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The neurobiology of values

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The neurobiology of values

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Editorial: The neurobiology of values

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Editorial on the Research Topic
The neurobiology of values

In recent years, the study of neurology and its implications for health equity has undergone significant development and progress. As our understanding of the brain continues to evolve, there's a growing desire to better understand the biology of social behavior and to integrate prosocial values into neurology research and practice. As editors, our aim is to explore fundamental questions: What do we mean by "values," and how do they impact the brain? The resulting collection of articles, titled "*The neurobiology of values*," takes a profound dive into how our brains shape and influence our values. This editorial aims to outline the main goals of the research in the Research Topic, summarizing important discoveries and putting them into a broader perspective.

Social engagement and brain health

In their perspective, "One step beyond the lab and clinic: "walking the dementia conversation"", Zegarra-Valdivia et al. take a bold step beyond the lab and clinic bringing together researchers, caregivers, and patients to "walk the talk" for dementia. This article not only shifts the focus from pathology to conversation but also emphasizes the importance of community engagement and real-world discussions in shaping our understanding of brain health and values.

Fitri et al. highlight the profound impact of empathy as a crucial skill in disrupting disparities in global brain health. This research advocates for a collective approach to address global mental health challenges, transcending geographical and cultural boundaries.

Ibanez et al. pose a compelling question in "Can prosocial values improve brain health?" Here, the focus shifts to the symbiotic relationship between prosocial values and the wellbeing of the brain, holding promises for advancing preventative and intervention strategies.

Berendzen's exploration of social attachment as a window into the neural basis of prosocial values offers valuable insights into the emotional underpinnings of our social behaviors. This research contributes to the growing body of knowledge surrounding empathy, cooperation, and the neural substrates that facilitate prosocial behavior.

Cultural perspectives on brain health

Stirland et al. invite us to consider the cultural basis of authenticity and leadership in brain health, prompting reflections on how cultural nuances influence cognitive wellbeing. The article further examines how societal values, when aligned with principles of respect and equity, contribute to overall cognitive health.

Hill-Jarrett invites us to explore "The Black radical imagination: a space of hope and possible futures," encouraging a departure from conventional perspectives. The cultural and social dimensions explored in this article inspire a reevaluation of the intersections between culture, identity, and brain health, challenging us to recognize the rich diversity of experiences that shape our values.

Person-centered approaches in brain health

Merrilees et al. shift attitudes toward aging, dementia, and caregiving by using personal narrative to promote person-centered values. Through the integration of personal stories, this research transcends traditional academic boundaries, providing a humanistic perspective on brain health and values.

Kaczmarska adds a unique rhythm to the Research Topic. Through the lens of dance, this research perspective not only offers insights into potential therapeutic avenues for those with dementia but also underscores the profound connection between embodiment and the brain. It highlights the significance of physical experiences in shaping our cognitive landscapes and the potential therapeutic benefits of embodied practices in promoting brain health and wellbeing.

Values and neurological disorders

Antoniou et al. explore the intricate moral landscapes of individuals grappling with frontotemporal dementia (FTD). This research delves into the ethical dimensions of cognitive challenges, urging us to reconsider societal structures and support systems for those navigating the complex terrain of moral decision-making amid neurodegenerative conditions.

A unique dimension is added to the Research Topic through the investigation of neuroanatomical and cellular degeneration in patients with social disorders characterized by new ritualistic belief systems (Ohm et al.). This comparative study between a TDP-C patient and a Pick patient sheds light on the intricate relationship between neural degeneration and social disorders. Understanding these connections may pave the way for innovative interventions and treatments in the realm of mental health.

Personality traits and neurobiology

In their exploration, Abu Raya, Ogunyemi, Broder et al. shed light on individual differences in personality traits with underlying neurobiological foundations. This piece expands our comprehension of how traits such as openness contribute to the diversity of values and cognitive processes, shaping our unique interactions with the world.

The reciprocal relationship between openness and creativity is a subject explored by Abu Raya, Ogunyemi, Rojas Carstensen et al.. From neurobiological perspectives to the influence of multicultural environments, the authors traverse the complex interplay between personality traits and neural processes. This research not only broadens our understanding of individual differences but also highlights the interconnectedness of neural processes with psychological traits, offering insights that extend beyond the laboratory into real-world scenarios.

Cross-cultural perspectives on respect, equity, and leadership in brain health

Khalaila et al. explore the neural underpinnings of respect across different cultures. Using a neuroscientific lens, the authors provide valuable insights into the mechanisms through which respect is processed in the brain, offering a nuanced understanding of this complex socio-cultural phenomenon.

Arshad et al. explore the impact of respect, equity, and leadership in brain health. This research extends beyond individual cognitive processes, examining the societal and organizational factors that contribute to overall brain health.

Economic and social values in decision-making

Messimeris et al., present an intriguing exploration of economic and social values by investigating the impact of lesions to the human ventromedial prefrontal cortex. By examining the neurological consequences of such lesions, the authors shed light on the neural substrates that govern our decision-making processes in social and economic contexts. This research not only informs our understanding of the brain's role in value-based choices but also holds implications for fields like economics, where the exploration of decision-making mechanisms is key.

