martin, A. (1999). Attribute-based neural substrates in temporal cortex for perceiving and knowing about objects. *Nat. Neurosci.* 2, 913–919. doi:10.1038/13217

Cheng, Y., Lee, S. Y., Chen, H. Y., Wang, P. Y., and Decety, J. (2012). Voice and emotion processing in the human neonatal brain. *J. Cogn. Neurosci.* 24, 1411–1419. doi:10.1162/jocn_a_00214

Christman, S. D. (2001). Individual differences in Stroop and local-global processing: a possible role of interhemispheric integration. *Brain Cogn.* 45, 97–118. doi:10.1006/brcg.2000.1259

Christman, S. D., Garvey, K. J., Propper, R. E., and Phaneuf, K. A. (2003). Bilateral eye movements enhance the retrieval of episodic memories. *Neuropsychology* 17, 221. doi:10.1037/0894-4105.17.2.221

Compton, R. J., Feigenson, K., and Widick, P. (2005). Take it to the bridge: an inter-hemispheric processing advantage for emotional faces. *Brain Res. Cogn. Brain Res.* 24, 66–72. doi:10.1016/j.cogbrainres.2004.12.002

Damoiseaux, J. S., Rombouts, S. A., Barkhof, F., Scheltens, P., Stam, C. J., Smith, S. M., et al. (2006). Consistent resting-state networks across healthy subjects. *Proc. Natl. Acad. Sci. U.S.A.* 103, 13848–13853. doi:10.1073/pnas.0601417103

Davidson, R. J. (1984). "Affect, cognition, and hemispheric specialization," in *Emotion, Cognition and Behavior*, eds C. E. Izard, J. Kagan, and R. B. Zajonc (New York: Cambridge University Press), 320–365.

Davidson, R. J. (1992). Anterior cerebral asymmetry and the nature of emotion. *Brain Cogn.* 20, 125–151. doi:10.1016/0278-2626(92)90065-T

Davidson, R. J. (1993). Cerebral asymmetry and emotion: conceptual and methodological conundrums. *Cogn. Emot.* 7, 115–138. doi:10.1016/j.ijpsycho.2008.12.003

Davidson, R. J. (2004). What does the prefrontal cortex "do" in affect: perspectives on frontal EEG asymmetry research. *Biol. Psychol.* 67, 219–233. doi:10.1016/j.biopsycho.2004.03.008

Davidson, R. J., and Fox, N. A. (1982). Asymmetrical brain activity discriminates between positive and negative affective stimuli in human infants. *Science* 218, 1235–1237. doi:10.1126/science.7146906

Davidson, R. J., and Hugdahl, K. (1995). *Brain Asymmetry*. Cambridge, MA: MIT Press.

Démonet, J. F., Price, C., Wise, R., and Frackowiak, R. S. J. (1994). A PET study of cognitive strategies in normal subjects during language tasks influence of phonetic ambiguity and sequence processing on phoneme monitoring. *Brain* 117, 671–682. doi:10.1093/brain/117.4.671

Dolcos, F., Kragel, P., Wang, L., and McCarthy, G. (2006). Role of the inferior frontal cortex in coping with distracting emotions. *Neuroreport* 17, 1591–1594. doi:10.1097/01.wnr.0000236860.24081.be

Drayer, B., Burger, I., and Hurwitz, B. (1989). Correlation of severity of panic disorder and neuroanatomical changes on magnetic resonance imaging. *Neuroscience* 1, 404–408.

Dronkers, N. F. (1996). A new brain region for coordinating speech articulation. *Nature* 384, 159–161. doi:10.1038/384159a0

Eidelberg, D., and Galaburda, A. M. (1982). Symmetry and asymmetry in the human posterior thalamus. I. Cytoarchitectonic analysis in normal persons. *Arch. Neurol.* 39, 325–332. doi:10.1001/archneur.1982.00510180003001

Eippert, F., Veit, R., Weiskopf, N., Erb, M., Birbaumer, N., and Anders, S. (2007). Regulation of emotional responses elicited by threat-related stimuli. *Hum. Brain Mapp.* 28, 409–423. doi:10.1002/hbm.20291

Farina, B., Mazzotti, E., Farina, F., Della Marca, G., Savoja, V., Kotzalidis, G. D., et al. (2012). Relationship between handedness and persistent emotional distress in adults experiencing an earthquake. *Riv. Psichiatr.* 47, 309–312. doi:10.1708/1139.12558

Faust, M., Kravetz, S., and Nativ-Safrai, O. (2004). The representation of aspects of the self in the two cerebral hemispheres. *Pers. Individ. Dif.* 37, 607–619. doi:10.1016/j.paid.2003.09.030

Fetterman, A. K., Ode, S., and Robinson, M. D. (2013). For which side the bell tolls: the laterality of approach-avoidance associative networks. *Motiv. Emot.* 37, 33–38. doi:10.1007/s11031-012-9306-5

Förstl, H., and Sahakian, B. (1991). A psychiatric presentation of abulia – three cases of left frontal lobe ischaemia and atrophy. *J. R. Soc. Med.* 84, 89.

Fox, M. D., and Raichle, M. E. (2007). Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nat. Rev. Neurosci.* 8, 700–711. doi:10.1038/nrn2201

Gainotti, G. (2012). Unconscious processing of emotions and the right hemisphere. *Neuropsychologia* 50, 205–218. doi:10.1016/j.neuropsychologia.2011.12.005

Gazzaniga, M. S. (1998). The split brain revisited. *Sci. Am.* 279, 35–39. doi:10.1038/scientificamerican0798-50

Gazzaniga, M. S., and LeDoux, J. E. (1978). *The Integrated Mind*. New York: Plenum Press.

Giardina, A., Caltagirone, C., and Oliveri, M. (2011). Temporo-parietal junction is involved in attribution of hostile intentionality in social interactions: an rTMS study. *Neurosci. Lett.* 495, 150–154. doi:10.1016/j.neulet.2011.03.059

Gorman, J. M., and Coplan, J. D. (1996). Comorbidity of depression and panic disorder. *J. Clin. Psychiatry* 57, 34–41.

Gorman, J. M., Fyer, M. R., Goetz, R., Askanazi, J., Liebowitz, M. R., Fyer, A. J., et al. (1988). Ventilatory physiology of patients with panic disorder. *Arch. Gen. Psychiatry* 45, 31–39. doi:10.1001/archpsyc.1988.01800250035006

Greenberg, L. S. (2007). Emotion coming of age. *Clin. Psychol.* 14, 414–421. doi:10.1111/j.1468-2850.2007.00101.x

Greicius, M. D., Srivastava, G., Reiss, A. L., and Menon, V. (2004). Default-mode network activity distinguishes Alzheimer's disease from healthy aging: evidence from functional MRI. *Proc. Natl. Acad. Sci. U.S.A.* 101, 4637–4642. doi:10.1073/pnas.0308627101

Greicius, M. D., Supekar, K., Menon, V., and Dougherty, R. F. (2009). Resting-state functional connectivity reflects structural connectivity in the default mode network. *Cereb. Cortex* 19, 72–78. doi:10.1093/cercor/bhn059

Grieve, K. L., Acuña, C., and Cudeiro, J. (2000). The primate pulvinar nuclei: vision and action. *Trends Neurosci.* 23, 35–39. doi:10.1016/S0166-2236(99)01482-4

Grimm, S., Boesiger, P., Beck, J., Schuepbach, D., Bermpohl, F., Walter, M., et al. (2008). Altered negative BOLD responses in the default-mode network during emotion processing in depressed subjects. *Neuropsychopharmacology* 34, 843–932. doi:10.1038/npp.2008.81

Gross, J. J. (1998). The emerging field of emotion regulation: an integrative review. *Rev. Gen. Psychol.* 2, 271–299. doi:10.1007/s11920-013-0407-y

Gross, J. J. (2002). Emotion regulation: affective, cognitive, and social consequences. *Psychophysiology* 39, 281–291. doi:10.1017/S0048577201393198

Gupta, R. K., Hasan, K. M., Trivedi, R., Pradhan, M., Das, V., Parikh, N. A., et al. (2005). Diffusion tensor imaging of the developing human cerebrum. *J. Neurosci. Res.* 81, 172–178. doi:10.1002/jnr.20547

Habel, U., Klein, M., Kellermann, T., Shah, N. J., and Schneider, F. (2005). Same or different? Neural correlates of happy and sad mood in healthy males. *Neuroimage* 26, 206–214. doi:10.1016/j.neuroimage.2005.01.014

Habib, M., Daquin, G., Pelletier, J., Montreuil, M., and Robichon, F. (2003). "Alexithymia as impaired callosal function: evidence from multiple sclerosis patients and normal individuals," in *The Parallel Brain: The Cognitive Neuroscience of the Corpus Callosum* (Cambridge: MIT Press), 415–422.

Hagemann, D., Hewig, J., Naumann, E., Seifert, J., and Bartussek, D. (2005). Resting brain asymmetry and affective reactivity: aggregated data support the right-hemisphere hypothesis. *J. Individ. Differ.* 26, 139–154. doi:10.1027/1614-0001.26.3.139

Harciarek, M., Heilman, K. M., and Jodzio, K. (2006). Defective comprehension of emotional faces and prosody as a result of right hemisphere stroke: modality versus emotion-type specificity. *J. Int. Neuropsychol. Soc.* 12, 774–781. doi:10.1017/S1355617706061121

Harker, L., and Keltner, D. (2001). Expressions of positive emotion in women's college yearbook pictures and their relationship to personality and life outcomes across adulthood. *J. Pers. Soc. Psychol.* 80, 112. doi:10.1037/0022-3514.80.1.112

Harmon-Jones, C., Schmeichel, B. J., Mennitt, E., and Harmon-Jones, E. (2011). The expression of determination: similarities between anger and approach-related positive affect. *J. Pers. Soc. Psychol.* 100, 172. doi:10.1037/a0020966

Harmon-Jones, E. (2004). On the relationship of frontal brain activity and anger: examining the role of attitude toward anger. *Cogn. Emot.* 18, 337–361. doi:10.1080/02699930341000059

Harmon-Jones, E., Abramson, L. Y., Sigelman, J., Bohlig, A., Hogan, M. E., and Harmon-Jones, C. (2002). Proneness to hypomania/mania symptoms or depression symptoms and asymmetrical frontal cortical responses to an anger-evoking event. *J. Pers. Soc. Psychol.* 82, 610–618. doi:10.1037/0022-3514.82.4.610

Harmon-Jones, E., and Harmon-Jones, C. (2010). On the relationship of trait PANAS positive activation and trait anger: evidence of a suppressor relationship. *J. Res. Pers.* 44, 120–123. doi:10.1016/j.jrp.2009.09.001

Harmon-Jones, E., Harmon-Jones, C., Abramson, L., and Peterson, C. K. (2009). PANAS positive activation is associated with anger. *Emotion* 9, 183. doi:10.1037/a0014959

Harmon-Jones, E., Harmon-Jones, C., and Price, T. F. (2013). What is approach motivation? *Emot. Rev.* 5, 291–295. doi:10.1177/1754073913477509

Harmon-Jones, E., Sigelman, J., Bohlig, A., and Harmon-Jones, C. (2003). Anger, coping, and frontal cortical activity: the effect of coping potential on anger-induced left frontal activity. *Cogn. Emot.* 17, 1–24. doi:10.1080/02699930302278

Hecht, D. (2010). Depression and the hyperactive right-hemisphere. *Neurosci. Res.* 68, 77–87. doi:10.1016/j.neures.2010.06.013

Heilman, K., and Bowers, D. (1990). "Neuropsychological studies of emotional changes induced by right and left hemispheric lesions," in *Psychological and Biological Approaches to Emotion*, eds N. Stein, B. Leventhal, and T. Trabasso (Hillsdale, NJ: Lawrence Erlbaum and Associates, Inc), 97–113.

Henriques, J. B., and Davidson, R. J. (1991). Left frontal hypoactivation in depression. *J. Abnorm. Psychol.* 100, 535. doi:10.1037/0021-843X.100.4.535

Hoppe, K. D., and Bogen, J. E. (1977). Alexithymia in twelve commissurotomized patients. *Psychother. Psychosom.* 28, 148–155. doi:10.1159/000287057

Hortensius, R., Schutter, D. J., and Harmon-Jones, E. (2012). When anger leads to aggression: induction of relative left frontal cortical activity with transcranial direct current stimulation increases the anger-aggression relationship. *Soc. Cogn. Affect. Neurosci.* 7, 342–347. doi:10.1093/scan/nsr012

Houtveen, J. H., Bermond, B., and Elton, M. R. (1997). Alexithymia: a disruption in a cortical network? An EEG power and coherence analysis. *J. Psychophysiol.* 11, 147–57.

Howard, M. F., and Reggia, J. A. (2007). A theory of the visual system biology underlying development of spatial frequency lateralization. *Brain Cogn.* 64, 111–123. doi:10.1016/j.bandc.2007.01.004

Hugdahl, K., Iversen, P. M., and Johnsen, B. H. (1993). Laterality for facial expressions: does the sex of the subject interact with the sex of the stimulus face? *Cortex* 29, 325–331. doi:10.1016/S0010-9452(13)80185-2

Hughes, A. J., and Rutherford, B. J. (2013). Hemispheric interaction, task complexity, and emotional valence: evidence from naturalistic images. *Brain Cogn.* 81, 167–175. doi:10.1016/j.bandc.2012.11.004

Ince, E., and Christman, S. D. (2002). Semantic representations of word meanings by the cerebral hemispheres. *Brain Lang.* 80, 393–420. doi:10.1006/brln.2001.2599

Irish, M., Kumfor, F., Hodges, J. R., and Piguet, O. (2013). A tale of two hemispheres: contrasting socioemotional dysfunction in right-versus left-lateralised semantic dementia. *Dement. Neuropsychol.* 7, 88–95.

Ivanov, I., Bansal, R., Hao, X., Zhu, H., Kellendonk, C., Miller, L., et al. (2010). Morphological abnormalities of the thalamus in youths with attention deficit hyperactivity disorder. *Am. J. Psychiatry* 167, 397–408. doi:10.1176/appi.ajp.2009.09030398

Iznak, A. F., Iznak, E. V., Kornilov, V. V., and Kontsevoi, V. A. (2011). Neuropsychophysiological correlates of reactive depression. *Hum. Physiol.* 37, 682–687. doi:10.1134/S0362119711060089

Jackson, D. C., Mueller, C. J., Dolski, I., Dalton, K. M., Nitschke, J. B., Urry, H. L., et al. (2003). Now you feel it, now you don't frontal brain electrical asymmetry and individual differences in emotion regulation. *Psychol. Sci.* 14, 612–617. doi:10.1046/j.0956-7976.2003.psci_1473.x

Jackson, M. C., Wolf, C., Johnston, S. J., Raymond, J. E., and Linden, D. E. (2008). Neural correlates of enhanced visual short-term memory for angry faces: an FMRI study. *PLoS ONE* 3:e3536. doi:10.1371/journal.pone.0003536

Jansari, A., Rodway, P., and Goncalves, S. (2011). Identifying facial emotions: valence specific effects and an exploration of the effects of viewer gender. *Brain Cogn.* 76, 415–423. doi:10.1016/j.bandc.2011.03.009

Jansari, A., Tranel, D., and Adolphs, R. (2000). A valence specific lateral bias for discriminating emotional facial expressions in free field. *Cogn. Emot.* 14, 341–353. doi:10.1080/026999300378860

Jasper, J. D., Barry, K., and Christman, S. D. (2008). Individual differences in counterfactual production. *Pers. Individ. Dif.* 45, 488–492. doi:10.1186/1471-2458-13-581

Janssen, L., Meulenbroek, R. G., and Steenbergen, B. (2011). Behavioral evidence for left-hemisphere specialization of motor planning. *Exp. Brain Res.* 209, 65–72. doi:10.1007/s00221-010-2519-5

Johnson, M. H. (2005). Subcortical face processing. *Nat. Rev. Neurosci.* 6, 766–786. doi:10.1038/nrn1766

Johnson-Frey, S. H., Newman-Norlund, R., and Grafton, S. T. (2005). A distributed left hemisphere network active during planning of everyday tool use skills. *Cereb. Cortex* 15, 681–695. doi:10.1093/cercor/bhh169

Kang, S. Y., and Kim, J. S. (2008). Anterior cerebral artery infarction: stroke mechanism and clinical-imaging study in 100 patients. *Neurology* 70, 2386–2393. doi:10.1212/01.wnl.0000314686.94007.d0

Karnath, H. O., Himmelbach, M., and Rorden, C. (2002). The subcortical anatomy of human spatial neglect: putamen, caudate nucleus and pulvinar. *Brain* 125, 350–360. doi:10.1093/brain/awf032

Keenan, J. P., and Gorman, J. (2007). The causal role of the right hemisphere in self-awareness: it is the brain that is selective. *Cortex* 43, 1074–1082. doi:10.1016/S0010-9452(08)70705-6

Kelley, N. J., Hortensius, R., and Harmon-Jones, E. (2013). When anger leads to rumination induction of relative right frontal cortical activity with transcranial direct current stimulation increases anger-related rumination. *Psychol. Sci.* 24, 475–481. doi:10.1177/0956797612457384

Kensinger, E. A., and Choi, E. S. (2009). When side matters: hemispheric processing and the visual specificity of emotional memories. *J. Exp. Psychol. Learn. Mem. Cogn.* 35, 247–253. doi:10.1037/a0013414

Kessler, R. C., Stang, P. E., Wittchen, H. U., Ustun, T. B., Roy-Burne, P. P., and Walters, E. E. (1998). Lifetime panic-depression comorbidity in the National Comorbidity Survey. *Arch. Gen. Psychiatry* 55, 801–808. doi:10.1001/archpsyc.55.9.801

Killgore, W. D., Gruber, S. A., and Yurgelun-Todd, D. A. (2008). Abnormal corticostriatal activity during fear perception in bipolar disorder. *Neuroreport*, 19, 1523–7. doi:10.1097/WNR.0b013e328310af58

Killgore, W. D., and Yurgelun-Todd, D. A. (2007). The right-hemisphere and valence hypotheses: could they both be right (and sometimes left)? *Soc. Cogn. Affect. Neurosci.* 2, 240–250. doi:10.1093/scan/nsm020

Kim, S. H., Cornwell, B., and Kim, S. E. (2012). Individual differences in emotion regulation and hemispheric metabolic asymmetry. *Biol. Psychol.* 89, 382–386. doi:10.1016/j.biopsycho.2011.11.013

Kinsbourne, M. (1978). "Biological determinants of functional bisymmetry and asymmetry," in *Asymmetrical Function of the Brain*, ed. M. Kinsbourne (London: Cambridge University Press), 3–16.

Kinsbourne, M., and Bemporad, B. (1984). "Lateralization of emotion: a model and the evidence," in *The Psychobiology of Affective Development*, eds N. Fox and R. J. Davidson (Hillsdale, NJ: Erlbaum), 259–291.

Kircher, T. T. J., Senior, C., Phillips, M. L., Benson, P. J., Bullmore, E. T., Brammer, M., et al. (2000). Toward a functional neuroanatomy of self-processing: effects of faces and words. *Brain Res. Cogn. Brain Res.* 10, 133–144. doi:10.1016/S0926-6410(00)00036-7

Koester, S. E., and O'Leary, D. D. (1994). Axons of early generated neurons in cingulate cortex pioneer the corpus callosum. *J. Neurosci.* 14, 6608–6620.

Koslov, K., Mendes, W. B., Pajtas, P. E., and Pizzagalli, D. A. (2011). Asymmetry in resting intracortical activity as a buffer to social threat. *Psychol. Sci.* 22, 641–649. doi:10.1177/0956797611403156

Kret, M. E., Denollet, J., Grèzes, J., and de Gelder, B. (2011). The role of negative affectivity and social inhibition in perceiving social threat: an fMRI study. *Neuropsychologia* 49, 1187–1193. doi:10.1016/j.neuropsychologia.2011.02.007

Kumar, D., and Srinivasan, N. (2011). Emotion perception is mediated by spatial frequency content. *Emotion* 11, 1144. doi:10.1037/a0025453

LaBerge, D., and Buchsbaum, M. S. (1990). Positron emission tomographic measurements of pulvinar activity during an attention task. *J. Neurosci.* 10, 613–619.

Lang, P. J., Bradley, M. M., and Cuthbert, B. N. (2008). *International Affective Picture System (IAPS): Affective Ratings of Pictures and Instruction Manual.* Technical Report A-8. Gainesville, FL: University of Florida.

Lausberg, H., Zaidel, E., Cruz, R. F., and Ptito, A. (2007). Speech-independent production of communicative gestures: evidence from patients with complete callosal disconnection. *Neuropsychologia* 45, 3092–3104. doi:10.1016/j.neuropsychologia.2007.05.010

Lazeron, R. H., Rombouts, S. A., Machielsen, W. C., Scheltens, P., Witter, M. P., Uylings, H. B., et al. (2000). Visualizing brain activation during planning: the tower of London test adapted for functional MR imaging. *Am. J. Neuroradiol.* 21, 1407–1414.

Le Sourn-Bissaoui, S., Caillies, S., Bernard, S., Deleau, M., and Brulé, L. (2012). Children's understanding of ambiguous idioms and conversational perspective-taking. *J. Exp. Child Psychol.* 112, 437–451. doi:10.1016/j.jecp.2012.02.003

Leckman, J. F., Weissman, M. M., Merikangas, K. R., Pauls, D. L., and Prusoff, B. A. (1983). Panic disorder and major depression: increased risk of depression, alcoholism, panic, and phobic disorders in families of depressed probands with panic disorder. *Arch. Gen. Psychiatry* 40, 1055. doi:10.1001/archpsyc.1983.01790090017002

LeDoux, J. (2007). The amygdala. *Curr. Biol.* 17, R868–R874. doi:10.1016/j.cub.2007.08.005

LeDoux, J. E. (ed.) (1996). *The Emotional Brain.* New York: Simon & Schuster.

Lee, G. P., Loring, D. W., Meader, K. J., and Brooks, B. B. (1990). Hemispheric specialization for emotional expression: a reexamination of results from intracarotid administration of sodium amobarbital. *Brain Cogn.* 12, 267–280. doi:10.1016/0278-2626(90)90019-K

Lembke, A., and Ketter, T. A. (2002). Impaired recognition of facial emotion in mania. *Am. J. Psychiatry* 159, 302–304.

Levy, J., Heller, W., Banich, M. T., and Burton, L. A. (1983). Asymmetry of perception in free viewing of chimeric faces. *Brain Cogn.* 2, 404–419. doi:10.1016/0278-2626(83)90021-0

Li, X., Sroubek, A., Kelly, M. S., Lesser, I., Sussman, E., He, Y., et al. (2012). Atypical pulvinar-cortical pathways during sustained attention performance in children with attention-deficit/hyperactivity disorder. *J. Am. Acad. Child Adolesc. Psychiatry* 51, 1197–1209. doi:10.1016/j.jaac.2012.08.013

Liddell, B. J., Brown, K. J., Kemp, A. H., Barton, M. J., Das, P., Peduto, A., et al. (2005). A direct brainstem–amygdala–cortical 'alarm' system for subliminal signals of fear. *Neuroimage* 24, 235–243. doi:10.1016/j.neuroimage.2004.08.016

Lindell, A. K. (2006). In your right mind: right hemisphere contributions to language processing and production. *Neuropsychol. Rev.* 16, 131–148. doi:10.1007/s11065-006-9011-9

Lozano, A. M., Giacobbe, P., Hamani, C., Rizvi, S. J., Kennedy, S. H., Kolivakis, T. T., et al. (2012). A multicenter pilot study of subcallosal cingulate area deep brain stimulation for treatment-resistant depression: clinical article. *J. Neurosurg.* 116, 315–322. doi:10.3171/2011.10.JNS102122

Lumley, M. A., and Sielky, K. (2000). Alexithymia, gender, and hemispheric functioning. *Compr. Psychiatry* 41, 352–359. doi:10.1053/comp.2000.9014

Lyle, K. B., Logan, J. M., and Roediger, H. L. (2008). Eye movements enhance memory for individuals who are strongly right-handed and harm it for individuals who are not. *Psychon. Bull. Rev.* 15, 515–520. doi:10.3758/PBR.15.3.515

Lyle, K. B., and Martin, J. M. (2010). Bilateral saccades increase intrahemispheric processing but not interhemispheric interaction: implications for saccade-induced retrieval enhancement. *Brain Cogn.* 73, 128–134. doi:10.1016/j.bandc.2010.04.004

Lyubomirsky, S., King, L., and Diener, E. (2005). The benefits of frequent positive affect: does happiness lead to success? *Psychol. Bull.* 131, 803. doi:10.1037/0033-2909.131.6.803

Maior, R. S., Hori, E., Tomaz, C., Ono, T., and Nishijo, H. (2010). The monkey pulvinar neurons differentially respond to emotional expressions of human faces. *Behav. Brain Res.* 215, 129–135. doi:10.1016/j.bbr.2010.07.009

Marsolek, C. J., DeYoung, C. G., Domansky, W. S., and Deason, R. G. (2013). Hemispheric asymmetries in motivation neurally dissociate self-description processes. *Emotion* 13, 462. doi:10.1037/a0030784

Matsunaga, M., Isowa, T., Kimura, K., Miyakoshi, M., Kanayama, N., Murakami, H., et al. (2009). Associations among positive mood, brain, and cardiovascular activities in an affectively positive situation. *Brain Res.* 1263, 93–103. doi:10.1016/j.brainres.2009.01.027

McGilchrist, I. (2010). Reciprocal organization of the cerebral hemispheres. *Dialogues Clin. Neurosci.* 12, 503–515.

McNally, R. J., Riemann, B. C., and Kim, E. (1990). Selective processing of threat cues in panic disorder. *Behav. Res. Ther.* 28, 407–412.

Mikkelson, A. C., Farinelli, L., and La Valley, A. G. (2006). The influences of brain dominance and biological sex on emotional expressivity, sensitivity, and control. *Commun. Quart.* 54, 427–446. doi:10.1080/01463370601035947

Miller, G. A., Crocker, L. D., Spielberg, J. M., Infantolino, Z. P., and Heller, W. (2013a). Issues in localization of brain function: the case of lateralized frontal cortex in cognition, emotion, and psychopathology. *Front. Integr. Neurosci.* 7:2. doi:10.3389/fnint.2013.00002

Miller, H. C., Chabriac, A. S., and Molet, M. (2013b). The impact of facial emotional expressions and sex on interpersonal distancing as evaluated in a computerized stop-distance task. *Can. J. Exp. Psychol.* 67, 188–194. doi:10.1037/a0030663

Minagawa-Kawai, Y., Matsuoka, S., Dan, I., Naoi, N., Nakamura, K., and Kojima, S. (2009). Prefrontal activation associated with social attachment: facial-emotion recognition in mothers and infants. *Cereb. Cortex* 19, 284–292. doi:10.1093/cercor/bhn081

Morris, J. S., Frith, C. D., Perrett, D. I., Rowland, D., Young, A. W., Calder, A. J., et al. (1996). A differential neural response in the human amygdala to fearful and happy facial expressions. *Nature* 383, 812–815. doi:10.1038/383812a0

Morris, J. S., Öhman, A., and Dolan, R. J. (1999). A subcortical pathway to the right amygdala mediating "unseen" fear. *Proc. Natl. Acad. Sci. U.S.A.* 96, 1680–1685. doi:10.1073/pnas.96.4.1680

Morris, R. G., Ahmed, S., Syed, G. M., and Toone, B. K. (1993). Neural correlates of planning ability: frontal lobe activation during the Tower of London test. *Neuropsychologia* 31, 1367–1378. doi:10.1016/0028-3932(93)90104-8

Najt, P., Bayer, U., and Hausmann, M. (2013). Models of hemispheric specialization in facial emotion perception – a reevaluation. *Emotion* 13, 159. doi:10.1037/a0029723

Nguyen, M. N., Hori, E., Matsumoto, J., Tran, A. H., Ono, T., and Nishijo, H. (2013). Neuronal responses to face-like stimuli in the monkey pulvinar. *Eur. J. Neurosci.* 37, 35–51. doi:10.1111/ejn.12020

Niebauer, C. L. (2004). Handedness and the fringe of consciousness: strong handers ruminate while mixed handers self-reflect. *Conscious. Cogn.* 13, 730–745. doi:10.1016/j.concog.2004.07.003

Nijboer, T. C., and Jellema, T. (2012). Unequal impairment in the recognition of positive and negative emotions after right hemisphere lesions: a left hemisphere bias for happy faces. *J. Neuropsychol.* 6, 79–93. doi:10.1111/j.1748-6653.2011.02007.x

Noriuchi, M., Kikuchi, Y., and Senoo, A. (2008). The functional neuroanatomy of maternal love: mother's response to infant's attachment behaviors. *Biol. Psychiatry* 63, 415423. doi:10.1016/j.biopsych.2007.05.018

Nummenmaa, L., Glerear, E., Viinikainen, M., Jääskeläinen, lP., Hari, R., and Sams, M. (2012). Emotions promote social interaction by synchronizing brain activity across individuals. *Proc. Natl. Acad. Sci. U.S.A.* 109, 9599–9604. doi:10.1073/pnas.1206095109

O'Brien, G. (1994). "The behavioral and developmental consequences of callosal agenesis," in *Callosal Agenesis: A Natural Split Brain?* eds M. Lassonde and M. A. Jeeves (New York: Plenum Press), 235–246.

Ochsner, K. N., and Gross, J. J. (2004). "Thinking makes it so: a social cognitive neuroscience approach to emotion regulation," in *Handbook of Self-Regulation: Research, Theory, and Applications.* eds R. F. Baumeistera and K. D. Vohs (New York: Guiford Press), 229–255.

Önal-Hartmann, C., Pauli, P., Ocklenburg, S., and Güntürkün, O. (2012). The motor side of emotions: investigating the relationship between hemispheres, motor reactions and emotional stimuli. *Psychol. Res.* 76, 311–316. doi:10.1007/s00426-011-0337-4

Onoda, K., Kuroda, Y., Yamamoto, Y., Abe, S., Oguro, H., Nagai, A., et al. (2010). Post-stroke apathy and hypoperfusion in basal ganglia: SPECT study. *Cerebrovasc. Dis.* 31, 6–11. doi:10.1159/000319771

Owen, A. M., Doyon, J., Petrides, M., and Evans, A. C. (1996). Planning and spatial working memory: a positron emission tomography study in humans. *Eur. J. Neurosci.* 8, 353–364. doi:10.1111/j.1460-9568.1996.tb01219.x

Padmala, S., Lim, S. L., and Pessoa, L. (2010). Pulvinar and affective significance: responses track moment-to-moment stimulus visibility. *Front. Hum. Neurosci.* 4:64. doi:10.3389/fnhum.2010.00064

Pandian, M. R. (2012). Idioms and proverbs: a philosophical standoff. *J. Engl. Lang. Lit. Stud.* 2, 42–50.

Paradiso, S., Johnson, D. L., Andreasen, N. C., O'Leary, D. S., Watkins, G. L., Ponto, L. L., et al. (1999). Cerebral blood flow changes associated with attribution of emotional valence to pleasant, unpleasant, and neutral visual stimuli in a PET study of normal subjects. *Am. J. Psychiatry* 156, 1618–1629.

Park, J. Y., Gu, B. M., Kang, D. H., Shin, Y. W., Choi, C. H., Lee, J. M., et al. (2010). Integration of cross-modal emotional information in the human brain: an fMRI study. *Cortex* 46, 161–169. doi:10.1016/j.cortex.2008.06.008

Parker, A., and Dagnall, N. (2010). Effects of handedness and saccadic bilateral eye movements on components of autobiographical recollection. *Brain Cogn.* 73, 93–101. doi:10.1016/j.bandc.2010.03.005

Parker, J. D., Keightley, M. L., Smith, C. T., and Taylor, G. J. (1999). Interhemispheric transfer deficit in alexithymia: an experimental study. *Psychosom. Med.* 61, 464–468.

Parvaz, M. A., MacNamara, A., Goldstein, R. Z., and Hajcak, G. (2012). Event-related induced frontal alpha as a marker of lateral prefrontal cortex activation during cognitive reappraisal. *Cogn. Affect. Behav. Neurosci.* 12, 730–740. doi:10.3758/s13415-012-0107-9

Paul, L. K., Lautzenhiser, A., Brown, W. S., Hart, A., Neumann, D., Spezio, M., et al. (2006). Emotional arousal in agenesis of the corpus callosum. *Int. J. Psychophysiol.* 61, 47–56. doi:10.1016/j.ijpsycho.2005.10.017

Paul, L. K., van Lancker-Sidtis, D., Schieffer, B., Dietrich, R., and Brown, W. S. (2003). Communicative deficits in agenesis of the corpus callosum: nonliteral language and affective prosody. *Brain Lang.* 85, 313–324. doi:10.1016/S0093-934X(03)00062-2

Paulhus, D. L., and Trapnell, P. D. (2008). "Self-presentation of personality," in *Handbook of Personality Psychology*. eds O. P. John, R. W. Robins, and L. A. Pervin (New York, NY: Guilford Press), 492–517.

Pedersen, W. C., Denson, T. F., Goss, R. J., Vasquez, E. A., Kelley, N. J., and Miller, N. (2011). The impact of rumination on aggressive thoughts, feelings, arousal, and behaviour. *Br. J. Soc. Psychol.* 50, 281–301. doi:10.1348/014466610X515696

Perria, L., Rosadini, G., and Rossi, G. (1961). Determination of side of cerebral dominance with amobarbital. *Arch. Neurol.* 4, 173. doi:10.1001/archneur.1961.00450080055006

Pessoa, L., and Adolphs, R. (2010). Emotion processing and the amygdala: from a 'low road' to 'many roads' of evaluating biological significance. *Nat. Rev. Neurosci.* 11, 773–783. doi:10.1038/nrn2920

Pietrek, C., Popov, T., Steffen, A., Miller, G. A., and Rockstroh, B. (2012). Neuromagnetic indication of dysfunctional emotion regulation in affective disorders. *Depress. Res. Treat.* 2012:156529. doi:10.1155/2012/156529

Prasko, J., Horácek, J., Zalesky, R., Kopecek, M., Novak, T., Paskova, B., et al. (2004). The change of regional brain metabolism (18FDG PET) in panic disorder during the treatment with cognitive behavioral therapy or antidepressants. *Neuroendocrinol. Lett.* 25, 340–348.

Previc, F. H. (1991). A general theory concerning the prenatal origins of cerebral lateralization in humans. *Psychol. Rev.* 98, 299. doi:10.1037/0033-295X.98.3.299

Price, T. F., and Harmon-Jones, E. (2011). Approach motivational body postures lean toward left frontal brain activity. *Psychophysiology* 48, 718–722. doi:10.1111/j.1469-8986.2010.01127.x

Propper, R. E., Brunyé, T. T., Christman, S. D., and Bologna, J. (2010). Negative emotional valence is associated with non-right-handedness and increased imbalance of hemispheric activation as measured by tympanic membrane temperature. *J. Nerv. Ment. Dis.* 198, 691–694. doi:10.1097/NMD.0b013e3181ef1f35

Propper, R. E., Christman, S. D., and Phaneuf, K. A. (2005). A mixed-handed advantage in episodic memory: a possible role of interhemispheric interaction. *Mem. Cognit.* 33, 751–757. doi:10.3758/BF03195341

Purushothaman, G., Marion, R., Li, K., and Casagrande, V. A. (2012). Gating and control of primary visual cortex by pulvinar. *Nat. Neurosci.* 15, 905–912. doi:10.1038/nn.3106

Raczkowski, D., and Diamond, I. T. (1980). Cortical connections of the pulvinar nucleus in Galago. *J. Comp. Neurol.* 193, 1–40. doi:10.1002/cne.901930102

Ramachandran, V. S. (1995). Anosognosia in parietal lobe syndrome. *Conscious. Cogn.* 4, 22–51. doi:10.1006/ccog.1995.1002

Rash, B. G., and Richards, L. J. (2001). A role for cingulate pioneering axons in the development of the corpus callosum. *J. Comp. Neurol.* 434, 147–157. doi:10.1002/cne.1170

Romanski, L. M., Giguere, M., Bates, J. F., and Goldman-Rakic, P. S. (1998). Topographic organization of medial pulvinar connections with the prefrontal cortex in the rhesus monkey. *J. Comp. Neurol.* 37, 313–332. doi:10.1002/(SICI)1096-9861(19970317)379:3<313::AID-CNE1>3.0.CO;2-6

Romei, V., De Gennaro, L., Fratello, F., Curcio, G., Ferrara, M., Pascual-Leone, A., et al. (2008). Interhemispheric transfer deficit in alexithymia: a transcranial magnetic stimulation study. *Psychother. Psychosom.* 77, 175–181. doi:10.1159/000119737

Root, J. C., Wong, P. S., and Kinsbourne, M. (2006). Left hemisphere specialization for response to positive emotional expressions: a divided output methodology. *Emotion* 6, 473. doi:10.1037/1528-3542.6.3.473

Ross, E. D. (1997). "Cortical representation of the emotions," in *Contemporary Behavioral Neurology*, eds M. R. Trimble and J. L. Cummings (Woburn, MA: Butterworth-Heinemann), 107–126.

Ross, E. D., Thompson, R. D., and Yenkosky, J. (1997). Lateralization of affective prosody in brain and the callosal integration of hemispheric language functions. *Brain Lang.* 56, 27–54. doi:10.1006/brln.1997.1731

Rottenberg, J. (2005). Mood and emotion in major depression. *Curr. Dir. Psychol. Sci.* 14, 167–170. doi:10.1111/j.0963-7214.2005.00354.x

Saalmann, Y. B., Pinsk, M. A., Wang, L., Li, X., and Kastner, S. (2012). The pulvinar regulates information transmission between cortical areas based on attention demands. *Science* 337, 753–756. doi:10.1126/science.1223082

Sackeim, H. A., Greenberg, M. S., Weiman, A. L., Gur, R. C., Hungerbuhler, J. P., and Geschwind, N. (1982). Hemispheric asymmetry in the expression of positive and negative emotions: neurological evidence. *Arch. Neurol.* 39, 210–218. doi:10.1001/archneur.1982.00510160016003

Saenger, V. M., Barrios, F. A., Martínez-Gudiño, M. L., and Alcauter, S. (2012). Hemispheric asymmetries of functional connectivity and grey matter volume in the default mode network. *Neuropsychologia* 50, 1308–1315. doi:10.1016/j.neuropsychologia.2012.02.014

Santos, C. O., Caeiro, L., and Ferro, J. M. (2013). "Mania," in *Neuropsychiatric Symptoms of Neurological Disease.* ed. J. M. Ferro (London: Springer), 65–79.

Schiffer, F., Zaidel, E., Bogen, J., and Chasan-Taber, S. (1998). Different psychological status in the two hemispheres of two split-brain patients. *Cogn. Behav. Neurol.* 11, 151–156.

Schore, A. N. (2005). Back to basics attachment, affect regulation, and the developing right brain: linking developmental neuroscience to pediatrics. *Pediatr. Rev.* 26, 204217. doi:10.1542/pir.26-6-204

Schulz, K. P., Fan, J., Magidina, O., Marks, D. J., Hahn, B., and Halperin, J. M. (2007). Does the emotional go/no-go task really measure behavioral inhibition?: convergence with measures on a non-emotional analog. *Arch. Clin. Neuropsychol.* 22, 151–160. doi:10.1016/j.acn.2006.12.001

Schutter, D. J., and Harmon-Jones, E. (2013). The corpus callosum: a commissural road to anger and aggression. *Neurosci. Biobehav. Rev.* 37, 2481–2488. doi:10.1016/j.neubiorev.2013.07.013

Sedda, A., Rivolta, D., Scarpa, P., Burt, M., Frigerio, E., Zanardi, G., et al. (2013). Ambiguous emotion recognition in temporal lobe epilepsy: the role of expression intensity. *Cogn. Affect. Behav. Neurosci.* 13, 452–463. doi:10.3758/s13415-013-0153-y

Shackman, A. J., Salomons, T. V., Slagter, H. A., Fox, A. S., Winter, J. J., and Davidson, R. (2011). The integration of negative affect, pain and cognitive control in the cingulate cortex. *Nat. Rev. Neurosci.* 12, 154–167. doi:10.1038/nrn2994

Sherman, S. M., and Guillery, R. W. (1996). Functional organization of thalamocortical relays. *J. Neurophysiol.* 76, 1367–1395.

Sherratt, S. (2007). Right brain damage and the verbal expression of emotion: a preliminary investigation. *Aphasiology* 21, 320–339. doi:10.1080/02687030600911401

Shipp, S. (2003). The functional logic of cortico-pulvinar connections. *Philos. Trans. R. Soc. London B Biol. Sci.* 358, 1605. doi:10.1098/rstb.2002.1213

Shobe, E. R., Ross, N. M., and Fleck, J. I. (2009). Influence of handedness and bilateral eye movements on creativity. *Brain Cogn.* 71, 204–214. doi:10.1016/j.bandc.2009.08.017

Silton, R. L., Heller, W., Towers, D. N., Engels, A. S., Spielberg, J. M., Edgar, J. C., et al. (2010). The time course of activity in dorsolateral prefrontal cortex and anterior cingulate cortex during top-down attentional control. *Neuroimage* 50, 1292–1302. doi:10.1016/j.neuroimage.2009.12.061

Smeets, G., and Merckelbach, H. (1997). Panic disorder and hemispheric reliance. *Anxiety Stress Coping* 10, 245–256. doi:10.1080/10615809708249303

Smith, S. D., and Bulman-Fleming, M. B. (2005). An examination of the right-hemisphere hypothesis of the lateralization of emotion. *Brain Cogn.* 57, 210–213. doi:10.1016/j.bandc.2004.08.046

Snodgrass, L. L., and Harring, K. E. (2000). Intensity affects the preconscious processing of emotionally toned words in college students. *Curr. Psychol.* 19, 249–257. doi:10.1007/s12144-000-1019-3

Snodgrass, L. L., and Harring, K. E. (2004). Right hemisphere positivity bias in preconscious processing: data from five experiments. *Curr. Psychol.* 23, 318–335. doi:10.1007/s12144-004-1004-3

Spence, S., Shapiro, D., and Zaidel, E. (1996). The role of the right hemisphere in the physiological and cognitive components of emotional processing. *Psychophysiology* 33, 112–122. doi:10.1111/j.1469-8986.1996.tb02115.x

Sperry, R. W., Zaidel, E., and Zaidel, D. (1979). Self recognition and social awareness in the deconnected minor hemisphere. *Neuropsychologia* 17, 153–66. doi:10.1016/0028-3932(79)90006-X

Spielberg, J. M., Heller, W., and Miller, G. A. (2013). Hierarchical brain networks active in approach and avoidance goal pursuit. *Front. Hum. Neurosci.* 7:284. doi:10.3389/fnhum.2013.00284

Spielberg, J. M., Heller, W., Silton, R. L., Stewart, J. L., and Miller, G. A. (2011a). Approach and avoidance profiles distinguish dimensions of anxiety and depression. *Cognit. Ther. Res.* 35, 359–371. doi:10.1007/s10608-011-9364-0

Spielberg, J. M., Miller, G. A., Engels, A. S., Herrington, J. D., Sutton, B. P., Banich, M. T., et al. (2011b). Trait approach and avoidance motivation: lateralized neural activity associated with executive function. *Neuroimage* 54, 661–670. doi:10.1016/j.neuroimage.2010.08.037

Sreenivas, S., Boehm, S. G., and Linden, D. E. J. (2012). Emotional faces and the default mode network. *Neurosci. Lett.* 506, 229–234. doi:10.1016/j.neulet.2011.11.012

Starkstein, S. E., Robinson, R. G., Honig, M. A., Parikh, R. M., Joselyn, J., and Price, T. R. (1989). Mood changes after right-hemisphere lesions. *Br. J. Psychiatry* 155, 79–85. doi:10.1192/bjp.155.1.79

Stosny, S. (2011). Anger in the age of entitlement: self-regulation. *Psychology Today*. Available at: http://www.psychologytoday.com/blog/anger-in-the-age-entitlement/201110/self-regulation

Taber, K. H., Wen, C., Khan, A., and Hurley, R. A. (2004). The limbic thalamus. *J. Neuropsychiatry Clin. Neurosci.* 16, 127–132. doi:10.1176/appi.neuropsych.16.2.127

Tamietto, M., and de Gelder, B. (2010). Neural bases of the non-conscious perception of emotional signals. *Nat. Rev. Neurosci.* 11, 697–709. doi:10.1038/nrn2889

Tapiero, I., and Fillon, F. (2007). "Hemispheric asymmetry in the processing of negative and positive emotional inferences," in *Higher Level Language Process in the Brain: Inference and Comprehension Processes.* eds F. Schmalhofer and C. A. Perfetti (Mahwah: Lawrence Erlbaum Associates, Inc.), 355–377.

Tomarken, A. J., Davidson, R. J., and Henriques, J. B. (1990). Resting frontal brain asymmetry predicts affective responses to films. *J. Pers. Soc. Psychol.* 59, 791. doi:10.1037/0022-3514.59.4.791

Tomarken, A. J., and Zald, D. H. (2009). Conceptual, methodological, and empirical ambiguities in the linkage between anger and approach: comment on Carver and Harmon-Jones (2009). *Psychol. Bull.* 135, 209–214. doi:10.1037/a0014735

Tranel, D., Damasio, H., and Damasio, A. R. (1997). A neural basis for the retrieval of conceptual knowledge. *Neuropsychologia* 35, 1329–1339. doi:10.1016/S0028-3932(97)00086-9

Troiani, V., and Schultz, R. T. (2013). Amygdala, pulvinar, and inferior parietal cortex contribute to early processing of faces without awareness. *Front. Hum. Neurosci.* 7:241. doi:10.3389/fnhum.2013.00241

Turk, A. A., Brown, W. S., Symington, M., and Paul, L. K. (2010). Social narratives in agenesis of the corpus callosum: linguistic analysis of the Thematic Apperception Test. *Neuropsychologia* 48, 43–50. doi:10.1016/j.neuropsychologia.2009.08.009

Tyler, L. K., Marslen-Wilson, W. D., Randall, B., Wright, P., Devereux, B. J., Zhuang, J., et al. (2011). Left inferior frontal cortex and syntax: function, structure and behaviour in patients with left hemisphere damage. *Brain* 134, 415–431. doi:10.1093/brain/awq369

van den Heuvel, M. P., and Hulshoff Pol, H. E. (2010). Exploring the brain network: a review on resting-state fMRI functional connectivity. *Eur. Neuropsychopharmacol.* 20, 519–534. doi:10.1016/j.euroneuro.2010.03.008

van den Heuvel, M. P., Mandl, R. C., Kahn, R. S., Pol, H., and Hilleke, E. (2009). Functionally linked resting-state networks reflect the underlying structural connectivity architecture of the human brain. *Hum. Brain Mapp.* 30, 3127–3141. doi:10.1002/hbm.20737

van Honk, J., and Schutter, D. J. (2007). "Vigilant and avoidant responses to angry facial expressions," in *Social Neuroscience: Integrating Biological and Psychological Explanations of Social Behavior*. eds E. Harmon-Jones and P. Winkielman (New York: Guiford Press), 197–223.

van Lancker, D. R., and Kempler, D. (1987). Comprehension of familiar phrases by left-but not by right-hemisphere damaged patients. *Brain Lang.* 32, 265–277. doi:10.1016/0093-934X(87)90128-3

Vecchio, F., Babiloni, C., Buffo, P., Rossini, P. M., and Bertini, M. (2013). Interhemispherical functional coupling of EEG rhythms during the perception of facial emotional expressions. *Clin. Neurophysiol.* 124, 263–272. doi:10.1016/j.clinph.2012.03.083

Versace, A., Thompson, W. K., Zhou, D., Almeida, J. R., Hassel, S., Klein, C. R., et al. (2010). Abnormal left and right amygdala-orbitofrontal cortical functional connectivity to emotional faces: state versus trait vulnerability markers of depression in bipolar disorder. *Biol. Psychiatry* 67, 422–431. doi:10.1016/j.biopsych.2009.11.025

Vocat, R., Staub, F., Stroppini, T., and Vuilleumier, P. (2010). Anosognosia for hemiplegia: a clinical-anatomical prospective study. *Brain* 133, 3578–3597. doi:10.1093/brain/awq297

Voyer, D., Voyer, S. D., and Tramonte, L. (2012). Free-viewing laterality tasks: a multilevel meta-analysis. *Neuropsychology* 26, 551–567. doi:10.1037/a0028631

Wada, J. (1949). A new method for the determination of the side of cerebral speech dominance: a preliminary report on the intracarotid injection of sodium amytal in man. *Igaku Seibutsugaku* 14, 221–222.

Wallentin, M., Nielsen, A. H., Vuust, P., Dohn, A., Roepstorff, A., and Lund, T. E. (2011). Amygdala and heart rate variability responses from listening to emotionally intense parts of a story. *Neuroimage* 58, 963–973. doi:10.1016/j.neuroimage.2011.06.077

Watson, D. (2009). Locating anger in the hierarchical structure of affect: comment on Carver and Harmon-Jones (2009). *Psychol. Bull.* 135, 205–208. doi:10.1037/a0014413

Webster, M. J., Bachevalier, J., and Ungerleider, L. G. (1993). Subcortical connections of inferior temporal areas TE and TEO in macaque monkeys. *J. Comp. Neurol.* 335, 73–91. doi:10.1002/cne.903350106

Weissman, D. H., and Banich, M. T. (2000). The cerebral hemispheres cooperate to perform complex but not simple tasks. Neuropsychology 14, 41–59. doi:10.1037//0894-4105.14.1.41

Whelan, D. C., and Zelenski, J. M. (2012). Experimental evidence that positive moods cause sociability. *Soc. Psychol. Pers. Sci.* 3, 430–437. doi:10.1177/1948550611425194

Wiebking, C., de Greck, M., Duncan, N. W., Heinzel, A., Tempelmann, C., and Northoff, G. (2011). Are emotions associated with activity during rest or interoception? An exploratory fMRI study in healthy subjects. *Neurosci. Lett.* 491, 87–92. doi:10.1016/j.neulet.2011.01.012

Wiedemann, G., Pauli, P., Dengler, W., Lutzenberger, W., Birbaumer, N., and Buchkremer, G. (1999). Frontal brain asymmetry as a biological substrate of emotions in patients with panic disorders. *Arch. Gen. Psychiatry* 56, 78. doi:10.1001/archpsyc.56.1.78

Wilde, E. A., Merkley, T. L., Bigler, E. D., Max, J. E., Schmidt, A. T., Ayoub, K. W., et al. (2012). Longitudinal changes in cortical thickness in children after traumatic brain injury and their relation to behavioral regulation and emotional control. *Int. J. Dev. Neurosci.* 30, 267–276. doi:10.1016/j.ijdevneu.2012.01.003

Wilhelm, F. H., Trabert, W., and Roth, W. T. (2001). Physiologic instability in panic disorder and generalized anxiety disorder. *Biol. Psychiatry* 49, 596–605. doi:10.1016/S0006-3223(00)01000-3

Witteman, J., van IJzendoorn, M. H., van de Velde, D., van Heuven, V. J., and Schiller, N. O. (2011). The nature of hemispheric specialization for linguistic and emotional prosodic perception: a meta-analysis of the lesion literature. *Neuropsychologia* 49, 3722–3738. doi:10.1016/j.neuropsychologia.2011.09.028

Wittling, W., Block, A., Schweiger, E., and Genzel, S. (1998). Hemisphere asymmetry in sympathetic control of the human myocardium. *Brain Cogn.* 38, 17–35. doi:10.1006/brcg.1998.1000

Yakovlev, P. I., Locke, S., Koskoff, D. Y., and Patton, R. A. (1960). Limbic nuclei of thalamus and connections of limbic cortex. *Arch. Neurol.* 3, 620–641. doi:10.1001/archneur.1960.00450060008002

Yuvaraj, R., Murugappan, M., Norlinah, M. I., Sundaraj, K., and Khairiyah, M. (2013). Review of emotion recognition in stroke patients. *Dement. Geriatr. Cogn. Disord.* 36, 179–196. doi:10.1159/000353440

Zhang, J., Zhou, R., and Oei, T. P. (2011). The effects of valence and arousal on hemispheric asymmetry of emotion. *J. Psychophysiol.* 25, 95–103. doi:10.1027/0269-8803/a000045

Zinner, L. R., Brodish, A. B., Devine, P. G., and Harmon-Jones, E. (2008). Anger and asymmetrical frontal cortical activity: evidence for an anger-withdrawal relationship. *Cogn. Emot.* 22, 1081–1093. doi:10.1080/02699930701622961

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Hierarchical brain networks active in approach and avoidance goal pursuit

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Effective approach/avoidance goal pursuit is critical for attaining long-term health and well-being. Research on the neural correlates of key goal-pursuit processes (e.g., motivation) has long been of interest, with lateralization in prefrontal cortex being a particularly fruitful target of investigation. However, this literature has often been limited by a lack of spatial specificity and has not delineated the precise aspects of approach/avoidance motivation involved. Additionally, the relationships among brain regions (i.e., network connectivity) vital to goal-pursuit remain largely unexplored. Specificity in location, process, and network relationship is vital for moving beyond gross characterizations of function and identifying the precise cortical mechanisms involved in motivation. The present paper integrates research using more spatially specific methodologies (e.g., functional magnetic resonance imaging) with the rich psychological literature on approach/avoidance to propose an integrative network model that takes advantage of the strengths of each of these literatures.

Keywords: goal pursuit, approach motivation, avoidance motivation, executive function, prefrontal cortex, laterality, abstraction gradient

> *If you want to live a happy life, tie it to a goal, not to people or things.*
>
> —Albert Einstein

APPROACH AND AVOIDANCE GOAL PURSUIT

The ability to pursue goals effectively is critical for attaining long-term health and well-being. In fact, independently meeting even our most basic needs requires some degree of successful goal pursuit. Goal pursuit can be defined as "responses intentionally performed to bring about or maintain a desired state" or "responses intentionally performed to control or prevent an undesired state," often termed approach and avoidance goal pursuit, respectively (Moskowitz and Grant, 2009). Research suggests that this approach/avoidance dichotomy is a central characteristic of goal pursuit and corresponds to two fundamental motivational systems (Elliot, 2006).

An extant body of neuroscience research provides a valuable foundation for understanding approach/avoidance functions. In particular, findings suggest that the prefrontal cortex (PFC) is lateralized with respect to motivational direction, with left PFC associated with approach and right PFC with avoidance (for review, see Spielberg et al., 2008). However, a number of factors limit the utility of this work (Miller et al., 2013). For example, research investigating approach/avoidance lateralization in PFC often fails to elucidate the specific aspects of approach/avoidance thought to be associated with prefrontal asymmetry (Tomarken and Zald, 2009). More broadly, neuroscience research on approach/avoidance goal pursuit and motivation has largely failed to take advantage of the rich psychological literature in this area, limiting the extent to which neural mechanisms involved in more complex goal-pursuit processes can be represented. Therefore, integration of the literature on goal pursuit in (lateralized) PFC with nuanced conceptualizations of approach/avoidance that deconstruct these fairly broad constructs into component processes will be necessary to achieve a full understanding of the neural mechanisms of goal pursuit.

Historically, an additional limiting factor in investigations of approach/avoidance lateralization in PFC has been a reliance on low-density electroencephalography (EEG), which does not allow for very precise spatial localization of activity (Tomarken and Zald, 2009). In the last two decades, functional magnetic resonance imaging (fMRI) has come to the fore as the dominant method to attain spatial specificity (although lateralization is often ignored or assessed inadequately; Herrington et al., 2005). However, the quest for spatial specificity has had an unfortunate consequence. Specifically, the vast majority of fMRI research has relied on what has been termed the "modular paradigm," in which processes are mapped simplistically onto specific brain regions, and connectivity among regions is not taken into consideration (Miller, 2010; Meehan and Bressler, 2012). Given that regions of the brain are nodes in highly interconnected networks rather than independent "islands" (Sporns, 2011), and changes in connectivity have a distributed impact throughout a network (Levit-Binnun and Golland, 2011), attempts to represent the neural mechanisms of goal pursuit and motivation will necessarily be limited until connectivity between network nodes is taken into account. Fortuitously, a recent explosion of methods for network identification and description (Bressler and Menon, 2010) has given us the tools to dramatically increase the complexity of the processes that we are able to represent, moving us closer to accurate representations of our constructs of interest (Chen and Berrios, 1998).

The present paper attempts to fill these gaps in the literature by presenting a network model of the neural instantiation of approach/avoidance goal pursuit. It reviews and integrates nuanced psychological models of approach/avoidance into a framework for understanding the extant neuroscience research, presents a preliminary structure of network connections, and outlines the way in which network nodes may interact to pursue goals. Importantly, this model incorporates hemispheric laterality, often ignored in fMRI research. Given the focus on cortical lateralization, the scope of the present paper is limited largely to PFC.

KEY GOAL-PURSUIT PROCESSES

As mentioned above, what have been termed the approach and avoidance motivational systems form the basis for the two types of goal pursuit. Although many definitions of motivation have been proposed, several functional aspects are fairly consistent. Specifically, many theories conceptualize motivation as internal processes that select goals based on their predicted value (e.g., reward or punishment), initiate behavior to achieve goals, and maintain goal-directed action (e.g., Jones, 1955; Lindsley, 1957; Campbell and Pritchard, 1976). Thus, motivation is necessary for an organism to pursue goals.

However, the construct of motivation does not encompass all processes needed to pursue goals. Many theorists have proposed that cognition interacts with motivational processes during goal pursuit (e.g., Sorrentino and Higgins, 1986; Locke and Latham, 2002). Although usually not explicitly defined, cognition has often been conceptualized as "those processes that mediate the acquisition and representation of knowledge about the world" (Kuhl, 1986, p. 407), including skills and abilities (Locke, 2000). This work rests on the assumption that motivation and cognition are separable processes (Kruglanski, 1999). However, there does not appear to be sufficient grounds to assume this dichotomy, with many theorists asserting that motivation and cognition are, at the very least, highly overlapping and interdependent (Lazarus, 1991; Miller, 1996, 2010; Sherman and Sherman, 1999; Crocker et al., 2013), if not simply different facets of the same construct (Sorrentino and Higgins, 1986; Kruglanski, 1999).

Distinguishing between motivational and cognitive processes becomes even more difficult when considering executive function. Similar to cognition, the construct of executive function is often defined imprecisely and with a large amount of variability (Martin and Failows, 2010). At a broad level, executive function is often conceptualized as the processes by which goal-directed action is carried out (Banich, 2009). Therefore, executive function shares with motivation a fundamental focus on goal pursuit. However, these constructs appear to have separable aspects. For example, processes involved in the energization of behavior are often considered to be solely the province of motivation. Additionally, executive function is associated with abilities, such as shifting, updating, and inhibition (Miyake et al., 2000), that are not usually considered to be part of the construct of motivation. The present paper provides a model of how the psychological processes involved in the pursuit of goals are instantiated in the brain, rather than delineating those processes which belong to motivation vs. executive function (or cognition more generally). Given that the present paper builds on psychological models of motivation, a motivational framework will be privileged. However, some of the processes discussed in the present paper under the rubric of motivation could just as validly be conceptualized as cognitive or executive function.

HIERARCHICAL APPROACH AND AVOIDANCE MOTIVATIONAL SYSTEMS

Approach and avoidance motivation are hypothesized to form the "basic building blocks that underlie the complexity of human behavior" (Carver et al., 2000, p. 741). Several researchers have suggested that these motivational systems are comprised of a number of hierarchical levels, with lower levels of these models subservient to higher levels (Lang et al., 1998; Elliot, 2006; Scholer and Higgins, 2008). For instance, Higgins and colleagues (for a review, see Scholer and Higgins, 2008) proposed a structure with three levels: the system, strategic, and tactical levels. These levels are thought to be hierarchical, but the selection of approach and avoidance is independent at each level.

SYSTEM LEVEL

At the system level, approach and avoidance are defined in relation to the goal that is currently held. Specifically, the goal can be to approach a potential desirable outcome or avoid a potential undesirable outcome. The critical determinant at this level is how the individual views the goal-object (the outcome of focus), rather than the properties of the goal-object itself. Therefore, the same goal-object can be part of either an approach or avoidance goal, depending on the individual's motivational orientation. Given two individuals striving to get an A on a test, one individual could view an A as an accomplishment that will bring them pleasure (a desirable outcome), whereas the other could view getting anything lower than an A as a failure that will bring them displeasure (an undesirable outcome). Based on their motivational orientation, the first individual wants to approach an A, whereas the second individual wants to avoid getting anything lower than an A.

Given that numerous conceptualizations of the goal construct are available in the literature, it is important to outline the specific operationalization used, in order to avoid confusion (Elliot and Fryer, 2008). Elliot and Niesta (2009, p. 58) suggested that a goal is defined as a "cognitive representation of a future object that the organism is committed to approach or avoid." In this conceptualization, the goal construct includes a commitment to pursue the goal-object. This commitment, along with the representation of the object (e.g., stimulus properties, associated value), must be sustained over time. Thus, one function of the system level is to maintain the goal construct over time.

STRATEGIC LEVEL

At the strategic level, approach and avoidance are defined in relation to the means or process of attaining a potential desirable outcome or preventing a potential undesirable outcome. As shown in **Figure 1**, at the strategic level one can approach matches to a desirable outcome (i.e., outcomes consistent with the desired state) or mismatches to an undesirable outcome (i.e., outcomes inconsistent with the undesired state). Similarly, one can avoid mismatches to a desirable outcome (i.e., outcomes inconsistent

		System Level	
		Approach Goal (desired outcome)	*Avoidance Goal (undesired outcome)*
Strategic Level	*Approach Strategy*	Approach matches to desired outcome	Approach mismatches to undesired outcome
	Avoidance Strategy	Avoid mismatches to desired outcome	Avoid matches to undesired outcome

FIGURE 1 | Relationship between the system and strategic levels of the hierarchical model of motivation. Figure adapted from Higgins et al. (1994).

with the desired state) or matches to an undesirable outcome (i.e., outcomes consistent with the undesired state). Therefore, when approaching a desirable outcome at the system level, one can either approach matches to that outcome or avoid mismatches to that outcome. For example, if the potential outcome was getting an A, approaching a match could be studying hard, and avoiding a mismatch could be staying away from situations that distract from studying. Similarly, when avoiding an undesirable outcome at the system level (e.g., not getting an A), one can either approach mismatches (e.g., studying hard) or avoid matches (e.g., avoiding distraction) to that outcome. Approach and avoidance at the strategic level reflect general/broad plans or means, rather than the specific instantiations of means, which are instead captured in the tactical level.

As discussed above, individuals commit to approaching or avoiding a certain end-state at the system level. In contrast, at the strategic level, a commitment can be made to the goal-pursuit plan, which Gollwitzer (1999) labeled an implementation intention (for reviews, see Gollwitzer, 1999; Parks-Stamm and Gollwitzer, 2009). Gollwitzer conceptualized implementation intentions as if-then plans that link goal-directed actions to anticipated opportunities to engage in these actions (i.e., committing to act in a certain way when a specific situation is encountered). For example, if a student commits to the goal of approaching an A, that student may form an approach plan to complete extra credit assignments (the action) whenever they are offered by the instructor (the situation).

Research indicates that forming implementation intentions increases the likelihood of goal attainment, especially for difficult-to-obtain goals (see Gollwitzer and Sheeran, 2006, for a meta-analysis of 94 studies indicating an effect size of $d = 0.65$). Gollwitzer (1999) attempted to explain this effect by suggesting that implementation intentions make the anticipated situation and planned response more cognitively accessible (i.e., primed). For instance, increasing the accessibility of the anticipated situation makes it easier to detect in the presence of distraction. Similarly, increasing the accessibility of the planned response makes it easier to select in the presence of competing responses. Research supports this hypothesis (for a review, see Gollwitzer et al., 2004), including in populations that experience executive dysfunction (e.g., children with Attention Deficit Hyperactivity Disorder, Gawrilow and Gollwitzer, 2008).

When implementation intentions are not formed, individuals must actively attend to the environment in order to detect opportunities to pursue the goal, which is more effortful and lacks the benefits discussed above (Gollwitzer, 1999). However, in some circumstances the formation of implementation intentions can be detrimental, and active monitoring may be the more successful choice. For example, implementation intentions can interfere with the pursuit of concurrent goals (Achtziger et al., 2012) unless the situation and action committed to in the implementation intention subserve both goals. Additionally, implementation intentions can be detrimental when novel goal-pursuit situations are encountered, because the heightened accessibility of the option committed to can direct attention away from novel situations (Parks-Stamm et al., 2007). In summary, at the strategic level, approach and avoidance goal-pursuit plans are selected and can either be committed to (i.e., the formation of implementation intentions) or actively managed.

TACTICAL LEVEL

At the tactical level, approach and avoidance are defined in relation to the specific ways a strategy could be implemented in a particular context. For example, if the strategy were to study hard, an approach tactic could be setting aside a specific time to study. An avoidance tactic could be making sure that no important study materials are missing. The tactical level is still at a higher level than the actual behavior implemented in a given situation, because an avoidance tactic can be implemented through physically approaching a stimulus and vice versa. For example, an avoidance tactic, such as ensuring that no important study materials are missing, could be implemented with approach behavior, such as approaching a classmate to ask them to show you their study materials or approaching the professor to ask them whether your study materials are adequate.

Although the levels are considered to be independent, Scholer and Higgins (2008) hypothesized that individuals tend to be consistent across levels. Higgins (2000, 2005) accounted for this consistency by proposing that inconsistency across levels leads to disruption in motivational orientation (i.e., approach or avoidance), which, in turn, leads to decreases in goal engagement (i.e., the amount of attention and effort invested in the goal). When there is consistency across levels, motivational orientation is maintained, and goal engagement is sustained.

TEMPERAMENT LEVEL

Elliot (2006) proposed a complementary hierarchical model of approach/avoidance motivation. This model consists of a temperament level comprised of individual differences in sensitivity to desired (approach temperament) or undesired (avoidance temperament) potential outcomes and adoption of approach or avoidance goals accordingly (at the system level). For example, a student high on avoidance temperament faced with an upcoming test will be sensitive to the potential for failure (e.g., appearing unintelligent) and is likely to adopt the goal of getting an A on the test in order to avoid failure. In contrast, a student high on approach temperament will be sensitive to the potential for success (e.g., appearing intelligent) and is likely to adopt the goal of getting an A in order to approach success. These students share the same goal-object (i.e., getting an A), but the underlying reasons for that goal differ.

Along with sensitivity to particular outcomes, the temperament level also involves general tendencies to adopt approach and avoidance means to attain goals (likely at both the strategic and tactical levels). Thus, the temperament level should lead to a tendency to engage the approach and/or avoidance systems overall, providing another method by which consistency across levels is attained.

INTEGRATED MODEL

In summary, combining Scholer and Higgins' (2008) and Elliot's (2006) models, the present proposal offers a hierarchical model of approach/avoidance motivation that consists of four levels: temperamental, system, strategic, and tactical. The temperamental level consists of broad tendencies to implement approach or avoidance goals and approach or avoidance means to attain these goals. The system level maintains the goals that are held, approaching desired outcomes and/or avoiding undesired outcomes. The strategic level represents the general means or process by which the goal will be pursued, and, at the tactical level, the strategy is instantiated in a specific context.

We propose that these levels can be conceptualized along a gradient of both abstraction and timescale, with higher levels being more abstract and typically having a longer timescale. For example, we posit that the system level has a longer time scale than the strategic level, because the goal must be maintained over time, during which a number of strategies can be employed. Thus, a goal must be maintained at the system level over longer periods than any particular strategy.

Similarly, we propose that the strategic level is more abstract than the tactical level, because the tactical level represents the implementation of the strategy in a given context. The system level is more abstract than the strategic level, because the same goal can be subserved by several strategies (i.e., equifinality, Martin and Tesser, 2009). Furthermore, goals themselves can range from concrete (e.g., get an A on a specific test) to abstract (e.g., be a nice person), whereas strategies are tied to specific goals. Thus, strategies can only be as abstract as the goals they are tied to. For example, it could be argued that a strategy such as "study hard" is more abstract than the goal of getting an A on a test. However, in this case, the strategy would be to study specific material (the material that will be tested) to the degree needed to attain an A in this particular class (which incorporates all the concrete information known about the class). If the strategy were simply to "study hard," it would not be a strategy for this particular goal, but likely the larger goal of doing well at one's studies overall. Thus, we suggest that, for a strategy to be tied to a particular goal, it must incorporate the parameters specific to that goal. This constrains the level of abstraction of a particular strategy, with the upper limit being the level of abstraction of the goal. Finally, the temperament level is the most abstract and has the longest time scale, as it reflects dispositions over the lifetime to activate a motivational orientation that is independent of specific goals.

The integrated hierarchical model proposed here implies that higher levels in the structure exert control over lower levels. For example, to attain a goal held at the system level, the goal must be maintained over time and appropriate strategies employed at appropriate times. Thus, processing at the strategic level is constrained by the particular goal held at the system level, and the system level must engage the strategic level when needed. Consequently, the role of the system level can be conceptualized as biasing processing in lower levels of the structure in support of an overarching goal. Given that multiple goals can be held at one time, the system level must also prioritize goals at any moment and bias processing accordingly. Therefore, one important function of this motivational system is to constrain processing at lower levels such that the organism continues to move toward the goal, accomplished through top-down biasing by levels higher in the hierarchy.

Although the proposed model is hierarchical, this is not to imply that communication between levels is always one-way (in fact, such a view is at odds with prefrontal neuroanatomy, e.g., Averbeck and Seo, 2008, as discussed below). Rather, bidirectional information flow between levels is vital to providing the feedback necessary to adaptively pursue goals (Fuster, 2008). In addition, the proposed hierarchy does not imply that inter-level communication must occur *only* through adjacent levels (e.g., the system level *must* bias the tactical level *only* through the strategic level). It appears likely that inter-level communication will occur in accordance with the hierarchy more often than not, because processing in adjacent levels will be more relevant that processing in non-adjacent levels. For example, information regarding the success of a particular tactic will have more utility for evaluating the larger strategy than for evaluating the larger goal (at the system level). However, information flow between non-adjacent levels is crucial in many cases. For example, given the complexity of our environment, the system level often maintains multiple goals simultaneously. In order to determine which particular goal to emphasize at any given moment, the tactical level must provide feedback to the system level about the estimated success of the tactics currently associated with each goal. Thus, the hierarchical nature of the proposed model still allows for the flexibility necessary to adaptively pursue goals.

The type of flexible communication described above is necessary in order to adaptively identify subgoals. That is, it is essential to set smaller, more proximal goals that comprise the steps necessary to attaining larger, distal goals (Kruglanski et al., 2002). For example, in order to obtain an academic degree, a student must complete a series of classes. Thus, completing each class is a subgoal necessary to the larger goal. An obvious question is *do subgoals differ from lower levels in the hierarchy*? We propose that these concepts, although similar, are relevant to different pieces of the process of pursuing longer-term goals. For example, a particular strategy is only relevant to the degree that it subserves the larger goal, whereas subgoals are themselves goals. That is, subgoals are committed to in and of themselves, which can become problematic when the subgoal becomes more important that the higher order goal it was meant to serve (D'Zurilla and Nezu, 2007). With relation to the proposed model, subgoals would be maintained by the system level once they were identified and committed to as goals. Thus, what may start out as a strategy/tactic becomes a subgoal once the individual identifies it as a discrete goal, apart from just a means to an end.

In conclusion, the integrated hierarchical model of approach/avoidance goal-pursuit proposed here is a nuanced conceptualization that deconstructs the fairly broad constructs of approach/avoidance into important component processes. We propose that this psychological model can serve as a framework for understanding the processes examined in neuroscience research on goal-pursuit systems.

NEURAL INSTANTIATION OF APPROACH/AVOIDANCE GOAL PURSUIT

Building on the proposed psychological model of approach and avoidance, we next attempt to integrate disparate bodies of neuroscience research to construct a preliminary model of the neural mechanisms instantiating the psychological model. In the present paper, we focus on PFC, given an overwhelming research base indicating that PFC is central to the pursuit of goals (Miller and Cohen, 2001; Fuster, 2008). Given that the approach/avoidance distinction is fundamental to the proposed model, we begin by reviewing research that has found such a distinction in prefrontal organization.

LATERALIZATION IN PREFRONTAL CORTEX ASSOCIATED WITH MOTIVATION

A long line of research suggests that PFC is lateralized with respect to motivational/emotional valence, with right PFC associated with avoidance motivation and unpleasant emotion, and left PFC associated with approach motivation and pleasant emotion (for review, see Heller et al., 2003; Miller et al., 2013). PFC lateralization with respect to motivational or emotional valence is supported by research using a number of different methodologies, including neuropsychological testing (e.g., Flor-Henry, 1976), brain lesion patients (e.g., Gainotti, 1972), and EEG (e.g., Davidson et al., 1990). Although PFC asymmetries have regularly been observed in EEG and other methodologies, they have been elusive in studies employing fMRI. This method complements EEG in that it provides better spatial resolution than traditional low-density EEG for locating specific areas of PFC involved in emotion and motivation. Herrington et al. (2005) were the first to demonstrate leftward lateralization for pleasant emotion using fMRI, which was localized to DLPFC. As discussed in Herrington et al. (2010), one reason why lateralization findings are uncommon in fMRI may be that lateralization is rarely tested directly. Indeed, region (including hemisphere) is almost never a factor or predictor in analyses of fMRI data. Statements are often made about what are in effect multiple simple-effects tests without a systematic evaluation of the underlying interaction.

MOTIVATION AND EXECUTIVE FUNCTION

Although motivation and executive function are both vital to goal-pursuit individually, we and others have argued that it is the interaction between these sets of processes that drives effective goal pursuit (e.g., Pessoa, 2009; Spielberg et al., 2011). Consider this scenario involving a student in her first year of college: it is the night before her first big test, and she planned to study for several hours and get a full night's rest. However, her roommate, with whom she has yet to develop a relationship, has just invited her to a party taking place that evening. If the student is motivated more strongly to obtain an A on her test, she must inhibit distraction (i.e., engage executive function) caused by reminders of the party (e.g., seeing her roommate's jacket) in order to fully concentrate on her material. However, if the student is motivated more strongly to build a friendship, she must inhibit distraction caused by reminders of her impending test (e.g., seeing a student from class at the party) in order to enjoy the party and fully interact with her roommate. In other words, what information is inhibited depends on which goal the student is motivated to pursue.

An emerging body of research consistently implicates areas of PFC in the integration of motivation and executive function processes (Gilbert and Fiez, 2004; Gray et al., 2005; Krawczyk et al., 2007; Locke and Braver, 2008; Rowe et al., 2008; Szatkowska et al., 2008). Such integration is consistent with conceptualizations of PFC as being necessary "to orchestrate thought and action in accordance with internal goals" (Miller and Cohen, 2001). For example, Pochon et al. (2002) examined the relation between reward processing, a facet of motivation, and performance on a working memory task. Results revealed that left DLPFC was activated by both working memory demands and increasing levels of reward. Taylor et al. (2004) conducted a similar study that examined the interaction between state motivation and working memory by manipulating motivation in terms of both reward and punishment. Consistent with the findings of Pochon et al. (2002), motivational processes interacted with working memory load in bilateral DLPFC. Several studies have also examined the interaction between motivation and inhibition-related processes. For example, Padmala and Pessoa (2010, 2011) found that monetary reward interacted with inhibition requirements in DLPFC (bilateral in one study, right only in the other study). In addition, Krebs et al. (2011) found that right DLPFC was activated when inhibiting goal-irrelevant reward associations.

Thus, several studies suggest that DLPFC is essential for the neural integration of motivation and executive function processes. These studies can be interpreted as manipulating the system level of the present hierarchical model of motivation, because they manipulate the reasons for the goal (i.e., to do well in order to obtain a reward or avoid a punishment). Thus, this research suggests that the system level is instantiated in (at least) DLPFC, which is consistent with research suggesting that DLPFC is involved in representing and maintaining goals (e.g., MacDonald et al., 2000). Although involvement of DLPFC was observed in all studies, there is inconsistency in the hemisphere which exhibited activation. Inconsistencies in the lateralization of DLPFC activation may be due several issues, including differences in the motivational manipulation used across the studies and the facet of executive function recruited. For example, Pochon et al. (2002) employed only a reward manipulation, consistent with the leftward lateralization found, whereas Taylor et al.'s (2004) motivational manipulation included both reward and punishment, consistent with the bilateral activation observed. However, all the studies recruiting inhibition used only reward and found right DLPFC activation (one study found bilateral activation), suggesting that task differences may play some part. The picture is further clouded by the fact that none of these studies actually tested laterality effects. Thus, the extent of the inconsistency is not clear.

MOTIVATIONAL TEMPERAMENT AND EXECUTIVE FUNCTION

Extending the work on state motivation and executive function, recent research has examined the interaction of motivational temperament with executive function. For example, Spielberg et al. (2011) investigated moderation of neural activation associated with the color-word Stroop (1935) task by approach and avoidance temperament. Neural activation associated with incongruent words was contrasted with activation associated with congruent words, and approach and avoidance temperament scores, computed using a confirmatory factor analysis of several self-report scales, were entered as between-subject predictors. Hemispheric lateralization was tested directly using methods similar to those of Herrington et al. (2010).

Consistent with research on state motivation and regional brain activity, approach temperament moderated activation in two regions of left DLPFC (a relatively anterior region in BA 8 and 9 and a more posterior area in BA 9 only), and avoidance temperament moderated activation in one region of right DLPFC (BA 9 and 6), all of which were lateralized effects. More specifically, higher levels of motivational temperament were associated with greater activation in the condition requiring stronger inhibition (incongruent, relative to congruent). Furthermore, higher levels of temperament were associated with better performance on the task, supporting the important moderating effect of such motivational tendencies on executive function.

The areas of DLPFC observed in Spielberg et al. (2011) have been associated with a number of other functions, including behavioral inhibition, planning action, attending to cues predicting the occurrence of a motivationally salient event, and responding when motivationally salient events occur (Volle et al., 2005; Abler et al., 2006; Bickel et al., 2009; Kaladjian et al., 2009). Incorporating this research with their findings, and consistent with Herrington et al. (2010), Spielberg et al. (2011) hypothesized that these regions of DLPFC are involved in implementing a motivational set that biases lower-order processing (i.e., attention to ink color vs. word meaning) to be congruent with goals. These findings have recently been replicated using an emotion-word Stroop task (Spielberg et al., 2012a), supporting the generalizability of these conclusions.

Although trait (e.g., motivational temperament) and state motivational manipulations are useful individually, it is likely that a deep understanding of the neural mechanisms involved in integrating motivation and executive function will occur only through a combination of these methods (e.g., investigating how trait phenomena moderate state manipulations). This is because a specific outcome can be viewed as an approach and/or avoidance goal depending on the motivational tendencies of each individual. For example, the potential to win a monetary reward will likely be viewed as an approach goal by many individuals, but may also be viewed as an avoidance goal (e.g., an opportunity to perform poorly and miss out on winning). Taking motivational temperament into account will allow for a greater level of certainty regarding the manner in which particular outcomes will be viewed.

INTERTEMPORAL CHOICE

Neuroscience research in the field of intertemporal choice, which investigates choices between outcomes that differ in temporal delay and reward/punishment magnitude, provides another avenue to examine the instantiation of motivational systems in the brain. Humans are often faced with choices between options that differ in the timescale of the potential outcomes. Often, one option is associated with a shorter delay and a smaller reward, whereas the delay in the other option is longer but the reward value greater. For example, an individual may have the goal of losing weight and be faced with the choice of whether to eat a high-calorie desert. In order to maximize gain/minimize loss over time, goals (e.g., losing weight) must be maintained in the face of competing options (e.g., sensory pleasure now), which is a process that can be associated with the system level of the hierarchical model of approach/avoidance. Although the choice with the longer delay has an objectively better outcome, this option is often not chosen, because humans discount the value of delayed rewards (Ainslie, 2001). The rate of future discounting can be thought of as a measure of impulsiveness, because it reflects the tendency to forego larger, long-term rewards in order to gain more immediate satisfaction (Ainslie, 1975). This proposal is supported by research indicating that more impulsive individuals (e.g., children with ADHD) discount future rewards more than less impulsive individuals (Barkley et al., 2001).

Recent research has attempted to identify brain regions involved in integrating temporal delay into the decision-making process. Several studies suggest that DLPFC, medial prefrontal cortex (MPFC), and posterior cingulate cortex (PCC) are involved in decisions to forego proximal reward or incur proximal punishment in order to maximize benefit over time, providing further support for the hypothesis that the system level is instantiated (in part) in DLPFC. Specifically, several studies have found that greater activation in DLPFC, MPFC, and PCC predicted the choice of the larger, later outcome (McClure et al., 2007; Wittmann et al., 2007; Weber and Huettel, 2008; Ballard and Knutson, 2009). As well, activation in DLPFC, MPFC, and PCC has been found to be positively correlated with the length of the delay associated with outcomes (Luhmann et al., 2008; Ballard and Knutson, 2009). Finally, gray-matter volume in DLPFC has been found to be positively associated with the tendency to choose the larger, later outcome over the smaller, more immediate outcome (Bjork et al., 2009).

In these studies, the delay and magnitude associated with each option were explicitly presented to participants. Therefore, maximizing reward over time required only the ability to resist the earlier option. In many real-world choices, however, the magnitude and delay of the outcome will not be explicit. For example, when choosing whether to forego eating (immediately available) cake in order to lose weight, the impact of cake eating on weight and how long it will be until the desired amount of weight will be lost (if cake is not eaten) will usually be unclear. In these situations, learning history can play an important role in determining which choice will be selected (e.g., how quickly a specific individual has lost weight in the past). Several studies have examined intertemporal choice when participants must learn the contingencies associated with different options. For example, Tanaka et al. (2004) employed a decision-making task in which participants had to learn to incur small, immediate losses in order to gain large, delayed rewards. Results revealed that learning to obtain larger, later rewards was associated with increased activation in left DLPFC, MPFC, and PCC, which is consistent with research linking these brain regions to foregoing proximal reward or incurring proximal punishment in order to maximize reward over time.

Yarkoni et al. (2005) employed a task similar to that of Tanaka et al. (2004). However, in their task, the strategy of foregoing more immediate rewards to obtain the delayed reward did not always maximize the total reward over time. Instead, it was optimal to choose the immediate reward in one of the conditions. Results revealed that DLPFC activation was associated with optimum performance (i.e., maximizing total reward) on the task. Specifically, when reward was maximized by sacrificing smaller, earlier rewards to obtain larger, later rewards, sustained activation in DLPFC across the entirety of the trials was greater than activation during the time at which participants actually made choices. When reward was maximized by choosing smaller, earlier rewards, DLPFC exhibited greater activation during the actual choice period, relative to the sustained activation across trials. This indicates that the involvement of DLPFC is not restricted to obtaining delayed rewards. Rather, DLPFC appears to be involved in maximizing overall benefit.

Taken together, this research supports the hypothesis that DLPFC is involved in maximizing benefit/minimizing harm over time. This would involve both the maintenance of appropriate goals in the face of competition (e.g., foregoing a small proximal reward for a larger, delayed reward) and the selection of appropriate strategies (e.g., determining whether obtaining proximal rewards or foregoing proximal rewards for larger, delayed rewards will maximize total benefit over time). Therefore, this research provides evidence that DLPFC is involved in instantiating both the system and strategic levels of the hierarchical model of motivation.

Both MPFC and PCC also appear to play significant roles in maximizing total reward over time. For example, research by Maddock (1999) indicates that PCC is involved in integrating emotional and motivational information with memory during recall. This suggests a role for MPFC and PCC in the anticipation of delayed rewards. When choosing between potential rewards, a representation of each outcome, incorporating motivationally relevant information based on past experience, is needed in order to evaluate the predicted subjective value of the outcome. In addition, the anticipation period itself can have value (Berns et al., 2007), because anticipation can be pleasant or unpleasant (or neutral). Greater incorporation of motivationally relevant information into mental simulations of a potential outcome will make an option seem more or less attractive.

The involvement of MPFC and PCC in the anticipation of potential outcomes is supported by several studies, including a study that found increased MPFC and PCC activation when participants self-reflected on both approach- and avoidance-related goals (Johnson et al., 2006). Additionally, dissociation in PCC activation to motivationally relevant stimuli has been found in relation to approach and avoidance (Touryan et al., 2007). Specifically, when an approach orientation was induced, greater activation in PCC was observed during the evaluation of pleasant stimuli (relative to unpleasant stimuli). In contrast, when an avoidance orientation was induced, greater activation in PCC was observed during the evaluation of unpleasant stimuli (relative to pleasant stimuli). Finally, Peters and Buchel (2010) directly investigated the impact of imagery associated with potential future outcomes on temporal discounting. Participants performed a classic delay discounting task in which they chose between immediate and delayed rewards. Before performing the task, participants identified a number of planned future events (e.g., going to a workshop, going to a friend's wedding). In one condition, the delayed reward choice was linked to one of the identified future events (i.e., the reward would be given on the day that the event occurred). Results revealed that rewards were discounted less heavily in this condition, relative to a control condition in which no links to future events were presented. Additionally, vividness ratings of future events correlated negatively with the rate of discounting, such that greater vividness was associated with less discounting. Importantly, both MPFC and PCC exhibited greater activation when links were presented, relative to the control condition, suggesting that these regions are involved in the representation of goals via imagery or other means. As well, the subjective value of the delayed reward option (i.e., the objective value multiplied by the delay discount rate) was correlated with brain activation in MPFC and PCC during the condition in which links to future events were presented, suggesting that these regions are involved in representing the value of future outcomes through associated imagery.

These findings are consistent with a model of the neural instantiation of prospection (Buckner and Carroll, 2007). Prospection is the process by which past memories are used to envision potential future scenarios, and this process can be used to assist in planning for future goals. Buckner and Carroll (2007) suggested that MPFC and PCC, along with other areas, are vital to the process of prospection.

In summary, the present review of the literature on intertemporal choice supports the hypothesis that DLPFC plays an essential role in goal pursuit and additionally implicates MPFC and PCC as being important components due to their involvement in the representation of motivationally salient aspects of potential future outcomes. In combination with the research reviewed above on the interaction of motivation and executive function, this research provides a starting point for a model of motivation in the brain.

A MODEL OF APPROACH/AVOIDANCE GOAL-PURSUIT PROCESSES IN THE BRAIN

Converging lines of research suggest that DLPFC implements a motivational set that biases lower-order neural processes to facilitate the achievement of goals. It is proposed here that this research can be interpreted by applying the framework of the hierarchical model of motivation (Elliot, 2006; Scholer and Higgins, 2008) to a set of proposals (for reviews, see Botvinick, 2008; Badre and D'Esposito, 2009) that superior, lateral prefrontal cortex (SLPFC), including DLPFC, is organized along a dimension of abstraction. Generally, more anterior regions (e.g., BA 10, DLPFC) are involved in the most abstract aspects of goal-directed processing (e.g., maintaining the ultimate goal), and more posterior regions (e.g., pre-motor cortex) are involved in processing the least abstract aspects (e.g., planning motor sequences).

There is some disagreement regarding the nature of the abstraction that organizes SLPFC. One proposal is that the abstraction is temporal in nature. Specifically, goals become more abstract as the timescale of the task they direct increases (Badre and D'Esposito, 2009). According to Botvinick (2008), timescale is likely the key parameter that governs the organization of SLPFC. Specifically, more anterior regions guide behavior over a longer time-span than do more posterior regions. Another proposal is policy abstraction, in which more abstract goal representations are more general than lower-level goal representations (Badre and D'Esposito, 2009).

It is proposed here that the gradient of abstraction and timescale evident in the hierarchical model of motivation can be mapped onto this SLPFC gradient, with the system level associated with more anterior SLPFC (e.g., BA 10, DLPFC) and lower levels (i.e., strategic, tactical) moving sequentially more posterior (e.g., BA 8, pre-motor cortex). The temperament level would be associated with the activity/reactivity of these regions (especially those instantiating the system level) rather than being associated with a specific region of SLPFC. Additionally, it is proposed here that SLPFC is lateralized with respect to motivational orientation, with left SLPFC associated with approach and right SLPFC associated with avoidance. This organization is illustrated in **Figure 2**. As shown, approach at the system level can recruit both approach and avoidance at the strategic level. However, approach at the system level is more likely to recruit approach at the strategic level, as indicated by the thicker arrows.

Support for this proposal can be found in a study by Kouneiher et al. (2009), which examined the integration of motivation and cognition in the context of a model of PFC abstraction proposed by Koechlin and colleagues (Koechlin et al., 2003; Koechlin and Summerfield, 2007). In this model, posterior DLPFC is hypothesized to be involved in contextual control (i.e., control based on rules related to the immediate context), whereas anterior DLPFC is hypothesized to be involved in episodic control (i.e., control based on a past event which indicates that a certain set of rules should be applied in the current context). The most anterior region, frontopolar PFC (e.g., BA 10), is hypothesized to be involved in branching control (i.e., maintaining a task set in memory while another task is carried out).

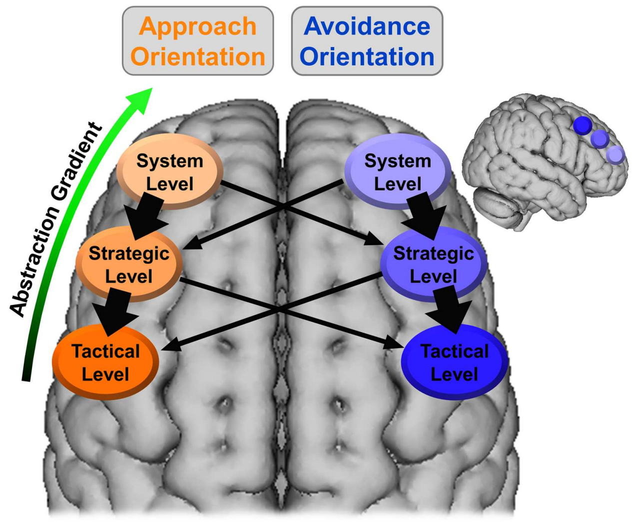

FIGURE 2 | Lateralized organization of superior, lateral prefrontal cortex with regard to the hierarchical model of motivation. The thickness of the arrows corresponds to the hypothesized strength of the relationship. The larger brain is an axial view of the superior surface of the brain viewed from above. The smaller brain is a sagittal view of the lateral surface of the right hemisphere. The location and coverage of the ovals/circles is meant to represent a relative placement rather than a delineation of specific cortex.

Kouneiher et al. (2009) found that rewards/punishments associated with the context (the current trial) and the episode (the current set of trials, which were preceded by a cue signaling the possible incentives) moderated posterior and anterior DLPFC activation, respectively. They also found an anterior-to-posterior gradient in medial PFC, with dorsal anterior cingulate cortex (dACC) activation moderated by episodic motivation and pre-supplementary motor area activation moderated by contextual motivation.

Support for the present proposal that the hierarchical model of approach/avoidance motivation can be mapped onto an anterior/posterior gradient of SLPFC can also be found in a recent study investigating the effect of forming implementation intentions on neural activation associated with goal pursuit (Gilbert et al., 2009). The task contained two conditions, which differed only in whether implementation intentions were externally provided to participants by experimenters. Given that the formation of implementation intentions reduces the need for active engagement of the strategic level (discussed above), and given that the conditions were of equal difficulty and potential monetary reward level, the conditions differed only on the extent to which the strategic level was actively engaged during the task. Consistent with the present proposal, engagement of the strategic level (i.e., when participants were not provided with implementations intentions) was positively associated with activation in two areas of left anterior SLPFC (BA 8 and 10). When participants were provided with implementation intentions, the only area of SLFPC exhibiting differential activation was left pre-motor cortex (BA 6).

ORBITOFRONTAL CORTEX

In addition to SLPFC, several other areas are likely to be important components of a model of motivation in the brain. As discussed above, MPFC and PCC appear to play important roles in anticipatory processes. Another potential region is orbitofrontal cortex (OFC), which has been linked to the maintenance of the current and expected motivational value of stimuli (O'Doherty and Dolan, 2006). This area likely provides information about stimulus value to superior areas such as DLPFC (Szatkowska et al., 2008).

However, there is some question regarding the nature of the value representations maintained in OFC (e.g., Roesch et al., 2007). Recent work by Schoenbaum and colleagues (Schoenbaum and Esber, 2010; Jones et al., 2012) suggests that OFC does not maintain cached value representations of a specific stimulus, *per se.* Rather, OFC appears to be necessary for calculating value on the fly in (at least somewhat) novel situations requiring integration of value information from several sources. In other words, OFC is required when an organism must infer the value of a stimulus – not based on direct past experience of the particular situation that is currently faced, but by integrating contingency and value information from different sources to estimate value. This view is supported by research indicating that Pavlovian or simple instrumental conditioning is not impacted by lesioning of OFC (this is not the case for amygdala lesions; Schoenbaum and Esber, 2010). Rather, OFC lesions prevent the suppression of old value when the current context signals a change in value (but no impact is observed after lesioning amygdala). Thus, OFC appears to be more involved in the types of value representations needed specifically in goal-directed behavior, as opposed to habit.

In addition, several studies suggest that the values maintained in OFC are relative to the individual's current state, rather than to potential future states involved in longer-term goals (e.g., Schoenbaum et al., 1998). For example, when an organism consumes a desired food to satiation (i.e., the food is no longer appealing), OFC tracks stimulus value relative to the current state of the individual (e.g., high value at the start, low or negative value at the end), rather than the long-term value of the food (which should remain high, otherwise that food would not be consumed in the future; Pickens et al., 2003). Additionally, several studies indicate that OFC is associated with choosing smaller, earlier rewards in intertemporal choice paradigms (e.g., Tanaka et al., 2004; Bjork et al., 2009). Therefore, it may be that OFC is involved in value maintenance for (usually shorter-term) goals related to the individual's current state (e.g., am I hungry now?). For (usually longer-term) goals related to potential future states of the individual (e.g., will I be hungry in the future?), MPFC and PCC may play a similar function by integrating motivationally salient information into memory that is recalled during anticipation. Alternatively, it is possible that OFC is involved in estimating stimulus value based on any state, whether that is the current state or an estimated future state. If so, MPFC/PCC may be more involved in the creation of the potential future state (e.g., estimating future needs/desires in a given circumstance). Future research separating estimation of value and internal state will be valuable in teasing apart these competing theories.

Research indicates that, like SLPFC, OFC may be organized along a gradient of abstraction. Specifically, a recent meta-analysis indicates that posterior OFC is closely associated with more primary reinforcers (e.g., sweet taste), whereas anterior OFC is closely associated with more abstract/secondary reinforcers (e.g., money, pride; Kringelbach and Rolls, 2004). Additionally, O'Doherty and Dolan (2006) have suggested that anterior, medial OFC is associated with maintaining a common neural currency, allowing the values of different types of reinforcers to be compared.

A medial vs. lateral distinction in OFC has been proposed by O'Doherty (2007). Specifically, medial OFC is thought to represent the value of rewards, whereas lateral OFC is thought to represent the value of punishments. However, there appears to be some disagreement regarding the role of lateral OFC. Specifically, Elliott et al. (2000) suggested that lateral OFC is activated when previously rewarded behavior must be inhibited, rather than representing the value of punishments *per se.* Kringelbach and Rolls (2004) incorporated both views and suggested that lateral OFC represents the value of punishments and signals that behavior should change.

This organization of OFC conflicts with the proposal that left PFC is associated with pleasant valence and approach motivation and right PFC with unpleasant valence and avoidance motivation (Heller, 1993; Davidson and Irwin, 1999). Additionally, recent meta-analysis suggests that OFC is lateralized with respect to emotional valence, although not in the predicted direction (Wager et al., 2008). Specifically, bilateral medial and right lateral OFC was associated with pleasant emotional experience, whereas left middle and lateral OFC was associated with unpleasant emotional experience. The association between bilateral, medial OFC and pleasant valence is consistent with O'Doherty's (2007) proposal. However, the findings of this meta-analysis raise questions regarding the role of lateral OFC that should be pursued in future research.

ANTERIOR CINGULATE CORTEX

Anterior cingulate cortex (ACC) is likely to be another important component of a model of motivation. One theory of ACC function is that ACC is involved in encoding the predicted value associated with actions (for a review, see Rushworth and Behrens, 2008). This includes the immediate reward or punishment value, as well as the value of potential information about future events prompted by the action. Additionally, ACC is hypothesized to influence the degree to which information gained from current actions influences future decisions (Rushworth and Behrens, 2008). Information represented in ACC is needed to efficiently create action plans to pursue goals, suggesting that ACC provides this information to SLPFC, including DLPFC. In relation to the hierarchical model of motivation, information held in ACC will be particularly relevant at the strategic and tactical levels.

An important consideration is to determine the regions of ACC that provide this information, given that several parcellations of ACC have been proposed. One influential parcellation (Bush et al., 2000; Mohanty et al., 2007) divided ACC into two sections; dorsal ACC was hypothesized to be more involved in putatively cognitive tasks such as error processing, whereas rostral ACC was hypothesized to be more involved in putatively emotional tasks. However, mounting evidence has called this parcellation into question. For example, Shackman et al. (2011) supported the association between dorsal ACC and putative cognitive control tasks but found that putatively emotional tasks were equally likely to activate dorsal or rostral ACC. In addition, they found that tasks involving pain were also more likely to activate dorsal ACC. In order to resolve this apparent discrepancy, they proposed that dorsal ACC is involved in using negative consequences (e.g., negative affect, pain) to adaptively modulate behavior, consistent with the proposal by Rushworth and Behrens (2008).

This proposal is also supported by a study that employed both diffusion tractography, which estimates the degree of white matter connectivity with other brain regions, and a meta-analysis of fMRI studies to parcellate cingulate (Beckmann et al., 2009). This analysis identified a region (roughly corresponding to the dorsal ACC region identified by Bush et al. (2000) but extending around the genu of the corpus callosum into rostral ACC) that is heavily connected to DLPFC and surrounding cortex and is reliably activated by reward manipulations. Given that this ACC region displays both motivation-related activation and connectivity to DLPFC, it is likely that this region provides motivational information regarding actions to DLPFC.

THE PROPOSED MODEL

The model proposed here (illustrated in **Figure 3**) posits that the system, strategic, and tactical levels of the hierarchical model of approach/avoidance motivation are instantiated along an anterior-to-posterior gradient of SLPFC (including DLFPC). Further, the present review suggests that OFC and ACC provide information about stimulus and action value, respectively, to these areas. Lastly, MPFC and PCC are involved in integrating motivationally salient information into the anticipation of potential future outcomes. Thus, we propose that all regions discussed are involved in instantiating the model, with SLPFC involved in overall coordination and maintenance over time of level-specific processing.

As an example of how the model may work with a specific goal, an individual may have the approach goal of losing weight in order to be more healthy, which would be maintained in anterior, left SLPFC (e.g., BA 10, anterior DLPFC). In order to pursue this goal, an area of left SLPFC posterior to this (e.g., posterior DLPFC) would be involved in the selection of an approach strategy and would engage ACC in order to obtain information regarding the potential value of different strategies. In this example, two approach strategies could be exercising regularly and eating healthy foods. The healthy eating strategy could be low value/high cost if the individual frequently encounters high-calorie food and has not been successful in the past in losing weight by eating healthily. In contrast, the exercise strategy could be high value/low cost if the individual has easy access to exercise equipment and has been successful in losing weight with exercise in the past, and this would likely be the strategy chosen. Anterior cingulate would also be engaged by a more posterior region of left SLPFC (e.g., pre-motor cortex) in order to determine the value of different approach tactics when judging which tactic to employ. For example, if the strategy were to exercise, an approach tactic could be going to the gym to participate in an exercise class or calling a friend to jog with. If the individual is embarrassed about showing their fitness level in front of strangers, the gym class tactic could be low value/high cost, whereas the tactic of jogging with a friend could be high value/low cost if the friend is sympathetic because they are also out of shape and attempting to lose weight, and this would likely be the tactic chosen. Finally, when faced with a conflicting goal, for example to enjoy a high-calorie dessert, anterior SLPFC would engage MPFC and PCC in anticipatory imagery of the future state of being thin. OFC would be involved in calculating the value of the dessert relative to the current state (though it may also be involved in calculating future value based on the anticipated future state of being thin).

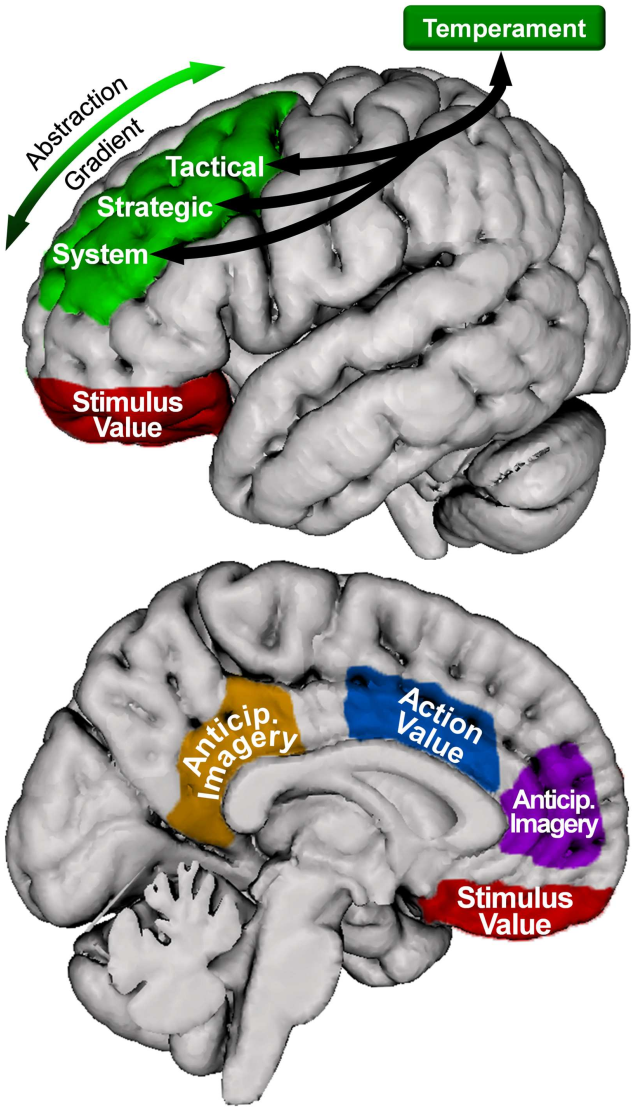

FIGURE 3 | Motivational organization of superior, lateral prefrontal cortex, and relationship with other brain areas in the model. Green = superior, lateral prefrontal cortex. Blue = anterior cingulate cortex. Red = orbitofrontal cortex. Purple = medial prefrontal cortex. Orange = posterior cingulate cortex. Only left hemisphere is shown; right hemisphere is similarly organized. The location and coverage of the areas is meant to represent a relative placement rather than a delineation of specific cortex.

Although the brain areas currently integrated into the model are proposed to be fundamental to the pursuit of goals, they are almost certainly not the only brain areas involved. Other brain regions are likely involved in instantiating fundamental components of motivation and are not yet incorporated into the present model. In addition, specific situations will necessitate the engagement of brain areas that instantiate processes more specific to the demands of that situation. For example, although engagement of Broca's area is not necessarily fundamental to goal-pursuit generally, it may be vital in situations where verbal rehearsal is needed to complete the task.

RELATIONSHIP TO EXTANT MODELS

The proposed model overlaps in a number of important dimensions with extant neural models of goal pursuit (although the models discussed are not necessarily labeled as such). For example, a number of models (e.g., Passingham and Wise, 2012) share a hierarchical structure (see Pessoa, 2009, for an example of a less hierarchical model), and this hierarchy is also mapped, at least to some degree, along an anterior-posterior gradient in PFC in some models (e.g., Fuster, 2008). In addition, the regions included in the proposed model are largely common across models (e.g., ACC, OFC).

The present model extends these models in a number of ways. First, the present model considers goal-pursuit related to approach and avoidance motivation separately, a division supported by a long line of research, as discussed above. In addition, the present model incorporates hemispheric asymmetry and the differential mapping of approach and avoidance therein. Furthermore, although previous models share a hierarchical structure, the present model incorporates well-researched psychological models of approach and avoidance to flesh out the nature of this hierarchy.

PRELIMINARY TESTS OF THE MODEL

A recent study provided preliminary support for the proposed network model (Spielberg et al., 2012b). In two independent samples, this study found that OFC, ACC, MPFC, and PCC interacted with regions of left and right DLPFC associated with approach and avoidance, respectively, to maintain difficult goals. Notably, approach and avoidance motivational temperament were associated with greater connectivity between OFC and left and right DLPFC, respectively, indicating that connections between DLPFC and OFC are of particular importance for motivational processes.

A recent explosion of methods for network identification and description will allow for further testing and refinement of the proposed model. Prominent among these methods is graph theory, which can characterize the role of different brain regions (nodes) within a network (see Bullmore and Sporns, 2009). For example, graph theory can identify that nodes are more central to a network (hubs) by examining the paths by which different nodes communicate with each other. Hubs are those nodes which are more often intermediaries through which different nodes communicate. Graph theory can also isolate specific circuits within the larger network (modules) by identifying nodes that tend to communicate more with nodes within the module than those outside. Importantly, graph theory can be used to test the importance of a node in a network by removing the node and assessing whether the network continues to function efficiently.

Use of graph theory has already begun to bear fruit. For example, Kinnison et al. (2012) examined brain networks during a task involving both motivational and executive function components. Results revealed that reward increased the efficiency of connections, especially between cortical and subcortical regions. With regard to the model proposed here, graph theory can be used to test a number of important components. For example, regions of superior-lateral PFC (e.g., DLPFC) are posited to be central to the pursuit of goals. Therefore, regions such as DLPFC should function as hubs when individuals are pursuing goals. In addition, we expect the regions posited to be nodes in the model to function as a module within the larger suite of brain regions active during goal pursuit. Finally, in combination with tasks that isolate specific aspects of the model (e.g., selection and implementation of tactics), graph theory can be used to test the importance of a particular node (e.g., dACC) to the isolated model aspect. In summary, graph theory, among other methods assessing networks (e.g., Astolfi et al., 2007; Popov et al., 2013), will likely be of great utility in testing and refining the proposed model.

MODEL IMPLICATIONS

The proposed model has a number of implications for future research. For example, the type of task manipulation used in a study (i.e., approach vs. avoidance) should be carefully considered, because this information should guide hypotheses about which hemisphere is primarily involved. If a task manipulation could be both approach- and avoidance-related (e.g., across participants), the power of the experiment may be diluted, because some participants primarily engage left SLPFC, whereas others engage right. Another implication is that when conducting research aimed at understanding goal pursuit or control processes in the brain, researchers should be aware of the motivational level(s) (e.g., system vs. tactical) manipulated by their task and examine specific areas of SLPFC (e.g., anterior DLPFC vs. pre-motor cortex) accordingly. If a task manipulation engages different levels at different times, and this is not accounted for in the analysis strategy, power may also be reduced, because SLPFC regions will not be consistently activated during the manipulation. Alternatively, if a task manipulation simultaneously engages multiple levels, specificity regarding regions of SLPFC involved may be lost. Another consideration implicated by the present model is the time frame in which goal manipulations operate (e.g., relative to a current or future state), which should be examined to determine whether value information is likely to be represented in OFC and/or MPFC/PCC.

The present model encourages the use of neuroscience data to drive psychological research on goal-pursuit processes. For example, novel hypotheses can be generated based on what is known about the brain regions involved in implementing those processes. Additionally, the present model is more spatially specific than previous models and provides an initial structure for the interactions among regions. This can be used, for example, to guide the placement of sources in EEG and MEG source localization research. This allows both for disentangling activity related to multiple, simultaneously occurring goal-pursuit processes associated with different brain areas in the model and for examination of the interactions among regions with great temporal specificity (see Silton et al., 2010, 2011, for examples of the utility of this technique). Finally, the present model can improve the utility of neuroscience research on goal-pursuit and control processes by providing a framework, incorporating a rich psychological conceptualization of approach/avoidance motivation, in which to place this research.

Reflected in the present model is an attempt to draw on nuanced psychological conceptualizations of approach/avoidance motivation (e.g., Elliot, 2006; Scholer and Higgins, 2008) to provide a more specific model (in terms of both brain regions and psychological processes involved) of how motivation is instantiated in brain networks. This model benefits from being informed by several often disconnected literatures, including psychological and neuroscience research on the structure of approach/avoidance approach/avoidance goal pursuit.

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REFERENCES

Abler, B., Walter, H., Erk, S., Kammerer, H., and Spitzer, M. (2006). Prediction error as a linear function of reward probability is coded in human nucleus accumbens. *Neuroimage* 31, 790–795. doi:10.1016/j.neuroimage.2006.01.001

Achtziger, A., Bayer, U. C., and Gollwitzer, P. M. (2012). Committing to implementation intentions: attention and memory effects for selected situation cues. *Motiv. Emot.* 36, 287–300. doi:10.1007/s11031-011-9261-6

Ainslie, G. (1975). Specious reward: a behavioral theory of impulsiveness and impulse control. *Psychol. Bull.* 82, 463–496. doi:10.1037/h0076860

Ainslie, G. (2001). *Breakdown of Will*. Cambridge: Cambridge University Press.

Astolfi, L., de Vico Fallani, F., Cincotti, F., Mattia, D., Marciani, M. G., Baccala, L. A., et al. (2007). Imaging functional brain connectivity patterns from high-resolution EEG and fMRI via graph theory. *Psychophysiology* 44, 880–893. doi:10.1111/j.1469-8986.2007.00556.x

Averbeck, B. B., and Seo, M. (2008). The statistical neuroanatomy of frontal networks in the macaque. *PLoS Comput. Biol.* 4:e1000050. doi:10.1371/journal.pcbi.1000050

Badre, D., and D'Esposito, M. (2009). Is the rostro-caudal axis of the frontal lobe hierarchical? *Nat. Rev. Neurosci.* 10, 659–669. doi:10.1038/nrn2667

Ballard, K., and Knutson, B. (2009). Dissociable neural representations of future reward magnitude and delay during temporal discounting. *Neuroimage* 45, 143–150. doi:10.1016/j.neuroimage.2008.11.004

Banich, M. T. (2009). Executive function: the search for an integrated account. *Curr. Dir. Psychol. Sci.* 18, 89–94. doi:10.1111/j.1467-8721.2009.01615.x

Barkley, R. A., Edwards, G., Laneri, M., Fletcher, K., and Metevia, L. (2001). Executive functioning, temporal discounting, and sense of time in adolescents with attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD). *J. Abnorm. Child Psychol.* 29, 541–556. doi:10.1023/A:1012233310098

Beckmann, M., Johansen-Berg, H., and Rushworth, M. (2009). Connectivity-based parcellation of human cingulate cortex and its relation to functional specialization. *J. Neurosci.* 29, 1175–1190. doi:10.1523/JNEUROSCI.3328-08.2009

Berns, G. S., Laibson, D., and Loewenstein, G. (2007). Intertemporal choice – toward an integrative framework. *Trends Cogn. Sci. (Regul. Ed.)* 11, 482–488. doi:10.1016/j.tics.2007.08.011

Bickel, W. K., Pitcock, J. A., Yi, R., and Angtuaco, E. J. (2009). Congruence of BOLD response across intertemporal choice conditions: fictive and real money gains and losses. *J. Neurosci.* 29, 8839–8846. doi:10.1523/JNEUROSCI.5319-08.2009

Bjork, J. M., Momenan, R., and Hommer, D. W. (2009). Delay discounting correlates with proportional lateral frontal cortex volumes. *Biol. Psychiatry* 65, 710–713. doi:10.1016/j.biopsych.2008.11.023

Botvinick, M. M. (2008). Hierarchical models of behavior and prefrontal function. *Trends Cogn. Sci. (Regul. Ed.)* 12, 201–208. doi:10.1016/j.tics.2008.02.009

Bressler, S. L., and Menon, V. (2010). Large-scale brain networks in cognition: emerging methods and principles. *Trends Cogn. Sci. (Regul. Ed.)* 14, 277–290. doi:10.1016/j.tics.2010.04.004

Buckner, R. L., and Carroll, D. C. (2007). Self-projection and the brain. *Trends Cogn. Sci. (Regul. Ed.)* 11, 49–57. doi:10.1016/j.tics.2006.11.004

Bullmore, E., and Sporns, O. (2009). Complex brain networks: graph theoretical analysis of structural and functional systems. *Nat. Rev. Neurosci.* 10, 186–198. doi:10.1038/nrn2575

Bush, G., Luu, P., and Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends Cogn. Sci. (Regul. Ed.)* 4, 215–222. doi:10.1016/S1364-6613(00)01483-2

Campbell, J. P., and Pritchard, R. D. (1976). "Motivation theory in industrial and organizational psychology," in *Handbook of Industrial and Organizational Psychology*, ed. M. D. Dunnette (Chicago, IL: Rand McNally), 63–130.

Carver, C. S., Sutton, S. K., and Scheier, M. F. (2000). Action, emotion, and personality: emerging conceptual integration. *Pers. Soc. Psychol. Bull.* 26, 741–751. doi:10.1177/0146167200268008

Chen, E. Y. H., and Berrios, G. E. (1998). "Neural network models in psychiatric diagnosis and symptom recognition," in *Neural Networks and Psychopathology*, eds D. J. Stein and J. Ludick (Cambridge: Cambridge University Press), 34–56.

Crocker, L. D., Heller, W., Warren, S. L., O'Hare, A., Infantolino, Z. P., and Miller, G. A. (2013). Relationships among cognition, emotion, and motivation: implications for intervention and neuroplasticity in psychopathology. *Front. Hum. Neurosci.* 7:261. doi:10.3389/fnhum.2013.00261

Davidson, R. J., Ekman, P., Saron, C. D., Senulis, J. A., and Friesen, W. V. (1990). Approach withdrawal and cerebral asymmetry: emotional expression and brain physiology I. *J. Pers. Soc. Psychol.* 58, 330–341. doi:10.1037/0022-3514.58.2.330

Davidson, R. J., and Irwin, W. (1999). The functional neuroanatomy of emotion and affective style. *Trends Cogn. Sci. (Regul. Ed.)* 3, 11–21. doi:10.1016/S1364-6613(98)01265-0

D'Zurilla, T. J., and Nezu, A. M. (2007). *Problem-Solving Therapy: A Positive Approach to Clinical Intervention.* New York: Springer.

Elliot, A. (2006). The hierarchical model of approach-avoidance motivation. *Motiv. Emot.* 30, 111–116. doi:10.1007/s11031-006-9028-7

Elliot, A. J., and Fryer, J. W. (2008). "The goal construct in psychology," in *Handbook of Motivation Science*, eds J. Shah and W. Gardner (New York, NY: Guilford Press), 235–250.

Elliot, A. J., and Niesta, D. (2009). "Goals in the context of the hierarchical model of approach avoidance motivation," in *The Psychology of Goals*, eds G. Moskowitz and H. Grant (New York, NY: Guilford Press), 56–76.

Elliott, R., Dolan, R. J., and Frith, C. D. (2000). Dissociable functions in the medial and lateral orbitofrontal cortex: evidence from human neuroimaging studies. *Cereb. Cortex* 10, 308–317. doi:10.1093/cercor/10.3.308

Flor-Henry, P. (1976). Lateralized temporal-limbic dysfunction and psychopathology. *Ann. N. Y. Acad. Sci.* 280, 777–795. doi:10.1111/j.1749-6632.1976.tb25541.x

Fuster, J. (2008). *The Prefrontal Cortex*, 4th Edn. London: Academic Press.

Gainotti, G. (1972). Emotional behavior and hemispheric side of the lesion. *Cortex* 8, 41–55. doi:10.1016/S0010-9452(72)80026-1

Gawrilow, C., and Gollwitzer, P. M. (2008). Implementation intentions facilitate response inhibition in children with ADHD. *Cogn. Ther. Res.* 32, 261–280. doi:10.1007/s10608-007-9150-1

Gilbert, A. M., and Fiez, J. A. (2004). Integrating rewards and cognition in the frontal cortex. *Cogn. Affect. Behav. Neurosci.* 4, 540–552. doi:10.3758/CABN.4.4.540

Gilbert, S. J., Gollwitzer, P. M., Cohen, A. L., Oettingen, G., and Burgess, P. W. (2009). Separable brain systems supporting cued versus self-initiated realization of delayed intentions. *J. Exp. Psychol. Learn. Mem. Cogn.* 35, 905–915. doi:10.1037/a0015535

Gollwitzer, P. M. (1999). Implementation intentions: strong effects of simple plans. *Am. Psychol.* 54, 493–503. doi:10.1037/0003-066X.54.7.493

Gollwitzer, P. M., Fujita, K., and Oettingen, G. (2004). "Planning and the implementation of goals," in *Handbook of Self-Regulation: Research, Theory, and Applications*, eds R. F. Baumeister and K. Vohs (New York, NY: Guilford Press), 211–228.

Gollwitzer, P. M., and Sheeran, P. (2006). Implementation intentions and goal achievement: a meta-analysis of effects and processes. *Adv. Exp. Soc. Psychol.* 38, 69–119. doi:10.1016/S0065-2601(06)38002-1

Gray, J. R., Burgess, G. C., Schaefer, A., Yarkoni, T., Larsen, R. J., and Braver, T. S. (2005). Affective personality differences in neural processing efficiency confirmed using fMRI. *Cogn. Affect. Behav. Neurosci.* 5, 182–190. doi:10.3758/CABN.5.2.182

Heller, W. (1993). Neuropsychological mechanisms of individual differences in emotion, personality, and arousal. *Neuropsychology* 7, 476–489. doi:10.1037/0894-4105.7.4.476

Heller, W., Koven, N. S., and Miller, G. A. (2003). "Regional brain activity in anxiety and depression, cognition/emotion interaction, and emotion regulation," in *The Asymmetrical Brain*, eds K. Hugdahl and R. J. Davidson (Cambridge, MA: MIT Press), 533–564.

Herrington, J. D., Heller, W., Mohanty, A., Engels, A. S., Banich, M. T., Webb, A., et al. (2010). Localization of asymmetric brain function in emotion and depression. *Psychophysiology* 47, 442–454. doi:10.1111/j.1469-8986.2009.00958.x

Herrington, J. D., Mohanty, A., Koven, N. S., Fisher, J. E., Stewart, J. L., Banich, M. T., et al. (2005). Emotion-modulated performance and activity in left dorsolateral prefrontal cortex. *Emotion* 5, 200–207. doi:10.1037/1528-3542.5.2.200

Higgins, E. T. (2000). Making a good decision: value from fit. *Am. Psychol.* 55, 1217–1230. doi:10.1037/0003-066X.55.11.1217

Higgins, E. T. (2005). Value from regulatory fit. *Curr. Dir. Psychol. Sci.* 14, 209–213. doi:10.1111/j.0963-7214.2005.00366.x

Higgins, E. T., Roney, C. J. R., Crowe, E., and Hymes, C. (1994). Ideal versus ought predilections for approach and avoidance: distinct self-regulatory systems. *J. Pers. Soc. Psychol.* 66, 276–286. doi:10.1037/0022-3514.66.2.276

Johnson, M., Raye, C., Mitchell, K., Touryan, S., Greene, E., Nolen-Hoeksema, S., et al. (2006). Dissociating medial frontal and posterior cingulate activity during self-reflection. *Soc. Cogn. Affect. Neurosci.* 1, 56–64. doi:10.1093/scan/nsl004

Jones, J. L., Esber, G. R., McDannald, M. A., Gruber, A. J., Hernandez, A., Mirenzi, A., et al. (2012). Orbitofrontal cortex supports behavior and learning using inferred but not cached values. *Science* 338, 953–956. doi:10.1126/science.1227489

Jones, M. R. (1955). *Nebraska Symposium on Motivation*, Vol. 3. Lincoln, NE: University of Nebraska Press.

Kaladjian, A., Jeanningros, R., Azorin, J. M., Nazarian, B., Roth, M., Anton, J. L., et al. (2009). Remission from mania is associated with a decrease in amygdala activation during motor response inhibition. *Bipolar Disord.* 11, 530–538. doi:10.1111/j.1399-5618.2009.00722.x

Kinnison, J., Padmala, S., Choi, J. M., and Pessoa, L. (2012). Network analysis reveals increased integration during emotional and motivational processing. *J. Neurosci.* 32, 8361–8372. doi:10.1523/JNEUROSCI.0821-12.2012

Koechlin, E., Ody, C., and Kouneiher, F. (2003). The architecture of cognitive control in the human prefrontal cortex. *Science* 302, 1181–1185. doi:10.1126/science.1088545

Koechlin, E., and Summerfield, C. (2007). An information theoretical approach to prefrontal executive function. *Trends Cogn. Sci. (Regul. Ed.)* 11, 229–235. doi:10.1016/j.tics.2007.04.005

Kouneiher, F., Charron, S., and Koechlin, E. (2009). Motivation and cognitive control in the human prefrontal cortex. *Nat. Neurosci.* 12, 939–947. doi:10.1038/nn.2321

Krawczyk, D. C., Gazzaley, A., and D'Esposito, M. (2007). Reward modulation of prefrontal and visual association cortex during an incentive working memory task. *Brain Res.* 1141, 168–177. doi:10.1016/j.brainres.2007.01.052

Krebs, R. M., Boehler, C. N., Egner, T., and Woldorff, M. G. (2011). The neural underpinnings of how reward associations can both guide and misguide attention. *J. Neurosci.* 31, 9752–9759. doi:10.1523/JNEUROSCI.0732-11.2011

Kringelbach, M. L., and Rolls, E. T. (2004). The functional neuroanatomy of the human orbitofrontal cortex: evidence from neuroimaging and neuropsychology. *Prog. Neurobiol.* 72, 341–372. doi:10.1016/j.pneurobio.2004.03.006

Kruglanski, A. W. (1999). Motivation, cognition, and reality: three memos for the next generation of research. *Psychol. Inq.* 10, 54–58. doi:10.1207/s15327965pli1001_8

Kruglanski, A. W., Shah, J. Y., Fishbach, A., Friedman, R., Chun, W. Y., and Sleeth-Keppler, D. (2002). "A theory of goal systems," in *Advances in Experimental Social Psychology*, Vol. 34, ed. M. P. Zanna (San Diego, CA: Academic Press), 331–378.

Kuhl, J. (1986). "Motivation and information processing: a new look at decision making, dynamic change, and action control," in *The Handbook of Motivation and Cognition: Foundations of Social Behavior*, eds R. M. Sorrentino and E. T. Higgins (New York, NY: Guilford Press), 404–434.

Lang, P. J., Bradley, M. M., and Cuthbert, B. N. (1998). Emotion, motivation, and anxiety: brain mechanisms and psychophysiology. *Biol. Psychiatry* 44, 1248–1263. doi:10.1016/S0006-3223(98)00275-3

Lazarus, R. S. (1991). Cognition and motivation in emotion. *Am. Psychol.* 46, 352–367. doi:10.1037/0003-066X.46.4.352

Levit-Binnun, N., and Golland, Y. (2011). Finding behavioral and network indicators of brain vulnerability. *Front. Neurosci.* 6:10. doi:10.3389/fnhum.2012.00010

Lindsley, D. B. (1957). "Psychophysiology and motivation," in *Nebraska Symposium on Motivation*, Vol. 5, ed. M. R. Jones (Lincoln, NE: University of Nebraska Press), 44–105.

Locke, E. A. (2000). Motivation, cognition, and action: an analysis of studies of task goals and knowledge. *Appl. Psychol.* 49, 408–429. doi:10.1111/1464-0597.00023

Locke, E. A., and Latham, G. P. (2002). Building a practically useful theory of goal setting and task motivation: a 35 year odyssey. *Am. Psychol.* 57, 705–717. doi:10.1037/0003-066X.57.9.705

Locke, H. S., and Braver, T. S. (2008). Motivational influences on cognitive control: behavior, brain activation, and individual differences. *Cogn. Affect. Behav. Neurosci.* 8, 99–112. doi:10.3758/CABN.8.1.99

Luhmann, C. C., Chun, M. M., Yi, D. J., Lee, D., and Wang, X. J. (2008). Neural dissociation of delay and uncertainty in intertemporal choice. *J. Neurosci.* 28, 14459–14466. doi:10.1523/JNEUROSCI.5058-08.2008

MacDonald, A. W., Cohen, J. D., Stenger, V. A., and Carter, C. A. (2000). Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science* 288, 1835–1838. doi:10.1126/science.288.5472.1835

Maddock, R. J. (1999). The retrosplenial cortex and emotion: new insights from functional neuroimaging of the human brain. *Trends Neurosci.* 22, 310–316. doi:10.1016/S0166-2236(98)01374-5

Martin, J., and Failows, L. (2010). "Executive function: theoretical concerns," in *Self and Social Regulation: Social Interaction and the Development of Social Understanding and Executive Functions*, eds B. Sokol, U. Muller, J. Carpendale, A. Young, and G. Iarocci (Oxford: Oxford University Press), 35–55.

Martin, L. L., and Tesser, A. (2009). "Five markers of motivated behavior," in *The Psychology of Goals*, eds G. Moskowitz and H. Grant (New York, NY: Guilford Press), 257–276.

McClure, S. M., Ericson, K. M., Laibson, D. I., Loewenstein, G., and Cohen, J. D. (2007). Time discounting for primary rewards. *J. Neurosci.* 27, 5796–5804. doi:10.1523/JNEUROSCI.4246-06.2007

Meehan, T. P., and Bressler, S. L. (2012). Neurocognitive networks: findings, models, and theory. *Neurosci. Biobehav. Rev.* 36, 2232–2247. doi:10.1016/j.neubiorev.2012.08.002

Miller, E. K., and Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annu. Rev. Neurosci.* 24, 167–202. doi:10.1146/annurev.neuro.24.1.167

Miller, G. A. (1996). Presidential address: how we think about cognition, emotion, and biology in psychopathology. *Psychophysiology* 33, 615–628. doi:10.1111/j.1469-8986.1996.tb02356.x

Miller, G. A. (2010). Mistreating psychology in the decades of the brain. *Perspect. Psychol. Sci.* 5, 716–743. doi:10.1177/1745691610388774

Miller, G. A., Crocker, L. D., Spielberg, J. M., Infantolino, Z. P., and Heller, W. (2013). Issues in localization of brain function: the case of lateralized frontal cortex in cognition, emotion, and psychopathology. *Front. Integr. Neurosci.* 7:2. doi:10.3389/fnint.2013.00002

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., Wager, T. D., et al. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: a latent variable analysis. *Cogn. Psychol.* 41, 49–100. doi:10.1006/cogp.1999.0734

Mohanty, A., Engels, A. S., Herrington, J. D., Heller, W., Ho, R. M., Banich, M. T., et al. (2007). Differential engagement of anterior cingulate cortex subdivisions for cognitive and emotional function. *Psychophysiology* 44, 343–351. doi:10.1111/j.1469-8986.2007.00515.x

Moskowitz, G. B., and Grant, H. (2009). "Introduction: four themes in the study of goals," in *The Psychology of Goals*, eds G. B. Moskowitz and H. Grant (New York, NY: Guilford Press), 1–24.

O'Doherty, J. P. (2007). Lights, camembert, action! The role of human orbitofrontal cortex in encoding stimuli, rewards, and choices. *Ann. N. Y. Acad. Sci.* 1121, 254–272. doi:10.1196/annals.1401.036

O'Doherty, J. P., and Dolan, R. J. (2006). "The role of human orbitofrontal cortex in reward prediction and behavioral choice: insights from neuroimaging," in *The Orbitofrontal Cortex*, eds D. H. Zald and S. L. Rauch (Oxford: Oxford University Press), 265–284.

Padmala, S., and Pessoa, L. (2010). Interactions between cognition and motivation during response inhibition. *Neuropsychologia* 48, 558–565. doi:10.1016/j.neuropsychologia.2009.10.017

Padmala, S., and Pessoa, L. (2011). Reward reduces conflict by enhancing attentional control and biasing visual cortical processing. *J. Cogn. Neurosci.* 23, 3419–3432. doi:10.1162/jocn_a_00011

Parks-Stamm, E., and Gollwitzer, P. M. (2009). "Goal implementation: the benefits and costs of if-then planning," in *The Psychology of Goals*, eds G. Moskowitz and H. Grant (New York, NY: Guilford Press), 362–391.

Parks-Stamm, E., Gollwitzer, P. M., and Oettingen, G. (2007). Action control by implementation intentions: effective cue detection and efficient response initiation. *Soc. Cogn.* 25, 247–264. doi:10.1521/soco.2007.25.2.248

Passingham, R. E., and Wise, S. P. (2012). *The Neurobiology of the Prefrontal Cortex: Anatomy, Evolution, and the Origin of Insight.* Oxford: Oxford University Press.

Pessoa, L. (2009). How do emotion and motivation direct executive control? *Trends Cogn. Sci. (Regul. Ed.)* 13, 160–166. doi:10.1016/j.tics.2009.01.006

Peters, J., and Buchel, C. (2010). Episodic future thinking reduces reward delay discounting through an enhancement of prefrontal-mediotemporal interactions. *Neuron* 66, 138–148. doi:10.1016/j.neuron.2010.03.026

Pickens, C. L., Setlow, B., Saddoris, M. P., Gallagher, M., Holland, P. C., and Schoenbaum, G. (2003). Different roles for orbitofrontal cortex and basolateral amygdala in a reinforcer devaluation task. *J. Neurosci.* 23, 11078–11084.

Pochon, J. B., Levy, R., Fossati, P., Lehericy, S., Poline, J. B., Pillon, B., et al. (2002). The neural system that bridges reward and cognition in humans: an fMRI study. *Proc. Natl. Acad. Sci. U.S.A.* 99, 5669–5674. doi:10.1073/pnas.082111099

Popov, T., Miller, G. A., Rockstroh, B., and Weisz, N. (2013). Modulation of alpha power and functional connectivity during facial affect recognition. *J. Neurosci.* 33, 6018–6026. doi:10.1523/JNEUROSCI.2763-12.2013

Roesch, M., Calu, D., Burke, K., and Schoenbaum, G. (2007). Should I stay or should I go? Transformation of time-discounted rewards in orbitofrontal cortex and associated brain circuits. *Ann. N. Y. Acad. Sci.* 1104, 21–34. doi:10.1196/annals.1390.001

Rowe, J. B., Eckstein, D., Braver, T., and Owen, A. M. (2008). How does reward expectation influence cognition in the human brain? *J. Cogn. Neurosci.* 20, 1–13. doi:10.1162/jocn.2008.20140

Rushworth, M., and Behrens, T. (2008). Choice, uncertainty and value in prefrontal and cingulate cortex. *Nat. Neurosci.* 11, 389–397. doi:10.1038/nn2066

Schoenbaum, G., Chiba, A. A., and Gallagher, M. (1998). Orbitofrontal cortex and basolateral amygdala encode expected outcomes during learning. *Nat. Neurosci.* 1, 155–159. doi:10.1038/407

Schoenbaum, G., and Esber, G. R. (2010). How do you (estimate you will) like them apples? Integration as a defining trait of orbitofrontal function. *Curr. Opin. Neurobiol.* 20, 205–211. doi:10.1016/j.conb.2010.01.009

Scholer, A., and Higgins, E. T. (2008). "Distinguishing levels of approach and avoidance: an analysis using regulatory focus theory," in *Handbook of Approach and Avoidance Motivation*, ed. A. J. Elliot (Hillsdale, NJ: Erlbaum), 362–391.

Shackman, A. J., Salomons, T. V., Slagter, H. A., Fox, A. S., Winter, J. J., and Davidson, R. J. (2011). The integration of negative affect, pain and cognitive control in the cingulate cortex. *Nat. Rev. Neurosci.* 12, 154–167. doi:10.1038/nrn2994

Sherman, S. J., and Sherman, J. W. (1999). Bring the troops back home: armistice between motivation and cognition. *Psychol. Inq.* 10, 65–68. doi:10.1207/s15327965pli1001_11

Silton, R. L., Heller, W., Towers, D. N., Engels, A. S., Edgar, J. C., Spielberg, J. M., et al. (2011). Depression and anxiety distinguish frontocingulate cortical activity during top-down attentional control. *J. Abnorm. Psychol.* 120, 272–285. doi:10.1037/a0023204

Silton, R. L., Miller, G. A., Towers, D. N., Engels, A. S., Edgar, J. C., Spielberg, J. M., et al. (2010). The time course of activity in dorsolateral prefrontal cortex and anterior cingulate cortex during top-down attentional control. *Neuroimage* 50, 1292–1302. doi:10.1016/j.neuroimage.2009.12.061

Sorrentino, R. M., and Higgins, E. T. (1986). "Motivation and cognition: warming to synergism," in *The Handbook of Motivation and Cognition: Foundations of Social Behavior*, eds R. M. Sorrentino and E. T. Higgins (New York, NY: Guilford Press), 3–19.

Spielberg, J. M., Miller, G. A., Engels, A. S., Herrington, J. D., Sutton, B. P., Banich, M. T., et al. (2011). Trait approach and avoidance motivation: lateralized neural activity associated with executive function. *Neuroimage* 54, 661–670. doi:10.1016/j.neuroimage.2010.08.037

Spielberg, J. M., Miller, G. A., Warren, S. L., Engels, A. S., Crocker, L. D., Sutton, B. P., et al. (2012a). Trait motivation moderates neural activation associated with goal pursuit. *Cogn. Affect. Behav. Neurosci.* 12, 308–322. doi:10.3758/s13415-012-0088-8

Spielberg, J. M., Miller, G. A., Warren, S. L., Engels, A. S., Crocker, L. D., Banich, M. T., et al. (2012b). A brain network instantiating approach and avoidance motivation. *Psychophysiology* 49, 1200–1214. doi:10.1111/j.1469-8986.2012.01443.x

Spielberg, J. M., Stewart, J. L., Levin, R. L., Miller, G. A., and Heller, W. (2008). Prefrontal cortex, emotion, and approach/withdrawal motivation. *Soc. Personal. Psychol. Compass* 2, 135–153. doi:10.1111/j.1751-9004.2007.00064.x

Sporns, O. (2011). *Networks of the Brain.* Cambridge, MA: The MIT Press.

Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *J. Exp. Psychol. Gen.* 18, 643–662. doi:10.1037/h0054651

Szatkowska, I., Bogorodzki, P., Wolak, T., Marchewka, A., and Szeszkowski, W. (2008). The effect of motivation on working memory: an fMRI and SEM study. *Neurobiol. Learn. Mem.* 90, 475–478. doi:10.1016/j.nlm.2008.06.001

Tanaka, S. C., Doya, K., Okada, G., Ueda, K., Okamoto, Y., Yamawaki, S., et al. (2004). Prediction of immediate and future rewards differentially recruits cortico-basal ganglia loops. *Nat. Neurosci.* 7, 887–893. doi:10.1038/nn1279

Taylor, S. F., Welsh, R. C., Wager, T. D., Phan, K. L., Fitzgerald, K. D., Gehring, W. J., et al. (2004). A functional neuroimaging study of motivation and executive function. *Neuroimage* 21, 1045–1054. doi:10.1016/j.neuroimage.2003.10.032

Tomarken, A. J., and Zald, D. H. (2009). Conceptual, methodological, and empirical ambiguities in the linkage between anger and approach: comment on Carver and Harmon-Jones. *Psychol. Bull.* 135, 209–214. doi:10.1037/a0014735

Touryan, S. R., Johnson, M. K., Mitchell, K. J., Farb, N., Cunningham, W. A., and Raye, C. L. (2007). The influence of self-regulatory focus on encoding of, and memory for, emotional words. *Soc. Neurosci.* 2, 14–27. doi:10.1080/17470910601046829

Volle, E., Pochon, J. B., Lehericy, S., Pillon, B., Dubois, B., Levy, R., et al. (2005). Specific cerebral networks for maintenance and response organization within working memory as evidenced by the double delay/double response paradigm. *Cereb. Cortex* 15, 1064–1074. doi:10.1093/cercor/bhh207

Wager, T. D., Feldman Barrett, L., Bliss-Moreau, E., Lindquist, K. A., Duncan, S., Kober, H., et al. (2008). "The neuroimaging of emotion," in *Handbook of Emotions*, 3rd Edn, eds M. Lewis, J. M. Haviland-Jones, and L. Feldman-Barrett (New York, NY: Guilford Press), 272–290.

Weber, B. J., and Huettel, S. A. (2008). The neural substrates of probabilistic and intertemporal decision making. *Brain Res.* 1234, 104–115. doi:10.1016/j.brainres.2008.07.105

Wittmann, M., Leland, D. S., and Paulus, M. P. (2007). Time and decision making: differential contribution of the posterior insular cortex and the striatum during a delay discounting task. *Exp. Brain Res.* 179, 643–653. doi:10.1007/s00221-006-0822-y

Yarkoni, T., Gray, J. R., Chrastil, E. R., Barch, D. M., Green, L., Braver, T. S., et al. (2005). Sustained neural activity associated with cognitive control during temporally extended decision making. *Cogn. Brain Res.* 23, 71–84. doi:10.1016/j.cogbrainres.2005.01.013

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Effects of saccadic bilateral eye movements on episodic and semantic autobiographical memory fluency

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Performing a sequence of fast saccadic horizontal eye movements has been shown to facilitate performance on a range of cognitive tasks, including the retrieval of episodic memories. One explanation for these effects is based on the hypothesis that saccadic eye movements increase hemispheric interaction, and that such interactions are important for particular types of memory. The aim of the current research was to assess the effect of horizontal saccadic eye movements on the retrieval of both episodic autobiographical memory (event/incident based memory) and semantic autobiographical memory (fact based memory) over recent and more distant time periods. It was found that saccadic eye movements facilitated the retrieval of episodic autobiographical memories (over all time periods) but not semantic autobiographical memories. In addition, eye movements did not enhance the retrieval of non-autobiographical semantic memory. This finding illustrates a dissociation between the episodic and semantic characteristics of personal memory and is considered within the context of hemispheric contributions to episodic memory performance.

Keywords: bilateral eye movements, autobiographical memory, episodic memory, semantic memory, memory fluency, hemispheric interaction

INTRODUCTION

Autobiographical memory refers to a range of stored information and knowledge pertaining to the self, and thus a form of personal memory. It is considered to comprise of both episodic (event and instance specific) and semantic (general self knowledge and facts about oneself) components (Conway, 1990, 2005; Dritschel et al., 1992; Conway and Pleydell-Pearce, 2000; Levine, 2004). The experiment presented here is concerned with the influence of saccadic bilateral (horizontal) eye movements on the retrieval of episodic and semantic components of autobiographical memory.

The reason for the interest in saccadic bilateral eye movements relates to a broader research literature regarding the role of hemispheric interaction in memory. It has been proposed that episodic memory processing is, in part, dependent upon hemispheric interactions (e.g., Christman et al., 2003; Habib et al., 2003; Christman and Propper, 2010). The importance of cerebral interaction in episodic memory comes from a range of findings. For example, research with commissurotomized patients or those with callosal agenesis show impaired performance on free recall and recognition, both of which are episodic memory tests (Phelps et al., 1991; Geffen et al., 1994; Cronin-Golomb et al., 1996; Jha et al., 1997).

Personal handedness has also been used as a behavioral marker for hemispheric interaction as several studies have found that mixed or inconsistent handed individuals have a relatively larger corpus callosum compared to right-handed individuals (e.g., Witelson, 1985; Denenberg et al., 1991; Habib et al., 1991; Clarke and Zaidel, 1994). The larger size of the corpus callosum subsequently provides a basis for greater hemispheric interaction (Christman, 1993, 1995; Niebauer et al., 2002). Results have revealed that mixed-handed individuals outperform those who are strongly right-handed on a range of episodic memory tasks including: free recall following incidental and intentional learning (Propper et al., 2005; Christman and Butler, 2011), enhanced remember responses in the remember-know paradigm (Propper and Christman, 2004), more accurate source/associative memory (Lyle et al., 2008b, 2012; Chu et al., 2012), and more successful learning of a foreign vocabulary (Kempe et al., 2009).

Research using neuroimaging procedures have also revealed interesting findings regarding the role of hemispheric interaction. Observations that the left and right prefrontal regions appeared to be preferentially activated during the encoding (vs. retrieval) of episodic information led to the proposal of the Hemispheric Encoding and Retrieval Asymmetry (HERA) model (Nyberg et al., 1996; Habib et al., 2003). This model essentially describes a functional asymmetry between the left and right hemispheres in terms of cognitive operations that are independent of the type of material being processed. A number of studies have found broad support for this idea using a range of techniques including PET (Tulving et al., 1994), fMRI (McDermott et al., 1999; Kompus et al., 2011), EEG (Babiloni et al., 2004, 2006), ERPs (Düzel et al., 1999), and TMS (Rossi et al., 2004, 2006; Gagnon et al., 2010; Manenti et al., 2011). In spite of the evidence in favor of the HERA model, not all research is equally supportive. For example, it has been argued that the main determinant of asymmetries is related to material-specific processing biases (e.g., Wagner et al., 1998; Miller et al., 2002) (but see Habib et al., 2003 for counter-arguments). Also, a case has been made for the hypothesis that when retrieval is effortful or demanding of resources, then retrieval itself elicits bilateral activations (Nolde et al., 1998). In some respects, Nolde et al. (1998) extend the HERA model by continuing to emphasize left hemisphere activity during encoding but either right or bilateral activity during retrieval depending on the complexity of the retrieval task. Despite some problems with HERA, it has been contended that successful performance on tasks of episodic memory are dependent upon the interaction between right hemisphere based retrieval processes operating upon the products of left hemisphere based encoding processes (Christman et al., 2003; Christman and Propper, 2010). Even if effortful retrieval involves bilateral activations, then presumably, successful interaction between the hemispheres would be important for retrieval success.

One particularly relevant avenue of research has focused on the effects of saccadic bilateral eye movements on memory. A number of experiments have demonstrated that episodic memory can be improved if retrieval is preceded by a period of 30 s of saccadic bilateral eye movements. For example, Christman et al. (2003), presented subjects with a list of words during the encoding phase of an experiment. This was followed by 30 s of bilateral eye movements prior to a test of episodic recognition memory. Compared to a range of control conditions, it was found that bilateral saccades improved overall memory accuracy. In addition, and consistent with predictions, bilateral enhancement was absent on a non-episodic test of implicit memory.

This and similar findings have been observed across a number of laboratory-based tests assessing different aspects of episodic memory such as: associative recognition and context memory (Parker et al., 2008; Lyle et al., 2012), visual scenes (Parker et al., 2009; Lyle and Jacobs, 2010), landmark shape and spatial location information (Brunyé et al., 2009), and free recall of neutral and emotional words (Samara et al., 2011; Nieuwenhuis et al., 2013).

Eye movements have also been shown to reduce false memory in paradigms that are designed to elicit high proportions of false memories, such as the Deese-Roediger-McDermott (DRM) paradigm (Christman et al., 2004; Parker and Dagnall, 2007). As a result, eye movements can be shown to increase memory accuracy by both increasing the hit rate and reducing the false alarm rate (e.g., Lyle et al., 2008a; Parker et al., 2008; Brunyé et al., 2009). Interestingly, a dissociation between eye movements and memory type has been found in one experiment. Christman et al. (2003) compared the effects of eye movements on performance on tests of both episodic recognition and the perceptual implicit test of word-fragment completion (WFC). Previous research has demonstrated that WFC is little influenced by encoding tasks that encourage meaning based analyses of the stimuli (e.g., Roediger et al., 1992). However, WFC is influenced by changes in perceptual characteristics of items between study and test (e.g., Blum and Yonelinas, 2001) and is largely considered to be dependent upon perceptual-lexical processing (e.g., Nelson et al., 1989; Richardson-Klavehn and Gardiner, 1998). The results of Christman et al. (2003) found that saccadic bilateral eye movements influenced episodic recognition only.

One explanation for these findings is that saccadic bilateral eye movements bring about increased hemispheric interaction. In particular, lateral eye movements have been found to be associated with activations in the contralateral hemisphere (Dean et al., 2004; Kastner et al., 2007). Consequently, performing a sequence of right-left eye movements is assumed to result in bihemispheric activation. This in turn leads to equalized activation between the two hemispheres and increased hemispheric interaction (Christman et al., 2003; Christman and Propper, 2010). Potentially therefore, this forms the foundation for superior episodic memory, by providing a basis for augmented encoding-retrieval interactions.

Both handedness and eye movement effects have been shown to extend beyond memories acquired in the laboratory and improve the recall of autobiographical information. For example, Propper et al. (2005) found that mixed-handed individuals recalled more actual (true) autobiographical events and were less prone to false recall. Subsequently, Christman et al. (2006) established both that mixed-handedness and bilateral saccades enhanced the recall of earlier childhood memories. Later, Parker and Dagnall (2010) furthered this work, observing similar enhancing effects of handedness and eye movements on the retrieval of recollective (and hence episodic) qualities associated with autobiographical remembering.

Thus far, research on autobiographical memory and saccadic eye movements (and handedness) has been limited to episodic autobiographical memory. As noted earlier, autobiographical memory consists of both episodic and semantic components. Episodic autobiographical memory refers to memory for event-specific details within a spatio-temporal context. Semantic autobiographical memory in contrast refers to personal facts and knowledge about the self and life experiences (Conway, 2005; Kopelman et al., 1989; Tulving, 2002). Research indicates that episodic and semantic components of autobiographical memory can be dissociated as a function of a range of factors such as: brain damage (e.g., Kopelman et al., 1989; Murphy et al., 2008; Coste et al., 2011), dementia (e.g., Greene et al., 1995; Smith et al., 2010), and aging (e.g., Levine et al., 2002; Piolino et al., 2002). Patterns of autobiographical memory dysfunction are also associated with cortical-specific changes in cell loss/damage (Gilboa et al., 2005).

The current research extends previous findings by considering the effects of eye movements on both episodic and semantic personal memory. To achieve this, it employs an autobiographical fluency task that enables both components to be measured on a common metric (Dritschel et al., 1992). In this test, participants are required to produce aloud as many exemplars as possible to a set of categories covering episodic and semantic personal memory (and general semantic memory as an additional point of comparison). The measure of interest is the number of exemplars produced per unit of time over 90 s (i.e., fluency). This technique (and similar fluency measures) has been employed in a variety of studies to assess the episodic and semantic aspects of autobiographical memory (e.g., Dritschel et al., 1992; Greene et al., 1995; Matuszewski et al., 2009; Smith et al., 2010; Coste et al., 2011; Unsworth et al., 2012).

In the current experiment, memory was assessed after a pre-task activity phase that involved either bilateral, vertical, or no-eye movements. A vertical condition was employed similar to previous work (e.g., Christman et al., 2003; Parker and Dagnall, 2007; Brunyé et al., 2009). The purpose of the vertical condition was to act as an additional control to assess the specificity of eye movement effects as opposed to influences due to increased oculomotor activity. According to Christman et al. (2003), finding effects specific to the horizontal condition is supportive of the importance of hemispheric interaction.

In the current experiment, the pre-task activity was repeated prior to the recall of each memory type. The reason for this relates to the likelihood that eye movement effects on cognition are likely to be time-limited. Although this is a reasonable idea, we are not aware of any specific experiments that have directly addresses this notion. However, some research does have some bearing upon the issue. For example, Brunyé et al. (2009) argued that the duration of the effects might be similar to the duration of increased neural excitability brought about by cortical transcranial magnetic stimulation that on average is up to about 4 min (Pasqual-Leone et al., 1994). In addition, in a test of divergent thinking, Shobe et al. (2009) found that eye movement effects lasted up to 3 or 9 min depending on the measure used. Consequently, it is considered that the influence of eye movements is limited to a particular time-window, although the precise duration of this window in relation to memory retrieval is not yet known.

Based upon previous research and ideas of Christman et al. (2003), it is hypothesized that bilateral saccades will facilitate the retrieval of episodic autobiographical memory. It is expected that both forms of semantic memory will be uninfluenced. Thus episodic and semantic memories are expected to dissociate as a function of bilateral saccades.

MATERIALS AND METHODS

DESIGN

The experiment had three independent variables and formed a three (eye movement condition; bilateral vs. vertical vs. no-eye movement) between-subjects by two (autobiographical memory period; age 5–11 vs. 12–18) within-subjects by three (recall period; 30 vs. 60 vs. 90 s) within-subjects mixed ANOVA. The dependent variable was the cumulative number of memories recalled in each of the conditions. In particular, the number of episodic memories, friends names, teachers names, and category examples.

PARTICIPANTS

A total of 69 participants took part in the experiment study and were aged between 18 and 37 years. A total of 23 were assigned randomly to each of the eye movement conditions. The mean ages of the participants within each condition were 22.96 for the bilateral group, 22.91 for the vertical group, and 23.13 for the no-eye movement group. They were recruited from both inside and outside the university campus building and took part voluntarily after providing informed consent.

MATERIALS AND APPARATUS

Test booklets were prepared that consisted of two main sections. The first section allowed for the recording of participant information. The second section contained the experimental instructions pertaining to the recall of episodic autobiographical memory, semantic autobiographical memory, and general semantic memory. With the exception of general semantic memory, each of the aforementioned was further subdivided into autobiographical memory periods covering memories from 5 to 11 and 12 to 18 years. The test booklets contained the experimental instructions and were later used to record the memory scores of the subjects across each of the conditions.

A digital timer was used to time the 90 s given for each memory recall test. A Dictaphone was used to record the memories produced by the subjects. This allowed the experimenter to assess memory recalls over the time period and remove any repeated responses from the participant recall protocol.

Following previous similar work, a computer program was designed to initiate eye movements. This was done by flashing a black circle against a white background from side to side (bilateral condition), up and down (vertical condition), or on and off in the center of the screen (fixation condition). The circle moved (flashed) once every 500 ms and in the eye movement conditions was located approximately 27°of visual angle apart. The average size of the computer monitor was 55 cm (diagonal) and viewing distance as adjusted to maintain 27°of visual angle.

PROCEDURE

All participants were tested individually and randomly assigned to the eye movement conditions. Initially, each participant was provided with the test booklet and asked to fill in the section requesting personal details. Once this had been done, the booklet was taken from the participant and retained by the experimenter.

The experimenter then requested the participant to face a computer monitor and was told that the next part of the experiment would begin. They were informed that this would consist of a repeating cycle of four phases in which they would be asked to view a moving (or stationary) dot on a screen followed by a test of memory. All instructions were presented aurally.

For those allocated to the bilateral (vs. vertical) condition, the instructions requested subjects to follow the moving dot from side to side (vs. up and down) by making horizontal (vs. vertical) eye movements. In the no-eye movement condition, subjects were asked to fixate their attention on the dot flashing on and off in the center of the screen. The experimenter monitored compliance with these instructions. After 30 s of the allotted condition, the memory test began. This procedure was repeated a total of four times, once prior to each recall test.

The standardized instructions (based on Dritschel et al., 1992) were read aloud by the experimenter to the participant according to the type of memory tested (specific personal events (episodic autobiographical), friends names (semantic autobiographical), teachers names (semantic autobiographical), and category examples (general semantic).

For episodic autobiographical memory the instructions read "For this test, I would like you to recall as many personal memories of events from two periods in your life. The first period is between 5 and 11 years old and the second period is between 12 and 18 years old. For each of these periods I would like you to recall as many memories as you can within 90 s. Please try to name specific event memories, such as "the time I beat my best friend in the school swimming competition" rather than general memories, such as "having a paper round." Please do not go into describe in detail about each memory, just state each one as it comes to mind and then move onto the next. Participants were informed that they did not have to disclose any memories they were not comfortable with recalling or sharing.

For semantic autobiographical memory the instructions read "For this test, I would like you to recall as many autobiographical facts as you can from two periods in your life. The first period is between 5 and 11 years old and the second period is between

12 and 18 years old. For each of these periods I would like you to recall as many autobiographical facts as you can within 90 s. By autobiographical facts, in this case I mean names of school friends (vs. teachers). You do not need to tell me each memory in detail, just try to recall as many facts as you can about your life."

For general semantic memory the instructions read "For this test, I would like you to generate as many examples from two semantic categories as you can. I will give you 90 s to generate from each semantic category. By generating examples from semantic categories what I mean is this, if I were to say transport then I would like you to say as many examples of transport that you can such as cars, trains, boats ships, etc. Just state out loud the examples that come to mind. You do not need to tell me each example in detail, just try to generate as many examples as you can." After presenting these instructions, the experimenter read aloud either animals or vegetables in a randomized order and the recall period commenced. Once the recall period had expired, the next category was presented and the second recall period for semantic memory commenced.

Once the participants understanding of each test was confirmed, the timer was set to 90 s and the participant would begin recall. Following Dritschel et al. (1992), subjects recalled information from the earlier autobiographical period first. Subsequent to the recall of each type of memory, there was a short pause of a few minutes, in which the experimenter prepared for the next phase and conversed with the subject at a general level. Following this, the next cycle of eye movements and testing began. The order in which episodic autobiographical, semantic, autobiographical (friends and teachers names), and general semantic memories were tested was counterbalanced. Thus the experiment consisted of a series of four eye movement and recall phases.

Following completion of the experiment, participants were debriefed and informed of their participant rights.

RESULTS

The number of memories recalled (minus repetitions or irrelevant information) for each memory type were entered into ANOVAs with eye movements as a between-subjects factor and autobiographical memory period and time period as within-subject factors. For episodic, friends and teacher memories this created the following design: three (eye movement; bilateral vs. vertical vs. central fixation) by two (autobiographical memory period; 5–11 vs. 12–18.) by three (recall period; 30 vs. 60 vs. 90) mixed ANOVA. For general semantic memory, the variable of autobiographical memory period was not relevant and the design was a three (eye movement; bilateral vs. horizontal vs. central fixation) by two (semantic category; animals vs. vegetables) by three (recall period; 30 vs. 60 vs. 90) mixed ANOVA.

EPISODIC AUTOBIOGRAPHICAL MEMORY

The cumulative number of specific autobiographical memories can be found in **Table 1** below.

Table 1 | Mean (SD) number of episodic memories recalled as a function of eye movement condition, autobiographical memory period, and recall period.

ABM period and recall period (s)	Eye movement		
	Bilateral	Vertical	Central
5–11 YEARS			
30	6.09 (3.36)	4.91 (2.15)	4.52 (1.44)
60	10.00 (4.22)	9.00 (3.87)	8.00 (2.43)
90	13.73 (4.78)	12.13 (4.69)	11.00 (3.50)
12–18 YEARS			
30	6.65 (2.53)	6.00 (2.45)	4.91 (2.69)
60	11.13 (3.25)	10.01 (3.25)	8.48 (3.63)
90	15.08 (4.19)	13.26 (3.73)	11.52 (4.44)

This revealed a main effect of autobiographical memory period, $F(1, 66) = 7.53$, $p = 0.008$, indicating more episodic memories recalled for the more recent period (M for 5–11 = 8.21; M for 12–18 = 9.67). The interaction between autobiographical memory period and eye movements was not significant $F(2, 66) = 0.39$, $p = 0.68$. The main effect of recall period was significant, $F(2, 132) = 564.56$, $p \leq 0.001$, indicating a greater number of memories recalled over the longer (90 s) time period. The interaction between recall period and eye movements started to approach significance, $F(4, 132) = 2.07$, $p = 0.09$. The three way interaction between autobiographical memory period, recall period, and eye movement was not significant, $F(4, 132) = 0.87$, $p = 0.42$. The main effect of eye movements was significant. $F(2, 66) = 3.57$, $p = 0.03$. The main effect of eye movements was assessed via t tests between each of the eye movement conditions. The difference between the central and vertical condition started to approach significance, $t(44) = -1.35$, $p = 0.09$ (with higher means for the vertical condition). The difference between vertical and bilateral condition also started to approach significance, $t(44) = -1.33$, $p = 0.09$ (higher means for the bilateral condition). The difference between the central and bilateral condition was significant, $t(44) = -2.66$, $p = 0.01$ (with higher means for the bilateral condition).

SEMANTIC AUTOBIOGRAPHICAL MEMORY – FRIENDS

The cumulative number of friends recalled can be found in **Table 2** below.

The main effect of autobiographical memory period was significant $F(1, 66) = 16.43$, $p \leq 0.01$, indicating more friend memories recalled for the more recent time period (M for 5–11 = 16.62; M for 12–18 = 19.15). The interaction between autobiographical memory period and eye movements was not significant, $F(2, 66) = 0.88$, $p = 0.42$. The main effect of recall period was significant, $F(2, 132) = 374.91$, $p \leq 0.01$, indicating a greater number of friend memories recalled over the longer (90 s) time period. The interaction between recall period and eye movement was not significant $F(4, 132) = 0.17$, $p = 0.94$. The interaction between autobiographical memory period and recall period was significant, $F(2, 132) = 10.37$, $p \leq 0.001$. This interaction was further assessed with simple main effects at each level of recall period. At the 30 s interval, the difference between 5–11 and 12–18 was significant, $t(69) = -2.70$, $p = 0.009$. At the 60 s interval, the difference between 5–11 and 12–18 was also significant, $t(69) = -3.46$, $p = 0.001$. At the 90 s interval, the difference between 5–11 and

Table 2 | Mean (SD) number of friend memories recalled as a function of eye movement condition, autobiographical memory period, and recall period.

ABM period and recall (s)	Eye movement		
	Bilateral	**Vertical**	**Central**
5–11 YEARS			
30	11.91 (2.89)	11.52 (3.55)	9.95 (4.64)
60	18.30 (3.53)	17.69 (5.41)	16.39 (8.87)
90	22.17 (6.29)	21.17 (6.56)	20.83 (10.60)
12–18 YEARS			
30	13.43 (2.50)	12.65 (3.46)	10.65 (3.58)
60	21.48 (4.88)	20.08 (4.74)	17.65 (6.55)
90	27.56 (8.08)	25.73 (5.32)	23.09 (9.46)

Table 3 | Mean (SD) number of teacher memories recalled as a function of eye movement condition, autobiographical memory period, and recall period.

ABM period and recall period (s)	Eye movement		
	Bilateral	**Vertical**	**Central**
5–11 YEARS			
30	5.26 (1.73)	5.39 (2.77)	6.17 (3.47)
60	7.17 (2.46)	7.43 (3.59)	9.00 (6.78)
90	8.26 (2.63)	8.47 (3.83)	10.47 (6.85)
12–18 YEARS			
30	6.47 (2.57)	7.08 (2.87)	6.26 (4.47)
60	10.56 (3.69)	11.13 (4.29)	10.70 (7.60)
90	13.73 (4.85)	13.91 (4.32)	13.70 (9.56)

12–18 was also significant, $t(69) = -4.19$, $p \leq 0.001$. Overall, this indicates that the difference in the number of memories recalled between time periods concerning friends becomes more significant over the recall interval. The three way interaction between time period, time interval, and eye movement was not significant, $F(4, 132) = 0.59$, $p = 0.67$. The main effect of eye movements was not significant. $F(2, 66) = 1.94$, $p = 0.15$.

SEMANTIC AUTOBIOGRAPHICAL MEMORY – TEACHERS

The cumulative number of teachers recalled can be found in **Table 3** below.

The main effect of autobiographical memory period was significant $F(1, 66) = 25.69$, $p \leq 0.001$, indicating more teacher memories recalled for the more recent time period (M for 5–11 = 7.51; M for 12–18 = 10.40). The interaction between autobiographical memory period and eye movements was not significant $F(2, 66) = 1.15$, $p = 0.32$. The main effect of recall period was significant, $F(2, 132) = 165.87$, $p \leq 0.001$, indicating a greater number of memories recalled over the longer (90 s) time period. The interaction between recall period and eye movements was not significant, $F(4, 132) = 0.50$, $p = 0.74$. The interaction between memory period and recall period was significant $F(2, 132) = 29.83$, $p \leq 0.001$. The interaction was assessed with simple main effects at each level of time interval. At the 30 s interval, the difference between 5–11 and 12–18 was significant, $t(69) = -2.43$, $p = 0.018$. At the 60 s interval, the difference between 5–11 and 12–18 was also significant, $t(69) = -4.85$, $p \leq 0.001$. At the 90 s interval, the difference between 5–11 and 12–18 was also significant, $t(69) = -5.78$, $p \leq 0.001$. Overall, this indicates that the difference in the number of memories recalled between time periods concerning teachers becomes more significant over the recall interval. The three way interaction between memory period, recall period and eye movement was not significant, $F(4, 132) = 0.23$, $p = 0.91$. The main effect of eye movements was not significant. $F(2, 66) = 0.27$, $p = 0.77$.

GENERAL SEMANTIC MEMORY

The cumulative number of semantic items recalled can be found in **Table 4** below.

Table 4 | Mean (SD) number of semantic memories recalled as a function of eye movement condition, semantic category, and recall period.

Semantic category and recall period (s)	Eye movement		
	Bilateral	**Vertical**	**Central**
VEGETABLES			
30	9.26 (2.70)	9.09 (3.17)	8.87 (2.83)
60	13.47 (4.71)	12.43 (3.53)	13.35 (4.10)
90	16.00 (4.76)	14.56 (4.25)	15.52 (5.08)
ANIMALS			
30	15.91 (5.45)	14.39 (3.49)	15.09 (2.90)
60	24.78 (6.34)	22.26 (4.23)	23.70 (5.57)
90	29.96 (6.45)	28.08 (5.12)	29.47 (6.80)

The main effect of semantic category was significant $F(1, 66) = 375.48$, $p \leq 0.001$. This indicates more items recalled for the category of animals (M for animals = 22.63; M for vegetables = 12.51). The interaction between semantic category and eye movements was not significant $F(2, 66) = 0.36$, $p = 0.70$. The main effect of recall period was significant, $F(2, 132) = 488.94$, $p \leq 0.001$, indicating a greater number of exemplars recalled over the longer (90 s) time period. The interaction between recall period and eye movements was not significant, $F(4, 132) = 0.57$, $p = 0.68$. The interaction of semantic category and recall period interval was significant, $F(2, 132) = 106.84$, $p \leq 0.001$. The interaction between semantic category and time interval was further assessed with simple main effects at each level of recall period. At the 30 s interval, the difference between vegetables and animals was significant, $t(69) = -12.72$, $p \leq 0.001$. At the 60 s interval, the difference between vegetables and animals was also significant, $t(69) = -18.51$, $p \leq 0.001$. At the 90 s interval, the difference between vegetables and animals was also significant, $t(69) = -18.93$, $p \leq 0.001$. Overall, this indicates that the difference in the number of memories recalled between semantic categories periods becomes more significant over the recall interval.

The three way interaction between semantic category, recall period and eye movements was not significant, $F(4, 132) = 0.24$, $p = 0.91$. The main effect of eye movement was not significant, $F(2, 66) = 0.90$, $p = 0.41$.

GENERAL SUMMARY

Bilateral saccades enhanced autobiographical memory fluency but only when this required the retrieval of episodic information. Bilateral eye movements did not influence fluency on the tests requiring the retrieval of personals semantic information or taxonomic semantic information.

DISCUSSION

The current experiment found a dissociation between episodic and semantic autobiographical memory as a function of bilateral saccadic eye movements. A dissociation was also found between episodic autobiographical memory and general semantic memory. In particular, saccadic bilateral eye movements improved fluency of memory retrieval but only for episodic memory.

These findings are congruent with the explanation offered by Christman et al. (2003) in which it is claimed that bilateral saccades influence only episodic memory. The rationale for this was rooted in research based on the HERA model (Habib et al., 2003) which states episodic memory is dependent upon the efficient interaction between the two cerebral hemispheres. Consequently, one way to explain the current findings is that increased/more efficient hemispheric interaction brought about by bilateral saccades enabled the more effective recovery of episodic (vs. semantic) memory traces.

An interesting point is that the autobiographical memory period did not interact with the eye movement manipulation; the effects were observed irrespective of whether the memories were more recent or more remote. Earlier work has demonstrated that bilateral saccades can enhance the recovery of earlier autobiographical memories, and hence lead to an earlier offset of infantile amnesia (Christman et al., 2006). However, that experiment did not specifically compare different time periods. Furthermore, in the current experiment, although lifetime periods were specified, the experimental instructions did not request specifically the retrieval of earliest memories.

The interaction between eye movements and recall period did not reach statistical significance therefore, eye movements enabled the more fluent recovery of episodic information over the three recall periods (30, 60, and 90 s). However, although not significant, the interaction between recall period and eye movements started to approach such a value. Inspection of the means in **Table 1** appears to show greater differences between the eye movement conditions for the longest recall period of 90 s. This may suggest that the effects of eye movements on recall could be greater when extended searches are required. This conjecture obviously requires further work.

The explanation for the effects of eye movements, as noted earlier, is based upon the original one formulated by Christman and colleagues (e.g., Christman et al., 2003; Christman and Propper, 2010). In some sense, direct evidence for the influence of bilateral saccades on hemispheric interaction has yet to found. Some suggestive evidence has shown that bilateral saccades alter prefrontal EEG coherence in the Gamma frequency range (Propper et al., 2007). However, this experiment did not measure memory performance. In another study, that did measure memory, no evidence was found for a specific effect of bilateral saccades on hemispheric interaction even though memory was improved following bilateral eye movements (Samara et al., 2011).

An alternative account of the results is that eye movements may enhance anterior-posterior interactions (Parker and Dagnall, 2007). Such interactions are of particular importance for episodic memory retrieval (Simons and Spiers, 2003; Summerfield and Mangels, 2005), and have been taken to indicate the functional coupling of frontal executive processes with more posterior regions, where the memory trace is stored. More recently, Lyle and colleagues (e.g., Lyle and Martin, 2010; Lyle and Orsborn, 2011) hypothesize that saccadic eye movements may result in the activation of neural regions that are involved in the allocation of attention and top-down control mechanisms. Their explanation is based on the findings that show making saccades activates a network of neural regions that include the frontal eye fields and more posterior regions such as the intraparietal sulcus. The latter region has been shown to play a role in episodic memory (Skinner and Fernandes, 2007; Cabeza, 2008; Ciaramelli et al., 2008) and the idea is that saccadic eye movements serve to pre-activate this region and thus enhance its functional contributions to task performance. These anterior-posterior interactions can occur *within* each hemisphere and thus in some respects, does not require interhemispheric interaction in order to support memory. Evidence for this has come from behavioral studies in which bilateral saccades were found to increase the accuracy of detection in a letter matching task, but only for within hemisphere trials (Lyle and Martin, 2010). Support has also been found from findings that demonstrate saccades do not increase effects that depends on interhemispheric interaction such as bilateral gain effects in face recognition (Lyle and Orsborn, 2011). More direct evidence for the role of saccade execution in attention control comes from Edlin and Lyle (2013), who found that bilateral saccades enhanced performance in the Attentional Network Task (ANT). In this task, subjects are required to detect and indicate the direction in which a target arrow is pointing. The position of the arrow can be cued (vs. uncued) and can be flanked by arrows that are either congruent (vs. incongruent) with the targets direction. The ANT allows for an assessment of various forms of attentional operations including, alerting, orienting, and control (executive functioning). Their results indicated an effect of bilateral saccades on the executive control component.

In relation to the current findings, the notion of enhanced top-down control and anterior-posterior interactions would make sense from some theoretical models of autobiographical memory and neuroimaging findings. For example, Conway (2001, 2005) and Conway and Pleydell-Pearce (2000), conceptualize autobiographical memory as organized in a hierarchical manner with distinct but interacting levels of representations. At the highest level are lifetime periods which represent personal information covering broad spans of time. Examples could include “my life whilst at secondary school” or “my relationship with my partner.” Also included at this level is general knowledge of other persons (e.g., teachers and friends), actions and plans. This type of representation is devoid of event-specific information and can be considered more schematic or semantic in nature. The next level of representation refers to general events and refers to both repeated and extended events such as "my holiday in the Lake District." The time span for this level typically ranges from days to weeks. The most detailed level of representation is that of event-specific knowledge. This level contains information of specific experiences rooted in perception and linked to occurrences in time and place. Consequently, this level of representation is episodic in nature.

Recalling autobiographical information can take the form of accessing event-specific information via higher levels of representation via control processes. Thus, recalling semantic information takes place prior to accessing the episodic details of an event. In relation to neural activations, this translates into initial processing in anterior regions, such as the left prefrontal cortex (representing cue specification and elaboration) followed by activations in posterior regions on the right or bilaterally (as the memory is recovered). This idea has received empirical support from studies of both slow cortical EEG potentials (e.g., Conway et al, 2001) and fMRI research (e.g., Botzung et al., 2008) (see also Cabeza and St Jacques, 2007 for a review of imaging studies implicating anterior-posterior interactions). More generally, a role for executive functioning in retrieving autobiographical memories has been implicated across a range of work, especially when access is required to event or episode-specific information. This is demonstrated by reduced executive control being associated with the increased likelihood of recalling more general (less specific) memories (e.g., Dalgleish et al., 2007), fewer episodic details (e.g., Matuszewski et al., 2009), and a reduced sense of autonoetic awareness and reliving of the episode (e.g., Piolino et al., 2007).

In terms of the present findings, this would suggest that bilateral saccades facilitate access to lower levels of representation. Higher levels of representation (semantic memory) are not influenced by such eye movements. Consequently, an alternative explanation of the current findings is that the dissociation between the retrieval of event-specific (episodic) and more general semantic memory arises as a direct result of top-down executive mechanisms as specified by Edlin and Lyle (2013). This would presumably take the form of saccades enhancing executive functioning, preactivating posterior regions involved in episodic memory, and enabling a more efficient and extended search through the store of event-specific information.

The idea of the importance of anterior-posterior interaction in autobiographical retrieval (and eye movement effects) does not have to be seen as excluding hemispheric interactions. Cooperation between the hemispheres would appear to be important in recalling episodic autobiographical memory as indicated by imaging studies that find bilateral activations during recall (e.g., Markowitsch et al., 2000; Greenberg et al., 2005; Vandekerckhove et al., 2005; Viard et al., 2010; Söderlund et al., 2012). Conceivably therefore, both accounts of eye movement effects could provide a plausible account of the findings; the experiment itself was not designed to assess one compared to the other.

Some of the findings of the present experiment deserve further comments; in particular, as related to recall period (and the duration of eye movement effects) and vertical saccades. Although the effect of eye movements did not interact with recall period (or ABM period), consideration of the means for episodic memory, appear to show slightly larger differences for the later segment of the recall period. Indeed the interaction started to approach significance for these variables. Whilst it is difficult to make too much of this finding, it is interesting to speculate why this might occur in relation to; (i) the potential time-limited effect of eye movements, and (ii) the means by which eye movements influence episodic retrieval. Pertaining to the former, the influence of eye movements must have at least spanned the recall period and thus show effects lasting over 180 s. This would certainly be within the potential time-window for eye movement effects as noted in the introduction. Pertaining to the latter, if it is assumed that recall in autobiographical memory may often start with the recall of the most accessible information or spontaneously retrieved memories (e.g., Conway and Pleydell-Pearce, 2000), then eye movements do not appear to influence this early stage of retrieval. Instead, the largest influence could arise at a later stage in the recall process that represents more effortful or attentionally demanding processing. This form of retrieval requires a generative recall process likely involving frontal/executive processes (Smith et al., 2010). This finding, if robust, fits in well with the hypothesis that saccade execution influences effortful recall by the implementation of top-down control processes.

It was noted in the introduction that only bilateral saccades were expected to enhance memory as this is in accordance with the idea that such influences are underpinned by hemispheric interaction. However, some research has found vertical saccades to enhance episodic memory (e.g., Lyle et al., 2008a), whereas other research has not found this to be the case (e.g., Christman et al., 2003; Parker et al., 2008; Brunyé et al., 2009). The current research found that vertical eye movements produced effects that were in-between those of bilateral and the central fixation condition (see **Table 1**). In the original paper by Christman et al. (2003), vertical eye movements (and other forms of eye movements) produced effects that were in-between the bilateral and no-eye movement condition. It is unclear why such differences have been observed in previous work and suggests additional research is required.

There are some limitations to the current experiment that need to be considered. One relates to the study of autobiographical memory more generally. In particular, because the events sampled come from the participants own life, then it is difficult to independently assess the veracity of the information recalled. One potential means of overcoming this would be to use diary based methods (e.g., Christman et al., 2003), but this would typically limit the time period over which memory could be studied. In relation to much autobiographical memory work that uses fluency measure or other forms of retrospective accounts (e.g., cue-word techniques), then it needs to be ensured that recalls are not contaminated by false memories, misleading reports (perhaps because of personal details), or retrieval from incorrect time periods. In the current experiment, the participants were fully assured that all responses would be treated anonymously and that they were not pressured into producing any personal details that they felt uncomfortable revealing. It would also seem unlikely that the results obtained here are due to any unintentional production of false memories or some form of source monitoring error by identifying memories from incorrect time periods. This is argued because previous laboratory-based work on bilateral eye movements has shown them to increase true and decrease false memory, even in situations that require a high degree of source monitoring to reduce such errors (e.g., Parker et al., 2008; Lyle and Jacobs, 2010). Consequently, to contend that the effects that were found here were the result of false autobiographical recall or faulty source monitoring would be incongruent with past research.

Another potential limitation is that handedness was not assessed. In some experiments, handedness and eye movements have been shown to interact such that greater eye movement effects are found with individuals who are strongly right-handed (Lyle et al., 2008b; Brunyé et al., 2009). However, other work has shown eye movements to enhance memory irrespective of handedness (Lyle and Jacobs, 2010). More recently, consistency of handedness (regardless of direction) has been shown to be of importance (Lyle et al., 2012). As a result, the precise relationship between handedness and eye movements is something that has yet to be explored further, both in general terms and in more specific contexts like the experiment reported here. In spite of this, the fact that an effect of bilateral eye movement was found suggests that even if stronger effects can be found with right-handed participants, they are not negligible in groups that likely contain a broader range of handedness types. In addition, given that most common behavioral profile is that of right-handedness (Peters and Murphy, 1992), then it could be safe to assume that most of the participants in the current experiment were right-handed.

Handedness itself has an influence on cognitive processes as outlined in the introduction; for example enhancing episodic memory. As some research has indicated similar effects of both eye movements and handedness (see Christman and Propper, 2010 for a review), then one might expect similar outcomes to the present results when comparing inconsistent with consistently strong right-handers. Although this research has not been undertaken, one recent report showed that general semantic memory fluency (number of exemplars produced) was not influenced by handedness (Sontam et al., 2009), and is thus consistent with the findings here. However, they did find a difference in which mixed-handed subjects demonstrated greater semantic switching (shifting from one taxonomic category to another) which was taken to indicate more widespread activation within semantic networks.

In summary, the present results found a dissociation between the episodic and semantic components of autobiographical memory as a function of eye movements. Subsequent research may consider investigating the influence of eye movements on other tasks of autobiographical memory and examining in a more direct manner, the influence of hemispheric interaction on both episodic and semantic autobiographical retrieval.

REFERENCES

Babiloni, C., Babiloni, F., Carducci, F., Cappa, S., Cincotti, F., Del Percio, C., et al. (2004). Human cortical EEG rhythms during long-term episodic memory task. A high-resolution EEG study of the HERA model. *Neuroimage* 21, 1576–1584. doi:10.1016/j.neuroimage.2003.11.023

Babiloni, C., Vecchio, F., Cappa, S., Pasqualetti, P., Rossi, S., Miniussi, C., et al. (2006). Functional frontoparietal connectivity during encoding and retrieval processes follows the HERA model: a high-resolution study. *Brain Res. Bull.* 68, 203–212. doi:10.1016/j.brainresbull.2005.04.019

Blum, S., and Yonelinas, A. P. (2001). Transfer across modality in perceptual implicit memory. *Psychon. Bull. Rev.* 8, 147–154.

Botzung, A., Denkova, E., Ciuciu, P., Scheiber, C., and Manning, L. (2008). The neural bases of the constructive nature of autobiographical memories studied with a self-paced fMRI design. *Memory* 16, 351–365. doi:10.1080/09658210801931222

Brunyé, T. T., Mahoney, C. R., Augustyn, J. S., and Taylor, H. A. (2009). Horizontal saccadic eye movements enhance the retrieval of landmark shape and location information. *Brain Cogn.* 70, 279–288. doi:10.1016/j.bandc.2009.03.003

Cabeza, R. (2008). Role of parietal regions in episodic memory retrieval: the dual attentional processes hypothesis. *Neuropsychologia* 46, 1813–1827. doi:10.1016/j.neuropsychologia.2008.03.019

Cabeza, R., and St Jacques, P. (2007). Functional neuroimaging of autobiographical memory. *Trends Cogn. Sci.* 11, 219–227. doi:10.1016/j.tics.2007.02.005

Christman, S. (1993). Handedness in musicians: bimanual constraints upon performance. *Brain Cogn.* 22, 266–272.

Christman, S. (1995). "Independence versus integration of right and left hemisphere processing: effects of handedness," in *Hemispheric Communication: Mechanisms and Models*, ed. F. L. Kitterle (Hillsdale, NJ: Erlbaum), 231–253.

Christman, S. D., and Butler, M. (2011). Mixed-handedness advantages in episodic memory obtained under conditions of intentional learning extend to incidental learning. *Brain Cogn.* 77, 17–22. doi:10.1016/j.bandc.2011.07.003

Christman, S. D., Garvey, K. J., Propper, R. E., and Phaneuf, K. A. (2003). Bilateral eye movements enhance the retrieval of episodic memories. *Neuropsychology* 17, 221–229. doi:10.1037/0894-4105.17.2.221

Christman, S. D., and Propper, R. E. (2010). "Episodic memory and hemispheric interaction: handedness and eye movements," in *Current Issues in Applied Memory Research*, eds G. M. Davies, and D. B. Wright (Hove: Psychology Press), 185–205.

Christman, S. D., Propper, R. E., and Brown, T. J. (2006). Increased interhemispheric interaction is associated with earlier offset of childhood amnesia. *Neuropsychology* 20, 336–345. doi:10.1037/0894-4105.20.3.336

Christman, S. D., Propper, R. E., and Dion, A. (2004). Increased interhemispheric interaction is associated with deceased false memories in a verbal converging semantic associates paradigm. *Brain Cogn.* 56, 313–319.

Chu, O., Abeare, C. A., and Bondy, M. A. (2012). Inconsistent vs consistent right-handers' performance on an episodic memory task: evidence from the California Verbal learning Test. *Laterality* 17, 306–317. doi:10.1080/1357650X.2011.568490

Ciaramelli, E., Grady, C. L., and Moscovitch, M. (2008). Top-down and bottom-up attention to memory: a hypothesis (AtoM) on the role of the posterior parietal cortex in memory retrieval. *Neuropsychologia* 46, 1828–1851. doi:10.1016/j.neuropsychologia.2008.03.022

Clarke, J. M., and Zaidel, E. (1994). Anatomical-behavioral relationships: corpus callosum morphometry and hemispheric specialization. *Behav. Brain Res.* 64, 185–202. doi:10.1016/0166-4328(94)90131-7

Conway, M. A. (1990). *Autobiographical Memory: An Introduction.* Buckingham: Open University Press.

Conway, M. A. (2001). Sensory-perceptual episodic memory and its context: autobiographical memory. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 356, 1375–1384. doi:10.1098/rstb.2001.0940

Conway, M. A. (2005). Memory & the self. *J. Mem. Lang.* 53, 594–628.

Conway, M. A., and Pleydell-Pearce, C. W. (2000). The construction of autobiographical memories in the self-memory system. *Psychol. Rev.* 107, 261–288. doi:10.1037/0033-295X.107.2.261

Conway, M. A., Pleydell-Pearce, C. W., and Whitecross, S. E. (2001). The neuroanatomy of autobiographical memory: A slow cortical potential study of autobiographical memory retrieval. *J. Mem. Lang.* 45, 493–524. doi:10.1006/jmla.2001.2781

Coste, C., Agar, N., Petitfour, E., Quinette, P., Guillery-Girard, B., Azouvi, P., et al. (2011). Exploring the roles of the executive and short-term feature binding functions in the retrieval of retrograde autobiographical memories in severe traumatic brain injury. *Cortex* 47, 771–786. doi:10.1016/j.cortex.2010.07.004

Cronin-Golomb, A., Gabrieli, J. D. E., and Keane, M. M. (1996). Implicit & explicit memory retrieval within and across the disconnected cerebral hemispheres. *Neuropsychology* 10, 254–262.

Dalgleish, T., Williams, J. M., Golden, A. M., Perkins, N., Barrett, L. F., Barnard, P. J., et al. (2007). Reduced specificity of autobiographical memory and depression: the role of executive control. *J. Exp. Psychol. Gen.* 136, 23–42. doi:10.1037/0096-3445.136.1.23

Dean, H. L., Crowley, J. C., and Platt, M. L. (2004). Visual and saccade-related activity in macaque posterior cingulate cortex. *J. Neurophysiol.* 92, 3056–3068. doi:10.1152/jn.00691.2003

Denenberg, V. H., Kertesz, A., and Cowell, P. E. (1991). A factor analysis of the human's corpus callosum. *Brain Res.* 548, 126–132. doi:10.1016/0006-8993(91)91113-F

Dritschel, B. H., Williams, J. M. G., Baddeley, A. D., and Nimmo-Smith, I. (1992). Autobiographical fluency – a method for the study of personal memory. *Mem. Cognit.* 20, 133–140.

Düzel, E., Cabeza, R., Pictons, T. W., Yonelinas, A. P., Scheich, H., Heinze, H.-J., et al. (1999). Task-related and item-related brain processes of memory retrieval. *Proc. Natl. Acad. Sci. U.S.A.* 96, 1794–1799. doi:10.1073/pnas.96.4.1794

Edlin, J. M., and Lyle, K. B. (2013). The effect of repetitive saccade execution on the attention network test: enhancing executive function with a flick of the eyes. *Brain Cogn.* 81, 345–351. doi:10.1016/j.bandc.2012.12.006

Gagnon, G., Blanchet, S., Grondin, S., and Schneider, C. (2010). Paired-pulse transcranial magnetic stimulation over the dorsolateral prefrontal cortex interferes with episodic encoding and retrieval for both verbal and non-verbal materials. *Brain Res.* 1344, 148–158. doi:10.1016/j.brainres.2010.04.041

Geffen, G. M., Forrester, G. M., Jones, D. L., and Simpson, D. A. (1994). "Auditory verbal learning and memory in cases of callosal agenesis," in *Callosal Agenesis*, eds M. Lassonde and M. A. Jeeves (New York, NY: Plenum Press), 247–260.

Gilboa, A., Ramirez, J., Kohler, S., Westmacott, R., Black, S. E., and Moscovitch, M. (2005). Retrieval of autobiographical memory in Alzheimer's disease: relation to volumes of medial temporal lobe and other structures. *Hippocampus* 15, 535–550. doi:10.1002/hipo.20090

Greenberg, D. L., Rice, H. J., Cooper, J. J., Cabeza, R., Rubin, D. C., and LaBar, K. S. (2005). Co-activation of the amygdala, hippocampus and inferior frontal gyrus during autobiographical memory retrieval. *Neuropsychologia* 43, 659–674. doi:10.1016/j.neuropsychologia.2004.09.002

Greene, J. D., Hodges, J. R., and Baddeley, A. D. (1995). Autobiographical memory and executive function in early dementia of Alzheimer's type. *Neuropsychologia* 33, 1647–1670. doi:10.1016/0028-3932(95)00046-1

Habib, R., Gayraud, D., Oliva, A., Regis, J., Salamon, G., and Khalil, R. (1991). Effects of handedness and sex on the morphology of the corpus callosum: a study with brain magnetic resonance imaging. *Brain Cogn* 16, 41–61.

Habib, R., Nyberg, L., and Tulving, E. (2003). Hemispheric asymmetries of memory: the HERA model revisited. *Trends Cogn. Sci.* 7, 241–245. doi:10.1016/S1364-6613(03)00110-4

Jha, A. P., Kroll, N., Baynes, K., and Gazzaniga, M. S. (1997). Memory encoding following complete commissurotomy. *J. Cogn. Neurosci.* 9, 143–159. doi:10.1162/jocn.1997.9.1.143

Kastner, S., DeSimone, K., Konen, C. S., Szczepanski, S., Weiner, K. S., and Schneider, K. A. (2007). Topographic maps in human frontal cortex revealed in delayed saccade and spatial working memory tasks. *J. Neurophysiol.* 97, 3494–3507. doi:10.1152/jn.00010.2007

Kempe, V., Brooks, P. J., and Christman, S. D. (2009). Inconsistent handedness is linked to more successful foreign language vocabulary learning. *Psychon. Bull. Rev.* 16, 480–485. doi:10.3758/PBR.16.3.480

Kompus, K., Kalpouzos, G., and Westerhausen, R. (2011). The size of the anterior corpus callosum correlates with the strength of hemispheric encoding-retrieval asymmetry in the ventrolateral prefrontal cortex. *Brain Res.* 1419, 61–67. doi:10.1016/j.brainres.2011.08.052

Kopelman, M. D., Wilson, B. A., and Baddeley, A. D. (1989). The autobiographical memory interview: a new assessment of autobiographical and personal semantic memory in amnesic patients. *J. Clin. Exp. Neuropsychol.* 11, 724–744. doi:10.1080/01688638908400928

Levine, B. (2004). Autobiographical memory and the self in time: brain lesion effects, functional neuroanatomy, and lifespan development. *Brain Cogn.* 55, 54–68.

Levine, B., Svoboda, E., Hay, J. F., Winocur, G., and Moscovitch, M. (2002). Aging and autobiographical memory: dissociating episodic from semantic retrieval. *Psychol. Aging* 17, 677–689. doi:10.1037/0882-7974.17.4.677

Lyle, K. B., Hanaver-Torrez, S. D., Hackländer, R. P., and Edlin, J. M. (2012). Consistency of handedness regardless of direction predicts baseline memory accuracy and potential for memory enhancement. *J. Exp. Psychol. Learn. Mem. Cogn.* 38, 187–193. doi:10.1037/a0024831

Lyle, K. B., and Jacobs, N. (2010). Is saccade-induced retrieval enhancement a potential means of improving eyewitness evidence? *Memory* 18, 581–594. doi:10.1080/09658211.2010.493891

Lyle, K. B., Logan, J. M., and Roediger, H. L. (2008a). Eye movements enhance memory for individuals who are strongly right-handed and harm it for individuals who are not. *Psychon. Bull. Rev.* 15, 515–520.

Lyle, K. B., McCabe, D. P., and Roediger, H. L. (2008b). Handedness is related to memory via hemispheric interaction: evidence from paired associate recall and source memory tasks. *Neuropsychology* 22, 523–530. doi:10.1037/0894-4105.22.4.523

Lyle, K. B., and Martin, J. M. (2010). Bilateral saccades increase intrahemispheric processing but not interhemispheric interaction: implications for saccade-induced retrieval enhancement. *Brain Cogn.* 73, 128–134. doi:10.1016/j.bandc.2010.04.004

Lyle, K. B., and Orsborn, A. E. (2011). Inconsistent handedness and saccade execution benefit face memory without affecting interhemispheric interaction. *Memory* 19, 613–624. doi:10.1080/09658211.2011.595418

Manenti, R., Cotelli, M., and Miniussi, C. (2011). Successful physiological aging and episodic memory: a brain stimulation study. *Behav. Brain Res.* 216, 153–158. doi:10.1016/j.bbr.2010.07.027

Markowitsch, H. J., Theiel, A., Reinkemeier, M., Kessler, J., Koyuncu, A., and Heiss, W. D. (2000). Right amygdalar and temporofrontal activation during autobiographic, but not during fictitious memory retrieval. *Behav. Neurol.* 12, 181–190.

Matuszewski, V., Piolino, P., Belliard, S., de la Sayette, V., Laisney, M., Lalevee, C., et al. (2009). Patterns of autobiographical memory impairment according to disease severity in semantic dementia. *Cortex* 45, 456–472. doi:10.1016/j.cortex.2007.11.006

McDermott, K. B., Ojemann, J. G., Petersen, S. E., Ollinger, J. M., Snyder, A. Z., Akbudak, E., et al. (1999). Direct comparison of episodic encoding and retrieval of words: an event-related fMRI study. *Memory* 7, 661–678. doi:10.1080/096582199387797

Miller, M. B., Kingstone, A., and Gazzaniga, M. S. (2002). Hemispheric encoding asymmetry is more apparent than real. *J. Cogn. Neurosci.* 14, 702–708. doi:10.1162/08989290260138609

Murphy, K. J., Troyer, A. K., Levine, B., and Moscovitch, M. (2008). Episodic, but not semantic, autobiographical memory is reduced in amnestic mild cognitive impairment. *Neuropsychologia* 46, 3116–3123. doi:10.1016/j.neuropsychologia.2008.07.004

Nelson, D. L., Keelean, P. D., and Negrao, M. (1989). Word-fragment cuing: the lexical search hypothesis. *J. Exp. Psychol. Learn. Mem. Cogn.* 15, 388–397.

Niebauer, C. L., Aselage, J., and Schutte, C. (2002). Interhemispheric interaction and consciousness: degree of handedness predicts the intensity of a sensory illusion. *Laterality* 7, 85–96.

Nieuwenhuis, S., Elzinga, B. M., Ras, P., Berends, F., Duijs, P., Samara, Z., et al. (2013). Bilateral saccadic eye movements and tactile stimulation, but not auditory stimulation, enhance memory retrieval. *Brain Cogn.* 81, 52–56. doi:10.1016/j.bandc.2012.10.003

Nolde, S. F., Johnson, M. K., and Raye, C. L. (1998). The role of prefrontal cortex during tests of episodic memory. *Trends Cogn. Sci.* 2, 399–406. doi:10.1016/S1364-6613(98)01233-9

Nyberg, L., Cabeza, R., and Tulving, E. (1996). PET studies of encoding and retrieval: the HERA model. *Psychon. Bull. Rev.* 3, 135–148.

Parker, A., Buckley, S., and Dagnall, N. (2009). Reduced misinformation effects following saccadic bilateral eye movements. *Brain Cogn.* 69, 89–97. doi:10.1016/j.bandc.2008.05.009

Parker, A., and Dagnall, N. (2007). Effects of bilateral eye movements on gist based false recognition in the DRM paradigm. *Brain Cogn.* 63, 221–225.

Parker, A., and Dagnall, N. (2010). Effects of handedness and saccadic bilateral eye movements on components of autobiographical recollection. *Brain Cogn.* 73, 93–101. doi:10.1016/j.bandc.2010.03.005

Parker, A., Relph, S., and Dagnall, N. (2008). Effects of bilateral eye movements on the retrieval of item, associative and contextual information. *Neuropsychology* 22, 136–145. doi:10.1037/0894-4105.22.1.136

Pasqual-Leone, A., Valls-Solé, J., Wassermann, E. M., and Hallett, M. (1994). Responses to rapid-rate transcranial magnetic stimulation of the human motor cortex. *Brain* 117, 847–858. doi:10.1093/brain/117.4.847

Peters, M., and Murphy, K. (1992). Cluster analysis reveals at least three, and possibly five, distinct handedness groups. *Neuropsychologia* 30, 373–380. doi:10.1016/0028-3932(92)90110-8

Phelps, E. A., Hirst, W., and Gazzaniga, M. S. (1991). Deficits in recall following partial and complete commissurotomy. *Cereb. Cortex* 1, 492–498. doi:10.1093/cercor/1.6.492

Piolino, P., Desgranges, B., Benali, K., and Eustache, F. (2002). Episodic and semantic remote autobiographical memory in ageing. *Memory* 10, 239–257. doi:10.1080/09658210143000353

Piolino, P., Desgranges, B., Manning, L., North, P., Jokic, F., and Eustache, F. (2007). Autobiographical memory and the sense of recollection and executive functions after closed head injury. *Cortex* 43, 176–195. doi:10.1016/S0010-9452(08)70474-X

Propper, R. E., and Christman, S. D. (2004). Mixed-versus strong right-handedness is associated with biases towards "remember" versus "know" judgements in recognition memory: role of interhemispheric interaction. *Memory* 12, 707–714. doi:10.1080/09658210344000503

Propper, R. E., Christman, S. D., and Phaneuf, K. A. (2005). A mixed-handed advantage in episodic memory: a possible role of interhemispheric interaction. *Mem. Cognit.* 33, 751–757.

Propper, R. E., Pierce, J., Bellorado, N., Geisler, M. W., and Christman, S. D. (2007). Effect of bilateral eye movements on frontal interhemispheric gamma EEG coherence: implications for EMDR therapy. *J. Nerv. Ment. Dis.* 195, 785–788. doi:10.1097/NMD.0b013e318142cf73

Richardson-Klavehn, A., and Gardiner, J. M. (1998). Depth of processing effects on priming is stem completion: test of the voluntary-contamination, conceptual-processing and lexical-processing hypotheses. *J. Exp. Psychol. Learn. Mem. Cogn.* 24, 593–609.

Roediger, H. L., Weldon, M. S., Stadler, M. L., and Riegler, G. L. (1992). Direct comparison of two implicit memory tests: word fragment completion and word stem completion. *J. Exp. Psychol. Learn. Mem. Cogn.* 18, 1251–1269.

Rossi, S., Miniussi, C., Pasqualetti, P., Babiloni, C., Rossini, P. M., and Cappa, S. F. (2004). Age-related functional changes of prefrontal cortex in long-term memory: a repetitive transcranial magnetic stimulation study. *J. Neurosci.* 24, 7939–7944. doi:10.1523/JNEUROSCI.0703-04.2004

Rossi, S., Pasqualetti, P., Zito, G., Vecchio, F., Cappa, S. F., Miniussi, C., et al. (2006). Prefrontal and parietal cortex in human episodic memory: an interference study by repetitive transcranial magnetic stimulation. *Eur. J. Neurosci.* 23, 793–800. doi:10.1111/j.1460-9568.2006.04600.x

Samara, Z., Elzinga, B. M., Slagter, H. A., and Nieuwenhuis, S. (2011). Do horizontal saccadic eye movements increase interhemispheric coherence? Investigation of a hypothesized neural mechanism underlying EMDR. *Front. Psychiatry* 2:4. doi:10.3389/fpsyt.2011.00004

Shobe, E. R., Ross, N. M., and Fleck, J. I. (2009). Influence of handedness and bilateral eye movements on creativity. *Brain Cogn.* 71, 204–214. doi:10.1016/j.bandc.2009.08.017

Simons, J. S., and Spiers, H. J. (2003). Prefrontal and medial temporal lobe interactions in long-term memory. *Nat. Rev. Neurosci.* 4, 637–648. doi:10.1038/nrn1178

Skinner, E. I., and Fernandes, M. A. (2007). Neural correlates of recollection and familiarity: a review of neuroimaging and patient data. *Neuropsychologia* 45, 2163–2179. doi:10.1016/j.neuropsychologia.2007.03.007

Smith, S. J., Souchay, C., and Conway, M. A. (2010). Overgeneral autobiographical memory in Parkinson's disease. *Cortex* 46, 787–793. doi:10.1016/j.cortex.2009.08.006

Söderlund, H., Moscovitch, M., Kumar, N., Mandic, M., and Levine, B. (2012). As time goes by: hippocampal connectivity changes with remoteness of autobiographical memory retrieval. *Hippocampus* 22, 670–679. doi:10.1002/hipo.20927

Sontam, V., Christman, S. D., and Jasper, J. D. (2009). Individual differences in semantic switching flexibility: effects of handedness. *J. Int. Neuropsychol. Soc.* 15, 1023–1027. doi:10.1017/S1355617709990440

Summerfield, C., and Mangels, J. A. (2005). Functional coupling between frontal and parietal lobes during recognition memory. *Neuroreport* 16, 117–122. doi:10.1097/00001756-200502080-00008

Tulving, E. (2002). "Episodic memory and common sense: how far apart?" in *Episodic Memory: New Directions in Research*, eds A. Baddeley, M. Conway, and J. Aggleton (Oxford: Oxford University Press), 269–287.

Tulving, E., Kapur, S., Craik, F. I. M., Markowitsch, H. J., and Houle, S. (1994). Hemispheric encoding and retrieval asymmetry in episodic memory: positron emission tomography findings. *Proc. Natl. Acad. Sci. U.S.A.* 91, 2016–2020. doi:10.1073/pnas.91.6.2016

Unsworth, N., Spillers, G. J., and Brewer, G. A. (2012). The role of working memory capacity in autobiographical retrieval: individual differences in strategic search. *Memory* 20, 167–176. doi:10.1080/09658211.2011.651087

Vandekerckhove, M. M. P., Markowitsch, H. J., Mertens, M., and Woermann, F. G. (2005). Bi-hemispheric engagement in the retrieval of autobiographical memories. *Behav. Neurol.* 16, 203–210.

Viard, A., Lebreton, K., Chételat, G., Desgranges, B., Landeau, B., Young, A., et al. (2010). Patterns of hippocampal-neocortical connectivity in the retrieval of autobiographical memories across the entire life-span of aged adults. *Hippocampus* 20, 153–165. doi:10.1002/hipo.20601

Wagner, A. D., Poldrack, R. A., Eldridge, L. L., Desmond, J. E., Glover, G. H., and Gabrieli, J. D. (1998). Material-specific lateralization of prefrontal activation during episodic encoding and retrieval. *Neuroreport* 9, 3711–3717. doi:10.1097/00001756-199811160-00026

Witelson, S. (1985). The brain connection: the corpus callosum is larger in left-handers. *Science* 229, 655–668. doi:10.1126/science.4023705

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Memory for hand-use depends on consistency of handedness

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Individuals who do not consistently use the same hand to perform unimanual tasks (inconsistent-handed) outperform consistent right- and left-handed individuals on tests of episodic memory. We explored whether the inconsistent-hander (ICH) memory advantage extends to memory for unimanual hand use itself. Are ICHs better able to remember which hand they used to perform actions? Opposing predictions are possible, stemming from the finding that some regions of the corpus callosum are larger in ICHs, especially those that connect motor areas. One hypothesis is that greater callosally mediated interhemispheric interaction produces ICHs' superior retrieval of episodic memories, and this may extend to episodic memories for hand use. Alternatively, we also hypothesized that greater interhemispheric interaction could produce more bilateral activation in motor areas during the performance and retrieval of unimanual actions. This could interfere with ICHs' ability to remember which hand they used. To test these competing predictions in the current study, consistent- and inconsistent-handers performed unimanual actions, half of which required manipulating objects and half of which did not. Each action was performed four times in one of five conditions that differed in the ratio of left to right hand use: always left (4:0), usually left (3:1), equal (2:2), usually right (1:3), or always right (0:4). We compared consistent- and inconsistent-handers on recall of the left:right ratio for each action. ICHs remembered how they performed actions better than consistent-handers, regardless of ratio. These findings provide another example of superior episodic retrieval in ICHs. We discuss how greater interaction might benefit memory for hand use.

Keywords: handedness, interhemispheric interaction, self-performed tasks, enactment, episodic memory, action memory, individual differences

INTRODUCTION

Individuals differ in the consistency with which they use a single preferred hand to perform unimanual tasks. Some individuals are highly consistent while others are relatively inconsistent, making greater use of both hands. We refer to this interindividual variable as handedness consistency, although it might also be called manual lateralization. Of interest to memory researchers, degree of handedness consistency, as measured by self-report, predicts performance on tests of episodic memory (for review, see Prichard et al., 2013). On average, inconsistent individuals remember events more accurately and with greater subjective vividness and detail than do consistent individuals.

Why is handedness consistency related to memory? The dominant theory in the literature is based on two assumptions: (1) inconsistent-handers (ICHs) have greater interhemispheric interaction than consistent-handers (CHs), and (2) greater interhemispheric interaction enhances some types of memory retrieval (Christman and Propper, 2001). The first assumption is tenuously supported by consistency-based anatomical differences in the corpus callosum. The corpus callosum is the major pathway for communication between the left and right cerebral hemispheres and has sometimes been found to be larger in ICHs than CHs (Witelson, 1985; Habib et al., 1991; Cowell et al., 1993; Luders et al., 2010), but not always (Jäncke and Steinmetz, 2003; Welcome et al., 2009). Differences in measurement techniques and measurement of different subregions of the corpus callosum may have led to these discrepancies. Because the corpus callosum is a bundle of fibers that branch to different cortical regions, consistency-based differences may exist in some callosal regions, but not others (Nowicka and Tacikowski, 2011). For example, Luders et al., found differences only in the anterior and posterior midbody of the corpus callosum, which primarily connect the sensory-motor cortices (Hofer and Frahm, 2006).

Behavioral studies provide more definitive evidence that ICHs have greater interhemispheric interaction than CHs. Interhemispheric transfer time, measured as the difference in response times for information processed in the hemisphere opposite the response hand and information processed in the same hemisphere as the response hand, is shorter in ICHs than CHs (Cherbuin and Brinkman, 2006; Bernard et al., 2011). Furthermore, ICHs exhibit greater interhemispheric transfer of skill learning (Chase and Seidler, 2008). Finally, Lyle and Martin (2010) found that ICHs were more accurate than CHs at detecting matches between letters (e.g., *A* and *a*) that were briefly flashed to separate visual fields.

The second assumption of the interhemispheric interaction hypothesis has sometimes (see Christman and Propper, 2001) been grounded in the hemispheric encoding/retrieval asymmetry (HERA) model (Tulving et al., 1994), according to which episodic memory is left lateralized in frontal regions at encoding and right lateralized at retrieval. If this is the case, then increased interhemispheric interaction could improve episodic retrieval by enhancing the transfer of information from the left to the right hemisphere. It appears, however, that the HERA model may only hold for relatively simple episodic retrieval tasks that require primarily familiarity-based judgments. Extensive neuroimaging evidence shows that more complex tasks that require recall of specific episodic details produce frontal activation bilaterally during retrieval (see Nolde et al., 1998; Miller et al., 2002). From this perspective, greater interhemispheric interaction may improve retrieval by enhancing coordination of retrieval areas across the hemispheres (Lyle et al., 2008b), but this should apply only to more complex tasks. Findings have so far supported this prediction with consistency-based differences limited to tasks that require recall. These tasks have included free recall (e.g., Propper et al., 2005; Lyle et al., 2008a; Christman and Butler, 2011), cued recall (Parker and Dagnall, 2010), associative recognition (Lyle et al., 2008b), and recall of source information (Christman et al., 2004; Lyle et al., 2008b). Differences have not been found on tasks with a small or non-existent recall component, including old/new recognition (Propper and Christman, 2004; Lyle et al., 2008a), short-term digit span (Lyle et al., 2008b), and implicit word-fragment completion (Propper et al., 2005).

Despite abundant evidence for consistency-based differences in episodic memory, memory for hand use itself has never been examined. If individuals perform unimanual actions multiple times with different combinations of their left and right hands, does their ability to recall how often they used a particular hand for each task depend on their consistency in everyday life? The question is of interest for three reasons. First, it is currently unclear to what extent consistency-based differences in memory occur for non-verbal information, including motoric and frequency information. Most studies that have documented a memory advantage for ICHs have employed word stimuli. We count among these Lyle et al.'s (2008b) tests of source memory. Although the tests revealed that ICHs were more likely than CHs to remember non-verbal source information, subjects were remembering the source of words. The only example of an inconsistently handed memory advantage for strictly non-verbal stimuli is Lyle and Jacobs's (2010) finding that ICHs were less likely than CHs to falsely remember visual details from a slideshow depicting a complex event. Although suggestive, an inconsistently handed advantage occurred in only one of two studies Lyle and Jacobs conducted. The studies had somewhat different procedures and Lyle and Jacobs reasoned that the advantage occurred in the procedure that necessitated greater recall of episodic details. Nonetheless, we consider this single result only preliminary evidence for an inconsistently handed memory advantage for non-verbal stimuli. Note also that, when Lyle et al., tested ICHs and CHs on memory for faces in an old/new recognition procedure, they did not find an advantage for ICHs. The authors attributed this null effect to the fact that interhemispheric interaction plays little role in face recognition (Gazzaniga and Smylie, 1983), but we cannot rule out that it was due to the non-verbal nature of the stimuli. If ICHs' memory advantage does extend to non-verbal information, then we would expect it to occur on a test of memory for the ratio of left to right-hand usage because such a test clearly requires *specific* recall.

The second reason for our interest in memory for hand use is that the hemispheric basis of unimanual action has been found to differ between ICHs and CHs and, from this, one could predict an inconsistently handed memory *dis*advantage. When using the dominant hand, both CHs and ICHs activate the contralateral motor cortex, but ICHs show greater activation of the ipsilateral motor cortex than CHs (Dassonville et al., 1997; Bernard et al., 2011). Greater ipsilateral activation may be related to the increased thickness of the corpus callosum that connects motor regions in ICHs. Callosal connections appear to be involved in spreading activation from one hemisphere to the other (e.g., Kinsbourne, 2003; Bloom and Hynd, 2005). When ICHs execute unimanual actions, greater callosal connectivity may cause activity in the controlling motor cortex (contralateral to the hand in use) to spread to the ipsilateral cortex. It is possible that this would have negative consequences for memory for hand use. Retrieval of action memories is associated with reactivation of primary motor areas that were active while performing the actions (Nyberg et al., 2001). This reactivation during retrieval is thought to aid memory for actions themselves (Masumoto et al., 2006), producing superior memory for self-performed actions than for verbally encoded action phrases (for review, see Cohen, 1989) or observed actions (e.g., Hornstein and Mulligan, 2001). Presumably, reactivation may also help individuals remember which hand they used to perform actions, with activity in a given hemisphere providing evidence that the action was performed with the contralateral hand. However, CHs and ICHs may not benefit equally from reactivation. Conceivably, ICHs' greater bilateral activation during unimanual action could be mirrored in greater bilateral activation during retrieval, causing confusion about which hand was used. More strictly unilateral activation/reactivation among CHs could lead to greater precision in memory.

The third and final reason for our interest in memory for hand use is that the study of consistency-based differences in memory has rested on the critical assumption that people can accurately remember how they use their hands in everyday life. In this area of research, consistency has invariably been measured by self-report on hand preference inventories. On these inventories, subjects report the frequency with which they use one hand or the other to perform everyday unimanual tasks (e.g., brushing one's teeth). These are reports of past behavior and therefore constitute a type of memory judgment. These judgments are generally assumed to be accurate. In other words, individuals who report consistency (or inconsistency) are assumed to actually perform everyday tasks in a consistent (or inconsistent) manner. However, memory is fallible in many respects and remembering contextual information, as opposed to item information, can be especially challenging (Johnson et al., 1993). It may be that people can remember that they performed certain actions (item information) without remembering how they performed them (contextual information). Therefore, we sought to conduct an initial investigation of memory for hand use. Although hand preference inventories probe memory for actions performed outside the laboratory, we felt a reasonable first step was to test memory for actions performed in a controlled laboratory setting.

In sum, our goal was to determine the relationship between handedness consistency and memory for hand use. ICHs' putatively greater interhemispheric interaction could give them an advantage over CHs if it facilitates recall of episodic detail. Alternatively, greater interaction between motor areas, and possible bilateral reactivation of these regions during retrieval, could reduce ICHs' ability to determine which hand or hands they used[1]. Given the centrality of handedness inventories in this research area, we modeled our memory test after the structure of those inventories. Namely, we measured memory for left:right hand-use ratios for actions. In addition, we examined memory for actions performed with and without objects. Hand preference inventories primarily consist of questions about actions performed with objects, so these types of actions were of greatest interest to us. However, we were also interested for exploratory purposes in whether the presence of an object would affect memory for hand-use or moderate any consistency-based memory differences.

MATERIALS AND METHODS

SUBJECTS

Subjects were undergraduates aged 18–30 who received credit in psychology courses for participating and provided informed consent under protocols approved by the University of Louisville IRB. Using the handedness inventory described below, and following the method from previous studies (e.g., Lyle et al., 2008b, 2012; Edlin and Lyle, 2013), we classified subjects according to their inventory scores. Subjects were classified as CHs if the absolute value of their inventory score was 80 or greater ($n = 50$, M absolute score = 92.8, eight males) or as ICHs if the absolute value of their inventory score was <80 ($n = 35$, M absolute score = 57.6, nine males, one unknown). Although we categorized subjects by consistency instead of direction of handedness, our sample included seven subjects who could be classified as left-handed due to negative inventory scores. Of these, two were CHs (M score = −92.5, one male) and five were ICHs (M score = −59, two males, one unknown).

MATERIALS

We assessed degree of handedness consistency using a modified version of Oldfield's (1971) Edinburgh Handedness Inventory. The inventory queries hand preferences for 10 activities (writing, drawing, using a spoon, opening jars, using a toothbrush, throwing, combing hair, using scissors, using a knife without a fork, and striking a match). For each activity, the response options (and corresponding point values) are Always Right (+10), Usually Right (+5), No Preference (0), Usually Left (−5), and Always Left (−10). Inventory scores range from −100 (consistently left-handed) to +100 (consistently right-handed) in 5-point increments.

For the hand-use task, we selected 20 actions (see **Table 1**), half of which required manipulating objects (e.g., roll the dice) and half of which did not (e.g., snap your fingers). The necessary objects were provided to subjects in a container at the beginning of the experiment. Actions were performed at one of five possible left:right hand-use ratios: always left (4:0), usually left (3:1), equal (2:2), usually right (1:3), or always right (0:4). Assignment of action to ratio was counterbalanced. For the performance/encoding phase of the procedure, we created four blocks of action commands. Each command instructed subjects to perform 1 of the 20 actions with a particular hand (e.g., "roll the dice with your left hand"). Thus, there were 20 commands per block. The commands were presented in pseudo-random order such that object actions and no-object actions were evenly distributed throughout each block. Commands were presented in a different order in each block. For actions assigned to the always-left and always-right ratios, the command was to use the same hand in every block. For actions assigned to the other three ratios, the commands varied in accordance with the particular ratio. Among actions assigned to the same ratio, the sequence of left/right commands was different for each action. For the retrieval phase of the procedure, a new random ordering of the 20 actions (without a performance command) was created for each subject.

Table 1 | Actions performed during the hand-use task.

Without objects	With objects[a]
Blow a kiss	Bounce the ball (small rubber ball)
Count to five	Drop a coin in the box (small box with slot and four pennies)
Cover your eye	Flip over the card (playing card)
Give a thumbs up	Move the mouse in a circle (mouse with cord removed)
Knock on the desk	Open the tupperware (small rubbermaid container)
Pat your head	Pull out your chair
Point to the monitor	Roll the die (six-sided die)
Snap your fingers	Take a piece of tape (roll of scotch tape)
Squeeze your hand	Take off the marker cap (dry erase marker)
Wave	Use the hole puncher (single hole punch and index card)

[a] *Subjects received the objects included in parenthesis.*

PROCEDURE

Subjects first completed the handedness inventory and were given the container of objects. Subjects then began the performance/encoding phase. Action commands appeared on a computer screen one at a time. For actions that required an object, subjects took the object out of the container, performed the action with the specified hand a single time, and replaced the object in the container. For no-object actions, subjects simply performed the action one time. Subjects were instructed to perform each action four times. Left:right hand-use ratio varied between actions such that each subject performed some actions in all five of the ratios. After each action, subjects rated the action on how difficult it was to perform the action with the specified hand and how natural it felt to do so. Ratings were made on a Likert scale ranging from 1 (*difficult/unnatural*) to 9 (*easy/natural*). Performance and ratings were self-paced. Subjects performed all 20 actions in each of 4 blocks. After the fourth and final block, there was a surprise memory

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[1] These two possibilities are of primary interest to the authors, but other predictions are certainly possible. For example, one might have expected CHs to have superior memory relative to ICHs for actions performed with the left hand due to the greater distinctiveness of left-hand usage for the former group than the latter (remembering that the vast majority of our subjects were right-hand dominant).

test. Each action was presented on the screen and subjects were instructed to select the hand-use ratio they remembered using to perform the task by pressing a number one through five that corresponded to always left, usually left, equal, usually right, or always right. Subjects were required to choose a ratio for each action.

RESULTS

RECALL

We submitted proportion of correct responses on the hand-use memory test to a 2 (consistency: CH or ICH) × 5 (ratio: always left, usually left, equal, usually right, or always right) × 2 (action type: object or no object) mixed-factorial ANOVA with consistency as a between-subjects factor and ratio and action type as within-subjects factors.

Addressing our primary research question, there was a main effect of consistency with ICHs ($M = 0.57$) producing more correct responses than CHs ($M = 0.47$), $F(1, 83) = 4.38$, $p = 0.039$, $\eta_p^2 = 0.05$. ICHs remembered all ratios numerically better than did CHs, as shown in **Figure 1** and as reflected in the non-significant consistency X ratio interaction, $F(4, 80) = 0.232$, $p = 0.920$, $\eta_p^2 = 0.011$. The consistency X action type interaction was also non-significant, $F(1, 83) = 1.41$, $p = 0.239$, $\eta_p^2 = 0.017$, indicating that the inconsistently handed advantage occurred regardless of whether actions were performed with or without objects.

There was also a main effect of ratio, $F(4, 80) = 12.72$, $p < 0.001$, $\eta_p^2 = 0.389$, indicating that some hand-use behaviors were better remembered than others (see **Figure 2**). Most strikingly, proportion correct for the always-right ratio ($M = 0.68$) was significantly higher than for all other ratios, smallest $t(84) = 2.97$, $p = 0.004$. Also, proportion correct was higher for the equal ratio ($M = 0.56$) than for the usually left ($M = 0.39$) or usually right ($M = 0.47$) ratios, smallest $t(84) = 2.34$, $p = 0.022$. In addition, proportion correct for usually right was higher than for usually left, $t(84) = 2.16$, $p = 0.033$, and always left ($M = 0.49$) was higher than usually left, $t(84) = 2.20$, $p = 0.030$. We examined the distribution of incorrect responses, which is shown in **Figure 3**. Three

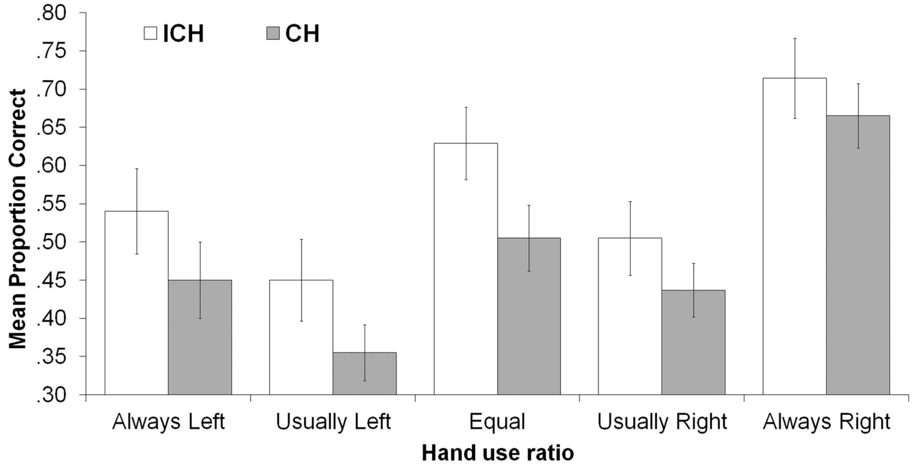

FIGURE 1 | Mean proportion correct as a function of hand-use ratio and consistency. Error bars indicate ±1 SEM.

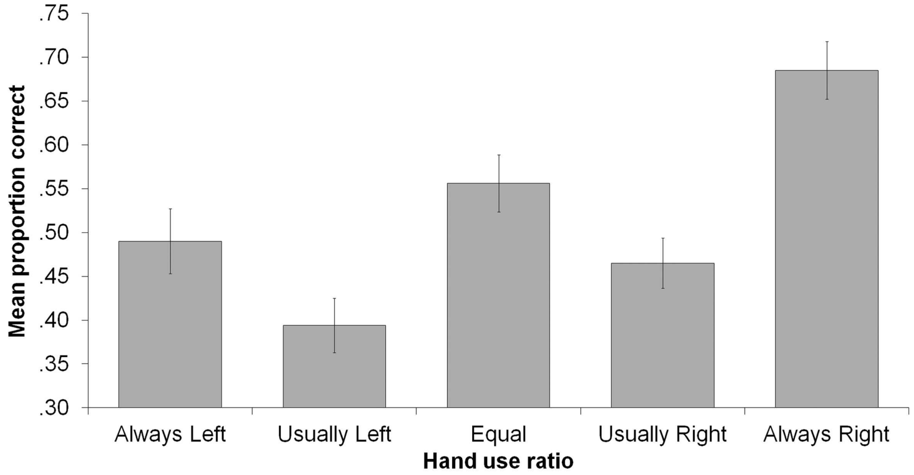

FIGURE 2 | Mean proportion correct as a function of hand-use ratio. Error bars indicate ±1 SEM.

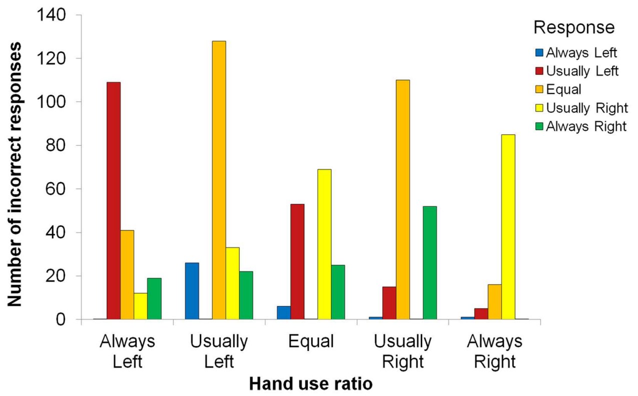

FIGURE 3 | Distribution of incorrect responses as a function of hand-use ratio.

patterns are evident. First, when the correct ratio was unequal, incorrect responses were usually shifted to a less extreme (versus more extreme) ratio than the actual one. Second, when the correct ratio was equal, incorrect responses tended to be shifted to the usually left or usually right ratio (rather than to one of the always ratios). Third, there was a slight tendency to respond with ratios in which there was more right-hand usage (rather than with ratios in which there was more left-hand usage); this can be seen most clearly in the equal ratio condition. None of these patterns suggest a strong response bias that could account for any of the significant between-ratio accuracy differences.

The ratio X action type interaction approached significance, $F(4, 80) = 2.32$, $p = 0.058$, $\eta_p^2 = 0.027$, but the trend was not readily interpretable. Briefly, proportion correct with and without objects was very similar and statistically indistinguishable for all ratios except usually right, for which object actions ($M = 0.55$) were remembered better than no-object actions ($M = 0.40$), $t(84) = 2.63$, $p = 0.01$.

RATINGS

Because difficulty and naturalness ratings were highly correlated, $r(85) = 0.53$, $p < 0.001$, we combined the two ratings into a composite fluency rating. We submitted ratings to a 2 (hand: left or right) × 2 (action type: object or no object) × 2 (consistency: CH or ICH) mixed-factorial ANOVA with hand and action type as within-subjects factors and consistency as a between-subjects factor.

The main effect of consistency was not significant, $F(1, 83) = 1.08$, $p = 0.302$, $\eta_p^2 = 0.013$, and neither were the interactions between consistency and hand or action type, $Fs < 1$, suggesting that the inconsistently handed memory advantage described above was not due to greater fluency when performing the actions.

There were significant main effects of hand, $F(1, 83) = 121.24$, $p < 0.001$, $\eta_p^2 = 0.594$, and action type, $F(1, 83) = 129.028$, $p < 0.001$, $\eta_p^2 = 0.609$, but these were qualified by a significant interaction between the two factors, $F(1, 83) = 68.479$, $p < 0.001$, $\eta^2 = 0.452$. Overall, subjects felt more fluent when performing right-hand actions ($M = 8.7$) than left-hand actions ($M = 7.5$), and when performing actions without objects (8.4) than with them (7.9). However, for right-hand actions, the fluency difference between actions performed without an object ($M = 8.8$) versus with one ($M = 8.7$) was very small, albeit significant, $t(84) = 4.10$, $p < 0.001$. For left-hand actions, the difference between actions performed without an object ($M = 7.9$) versus with one ($M = 7.2$) was markedly larger, $t(84) = 10.85$, $p < 0.001$.

DISCUSSION

The primary goal of this study was to compare the ability of ICHs and CHs to remember how they used their hands. Recent studies have found that ICHs have superior episodic memory but have not revealed whether this advantage extends to non-verbal stimuli or to memory for hand use, in particular. Empirically, many studies have shown an inconsistently handed advantage for verbal stimuli (e.g., Propper et al., 2005; Lyle et al., 2008a; Christman and Butler, 2011), but, to our knowledge, only one has done the same for non-verbal stimuli (Lyle and Jacobs, 2010). Given that ICHs differ from CHs in language lateralization (Knecht et al., 2000) and that ICHs have more diffuse semantic networks (Sontam and Christman, 2012), it was conceivable that these factors resulted in a memory advantage specifically for verbal stimuli. Theoretically, ICHs' putatively greater interhemispheric interaction (Christman and Propper, 2001; Lyle et al., 2008b) fostered opposing predictions about memory for hand use. Greater interaction could benefit memory by increasing recall of episodic details or harm it by producing bilateral reactivation in motor cortex during retrieval of unimanual actions. Our results resolved these empirical and theoretical uncertainties by clearly showing that ICHs performed better than CHs on our test of memory for hand-use ratio. This finding supports the conclusion that the inconsistently handed memory advantage does extend to non-verbal events, including self-performed actions.

Although we found a consistency-based difference in memory for hand use, elucidating the cause of this difference requires additional research. The results of our ratings data argue against the possibility that the memory difference was due to differences between ICHs and CHs in hand-use fluency, because the groups provided similar fluency ratings. Following, we consider three other possible explanations for ICHs' superior ability to remember which hand they used to perform actions. One is that, while reactivation of motor cortex at retrieval can potentially be used by either CHs or ICHs to determine which hand or hands were used at performance/encoding, ICHs are more skilled at interpreting this reactivation. If ICHs routinely experience bilateral activation during performance (Dassonville et al., 1997) and corresponding bilateral reactivation during retrieval (Nyberg et al., 2001), they may have adapted some means of differentiating between contralateral activation due to hand-use and ipsilateral activation from callosal "overflow." This could make ICHs more sophisticated decision makers than CHs when recalling which hand or hands they used to perform an action during instances of bilateral motor cortex reactivation.

Alternatively, individuals may use motor cortex reactivation only to determine that an action was performed versus not, and not to determine exactly which hand or hands were used to perform the action. Prior studies showing a memory advantage for performed actions compared to actions encoded using other methods (e.g., reading action phrases; see Cohen, 1989) have focused on remembering the presence or absence of an action and not specific details of the action. If specific hand-use information is not gleaned from motor cortex reactivation, then correctly remembering hand use would presumably rely on recollecting specific episodic details encoded during the act of performance (e.g., visual details, cognitive operations). If this explanation is correct, we could attribute the superior performance of ICHs on this task to the already established fact that ICHs are superior to CHs when recalling episodic details.

A third possible explanation for ICHs' superior memory for hand-use assumes, like our first explanation, that motor cortex reactivation at retrieval can serve as a useful source of information about which hand or hands were used, but that ICHs are less reliant on it than CHs. ICHs' hand-use memories may be based on both motor cortex reactivation and, as proposed in our second explanation, recall of additional episodic details. In contrast, CHs may rely largely on motor cortex reactivation, which may be insufficient to remember specific hand-use ratios. Propper and Christman (2004) found that ICHs' memories are more likely than CHs' to be accompanied by a rich recollective experience (indexed by "Remember" responses), whereas CHs' memories are more likely than ICHs' to be accompanied only by a non-specific sense of familiarity (indexed by "Know" responses). In the context of remembering hand use, CHs' reliance on motor cortex reactivation may give rise to a similar sense of familiarity while ICHs' use of additional episodic details may produce a sense of recollection.

Consideration of these possibilities raises the important lingering question of exactly how ICHs' putatively greater interhemispheric interaction might cause them to remember the episodic past more accurately and in greater detail. One idea not yet put forth in the literature is that ICHs' threshold for recruiting both hemispheres, versus only one, during episodic memory tests may be lower than CHs'. As mentioned in the introduction, complex memory tasks produce bilateral frontal activation (see Nolde et al., 1998; Miller et al., 2002) and greater connectivity between the hemispheres via the corpus callosum has been proposed as an explanation for ICHs' superior memory performance on these tasks. However, recruitment of both hemispheres to perform a task comes at a cost, which is dependent on interhemispheric transfer times. Banich (1998) proposed that simple tasks with low attentional demands are more efficiently processed by a single hemisphere specialized for that task. As task complexity increases, processing load overcomes the cost of transferring information across the corpus callosum. The threshold at which it is more efficient to recruit both hemispheres than rely on a single specialized hemisphere would theoretically be lower for individuals who have faster interhemispheric transfer times, including ICHs (Cherbuin and Brinkman, 2006; Bernard et al., 2011). Therefore, in addition to ICHs having an advantage on memory tasks that typically induce bilateral processing in all individuals (ICHs and CHs alike), ICHs may also be more likely to recruit additional hemispheric processing capability on tasks are not typically associated with bilateral activation (that is, not associated with bilateral activation in CHs, who constitute the majority of the population).

Our finding that ICHs were better at recalling hand-use ratios than CHs might be considered worrisome given that, in research examining the relationship between consistency and cognition (as well as consistency and personality; e.g., Christman et al., 2008; Lyle and Grillo, 2013) classification as ICHs or CHs is based on self-reported hand use. If ICHs are superior to CHs at recalling instances in which they used a combination of their left and right hands to perform tasks in everyday life, as they were better at remembering these instances in the laboratory, then a troubling possibility presents itself. ICHs and CHs could conceivably have similar real-world hand-use behaviors for the actions queried on hand preference inventories, including a similar rate of inconsistent behavior, but ICHs may be more likely to remember that they behaved inconsistently. If this were the case, it would undercut the idea that people who use their hands inconsistently have better episodic memory, and instead mean that people who have better episodic memory are more likely to remember instances of inconsistency when completing handedness questionnaires. Of course, recalling the exact left:right ratios for laboratory tasks performed only four times and after a retention interval of only a few minutes is different in many respects than recalling one's pattern of behavior for real-world actions performed innumerable times outside of the laboratory. Nonetheless, ICHs have been found to have more accurate and more detailed memories for events outside of the lab (Christman et al., 2003; Propper et al., 2005; Parker and Dagnall, 2010). Of course, it is also possible that people rely more on semantic memory instead of retrieving specific events when recalling patterns of behavior for real-world actions. There is some evidence that consistency-based differences do not extend to semantic memory (Propper et al., 2005), therefore ICHs and CHs may be equally accurate when reporting hand-use on handedness inventories. Future research is needed to explore the accuracy of responses on handedness questionnaires.

Finally, we consider our finding that, regardless of consistency, some hand-use ratios were remembered better than others. In particular, the always-right ratio was remembered significantly better than all others. In interpreting this finding, recall that our sample included only seven left-handed subjects (i.e., subjects with negative scores on the handedness inventory). The strong representation of right-handers was evident in the subjective fluency data where subjects rated left-hand actions as being more difficult and less natural than right-hand actions. Hence, most subjects in our sample, regardless of consistency, were right-hand dominant and we found that memory was best for actions that were always performed with the dominant hand. This may be due to the strength of motor cortex reactivation during recall. Prior studies have reported greater activation in the contralateral hemisphere when performing tasks with the dominant hand than with the non-dominant hand (Dassonville et al., 1997). If this pattern is mirrored in reactivation at retrieval, and individuals rely on reactivation to determine the hand used to perform an action, then stronger reactivation following right- than left-hand actions should have resulted in superior memory for always-right actions than always-left actions. This is the result we obtained. For actions performed with both hands, both motor cortices may have been reactivated, but there may have been stronger reactivation in the dominant (left) hemisphere than in the non-dominant (right) hemisphere, and the former may have masked the latter. This could lead to failures to remember that these actions were performed with both hands, reducing accuracy for the usually left, equal, and usually right ratios.

Also, right-handers have been found to exhibit bilateral activation in motor cortex when performing tasks with their left hand (e.g., Kim et al., 1993; Cramer et al., 1999). The unexpected ipsilateral (left hemisphere) activation may be related to the increased complexity of using the non-dominant hand (Haaland et al., 2004). If bilateral activation during performance is mirrored at retrieval, and individuals use patterns of reactivation to determine which hand was used, this could have contributed to poorer memory for always-left actions than always-right actions.

In summary, we compared the ability of ICHs and CHs to remember left:right hand-use ratios for actions and found that ICHs outperformed CHs. Both groups were significantly better at remembering the actions performed in the always-right ratio than all other ratios.

REFERENCES

Banich, M. T. (1998). The missing link: the role of interhemispheric interaction in attentional processing. *Brain Cogn.* 36, 128–157. doi:10.1006/brcg.1997.0950

Bernard, J. A., Taylor, S. F., and Seidler, R. D. (2011). Handedness, dexterity, and motor cortical representations. *J. Neurophysiol.* 105, 88–99. doi:10.1152/jn.00512.2010

Bloom, J. S., and Hynd, G. W. (2005). The role of the corpus callosum in interhemispheric transfer of information: excitation or inhibition? *Neuropsychol. Rev.* 15, 59–71. doi:10.1007/s11065-005-6252-y

Chase, C., and Seidler, R. (2008). Degree of handedness affects intermanual transfer of skill learning. *Exp. Brain Res.* 190, 317–328. doi:10.1007/s00221-008-1472-z

Cherbuin, N., and Brinkman, C. (2006). Hemispheric interactions are different in left-handed individuals. *Neuropsychology* 20, 700–707. doi:10.1037/0894-4105.20.6.700

Christman, S. D., and Butler, M. (2011). Mixed-handedness advantages in episodic memory obtained under conditions of intentional learning extend to incidental learning. *Brain Cogn.* 77, 17–22. doi:10.1016/j.bandc.2011.07.003

Christman, S. D., Garvey, K. J., Propper, R. E., and Phaneuf, K. A. (2003). Bilateral eye movements enhance the retrieval of episodic memories. *Neuropsychology* 17, 221–229. doi:10.1037/0894-4105.17.2.221

Christman, S. D., Henning, B., Geers, A. L., Propper, R. E., and Niebauer, C. L. (2008). Mixed-handed persons are more easily persuaded and are more gullible: interhemispheric interaction and belief updating. *Laterality* 13, 403–426. doi:10.1080/13576500802079646

Christman, S. D., and Propper, R. E. (2001). Superior episodic memory is associated with interhemispheric processing. *Neuropsychology* 15, 607–616. doi:10.1037/0894-4105.15.4.607

Christman, S. D., Propper, R. E., and Dion, A. (2004). Increased interhemispheric interaction is associated with decreased false memories in a verbal converging semantic associates paradigm. *Brain Cogn.* 56, 313–319. doi:10.1016/j.bandc.2004.08.005

Cohen, R. L. (1989). Memory for action events: the power of enactment. *Educ. Psychol. Rev.* 1, 57–80. doi:10.1007/BF01326550

Cowell, P. E., Kertesz, A., and Denenberg, V. H. (1993). Multiple dimensions of handedness and the human corpus callosum. *Neurology* 43, 2353–2357. doi:10.1212/WNL.43.11.2353

Cramer, S. C., Finklestein, S. P., Schaechter, J. D., Bush, G., and Rosen, B. R. (1999). Activation of distinct motor cortex regions during ipsilateral and contralateral finger movements. *J. Neurophysiol.* 81, 383–387.

Dassonville, P., Zhu, X. H., Ugurbil, K., Kim, S. G., and Ashe, J. (1997). Functional activation in motor cortex reflects the direction and the degree of handedness. *Proc. Natl. Acad. Sci. U.S.A.* 94, 14015–14018. doi:10.1073/pnas.94.25.14015

Edlin, J. M., and Lyle, K. B. (2013). The effect of repetitive saccade execution on the attention network test: enhancing executive function with a flick of the eyes. *Brain Cogn.* 81, 345–351. doi:10.1016/j.bandc.2012.12.006

Gazzaniga, M. S., and Smylie, C. S. (1983). Facial recognition and brain asymmetries – clues to underlying mechanisms. *Ann. Neurol.* 13, 536–540. doi:10.1002/ana.410130511

Haaland, K. Y., Elsinger, C. L., Mayer, A. R., Durgerian, S., and Rao, S. M. (2004). Motor sequence complexity and performing hand produce differential patterns of hemispheric lateralization. *J. Cogn. Neurosci.* 16, 621–636. doi:10.1162/089892904323057344

Habib, M., Gayraud, D., Oliva, A., Regis, J., Salamon, G., and Khalil, R. (1991). Effects of handedness and sex on the morphology of the corpus callosum – a study with brain magnetic resonance imaging. *Brain Cogn.* 16, 41–61. doi:10.1016/0278-2626(91)90084-L

Hofer, S., and Frahm, J. (2006). Topography of the human corpus callosum revisited – comprehensive fiber tractography using diffusion tensor magnetic resonance imaging. *Neuroimage* 32, 989–994. doi:10.1016/j.neuroimage.2006.05.044

Hornstein, S. L., and Mulligan, N. W. (2001). Memory of action events: the role of objects in memory of self- and other-performed tasks. *Am. J. Psychol.* 114, 199–217. doi:10.2307/1423515

Jäncke, L., and Steinmetz, H. (2003). "Brain size: a possible source of interindividual variability in corpus callosum morphology," in *The Parallel Brain: The Cognitive Neuroscience of the Corpus Callosum*, eds E. Zaidel, and M. Iacoboni (Cambridge, MA: MIT Press), 51–63.

Johnson, M. K., Hashtroudi, S., and Lindsay, D. S. (1993). Source monitoring. *Psychol. Bull.* 114, 3–28. doi:10.1037/0033-2909.114.1.3

Kim, S. G., Ashe, J., Hendrich, K., Ellermann, J. M., Merkle, H., Ugurbil, K., et al. (1993). Functional magnetic resonance imaging of motor cortex – hemispheric asymmetry and handedness. *Science* 261, 615–617. doi:10.1126/science.8342027

Kinsbourne, M. (2003). "The corpus callosum equilibrates the cerebral hemispheres," in *The Parallel Brain: The Cognitive Neuroscience of the Corpus Callosum*, eds E. Zaidel, and M. Iacoboni (Cambridge, MA: MIT Press), 271–281.

Knecht, S., Drager, B., Deppe, M., Bobe, L., Lohmann, H., Floel, A., et al. (2000). Handedness and hemispheric language dominance in healthy humans. *Brain* 123, 2512–2518. doi:10.1093/brain/123.12.2512

Luders, E., Cherbuin, N., Thompson, P. M., Gutman, B., Anstey, K. J., Sachdev, P., et al. (2010). When more is less: associations between corpus callosum size and handedness lateralization. *Neuroimage* 52, 43–49. doi:10.1016/j.neuroimage.2010.04.016

Lyle, K. B., and Grillo, M. C. (2013). Consistent-handed individuals are more authoritarian. *Laterality*. Available at: http://pubget.com/paper/23586369

Lyle, K. B., Hanaver-Torrez, S. D., Häcklander, R. P., and Edlin, J. M. (2012). Consistency of handedness, regardless of direction, predicts baseline memory accuracy and potential for memory enhancement. *J. Exp. Psychol. Learn. Mem. Cogn.* 38, 187–193.

Lyle, K. B., and Jacobs, N. E. (2010). Is saccade-induced retrieval enhancement a potential means of improving eyewitness evidence? *Memory* 18, 581–594. doi:10.1080/09658211.2010.493891

Lyle, K. B., Logan, J. M., and Roediger, H. L. (2008a). Eye movements enhance memory for individuals who are strongly right-handed and harm it for individuals who are not. *Psychon. Bull. Rev.* 15, 515–520. doi:10.3758/PBR.15.3.515

Lyle, K. B., McCabe, D. P., and Roediger, H. L. (2008b). Handedness is related to memory via hemispheric interaction: evidence from paired associate recall and source memory tasks. *Neuropsychology* 22, 523–530. doi:10.1037/0894-4105.22.4.523

Lyle, K. B., and Martin, J. M. (2010). Bilateral saccades increase intrahemispheric processing but not interhemispheric interaction: implications for saccade-induced retrieval enhancement. *Brain Cogn.* 73, 128–134. doi:10.1016/j.bandc.2010.04.004

Masumoto, K., Yamaguchi, M., Sutani, K., Tsuneto, S., Fujita, A., and Tonoike, M. (2006). Reactivation of physical motor information in the memory of action events. *Brain Res.* 1101, 102–109. doi:10.1016/j.brainres.2006.05.033

Miller, M. B., Kingstone, A., and Gazzaniga, M. S. (2002). Hemispheric encoding asymmetry is more apparent than real. *J. Cogn. Neurosci.* 14, 702–708. doi:10.1162/08989290260138609

Nolde, S. F., Johnson, M. K., and Raye, C. L. (1998). The role of prefrontal cortex during tests of episodic memory. *Trends Cogn. Sci.* 2, 399–406. doi:10.1016/S1364-6613(98)01233-9

Nowicka, A., and Tacikowski, P. (2011). Transcallosal transfer of information and functional asymmetry of the human brain. *Laterality* 16, 35–74. doi:10.1080/13576500903154231

Nyberg, L., Petersson, K. M., Nilsson, L. G., Sandblom, J., Aberg, C., and Ingvar, M. (2001). Reactivation of motor brain areas during explicit memory for actions. *Neuroimage* 14, 521–528. doi:10.1006/nimg.2001.0801

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9, 97–113. doi:10.1016/0028-3932(71)90067-4

Parker, A., and Dagnall, N. (2010). Effects of handedness and saccadic bilateral eye movements on components of autobiographical recollection. *Brain Cogn.* 73, 93–101. doi:10.1016/j.bandc.2010.03.005

Prichard, E., Propper, R. E., and Christman, S. D. (2013). Degree of handedness, but not direction, is a systematic predictor of cognitive performance. *Front. Psychol.* 4:9. doi:10.3389/fpsyg.2013.00009

Propper, R. E., and Christman, S. D. (2004). Mixed-versus strong right-handedness is associated with biases towards "remember" versus "know" judgements in recognition memory: role of interhemispheric interaction. *Memory* 12, 707–714. doi:10.1080/09658210344000503

Propper, R. E., Christman, S. D., and Phaneuf, K. A. (2005). A mixed-handed advantage in episodic memory: a possible role of interhemispheric interaction. *Mem. Cognit.* 33, 751–757.

Sontam, V., and Christman, S. D. (2012). Semantic organisation and handedness: mixed-handedness is associated with more diffuse activation of ambiguous word associates. *Laterality* 17, 38–50.

Tulving, E., Kapur, S., Craik, F. I. M., Moscovitch, M., and Houle, S. (1994). Hemispheric encoding/retrieval asymmetry in episodic memory – positron emission tomography findings. *Proc. Natl. Acad. Sci. U.S.A.* 91, 2016–2020. doi:10.1073/pnas.91.6.2016

Welcome, S. E., Chiarello, C., Towler, S., Halderman, L. K., Otto, R., and Leonard, C. M. (2009). Behavioral correlates of corpus callosum size: anatomical/behavioral relationships vary across sex/handedness groups. *Neuropsychologia* 47, 2427–2435. doi:10.1016/j.neuropsychologia.2009.04.008

Witelson, S. F. (1985). The brain connection – the corpus callosum is larger in left-handers. *Science* 229, 665–668. doi:10.1126/science.4023705

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Continuities in emotion lateralization in human and non-human primates

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Where hemispheric lateralization was once considered an exclusively human trait, it is increasingly recognized that hemispheric asymmetries are evident throughout the animal kingdom. Emotion is a prime example of a lateralized function: given its vital role in promoting adaptive behavior and hence survival, a growing body of research in affective neuroscience is working to illuminate the cortical bases of emotion processing. Presuming that human and non-human primates evolved from a shared ancestor, one would anticipate evidence of organizational continuity in the neural substrate supporting emotion processing. This paper thus reviews research examining the patterns of lateralization for the expression and perception of facial emotion in non-human primates, aiming to determine whether the patterns of hemispheric asymmetry that characterize the human brain are similarly evident in other primate species. As such, this review seeks to enhance understanding of the evolution of hemispheric specialization for emotion, using emotion lateralization in non-human primates as a window through which to view emotion lateralization in humans.

Keywords: perception, expression, asymmetry, hemisphere, face, chimpanzee, macaque, baboon

For much of the past 150 years, hemispheric lateralization has been considered an exclusive characteristic of the human brain. However, where once cerebral asymmetry was thought “the most imposing difference between man and animal,” (Pruner-Bey, 1865, p. 558), it is increasingly recognized that cerebral asymmetries present throughout the animal kingdom (e.g., Rogers and Andrew, 2002; Ocklenburg and Güntürkün, 2012), across both vertebrates (e.g., Corballis, 2009) and invertebrates (e.g., Taylor et al., 2010). Far from being exclusive to humans, species from amphibians (e.g., Vallortigara, 2006) and fish (e.g., Lippolis et al., 2009), to reptiles (e.g., Csermely et al., 2010), birds (e.g., Rogers, 2008), and mammals (e.g., Levy, 1977), evidence asymmetries in brain and behavior, suggesting that lateralization is a fundamental principle of nervous system organization. Despite this, the popularity of the presumption that lateralization was restricted to humans has limited the integration of research across human and non-human species. Such integration is needed to help shed light on the phylogeny of hemispheric asymmetry.

The notion that the human brain is functionally lateralized was first mooted by Broca (1861) following his observation that left hemisphere insult was intimately linked with language impairment. Whilst language is undoubtedly the paradigmatic lateralized function, it is not alone: emotion processing also exhibits clear evidence of functional lateralization in humans. Although the precise nature of the lateral division of emotion remains somewhat contentious (for review please see Demaree et al., 2005; Harmon-Jones et al., 2010; Rutherford and Lindell, 2011), the right hemisphere is widely regarded to play the dominant role in emotion processing. This lateralization of function confers efficiency benefits, removing redundancy associated with the reduplication of function, preventing conflict between the hemispheres, and facilitating performance of multiple simultaneous tasks (e.g., Rogers et al., 2004; Reddon and Hurd, 2009; Salva et al., 2012).

The purpose of emotion is to facilitate adaptive behavior and decision making in response to salient events (Davidson et al., 2007). As such, emotion is vital to survival. Emotional expressions play a powerful communicative role for we convey emotional states to others via the stereotypic posturing of facial features (Leopold and Rhodes, 2010). Emotional expressions are thus a key component of social interactions, indicating the likely future behavior of the displaying animal (Andrew, 1963), communicating intentions and desires, and influencing others’ emotional states. In highly social species like primates, the ability to decode emotional facial expressions efficiently and effectively confers significant evolutionary advantage (e.g., efficient threat detection aids self-preservation by prompting a fight/flight response). Given the importance of emotion to primate survival, a growing body of research in affective neuroscience is dedicated to shedding light on the neural substrates supporting emotion processing, and providing clues concerning phylogenies in human and non-human primates.

Presuming that human and non-human primates evolved from a shared ancestor (Stewart and Disotell, 1998), one would expect evidence of organizational continuity in the neural substrates supporting emotion processing. This paper thus reviews research examining patterns of lateralization for the expression and perception of facial emotion in non-human primates, assessing whether the characteristic right hemisphere dominance for emotion processing seen in humans is similarly evident in other primate species. As such, this review seeks to enhance understanding of the evolution of hemispheric specialization for emotion by using emotion lateralization in non-human primates as a powerful window through which to view emotion lateralization in humans.

EMOTION LATERALIZATION IN HUMANS

Following Broca's (1861) discovery that language was functionally lateralized in the human brain, Hughlings-Jackson (1874/1915) reported that emotion was also lateralized. Based on his repeated clinical observation that right hemisphere damage led to deficits in producing and perceiving emotion, Hughlings-Jackson proposed that emotion was lateralized to the right hemisphere (*the right hemisphere hypothesis*; see also Demaree et al., 2005, for review of an alternate model: *the valence hypothesis*). Subsequent observations of clinical patients offer further support for the right hemisphere hypothesis, demonstrating that damage to the right hemisphere compromises both the perception (e.g., Bowers et al., 1985; Borod et al., 1992) and the production of emotion (e.g., Borod et al., 1986; Blonder et al., 1993). These clinical findings converge with the results of behavioral investigations in neurotypical populations (e.g., Wittling and Roschmann, 1993; Calvo and Avero, 2008), confirming right hemisphere dominance for emotion processing.

The cortical asymmetry evident for emotion processing leads to an expressional asymmetry: though we are rarely conscious of it, human emotional expressions are asymmetric. Thus, whether we are grinning or grimacing, we show stronger emotion on the left side of the face (e.g., Indersmitten and Gur, 2003). As the lower two-thirds of the face is innervated contralaterally (Rinn, 1984; Patten, 1996), with bilateral projections increasing in the upper face (Matsumoto and Lee, 1993), the left side of the face is predominantly controlled by the right hemisphere. Given the right hemisphere's dominance for emotion control (e.g., Demaree et al., 2005), the muscles on the left side of the face move more than those on the right side of the face during emotional expression (e.g., Dimberg and Petterson, 2000), consequently producing a more intense expression. Not surprisingly then, Borod's (1993) review of 47 studies examining facial expression asymmetries in the normal population concluded that the left hemiface produces more intense emotional expressions than the right hemiface. As the left side of the face is more emotionally expressive, chimeric faces composed of mirrored left-cheeks are perceived as showing stronger emotion than mirrored right-cheek composites (Sackeim et al., 1978; please refer to **Figure 1**), and left cheek portraits appear more emotionally expressive than those showing the right cheek (e.g., Nicholls et al., 2002; see Lindell, in press, for review).

The observation that human facial expressions are asymmetric is not new. Darwin (1872) first reported that for expressions such as "sneering defiance," the upper lip is "raised on one side alone in sneering at or defying any one. . . (although) movement being confined to one side may not be an essential part of the expression, but may depend on the proper muscles being incapable of movement excepting on one side," (p. 253). In Darwin's view, human expressions shared much with those of other animals, contrary to facial anatomist Sir Charles Bell's claims that God designed humans with unique facial muscles to express uniquely human emotions (Matsumoto and Ekman, 2008); by adopting a comparative, evolutionary approach, Darwin noted commonalities between human expressions and those of our "semi-human progenitors," (p. 254). Unfortunately however, this comparative, evolutionary study of facial expressions has attracted little interest, as researchers from Andrew (1963) to Leopold and Rhodes (2010) lament.

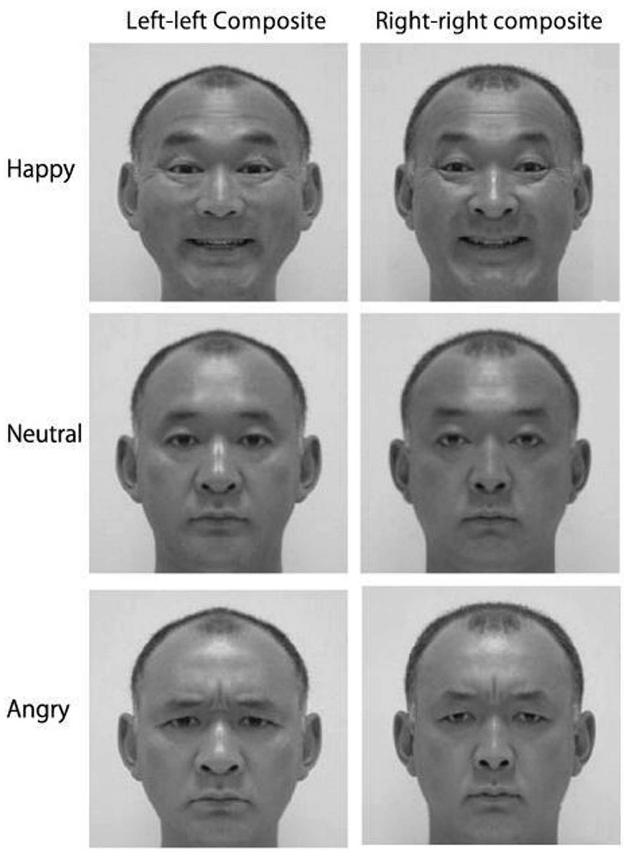

FIGURE 1 | Examples of mirrored chimeric face stimuli; people tend to select the left–left chimeras as showing stronger emotion than the right–right chimeras (Reprinted from Okubo et al., 2013, Copyright with permission from Elsevier).

Beyond asymmetries in the expression of emotion, the right hemisphere's superiority for emotion processing also manifests in asymmetries when perceiving emotion. Clinical research confirms that damage to the right hemisphere impairs the ability to identify and discriminate facial emotions, whereas damage restricted to the left hemisphere does not affect emotion recognition (e.g., Adolphs et al., 1996). The emotion perception impairment resulting from right hemisphere damage is not restricted to emotion conveyed via the facial channel: right hemisphere damage also compromises the perception of emotional words (Borod et al., 1998), and impairs the ability to interpret emotional prosody (Tucker et al., 1977). Consistently, anesthetizing the right hemisphere causes patients to judge facial emotional expressions as less intense than when the left hemisphere is anesthetized (Ahern et al., 1991). As such, the clinical data clearly implicate a dominant right hemisphere role in emotion perception.

Data from both imaging and behavioral studies similarly highlight strong right hemisphere involvement when we perceive emotion. Across a range of paradigms and communicative channels, functional imaging research indicates that perceiving emotion expressed via faces (Gorno-Tempini et al., 2001), prosody (Wildgruber et al., 2005), and even music (Blood et al., 1999), prompts more pronounced activation in the right than left hemisphere. Results of behavioral investigations appear congruent, with participants exhibiting a left visual field (right hemisphere) advantage for recognizing emotional expressions in faces (Ley and Bryden, 1979), leading to a perceptual bias when viewing emotional/neutral chimeric faces: chimeras showing emotion in the viewer's left visual appear more emotionally expressive than chimeras showing emotion in the viewer's right visual field (Failla et al., 2003; please refer to **Figure 2**). This emotional asymmetry is similarly evident for audition, with participants showing a left ear (right hemisphere) advantage for recognizing emotional words (Sim and Martinez, 2005), and emotional tones (Bryden et al., 1982).

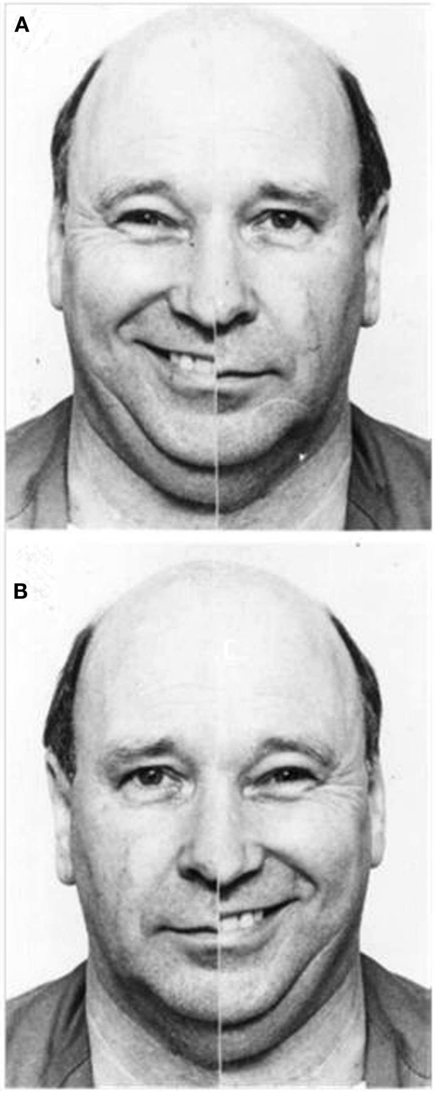

FIGURE 2 | Examples of emotional/neutral chimeric face stimuli; people tend to select the image in which emotion is presented in the left visual field (A) as more expressive than the identical image reversed to show emotion in the right visual field (B) (Reprinted from Failla et al., 2003, Copyright with permission from Elsevier).

In sum, the evidence indicates that the right hemisphere plays a crucial role in emotion processing in humans. Across a broad range of research paradigms, including clinical, functional imaging, and behavioral investigations, the data highlight the importance of the right hemisphere in both the expression and perception of facial emotion. The question to which we now turn is whether the hemispheric asymmetry for emotion processing present in humans is similarly evident in non-human primates, thus suggesting conservation across phylogeny.

EMOTIONAL EXPRESSION IN PRIMATES

Across the animal kingdom, species convey information regarding emotional state via different communicative channels (e.g., vision, olfaction, audition). A visual means of emotional expression is widely used by diurnal social mammals, including primates (Tate et al., 2006); in non-human primates, facial expressions of emotion are typically accompanied by vocalization (e.g., Hauser, 1993). The facial expression of emotion necessitates exquisite facial mobility: to communicate effectively, faces must be configurable into a variety of postures (please refer to **Figure 3**). Not surprisingly then, facial mobility has increased over the course of primate evolution (Andrew, 1963), facilitating a greater variety and more precise expressional displays that serve to reduce uncertainty about behavioral intent and thus promote social cohesion (Parr et al., 2007a). Such displays offer more specific information about the probable future behavior of the displaying animal, conferring an evolutionary advantage for highly social animals, hence the trend toward increased facial mobility across primates' evolutionary history (Andrew, 1963).

Of all the mammals, primates are argued to possess the most complex facial musculature, thus enabling the most intricate facial displays (Burrows, 2008). Though it was once thought that the complexity of primates' facial musculature increased as you traveled up the phylogenetic tree (i.e., low complexity for galagos, lorises, and lemurs; high complexity for chimpanzees and humans; Huber, 1931), more recent research indicates that the number of facial muscles in the lower primates (17 muscles in galagos and lemurs; Burrows, 2008) is much closer to that of the higher primates (23 muscles in humans and chimpanzees; Burrows et al.,

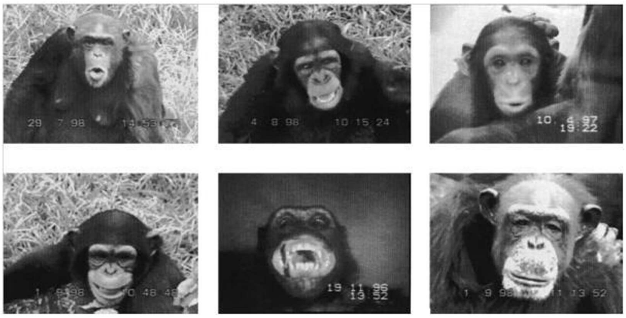

FIGURE 3 | Examples of chimpanzee facial expressions. Top row from left to right: pant-hooting, play face, silent pout. Bottom row from left to right: silent bared-teeth display, staring bared-teeth scream face, neutral face (Reprinted from Fernández-Carriba et al., 2002a, Copyright with permission from Elsevier).

2006) than previously estimated. Looking particularly at humans and our closest relative, the chimpanzee, Burrows et al.'s anatomical work confirms that the 23 facial muscles present in humans are *all* present in chimpanzees. Indeed, comparative research confirms that intramuscular electrical stimulation of the individual facial muscles prompts functionally similar changes in appearance in both chimpanzees and humans (Waller et al., 2006). Not surprisingly then, this similarity in musculature means that the basic repertoire of facial expressions available to humans is similar to that observed in chimpanzees (Parr et al., 2007a,b).

Studies of reflexive facial expressions in response to different tastes offer evidence of expressional congruity across primate species, with salty and bitter tastes prompting aversive emotional expressions whereas sweet tastes elicit positive emotional expressions (Erickson and Schulkin, 2003). These emotional responses to sweet and bitter tastes are homologously observed across primate species, including lemurs, Old and New World monkeys, great apes, and humans (Steiner et al., 2001). Critically, the degree of similarity in pattern of expression closely reflects phylogenetic proximity: human expressions are more similar to those of the great apes than either species' expressions are to Old or New World monkeys. Given that humans and great apes are thought to have shared a common ancestor within the last 10–20 million years (Stewart and Disotell, 1998), and their hominoid ancestors both diverged from Old World monkeys 20–40 million years ago (Arnason et al., 1996), the congruity in expression for more closely related species appears apposite and is consistent with cytoarchitectural differences in oro-facial motor cortex between the hominoid species (humans and great apes) and Old World monkeys (Sherwood et al., 2004).

EMOTION LATERALIZATION IN NON-HUMAN PRIMATES: EXPRESSION

Analysis of facial expression asymmetries in non-human primates suggests that the right hemisphere/left hemiface emotion bias evident in human expression has its precursors in non-human primate evolution. Across a variety of non-human primate species, including rhesus macaques (e.g., Hauser, 1993), baboons (e.g., Wallez and Vauclair, 2011), and chimpanzees (e.g., Fernández-Carriba et al., 2002a,b), the left side of the face produces more pronounced emotional expressions, with the left side of the mouth opening wider and mobilizing earlier during emotional calls. Given that the left side of the face/mouth is contralaterally controlled by the right hemisphere in both human and non-human primates (e.g., Patten, 1996; Morecraft et al., 2001), more pronounced expressivity in the left side of the face is taken to index right hemisphere dominance for emotional expression.

When Hauser (1993) assessed asymmetries in adult rhesus macaques' facial expressions (fear grimace, copulation grimace, open mouth threat, ear flap), results indicated that the left side of the face was both more expressive and more mobile. For example, when producing a fear grimace, there were more expression folds on the left side of the face, and the left corner of the mouth reached a higher position, than the right. As the left side of the face is predominantly controlled by the right hemisphere in macaques (e.g., Morecraft et al., 2001), Hauser's findings suggest right hemisphere dominance for emotion control in macaques. Moreover, analysis of the timings of expression emergence indicated that the left side of the face commenced movement first (fear grimace, open mouth threat) and maintained the expression for longer (copulation grimace) than the right side. This finding has subsequently been replicated by Hauser and Akre (2001), with both infant and adult macaques showing earlier initiation of emotional expressions on the left side of the face, again implicating a greater right hemisphere role in emotional control.

This left side bias has also been reported for screeching in adult baboons (Wallez and Vauclair, 2011, in press), with recent research confirming that it is evident early in development, being present in both infant macaques (cooing) and infant baboons (gecking; Wallez and Vauclair, 2012; please refer to **Figure 4**). Given that both baboons and macaques are Old World monkey species, these data suggest that the right hemisphere's specialization for the control of emotional expression must have emerged early in primate evolution (at least 30–40 million years ago, Boyed and Silk, 2000) and was conserved in later-evolving primate species, including both chimpanzees and humans.

Fernández-Carriba et al.'s (2002a,b) research on chimpanzee facial expressions again implicates a strong right hemisphere role in emotional expression. They made natural observations of chimpanzees interacting over two 9-month periods, and recorded/coded five categories of facial expressions (pant-hooting, play face, silent pout, silent bare-teeth display, staring bared-teeth scream face). Quantitative analysis of the resulting 183 facial images indicated that the left hemi-mouth subtended a larger area than the right (hooting, play, silent bared-teeth), and extended laterally more than the right (hooting, silent bared-teeth, scream face). As such, these findings appear consistent with a right hemisphere dominant functional asymmetry for emotion control.

Importantly, research comparing oro-facial asymmetries in non-human primates' emotional and intentional communicative vocalizations confirms differential patterns of lateralization. Whereas the left side of the face moves earlier and more during facial expressions of emotion (e.g., Hauser, 1993; Fernández-Carriba et al., 2002a,b), Losin et al. (2008) found that chimpanzees' intentional communicative vocalizations were associated with greater movement on the right side of the face. They compared oro-facial asymmetries for emotional signals (pant-hoot, food-bark) and referential, communicative signals that the captive chimpanzees had learned to use to intentionally attract the attention of humans (raspberry, extended grunt). Results indicated that the emotional signals were expressed more intensely on the left side

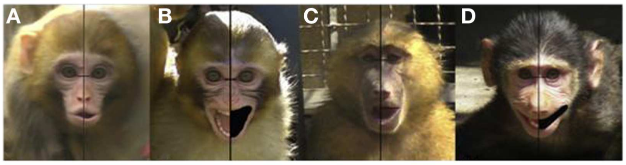

FIGURE 4 | Examples of asymmetries in expressions in infant macaques [(A) cooing; (B) screaming] and infant baboons [(C) moaning; (D) gecking] (Reprinted from Wallez and Vauclair, 2012, Copyright with permission from Elsevier).

of the chimpanzees' faces, but in striking contrast, the intentional communicative signals prompted greater movement in the right hemiface, suggesting left hemisphere control of learned oro-facial movements. This pattern of results was recently replicated in a second colony of captive chimpanzees (Wallez et al., 2012). As such, these findings suggest that just as humans show predominantly left lateralization for intentional communication (language) and right hemisphere lateralization for emotion, non-human primates like chimpanzees show left lateralization for intentional communication (learned, attention-getting sounds) and right hemisphere lateralization for emotion.

In addition, studies asking humans to judge the emotional expressivity of non-human primate faces confirm that we perceive the left hemiface as being more expressive. Hauser (1993) created left–left and right–right chimeric faces of rhesus macaques' fear grimaces and asked human participants to indicate which appeared more emotionally expressive. The overwhelming majority of participants (41/43) deemed the left–left chimeras more emotionally expressive than the right–right chimeras, consistent with greater expressivity in the left side of the monkey's faces as a consequence of predominant right hemisphere innervation. Similar findings have been reported for judgments of baboon (Wallez and Vauclair, in press) and chimpanzee chimeric faces (Fernández-Carriba et al., 2002a), with the consistent left–left chimera preference confirming right hemisphere dominance for the expression of emotion in non-human primates.

Although Hauser's (1993) and Fernández-Carriba et al.'s (2002a,b) findings appear consistent with a right hemisphere model of emotional control, Hook-Costigan and Rogers' (1998) marmoset research supports an alternate, valence-based conceptualization. According to *the valence hypothesis*, both hemispheres contribute to emotion processing: the right hemisphere is argued to control negative emotion, whereas the left hemisphere controls positive emotion (see Demaree et al., 2005, for review in humans). This valence-based asymmetry may reflect a more basic lateralization of behavioral tendencies to approach positive stimuli and avoid/withdraw from aversive stimuli (see Rutherford and Lindell, 2011, for review of approach/avoidance lateralization; Harmon-Jones, 2004, and Carver and Harmon-Jones, 2009, for detailed discussion of anger as an approach-related emotion). Hook-Costigan and Rogers reported greater expressivity on the left side of marmosets' faces for expressions and vocalizations of fear, however the right side of the face was more expressive when marmosets made social contact calls. Consequently their data appear consistent with right hemisphere control of negative, and left hemisphere control of positive, emotion. To date these are the only non-human primate data supporting the valence hypothesis and until further consistent evidence is available, should be interpreted cautiously. It is interesting to note, however, that just as there is conflicting evidence supporting the right hemisphere and valence hypotheses in humans, the contention is mirrored in the non-human primate research. Indeed, some recent evidence fails to support either the right hemisphere or valence hypothesis, with Wallez and Vauclair (2012) reporting a right cheek (i.e., left hemisphere) bias for screaming in infant macaques.

Overall, however, the majority of research investigating the lateralization of emotional expression in non-human primates indicates right hemisphere dominance for emotion control. Data from investigations assessing species including macaques (e.g., Hauser, 1993), baboons (e.g., Wallez and Vauclair, 2011), and chimpanzees (e.g., Fernández-Carriba et al., 2002a,b), indicate that the left side of these non-human primates' faces is more emotionally expressive, mobilizing earlier and moving more. Given this anatomical expressional asymmetry, it is not surprising that chimeras composed of two left chimpanzee hemifaces are overwhelming perceived as more emotionally expressive than right–right chimeras (e.g., Hauser, 1993). As such, the non-human primate findings appear consistent with those observed in human studies, indicating right hemisphere dominance for emotion control. Moreover, the fact that the expressional asymmetry is evident in Old World monkey species like baboons and macaques implies that right hemisphere specialization emerged early in primate evolution (at least 30–40 million years ago, Boyed and Silk, 2000) and was phylogenetically conserved in later-evolving primate species, such as chimpanzees and humans. Thus far from being an exclusively human trait, hemispheric lateralization for emotional expression is evident across primate species.

EMOTION LATERALIZATION IN NON-HUMAN PRIMATES: PERCEPTION

The ability to read others' emotional expressions provides valuable information about affective state and allows an animal to modify its own behavior in light of the information gained. As such, the ability to accurately and efficiently distinguish facial emotions is a vital skill. Not surprisingly then, primates have evolved to develop exquisite mechanisms for recognizing emotions. For example, within a few days of birth, human babies can distinguish between happy, sad, and surprised expressions (e.g., Field et al., 1982), and by 6 months, human infants have gained the ability to distinguish between the negative emotions of fear, anger, and sadness (Serrano et al., 1992). Whilst there is a considerable body of research assessing facial emotion expression in non-human primates, research investigating facial emotion perception in non-human primates is rather more scarce. The lack of research in this area presumably reflects the challenges inherent in such an endeavor: while expressional asymmetries can be easily assessed using an observational paradigm, assessment of perceptual asymmetries may appear less amenable to naturalistic observation. That said, a number of researchers have investigated emotion perception in non-human primates, and these data are again consistent in supporting a greater role for the right hemisphere in emotion processing.

For example, when gelada baboons engage in agonistic behavior, they preferentially favor their left visual field (right hemisphere; Casperd and Dunbar, 1996). The authors assessed orientational asymmetries of male baboons during fights, threats, and approaches, and found that both members of a conflict pair used their left visual field more often than the right. As the authors write, ". . . an animal which orients its head so as to hold its opponent on the left side. . . does so in order to ensure that signal information is transmitted disproportionately to the right cerebral hemisphere," (p. 58), consistent with right hemisphere dominance for emotion processing. Similar findings have been reported for approach behaviors in mangabeys, suggesting that the left visual field bias is not restricted to negative interactions in primates. Baraud et al. (2009) found that mangabeys (a type of Old World monkey) are more inclined to approach a conspecific on the left. Such an approach privileges visual access to the more expressive left side of the face, presumably facilitating efficient emotion communication.

Whereas Casperd and Dunbar (1996) and Baraud et al. (2009) used natural observational methods to assess emotion perception in non-human primates, other researchers have employed experimental paradigms, including split brain research. In humans, the split brain operation is performed to relieve intractable epilepsy; by severing the corpus callosum the two sides of the brain are functionally isolated, preventing epileptiform activity from traveling between the hemispheres (Sperry, 1968). Following split brain operations on 26 rhesus macaques, Vermeire and Hamilton (1998) trained the macaques to discriminate macaque faces on the basis of emotional expression. When faces were presented to the macaques' isolated right hemispheres, emotion discrimination performance was significantly better than when the faces were presented to the isolated left hemispheres, indicating a right hemisphere advantage for the perception of facial emotion in Old World monkeys.

Research investigating emotion perception in chimpanzees similarly indicates a right hemisphere advantage. Parr and Hopkins (2000) showed six chimpanzees emotionally evocative videos depicting play (positive), scenery (neutral), and severe aggression (negative); whilst the chimpanzees watched the videos their tympanic membrane temperature (Tty) was recorded (Tty provides an indirect but reliable measure of brain temperature, indexing changes in autonomic and behavioral activity). Parr and Hopkins' data indicted that right ear Tty increased for all chimpanzees when they were viewing the negative emotional video, consistent with greater right hemisphere involvement in processing negative emotion.

Importantly, this right hemisphere emotion perception bias is not restricted to the perception of emotion in conspecifics: chimpanzees also show a right hemisphere bias when perceiving facial emotion in humans (Morris and Hopkins, 1993). Morris and Hopkins (1993) trained three chimpanzees to discriminate between pairs of human chimeric faces on the basis of which chimera appeared happier (each chimera was composed of one neutral and one smiling half). During the test phase the researchers found that the chimpanzees were more likely to select the chimera with the smiling half falling in the left visual field (right hemisphere). Previous human research using an identical task similarly indicated a preference for chimeras with the emotion falling in the left visual field (Levy et al., 1983), indicating a high degree of consistency in the lateralization of emotion perception in these closely related primates.

In sum, the results of studies investigating the perception of emotion in non-human primates echo the results of studies assessing the expression of emotion in non-human primates, indicating right hemisphere dominance for emotion control. Although studies examining emotion perception in non-human primate species have investigated only a few species (i.e., macaques, baboons, chimpanzees), the data from those investigations indicate a left visual field (right hemisphere) bias for the perception of emotion in both conspecific (e.g., Vermeire and Hamilton, 1998) and human faces (e.g., Morris and Hopkins, 1993), and during natural interactions (Casperd and Dunbar, 1996; Baraud et al., 2009). Given that this bias is consistent across both Old World monkeys and great ape species, and is similarly evident in humans, it seems reasonable to suggest that just as the asymmetry for emotion expression is evident across primate phylogeny, a right hemisphere bias for emotion perception is conserved across primate species.

CONCLUSION AND FUTURE DIRECTIONS

Far from being a uniquely human trait, the research reviewed suggests that lateralization of function is a universal characteristic of primate species. In particular, the right hemisphere asymmetry that characterizes the expression and perception of emotion in humans appears to be pervasive across primate phylogeny. From Old World monkeys like baboons and macaques, to great apes and humans, species thought to have evolved from a shared ancestor over 30–40 million years ago (Stewart and Disotell, 1998; Boyed and Silk, 2000) show similar emotional asymmetries. Across primate species the right hemisphere's dominance in emotion processing is manifest, leading to greater emotional expressivity in human and non-human primates' left hemifaces (e.g., Borod, 1993; Fernández-Carriba et al., 2002a,b), and greater perceptual sensitivity to emotion in human and non-human primates' left visual fields (controlled by the right hemisphere; e.g., Ley and Bryden, 1979; Morris and Hopkins, 1993). Given that these emotional asymmetries are present in Old World monkey species, the right hemisphere's specialization for emotion processing is likely to have emerged early in primate evolution, with evidence implying phylogenetic conservation in later-evolving primate species, including humans. As such, the research reviewed strongly supports the notion of organizational continuity in the neural substrates supporting emotion processing in primate species.

This review has argued that the right hemisphere asymmetry for emotion reflects homology across primate species (i.e., results from shared primate ancestry), however it is important to note an alternate possibility. Hopkins and Cantalupo (2008) point out that continuity in patterns of asymmetry may result from homology but could alternately reflect homoplasy: convergent evolution of common patterns of asymmetry that evolved independently. However, given that the patterns of lateralization in lower and higher primates are conserved despite marked changes in the organization of sensory systems (e.g., vision), it appears probable that the consistency in patterns of primate lateralization reflects homology (see Hopkins and Cantalupo, 2008, for discussion).

Beyond the suggestion of continuity in emotion lateralization for human and non-human primates, this review makes it strikingly apparent that there are significant gaps in the non-human primate literature. Whilst emotional expression has been subject to comparatively greater investigation than emotion perception in non-human primates, even there the studies are restricted to only a few species (i.e., macaques, baboons, chimpanzees, marmosets). Whether the right hemisphere's dominance for emotion extends to prosimians remains an open question. Though it appears probable that the left side expressivity bias seen in Old World monkeys, New World Monkeys, great apes, and humans will be similarly evident in their more phylogenetically distant primate relatives, only investigation of facial displays in more primitive primates, such as lemurs, galagos, and lorises, will resolve the question.

As Ward (1991) notes, examination of prosimian species offers unique opportunities in the investigation of the evolution of primate lateralization: prosimians are less complex than anthropoid primates in terms of behavior and brain structure, yet being primates, can serve as models of human laterality. Given that prosimians, such as galagos, are thought to retain many of the characteristics ancestral to those of all living primates (Brothers, 1990), examination of their facial expressions may help shed light on the degree to which expressional asymmetries are likely to have developed over the course of primate evolution. Moreover, prosimians present in the potentially unique position of serving as a bridge between non-primate mammals and anthropoid primates. Research investigating emotion lateralization in non-primate mammals such as dogs (e.g., Quaranta et al., 2007; Siniscalchi et al., 2010) and horses (e.g., De Boyer Des Roches et al., 2008; Farmer et al., 2010) offers evidence indicating the lateralization of emotion perception in these species; however studies assessing asymmetries in the expression of facial emotion in non-primate mammal have yet to be conducted. Should examination of prosimian species confirm hemifacial asymmetries in emotion expression, assessment of asymmetries in the facial expressions of non-primate mammals appears a logical next step.

Investigation of emotion lateralization in the owl monkey family *Aotus* (also known as the night monkey) also offers intriguing possibilities. Being a nocturnal anthropoid, this group of non-human primates has evolved to possess comparatively less differentiated facial musculature than diurnal primates and is reported to have virtually no facial expressions (Huber, 1931; Chevalier-Skolnikoff, 1973). Examination of both expressional and perceptual asymmetries in this family thus affords a unique opportunity to assist in determining the extent to which nature and nurture shape patterns of emotion lateralization in primates. By examining the magnitude of the emotion asymmetry present in the nocturnal *Aotus* and comparing it with that seen in a similar but diurnal (e.g., *Cebidae*) or cathmeral anthropoid species (e.g., *Aotus azarae azarae* which is sporadically active during the day and night), one may speculate on the influence of experience on emotion lateralization. Observation of others' emotion expressions may increase the magnitude of the hemispheric asymmetry for emotion processing in diurnal primates via experience-dependent processes; such influences may be less likely to induce changes in nocturnal and cathmeral primates like *Aotus*.

The fact that hemispheric asymmetries are evident across primate species has implications beyond the lateralization of emotion. Where once lateralization was thought to be a defining human attribute (e.g., Pruner-Bey, 1865), the studies reviewed indicate that emotion lateralization is the rule rather than the exception among primates, confirming that the emergence of hemispheric asymmetry was independent of language. Whilst theorists seek to distinguish uniquely human characteristics (mooting language, tool use, and creativity as likely contenders), it appears increasingly apparent that such anthropocentric goals are of limited utility; human and non-human primates are far more similar than we are different. The research reviewed indicates that the right hemisphere asymmetry for emotion processing is pervasive from Old World monkeys to chimpanzees and humans, and future research will determine whether this pattern of lateralization similarly extends to more distantly related prosimians. If right hemisphere emotion lateralization is confirmed in prosimians, investigation of lateralization in non-primate mammals offers a logical next step in the journey toward understanding the evolution of emotion lateralization.

REFERENCES

Adolphs, R., Damasio, H., Tranel, D., and Damasio, A. R. (1996). Cortical systems for the recognition of emotion in facial expressions. *J. Neurosci.* 16, 7678–7687.

Ahern, G. L., Schomer, D. L., Kleefield, J., Blume, H., Cosgrove, G. R., Weintraub, S., et al. (1991). Right hemisphere advantage for evaluating emotional facial expressions. *Cortex* 27, 193–202. doi:10.1016/S0010-9452(13)80123-2

Andrew, R. J. (1963). Evolution of facial expression. *Science* 142, 1034–1041. doi:10.1126/science.142.3595.1034

Arnason, U., Gullberg, A., Janke, A., and Xu, X. F. (1996). Pattern and timing of evolutionary divergences among hominoids based on analyses of complete mtDNAs. *J. Mol. Evol.* 43, 650–661. doi:10.1007/BF02202113

Baraud, I., Buytet, B., Bec, P., and Blois-Heulin, C. (2009). Social laterality and 'transversality' in two species of mangabeys: influences of rank and implication for hemispheric specialization. *Behav. Brain Res.* 198, 449–458. doi:10.1016/j.bbr.2008.11.032

Blonder, L. X., Burns, A., and Bowers, D. (1993). Right hemisphere facial expressivity during natural conversation. *Brain Cogn.* 21, 44–56. doi:10.1006/brcg.1993.1003

Blood, A. J., Zatorre, R. J., Bermudez, P., and Evans, A. C. (1999). Emotional responses to pleasant and unpleasant music correlate with activity in paralimbic brain regions. *Nat. Neurosci.* 2, 382–387. doi:10.1038/7299

Borod, J. C. (1993). Cerebral mechanisms underlying facial, prosodic, and lexical emotional expression: a review of neuropsychological studies and methodological issues. *Neuropsychology* 7, 445–463. doi:10.1037/0894-4105.7.4.445

Borod, J. C., Andelman, F., Obler, L. K., Tweedy, J. R., and Welkowitz, J. (1992). Right hemisphere specialization for the identification of emotional words and sentences: evidence from stroke patients. *Neuropsychologia* 30, 827–844. doi:10.1016/0028-3932(92)90086-2

Borod, J. C., Cicero, B. A., Obler, L. K., Welkowitz, J., Erhan, H. M., Santschi, C., et al. (1998). Right hemisphere emotional perception: evidence across multiple channels. *Neuropsychology* 12, 446–458. doi:10.1037/0894-4105.12.3.446

Borod, J. C., Koff, E., Lorch, M. P., and Nicholas, M. (1986). The expression and perception of facial emotion in brain-damaged patients. *Neuropsychologia* 24, 169–180. doi:10.1016/0028-3932(86)90050-3

Bowers, D., Bauer, R., Coslett, B., and Heilman, K. (1985). Processing of faces by patients with unilateral hemisphere lesions. I. Dissociation between judgements of facial affect and facial identity. *Brain Cogn.* 4, 258–272. doi:10.1016/0278-2626(85)90020-X

Boyed, R., and Silk, J. B. (2000). *How Humans Evolved*. New York: WW Norton.

Broca, P. (1861). Sur le principe des localisations cérébrales. *Bull. Soc. Anthropol.* 2, 190–204.

Brothers, L. (1990). The neural basis of primate social communication. *Motiv. Emot.* 14, 81–91. doi:10.1007/BF00991637

Bryden, M. P., Ley, R. G., and Sugarman, J. H. (1982). A left-ear advantage for identifying the emotional quality of tonal sequences. *Neuropsychologia* 20, 83–87. doi:10.1016/0028-3932(82)90089-6

Burrows, A. M. (2008). The facial expression musculature in primates and its evolutionary significance. *Bioessays* 30, 212–225. doi:10.1002/bies.20719

Burrows, A. M., Waller, B. M., Parr, L. A., and Bonar, C. J. (2006). Muscles of facial expression in the chimpanzee (*Pan troglodytes*): descriptive, comparative, and phylogenetic contexts. *J. Anat.* 208, 153–168. doi:10.1111/j.1469-7580.2006.00523.x

Calvo, M. G., and Avero, P. (2008). Affective priming of emotional pictures in parafoveal vision: left visual field advantage. *Cogn. Affect. Behav. Neurosci.* 8, 41–53. doi:10.3758/CABN.8.1.41

Carver, C. S., and Harmon-Jones, E. (2009). Anger is an approach-related affect: evidence and implications. *Psychol. Bull.* 135, 185–204. doi:10.1037/a0013965

Casperd, J. M., and Dunbar, R. I. M. (1996). Asymmetries in the visual processing of emotional cues during agonistic interactions by gelada baboons. *Behav. Processes* 37, 57–65. doi:10.1016/0376-6357(95)00075-5

Chevalier-Skolnikoff, S. (1973). "Facial expression of emotion in nonhuman primates," in *Darwin and Facial Expression*, ed. P. Ekman (New York: Academic Press), 11–90.

Corballis, M. C. (2009). The evolution and genetics of cerebral asymmetry. *Phil. Trans. R. Soc. B* 364, 867–879. doi:10.1098/rstb.2008.0232

Csermely, D., Bonati, B., and Romani, R. (2010). Lateralisation in a detour test in the common wall lizard (Podarcis muralis). *Laterality* 15, 535–547. doi:10.1080/13576500903051619

Darwin, C. (1872). *The Expression of Emotions in Man and Animals*. Chicago: The University of Chicago Press.

Davidson, R. J., Fox, A., and Kalin, N. H. (2007). "Neural bases of emotion regulation in nonhuman primates and humans," in *Handbook of Emotion Regulation*, ed. J. J. Gross (New York: Guilford Press), 47–68.

De Boyer Des Roches, A., Richard-Yris, M.-A., Henry, S., Mohammad, E., and Hausberger, M. (2008). Laterality and emotions: visual laterality in the domestic horse (*Equus caballus*) differs with objects' emotional value. *Physiol. Behav.* 94, 487–490. doi:10.1016/j.physbeh.2008.03.002

Demaree, H. A., Everhart, D. E., Youngstrom, E. A., and Harrison, D. W. (2005). Brain lateralisation of emotional processing: historical roots and a future incorporating "dominance". *Behav. Cogn. Neurosci. Rev.* 4, 3–20. doi:10.1177/1534582305276837

Dimberg, U., and Petterson, M. (2000). Facial reactions to happy and angry facial expressions: evidence for right hemisphere dominance. *Psychophysiology* 37, 693–696. doi:10.1111/1469-8986.3750693

Erickson, K., and Schulkin, J. (2003). Facial expressions of emotion: a cognitive neuroscience perspective. *Brain Cogn.* 52, 52–60. doi:10.1016/S0278-2626(03)00008-3

Failla, C. V., Sheppard, D. M., and Bradshaw, J. L. (2003). Age and responding-hand related changes in performance of neurologically normal subjects on the line-bisection and chimeric-faces tasks. *Brain Cogn.* 52, 353–363. doi:10.1016/S0278-2626(03)00181-7

Farmer, K., Krueger, K., and Byrne, R. W. (2010). Visual laterality in the domestic horse (*Equus caballus*) interacting with humans. *Anim. Cogn.* 13, 229–238. doi:10.1007/s10071-009-0260-x

Fernández-Carriba, S., Loeches, Á, Morcillo, A., and Hopkins, W. D. (2002a). Asymmetry in facial expression of emotions by chimpanzees. *Neuropsychologia* 40, 1523–1533. doi:10.1016/S0028-3932(02)00028-3

Fernández-Carriba, S., Loeches, Á, Morcillo, A., and Hopkins, W. D. (2002b). Functional asymmetry of emotions in primates: new findings in chimpanzees. *Brain Res. Bull.* 57, 561–564. doi:10.1016/S0361-9230(01)00685-2

Field, T. M., Woodson, R., Greenberg, R., and Cohen, D. (1982). Discrimination and imitation of facial expressions by neonates. *Science* 218, 179–181. doi:10.1126/science.7123230

Gorno-Tempini, M. L., Pradelli, S., Serafini, M., Pagnoni, G., Baraldi, P., Porro, C., et al. (2001). Explicit and incidental facial expression processing: an fMRI study. *Neuroimage* 14, 465–473. doi:10.1006/nimg.2001.0811

Harmon-Jones, E. (2004). On the relationship of anterior brain activity and anger: examining the role of attitude toward anger. *Cogn. Emot.* 18, 337–361. doi:10.1080/02699930341000059

Harmon-Jones, E., Gable, P. A., and Peterson, C. K. (2010). The role of asymmetric frontal cortical activity in emotion-related phenomena: a review and update. *Biol. Psychol.* 84, 451–462. doi:10.1016/j.biopsycho.2009.08.010

Hauser, M. D. (1993). Right hemisphere dominance for the production of facial expression in monkeys. *Science* 261, 475–477. doi:10.1126/science.8332914

Hauser, M. D., and Akre, K. (2001). Asymmetries in the timing of facial and vocal expressions by rhesus monkeys: implications for hemispheric specialization. *Anim. Behav.* 61, 391–400. doi:10.1006/anbe.2000.1588

Hook-Costigan, M. A., and Rogers, L. J. (1998). Lateralized use of the mouth in production of vocalizations by marmosets. *Neuropsychologia* 36, 1265–1273. doi:10.1016/S0028-3932(98)00037-2

Hopkins, W. D., and Cantalupo, C. (2008). Theoretical speculations on the evolutionary origins of hemispheric specialization. *Curr. Dir. Psychol. Sci.* 17, 233–237. doi:10.1111/j.1467-8721.2008.00581.x

Huber, E. (1931). *Evolution of Facial Musculature and Expression*. Baltimore: The Johns Hopkins Press.

Hughlings-Jackson, J. (1874/1915). On the nature of duality of the brain. *Brain* 38, 80–103. doi:10.1093/brain/38.1-2.80 (Original work published 1874).

Indersmitten, T., and Gur, R. C. (2003). Emotion processing in chimeric faces: hemispheric asymmetries in expression and recognition of emotions. *J. Neurosci.* 23, 3820–3825.

Leopold, D. A., and Rhodes, G. (2010). A comparative view of face perception. *J. Comp. Psychol.* 124, 233–251. doi:10.1037/a0019460

Levy, J. (1977). The mammalian brain and the adaptive advantage of cerebral asymmetry. *Ann. N. Y. Acad. Sci.* 299, 264–272. doi:10.1111/j.1749-6632.1977.tb41913.x

Levy, J., Heller, W., Banich, M. T., and Burton, L. A. (1983). Asymmetry of perception in free viewing of chimeric faces. *Brain Cogn.* 2, 404–419. doi:10.1016/0278-2626(83)90021-0

Ley, R. G., and Bryden, M. P. (1979). Hemispheric differences in processing emotions and faces. *Brain Lang.* 7, 127–138. doi:10.1016/0093-934X(79)90010-5

Lindell, A. K. (in press). The silent social/emotional signals in left and right cheek poses: a literature review. *Laterality* doi:10.1080/1357650X.2012.737330

Lippolis, G., Joss, J. M., and Rogers, L. J. (2009). Australian lungfish (*Neoceratodus forsteri*): a missing link in the evolution of complementary side biases for predator avoidance and prey capture. *Brain Behav. Evol.* 73, 295–303. doi:10.1159/000230674

Losin, E. A. R., Russell, J. L., Freeman, H., Meguerditchian, A., and Hopkins, W. D. (2008). Left hemisphere specialization for oro-facial movements of learned vocal signals by captive chimpanzees. *PLoS ONE* 3:e2529. doi:10.1371/journal.pone.0002529

Matsumoto, D., and Ekman, P. (2008). Facial expression analysis. *Scholarpedia* 3:4237. doi:10.4249/scholarpedia.4237

Matsumoto, D., and Lee, M. (1993). Consciousness, volition, and the neuropsychology of facial expressions of emotion. *Conscious. Cogn.* 2, 237–254. doi:10.1006/ccog.1993.1022

Morecraft, R. J., Louie, J. L., Herrick, J. L., and Stilwell-Morecraft, K. S. (2001). Cortical innervation of the facial nucleus in the non-human primate: a new interpretation of the effects of stroke and related subtotal brain trauma on the muscles of facial expression. *Brain* 124, 176–208. doi:10.1093/brain/124.1.176

Morris, R. D., and Hopkins, W. D. (1993). Perception of human chimeric faces by chimpanzees: evidence for a right hemisphere advantage. *Brain Cogn.* 21, 111–122. doi:10.1006/brcg.1993.1008

Nicholls, M. E. R., Wolfgang, B. J., Clode, D., and Lindell, A. K. (2002). The effect of left and right poses on the expression of facial emotion. *Neuropsychologia* 40, 1662–1665. doi:10.1016/S0028-3932(02)00024-6

Ocklenburg, S., and Güntürkün, O. (2012). Hemispheric asymmetries: the comparative view. *Front. Psychol.* 3:5. doi:10.3389/fpsyg.2012.00005

Okubo, M., Ishikawa, K., and Kobayashi, A. (2013). No trust on the left side: hemifacial asymmetries for trustworthiness and emotional expressions. *Brain Cogn.* 82, 181–186.

Parr, L. A., and Hopkins, W. D. (2000). Brain temperature and emotional perception in chimpanzees, *Pan troglodytes. Physiol. Behav.* 71, 363–371. doi:10.1016/S0031-9384(00)00349-8

Parr, L. A., Waller, B. M., and Vick, S. J. (2007a). New developments in understanding emotional facial signals in chimpanzees. *Curr. Dir. Psychol. Sci.* 16, 117–122. doi:10.1111/j.1467-8721.2007.00487.x

Parr, L. A., Waller, B. M., Vick, S. J., and Bard, K. A. (2007b). Classifying chimpanzee facial expressions by muscle action. *Emotion* 7, 172–181. doi:10.1037/1528-3542.7.1.172

Patten, J. (1996). *Neurological Differential Diagnosis*, 2nd Edn. New York: Springer-Verlag.

Pruner-Bey. (1865). L'homme et l'animal. *Bull. Soc. Anthropol.* 6, 522–562. doi:10.3406/bmsap.1865.9508

Quaranta, A., Siniscalchi, M., and Vallortigara, G. (2007). Asymmetric tail-wagging responses by dogs to different emotive stimuli. *Curr. Biol.* 17, R199–R201. doi:10.1016/j.cub.2007.02.008

Reddon, A. R., and Hurd, P. L. (2009). Acting unilaterally: why do animals with strongly lateralized brains behave differently than those with weakly lateralized brains? *Biosci. Hypotheses* 2, 383–387. doi:10.1016/j.bihy.2009.06.007

Rinn, W. B. (1984). The neuropsychology of facial expression: a review of the neurological and psychological mechanisms for producing facial expressions. *Psychol. Bull.* 95, 52–77. doi:10.1037/0033-2909.95.1.52

Rogers, L. J. (2008). Development and function of lateralization in the avian brain. *Brain Res. Bull.* 76, 235–244. doi:10.1016/j.brainresbull.2008.02.001

Rogers, L. J., and Andrew, J. R. (2002). *Comparative Vertebrate Lateralization.* Cambridge: Cambridge University Press.

Rogers, L. J., Zucca, P., and Vallortigara, G. (2004). Advantages of having a lateralized brain. *Proc. Biol. Sci.* 271, S420–S422. doi:10.1098/rsbl.2004.0200

Rutherford, H. J. V., and Lindell, A. K. (2011). Thriving and surviving: approach and avoidance motivation and lateralisation. *Emot. Rev.* 3, 333–343. doi:10.1177/1754073911402392

Sackeim, H. A., Gur, R. C., and Saucy, M. C. (1978). Emotions are expressed more intensely on the left side of the face. *Science* 202, 434–436. doi:10.1126/science.705335

Salva, O. R., Regolin, L., Mascalzoni, E., and Vallortigara, G. (2012). Cerebral and behavioural asymmetries in animal social recognition. *Comp. Cogn. Behav. Rev.* 7, 110–138. doi:10.3819/ccbr.2012.70006

Serrano, J. M., Iglesias, J., and Loeches, A. (1992). Visual discrimination and recognition of facial expressions of anger, fear, and surprise in 4- to 6-month-old infants. *Dev. Psychobiol.* 25, 411–425. doi:10.1002/dev.420250603

Sherwood, C. C., Holloway, R. L., Erwin, J. M., and Hof, P. R. (2004). Cortical orofacial motor representation in old World monkeys, great apes, and humans. *Brain Behav. Evol.* 63, 82–106. doi:10.1159/000075672

Sim, T.-C., and Martinez, C. (2005). Emotion words are remembered better in the left ear. *Laterality* 10, 149–159. doi:10.1080/13576500342000365

Siniscalchi, M., Sasso, R., Pepe, A. M., Vallortigara, G., and Quaranta, A. (2010). Dogs turn left to emotional stimuli. *Behav. Brain Res.* 208, 516–521. doi:10.1016/j.bbr.2009.12.042

Sperry, R. W. (1968). Mental unity following surgical disconnection of the cerebral hemispheres. *Harvey Lect.* 62, 293–323.

Steiner, J. E., Glaser, D., Hawilo, M. E., and Berridge, K. C. (2001). Comparative expression of hedonic impact: affective reactions to taste by human infants and other primates. *Neurosci. Biobehav. Rev.* 25, 53–74. doi:10.1016/S0149-7634(00)00051-8

Stewart, C.-B., and Disotell, T. R. (1998). Primate evolution – in and out of Africa. *Curr. Biol.* 8, R582–R588. doi:10.1016/S0960-9822(07)00367-3

Tate, A. J., Fischer, H., Leigh, A. E., and Kendrick, K. M. (2006). Behavioral and neurophysiological evidence for face identity and face emotion processing in animals. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 361, 2155–2172. doi:10.1098/rstb.2006.1937

Taylor, R. W., Hsieh, Y. W., Gamse, J. T., and Chuang, C. F. (2010). Making a difference together: reciprocal interactions in *C. elegans* and zebrafish asymmetric neural development. *Development* 137, 681–691. doi:10.1242/dev.038695

Tucker, D. M., Watson, R. T., and Heilman, K. M. (1977). Discrimination and evocation of affectively intoned speech in patients with right parietal disease. *Neurology* 27, 947–950. doi:10.1212/WNL.27.10.947

Vallortigara, G. (2006). The evolutionary psychology of left and right: costs and benefits of lateralization. *Dev. Psychobiol.* 48, 418–427. doi:10.1002/dev.20166

Vermeire, B. A., and Hamilton, C. R. (1998). Effects of facial identity, facial expression, and subject's sex on laterality in monkeys. *Laterality* 3, 1–19. doi:10.1080/135765098397377

Waller, B. M., Vick, S.-J., Parr, L. A., Bard, K. A., Pasqualini, M. C. S., Gothard, K. M., et al. (2006). Intramuscular electrical stimulation of facial muscles in humans and chimpanzees: duchenne revisited and extended. *Emotion* 6, 367–382. doi:10.1037/1528-3542.6.3.367

Wallez, C., Schaeffer, J., Meguerditchian, A., Vauclair, J., Schapiro, S. J., and Hopkins, W. D. (2012). Contrast of hemispheric lateralization for oro-facial movements between learned attention-getting sounds and species-typical vocalizations in chimpanzees: extension in a second colony. *Brain Lang.* 123, 75–79. doi:10.1016/j.bandl.2012.07.002

Wallez, C., and Vauclair, J. (2011). Right hemisphere dominance for emotion processing in baboons. *Brain Cogn.* 75, 164–169. doi:10.1016/j.bandc.2010.11.004

Wallez, C., and Vauclair, J. (2012). First evidence of population-level oro-facial asymmetries during the production of distress calls by macaque (*Macaca mulatta*) and baboon (*Papio anubis*) infants. *Behav. Brain Res.* 234, 69–75. doi:10.1016/j.bbr.2012.06.004

Wallez, C., and Vauclair, J. (in press). Human (*Homo sapiens*) and baboon (*Papio papio*) chimeric face processing: right hemisphere involvement. *J. Comp. Psychol.* doi:10.1037/a0031494

Ward, J. P. (1991). "Prosimians as animal models in the study of neural lateralization," in *Cerebral Laterality: Theory and Research*, ed. F. L. Kitterle (Hillsdale, NJ: Lawrence Erlbaum Associates, Inc), 1–18.

Wildgruber, D., Riecker, A., Hertrich, I., Erb, M., Grodd, W., Ethofer, T., et al. (2005). Identification of emotional intonation evaluated by fMRI. *Neuroimage* 24, 1233–1241. doi:10.1016/j.neuroimage.2004.10.034

Wittling, W., and Roschmann, R. (1993). Emotion-related hemisphere asymmetry: subjective emotional responses to laterally presented films. *Cortex* 29, 431–448. doi:10.1016/S0010-9452(13)80252-3

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Hemispheric lateralization interrupted: material-specific memory deficits in temporal lobe epilepsy

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The hemispheric lateralization of memory has largely been informed through the study of patients with temporal lobe epilepsy originating from medial temporal sources (mTLE). The material-specific model of memory relies on the basic framework that the left temporal lobe mediates verbal memories, while the right temporal lobe mediates non-verbal memories. Over the years, this model has been refined, and even challenged, as our understanding of the material-specific memory deficits in mTLE has been further elaborated in the neuropsychological and neuroimaging literature. The first goal of this mini-review is to highlight the major findings in the mTLE literature that have advanced and expanded our understanding of material-specific memory deficits in mTLE. Second, we will review how functional neuroimaging patterns of material-specific hemispheric lateralization in mTLE are being translated into the innovative clinical application of preoperative fMRI memory mapping.

Keywords: material-specific, memory, hemispheric lateralization, temporal lobe epilepsy, fMRI

INTRODUCTION

Temporal lobe epilepsy (TLE) is the most common form of localization-related epilepsy in adults, accounting for approximately 60% of cases (Hauser et al., 1991). The most common site of epileptogenesis in TLE originates from medial temporal lobe (MTL) structures, including the hippocampus and anterior subregions (including anterior parahippocampal cortex) (McMillan et al., 1987; Meencke and Veith, 1992; Wolf et al., 1993; Blume, 2006). Medial TLE (mTLE) is often poorly controlled with medications and class I evidence supports the use of surgical resections, specifically anterior temporal lobe resections (ATLR). Both the underlying disease focus and surgical management of mTLE can lead to significant disruption of function within regions and networks that are critically involved in memory function (Fisher et al., 2000; Lee et al., 2002; Sabsevitz et al., 2003; Stroup et al., 2003; Gleissner et al., 2004; Baxendale et al., 2006; Lineweaver et al., 2006; Binder et al., 2008; Hermann and Seidenberg, 2008). The study of memory deficits resulting from the underlying pathology and surgical management of mTLE has been the foundation for much of our understanding regarding memory function (Scoville and Milner, 1957; Penfield and Milner, 1958; Milner, 1970). One of the most influential frameworks describes the hemispheric specialization of memory based on verbal and non-verbal characteristics. The material-specific model dates back to Brenda Milner's observation that post-operative lesions in the left MTL resulted in abnormalities in verbal memory, while right temporal lobe lesions caused reductions in memory for non-verbal material (assuming left cerebral language dominance) (Milner, 1966). Based on the foundation of material-specific memory deficits, our understanding of hemispheric lateralization of memory function has expanded over time (for a review, see Saling, 2009) and continues to be a heuristic employed in clinical practice and surgical decision making in mTLE (Baxendale, 2008). In fact, material-specific fMRI patterns of hemispheric asymmetry are currently being investigated as a means to estimate the risk for memory decline following ATLR in mTLE. Unlike other reviews on the material-specific memory in mTLE, we focus that later part of this mini-review on the translation of these imaging methods to preoperative clinical mapping.

MATERIAL-SPECIFIC MEMORY MODEL
Hemispheric specialization of memory, such that verbal learning and memory is more dependent on dominant (usually left) hemisphere medial temporal lobe structures, and visuospatial learning is more dependent on medial temporal structures within the non-dominant hemisphere

PRESURGICAL DECISION MAKING
The decision to pursue surgical options (lesionectomy, lobectomy, etc.) is based on information gathered regarding: clinical history, electroencephalographic (EEG) data, neuroimaging data (MRI, PET, MEG), neuropsychological testing, and psychosocial functioning

SURGICAL MANAGEMENT OF FOCAL EPILEPSIES
The goal of epilepsy surgery is to identify an area of abnormal cortex from which seizures originate and remove it without causing damage to surrounding functioning tissue

A number of neuropsychological and neuroimaging studies have demonstrated a relationship between material-specific memory impairment and lateralized MTL dysfunction in mTLE (Jones-Gotman, 1986; Seidenberg et al., 1996; Helmstaedter et al., 1997, 2003; Jones-Gotman et al., 1997, 2010; Gleissner et al., 1998; Pillon et al., 1999; Golby et al., 2002; Powell et al., 2005).

However, inconsistencies have also been reported (for a review, see Saling, 2009) and our understanding of the functional specialization of temporal regions in material-specific memory and the participation of these functionally specialized nodes in a larger network framework of memory processes is still evolving. The variability in the material-specific findings in mTLE has also broadened our understanding of mTLE as a network disease that can affect the function of or connections between any number of nodes that are critical for memory. For instance, material-specific memory deficits in pre- and post-operative mTLE can result from focal dysfunction in subregions within the MTL, including the hippocampus and parahippocampal and entorhinal cortices, dysfunction within the lateral temporal lobe, and disconnections between MTL and ipsilateral cortical connections. mTLE has also been associated with patterns of disrupted functional localization and lateralization resulting from functional reorganization or compensatory regional involvement (Adcock et al., 2003; Thivard et al., 2005), which has allowed for the investigation of the functional implications of neuroplastic changes.

MATERIAL-SPECIFIC MEMORY DEFICITS AND mTLE

The link between verbal memory deficits and the language-dominant mTLE is one of the most consistent patterns of material-specific memory deficits in mTLE (Jones-Gotman et al., 2000), although variability in verbal memory findings can be elicited by accounting for certain task-specific factors (Saling et al., 2002; Saling, 2009). In the non-verbal domain, evidence for a specific link between the right temporal lobe and spatial memory is considerably weaker. Some have argued that visual-spatial memory is a bilateral process, which may largely be mediated by the verbalizability of the information to be learned (van Asselen et al., 2006). To-date, pre- and post-operative ATLR studies using neuropsychological and neuroimaging techniques have produced a myriad of inconclusive data that support non-lateralized findings, including measures of navigation (Maguire et al., 1996; Jokeit et al., 2001), maze learning (Bohbot et al., 1998; Astur et al., 2002), scene recognition (Maguire and Cipolotti, 1998; Spiers et al., 2001a), plan drawing (Spiers et al., 2001b), abstract design (Piguet et al., 1994; Dige and Wik, 2001), and faces (Hermann et al., 1997; Reminger et al., 2004). Furthermore, a number of standard tests of visuospatial memory, including the Rey–Osterrieth Complex Figure, commonly used in evaluation of mTLE, do not reliably distinguish between left and right mTLE (Lee et al., 2002; McConley et al., 2008).

Studies focused on understanding the inconsistencies in the patterns of material-specific memory deficits in mTLE have found evidence for functional dissociations based on the variable influence of extratemporal, intratemporal, and intra-MTL regional dysfunction and highlight the larger network context that can be disrupted by mTLE pathology and surgical management.

EXTRATEMPORAL CORTICAL INFLUENCES

Extratemporal neocortical and connectivity abnormalities in mTLE have been reported both contralateral and ipsilateral to the side of seizure onset (Oyegbile et al., 2004; McDonald et al., 2008; Mueller et al., 2010; Ji et al., 2013). Below we discuss three examples of extratemporal influence over material-specific findings in unilateral mTLE.

Frontal lobe language functions

In cases of language-dominant mTLE, extent of hemispheric disruption has the potential to impact language functioning or adequacy (Hermann et al., 1988, 1992). It has been suggested that the strong connections between the inferior frontal cortex and the MTL make frontal lobe language functions particularly sensitive to MTL pathology (Powell et al., 2004). In fact, diffusion tensor imaging (DTI) evidence for reduced left hemisphere language connections in patients with left mTLE compared to both controls and right mTLE patients has been reported (Powell et al., 2007). Functionally, language adequacy has been shown to act as a significant confound when lateralizing verbal memory encoding (Hermann et al., 1988, 1992; Saling et al., 2002). That is, when controlling for language adequacy on a word-list learning task, performance does not correspond with side of seizure focus (right or left) (Hermann et al., 1988, 1992; Saling et al., 2002). Therefore, list-learning performance appears to be less specific to unilateral MTL pathology, and instead corresponds more strongly to extratemporal language processes. Interestingly, retention of verbal information over a delay period has been shown to be less influenced by language adequacy making it a stronger marker of MTL function in left mTLE (Hermann et al., 1988, 1992; Saling et al., 2002).

Frontal lobe memory functions

In addition to material-specific patterns of hemispheric asymmetry, neuroimaging studies have found evidence for hemispheric asymmetries within the frontal lobes that corresponds to the component stages of memory (encoding and retrieval) (for reviews, see Desgranges et al., 1998; Cabeza and Nyberg, 2000; Lepage et al., 2000; Fletcher and Henson, 2001). The "hemispheric encoding and retrieval asymmetry" (HERA) model argues that there are observable hemispheric differences according to the stage of memory processing – encoding being preferentially associated with left frontal regions, and memory retrieval showing greater right-sided frontal activation regardless of material type (Desgranges et al., 1998; McDermott et al., 1999; Cabeza and Nyberg, 2000; Lepage et al., 2000; Nyberg et al., 2000; Fletcher and Henson, 2001; Grady et al., 2001; Johnson et al., 2003). Kennepohl et al. (2007) reported convincing evidence within the MTL that aligns with the HERA pattern – the left entorhinal cortex was significantly more active than the right regardless of material type during encoding trials. They found less convincing evidence for the lateralization of retrieval to the right MTL. The work of Kennepohl et al. (2007) raises the possibility that some variability associated with material-specific memory deficits in mTLE could be accounted for by other factors related to hemispheric asymmetries. Future studies in mTLE could be designed to take the HERA pattern into account to further deconstruct the functional specialization of MTL regions and their relationship to post-operative memory outcomes.

Parietal and striatal contributions

The neuroimaging literature suggests that a consistent network of brain regions participates in spatial navigation, including the hippocampus proper, the parietal lobe, striatum, occipitotemporal regions, cingulate cortex, and parahippocampal cortices

(Aguirre et al., 1996, 1998; Maguire, 1997; Maguire et al., 1998; Jokeit et al., 2001). Two basic strategies in spatial navigation have been described – egocentric and allocentric (Iaria et al., 2003). Allocentric navigation strategies use landmarks and the spatial relationship to a target in order to create a visual map of the environment. Animal and human studies have found support to link allocentric navigation to MTL structures, including the hippocampus and parahippocampal cortex (O'Keefe and Dostrovsky, 1971; Morris et al., 1982; Bohbot et al., 1998, 2004). Egocentric navigation, which describes determining the position of targets in an environment relative to one's body or position, has been localized to regions within the parietal lobe and striatum in animals and humans (Wiener, 1993; Weniger et al., 2009). Therefore, task-specific features and the extent of potential extratemporal mTLE-related pathology, mainly along MTL-parietal and MTL-striatal connections, may account for variability of visuospatial memory in mTLE.

Spatial navigation studies have also shown patterns of dynamic interaction between right and left temporal regions, and both left and right mTLE patients have demonstrated impairment (Maguire et al., 1996; Astur et al., 2002; Glikmann-Johnston et al., 2008; Canovas et al., 2011). Similarly, measures of object-location have found evidence for bilateral temporal contributions (Baxendale et al., 1998; Incisa della Rochetta et al., 2004; Kessels et al., 2004; Stepankova et al., 2004); although, most studies suggest that the ability to navigate, learn, and recall arbitrarily related objects and locations is right lateralized (Abrahams et al., 1997, 1999; Bohbot et al., 1998; Johnsrude et al., 1999; Duzel et al., 2003; Crane and Milner, 2005; Parslow et al., 2005; Diaz-Asper et al., 2006; Piekema et al., 2006). Overall, the potential bilateral nature of spatial memory may limit the detection of material-specific patterns, particularly during spatial navigation tasks.

INTRATEMPORAL ORGANIZATION

Medial and lateral divisions of the temporal lobes are variably affected by mTLE and surgical resections (Fisher et al., 2000; Lee et al., 2002; Sabsevitz et al., 2003; Stroup et al., 2003; Gleissner et al., 2004; Baxendale et al., 2006; Lineweaver et al., 2006; Binder et al., 2008; Hermann and Seidenberg, 2008) and can influence the nature and extent of memory deficits. Below we discuss the findings related to the underlying semantic structure of verbal memory tasks and contributions of task-specific factors to material-specific verbal memory deficits in mTLE.

Semantic-arbitrary distinction

Performance on verbal memory tasks consistently varies relative to the degree the task draws on pre-existing semantic associations (Saling et al., 2002; Saling, 2009). Verbal paired-associate learning studies have shown that patients with language-dominant seizure foci are typically impaired when it comes to learning arbitrary word-pairs. This is known as the semantic-arbitrary distinction and is also supported by studies of story memory (Rausch and Babb, 1987; Saling et al., 1993). However, language-dominant MTL seizure foci do not reliably interfere with learning semantically related word-pairs (Saling et al., 1993, 2002). Similarly, both patients with right and left mTLE tend to be mildly impaired on story memory tasks, which are rich in semantic context (Saling et al., 1993, 2002). Findings related to the semantic-arbitrary distinction also extend to list-learning tasks that allow for semantic clustering (Helmstaedter et al., 1997; Saling et al., 2002), such that the presence of a semantic clustering component may mask a performance deficit on a list-learning task and interfere with the detection of memory impairment linked to underlying language-dominant MTL dysfunction.

In contrast, arbitrary paired-associate learning has been correlated with imaging findings in left mesial temporal structures, specifically the perirhinal cortex (Lillywhite et al., 2007) and the arbitrary-semantic effect has been confirmed in left mTLE patients following standard *en bloc* resections (Helmstaedter and Elger, 1996; Helmstaedter et al., 1997; Saling et al., 2002). More specifically, a lateral to medial gradient has been reported, such that medial structures have been shown to play a critical role in forming arbitrary associations, but are not necessary if semantic associations are pre-existing (Saling et al., 2002). In the pre-existing semantic conditions, cortical or lateral regions are recruited due to their involvement in housing semantic stores (Lillywhite et al., 2007; Saling, 2009).

INTRA-MTL REGIONAL SPECIALIZATION

The exact nature of the discrete functional contributions of MTL structures to memory processes remains a matter of intense debate, particularly within the literature on component processes of recognition memory (Aggleton and Brown, 2006; Eichenbaum et al., 2007, 2012; Squire et al., 2007; Henke, 2010). Below we discuss the predominant models of intra-MTL functional specialization during encoding and recognition.

Item-in-context model of encoding

Based on the collection of findings from the recollection and familiarity literature (for reviews, see Davachi, 2006; Diana et al., 2007; Eichenbaum et al., 2007), Eichenbaum et al. (2012) proposed a model of episodic memory encoding or "item-in-context" memory. Work in both animals and humans, argues that cortical inputs along the ventral "what" stream first process information regarding objects and events in perirhinal and lateral entorhinal regions, while information regarding spatial context from the dorsal "where" stream is processed by the medial entorhinal and parahippocampal cortex (Suzuki and Amaral, 1994; Furtak et al., 2007; Kerr et al., 2007; van Strien et al., 2009; Wang et al., 2011). Encoding of episodic memories is then proposed to involve the binding or convergence of object and context information from these regions within the hippocampus. Retrieval of episodic memories when cued by either an object or context would reactivate the bound representation within the hippocampus and retrieve the corresponding item or context information by reactivating the "what" and "where" streams (Eichenbaum et al., 2012). The item-in-context model of encoding is consistent with the idea of a medial-lateral gradient of temporal lobe functional specialization discussed above, wherein medial structures are necessary to form novel or arbitrary associations.

Recollection and familiarity

Most agree that recognition memory consists of two processes: recollection and familiarity. Recollection refers to the recognition of a stimulus that is bound to contextual details, while familiarity describes an awareness of a stimulus in the absence of contextual details from the original encoding episode (for reviews, see Yonelinas and Levy, 2002; Skinner and Fernandes, 2007). The dual process model suggests that these two processes are mediated by distinct MTL systems; with recollection linked to hippocampal function and familiarity associated with the perirhinal cortex (Aggleton and Brown, 1999, 2006; Yonelinas and Levy, 2002; Eichenbaum et al., 2007). The study of surgical mTLE patients has made a strong case for the dual process model. In fact, Bowles et al. (2007, 2010) have demonstrated a double dissociation, wherein standard ATLR mTLE patients exhibited isolated impairments in recollection and sparing of familiarity processes, while patient NB, who underwent a resection localized to the perirhinal and entorhinal cortices, displayed a selective familiarity impairment (Bowles et al., 2007, 2010). A number of functional imaging studies have also reported that activation of the hippocampus occurs with episodic recollection and memory for associations and context, whereas activation of the perirhinal and parahippocampal cortex is linked with familiarity (for reviews, see Davachi, 2006; Diana et al., 2007; Eichenbaum et al., 2007). Bowles et al. (2010) also showed that overall recognition performance was comparable between the ATLR patients and patient NB, which provides evidence against the main counterargument to the dual process model that states the functional specialization of MTL regions is primarily related to memory strength (Squire et al., 2004, 2007; Wais et al., 2008).

fMRI MEMORY MAPPING FOR PREOPERATIVE PREDICTION OF MEMORY OUTCOMES

Mapping brain memory patterns using Blood oxygen dependent (BOLD) fMRI has been gaining momentum in clinical practice as a means to estimate the risk for memory decline following ATLR in mTLE. The foundation for clinical fMRI mapping is based on the patterns of material-specific findings discussed above, as well as patterns of neuroplasticity and reorganization and their relationship to outcome measures. While there are still methodological and even material-specific challenges (Jansen et al., 2009; Binder, 2011), preoperative fMRI memory mapping has the potential to be a promising addition to the current methods of outcome prediction and as a non-invasive alternative to the intracarotid amytal test (IAT).

ESTIMATING POTENTIAL FUNCTIONAL DEFICITS

Neuropsychological testing, the intracarotid amytal test (IAT), and electrocorticography are the current gold standard for determining whether cognitive or functional decline might be anticipated following ATLR

Neuroimaging studies in mTLE have revealed functionally asymmetric patterns of activation within MTL structures contralateral to the seizure foci during material-specific encoding (Golby et al., 2002; Powell et al., 2007; Banks et al., 2012; Alessio et al., 2013; Sidhu et al., 2013). Functional asymmetries have been associated with variability in neural reorganization within different populations of mTLE patients (Mechanic-Hamilton et al., 2009), with greater asymmetries in mTLE patients with an early age of onset compared to patients with later onset (corresponding to the literature on language lateralization in mTLE). However, it is unclear how well patterns of contralateral activation reflect compensatory activation, as performance levels do not always equate between control subjects and patients (Richardson et al., 2006; Powell et al., 2007). As a result, some have argued that contralateral activation is more appropriately regarded as a marker of network disruption (Powell et al., 2007).

Predictive studies of memory outcomes following ATLR have generally relied on two perspectives to guide decision making (Chelune et al., 1991; Chelune, 1995). The functional reserve hypothesis proposes that the level of functioning of the hippocampus contralateral to the seizure focus will determine the memory outcome. In contrast, the functional adequacy model predicts that post-operative memory outcome will be inversely related to the level of preoperative functioning of the tissue to be resected (Chelune, 1995; Chelune and Najm, 2000).

The functional adequacy model is supported by findings that demonstrate mTLE patients with better preoperative memory functioning are at greater risk for significant memory declines, than patients with low average or poor preoperative memory functioning (Chelune et al., 1991; Hermann et al., 1995; Helmstaedter and Elger, 1996; Jokeit et al., 1997; Davies et al., 1998; Stroup et al., 2003; Gleissner et al., 2004; Baxendale et al., 2006, 2007; Lineweaver et al., 2006; Bonelli et al., 2010). fMRI studies have also been supportive of the functional adequacy model, suggesting that patients with greater ipsilateral activation compared to contralateral MTL activation have greater memory decline following temporal lobectomy (Binder et al., 2008; Frings et al., 2008; Powell et al., 2008; Bonelli et al., 2010; Dupont et al., 2010). Interestingly, a recent DTI study has also shown that stronger connectivity between a default mode network node in the posterior cingulate cortex and the epileptogenic hippocampus, compared to the contralateral hippocampus, has also been linked to greater post-operative memory decline, suggesting a broader network adequacy model (McCormick et al., 2013).

The functional reserve hypothesis has received less support; however, recent neuroimaging work has found evidence for a more nuanced understanding of the functional reserve hypothesis based on anterior and posterior divisions of the MTL (Bonelli et al., 2010). Support for the functional adequacy model was found in patterns of anterior MTL activation, such that the greater asymmetry toward the left was associated with greater decline in verbal memory (Bonelli et al., 2010). However, support for a functional reserve hypothesis was found in patterns of activation in the posterior MTL ROI such that greater asymmetry toward the left was associated *less* verbal memory decline after ATLR (Bonelli et al., 2010). The authors interpreted the posterior findings as intrahemispheric or intra-MTL reorganization of anterior MTL function. Recent data also suggests that the functional reserve and adequacy models may apply differently in the context of right or left MTL seizure foci: memory outcomes for patients with left mTLE may be best predicted by well-functioning right MTL, while patients with right mTLE might be more dependent on the extent of remaining memory function with ipsilateral MTL structures (Banks et al., 2012).

SUMMARY

The underlying focal pathology and surgical management of mTLE has informed much of our understanding about the material-specific lateralization of memory function. As research methodologies and cognitive theories have been developed, their application to the study of memory deficits in mTLE has refined and even challenged the model of material-specificity. Within the verbal domain, recent work has highlighted the importance of accounting for language adequacy and pre-existing semantic associations. The association between non-verbal deficits and right mTLE has been less consistent than the link between verbal memory and left mTLE, but tasks such as object-location binding have demonstrated promise. Finally, mTLE patients demonstrate aberrant lateralization of activation patterns on functional neuroimaging studies during material-specific memory tasks. These patterns are now being investigated as potential tools for clinical mapping to estimate post-operative memory outcomes following ATLRs.

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REFERENCES

Abrahams, S., Morris, R. G., Polkey, C. E., Jarosz, J. M., Cox, T. C., Graves, M., et al. (1999). Hippocampal involvement in spatial and working memory: a structural MRI analysis of patients with unilateral mesial temporal lobe sclerosis. *Brain Cogn.* 41, 39–65. doi:10.1006/brcg.1999.1095

Abrahams, S., Pickering, A., Polkey, C. E., and Morris, R. G. (1997). Spatial memory deficits in patients with unilateral damage to the right hippocampal formation. *Neuropsychologia* 35, 11–24. doi:10.1016/S0028-3932(96)00051-6

Adcock, J. E., Wise, R. G., Oxbury, J. M., Oxbury, S. M., and Matthews, P. M. (2003). Quantitative fMRI assessment of the differences in lateralization of language-related brain activation in patients with temporal lobe epilepsy. *Neuroimage* 18, 423–438. doi:10.1016/S1053-8119(02)00013-7

Aggleton, J. P., and Brown, M. W. (1999). Episodic memory, amnesia, and the hippocampal-anterior thalamic axis. *Behav. Brain Sci.* 22, 425–444. doi:10.1017/S0140525X99002034 discussion 444-489,

Aggleton, J. P., and Brown, M. W. (2006). Interleaving brain systems for episodic and recognition memory. *Trends Cogn. Sci. (Regul. Ed.)* 10, 455–463. doi:10.1016/j.tics.2006.08.003

Aguirre, G. K., Detre, J. A., Alsop, D. C., and D'Esposito, M. (1996). The parahippocampus subserves topographical learning in man. *Cereb. Cortex* 6, 823–829. doi:10.1093/cercor/6.6.823

Aguirre, G. K., Zarahn, E., and D'Esposito, M. (1998). Neural components of topographical representation. *Proc. Natl. Acad. Sci. U.S.A.* 95, 839–846. doi:10.1073/pnas.95.3.839

Alessio, A., Pereira, F. R., Sercheli, M. S., Rondina, J. M., Ozelo, H. B., Bilevicius, E., et al. (2013). Brain plasticity for verbal and visual memories in patients with mesial temporal lobe epilepsy and hippocampal sclerosis: an fMRI study. *Hum. Brain Mapp.* 34, 186–199. doi:10.1002/hbm.21432

Astur, R. S., Taylor, L. B., Mamelak, A. N., Philpott, L., and Sutherland, R. J. (2002). Humans with hippocampus damage display severe spatial memory impairments in a virtual Morris water task. *Behav. Brain Res.* 132, 77–84. doi:10.1016/S0166-4328(01)00399-0

Banks, S. J., Sziklas, V., Sodums, D. J., and Jones-Gotman, M. (2012). fMRI of verbal and nonverbal memory processes in healthy and epileptogenic medial temporal lobes. *Epilepsy Behav.* 25, 42–49. doi:10.1016/j.yebeh.2012.07.003

Baxendale, S. (2008). The impact of epilepsy surgery on cognition and behavior. *Epilepsy Behav.* 12, 592–599. doi:10.1016/j.yebeh.2007.12.015

Baxendale, S., Thompson, P., Harkness, W., and Duncan, J. (2006). Predicting memory decline following epilepsy surgery: a multivariate approach. *Epilepsia* 47, 1887–1894. doi:10.1111/j.1528-1167.2006.00810.x

Baxendale, S., Thompson, P., Harkness, W., and Duncan, J. (2007). The role of the intracarotid amobarbital procedure in predicting verbal memory decline after temporal lobe resection. *Epilepsia* 48, 546–552. doi:10.1111/j.1528-1167.2006.00940.x

Baxendale, S. A., Thompson, P. J., and Van Paesschen, W. (1998). A test of spatial memory and its clinical utility in the pre-surgical investigation of temporal lobe epilepsy patients. *Neuropsychologia* 36, 591–602. doi:10.1016/S0028-3932(97)00163-2

Binder, J. R. (2011). Functional MRI is a valid noninvasive alternative to Wada testing. *Epilepsy Behav.* 20, 214–222. doi:10.1016/j.yebeh.2010.08.004

Binder, J. R., Sabsevitz, D. S., Swanson, S. J., Hammeke, T. A., Raghavan, M., and Mueller, W. M. (2008). Use of preoperative functional MRI to predict verbal memory decline after temporal lobe epilepsy surgery. *Epilepsia* 49, 1377–1394. doi:10.1111/j.1528-1167.2008.01625.x

Blume, W. T. (2006). The progression of epilepsy. *Epilepsia* 47(Suppl. 1), 71–78. doi:10.1111/j.1528-1167.2006.00665.x

Bohbot, V. D., Iaria, G., and Petrides, M. (2004). Hippocampal function and spatial memory: evidence from functional neuroimaging in healthy participants and performance of patients with medial temporal lobe resections. *Neuropsychology* 18, 418–425. doi:10.1037/0894-4105.18.3.418

Bohbot, V. D., Kalina, M., Stepankova, K., Spackova, N., Petrides, M., and Nadel, L. (1998). Spatial memory deficits in patients with lesions to the right hippocampus and to the right parahippocampal cortex. *Neuropsychologia* 36, 1217–1238. doi:10.1016/S0028-3932(97)00161-9

Bonelli, S. B., Powell, R. H., Yogarajah, M., Samson, R. S., Symms, M. R., Thompson, P. J., et al. (2010). Imaging memory in temporal lobe epilepsy: predicting the effects of temporal lobe resection. *Brain* 133, 1186–1199. doi:10.1093/brain/awq006

Bowles, B., Crupi, C., Mirsattari, S. M., Pigott, S. E., Parrent, A. G., Pruessner, J. C., et al. (2007). Impaired familiarity with preserved recollection after anterior temporal-lobe resection that spares the hippocampus. *Proc. Natl. Acad. Sci. U.S.A.* 104, 16382–16387. doi:10.1073/pnas.0705273104

Bowles, B., Crupi, C., Pigott, S., Parrent, A., Wiebe, S., Janzen, L., et al. (2010). Double dissociation of selective recollection and familiarity impairments following two different surgical treatments for temporal-lobe epilepsy. *Neuropsychologia* 48, 2640–2647. doi:10.1016/j.neuropsychologia.2010.05.010

Cabeza, R., and Nyberg, L. (2000). Imaging cognition II: an empirical review of 275 PET and fMRI studies. *J. Cogn. Neurosci.* 12, 1–47. doi:10.1162/08989290051137585

Canovas, R., Leon, I., Serrano, P., Roldan, M. D., and Cimadevilla, J. M. (2011). Spatial navigation impairment in patients with refractory temporal lobe epilepsy: evidence from a new virtual reality-based task. *Epilepsy Behav.* 22, 364–369. doi:10.1016/j.yebeh.2011.07.021

Chelune, G., and Najm, I. M. (2000). "Risk factors associated with post-surgical decrements in memory," in *Epilepsy Surgery*, eds H. Luders and Y. Comair (Philadelphia: Lippincott), 497–504.

Chelune, G. J. (1995). Hippocampal adequacy versus functional reserve: predicting memory functions following temporal lobectomy. *Arch. Clin. Neuropsychol.* 10, 413–432. doi:10.1093/arclin/10.5.413

Chelune, G. J., Naugle, R. I., Luders, H., and Awad, I. A. (1991). Prediction of cognitive change as a function of preoperative ability status among temporal lobectomy patients seen at 6-month follow-up. *Neurology* 41, 399–404. doi:10.1212/WNL.41.3.399

Crane, J., and Milner, B. (2005). What went where? Impaired object-location learning in patients with right hippocampal lesions. *Hippocampus* 15, 216–231. doi:10.1002/hipo.20043

Davachi, L. (2006). Item, context and relational episodic encoding in humans. *Curr. Opin. Neurobiol.* 16, 693–700. doi:10.1016/j.conb.2006.10.012

Davies, K. G., Bell, B. D., Bush, A. J., and Wyler, A. R. (1998). Prediction of verbal memory loss in individuals after anterior temporal lobectomy. *Epilepsia* 39, 820–828. doi:10.1111/j.1528-1157.1998.tb01175.x

Desgranges, B., Baron, J. C., and Eustache, F. (1998). The functional neuroanatomy of episodic memory: the role of the frontal lobes, the hippocampal formation, and other areas. *Neuroimage* 8, 198–213. doi: 10.1006/nimg.1998.0359

Diana, R. A., Yonelinas, A. P., and Ranganath, C. (2007). Imaging recollection and familiarity in the medial temporal lobe: a three-component model. *Trends Cogn. Sci. (Regul. Ed.)* 11, 379–386. doi:10.1016/j.tics.2007.08.001

Diaz-Asper, C. M., Dopkins, S., Potolicchio, S. J. Jr., and Caputy, A. (2006). Spatial memory following temporal lobe resection. *J. Clin. Exp. Neuropsychol.* 28, 1462–1481. doi:10.1080/13803390500434359

Dige, N., and Wik, G. (2001). A visual learning and memory test for preoperative evaluation of patients with temporal lobe epilepsy. *Int. J. Neurosci.* 111, 167–174. doi:10.3109/00207450108994228

Dupont, S., Duron, E., Samson, S., Denos, M., Volle, E., Delmaire, C., et al. (2010). Functional MR imaging or Wada test: which is the better predictor of individual postoperative memory outcome? *Radiology* 255, 128–134. doi:10.1148/radiol.09091079

Duzel, E., Habib, R., Rotte, M., Guderian, S., Tulving, E., and Heinze, H. J. (2003). Human hippocampal and parahippocampal activity during visual associative recognition memory for spatial and nonspatial stimulus configurations. *J. Neurosci.* 23, 9439–9444.

Eichenbaum, H., Sauvage, M., Fortin, N., Komorowski, R., and Lipton, P. (2012). Towards a functional organization of episodic memory in the medial temporal lobe. *Neurosci. Biobehav. Rev.* 36, 1597–1608. doi: 10.1016/j.neubiorev.2011.07.006

Eichenbaum, H., Yonelinas, A. P., and Ranganath, C. (2007). The medial temporal lobe and recognition memory. *Annu. Rev. Neurosci.* 30, 123–152. doi:10.1146/annurev.neuro.30.051606.094328

Fisher, R. S., Vickrey, B. G., Gibson, P., Hermann, B., Penovich, P., Scherer, A., et al. (2000). The impact of epilepsy from the patient's perspective I. Descriptions and subjective perceptions. *Epilepsy Res.* 41, 39–51. doi:10.1016/S0920-1211(00)00128-5

Fletcher, P. C., and Henson, R. N. (2001). Frontal lobes and human memory: insights from functional neuroimaging. *Brain* 124, 849–881. doi:10.1093/brain/124.5.849

Frings, L., Wagner, K., Halsband, U., Schwarzwald, R., Zentner, J., and Schulze-Bonhage, A. (2008). Lateralization of hippocampal activation differs between left and right temporal lobe epilepsy patients and correlates with postsurgical verbal learning decrement. *Epilepsy Res.* 78, 161–170. doi:10.1016/j.eplepsyres.2007.11.006

Furtak, S. C., Wei, S. M., Agster, K. L., and Burwell, R. D. (2007). Functional neuroanatomy of the parahippocampal region in the rat: the perirhinal and postrhinal cortices. *Hippocampus* 17, 709–722. doi:10.1002/hipo.20314

Gleissner, U., Helmstaedter, C., and Elger, C. E. (1998). Right hippocampal contribution to visual memory: a presurgical and postsurgical study in patients with temporal lobe epilepsy. *J. Neurol. Neurosurg. Psychiatr.* 65, 665–669. doi:10.1136/jnnp.65.5.665

Gleissner, U., Helmstaedter, C., Schramm, J., and Elger, C. E. (2004). Memory outcome after selective amygdalohippocampectomy in patients with temporal lobe epilepsy: one-year follow-up. *Epilepsia* 45, 960–962. doi:10.1111/j.0013-9580.2004.42203.x

Glikmann-Johnston, Y., Saling, M. M., Chen, J., Cooper, K. A., Beare, R. J., and Reutens, D. C. (2008). Structural and functional correlates of unilateral mesial temporal lobe spatial memory impairment. *Brain* 131, 3006–3018. doi:10.1093/brain/awn213

Golby, A. J., Poldrack, R. A., Illes, J., Chen, D., Desmond, J. E., and Gabrieli, J. D. (2002). Memory lateralization in medial temporal lobe epilepsy assessed by functional MRI. *Epilepsia* 43, 855–863. doi:10.1046/j.1528-1157.2002.20501.x

Grady, C. L., McIntosh, A. R., Beig, S., and Craik, F. I. (2001). An examination of the effects of stimulus type, encoding task, and functional connectivity on the role of right prefrontal cortex in recognition memory. *Neuroimage* 14, 556–571. doi: 10.1006/nimg.2001.0865

Hauser, W. A., Annegers, J. F., and Kurland, L. T. (1991). Prevalence of epilepsy in Rochester, Minnesota: 1940-1980. *Epilepsia* 32, 429–445. doi:10.1111/j.1528-1157.1991.tb04675.x

Helmstaedter, C., and Elger, C. E. (1996). Cognitive consequences of two-thirds anterior temporal lobectomy on verbal memory in 144 patients: a three-month follow-up study. *Epilepsia* 37, 171–180. doi:10.1111/j.1528-1157.1996.tb00009.x

Helmstaedter, C., Grunwald, T., Lehnertz, K., Gleissner, U., and Elger, C. E. (1997). Differential involvement of left temporolateral and temporomesial structures in verbal declarative learning and memory: evidence from temporal lobe epilepsy. *Brain Cogn.* 35, 110–131. doi:10.1006/brcg.1997.0930

Helmstaedter, C., Kurthen, M., Lux, S., Reuber, M., and Elger, C. E. (2003). Chronic epilepsy and cognition: a longitudinal study in temporal lobe epilepsy. *Ann. Neurol.* 54, 425–432. doi:10.1002/ana.10692

Henke, K. (2010). A model for memory systems based on processing modes rather than consciousness. *Nat. Rev. Neurosci.* 11, 523–532. doi:10.1038/nrn2850

Hermann, B., and Seidenberg, M. (2008). "Memory impairment and its cognitive context in epilepsy," in *Behavioral Aspects of Epilepsy: Principles and Practice*, eds D. L. Schacter, G. L. Holmes, and K.-N. Dga (New York: Demos), 147–153.

Hermann, B. P., Seidenberg, M., Haltiner, A., and Wyler, A. R. (1992). Adequacy of language function and verbal memory performance in unilateral temporal lobe epilepsy. *Cortex* 28, 423–433. doi:10.1016/S0010-9452(13)80152-9

Hermann, B. P., Seidenberg, M., Haltiner, A., and Wyler, A. R. (1995). Relationship of age at onset, chronologic age, and adequacy of preoperative performance to verbal memory change after anterior temporal lobectomy. *Epilepsia* 36, 137–145. doi:10.1111/j.1528-1157.1995.tb00972.x

Hermann, B. P., Seidenberg, M., Schoenfeld, J., and Davies, K. (1997). Neuropsychological characteristics of the syndrome of mesial temporal lobe epilepsy. *Arch. Neurol.* 54, 369–376. doi:10.1001/archneur.1997.00550160019010

Hermann, B. P., Wyler, A. R., Steenman, H., and Richey, E. T. (1988). The interrelationship between language function and verbal learning/memory performance in patients with complex partial seizures. *Cortex* 24, 245–253. doi:10.1016/S0010-9452(88)80033-9

Iaria, G., Petrides, M., Dagher, A., Pike, B., and Bohbot, V. D. (2003). Cognitive strategies dependent on the hippocampus and caudate nucleus in human navigation: variability and change with practice. *J. Neurosci.* 23, 5945–5952.

Incisa della Rochetta, A., Samson, S., Ehrle, N., Denos, M., Hasboun, D., and Baulad, M. (2004). Memory for visuospatial location following selective hippocampal sclerosis: the use of different coordinate systems. *Neuropsychology* 18, 15–28. doi:10.1037/0894-4105.18.1.15

Jansen, A., Sehlmeyer, C., Pfleiderer, B., Sommer, J., Konrad, C., Zwitserlood, P., et al. (2009). Assessment of verbal memory by fMRI: lateralization and functional neuroanatomy. *Clin. Neurol. Neurosurg.* 111, 57–62. doi:10.1016/j.clineuro.2008.08.005

Ji, G. J., Zhang, Z., Zhang, H., Wang, J., Liu, D. Q., Zang, Y. F., et al. (2013). Disrupted causal connectivity in mesial temporal lobe epilepsy. *PLoS ONE* 8:e63183. doi:10.1371/journal.pone.0063183

Johnson, M. K., Raye, C. L., Mitchell, K. J., Greene, E. J., and Anderson, A. W. (2003). FMRI evidence for an organization of prefrontal cortex by both type of process and type of information. *Cereb. Cortex* 13, 265–273. doi:10.1093/cercor/13.3.265

Johnsrude, I. S., Owen, A. M., Crane, J., Milner, B., and Evans, A. C. (1999). A cognitive activation study of memory for spatial relationships. *Neuropsychologia* 37, 829–841. doi:10.1016/S0028-3932(98)00136-5

Jokeit, H., Ebner, A., Holthausen, H., Markowitsch, H. J., Moch, A., Pannek, H., et al. (1997). Individual prediction of change in delayed recall of prose passages after left-sided anterior temporal lobectomy. *Neurology* 49, 481–487. doi:10.1212/WNL.49.2.481

Jokeit, H., Okujava, M., and Woermann, F. G. (2001). Memory fMRI lateralizes temporal lobe epilepsy. *Neurology* 57, 1786–1793. doi:10.1212/WNL.57.10.1786

Jones-Gotman, M. (1986). Right hippocampal excision impairs learning and recall of a list of abstract designs. *Neuropsychologia* 24, 659–670. doi: 10.1016/0028-3932(86)90005-9

Jones-Gotman, M., Harnadek, M. C., and Kubu, C. S. (2000). Neuropsychological assessment for temporal lobe epilepsy surgery. *Can. J. Neurol. Sci.* 27(Suppl. 1), S39–S43. discussion S50-32,

Jones-Gotman, M., Smith, M. L., Risse, G. L., Westerveld, M., Swanson, S. J., Giovagnoli, A. R., et al. (2010). The contribution of neuropsychology to diagnostic assessment in epilepsy. *Epilepsy Behav.* 18, 3–12. doi:10.1016/j.yebeh.2010.02.019

Jones-Gotman, M., Zatorre, R. J., Olivier, A., Andermann, F., Cendes, F., Staunton, H., et al. (1997). Learning and retention of words and designs following excision from medial or lateral temporal-lobe structures. *Neuropsychologia* 35, 963–973. doi:10.1016/S0028-3932(97)00024-9

Kennepohl, S., Sziklas, V., Garver, K. E., Wagner, D. D., and Jones-Gotman, M. (2007). Memory and the medial temporal lobe: hemispheric specialization reconsidered. *Neuroimage* 36, 969–978. doi:10.1016/j.neuroimage.2007.03.049

Kerr, K. M., Agster, K. L., Furtak, S. C., and Burwell, R. D. (2007). Functional neuroanatomy of the parahippocampal region: the lateral and medial entorhinal areas. *Hippocampus* 17, 697–708. doi:10.1002/hipo.20315

Kessels, R. P., Hendriks, M., Schouten, J., Van Asselen, M., and Postma, A. (2004). Spatial memory deficits in patients after unilateral selective amygdalohippocampectomy. *J. Int. Neuropsychol. Soc.* 10, 907–912. doi:10.1017/S1355617704106140

Lee, T. M., Yip, J. T., and Jones-Gotman, M. (2002). Memory deficits after resection from left or right anterior temporal lobe in humans: a meta-analytic review. *Epilepsia* 43, 283–291. doi:10.1046/j.1528-1157.2002.09901.x

Lepage, M., Ghaffar, O., Nyberg, L., and Tulving, E. (2000). Prefrontal cortex and episodic memory retrieval mode. *Proc. Natl. Acad. Sci. U.S.A.* 97, 506–511. doi:10.1073/pnas.97.1.506

Lillywhite, L. M., Saling, M. M., Briellmann, R. S., Weintrob, D. L., Pell, G. S., and Jackson, G. D. (2007). Differential contributions of the hippocampus and rhinal cortices to verbal memory in epilepsy. *Epilepsy Behav.* 10, 553–559. doi:10.1016/j.yebeh.2007.03.002

Lineweaver, T. T., Morris, H. H., Naugle, R. I., Najm, I. M., Diehl, B., and Bingaman, W. (2006). Evaluating the contributions of state-of-the-art assessment techniques to predicting memory outcome after unilateral anterior temporal lobectomy. *Epilepsia* 47, 1895–1903. doi:10.1111/j.1528-1167.2006.00807.x

Maguire, E. A. (1997). Hippocampal involvement in human topographical memory: evidence from functional imaging. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 352, 1475–1480. doi:10.1098/rstb.1997.0134

Maguire, E. A., Burke, T., Phillips, J., and Staunton, H. (1996). Topographical disorientation following unilateral temporal lobe lesions in humans. *Neuropsychologia* 34, 993–1001. doi:10.1016/0028-3932(96)00022-X

Maguire, E. A., and Cipolotti, L. (1998). Selective sparing of topographical memory. *J. Neurol. Neurosurg. Psychiatr.* 65, 903–909. doi:10.1136/jnnp.65.6.903

Maguire, E. A., Frith, C. D., Burgess, N., Donnett, J. G., and O'Keefe, J. (1998). Knowing where things are parahippocampal involvement in encoding object locations in virtual large-scale space. *J. Cogn. Neurosci.* 10, 61–76. doi:10.1162/089892998563789

McConley, R., Martin, R., Palmer, C. A., Kuzniecky, R., Knowlton, R., and Faught, E. (2008). Rey Osterrieth complex figure test spatial and figural scoring: relations to seizure focus and hippocampal pathology in patients with temporal lobe epilepsy. *Epilepsy Behav.* 13, 174–177. doi:10.1016/j.yebeh.2008.03.003

McCormick, C., Quraan, M., Cohn, M., Valiante, T. A., and McAndrews, M. P. (2013). Default mode network connectivity indicates episodic memory capacity in mesial temporal lobe epilepsy. *Epilepsia* 54, 809–818. doi:10.1111/epi.12098

McDermott, K. B., Buckner, R. L., Petersen, S. E., Kelley, W. M., and Sanders, A. L. (1999). Set- and code-specific activation in frontal cortex: an fMRI study of encoding and retrieval of faces and words. *J. Cogn. Neurosci.* 11, 631–640. doi:10.1162/089892999563698

McDonald, C. R., Ahmadi, M. E., Hagler, D. J., Tecoma, E. S., Iragui, V. J., Gharapetian, L., et al. (2008). Diffusion tensor imaging correlates of memory and language impairments in temporal lobe epilepsy. *Neurology* 71, 1869–1876. doi:10.1212/01.wnl.0000327824.05348.3b

McMillan, T. M., Powell, G. E., Janota, I., and Polkey, C. E. (1987). Relationships between neuropathology and cognitive functioning in temporal lobectomy patients. *J. Neurol. Neurosurg. Psychiatr.* 50, 167–176. doi:10.1136/jnnp.50.2.167

Mechanic-Hamilton, D., Korczykowski, M., Yushkevich, P. A., Lawler, K., Pluta, J., Glynn, S., et al. (2009). Hippocampal volumetry and functional MRI of memory in temporal lobe epilepsy. *Epilepsy Behav.* 16, 128–138. doi:10.1016/j.yebeh.2009.07.012

Meencke, H. J., and Veith, G. (1992). Migration disturbances in epilepsy. *Epilepsy Res. Suppl.* 9, 31–39. discussion 39-40.

Milner, B. (1966). "Amnesia following operation on the temporal lobes," in *Amnesia*, eds C. Whitty and O. Zangwill (London: Butterworth), 109–133.

Milner, B. (1970). "Memory and the medial temporal regions of the brain," in *Biology of Memory*, eds P. Kh and D. Broadbent (New York: Academic Press), 29–50.

Morris, R. G., Garrud, P., Rawlins, J. N., and O'Keefe, J. (1982). Place navigation impaired in rats with hippocampal lesions. *Nature* 297, 681–683. doi:10.1038/297681a0

Mueller, S. G., Laxer, K. D., Barakos, J., Cheong, I., Finlay, D., Garcia, P., et al. (2010). Involvement of the thalamocortical network in TLE with and without mesiotemporal sclerosis. *Epilepsia* 51, 1436–1445. doi:10.1111/j.1528-1167.2009.02413.x

Nyberg, L., Persson, J., Habib, R., Tulving, E., Mcintosh, A. R., Cabeza, R., et al. (2000). Large scale neurocognitive networks underlying episodic memory. *J. Cogn. Neurosci.* 12, 163–173. doi:10.1162/089892900561805

O'Keefe, J., and Dostrovsky, J. (1971). The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Res.* 34, 171–175. doi:10.1016/0006-8993(71)90358-1

Oyegbile, T. O., Dow, C., Jones, J., Bell, B., Rutecki, P., Sheth, R., et al. (2004). The nature and course of neuropsychological morbidity in chronic temporal lobe epilepsy. *Neurology* 62, 1736–1742. doi:10.1212/01.WNL.0000125186.04867.34

Parslow, D. M., Morris, R. G., Fleminger, S., Rahman, Q., Abrahams, S., and Recce, M. (2005). Allocentric spatial memory in humans with hippocampal lesions. *Acta Psychol. (Amst.)* 118, 123–147. doi:10.1016/j.actpsy.2004.10.006

Penfield, W., and Milner, B. (1958). Memory deficit produced by bilateral lesions in the hippocampal zone. *AMA Arch. Neurol. Psychiatry* 79, 475–497. doi:10.1001/archneurpsyc.1958.02340050003001

Piekema, C., Kessels, R. P., Mars, R. B., Petersson, K. M., and Fernandez, G. (2006). The right hippocampus participates in short-term memory maintenance of object-location associations. *Neuroimage* 33, 374–382. doi:10.1016/j.neuroimage.2006.06.035

Piguet, O., Saling, M. M., O'Shea, M. F., Berkovic, S. F., and Bladin, P. F. (1994). Rey figure distortions reflect nonverbal recall differences between right and left foci in unilateral temporal lobe epilepsy. *Arch. Clin. Neuropsychol.* 9, 451–460. doi:10.1016/0887-6177(94)90007-8

Pillon, B., Bazin, B., Deweer, B., Ehrle, N., Baulac, M., and Dubois, B. (1999). Specificity of memory deficits after right or left temporal lobectomy. *Cortex* 35, 561–571. doi:10.1016/S0010-9452(08)70819-0

Powell, H. W., Koepp, M. J., Richardson, M. P., Symms, M. R., Thompson, P. J., and Duncan, J. S. (2004). The application of functional MRI of memory in temporal lobe epilepsy: a clinical review. *Epilepsia* 45, 855–863. doi:10.1111/j.0013-9580.2004.41603.x

Powell, H. W., Koepp, M. J., Symms, M. R., Boulby, P. A., Salek-Haddadi, A., Thompson, P. J., et al. (2005). Material-specific lateralization of memory encoding in the medial temporal lobe: blocked versus event-related design. *Neuroimage* 27, 231–239. doi:10.1016/j.neuroimage.2005.04.033

Powell, H. W., Parker, G. J., Alexander, D. C., Symms, M. R., Boulby, P. A., Wheeler-Kingshott, C. A., et al. (2007). Abnormalities of language networks in temporal lobe epilepsy. *Neuroimage* 36, 209–221. doi:10.1016/j.neuroimage.2007.02.028

Powell, H. W., Richardson, M. P., Symms, M. R., Boulby, P. A., Thompson, P. J., Duncan, J. S., et al. (2008). Preoperative fMRI predicts memory decline following anterior temporal lobe resection. *J. Neurol. Neurosurg. Psychiatr.* 79, 686–693. doi:10.1136/jnnp.2007.115139

Rausch, R., and Babb, T. L. (1987). "Evidence for memory specialization within the mesial temporal lobe of man," in *Fundamental Mechanisms of Human Brain Function*, ed. J. Engel Jr. (New York: Raven Press), 103–109.

Reminger, S. L., Kaszniak, A. W., Labiner, D. M., Littrell, L. D., David, B. T., Ryan, L., et al. (2004). Bilateral hippocampal volume predicts verbal memory function in temporal lobe epilepsy. *Epilepsy Behav.* 5, 687–695. doi:10.1016/j.yebeh.2004.06.006

Richardson, M. P., Strange, B. A., Duncan, J. S., and Dolan, R. J. (2006). Memory fMRI in left hippocampal sclerosis: optimizing the approach to predicting postsurgical memory. *Neurology* 66, 699–705. doi:10.1212/01.wnl.0000201186.07716.98

Sabsevitz, D. S., Swanson, S. J., Hammeke, T. A., Spanaki, M. V., Possing, E. T., Morris, G. L. III, et al. (2003). Use of preoperative functional neuroimaging to predict language deficits from epilepsy surgery. *Neurology* 60, 1788–1792. doi:10.1212/01.WNL.0000068022.05644.01

Saling, M. M. (2009). Verbal memory in mesial temporal lobe epilepsy: beyond material specificity. *Brain* 132, 570–582. doi:10.1093/brain/awp012

Saling, M. M., Berkovic, S. F., O'Shea, M. F., Kalnins, R. M., Darby, D. G., and Bladin, P. F. (1993). Lateralization of verbal memory and unilateral hippocampal sclerosis: evidence of task-specific effects. *J. Clin. Exp. Neuropsychol.* 15, 608–618. doi:10.1080/01688639308402582

Saling, M. M., O'Shea, M. F., Weintrob, D. L., Wood, A. G., Reutens, D. C., and Berkovic, S. (2002). "Medial and lateral contributions to verbal memory: evidence from temporal lobe epilepsy," in *Frontiers of Memory*, eds A. Yamadori, K. R. T. Fujii, and K. Suzuki (Sendai: Tohoku University Press), 151–158.

Scoville, W. B., and Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *J. Neurol. Neurosurg. Psychiatr.* 20, 11–21. doi:10.1136/jnnp.20.1.11

Seidenberg, M., Hermann, B. P., Dohan, F. C. Jr., Wyler, A. R., Perrine, A., and Schoenfeld, J. (1996). Hippocampal sclerosis and verbal encoding ability following anterior temporal lobectomy. *Neuropsychologia* 34, 699–708. doi:10.1016/0028-3932(95)00146-8

Sidhu, M. K., Stretton, J., Winston, G. P., Bonelli, S., Centeno, M., Vollmar, C., et al. (2013). A functional magnetic resonance imaging study mapping the episodic memory encoding network in temporal lobe epilepsy. *Brain* 136, 1868–1888. doi:10.1093/brain/awt099

Skinner, E. I., and Fernandes, M. A. (2007). Neural correlates of recollection and familiarity: a review of neuroimaging and patient data. *Neuropsychologia* 45, 2163–2179. doi:10.1016/j.neuropsychologia.2007.03.007

Spiers, H. J., Burgess, N., Hartley, T., Vargha-Khadem, F., and O'Keefe, J. (2001a). Bilateral hippocampal pathology impairs topographical and episodic memory but not visual pattern matching. *Hippocampus* 11, 715–725. doi:10.1002/hipo.1087

Spiers, H. J., Burgess, N., Maguire, E. A., Baxendale, S. A., Hartley, T., Thompson, P. J., et al. (2001b). Unilateral temporal lobectomy patients show lateralized topographical and episodic memory deficits in a virtual town. *Brain* 124, 2476–2489. doi:10.1093/brain/124.12.2476

Squire, L. R., Stark, C. E., and Clark, R. E. (2004). The medial temporal lobe. *Annu. Rev. Neurosci.* 27, 279–306. doi:10.1146/annurev.neuro.27.070203.144130

Squire, L. R., Wixted, J. T., and Clark, R. E. (2007). Recognition memory and the medial temporal lobe: a new perspective. *Nat. Rev. Neurosci.* 8, 872–883. doi:10.1038/nrn2154

Stepankova, K., Fenton, A. A., Pastalkova, E., Kalina, M., and Bohbot, V. D. (2004). Object-location memory impairment in patients with thermal lesions to the right or left hippocampus. *Neuropsychologia* 42, 1017–1028. doi:10.1016/j.neuropsychologia.2004.01.002

Stroup, E., Langfitt, J., Berg, M., Mcdermott, M., Pilcher, W., and Como, P. (2003). Predicting verbal memory decline following anterior temporal lobectomy (ATL). *Neurology* 60, 1266–1273. doi:10.1212/01.WNL.0000058765.33878.0D

Suzuki, W. A., and Amaral, D. G. (1994). Perirhinal and parahippocampal cortices of the macaque monkey: cortical afferents. *J. Comp. Neurol.* 350, 497–533. doi:10.1002/cne.903500402

Thivard, L., Hombrouck, J., Du Montcel, S. T., Delmaire, C., Cohen, L., Samson, S., et al. (2005). Productive and perceptive language reorganization in temporal lobe epilepsy. *Neuroimage* 24, 841–851. doi:10.1016/j.neuroimage.2004.10.001

van Asselen, M., Kessels, R. P., Neggers, S. F., Kappelle, L. J., Frijns, C. J., and Postma, A. (2006). Brain areas involved in spatial working memory. *Neuropsychologia* 44, 1185–1194. doi:10.1016/j.neuropsychologia.2005.10.005

van Strien, N. M., Cappaert, N. L., and Witter, M. P. (2009). The anatomy of memory: an interactive overview of the parahippocampal-hippocampal network. *Nat. Rev. Neurosci.* 10, 272–282. doi:10.1038/nrn2614

Wais, P. E., Mickes, L., and Wixted, J. T. (2008). Remember/know judgments probe degrees of recollection. *J. Cogn. Neurosci.* 20, 400–405. doi:10.1162/jocn.2008.20041

Wang, Q., Gao, E., and Burkhalter, A. (2011). Gateways of ventral and dorsal streams in mouse visual cortex. *J. Neurosci.* 31, 1905–1918. doi:10.1523/JNEUROSCI.3488-10.2011

Weniger, G., Ruhleder, M., Wolf, S., Lange, C., and Irle, E. (2009). Egocentric memory impaired and allocentric memory intact as assessed by virtual reality in subjects with unilateral parietal cortex lesions. *Neuropsychologia* 47, 59–69. doi:10.1016/j.neuropsychologia.2008.08.018

Wiener, S. I. (1993). Spatial and behavioral correlates of striatal neurons in rats performing a self-initiated navigation task. *J. Neurosci.* 13, 3802–3817.

Wolf, H. K., Campos, M. G., Zentner, J., Hufnagel, A., Schramm, J., Elger, C. E., et al. (1993). Surgical pathology of temporal lobe epilepsy. Experience with 216 cases. *J. Neuropathol. Exp. Neurol.* 52, 499–506. doi:10.1097/00005072-199309000-00008

Yonelinas, A. P., and Levy, B. J. (2002). Dissociating familiarity from recollection in human recognition memory: different rates of forgetting over short retention intervals. *Psychon. Bull. Rev.* 9, 575–582. doi:10.3758/BF03196315

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Pupil dilations reflect why Rembrandt biased female portraits leftward and males rightward

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Portrait painters are experts at examining faces and since emotional content may be expressed differently on each side of the face, consider that Rembrandt biased his male portraits to show their right-cheek more often and female portraits to show their left-cheek more often. This raises questions regarding the emotional significance of such biased positions. I presented rightward and leftward facing male and female portraits. I measured observers' pupil size while asking observers to report how (dis)pleasing they found each image. This was a methodological improvement over the type of research initially done by Eckhard Hess who claimed that pupils dilate to pleasant images and constrict to unpleasant images. His work was confounded since his images' luminances and contrasts across conditions were inconsistent potentially affecting pupil size. To overcome this limitation I presented rightward or leftward facing male and female portraits by Rembrandt to observers in either their original or mirror-reversed position. I found that in viewing male portraits pupil diameter was a function of arousal. That is, larger pupil diameter occurred for images rated both low and high in pleasantness. This was not the case with female portraits. I discuss these findings in regard to the perceived dominance of males and how emotional expressions may be driven by hemispheric laterality.

Keywords: hemispheric laterality, pupil size, face perception, emotion, esthetic judgments

INTRODUCTION

Portraitures have been shown to exhibit a leftward bias, where the left check is exposed more often than the right. This occurs more often in female than male portraits which may be due to a desire to portray female's more emotive left-side. Hemispheric lateralization may also play a role by projecting negative emotions to the left-side of the face and positive emotions to the right-side of the face. This distinction will be addressed. Given that conscious judgments of pleasingness are beset with problems, it is important to also use an unconscious measure such as pupil size. Hess (1965, 1972) claimed that pupils enlarge when viewing pleasant images and constrict when viewing unpleasant images. Yet since pupil size also covaries with luminance, a novel technique was employed to measure pupil size in response to portraits and their mirror image. I found that Hess was incorrect to focus on valence and should have emphasized arousal instead. This finding was evident in male but not female portraits, which may be due to the dominance exhibited in male portraitures.

PORTRAITURE'S LEFTWARD BIAS

Portraits often expose more of one side of their face than the other side (McManus and Humphrey, 1973; Grüsser et al., 1988). For example, in a study of 1,474 Western European portraits created from the fourteenth to the twentieth century, 891 posers (~60%) exposed more of their left-cheek, whereas 583 (~40%) exposed more of their right-check (McManus and Humphrey, 1973). This left-cheek asymmetry is stronger for women portraits (Gordon, 1974; Grüsser et al., 1988; Conesa et al., 1995). That is, ~68% of women's portraits, but only 56% of male portraits have a leftward bias (McManus and Humphrey, 1973).

This gender difference has had several explanations (Lindell, 2013). One promising interpretation suggests that the leftward bias results from the poser's preference to portray the left-side of the face's emotional qualities (Nicholls et al., 1999). Nicholls et al., 1999, p. 665) instructed participants to pose for a portrait to either "put as much real emotion and passion into a portrait as you can" or "to avoid depicting any emotion at all." In the first case, participants were more likely to turn their left-cheek toward a camera during a picture-taking session, whereas in the second case participants were more likely to turn their right-cheek toward the camera. Likewise, multiple studies report that the left-side of the face is more intense in exhibiting voluntary emotional expression, especially for women (Sackeim and Gur, 1978; Sackeim et al., 1978; Borod and Caron, 1980; Borod et al., 1988; Nicholls et al., 2000). For example, Nicholls et al. (2002a) demonstrated that people who are more emotionally expressive are more likely to pose for a portrait offering the left-cheek; the paper argues that as females score higher on measures of emotional expressivity, they are more likely to pose offering the left-cheek. Nicholls et al. (2002b) then demonstrated that viewers perceive images of models offering the left-cheek as more emotionally expressive. Lindell (2013) offers a review of this literature. These findings are consistent with the idea that facial expressions are related to cerebral hemispheric laterality, and that the right brain hemisphere is dominant in processing and also displaying emotional expressions (to the left-side of the face) (Bryden and Ley, 1983).

Given these findings, males may not want to portray their emotive left-side as much as females (or by the behest of the artist). Likewise, artists may prefer to portray women as being more emotive than men, thereby exposing their left-cheek more often. These notions are supported by Grüsser et al. (1988), who examined fifteenth to twentieth century portraits and found a left-cheeked bias, which was always stronger for female than for male portraits. Thus, the current study examines the bias a portrait conveys, not the viewer's preference for a right or left-side of an image. This tests the sitter's hemispheric asymmetry (contralateral control of facial musculature) rather than the perceiver will produce differences in valence or arousal.

Alternatively, a valence hypothesis suggests that since each cerebral hemisphere controls predominantly the musculature on the lower two-thirds of the contralateral side of the face (Brodal, 1965) each side of the face portrays different emotive qualities. So, positive emotions should be more prevalent on the right-side of the face (since it is governed by the left cerebral hemisphere) and negative emotional expressions should be more prevalent on the left-side of the face (since it is governed by the right cerebral hemisphere) (Rossi and Rosadini, 1967; Gainotti, 1969, 1972; Ahern and Schwartz, 1979; Schwartz et al., 1979; Sackeim et al., 1982; Fridlund and Izard, 1983; Natale et al., 1983; Sackeim and Gur, 1983; Davidson, 1984; Silberman and Weingartner, 1986; Schiff and Lamon, 1989; Mandal et al., 1991; Borod et al., 1997; Jasari et al., 2000; for a literature review see Powell and Schirillo, 2009). This makes it peculiar to portray the left-cheek more often. Logically it may follow that the valence hypothesis is less compelling than the lateralized one.

Thus, the field of lateralized portraiture has sought to determine whether one side of the face is more pleasant than the other. Schirillo and Fox (2006) (**Figure 1**) showed observers all 373 of Rembrandt's portraits and found that left-cheeked females were assessed as more approachable than right-cheeked females portraits while males portraits (for both sides of the face) were assessed as preferably avoided. Thus, observers were more likely overall to want to approach female rather than male Rembrandt portraits. Unfortunately, this study did not use mirror-reversed images so it could not determine overall effect of cheek.

CONSCIOUS EMOTIONAL JUDGMENTS MEASURED USING AN UNCONSCIOUS PUPIL SIZE MEASURE

Research investigating the interaction of lateralized portraiture and pleasantness ratings is beset with problems (Rinn, 1984). For example, the most popular methodology is to obtain an observer's subjective impression of the stimuli such as degree of liking (Russell and George, 1990). This method may cause observers to use separate, immeasurable, criteria in making judgments (e.g., one observer may use an image's contrast, whereas another may use facial features, such as eyebrows). This obfuscates linking esthetic judgments to cerebral laterality. Thus, it makes sense to

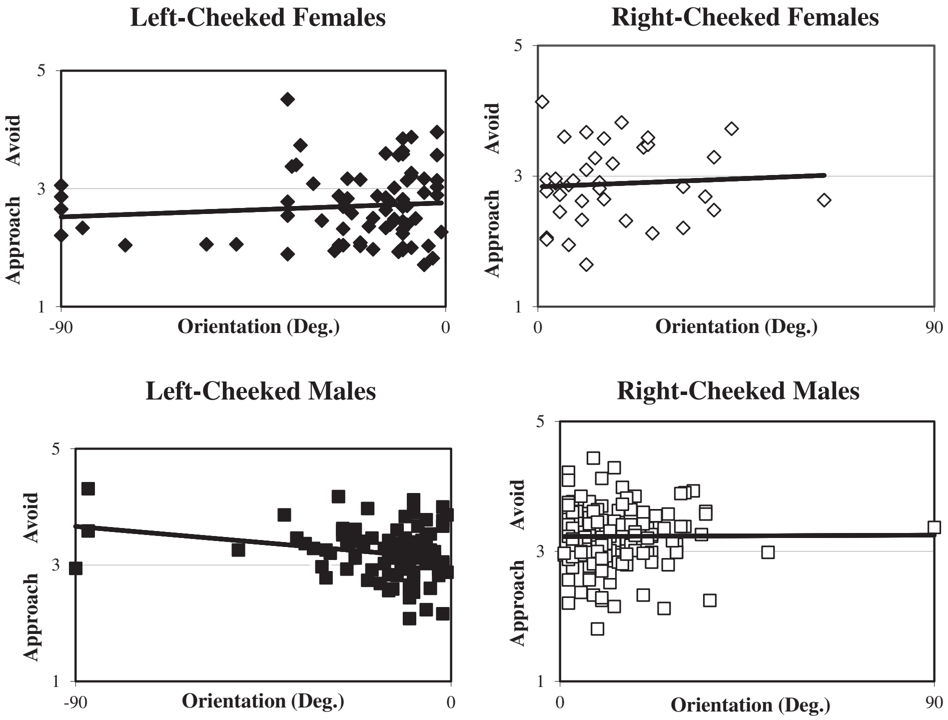

FIGURE 1 | Scatterplots of the distribution of each of 373 Rembrandt portrait angles as a function of ratings of approach/avoidance ratings (collapsed over 73 subjects' ratings). Upper left (closed squares) – shows left-cheeked males (−90° to −1° orientation), upper right (open squares) – shows right-cheeked males (+1° to +90° orientation), lower left (closed diamonds) – shows left-cheeked females (−90° to −1° orientation), lower right (open diamonds) – shows right-cheeked females (+1° to +90° orientation). Linear regressions are plotted for each graph. Here 2 indicates a rating of "mildly approach," 3 indicates "neutral," and 4 indicates "mildly avoid."

try to understand portrait laterality to what may be a correlate to automatic affective reactions.

Pupil size is one previously measured unconscious indicator of affective processing (Hess and Polt, 1960; Hess, 1965, 1972; Janisse, 1974; Loewenfeld, 1999). Hess (1965, 1972), attempted to transform the field of esthetics by claiming that pupils enlarge when viewing pleasant images and constrict when viewing unpleasant images (see also Hess and Polt, 1960; Hess et al., 1965; Simms, 1967; Fitzgerald, 1968; Goldwater, 1972). However, pupil size also varies with luminance (Loewenfeld, 1966, 1999; Woodmansee, 1966; Miller, 1967; Kohn and Clynes, 1969; Goldwater, 1972; Janisse, 1973, 1974; Loftus, 1985; Mannan et al., 1995; Locher, 1996), and since Hess compared different images with different intensities and contrast levels (e.g., a snake versus a naked women), his work was confounded.

A NOVEL METHODOLOGY

Since I used original and mirror-reversed portraits, I was also able to explore the hemispheric laterality of emotional expression. Rembrandt may have turned his subject's faces sideways to display specific emotional content of their facial musculature. If this is the case, self-reports regarding dominance especially of male subjects should show up as emotional responses which might be quantified by pupil size relationships. It was found that Hess was incorrect to focus on valence. Instead, he should have focused on arousal, since it was found that arousal, not valence, drives pupil diameter for male portraits. That is pupils dilated for males that were rated both most pleasant and most unpleasant (Powell and Schirillo, 2009). Thus, verbal ratings of pleasantness are a self-report measure which relate to an unconscious indicator of pleasantness (i.e., pupil diameter) as suggested by Hess and others (Hess and Polt, 1960; Hess, 1965, 1972; Hess et al., 1965).

DOMINANCE, VALENCE, AND AROUSAL

Dominance (typically associated with positive, e.g., self-assurance, arrogance, and feeling bold or triumphant) or negative affective states (e.g., hostility, irritability, and anger) (Demaree et al., 2005) can lead to larger pupil size (Darwin, 1872). These arousal differences should only be present in viewing male portraits since they accentuate dominance (Dunbar and Burgoon, 2005). This is emphasized in images where each side of the face reflects different emotional expressions a concept first posited by Darwin (1872), especially as it relates to dominance.

The use of Rembrandt portraits allowed for the exploration of esthetic judgments of a famous artist while investigations of Rembrandt's work in the context of hemispheric laterality provide also examining potential differences in facial emotion expression. First, using artwork should elicit stronger esthetic reactions than photographs of faces. Second, prior preliminary evidence that perceived dominance is greater when viewing his right-cheeked male portraits (Schirillo, 2000). It is possible that this is the reason for their prevalence; however due to the correlational nature of the data it may also be that Rembrandt may have chosen to selectively portray the right-cheeks of more dominant males. Thus, I attempt to show how hemispheric asymmetries may regulate displays of facial emotion which are reflected by an observer's esthetic judgment of a portrait. It is interesting that Schirillo's (2000) study of "social appealingness" of male and female right and left-cheeked portraits differs from Schirillo and Fox's (2006) study of approach/avoidance of the same? Seemingly, "social appeal" differs from the desire to approach or avoid. Further work on this discrepancy is needed.

Given that verbal ratings of pleasingness are a self-report measure, it is of interest to determine their relationship with an unconscious indicator of pleasingness (i.e., pupil diameter) as suggested by Hess and others, and how this in turn might be related to the emotional content of facial musculature. If self-report interpretations drive assumptions regarding dominance, they may show up in the portraits' emotional qualities which are reflected in pupil size relationships. However, it may be that pupil diameter is more related to arousal rather than pleasingness. The current study will help clarify this dependent variable.

In an earlier study of Rembrandt portraits (Schirillo, 2000) a factor analysis revealed that females with their left-cheek exposed were judged to be much less socially appealing than less commonly painted right-cheeked females. Conversely, the more commonly painted right-cheeked males were judged to be more socially appealing than either left-cheeked males or females facing either direction. It was hypothesized that hemispheric asymmetries regulating emotional facial displays of approach and avoidance influenced the side of the face Rembrandt's models exposed due to prevailing social norms. Thus, females would be considered more appealing than males and left facing males would be considered the least appealing. A second experiment had different subjects judge a different collection of 40 portraits by Rembrandt and their mirror images. Portraits were matched for valence, arousal and dominance by a second set of 20 subjects. I hypothesized that mirror-reversed images would produce the same pattern of results as their original orientation counterparts. I also hypothesized that hemispheric asymmetries that specify the emotional expression on each side of the face will account for the obtained results, that is, original left-cheeked males will be preferred, due to their perceived dominance while there will be no difference in female portraits.

MATERIALS AND METHODS

SUBJECTS

Forty right-handed observers (20 males; ages 18–23) with normal or corrected-to-normal vision (but no eyeglasses) from the introductory psychology research pool at Wake Forest University participated in the study. Handedness was determined using Annett's Peg-Moving task as right-minus-left latency (peg-moving speed) (Annett and Kilshaw, 1983). The study was performed in accordance with the ethical standards of the Declaration of Helsinki.

STIMULI

Forty black and white images taken from oil paintings were chosen from a collection of 373 portraits painted by Rembrandt. The specific portraits chosen represent his most rightward and leftward facing portraits (Schirillo and Fox, 2006). Grayscale images were used instead of colored images because color can lead to changes in pupil diameter (Miller, 1967; Kohn and Clynes, 1969). Ten were right-cheeked males (none were self-portraits of Rembrandt), 10 were left-cheeked males, 10 were right-cheeked females, and 10 were left-cheeked females (Lists Painting Names in Appendix). Next, these images were used to produce 40 mirror-reversed images using PhotoShop IBM. The portraits were only of busts. Each portrait was scanned into PhotoShop and was projected to each observer individually using an IBM CRT computer monitor using Microsoft PowerPoint. Viewing distance was 24″ making the image size range from 11.7°(height) × 8.5°(width) to 11.8° × 12.4°. The observers close distance to the screen limited their ability to spend considerable time viewing off-screen. To verify this notion, since the head-mounted Applied Science Laboratories (ASL; series 6000) eye-tracker could also measure eye position, I determined that observers were only off-screen ~3% of their total viewing time. My data also showed that time with no record (due to eye closure) was minimal. In addition, 80 blurred images were created (40 from original and 40 from mirror-reversed images) in PhotoShop using a Gaussian blur function (See **Figure 2**). There was no ambient lightning in the experimental chamber, in that it was a room without windows. Since the door was closed, the only light available came directly from the computer screen that showed the images.

The eye tracking device was used to determine the pupil size of the left-eye. The right-eye pupil size was not measured because pupil size is believed to be conjugate across the two eyes (Loewenfeld, 1999). Pupil diameter was recorded automatically every 17 ms for each entire 15 s trial. The average size across the entire 15 s viewing period was computed minus any time the pupil computation was off-line (due to blinks, etc.). Given that the ASL eye-tracker stops recording when the eye closes more than 50% (assumedly due to blinks or partial eye closure) I have no record of this data.

Instead of using linear interpolation to estimate the pupil size during this off-line period (Steinhauer et al., 2004) I felt it best to simply eliminate these segments from my dataset since blinks can alter pupil size (Nakayama, 2006). Given that the ASL eye-tracker is fixed to the head, head-movements did not alter pupil diameter recordings or result in loss of tracking. Thus, other than eye-blink time I did not remove any artifacts from the data. The remaining data was imported into Excel to do the data cleaning which was then converted to SPSS to do the statistical analysis. Average pupil size was calculated for each image across the observation period which excluded instances where the observer blinked or had partial eye lid closures (since when the eye closes the ASL machine cannot record any pupil size). Observers used a chinrest to ensure a fixed 24″ distance between themselves and the screen to retain a constant depth of field across the images (Simms, 1967).

To circumvent Hess' luminance and contrast confounds, I had observers view left- and right-cheeked portraits, and their mirror images (e.g., see **Figures 2B,D**), while they determined the esthetic pleasantness of each face. Simultaneously, I monitored their pupil size allowing for a correlate between portrait pleasantness and pupil size. Since original and mirror images have the same luminance profiles, and I only compared pupil size and pleasantness ratings across matched pairs of faces, Hess' confounds were eliminated.

Since Woodmansee (1966, p. 133) found "significant pupillary constriction with shifts in gaze from darker to brighter areas of the picture," I, like him, presented a blurred image prior to its clear image to minimize changes in pupil size. For example, **Figure 2** shows images in their original and mirror-reverse orientation (**Figures 2B,D**) along with their corresponding preceding blurred images (**Figures 2A,C**). These images are significantly blurred, so that facial pleasantness cannot be extracted from the blurred images (Bachman, 2007).

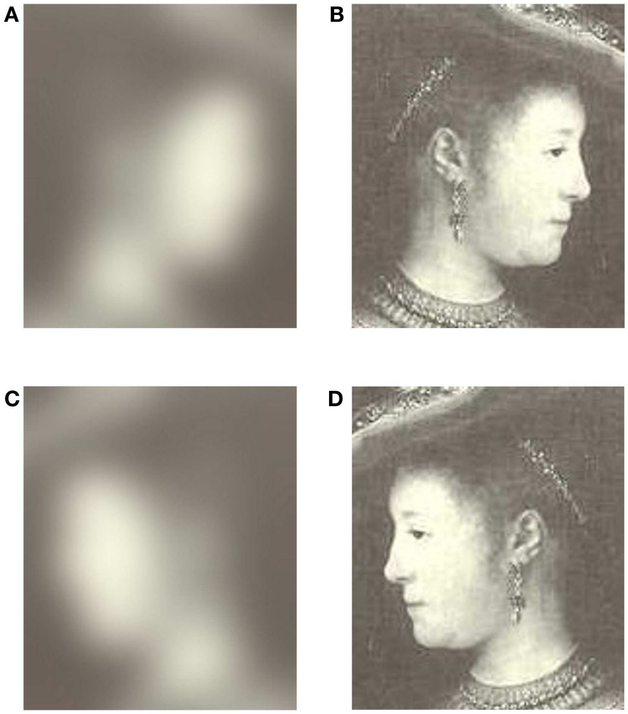

FIGURE 2 | (A) Blurred original orientation, **(B)** original orientation of a left-cheeked female, **(C)** blurred mirror-reverse, and **(D)** mirror-reverse orientation (A woman in fanciful costume). Baltimore, The Walters Art Gallery; Br. 386). Copyright 1969 Phaidon Press Ltd. Rembrandt, *The Complete Edition of Paintings*. A. Bredius, revised by H. Gerson.

Observers viewed 40 images in their original posed orientation, and in their mirror-reversed orientation (resulting in 80 images in total). Since I only compared pupil size across original versus mirror-reversed images, my within-subject's design eliminates potential confounding factors such as age and medication. Right-cheeked mirror-reversed images are portraits that originally faced rightward but due to reversal appeared to be of original left-cheeked images. Likewise, left-cheek mirror-reversed images appeared to be of original right-cheek portraits. Images were randomized, and presented to each observer in random order. Each of the 80 images was viewed for 15 s and was preceded by a blurred version of the image for 15 s. Fifteen seconds was decided upon because of three previous findings. First, Smith and Smith (2001) found that art viewers examined The Metropolitan Museum of Art paintings for a median of 17 s. Second, Aboyoun and Dabbs (1998) showed that pupil size rapidly decreases upon image presentation, which then recovers to either baseline or above baseline levels. Consequently, pupil size must be measured for at least several seconds to overcome this initial depression. Lastly, Richer et al. (1983) found that pupil size increases begin about 1.5 s before stimulus presentation and peak around a second after presentation. As a result, I gave observers more time than needed to generate an entire response to an image. Observers' pupil size was measured during each non-blurred image presentation while they contemplated how pleasant they found the non-blurred images. Observers were instructed to think about the esthetic pleasingness of each image for the entire 15 s it was shown and then report their judgment after the image was removed. This occurred during the presentation of the subsequent blurry image.

The rationale for presenting a blurred image of a given portrait prior to presenting that portrait was to avoid the following confound prevalent in the pupillometry literature. That is, if a constant blank gray screen was used as a baseline the subsequent test-image would produce the following effect (See **Figure 2** taken from Bradley et al., 2008). That is, the most important natural function of the pupil is to dynamically respond to changes in environmental illumination with an initial constriction (i.e., the light reflex) that is related to stimulus luminosity (Beatty and Lucero-Wagoner, 2000). Thus, if a constant blank gray screen were used as a baseline the brighter images would produce a larger constriction than the dimmer images. This effect takes up to 6 s before reaching a plateau. To circumvent this effect I choose to first present for 15 s a blurred image of the subsequent test-portrait. This does two things. First, it makes the large constriction (i.e., light reflex) occur during the blurred image rather than during the test-image. By the end of the 15 s of viewing the blurred image the pupil has adjusted to the light level of the image that will subsequently be presented. Given this very long duration the pupil will no longer carry-over any information from the previous clear portrait. This is because the pupil is reflexive and does not contain a memory loop so by the end of presenting a blurred image there are no residual effects from the proceeding clear image. However, the blurred images differ in luminance thus setting a different baseline for the subsequent portrait. This is actually desired, so that the magnitude of the effect is not the result of a shift in overall luminance level (as occurs in **Figure 2**). Instead, each original and mirror-reversed blurred image sets the same baseline for their subsequent clear image. This is important since it is only the results of these two (original and mirror-reversed test-image) pupil diameters that will be compared against each other.

I manually recorded pleasantness scores for each face by taking verbal esthetic judgments using a 1–9 numerical scale, with one meaning most displeasing, five meaning neutral, and nine meaning most pleasing. Pleasingness is just one dimension of esthetics, but seemed to be appropriate based on a study that used five evaluative scales (e.g., pleasingness, likeability, preferability, interestingness, and complexity) (Russell and George, 1990). In Russell and George's (1990) study, pleasingness was highly correlated with likeability and preferability, and was the highest in inter-subject agreement. The difference in verbal rating between the original and mirror-reverse images was then correlated with the difference between the average pupil diameters.

Following the stimulus presentation, observers were administered a questionnaire that pertained to their art training and their familiarity with the portraits. They were not told prior to the experimental session that they would see original and mirror-reversed images, but they may have become aware of this as the session progressed. To determine if observers noticed these mirror duplications, I asked whether they noticed anything unusual about the images at the end of the session. Sixteen of 40 observers reported noticing that a number of images were mirror-reversed. Only three observers had formal art training and nine reported that they had seen less than 25% of the portraits before. Thus, while many of these images are famous, most observers were not familiar with them.

RESULTS

PLEASANTNESS RATINGS

Before examining individual pleasantness ratings, I obtained each observer's average pleasantness ratings for each of the eight portrait types (e.g., original right and left, mirror-reverse right and left, males and females). This resulted in each observer having eight data points. Then, pleasantness ratings for male and female portraits were submitted to a 2 (Portrait Gender: male vs. female) × 2 (Orientation: original vs. mirror-reversed) × 2 (Side of Face: left vs. right) repeated measures ANOVA. Males and female observers were included as a between-subjects factor, but showed no effect.

Figure 4 shows the means for each portrait group. There was a main effect for Side of Face with left-cheeks rated higher than right-cheeked individuals $F(1, 39) = 11.55$, $p = 0.002$, $d = 1.07$. Additionally, there were three significant interactions. First, there was a Side of Face by Orientation interaction $F(1, 39) = 12.54$, $p = 0.001$, $d = 1.12$. While left-side portraits (original and reversed) were rated higher than right portraits (see Side of Face main effect), right mirror reversals were rated higher than right originals ($M = 4.23$ vs. $M = 4.13$), while left originals were rated higher than left mirror reversals ($M = 4.75$ vs. $M = 4.57$, respectively) [$t(1, 78) = 2.56$, $p = 0.01$, $d = 0.59$; $t(1, 78) = 2.91$, $p = 0.005$, $d = 0.65$]. That is, leftward appearing portraits, left originals and right reversals whose appearance to the observer seems to be left faced, are rated higher than right faced originals and left mirror-reversed (portraits viewed as seemingly right faced). Second, a Side of Face by Portrait Gender interaction was found $F(1, 39) = 15.12$, $p = 0.001$, $d = 1.23$ with left-side females portraits rated higher than right-side females portraits ($M = 5.07$ vs. $M = 4.38$), whereas the opposite is true for males portraits though to a lesser degree ($M = 4.23$ for left male portraits and $M = 4.41$ for right male portraits) [$t(1, 78) = 3.22$, $p = 0.002$, $d = 0.72$; $t(1, 78) = 2.96$, $p = 0.004$, $d = 0.66$]. Third, there was an Portrait Gender by Orientation $F(1, 39) = 7.42$ $p = 0.097$, $d = 0.86$, such that female mirror reversals were rated lower than original female portraits ($M = 4.38$ vs. $M = 4.58$), whereas the opposite relationship was found for males ($M = 4.35$ vs. $M = 4.29$) [$t(1, 78) = 2.72$, $p = 0.008$, $d = 0.61$; $t(1, 78) = 2.51$, $p = 0.015$, $d = 0.015$].

PUPIL SIZE

Before examining individual pupil size, I obtained each observer's average pupil size for each of the eight types of portraits. Mean pupil sizes for these groups are shown in **Figure 3** alongside the means of the previous three-way ANOVA conducted for verbal pleasingness. There was a main effect of portrait gender across the eight types of portraits $F(1, 39) = 39.14$, $p < 0.0001$, $d = 1.98$ (**Figure 4**). Average pupil diameter when viewing male portraits was larger ($M = 5.5$) than when viewing

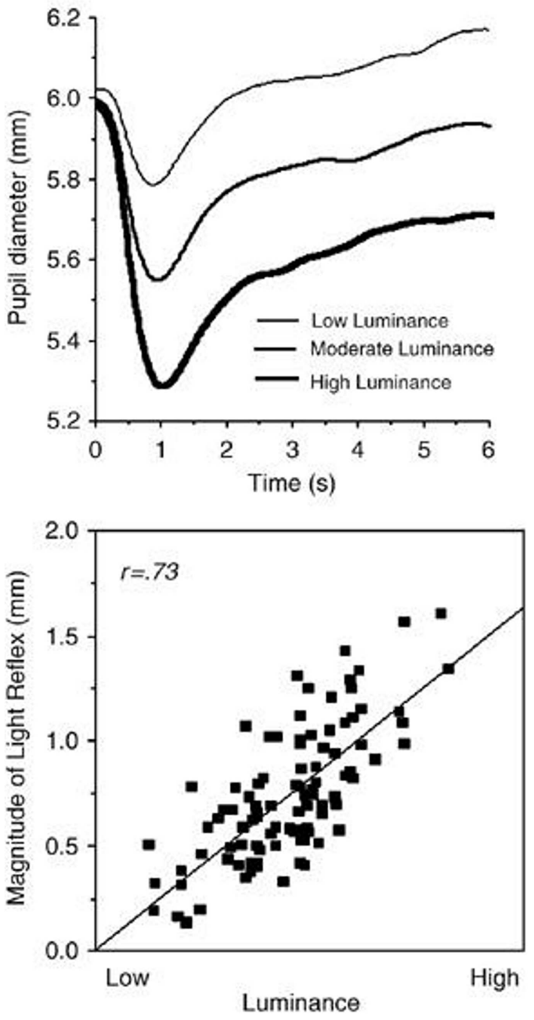

FIGURE 3 | (Top) Average pupil diameter over time as a function of luminance of the image viewed. This variation is termed the light reflex. (Bottom) correlation of the magnitude of the light reflex as a function of image luminance (Taken from Bradley et al., 2008).

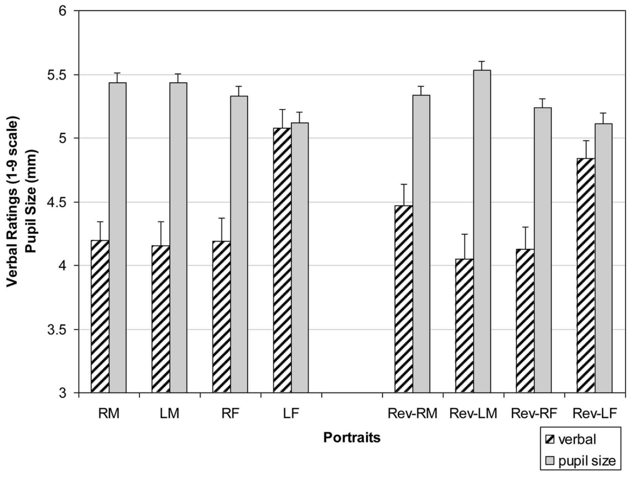

FIGURE 4 | Verbal ratings (striped bars) as a function of portrait type on a 1–9 scale, with 1 indicating most displeasing, 5 indicating neutral, and 9 indicating most pleasant. Pupil size in mm (solid bars) as a function of portrait type (R = Right-cheeked, L = Left-cheeked, M = Males, F = Females, Rev = Mirror-reversed images). Error bars = SEM.

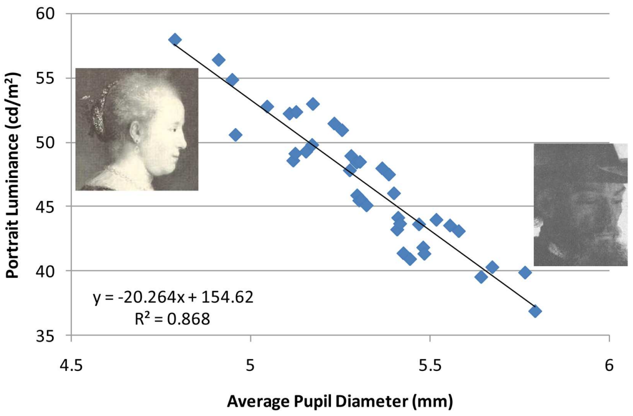

FIGURE 5 | Correlation between pupil diameter given the average luminance for each portrait (*n* = 40 observers). The figure includes the portraits with the highest and lowest average luminance.

females portraits ($M = 5.3$) [$t(1, 78) = 3.07$, $p = 0.003$, $d = 0.69$]. This analysis also yielded a significant Side of Face × Orientation interaction $F(1, 39) = 14.72$, $p = 0.001$, $d = 1.21$. Original right-cheeked portraits ($M = 5.42$) elicited greater average pupil size than right-cheeked reversed portraits ($M = 5.15$) [$t(1, 78) = 3.55$, $p = 0.001$, $d = 0.76$]. Conversely, average pupil size was largest for left-cheeked reversed portraits ($M = 5.44$) than for original left-cheeked portraits ($M = 5.23$) [$t(1, 78) = 3.13$, $p = 0.002$, $d = 0.72$]. When these findings are examined alongside the Side of Face × Orientation interaction for verbal ratings, I find that images with the appearance of being right-cheeked yielded larger average pupil size and lower verbal ratings.

Overall, pupil diameters were well within the normal range, where, as expected, the luminance of the portrait viewed dramatically affected pupil size (**Figure 5**; range = 4.71–5.82 mm). The fact that pupil contraction increased with an increase in image luminance reinforces my decision to use mirror-reversed images.

LINEAR AND QUADRATIC RELATIONSHIPS BETWEEN PLEASANTNESS RATINGS AND PUPIL DIAMETER

I examined linear and quadratic relationships between pleasantness and pupil size. First, a regression was computed to examine whether there was a linear relationship between pleasantness and pupil diameter. This was done by taking each portrait (original or mirror-reversed) for each observer as an individual case. Then difference scores between verbal pleasingness were regressed using the predictor variables of pupil size difference and quadric pupil size difference. **Figure 6A** shows that, for males, as the original verbal ratings became more positive (represented on the *x*-axis by verbal rating differences that were greater than zero), the original pupil size got smaller. Likewise, as original ratings became more negative (represented on the *x*-axis by verbal rating differences that were less than zero), the original pupil size got larger. This negative slope was statistically significant for male portraits $r(39) = -0.41$, $p < 0.009$, $d = -0.90$ (**Figure 6A**) but I failed to find a relationship for female portraits $r(39) = -0.22$, $p = 0.178$, $d = -0.90$ (**Figure 6B**). This means that when an original male portrait was preferred (whether right- or left-cheeked) the pupil was smaller while viewing the original portrait compared to the mirror-reversed image. Yet, when the mirror-reversed portrait was preferred (whether right- or left-cheeked) the pupil was smaller while viewing the mirror-reversed portrait compared to the original.

Next, linear and quadratic functions were entered into a regression model to evaluate if the relationship is better categorized by a quadratic function. The following quadratic regression model was computed separately for male and female portraits:

$$\text{Pupil} = b_0 + b_1\left(\text{pleasantness}\right) + b_2\left(\text{pleasantness}^2\right)$$

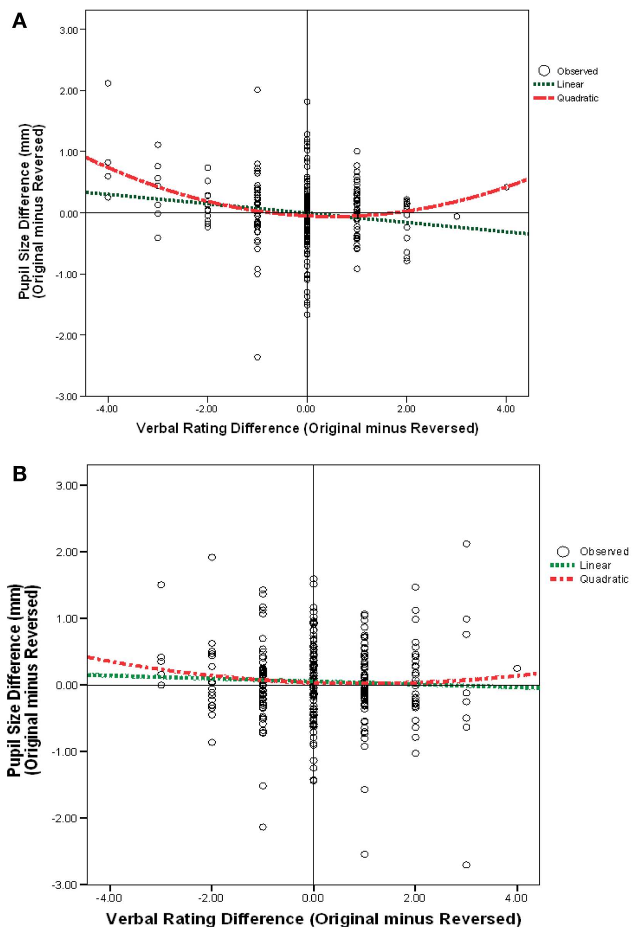

FIGURE 6 | Pupil size difference score (original-minus mirror-reversed) as a function of the difference in 1–9 verbal rating scores (between an original-minus mirror-reversed image) for all (A) male portraits, (B) female portraits.

Figure 6A shows that there was a significant quadratic effect for male portraits $b = 0.40$, $t(797) = 3.22$, $p = 0.002$, $d = 0.22$ when the linear relationship was held constant. Pupil diameter was largest when there were the greatest differences in verbal ratings between an original and mirror-reversed male image. That is, when images were extremely liked or disliked, pupil size increased. This quadratic relationship accounted for significantly more of the variance than the linear relationship, R^2 change $= 0.32$, $p < 0.004$, $d = 0.22$. However, for female portraits, the regression model failed to find a significant linear or quadratic relationship between pupil diameter and pleasantness $F(2, 797) = 0.59$, $p = 0.32$, $d = 0.07$ (**Figure 6B**). Pupil size could be confounded by the luminance of an image, so difference scores were calculated to compare across images. If difference scores were not used, and instead, pupil size for original and mirror-reversed images were used in the regression, then my findings would be seriously confounded because these values do not account for the changes in luminance/contrast across images and comparisons across images would be misleading. In sum, there were 800 total cases [i.e., 40 observers × 40 portraits (original-minus mirror-reversed)] used in the analysis.

$$\begin{aligned}\text{Outcome (DV) variable} &= \text{pupil difference}\\ \text{Predictor (IVs) variable} &= \text{verbal rating difference;}\\ &\quad \times \text{ quadratic verbal difference}\end{aligned}$$

It is important to realize that my images were not necessarily less pleasing in their non-original orientation. Instead, what I found was that only if there were a large difference in the rating between original and mirror-reversed images (where either orientation could have been the more pleasing image) there would also be a large difference in pupil size between those images.

As expected, there were almost as many zero differences between original and reversed image verbal ratings as there were difference scores (**Figure 7**). This inevitable outcome can potentially affect any of my linear and quadratic relationships.

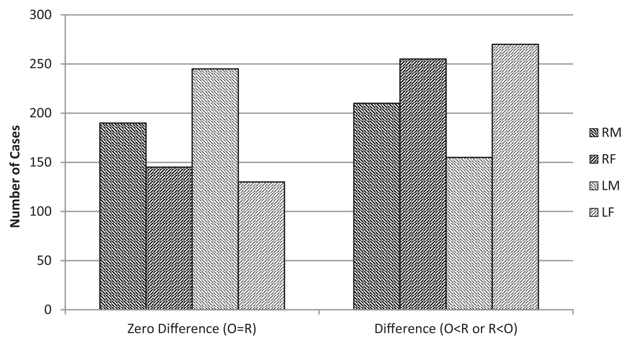

FIGURE 7 | Number of cases for all observers in which there was either a zero difference in verbal rating or there was a difference of any magnitude (with the original score being either more or less than the mirror-reversed image). (R = Right-cheeked, L = Left-cheeked, M = Males, F = Females).

DISCUSSION

While it has been shown that pupils get larger to intense (arousing) stimuli, I only replicated this for male portraits. Schirillo's (2000) analysis of Rembrandt's portraits suggests this may be because the perceived dominance of male portraits was rated higher than for female portraits. Dominance may be associated with positive (e.g., self-assurance, arrogance, and feeling bold or triumphant) or negative affective states (e.g., hostility, irritability, and anger) (Demaree et al., 2005). It is possible that while Rembrandt painted males to exhibit these positive dominant traits (see Humphrey and McManus, 1973), negative dominance traits may have also been captured. Thus, the negative linear relationship between pleasantness ratings and pupil diameter for males is consistent with Tinio and Robertson (1969), who found that aggressive Thematic Apperception Test cards elicited larger pupil size than control cards. This implies that Rembrandt's male portraits may actually be perceived as domineering which is consistent with Libby et al. (1973) and Woodmansee (1967) who found that unpleasant images were associated with larger pupil sizes compared to pleasant images.

Given that my verbal ratings of pleasingness are a self-report measure of what may be an emotive expression, it was of interest to determine their relationship with an unconscious indicator of pleasingness (i.e., pupil diameter) as suggested by Hess and others, and how this in turn might be related to the emotional content of the facial musculature displayed in the images. For example, self-report assumptions regarding dominance can be present in the emotional qualities of the portraits, which may be captured by pupil size relationships. I have explored these variables while simultaneously eliminating Stern and Strock's (1987) concern that one drawback to pupillometry is that changes associated with such variables are considerably smaller than those associated with illumination effects.

This new methodology eliminates Hess' (1972) fluctuations in luminance and contrast across images allowing us to observe how pupil size varies as a function of the differences in verbal reports of pleasant and less pleasant original and mirror-reversed portraits. This was done by *only* comparing measurements between original and mirror-reversed images which makes image contrast and luminance irrelevant. This also means I do not require a baseline pupil size from the blurred images; since pupil size should not vary between original and mirror-reversed images because such images do not vary in image contrast and luminance. If they do differ, this must be because the emotional content of the images vary, not their image contrast or luminance.

Given that it is impossible to equate apparent contrast or mean luminance across images, research testing Hess' hypothesis had ceased. However, my improved methodology does not need to equate apparent contrast or mean luminance since this automatically occurs by comparing pupil size only across an original and its mirror-reversed image. In essence, I created a methodology that reexamined the relationship between a self-report and emotive measure (i.e., pleasingness) and an unconscious physiological measure (i.e., pupil size). I show that Hess (1965, 1972) was incorrect by focusing on valence. Instead he should have focused on arousal, since arousal drives the effect for male portraits not valence.

Male portraits showed both a linear and quadratic relationship between pupil diameter and esthetic judgments of pleasantness. The linear model indicates that pupil diameter increased when viewing negative male portraits and decreased when viewing positive male portraits, whereas a quadratic model shows that pupil diameter increases to both highly pleasant and unpleasant male portraits. Thus, it is plausible that researchers who used only a linear function found that unpleasant images were associated with larger pupil sizes compared to pleasant images (Woodmansee, 1967; Tinio and Robertson, 1969; Libby et al., 1973). These findings do not support Hess' (1965) prediction, which suggested that unpleasant images would have been associated with a smaller pupil diameter.

However, a quadratic relationship accounts for significantly more variance than a linear relationship. In this case, pupil size increased with large differences among pleasantness ratings for male faces. This is consistent with previous findings that pupil size is related to stimulus intensity rather than their specific positive or negative content (Janisse, 1973, 1974, 1977; Aboyoun and Dabbs, 1998). For example, arousing situations have been shown to produce larger pupil diameter in non-visual stimuli studies. Nunnally et al. (1967) found that painfully loud sounds increased muscle tension causing larger pupil size. They also found an increase in pupil diameter when observers expected to hear a gunshot. Likewise, Polt (1970) found larger pupil size during mental arithmetic tasks when observers believed they would be shocked for incorrect answers. This may also account for why females failed to show an effect of arousal. I suggest that females are considered pleasing (not aversive) compared to males, thus when viewing female portraits one's pupil size is already approaching the floor, and thereby has less room to show arousal effects.

The esthetic verbal pleasantness judgments suggest that the observers were attending to the actual facial physiognomy of the posers and that pleasantness was determined to a lesser degree by the orientation the portrait faced. In agreement with prior research (Schirillo and Fox, 2006), the left-side of women's faces were rated as more esthetically pleasant than their right-side. This suggests that for women it is important to express more emotive facial qualities than males, in agreement with Nicholls et al. (1999) and the right-hemisphere model of emotion lateralization. Yet how emotion may be lateralized in the cerebral hemispheres is still under debate (Davidson, 1995; Demaree et al., 2005; Killgore and Yurgelun-Todd, 2007). One recent argument is that an approach/withdrawal model may provide a more appropriate fit to the data as opposed to the positive/negative hemispheric difference model (Demaree et al., 2005). Davidson and others interpretation of the left/right differences in emotion valence is that the right cerebral hemisphere regulates withdrawal behaviors whereas the left cerebral hemisphere regulates approach behaviors (Kinsbourne, 1982; Davidson, 1984, 1992, 1995; Davidson et al., 1990; Fox, 1991). If this is the case, as stated in Schirillo (2000), I speculate that Rembrandt preferred to paint females left-side because it captured the attractive quality of being demure.

Prehn et al. (2013) demonstrated that oxytocin increased saliency of all social stimuli regardless whether faces were male or female. In the placebo group (without oxytocin treatment), however, they found a strong gender effect (which decreased after oxytocin treatment). However, they used Winmorph 3.01 (www.debugmode.com/winmorph) to transform neutral expressions into all of the emotional ones in 5% steps. My study had no such control. Interestingly, their placebo "happy" male and female faces did not significantly differ in recorded intensity levels, nor recorded pupil size. This would have been the condition that I most like replicated. Like me, they found increased pupil dilations during the processing of male compared with female faces, which they attribute to reflecting men's (they only used male subjects) lower interest in male faces. However, I used both sexes as subjects and found no significant differences between groups. Yet their oxytocin manipulation is evidence that increased pupillary responses have been observed when stimuli are emotionally salient. But I controlled for saliency as much as possible by matching for valence and dominance, so I do not believe this was a factor in my experiment.

In summary, this study provides a new methodology to research the association between pupil diameter and esthetic verbal judgments. Based on its findings, Hess' (1965, 1972) hypothesis that pupils dilate to pleasant images and constrict to displeasing images seems incorrect. Instead, at least for male portraits, pupil size is a function of arousal such that pupil size difference increases when the difference in verbal reports are both most pleasant and most displeasing. I consider the possibility that this is related to perceived dominance (Ellis, 2006), in that a linear function showed that faces rated low in esthetic pleasantness evoked the largest pupil diameter. I consider the possibility that this is related to disliking perceived threat (Darwin, 1872), which may have been a dominance trait that Rembrandt inadvertently depicted.

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REFERENCES

Aboyoun, D. C., and Dabbs, J. M. (1998). The Hess pupil dilation findings: sex or novelty? *Soc. Behav. Pers.* 26, 415–420. doi:10.2224/sbp.1998.26.4.415

Ahern, G. L., and Schwartz, G. E. (1979). Differential lateralization for positive versus negative emotion. *Neuropsychologia* 17, 693–698. doi:10.1016/0028-3932(79)90045-9

Annett, M., and Kilshaw, D. (1983). Right and left-hand skill. 1. Estimating the parameters of the distribution of L-R differences in males and females. *Br. J. Psychol.* 74, 269–283. doi:10.1111/j.2044-8295.1983.tb01862.x

Bachman, T. (2007). When beauty breaks down: investigation of the effect of spatial quantisation on aesthetic evaluation of facial images. *Perception* 36, 840–849. doi:10.1068/p5509

Beatty, J., and Lucero-Wagoner, B. (2000). "The pupillary system," in *Handbook of Psychophysiology*, eds J. T. Cacioppo, L. G. Tassinary, and G. G. Berntson (Cambridge: Cambridge University Press), 14–162.

Borod, J. C., and Caron, H. S. (1980). Facedness and emotion related to lateral dominance, sex and expression type. *Neuropsychologia* 18, 237–241. doi:10.1016/0028-3932(80)90070-6

Borod, J. C., Haywood, C. S., and Koff, E. (1997). Neuropsychological aspects of facial asymmetry during emotional expression: a review of the normal adult literature. *Neuropsychol. Rev.* 7, 41–60. doi:10.1007/BF02876972

Borod, J. C., Kent, J., Koff, E., Martin, C., and Alpert, M. (1988). Facial asymmetry while posing positive and negative emotions: support for the right hemisphere hypothesis. *Neuropsychologia* 26, 759–764. doi:10.1016/0028-3932(88)90013-9

Bradley, M. M., Miccoli, L., Escrig, M. A., and Lang, P. (2008). The pupil as a measure of emotional arousal and autonomic activation. *Psychophysiology* 45, 602–607. doi:10.1111/j.1469-8986.2008.00654.x

Brodal, A. (1965). *The Cranial Nerves*. Oxford: Blackwell.

Bryden, M. P., and Ley, R. G. (1983). "Right-hemispheric involvement in the perception and expression of emotion in normal humans," in *Neuropsychology of Human Emotion*, eds K. M. Heilman, and P. Satz (New York: Guilford Press), 6–44.

Conesa, J., Brunold-Conesa, C., and Miron, M. (1995). Incidence of the half-left profile pose in single-subject portraits. *Percept. Mot. Skills* 81, 920–922. doi:10.2466/pms.1995.81.3.920

Darwin, C. (1872). *The Expression of the Emotions in Man and Animals*. New York: D. Appleton and Co.

Davidson, R. J. (1984). "Affect, cognition, and hemispheric specialization," in *Emotions, Cognition, and Behavior*, eds C. E. I. Izard, J. Kagan, and R. B. Zajonc (Cambridge, MA: Cambridge University Press), 320–365.

Davidson, R. J. (1992). Emotion and affective style: hemispheric substrates. *Psychol. Sci.* 3, 39–43. doi:10.1111/j.1467-9280.1992.tb00254.x

Davidson, R. J. (1995). "Cerebral asymmetry, emotion, and affective style," in *Brain Asymmetry*, eds R. J. Davidson, and K. Hughdahl (Cambridge, MA: MIT Press), 361–388.

Davidson, R. J., Ekman, P., Saron, C. D., Senuluis, J. A., and Friesen, W. V. (1990). Approach-withdrawal and cerebral asymmetry: emotional expression and brain physiology I. *J. Pers. Soc. Psychol.* 58, 330–341. doi:10.1037/0022-3514.58.2.330

Demaree, H. A., Everhart, D. E., Youngstrom, E. A., and Harrison, D. W. (2005). Brain lateralization of emotional processing: historical roots and a future incorporating "dominance." *Behav. Cogn. Neurosci. Rev.* 4, 3–20. doi:10.1177/1534582305276837

Dunbar, N. E., and Burgoon, J. K. (2005). Perceptions of power and interactional dominance in interpersonal relationships. *J. Soc. Pers. Relat.* 22, 207–233. doi:10.1177/0265407505050944

Ellis, L. (2006). Gender differences in smiling: an evolutionary neuroandrogenic theory. *Physiol. Behav.* 88, 303–308. doi:10.1016/j.physbeh.2006.03.034

Fitzgerald, H. E. (1968). Autonomic pupillary reflex activity during early infancy and its relation to social and non-social and non-social visual stimuli. *Diss. Abstr.* 28, 3896B–3897B.

Fox, N. A. (1991). If it's not left, it's right: electroencephalograph asymmetry and the development of emotion. *Am. Psychol.* 46, 863–872. doi:10.1037/0003-066X.46.8.863

Fridlund, A. J., and Izard, C. (1983). "Electromyographic studies of facial expressions of emotions and patterns of emotion," in *Social Psychophysiology: A Sourcebook*, eds J. T. Cacioppo and R. E. Petty (New York: Guilford Press), 254–261.

Gainotti, G. (1969). "Catastrophic" reactions and manifestations of indifferences during cerebral disorders. *Neuropsychologia* 7, 195–204. doi:10.1016/0028-3932(69)90017-7

Gainotti, G. (1972). Emotional behavior and hemispheric side of lesion. *Cortex* 8, 41–55. doi:10.1016/S0010-9452(72)80026-1

Goldwater, B. C. (1972). Psychological significance of pupillary movements. *Psychol. Bull.* 77, 340–355. doi:10.1037/h0032456

Gordon, I. (1974). "Left and right in art," in *Psychology and the Arts*, ed. D. O'Hare (Brighton: Harevesor), 211–241.

Grüsser, O. J., Selke, T., and Zynda, B. (1988). "Cerebral lateralization and some implications for art, aesthetic perception, and artistic creativity," in *Beauty & The Brain: Biological Aspects of Aesthetics*, eds I. Reutshcler, B. Herzberger, and D. Epstein (Boston: Berkhäuer Verlag), 257–293.

Hess, E. H. (1965). Attitude and pupil size. *Sci. Am.* 212, 46–54. doi:10.1038/scientificamerican0465-46

Hess, E. H. (1972). "Pupillometrics: a method of studying mental, emotional, and sensory processes," in *Handbook of Psychophysiology*, eds N. S. Greenfield and R. A. Sternbach (New York: Holt, Rinehart & Winston), 491–531.

Hess, E. H., and Polt, J. M. (1960). Pupil size as related to interest value of visual stimuli. *Science* 132, 349–350. doi:10.1126/science.132.3423.349

Hess, E. H., Seltzer, A. L., and Shlien, J. M. (1965). Pupil response of hetero- and homosexual males to pictures of men and women: a pilot study. *J. Abnorm. Psychol.* 70, 165–168. doi:10.1037/h0021978

Humphrey, N., and McManus, C. (1973). Status and the left cheek. *New Sci.* 23, 437–439.

Janisse, M. P. (1973). Pupil size and affect: a critical review of the literature since 1960. *Can. Psychol.* 14, 311–329. doi:10.1037/h0082230

Janisse, M. P. (1974). Pupil size, affect and exposure frequency. *Soc. Behav. Pers.* 2, 125–146. doi:10.2224/sbp.1974.2.2.125

Janisse, M. P. (1977). *Pupillometry: The Psychology of the Pupillary Response*. New York, NY: John Wiley & Sons.

Jasari, A., Tranel, D., and Adolphs, R. (2000). A valence-specific lateral bias for discriminating emotional facial expressions in free field. *Cogn. Emot.* 14, 341–353. doi:10.1080/026999300378860

Killgore, W. D. S., and Yurgelun-Todd, D. A. (2007). The right-hemisphere and valence hypotheses: could they both be right (and sometimes left)? *Soc. Cogn. Affect. Neurosci.* 2, 240–250. doi:10.1093/scan/nsm020

Kinsbourne, M. (1982). Hemispheric specialization and the growth of human understanding. *Am. Psychol.* 37, 411–420. doi:10.1037/0003-066X.37.4.411

Kohn, M., and Clynes, M. (1969). Color dynamics of the pupil. *Ann. N. Y. Acad. Sci.* 156, 931–950. doi:10.1111/j.1749-6632.1969.tb14024.x

Libby, W. L., Lacey, B. C., and Lacey, J. I. (1973). Pupillary and cardiac activity during visual attention. *Psychophysiology* 10, 270–294. doi:10.1111/j.1469-8986.1973.tb00526.x

Lindell, A. K. (2013). Continuities in emotion lateralization in human and non-human primates. *Front. Hum. Neurosci.* 7:464. doi:10.3389/fnhum.2013.00464

Locher, P. L. (1996). The contribution of eye-movement research to an understanding of pictorial balance perception: a review of the literature. *Empiric. Stud. Arts* 14, 143–163. doi:10.2190/D77M-3NU4-DQ88-H1QG

Loewenfeld, I. E. (1966). Comment on Hess' findings. *Surv. Ophthalmol.* 11, 293–294.

Loewenfeld, I. E. (1999). *The Pupil: Anatomy, Physiology, and Clinical Applications*. Boston: Butterworth-Heinemann.

Loftus, G. R. (1985). Picture perception: effects of luminance on available information and information-extraction rate. *J. Exp. Psychol. Gen.* 114, 342–356. doi:10.1037/0096-3445.114.3.342

Mandal, M. K., Tandon, S. C., and Asthana, H. S. (1991). Right brain damage impairs recognition of negative emotions. *Cortex* 27, 247–253. doi:10.1016/S0010-9452(13)80129-3

Mannan, S., Ruddock, K. H., and Wooding, D. S. (1995). Automatic control of saccadic eye movements made in visual inspection of briefly presented 2-D images. *Spat. Vis.* 9, 363–386. doi:10.1163/156856895X00052

McManus, C., and Humphrey, N. (1973). Turning the left cheek. *Nature* 243, 271–272. doi:10.1038/243271a0

Miller, R. L. (1967). *The Clinical Validation of the Pupillary Response: The Effect of Chromatic and Achromatic Stimuli Upon Pupil Responsivity*. Doctoral Dissertation, Michigan State University, East Lansing.

Nakayama, M. (2006). "Influence of blink on pupillary indices," in *Biomedical Circuits and Systems Conference* (London: IEEE BioCAS 2006), 29–32.

Natale, M., Gur, R. E., and Gur, R. C. (1983). Hemispheric asymmetries in processing emotional expressions. *Neuropsychologia* 21, 555–565. doi:10.1016/0028-3932(83)90011-8

Nicholls, M. E. R., Clode, D., Lindell, A. K., and Wood, A. G. (2002a). Which cheek to turn? The effect of gender and emotional expressivity on posing behavior. *Brain Cogn.* 48, 480–484. doi:10.1006/brcg.2001.1402

Nicholls, M. E. R., Wolfgang, B. J., Clode, D., and Lindell, A. K. (2002b). The effect of left and right poses on the expression of facial emotion. *Neuropsychologia* 40, 1662–1665. doi:10.1016/S0028-3932(02)00024-6

Nicholls, M. E. R., Clode, D., Wood, S. J., and Wood, A. G. (1999). Laterality of expression in portraiture: putting your best cheek forward. *Proc. R. Soc. Lond.* 226, 1517–1522. doi:10.1098/rspb.1999.0809

Nicholls, M. E. R., Ellis, B. E., Clement, J. G., and Yoshino, M. (2000). Detecting hemifacial asymmetries in emotional expression with three-dimensional computerized image analysis. *Proc. R. Soc. Lond. Biol. Sci.* 271, 663–668. doi:10.1098/rspb.2003.2660

Nunnally, J. C., Knott, P. D., Duchnowski, A., and Parker, R. (1967). Pupillary responses as a general measure of activation. *Percept. Psychophys.* 2, 149–155.

Polt, J. M. (1970). Effect of threat of shock on pupillary response in a problem-solving task. *Percept. Mot. Skills* 31, 587–593. doi:10.2466/pms.1970.31.2.587

Powell, W. R., and Schirillo, J. A. (2009). Asymmetrical facial expressions in portraits and hemispheric laterality: a literature review. *Laterality* 14, 545–572. doi:10.1080/13576500802680336

Prehn, K., Kazzer, P., Lischke, A., Heinrichs, M., Herpertz, S. C., and Domes, G. (2013). Effects of intranasal oxytocin on pupil dilation indicate increased salience of socioaffective stimuli. *Psychophysiology* 50, 528–537. doi:10.1111/psyp.12042

Richer, F., Silverman, C., and Beatty, J. (1983). Response selection and initiation in speeded reactions: a pupillometric analysis. *J. Exp. Psychol. Hum. Percept. Perform.* 3, 360–370.

Rinn, W. E. (1984). The neuropsychology of facial expression: a review of the neurological and psychological mechanisms for producing facial expressions. *Psychol. Bull.* 95, 52–77. doi:10.1037/0033-2909.95.1.52

Rossi, G. F., and Rosadini, G. (1967). "Experimental analysis of cerebral dominance in man," in *Brain Mechanisms Underlying Speech and Language*, eds C. H. Millikan, and F. L. Darley (New York: Grune and Stratton), 167–189.

Russell, P. A., and George, D. A. (1990). Relationships between aesthetic response scales applied to paintings. *Empiric. Stud. Arts* 8, 15–30. doi:10.2190/AU1R-6UXE-T14R-04WQ

Sackeim, H. A., Greenberg, M. S., Weiman, A. L., and Gurr, R. C. (1982). Hemispheric asymmetry in the expression of positive and negative emotions. *Arch. Neurol.* 39, 210–218. doi:10.1001/archneur.1982.00510160016003

Sackeim, H. A., and Gur, R. C. (1978). Lateral asymmetry in intensity of emotional expression. *Neuropsychologia* 16, 473–481. doi:10.1016/0028-3932(78)90070-2

Sackeim, H. A., and Gur, R. C. (1983). "Facial asymmetry and the communication of emotion," in *Social Psychophysiology*, eds J. T. Cacioppo, and R. E. Petty (New York: Guilford), 307–352.

Sackeim, H. A., Gur, R. C., and Saucy, M. C. (1978). Emotions are expressed more intensely on the left side of the face. *Science* 202, 434–436. doi:10.1126/science.705335

Schiff, B. B., and Lamon, M. (1989). Inducing emotion by unilateral contraction of facial muscles: a new look at hemispheric specialization and the experience of emotion. *Neuropsychologia* 27, 923–935. doi:10.1016/0028-3932(89)90068-7

Schirillo, J., and Fox, M. (2006). Rembrandt's portraits: approach or avoid? *Leonardo* 39, 253–256. doi:10.1162/leon.2006.39.3.253

Schirillo, J. A. (2000). Hemispheric asymmetries and gender influence Rembrandt's portrait orientations. *Neuropsychologia* 38, 1593–1606. doi:10.1016/S0028-3932(00)00063-4

Schwartz, G. E., Ahern, G. L., and Brown, S. (1979). Lateralized facial muscle response to positive and negative emotional stimuli. *Psychophysiology* 16, 561–571. doi:10.1111/j.1469-8986.1979.tb01521.x

Silberman, E. K., and Weingartner, H. (1986). Hemispheric lateralization of functions related to emotion. *Brain Cogn.* 5, 322–353. doi:10.1016/0278-2626(86)90035-7

Simms, T. M. (1967). Pupillary response of male and female subjects to pupillary difference in male and female picture stimuli. *Percept. Psychophys.* 2, 553–555.

Smith, J. K., and Smith, L. F. (2001). Spending time on art. *Empiric. Stud. Arts* 19, 229–236. doi:10.2190/5MQM-59JH-X21R-JN5J

Steinhauer, S. R., Siegle, G. J., Condray, R., and Pless, M. (2004). Sympathetic and parasympathetic innervation of pupillary dilation during sustained processing. *Int. J. Psychophysiol.* 52, 77–86. doi:10.1016/j.ijpsycho.2003.12.005

Stern, J. A., and Strock, B. D. (1987). "Oculomotor activity and user-system interaction in the workplace," in *Psychophysiology and the Electronic Workplace*, eds A. Gale, and B. Christie (Oxford: John Wiley & Sons), 239–254.

Tinio, F., and Robertson, M. (1969). Examination of two indices of hostility: fantasy and change in pupil size. *Proc. Annu. Convent. Am. Psychol. Assoc.* 4, 173–174.

Woodmansee, J. J. (1966). "Methodological problems in pupillographic experiments," in *Proceedings of the Annual Convention of the American Psychological Association*, 133–134.

Woodmansee, J. J. (1967). The pupil reaction as an index of positive and negative affect. *Paper Presented at the Convention of the American Psychological Association*, Washington, DC.

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APPENDIX

LISTING OF PAINTING TITLES (TAKEN FROM BREDIUS, 1969).

Left facing females

1. Rembrandt's Sister, 1632. Stockholm, National Museum (Br. 85)
2. Saskia. 1643. Cassel, Gemaldegalerie (Br. 101).
3. Saskia. 1636. Hartford, Conn., Wadsworth Atheneum (Br. 105).
4. Hendrickje Stoffels as Flora. 1654. New York, Metropolitain of Art (Br. 114).
5. Amalia van Solms. 1632. Paris, Musee Jacquemart-Andre (Br. 99).

Right facing females

1. Rembrandt's Mother as a Biblical Prophetess (Hannah?). 1631. Amsterdam, Rijksmuseum (Br. 69).
2. Saskia. 1633. Washington, National Gallery of Art (Widener Collection) (Br. 96).
3. Rembrandt's Sister. 1634. Indianapolis, John Herron Art Museum (Br. 100).
4. A Woman in Fanciful Costume. 1648. Baltimore, The Walters Art Gallery (Br. 386).
5. A Young Girl Seated. 1660. London, E. S. Borthwick Norton Sale, May 15. 1953 (Br. 393).

Left facing males

1. Head of an Old Man. Copenhagen, Statens Museum (Br. 136).
2. A Man in Oriental Costume. 1633. Munich, Alte Pinakothek (Br. 178).
3. A Bearded Man. 1646. Cassel, Germaldegalerie (Br. 230).
4. Study of an Old Man. 1640. Detroit, Mrs. Standish Backus (Br. 244).
5. Portrait of an Old Man in a Pearl-Trimmed Hat. 1662. Dresden, Gemaldegalirie (Br. 324).

Right facing males

1. Self-Portrait. 1629. Munich, Alte Pinakothek (Br. 2).
2. Self-Portrait. Not dated. The Hague, Mauritshuis (Br. 24).
3. An Old Man with a Gold Chain. 1630. Los Angeles, Hans Cohn (Br. 149).
4. Portrait of a Man Reading. 1645. Williamstown, Mass., The Sterling and Francine Clark Art Museum (Br. 238).
5. Study of the Head of an Old Man. 1661. New York, John Hay Whitney (Br. 261).

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Caffeine promotes global spatial processing in habitual and non-habitual caffeine consumers

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Information processing is generally biased toward global cues, often at the expense of local information. Equivocal extant data suggests that arousal states may accentuate either a local or global processing bias, at least partially dependent on the nature of the manipulation, task, and stimuli. To further differentiate the conditions responsible for such equivocal results we varied caffeine doses to alter physiological arousal states and measured their effect on tasks requiring the retrieval of local versus global spatial knowledge. In a double-blind, repeated-measures design, non-habitual (Experiment 1; $N = 36$, $M = 42.5 \pm 28.7$ mg/day caffeine) and habitual (Experiment 2; $N = 34$, $M = 579.5 \pm 311.5$ mg/day caffeine) caffeine consumers completed four test sessions corresponding to each of four caffeine doses (0, 100, 200, 400 mg). During each test session, participants consumed a capsule containing one of the three doses of caffeine or placebo, waited 60 min, and then completed two spatial tasks, one involving memorizing maps and one spatial descriptions. A spatial statement verification task tested local versus global spatial knowledge by differentially probing memory for proximal versus distal landmark relationships. On the map learning task, results indicated that caffeine enhanced memory for distal (i.e., global) compared to proximal (i.e., local) comparisons at 100 (marginal), 200, and 400 mg caffeine in non-habitual consumers, and marginally beginning at 200 mg caffeine in habitual consumers. On the spatial descriptions task, caffeine enhanced memory for distal compared to proximal comparisons beginning at 100 mg in non-habitual but not habitual consumers. We thus provide evidence that caffeine-induced physiological arousal amplifies global spatial processing biases, and these effects are at least partially driven by habitual caffeine consumption.

Keywords: caffeine, arousal, spatial memory, global, local

INTRODUCTION

The way we perceive our environment has implications for our ability to attend to environmental cues and successfully navigate from one point to another. Visual perception research suggests that information processing shows a global precedence, with processing beginning at global levels and then progressing to relatively local levels (Navon, 1977, 2003; Kimchi, 1992), even as early as infancy (Cassia et al., 2002). Some recent findings suggest that this global precedence is not a stable trait but rather subject to change under conditions of emotional and physiological arousal. The directionality of these changes, however, remains under debate; indeed some studies find evidence of arousal-induced global processing advantages, and yet others find the opposite. Further, the generalizability of these effects across information types has not been fully explored. Several studies have examined these issues with visual perception and verbal memory, but would they also carry over to the processing and mental representation of relatively real-world spatial information? Toward further elucidating the directionality and breadth of arousal effects on local versus global processing, the present research examines whether physiological arousal states modulate global precedence on tasks involving the processing, representation, and retrieval of spatial information. Below we review extant literature related to arousal influences on perception and memory, and then briefly review emerging evidence related to caffeine's influence on these processes as a basis for motivating our manipulation and hypotheses.

AROUSAL AND MEMORY

Equivocal extant data suggests that arousal states may accentuate either a local or global processing bias, at least partially dependent on the nature of the manipulation, task, and stimuli. Emotional information may be conceptualized in two orthogonal dimensions: valence (positive or negative) and arousal (high or low), which utilize somewhat distinct neural processes (Kensinger and Corkin, 2004).

Two different research methods have been used to determine the relationship between emotional state and global/local processing biases, the first of which investigates memory and attention to emotional stimuli. Exposure to emotional stimuli generally narrows attention and impairs memory for details peripheral to the salient image features (Loftus, 1979; Loftus and Burns, 1982). At the same time, memory for certain details, mainly the central details (e.g., a weapon), are enhanced in arousing relative to neutral scenes (Kensinger and Schacter, 2006, 2007). Enhanced memory for central, emotionally arousing elements of a scene is not necessarily due to increased attention for those elements; this enhancement is present after as little as one eye fixation (Christianson et al., 1991). These findings are generally aligned with Easterbrook's (1959) seminal arousal hypothesis, which proposed that heightened emotional arousal reduces the range of cues an individual uses to gather information from ongoing events (Easterbrook, 1959).

The second method entails experimentally inducing emotional states, and assessing the influence on memory and attention to neutral stimuli. Emotional states may act as information cues, i.e., *affect as information* approach (Schwarz and Clore, 1983; Clore and Palmer, 2009). Gasper and Clore (2002) proposed the *levels of focus* approach, in which mood states differentially guide attention to global versus local cues. Individuals in sad emotional states are less likely to attend to global perceptual cues than individuals in happy emotional states (Gasper and Clore, 2002); specifically, when asked to indicate whether a target figure is most similar to a figure that matches either the local or global features of the target figure, participants showed a marked tendency to match on global features when in a positive versus negative or neutral mood. Similar results were found with verbal stimuli: when participants were placed in a positive versus negative mood they tended to falsely recall a higher proportion of highly associated but never presented words, i.e., critical lures, suggesting increased "gist" or global verbal associative processing (Storbeck and Clore, 2005).

Other studies suggest that arousal, rather than valence, may be responsible for at least some of the above findings. For instance, Corson and Verrier (2007) argue that earlier verbal memory results can be attributed to arousal alone rather than accompanying valence (Corson and Verrier, 2007); specifically, when valence was held constant, high arousal states showed the global verbal associative processing found by Storbeck and Clore (2005). Arousal also influences the ability to switch between local and global attentional focuses, as trained soccer players have impaired local attention relative to non-athletes, but are better able to switch from local to global perspectives during periods of high physiological arousal (Pesce et al., 2007). More chronic arousal, such as that experienced by individuals with post-traumatic stress disorder (PTSD) with heightened basal arousal levels, also leads to global processing biases (Vasterling et al., 2004).

Whether emotional states or cues contribute to a global or local focus may be driven, in part, by their motivational intensity. Motivational intensity as defined by Gable and Harmon-Jones (2010) is the "impetus to act." They propose that within positive affective states, low approach motivation (e.g., content) broadens attentional scope whereas high approach motivation (e.g., enthusiastic) narrows attentional scope (Harmon-Jones and Gable, 2008). The same has been found within negative affective states, as viewing a series of images low in approach intensity (i.e., sad) accentuated global attention whereas viewing a series of images high in approach intensity (i.e., disgusting) reduced global attention relative to neutral images (Gable and Harmon-Jones, 2010). Such results are likely not attributable to differences in arousal, as viewing images characterized as negative in affect and high in arousal and approach motivation (i.e., appetitive desserts) narrowed attentional scope, whereas pedaling on a bicycle, which increases cardiovascular arousal but does not affect or approach motivation, had no influence on attentional scope (Gable and Harmon-Jones, 2013).

Thus, there is converging evidence that arousal states (with or without specific valence or motivational attributes) may influence both the processing and representation of abstract shapes (e.g., Gasper and Clore, 2002) and word lists (e.g., Storbeck and Clore, 2005; Corson and Verrier, 2007). Further, when individuals attend to affectively salient images there appears to be an arousal-related increase in local processing (Loftus, 1979; Kensinger and Schacter, 2006); in contrast, when individuals attend to affectively neutral information while in a heightened arousal state there appears to be an increase in global processing.

Some recent research specifically asked whether the valence or arousal accompanying affective states modulated local versus global processing of spatial information. Brunyé et al. (2009) manipulated subjects' emotional states by crossing arousal (high versus low) with valence (happy versus sad) and assessed memory for landmark relationships. They found that high arousal augmented global spatial processing, such that accuracy and response time for distal relative to proximal landmark judgments were higher and faster (respectively) for individuals in high relative to low arousal states, regardless of positive or negative valence (Brunyé et al., 2009). This adds converging evidence to suggest that heightened arousal, regardless of valence, promotes global processing advantages with map-based spatial information.

CAFFEINE, AROUSAL, AND GLOBAL PROCESSING

The research reviewed above highlights the importance of selectively targeting arousal mechanisms without altering the valence or motivational intensity of subjective mood states; in the behavioral paradigms frequently used in laboratory settings, this can be difficult. Indeed the pictures, music, and/or autobiographical recall instructions typically selected for mood induction tend to be selected to specifically induce single affective states such as happiness, sadness, anger, or fear (Lang et al., 1993, 1998; Husain et al., 2002; Jallais and Gilet, 2010). Indeed it is difficult to imagine images or music that can induce a heightened arousal state without also being associated with anger, anxiety, fear, or excitement; similarly, it is difficult to induce a suppressed arousal state without it being associated with sadness or a positive state of relaxation/contentment.

A relatively selective approach to influencing arousal states is to manipulate subjective and physiological arousal by administering a psychostimulant such as caffeine. Caffeine is the most common behaviorally active substance in the world. Almost 90% of the individuals in the United States consume caffeine, and daily caffeine intake averages approximately 200 mg/day (Frary et al., 2005; Smith, 2011). Habitual caffeine consumption may stem, in part, from its perceived beneficial effects on arousal and vigilance (Nehlig et al., 1992b; Lieberman, 2001). Biochemically, caffeine consumption results in increased dopamine and serotonin, which have been linked to the enhancement of processes that require executive control (Ferre et al., 1997; Abrams et al., 2005; Brunyé et al., 2010b; Mahoney et al., 2011). In addition, caffeine consumption has been shown to increase cortisol, an index of physiological arousal (Lovallo et al., 2005), and enhance alertness, vigilance, and psychomotor performance (Lieberman, 2003). Other cognitive influences of caffeine, including attention, depend more on environmental factors such as sleep deprivation as well as individuals' habitual caffeine intake (Rogers et al., 2005; Brunyé et al., 2010a,b).

Caffeine reliably increases arousal in habitual and non-habitual caffeine consumers (Childs and de Wit, 2006). Similarly, caffeine withdrawal reduces arousal (i.e., lower rated vigor and higher rated fatigue) in habitual consumers (Lane, 1997; Lane and Phillips-Brute, 1998; Haskell et al., 2005). However, evidence is mixed as to whether caffeine influences affective valence. Caffeine increased anxiety and tension, but only at a high dose (Childs and de Wit, 2006; Mahoney et al., 2011), but did not influence anxiety or hedonic tone in habitual and non-habitual caffeine consumers (Smith et al., 2006a). Caffeine withdrawal may also influence affective valence, as high habitual caffeine consumers reported feeling less vigorous and more angry, confused, depressed, and fatigued after abstaining from their normal caffeine intake than after consuming caffeine *ad libitum* (Lane, 1997; Lane and Phillips-Brute, 1998). Thus caffeine reliably increases arousal but not affective valence, but the caffeine withdrawal from overnight abstinence could partially account for mixed findings in high habitual caffeine consumers.

Recent research suggests that caffeine accentuates global processing biases in both visual perception (Mahoney et al., 2011) and language-based tasks (Brunyé et al., 2012). Mahoney et al. (2011) administered a range of caffeine doses (0–400 mg) and asked participants to complete two visual attention tasks, i.e., the Hierarchical Shape Task (Kimchi and Palmer, 1982) and Hierarchical Letter Task (Navon, 1977). Individuals responded faster to global relative to local comparisons, and this effect became pronounced with caffeine administration. Brunyé et al. (2012) used the same dose-ranging design, and used a language tasks that required subjects to identify and correct errors in an extended text. Caffeine enhanced error detection rates for global (e.g., subject-verb agreement errors), but not local (e.g., spelling errors) elements of the text beginning at 200 mg in non-habitual caffeine consumers and at 400 mg in habitual caffeine consumers.

PRESENT STUDY

The primary aim of the present study is to assess the influence of arousal on global versus local spatial memory, in order to better understand the relationship between arousal and memory for "gist" and detail information without the potential confounding influence of emotional valence. The extant literature provides a strong basis for generating hypotheses regarding caffeine's influence on the processing and representation of local versus global spatial information. A number of studies have suggested that encoding of spatial information is an automatic rather than effortful process (Hasher and Zacks, 1979; Ellis, 1990; Andrade and Meudell, 1993) and thus unlikely to be influenced by arousal states; other studies, however suggest the opposite (Light and Zelinski, 1983; Arbuckle et al., 1994; Kessels et al., 2005). Indeed a growing body of evidence suggests that the ability to accurately process and mentally represent spatial information is contingent upon several factors such as goals, affective states, working memory load, and strategies (McNamara et al., 1992; Taylor et al., 1999; Waller, 2000; Hegarty et al., 2006; Brunye and Taylor, 2008; Maddox et al., 2008; Brunyé et al., 2009; Gyselinck et al., 2009; Meneghetti et al., 2009; Gardony et al., 2011). Thus, a number of studies suggest that there is limited automaticity to the encoding of spatial location information, although it may be processed less effortfully than some other types of information (Thomas et al., 2012). Our first hypothesis, therefore, is that the arousal states produced via caffeine administration will influence participants' ability to accurately memorize spatial information.

The effect of caffeine on spatial memory is expected to manifest specifically when assessing memory for local versus global details of a spatial scene. Previous work suggests that arousal but not valence enhances memory for global spatial relationships (Brunyé et al., 2009) and that caffeine amplifies global processing biases (Mahoney et al., 2011). To examine whether these results hold for caffeine and spatial stimuli, we assess participants' ability to make inferences about proximal (two landmarks close to one another) versus distal (two landmarks far from one another) spatial relationships after consuming one of four caffeine doses. Given earlier findings, our second hypothesis states that increasing doses of caffeine will induce an increasingly global focus in spatial memory.

Finally, because chronic caffeine consumption can increase adenosine receptor density in the brain (Daval et al., 1989; Rudolphi et al., 1989; Varani et al., 1999) and influence necessary doses required to achieve cognitive effects (Evans and Griffiths, 1992; Jacobson and Thurman-Lacey, 1992; Lyvers et al., 2004; Attwood et al., 2007; Brunyé et al., 2010a, 2012), consumption patterns may modulate our hypothesized effects. To address this issue, we separately recruited participants who rarely (Experiment 1) or regularly (Experiment 2) consume caffeine. Our final hypothesis states that the influence of caffeine on spatial memory will be evident at lower doses in low habitual caffeine consumers than in high habitual consumers.

MATERIALS AND METHODS

PARTICIPANTS

Thirty six undergraduate students who were low habitual caffeine consumers (less than 100 mg/day, $M = 42.45 \pm 28.68$ mg/day) participated in Experiment 1 and 34 students who were high habitual caffeine consumers (at least 300 mg/day, $M = 579.51 \pm 311.48$ mg/day) participated in Experiment 2 (see **Table 1**). Students participated for monetary compensation ($10 USD/h). All students were non-nicotine users, in good health, and did not use prescription medication other than oral contraceptives. Written informed consent was obtained, and all procedures were jointly approved by the Tufts University Institutional Review Board and the Human Use Review Committee of the U.S. Army Research Institute for Environmental Medicine.

DESIGN

Both Experiment 1 and Experiment 2 used a double-blind, repeated-measures design with four levels of caffeine (0, 100, 200, 400 mg caffeine). The highest dose of caffeine approximates that found in a 20 oz coffee portion served at a major franchise coffee house (i.e., 415 mg; www.starbucks.com). Caffeine order was counterbalanced across participants. In order to control for taste, caffeine or placebo was administered in capsule form; capsules

Table 1 | Age, gender, BMI, and caffeine intake distribution for study subjects.

Habitual caffeine intake	n (female)	Age	BMI	Caffeine intake
		M ± SD	M ± SD	M ± SD
Low (<100 mg/day)	36 (20)	19.08 ± 1.32	23.15 ± 3.01	42.45 ± 28.68
High (>300 mg caffeine/day)	34 (26)	20.00 ± 1.46	22.65 ± 4.64	579.51 ± 311.48

were identical in color, size, weight, and shape. The caffeine was 99.8% pure anhydrous USP-grade powder. Placebo capsules were filled with physiologically inert microcrystalline cellulose powder, which was also used as filler material in the two lower-dose caffeine capsules.

QUESTIONNAIRES AND COGNITIVE TASKS

Brief mood introspection scale

The Brief Mood Introspection Scale (BMIS) involves rating current mood state in accordance with 16 adjectives (8 positive and 8 negative) on a series of 4 point Likert scales anchored at 1 (definitely do not feel) and 4 (definitely feel) (Mayer and Gasche, 1988). The BMIS was factored into four subscales: pleasant, unpleasant, arousal and calm, and served as a manipulation check to ensure that caffeine increased feelings of arousal but did not reliably alter feelings of positive or negative affect.

Map learning task

Four maps were adapted from Grinnell, St. Olaf's, and Occidental campus maps (i.e., Brunye et al., 2007). Each map was standardized to include 14 labeled buildings, 6 labeled roads, and a compass rose. Participants had 5 min to study a map, which was followed by a brief distraction task (i.e., simple arithmetic calculations) and then a spatial statement verification task. The statement verification task involved 56 sentences describing the relative spatial location between map locations (e.g., The Psychology Building is west of Anderson Hall) across two comparison distances (28 proximal, 28 distal). Participants responded "true" or "false" and dependent measures include accuracy and response time.

Spatial description task

This task followed the same procedure as the map learning task with the exception that participants read a description of an environment, instead of studying a map. Four sets of text were adapted from (Taylor and Tversky, 1992, see also Brunye and Taylor, 2008; Brunye et al., 2008). Each set of texts described an environment that included 7–10 landmarks. Participants had approximately 5 min to study the description, followed by the brief arithmetic distracter task and then the statement verification task. Dependent measures include accuracy and response time.

PROCEDURE

Participants completed one practice session and all four caffeine conditions on separate days, resulting in five test sessions. There was a minimum three day wash-out period between test sessions. Participants were instructed not to eat or drink anything (with the exception of water) after 9:00 p.m. the night before a test session and not to use any over-the-counter medications or herbal supplements 24 h prior to testing. A 12-h abstinence period is thought to be a sufficient wash-out period to attenuate the effects of earlier caffeine consumption, given that the mean plasma and elimination half-life of caffeine ranges from 3 to 10 h (Blanchard and Sawers, 1983; Scott et al., 1989; Nehlig et al., 1992a). Test sessions began between 7:00 and 9:30 a.m.

When participants arrived in the morning, they consumed a capsule containing one of the three doses of caffeine or placebo along with a cup of water. Sixty minutes after consuming the capsule, participants completed the BMIS, map task, and spatial description task, in the same order within-participants and counterbalanced order across participants. Timing of testing was based on previous research showing that caffeine peak plasma concentrations vary between individuals and occur between 30 and 120 min after consumption (Blanchard and Sawers, 1983; Arnaud, 1987; Smith, 2002).

STATISTICS

The BMIS was analyzed using an Analyses of Variance (ANOVA) with Caffeine condition (0, 100, 200, 400 mg) and Subscale (Positive, Negative, Arousal, Calm) as within-participants factors. The map task and spatial descriptions tasks were analyzed using an ANOVA with Caffeine condition (0, 100, 200, 400) and test Distance (proximal, distant) as the within-participants factors. Dependent measures include response time and accuracy. An effect was deemed statistically significant if the likelihood of its occurrence by chance was $p < 0.05$. When sphericity was violated, Greenhouse–Geisser corrected p-values were used. When an ANOVA yielded a significant main effect, *post hoc* tests using the Bonferroni correction were conducted. All statistical analyses were performed using SPSS 12.0.

RESULTS

MANIPULATION CHECK

In low habitual caffeine consumers, analysis of BMIS data indicated main effects of Subscale $F(3, 105) = 155.094$, $p < 0.001$ ($\eta^2 = 0.714$), and marginal effects of Caffeine, $F(3, 105) = 2.251$, $p < 0.09$ ($\eta^2 = 0.003$); these effects were qualified by an interaction between Subscale and Caffeine, $F(9, 315) = 2.262$, $p < 0.05$ ($\eta^2 = 0.004$). Follow-up analyses demonstrated that caffeine did not influence rated positive ($p > 0.33$), negative ($p > 0.17$), or calm mood ($p > 0.26$) but increased rated arousal $F(3, 105) = 4.882$, $p < 0.01$ ($\eta^2 = 0.310$). Paired t-tests showed that rated arousal was marginally higher after 200 mg $t(35) = 1.858$, $p < 0.08$ ($d = 0.310$) and significantly higher after 400 mg caffeine $t(35) = 3.388$, $p < 0.01$ ($d = 0.565$) than placebo (**Table 2**).

In high habitual caffeine consumers, main effects of Subscale $F(3, 99) = 115.827$, $p < 0.001$ ($\eta^2 = 0.707$), and marginal effects of Caffeine, $F(3, 99) = 2.267$, $p < 0.09$ ($\eta^2 = 0.003$) were

Table 2 | Brief mood introspection scale (BMIS).

		Pleasant		Unpleasant		Arousal		Calm	
		M	SE	M	SE	M	SE	M	SE
Low habitual caffeine consumer	0 mg	20.06	0.82	23.58	0.69	12.31	0.36	13.11	0.27
	100 mg	21.06	0.85	24.61	0.73	12.78	0.44	13.11	0.35
	200 mg	21.22	0.78	24.36	0.69	13.28	0.50	13.19	0.29
	400 mg	20.64	0.85	23.78	0.67	14.28	0.52	13.64	0.26
High habitual caffeine consumer	0 mg	20.44	0.66	22.91	0.71	12.59	0.49	12.71	0.29
	100 mg	20.68	0.79	23.65	0.73	12.76	0.50	12.85	0.29
	200 mg	21.09	0.70	23.59	0.73	13.44	0.49	13.24	0.35
	400 mg	21.06	0.66	22.91	0.70	13.76	0.45	13.47	0.29

Paired t-tests demonstrated that 200 and 400 mg caffeine resulted in higher feelings of arousal (arousal-calm) than placebo (p's < 0.01), but did not influence valence ratings (pleasant-unpleasant).

not qualified by a Subscale by Caffeine interaction ($p > 0.26$). Thus 200 and 400 mg caffeine increased feelings of arousal, but not valence, in low habitual caffeine consumers, and such doses did not influence mood in high consumers.

CAFFEINE ORDER

Caffeine order was counterbalanced across participants to circumvent order effects. Nonetheless, all measures were subjected to analyses testing whether the first dose received, either low (i.e., 0 or 100 mg) or high (i.e., 200 or 400 mg) influenced results. In low habitual caffeine consumers, a low versus high first dose did not impact the BMIS (p's > 0.13) or spatial descriptions task (p's > 0.15). On the map learning task, no effects were found for reaction time (p's > 0.16) but a marginal Caffeine by First Dose interaction on accuracy $F(3, 102) = 2.262$, $p < 0.09$ $(\eta^2 = 0.029)$ showed that accuracy was higher after 200 and 400 mg caffeine (p's < 0.05) relative to placebo when the low dose was given first $F(3, 18) = 2.859$, $p < 0.05$ $(\eta^2 = 0.068)$ but no differences in accuracy when the high dose was given first ($p > 0.59$).

In high habitual caffeine consumers, a low versus high first dose did not impact the BMIS (p's > 0.13). On the map learning task, no effects were found for accuracy (p's > 0.43) but a marginal effect of First Dose on reaction time $F(1, 30) = 3.017$, $p < 0.1(\eta^2 = 0.189)$ in which reaction time was higher overall when subject were given the high relative to low dose first. On the spatial descriptions task, no effects were found for accuracy (p's > 0.28). A Distance by First Dose interaction was found on reaction time $F(1, 32) = 4.285$, $p < 0.05$ $(\eta^2 = 0.028)$, but showed no differences between distal and proximal landmarks when either the low ($p > 0.19$) or high ($p > 0.13$) dose was given first. Thus caffeine order exerted only marginal effects on results.

EXPERIMENT 1: NON-HABITUAL CAFFEINE CONSUMERS

Map learning task

Accuracy data replicated earlier results with a main effect of Distance $F(1, 35) = 82.45$, $p < 0.001(\eta^2 = 0.200)$, in which accuracy was higher for distant relative to proximal distances (Mean ± SEM Proximal = 0.77 ± 0.02; Distant = 0.89 ± 01). There was also a Distance × Caffeine interaction $F(2.313, 80.962) = 4.695$, $p < 0.01$ $(\eta^2 = 0.027)$. As shown in **Table 3**, verification accuracy rates for distant landmarks increased as a function of caffeine dose; specifically, for distant landmarks $F(3, 105) = 7.072$, $p < 0.001$ $(\eta^2 = 0.168)$ accuracy was marginally higher at 100 mg versus Placebo $t(35) = 1.920$, $p < 0.07$ $(d = 0.32)$ and showed higher accuracy at 200 mg versus Placebo $t(35) = 2.912$, $p < 0.01$ $(d = 0.485)$, and 400 mg versus Placebo $t(35) = 4.333$, $p < 0.001$ $(d = 0.722)$. This same effect was not found when verifying landmarks close together (p's > 0.65). These results replicate the symbolic distance effect, showing greater accuracy for landmarks that are farther apart than closer together, and show that caffeine amplifies the effect beginning at 100 mg caffeine intake.

Analysis of response time showed main effects for Distance $F(1, 35) = 94.139$, $p < 0.001$ $(\eta^2 = 0.241)$, in which response time was lower for distant relative to proximal landmarks, again replicating the symbolic distance effect (Proximal = 3765.43 ± 185.07 ms; Distant = 3058.36 ± 140.87 ms). No effects of Caffeine or interactions were found for response time.

Spatial description task

Accuracy data replicated earlier results with a main effect of Distance $F(1, 34) = 85.421$, $p < 0.001$ $(\eta^2 = 0.139)$, in which accuracy was higher for distant relative to proximal distances (Proximal = 0.73 ± 0.02; Distant = 0.86 ± 01). A marginal effect of Caffeine $F(3, 102) = 2.227$, $p < 0.100$ $(\eta^2 = 0.031)$ showed that accuracy did not differ from placebo after 100 mg caffeine, but was higher after 200 mg and marginally higher after 400 mg caffeine. As with the map task, there was also a Distance × Caffeine interaction $F(2.382, 80.972) = 3.556$, $p < 0.05$ $(\eta^2 = 0.029)$. As shown in **Table 3**, distant trial accuracy rates increased as a function of caffeine dose $F(3, 102) = 9.094$, $p < 0.001$ $(\eta^2 = 0.211)$; specifically, within the distant condition accuracy was higher at 100 mg versus Placebo $t(34) = 3.891$, $p < 0.001$ $(d = 0.658)$, 200 mg versus Placebo $t(34) = 3.490$, $p < 0.01$ $(d = 0.590)$, and 400 mg versus Placebo $t(34) = 4.708$, $p < 0.001$ $(d = 0.798)$. This same effect was not found in the proximal condition (p's > 0.58). These results replicate the symbolic distance effect and show that caffeine promotes the global spatial processing bias beginning at 100 mg caffeine intake.

No effects were found for response time (p's > 0.70).

Table 3 | Experiment 1 map learning task and spatial description task mean accuracy and response time in low habitual caffeine consumers ($n = 36$).

		Map learning task				Spatial descriptions task			
		Proximal		Distal		Proximal		Distal	
		M	SE	M	SE	M	SE	M	SE
Accuracy	0 mg	0.78	0.03	0.84	0.02	0.73	0.03	0.76	0.03
	100 mg	0.79	0.03	0.88	0.02	0.71	0.04	0.87	0.03
	200 mg	0.76	0.03	0.92	0.02	0.75	0.03	0.89	0.02
	400 mg	0.78	0.03	0.93	0.01	0.72	0.04	0.92	0.01
Response time	0 mg	3686.95	220.98	2938.86	168.88	2918.88	258.75	3100.91	294.12
	100 mg	3930.92	205.45	3205.35	161.19	3210.21	362.67	3233.22	276.08
	200 mg	3729.28	221.54	3089.34	180.49	2933.97	384.31	2948.43	344.09
	400 mg	3714.59	204.46	2999.88	157.26	2909.13	291.77	2830.50	270.01

The table represents proximal relative to distant distal comparisons for each of the four Caffeine doses (0, 100, 200, 400 mg). In the map learning task, within the distant condition accuracy was not higher at 100 mg versus Placebo, but showed higher accuracy at 200 mg versus Placebo ($p < 0.01$), and 400 mg versus Placebo ($p < 0.001$). This same effect was not found in the proximal condition. In the spatial description task, distal distance accuracy rates increased as a function of caffeine dose; specifically, within the distant condition accuracy was higher at 100 mg versus Placebo ($p < 0.001$), 200 mg versus Placebo ($p < 0.01$), and 400 mg versus Placebo ($p < 0.001$). This same effect was not found in the proximal condition.

EXPERIMENT 2: HABITUAL CAFFEINE CONSUMERS

Map learning task and spatial description task data reflect 32 complete data sets, as one subject failed to complete tasks during the 200 mg dose test session, and one other subject failed to complete tasks during the 400 mg dose test session.

Map learning task

Accuracy data replicated earlier results with a main effect of Distance $F(1, 31) = 35.133$, $p < 0.001$ ($\eta^2 = 0.108$), in which accuracy was higher for distant relative to proximal distances (Proximal $= 0.70 \pm 0.02$; Distant $= 0.78 \pm 03$). There was also a Distance × Caffeine interaction $F(3, 93) = 3.196$, $p < 0.05$ ($\eta^2 = 0.018$). As depicted in **Table 4**, distant distance accuracy rates marginally increased as a function of caffeine dose; specifically, within the distant condition $F(3, 93) = 2.633$, $p < 0.06$, accuracy was not higher at 100 mg ($p > 0.95$) or 200 mg ($p > 0.13$) versus Placebo but was marginally accuracy at 400 mg versus Placebo $t(31) = 1.955$, $p < 0.07$ ($d = 0.346$). This same effect was not found in the proximal condition (p*'s* > 0.45). These results replicate the symbolic distance effect and show that caffeine exacerbates the effect, only marginally after 400 mg caffeine intake in high habitual caffeine consumers.

Analysis of response time showed main effects for Distance $F(1, 31) = 103.521$, $p < 0.001$ ($\eta^2 = 0.184$), in which response time was higher for distant relative to proximal distances, again replicating the symbolic distance effect (Proximal $= 3310.02 \pm 202.66$ ms; Distant $= 2688.57 \pm 176.03$ ms). No effects of Caffeine or interactions were found for response time.

Spatial description task

Accuracy data replicated earlier results with a main effect of Distance $F(1, 33) = 28.830$, $p < 0.001$ ($\eta^2 = 0.039$), in which accuracy was higher for distant relative to proximal distances, demonstrating greater accuracy for landmarks that are farther apart than closer together (Proximal $= 0.69 \pm 0.03$; Distant $= 0.74 \pm 0.03$). No effects of Caffeine or interactions were found for accuracy (p's > 0.28).

No effects were found for response time (p's > 0.10).

COMPARING HIGH AND LOW CONSUMERS

To specifically test differences across consumption profiles, we calculated change scores by subtracting the mean accuracy proximal from distant distal comparisons for both the Map Learning and spatial descriptions tasks. Analysis of the map learning task replicated findings of Experiments 1 and 2, finding a main effect of Caffeine $F(3, 198) = 6.692$, $p < 0.001$ ($\eta^2 = 0.084$), such that the difference in accuracy between distant and proximal distances was not higher at 100 mg versus Placebo ($p > 0.43$), but was higher at 200 mg versus Placebo $t(68) = 3.056$, $p < 0.01$ ($d = 0.368$) and 400 mg versus Placebo $t(67) = 4.102$, $p < 0.001$ ($d = 0.497$). These results show that caffeine exacerbates the global processing bias beginning at 200 mg caffeine intake across habitual consumption profiles.

As depicted in **Figure 1**, a main effect of Consumption profile $F(1, 66) = 4.54$, $p < 0.05$ ($\eta^2 = 0.244$) showed that the difference in accuracy between distant and proximal distances was higher in low relative to high habitual caffeine consumers (Low $= 0.12 \pm 0.01$; High $= 0.08 \pm 0.01$; **Figure 2**). This finding indicates that at relevant doses, caffeine has greater effects on spatial processing in low relative to high habitual caffeine consumers. No Caffeine × Consumption interaction was found ($p > 0.54$).

Analysis of the spatial description task replicated findings of Experiments 1 and 2, showing a main effect of Caffeine $F(3, 201) = 4.652$, $p < 0.001$ ($\eta^2 = 0.060$), such that the difference in accuracy between distant and proximal distances was higher after 100 mg $t(68) = 3.045$, $p < 0.01$ ($d = 0.366$), 200 mg $t(68) = 2.567$, $p < 0.05$ ($d = 0.309$), and 400 mg caffeine $t(68) = 3.697$, $p < 0.001$ ($d = 0.445$) than placebo. As depicted in **Figure 2**, a main effect

Table 4 | Map learning task and spatial description task mean accuracy and response time (SE) in high habitual caffeine consumers ($n = 36$).

		Map learning task				Spatial descriptions task			
		Proximal		Distal		Proximal		Distal	
		M	SE	M	SE	M	SE	M	SE
Accuracy	0 mg	0.70	0.03	0.74	0.03	0.73	0.03	0.75	0.04
	100 mg	0.69	0.03	0.75	0.03	0.67	0.04	0.74	0.04
	200 mg	0.73	0.03	0.80	0.03	0.70	0.03	0.75	0.03
	400 mg	0.67	0.03	0.81	0.03	0.65	0.04	0.72	0.03
Response time	0 mg	3254.28	275.64	2790.53	230.40	2701.23	240.52	2793.07	240.49
	100 mg	3238.95	236.98	2437.73	203.94	2678.42	199.98	2706.29	196.47
	200 mg	3375.27	240.27	2731.90	208.05	2662.35	205.99	2787.82	235.65
	400 mg	3340.47	221.65	2783.42	190.40	2447.75	218.53	2642.49	230.92

The table represents proximal relative to distant distal comparisons for each of the four Caffeine doses (0, 100, 200, 400 mg). In the map learning task, distal distance accuracy rates marginally increased as a function of caffeine dose; specifically, within the distant condition accuracy was not higher at 100 mg versus Placebo, but showed marginally higher accuracy at 200 mg versus Placebo ($p < 0.10$), and 400 mg versus Placebo ($p < 0.07$). This same effect was not found in the proximal condition. No effects were found for the spatial description task.

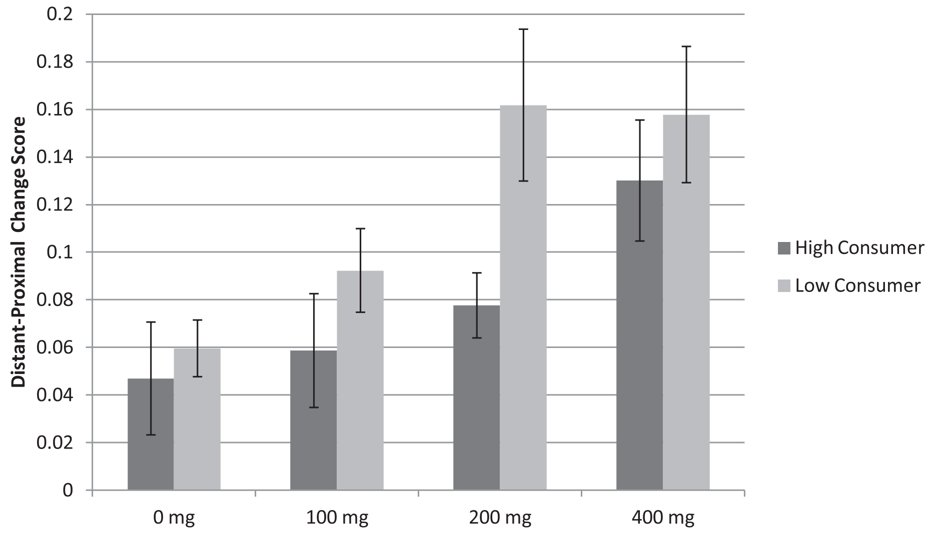

FIGURE 1 | Map learning task mean accuracy (SE) in both low and high habitual consumers ($n = 70$). The graph represents change scores for distant minus proximal distal comparisons. Accuracy was higher in low relative to high habitual caffeine consumers ($p < 0.05$).

of Consumption profile $F(1, 67) = 19.427$, $p < 0.001$ ($\eta^2 = 0.122$) showed that accuracy was higher in low relative to high habitual caffeine consumers (Low $= 0.13 \pm 0.01$; High $= 0.05 \pm 0.01$), again showing that caffeine influences spatial processing more so in low than high habitual caffeine consumers. No Caffeine × Consumption interaction was found ($p > 0.39$).

DISCUSSION

We evaluated the influence of caffeine on proximal and distant landmark comparisons in low habitual (Experiment 1) and high habitual (Experiment 2) caffeine consumers. We used two tasks in which subjects studied either maps or spatial descriptions of environments and later completed spatial statement verification tasks that related landmark pairs that were either close (proximal) or far (distal) from one another. Across both experiments and tasks, we replicated previous findings that accuracy is higher for comparisons between landmarks that are farther apart relative to closer together, i.e., the symbolic distance effect (Moyer and Bayer, 1976; Navon, 1977). On the map learning task, caffeine enhanced memory for distal (i.e., global) compared to proximal (i.e., local) comparisons at 100 (marginal), 200, and 400 mg caffeine in non-habitual consumers, and marginally beginning at 400 mg caffeine in habitual consumers. On the spatial descriptions task, caffeine enhanced memory for distal compared to proximal comparisons beginning at 100 mg in non-habitual but not habitual consumers. These findings support extant evidence

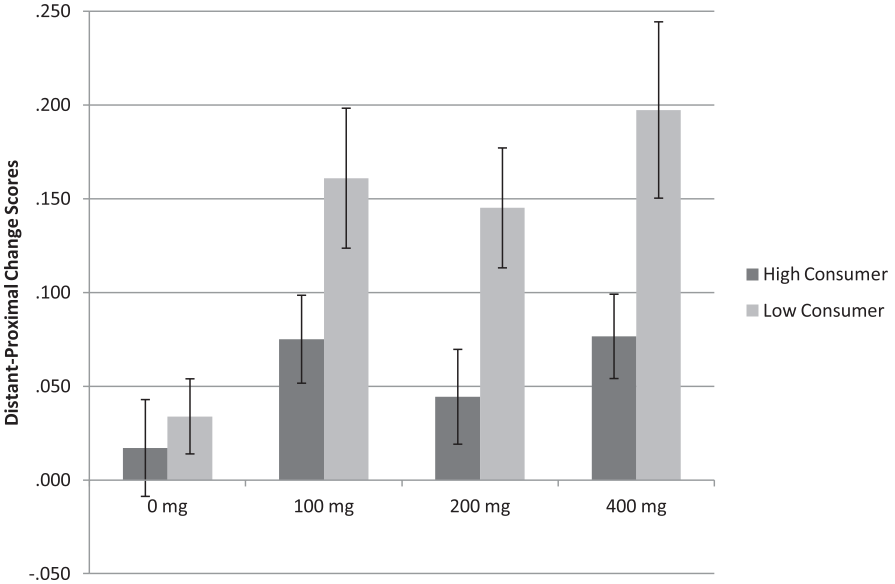

FIGURE 2 | Spatial description task mean accuracy (SE) in both low and high habitual consumers ($n = 70$). The graph represents change scores for distant minus proximal distal comparisons. The difference in accuracy between distant and proximal distances was higher after all doses caffeine intake than placebo ($p < 0.001$) and higher in low relative to high habitual caffeine consumers ($p < 0.001$).

that caffeine-induced physiological arousal amplifies global spatial processing biases, and these effects are at least partially driven by participants' caffeine consumption levels. Critically, our results are unique to physiological arousal, as we showed no reliable evidence that caffeine influenced rated pleasant or unpleasant mood.

CAFFEINE INCREASES GLOBAL FOCUS IN SPATIAL MEMORY

We found only marginal effects of caffeine to support our first hypothesis, i.e., the arousal states produced via caffeine administration would influence participants' ability to accurately memorize spatial information. Such effects were found in the spatial descriptions task, in which 200 and 400 mg caffeine marginally improved accuracy relative to placebo in low habitual caffeine consumers. However the data support our second hypothesis that increasing doses of caffeine would induce an increasingly global focus in spatial memory. The results are in line with previous findings that emotional arousal strengthens the representation of distal spatial relationships (Brunyé et al., 2009) and extend these findings by providing evidence that physiological arousal devoid of any valence manipulation, as induced by caffeine, accentuates the global processing bias. The results also support data showing that caffeine augments the global processing bias using hierarchical visual attention (Mahoney et al., 2011) and language-based materials (Brunyé et al., 2012). The results extend such extant findings in several ways. Mahoney and colleagues evaluated the influence of a range of caffeine doses, i.e., 0, 100, 200, and 400 mg caffeine as in the present study, on the Hierarchical Shape and Hierarchical Letter Tasks, which are compound stimuli tasks (i.e., smaller stimuli made of larger stimuli; Navon, 2003) in low habitual caffeine consumers. Although the present study is similar in design and shows a similar global processing accentuation to Mahoney et al. (2011), it goes further in demonstrating that the effect applies during tasks involving both spatial perception (i.e., perceiving the map) and spatial memory (i.e., representing then retrieving the map). Furthermore, we extend the literature to a relatively ecologically relevant task that involves spatial processes demanded on a daily basis such as during navigation through familiar or unfamiliar environments. Additionally, the present findings indicate that at similar doses, caffeine augments global processing to a greater extent in low relative to high habitual caffeine consumers.

Caffeine's influence on global and local spatial representations may stem, in part, from up-regulation of norepinephrine and serotonin activity. Caffeine is a non-selective competitive adenosine receptor antagonist which exerts its effects primarily through adenosine A_1 and A_{2A} receptors (Ferre, 2010). Adenosine, in turn, influences other central ascending neurotransmitter systems, including the dopaminergic, noradrenergic, and acetylcholinergic systems. Normally, endogenous adenosine inhibits neurotransmission but caffeine blocks this inhibition, thus increasing extracellular dopamine, noradrenalin, and acetylcholine concentrations (Ferre et al., 1997; Koppelstaetter et al., 2010). Caffeine increases resting-state arousal (Barry et al., 2005), and, though tentative, arousal may be associated with greater right than left hemisphere activity (Nitschke et al., 1999).

Several decades of work suggest a right-hemisphere advantage for global processing, and there is some suggestion of increased right-hemisphere activity during physiological arousal-induced via exercise or caffeine administration. Patients with left versus right-hemisphere neurological lesions tend to show impaired local and global perceptual processing, respectively (Robertson et al., 1988; Christie et al., 2012). In healthy adults, studies using event-related potential (ERP) show right-hemisphere dominance for global, and left for local, visual attention (Heinze and Munte, 1993; Proverbio et al., 1998; Yamaguchi et al., 2000). The right-hemisphere is also more active than the left during states of physiological arousal, such as during aerobic exercise (Woo et al., 2009). Evidence specifically regarding caffeine's selective influence on brain activation and relative hemispheric activity is very limited. Whereas a few studies suggest increased right versus left activity following caffeine consumption (Lorist and Snel, 1997; Koppelstaetter et al., 2008), some suggest no hemispheric differences (Kennedy and Haskell, 2011), and others suggest increased left versus right activity (Kuchinke and Lux, 2012). Overall, caffeine may upregulate levels of brain dopamine, serotonin, and norepinephrine, neurotransmitter systems that appear to be at least partially lateralized to the right-hemisphere (Oke et al., 1978, 1980; Arato et al., 1991; Davidson et al., 2004; Smith et al., 2006b). The right-hemisphere has also been implicated in the processing and representation of spatial information including relative landmark locations (Smith et al., 1996; Bohbot et al., 1998). Overlapping right-hemisphere neural mechanisms engaged during global processing, spatial cognition, and states of physiological arousal may prove responsible for the present results; future work might directly consider this possibility by complementing our design with functional neuroimaging.

CAFFEINE ACCENTUATES GLOBAL PROCESSING IN BOTH HIGH AND LOW CAFFEINE CONSUMERS

To specifically test differences across consumption profiles, we calculated change scores by subtracting the mean accuracy proximal from distant distal comparisons and compared these scores across the two consumption profiles. We found that the difference between low and high accuracy levels was higher in low relative to high habitual caffeine consumers in both tasks, but found no interactions with dose. Thus we support the final hypothesis that the influence of caffeine on spatial representation will be greater in low versus high consumers by showing greater difference in accuracy between distant and proximal distal comparisons in individuals who do not typically consume caffeine.

The argument over whether caffeine influences cognition or merely reverses withdrawal effects is ongoing. Although this is the first study to compare the impact of caffeine on memory for spatial relationships, previous studies assessing caffeine and other types of memory provide conflicting reports, e.g., caffeine improved working memory regardless of habitual consumption profile in one study (Addicott and Laurienti, 2009) but neither caffeine, habitual caffeine consumption, nor caffeine withdrawal influenced working memory, short-term, or delayed memory in other studies (Mitchell and Redman, 1992; Hewlett and Smith, 2007; Koppelstaetter et al., 2008).

In order to better determine whether caffeine's influence on spatial processing is influenced by caffeine withdrawal, future studies should employ a "normal caffeine consumption" condition, which could be compared to the placebo condition. Regardless of this limitation to our study design, comparing the high and low caffeine consumers' results, separately, indicates that caffeine enhances the global processing bias in both habitual and non-habitual caffeine consumers, and that a larger caffeine dose is necessary to achieve the same effect in high habitual caffeine consumers, in that for distal landmark comparisons, caffeine improved accuracy beginning between 100 mg (map learning task) and 200 mg (spatial descriptions task) in low habitual consumers, but only marginally improved accuracy at 400 mg in high habitual caffeine consumers.

Comparisons between high and low habitual caffeine consumers provide convincing evidence that caffeine accentuates global processing across habitual consumption profiles. These findings refute the contention that caffeine's effects are primarily due to reversal of caffeine withdrawal, as past work has found that caffeine abstinence impairs cognitive performance and caffeine intake does not reverse withdrawal effects (Rogers et al., 2005). However, the present results indicate that caffeine promotes the global processing bias across habitual consumption profiles, after as little as 200 mg caffeine intake. The role of caffeine withdrawal in caffeine-induced changes to cognitive performance may be domain-dependent, in that caffeine enhanced working memory following caffeine abstinence and normal consumption but improved psychomotor performance following caffeine abstinence only (Addicott and Laurienti, 2009), and caffeine enhances executive function in both habitual and non-habitual caffeine consumers (Brunyé et al., 2010a,b). Thus, habitual consumption profiles may play a role in caffeine's influence on psychomotor performance, but not on other cognitive domains, including global spatial processing.

However, we found no interaction between Caffeine dose and Consumption profile on the global processing bias (i.e., difference in accuracy for distal minus proximal landmark comparisons), which indicates that caffeine did not differentially influence accuracy for distal and proximal comparisons between low and high habitual caffeine consumers in a dose-dependent manner with the range of doses administered. Further, we found no main effects or interactions between caffeine and distance on the spatial descriptions task in high habitual caffeine consumers, which leaves open the question of whether a higher dose is necessary to see the global processing bias in habitual caffeine consumers or, conversely, whether caffeine does not influence spatial processing on this task in individuals who regularly consume caffeine.

CONCLUSION

In summary, caffeine amplified a globally focused spatial representation after as little as 100 mg caffeine, less than the amount of caffeine in Starbucks 12 oz brewed coffee (260 mg). The results have implications in everyday life, as daily caffeine intake could potentially lead to more global spatial representations. A morning cup of coffee, for example, could enhance memory for the general location of key landmarks or regions (e.g., theater district, Empire State Building), but perhaps at the expense of knowledge (e.g., particular theaters, buildings adjacent to the Empire State Building).

The globally focused spatial representation is evident in both habitual and non-habitual consumers, although it appears to require more caffeine to achieve the same global bias in habitual consumers. Thus the caffeine's influence on spatial representation and memory may be vulnerable to influences of caffeine tolerance and withdrawal. Thus an increasingly large cup of coffee may be needed for enhanced memory for global environmental features.

REFERENCES

Abrams, J. K., Johnson, P. L., Hay-Schmidt, A., Mikkelsen, J. D., Shekhar, A., and Lowry, C. A. (2005). Serotonergic systems associated with arousal and vigilance behaviors following administration of anxiogenic drugs. *Neuroscience* 133, 983–997. doi:10.1016/j.neuroscience.2005.03.025

Addicott, M. A., and Laurienti, P. J. (2009). A comparison of the effects of caffeine following abstinence and normal caffeine use. *Psychopharmacology (Berl.)* 3, 423–431. doi:10.1007/s00213-009-1668-3

Andrade, J., and Meudell, P. (1993). Short report: is spatial information encoded automatically in memory? *Q. J. Exp. Psychol. A* 46, 365–375. doi:10.1080/14640749308401051

Arato, M., Frecska, E., MacCrimmon, D. J., Guscott, R., Saxena, B., Tekes, K., et al. (1991). Serotonergic interhemispheric asymmetry: neurochemical and pharmaco-EEG evidence. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 15, 759–764.

Arbuckle, T. Y., Cooney, R., Milne, J., and Melchior, A. (1994). Memory for spatial layouts in relation to age and schema typicality. *Psychol. Aging* 9, 467–480. doi:10.1037/0882-7974.9.3.467

Arnaud, M. J. (1987). The pharmacology of caffeine. *Prog. Drug Res.* 31, 273–313.

Attwood, A. S., Higgs, S., and Terry, P. (2007). Differential responsiveness to caffeine and perceived effects of caffeine in moderate and high regular caffeine consumers. *Psychopharmacology (Berl.)* 190, 469–477. doi:10.1007/s00213-006-0643-5

Barry, R. J., Rushby, J. A., Wallace, M. J., Clarke, A. R., Johnstone, S. J., and Zlojutro, I. (2005). Caffeine effects on resting-state arousal. *Clin. Neurophysiol.* 116, 2693–2700. doi:10.1016/j.clinph.2005.08.008

Blanchard, J., and Sawers, S. J. A. (1983). The absolute bioavailability of caffeine in man. *Eur. J. Clin. Pharmacol.* 24, 93–98. doi:10.1007/BF00613933

Bohbot, V. D., Kalina, M., Stepankova, K., Spackova, N., Petrides, M., and Nadel, L. (1998). Spatial memory deficits in patients with lesions to the right hippocampus and to the right parahippocampal cortex. *Neuropsychologia* 36, 1217–1238. doi:10.1016/S0028-3932(97)00161-9

Brunyé, T. T., Mahoney, C. R., Augustyn, J. S., and Taylor, H. A. (2009). Emotional state and local versus global spatial memory. *Acta Psychol.* 130, 138–146. doi:10.1016/j.actpsy.2008.11.002

Brunyé, T. T., Mahoney, C. R., Lieberman, H. R., Giles, G. E., and Taylor, H. A. (2010a). Acute caffeine consumption enhances the executive control of visual attention in habitual consumers. *Brain Cogn.* 72, 186–192. doi:10.1016/j.bandc.2010.07.006

Brunyé, T. T., Mahoney, C. R., Lieberman, H. R., and Taylor, H. A. (2010b). Caffeine modulates attention network function. *Brain Cogn.* 72, 181–188. doi:10.1016/j.bandc.2009.07.013

Brunyé, T. T., Mahoney, C. R., Rapp, D. N., Ditman, T., and Taylor, H. A. (2012). Caffeine enhances real-world language processing: evidence from a proofreading task. *J. Exp. Psychol. Appl.* 18, 95–108. doi:10.1037/a0025851

Brunye, T. T., Rapp, D. N., and Taylor, H. A. (2008). Representational flexibility and specificity following spatial descriptions of real-world environments. *Cognition* 108, 418–443. doi:10.1016/j.cognition.2008.03.005

Brunye, T. T., and Taylor, H. A. (2008). Extended experience benefits spatial mental model development with route but not survey descriptions. *Acta Psychol.* 127, 340–354. doi:10.1016/j.actpsy.2007.07.002

Brunye, T. T., Taylor, H. A., and Worboys, M. (2007). Levels of detail in descriptions and depictions of geographic space. *Spat. Cogn. Comput.* 7, 227–266. doi:10.1080/13875860701515472

Cassia, V. M., Simion, F., Milani, I., and Umilta, C. (2002). Dominance of global visual properties at birth. *J. Exp. Psychol. Gen.* 131, 398–411. doi:10.1037/0096-3445.131.3.398

Childs, E., and de Wit, H. (2006). Subjective, behavioral, and physiological effects of acute caffeine in light, nondependent caffeine users. *Psychopharmacology* 185, 514–523. doi:10.1007/s00213-006-0341-3

Christianson, S. A., Loftus, E. F., Hoffman, H., and Loftus, G. R. (1991). Eye fixations and memory for emotional events. *J. Exp. Psychol. Learn. Mem. Cogn.* 17, 693–701. doi:10.1037/0278-7393.17.4.693

Christie, J., Ginsberg, J. P., Steedman, J., Fridriksson, J., Bonilha, L., and Rorden, C. (2012). Global versus local processing: Seeing the left side of the forest and the right side of the trees. *Front. Hum. Neurosci.* 6:28. doi:10.3389/fnhum.2012.00028

Clore, G. L., and Palmer, J. E. (2009). Affective guidance of intelligent agents: how emotion controls cognition. *Cogn. Syst. Res.* 10, 21–30. doi:10.1016/j.cogsys.2008.03.002

Corson, Y., and Verrier, N. (2007). Emotions and false memories: valence or arousal? *Psychol. Sci.* 18, 208–211. doi:10.1111/j.1467-9280.2007.01874.x

Daval, J. L., Deckert, J., Weiss, S. R., Post, R. M., and Marangos, P. J. (1989). Upregulation of adenosine A1 receptors and forskolin binding sites following chronic treatment with caffeine or carbamazepine: a quantitative autoradiographic study. *Epilepsia* 30, 26–33. doi:10.1111/j.1528-1157.1989.tb05276.x

Davidson, M. C., Horvitz, J. C., Tottenham, N., Fossella, J. A., Watts, R., Ulug, A. M., et al. (2004). Differential cingulate and caudate activation following unexpected nonrewarding stimuli. *Neuroimage* 23, 1039–1045. doi:10.1016/j.neuroimage.2004.07.049

Easterbrook, J. A. (1959). The effect of emotion on cue utilization and the organization of behavior. *Psychol. Rev.* 66, 183–201. doi:10.1037/h0047707

Ellis, N. R. (1990). Is memory for spatial location automatically encoded? *Mem. Cognit.* 18, 584–592.

Evans, S. M., and Griffiths, R. R. (1992). Caffeine tolerance and choice in humans. *Psychopharmacology* 108, 51–59. doi:10.1007/BF02245285

Ferre, S. (2010). Role of the central ascending neurotransmitter systems in the psychostimulant effects of caffeine. *J. Alzheimers Dis.* 20(Suppl. 1), S35–S49. doi:10.3233/JAD-2010-1400

Ferre, S., Fredholm, B. B., Morelli, M., Popoli, P., and Fuxe, K. (1997). Adenosine-dopamine receptor-receptor interactions as an integrative mechanism in the basal ganglia. *Trends Neurosci.* 20, 482–487. doi:10.1016/S0166-2236(97)01096-5

Frary, C. D., Johnson, R. K., and Wang, M. Q. (2005). Food sources and intakes of caffeine in the diets of persons in the united states. *J. Am. Diet. Assoc.* 105, 110–113. doi:10.1016/j.jada.2004.10.027

Gable, P., and Harmon-Jones, E. (2010). The blues broaden, but the nasty narrows: attentional consequences of negative affects low and high in motivational intensity. *Psychol. Sci.* 21, 211–215. doi:10.1177/0956797609359622

Gable, P. A., and Harmon-Jones, E. (2013). Does arousal per se account for the influence of appetitive stimuli on attentional scope and the late positive potential? *Psychophysiology* 50, 344–350. doi:10.1111/psyp.12023

Gardony, A., Brunyé, T. T., Mahoney, C. R., and Taylor, H. A. (2011). Affective states influence spatial cue utilization during navigation. *Presence* 20, 223–240. doi:10.1162/PRES_a_00046

Gasper, K., and Clore, G. L. (2002). Attending to the big picture: Mood and global versus local processing of visual information. *Psychol. Sci.* 13, 34–40. doi:10.1111/1467-9280.00406

Gyselinck, V., Meneghetti, C., De Beni, R., and Pazzaglia, F. (2009). The role of working memory in spatial text processing: what benefit of imagery strategy and visuospatial abilities? *Learn. Individ. Differ.* 19, 12–20. doi:10.1016/j.lindif.2008.08.002

Harmon-Jones, E., and Gable, P. A. (2008). Incorporating motivational intensity and direction into the study of emotions: Implications for brain mechanisms of emotion and cognition-emotion interactions. *Neth. J. Psychol.* 64, 132. doi:10.1007/BF03076416

Hasher, L., and Zacks, R. T. (1979). Automatic and effortful processes in memory. *J. Exp. Psychol. Gen.* 108, 356–388. doi:10.1037/0096-3445.108.3.356

Haskell, C. F., Kennedy, D. O., Wesnes, K. A., and Scholey, A. B. (2005). Cognitive and mood improvements of caffeine in habitual consumers and habitual non-consumers of caffeine. *Psychopharmacology* 179, 813–825. doi:10.1007/s00213-004-2104-3

Hegarty, M., Montello, D. R., Richardson, A. E., Ishikawa, T., and Lovelace, K. (2006). Spatial abilities at different scales: individual differences in aptitude-test performance and spatial-layout learning. *Intelligence* 34, 151–176. doi:10.1016/j.intell.2005.09.005

Heinze, H. J., and Munte, T. F. (1993). Electrophysiological correlates of hierarchical stimulus processing: dissociation between onset and later stages of global and local target processing. *Neuropsychologia* 31, 841–852. doi:10.1016/0028-3932(93)90132-J

Hewlett, P., and Smith, A. (2007). Effects of repeated doses of caffeine on performance and alertness: new data and secondary analyses. *Hum. Psychopharmacol.* 22, 339–350. doi:10.1002/hup.854

Husain, G., Thompson, W. F., and Schellenberg, E. G. (2002). Effects of musical tempo and mode on arousal, mood, and spatial abilities. *Music Percept.* 20, 151–171. doi:10.1525/mp.2002.20.2.151

Jacobson, B. H., and Thurman-Lacey, S. R. (1992). Effect of caffeine on motor performance by caffeine-naive and -familiar subjects. *Percept. Mot. Skills* 74, 151–157. doi:10.2466/pms.1992.74.1.151

Jallais, C., and Gilet, A. L. (2010). Inducing changes in arousal and valence: comparison of two mood induction procedures. *Behav. Res. Methods* 42, 318–325. doi:10.3758/BRM.42.1.318

Kennedy, D. O., and Haskell, C. F. (2011). Cerebral blood flow and behavioural effects of caffeine in habitual and non-habitual consumers of caffeine: a near infrared spectroscopy study. *Biol. Psychol.* 86, 298–306. doi:10.1016/j.biopsycho.2010.12.010

Kensinger, E. A., and Corkin, S. (2004). Two routes to emotional memory: distinct neural processes for valence and arousal. *Proc. Natl. Acad. Sci. U.S.A.* 101, 3310–3315. doi:10.1073/pnas.0306408101

Kensinger, E. A., and Schacter, D. L. (2006). Reality monitoring and memory distortion: Effects of negative, arousing content. *Mem. Cognit.* 34, 251–260. doi:10.3758/BF03193403

Kensinger, E. A., and Schacter, D. L. (2007). Remembering the specific visual details of presented objects: neuroimaging evidence for effects of emotion. *Neuropsychologia* 45, 2951–2962. doi:10.1016/j.neuropsychologia.2007.05.024

Kessels, R. P., Boekhorst, S. T., and Postma, A. (2005). The contribution of implicit and explicit memory to the effects of errorless learning: a comparison between young and older adults. *J. Int. Neuropsychol. Soc.* 11, 144–151. doi:10.1017/S1355617705050174

Kimchi, R. (1992). Primacy of wholistic processing and global/local paradigm: a critical review. *Psychol. Bull.* 112, 24–38. doi:10.1037/0033-2909.112.1.24

Kimchi, R., and Palmer, S. E. (1982). Form and texture in hierarchically constructed patterns. *J. Exp. Psychol. Hum. Percept. Perform.* 8, 521–535. doi:10.1037/0096-1523.8.4.521

Koppelstaetter, F., Poeppel, T. D., Siedentopf, C. M., Ischebeck, A., Kolbitsch, C., Mottaghy, F. M., et al. (2010). Caffeine and cognition in functional magnetic resonance imaging. *J. Alzheimers Dis.* 20, S71–S84. doi:10.3233/JAD-2010-1417

Koppelstaetter, F., Poeppel, T. D., Siedentopf, C. M., Ischebeck, A., Verius, M., Haala, I., et al. (2008). Does caffeine modulate verbal working memory processes? An fMRI study. *Neuroimage* 39, 492–499. doi:10.1016/j.neuroimage.2007.08.037

Kuchinke, L., and Lux, V. (2012). Caffeine improves left hemisphere processing of positive words. *PLoS ONE* 7:e48487. doi:10.1371/journal.pone.0048487

Lane, J. D. (1997). Effects of brief caffeinated-beverage deprivation on mood, symptoms, and psychomotor performance. *Pharmacol. Biochem. Behav.* 58, 203–208. doi:10.1016/S0091-3057(97)00007-5

Lane, J. D., and Phillips-Brute, B. G. (1998). Caffeine deprivation affects vigilance performance and mood. *Physiol. Behav.* 65,

Lang, P. J., Bradley, M. M., and Cuthbert, B. N. (1998). Emotion, motivation, and anxiety: brain mechanisms and psychophysiology. *Biol. Psychiatry* 44, 1248–1263. doi:10.1016/S0006-3223(98)00275-3

Lang, P. J., Greenwald, M. K., Bradley, M. M., and Hamm, A. O. (1993). Looking at pictures: affective, facial, visceral, and behavioral reactions. *Psychophysiology* 30, 261–273. doi:10.1111/j.1469-8986.1993.tb03352.x

Lieberman, H. R. (2001). The effects of ginseng, ephedrine, and caffeine on cognitive performance, mood and energy. *Nutr. Rev.* 59, 91–102. doi:10.1111/j.1753-4887.2001.tb06995.x

Lieberman, H. R. (2003). Nutrition, brain function and cognitive performance. *Appetite* 40, 245–254. doi:10.1016/S0195-6663(03)00010-2

Light, L. L., and Zelinski, E. M. (1983). Memory for spatial information in young and old adults. *Dev. Psychol.* 19, 901–906. doi:10.1037/0012-1649.19.6.901

Loftus, E. F. (1979). The malleability of human memory. *Am. Sci.* 67, 312–320.

Loftus, E. F., and Burns, T. E. (1982). Mental shock can produce retrograde amnesia. *Mem. Cognit.* 10, 318–323.

Lorist, M. M., and Snel, J. (1997). Caffeine effects on perceptual and motor processes. *Electroencephalogr. Clin. Neurophysiol.* 102, 401–413. doi:10.1016/S0921-884X(97)95729-5

Lovallo, W. R., Whitsett, T. L., al'Absi, M., Sung, B. H., Vincent, A. S., and Wilson, M. F. (2005). Caffeine stimulation of cortisol secretion across the waking hours in relation to caffeine intake levels. *Psychosom. Med.* 67, 734–739. doi:10.1097/01.psy.0000181270.20036.06

Lyvers, M., Brooks, J., and Matica, D. (2004). Effects of caffeine on cognitive and autonomic measures in heavy and light caffeine consumers. *Aus. J. Psychol.* 56, 33–41. doi:10.1080/00049530410001688119

Maddox, K. B., Rapp, D. N., Brion, S., and Taylor, H. A. (2008). Social influences on spatial memory. *Mem. Cognit.* 36, 479–494. doi:10.3758/MC.36.3.479

Mahoney, C. R., Brunyé, T. T., Giles, G., Lieberman, H. R., and Taylor, H. A. (2011). Caffeine-induced physiological arousal accentuates global processing biases. *Pharmacol. Biochem. Behav.* 99, 59–65. doi:10.1016/j.pbb.2011.03.024

Mayer, J. D., and Gasche, Y. N. (1988). The experience and meta-experience of mood. *J. Pers. Soc. Psychol.* 55, 102–111. doi:10.1037/0022-3514.55.1.102

McNamara, T. P., Halpin, J. A., and Hardy, J. K. (1992). Spatial and temporal contributions to the structure of spatial memory. *J. Exp. Psychol. Learn. Mem. Cogn.* 18, 555–564. doi:10.1037/0278-7393.18.3.555

Meneghetti, C., Gyselinck, V., Pazzaglia, F., and De Beni, R. (2009). Individual differences in spatial text processing: high spatial ability can compensate for spatial working memory interference. *Learn. Individ. Differ.* 19, 577–589. doi:10.1016/j.lindif.2009.07.007

Mitchell, P. J., and Redman, J. R. (1992). Effects of caffeine, time of day and user history on study-related performance. *Psychopharmacology (Berl.)* 109, 121–126. doi:10.1007/BF02245489

Moyer, R. S., and Bayer, R. H. (1976). Mental comparisons and the symbolic distance effect. *Cogn. Psychol.* 8, 228–246. doi:10.1016/0010-0285(76)90025-6

Navon, D. (1977). Forest before trees: the precedence of global features in visual perception. *Cogn. Psychol.* 9, 353–383. doi:10.1016/0010-0285(77)90012-3

Navon, D. (2003). What does a compound letter tell the psychologist's mind? *Acta Psychol.* 114, 273–309. doi:10.1016/j.actpsy.2003.06.002

Nehlig, A., Daval, J. L., and Debry, G. (1992a). Caffeine and the central nervous system: mechanisms of action, biochemical, metabolic and psychostimulant effects. *Brain Res. Rev.* 17, 139–170. doi:10.1016/0165-0173(92)90012-B

Nehlig, A., Daval, J. L., and Debry, G. (1992b). Caffeine and the central nervous system: mechanisms of action, biochemical, metabolic and psychostimulant effects. *Brain Res. Rev.* 17, 139–170. doi:10.1016/0165-0173(92)90012-B

Nitschke, J. B., Heller, W., Palmieri, P. A., and Miller, G. A. (1999). Contrasting patterns of brain activity in anxious apprehension and anxious arousal. *Psychophysiology* 36, 628–637. doi:10.1111/1469-8986.3650628

Oke, A., Keller, R., Mefford, I., and Adams, R. N. (1978). Lateralization of norepinephrine in human thalamus. *Science* 200, 1411–1413. doi:10.1126/science.663623

Oke, A., Lewis, R., and Adams, R. N. (1980). Hemispheric asymmetry of norepinephrine distribution in rat thalamus. *Brain Res.* 188, 269–272. doi:10.1016/0006-8993(80)90575-2

Pesce, C., Tessitore, A., Casella, R., Pirritano, M., and Capranica, L. (2007). Focusing of visual attention at rest and during physical exercise in soccer players. *J. Sports Sci.* 25, 1259–1270. doi:10.1080/02640410601040085

Proverbio, A. M., Minniti, A., and Zani, A. (1998). Electrophysiological evidence of a perceptual precedence of global vs. local visual information. *Brain Res. Cogn. Brain Res.* 6, 321–334. doi:10.1016/S0926-6410(97)00039-6

Robertson, L. C., Lamb, M. R., and Knight, R. T. (1988). Effects of lesions of temporal-parietal junction on perceptual and attentional processing in humans. *J. Neurosci.* 8, 3757–3769.

Rogers, P. J., Heatherley, S. V., Hayward, R. C., Seers, H. E., Hill, J., and Kane, M. (2005). Effects of caffeine and caffeine withdrawal on mood and cognitive performance degraded by sleep restriction. *Psychopharmacology* 179, 742–752. doi:10.1007/s00213-004-2097-y

Rudolphi, K. A., Keil, M., Fastbom, J., and Fredholm, B. B. (1989). Ischaemic damage in gerbil hippocampus is reduced following upregulation of adenosine (A1) receptors by caffeine treatment. *Neurosci. Lett.* 103, 275–280. doi:10.1016/0304-3940(89)90112-2

Schwarz, N., and Clore, G. L. (1983). Mood, misattribution, and judgments of well-being: Informative and directive functions of affective states. *J. Pers. Soc. Psychol.* 45, 513–523. doi:10.1037/0022-3514.45.3.513

Scott, N. R., Stambuk, D., Chakraborty, J., Marks, V., and Morgan, M. Y. (1989). The pharmacokinetics of caffeine and its dimethylxanthine metabolites in patients with chronic liver disease. *Br. J. Clin.*

Pharmacol. 27, 205–213. doi:10.1111/j.1365-2125.1989.tb05352.x

Smith, A. (2002). Effects of caffeine on human behavior. *Food Chem. Toxicol.* 49, 1243–1255. doi:10.1016/S0278-6915(02)00096-0

Smith, A. P. (2011). "Caffeine: Practical implications," in *Diet, Brain, Behavior: Practical Implications*, eds R. B. Kanarek, and H. R. Lieberman (Boca Raton, FL: CRC Press), 271–292.

Smith, A. P., Christopher, G., and Sutherland, D. (2006a). Effects of caffeine in overnight withdrawn consumers and non-consumers. *Nutr. Neurosci.* 9, 63–71. doi:10.1080/10284150600582927

Smith, A. B., Taylor, E., Brammer, M., Toone, B., and Rubia, K. (2006b). Task-specific hypoactivation in prefrontal and temporoparietal brain regions during motor inhibition and task switching in medication-naive children and adolescents with attention deficit hyperactivity disorder. *Am. J. Psychiatry* 163, 1044–1051. doi:10.1176/appi.ajp.163.6.1044

Smith, E. E., Jonides, J., and Koeppe, R. A. (1996). Dissociating verbal and spatial working memory using PET. *Cereb. Cortex* 6, 11–20. doi:10.1093/cercor/6.1.11

Storbeck, J., and Clore, G. L. (2005). With sadness comes accuracy; with happiness, false memory: mood and the false memory effect. *Psychol. Sci.* 16, 785–791. doi:10.1111/j.1467-9280.2005.01615.x

Taylor, H. A., Naylor, S. J., and Chechile, N. A. (1999). Goal-specific influences on the representation of spatial perspective. *Mem. Cognit.* 27, 309–319.

Taylor, H. A., and Tversky, B. (1992). Spatial mental models derived from survey and route descriptions. *J. Mem. Lang.* 31, 261–282. doi:10.1016/0749-596X(92)90014-O

Thomas, A. K., Bonura, B. M., Taylor, H. A., and Brunye, T. T. (2012). Metacognitive monitoring in visuospatial working memory. *Psychol. Aging* 27, 1099–1110. doi:10.1037/a0028556

Varani, K., Portaluppi, F., Merighi, S., Ongini, E., Belardinelli, L., and Borea, P. A. (1999). Caffeine alters A2A adenosine receptors and their function in human platelets. *Circulation* 99, 2499–2502. doi:10.1161/01.CIR.99.19.2499

Vasterling, J. J., Duke, L. M., Tomlin, H., Lowery, N., and Kaplan, E. (2004). Global-local visual processing in posttraumatic stress disorder. *J. Int. Neuropsychol. Soc.* 10, 709–718. doi:10.1017/S1355617704105031

Waller, D. (2000). Individual differences in spatial learning from computer-simulated environments. *J. Exp. Psychol. Appl.* 6, 307–321. doi:10.1037/1076-898X.6.4.307

Woo, M., Kim, S., Kim, J., Petruzzello, S. J., and Hatfield, B. D. (2009). Examining the exercise-affect dose-response relationship: does duration influence frontal EEG asymmetry? *Int. J. Psychophysiol.* 72, 166–172. doi:10.1016/j.ijpsycho.2008.12.003

Yamaguchi, S., Yamagata, S., and Kobayashi, S. (2000). Cerebral asymmetry of the "top-down" allocation of attention to global and local features. *J. Neurosci.* 20, RC72.

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