Fairness and equity in brain health

The article by Avelino-Silva et al. delves into the intricate relationship between fairness and the brain. From the depths of our guts to the complexities of neural processes, the authors critically examine the neurological mechanisms that establish our sense of fairness. Their insights contribute to a deeper understanding of the cognitive processes involved in shaping our ethical values, with potential implications for fields ranging from psychology to ethics.

Hope and positive impact on society

Dasgupta et al. inject a note of optimism with "Hope for brain health: impacting the life course and society." By examining interventions across the life course, the research suggests that positive impacts on individuals can resonate on a societal level. This article challenges us to consider brain health as a collective responsibility, urging society to invest in strategies that promote cognitive wellbeing throughout the lifespan.

The articles in "*The neurobiology of values*" Research Topic create a fascinating picture of how our brains and values are closely connected. Each article, like a unique thread, adds something special to our understanding, whether it's about the brain's role in fairness or how our brains shape our social behavior. This Research Topic helps us see that our values aren't just abstract ideas; they're deeply woven into our brains, impacting how we think, decide, and act. It's an exciting journey through the neural pathways of human values, offering a complete view that goes beyond labs and clinics into the diverse landscapes of culture, society, and our everyday experiences.

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Can prosocial values improve brain health?

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Prosocial values play a critical role in promoting care and concern for the well-being of others and prioritizing the common good of society. Evidence from population-based reports, cognitive neuroscience, and clinical studies suggests that these values depend on social cognition processes, such as empathy, deontological moral cognition, moral emotions, and social cooperation. Additionally, indirect evidence suggests that various forms of prosocial behaviors are associated with positive health outcomes at the behavioral, cardiovascular, immune, stress-related, and inflammatory pathways. However, it is unclear whether prosociality can positively influence brain health outcomes. In this perspective, we propose that prosocial values are not only influenced by brain conditions but could also potentially play a role in protecting brain health. We review studies from various fields that support this claim, including recent reports of prosociality-based interventions impacting brain health. We then explore potential multilevel mechanisms, based on the reduction of allostatic overload at behavioral, cardiovascular, immune, stress-related, and inflammatory levels. Finally, we propose potential prosociality-based interventions for improving brain health in at-risk populations, such as psychiatric and neurological patients, and individuals exposed to poverty or violence. Our perspective suggests that prosocial values may play a role in promoting and maintaining healthy brains.

KEYWORDS

prosocial values, prosociality, social cognition, brain health, Allostasis, empathy, cooperation, moral cognition

Prosocial values and social cognition

Prosocial values are defined as the beliefs, attitudes, and behaviors that promote the well-being and welfare of others, with an emphasis on cooperation, helping, sharing, and altruism (1). Prosocial values promote care and concern for the welfare of others and are critical for prioritizing the common good of society at large. These include cognitive, moral, and socioemotional processes that prioritize the well-being of others and society over one's own interests. These values are important for building strong and healthy communities, promoting positive social interactions, and creating a sense of social connectedness.

Studies in economics and psychology suggest that prosocial behavior improves common goods, such as increased cooperation and trust among individuals, better outcomes for collective action problems, and improved resource management. This effect has been particularly observed in challenging contexts like the pandemic (2–6). In social decision-making contexts, individuals tend to contribute more to a common pool of resources when they believe that others are also making contributions (7). Similarly, from childhood to adulthood, prosocial behavior can increase levels of cooperation and trust, leading to improved relationships and increased cooperation in both social and economic contexts (8–10). Overall, prosocial behavior can have a positive impact on common goods and improve the overall well-being of society.

Population-based reports, cognitive neuroscience, and clinical studies have linked prosocial behaviors with different social cognition processes, such as empathy, deontological moral cognition, moral emotions, and social cooperation. Empathy, or the ability to understand and share the feelings of others (11), has been closely linked to prosocial behavior (12). People who score higher on empathy measures are more likely to engage in behaviors that benefit others. Similarly, compassion involves an emotional response of understanding, caring, and alleviating the suffering of others. While empathy focuses on sharing and mirroring emotions, compassion goes further by involving active help and support. Deontological moral cognition refers to the beliefs and values supporting the groups' benefits, even at the expense of potential negative individual consequences. It also emphasizes adherence to rules, duties, or principles, regardless of the consequences or outcomes. These moral processes have been found to play a significant role in shaping prosocial behavior (13). Moral emotions, such as guilt, shame, or counter-empathic emotions (envy, Schadenfreude), are complex affective processes linked to the ethical aspects of one's actions or thoughts and have also been linked to prosocial behavior (14). Although typically seen as negative, counter-empathic emotions can promote prosocial behavior (15). Envy can inspire self-improvement or goal-setting, leading to positive outcomes for individuals and society. Meanwhile, Schadenfreude can foster social cohesion by highlighting unfairness or promoting group norms as a form of social regulation. Finally, social cooperation, or working together with others toward a common goal (i.e., sharing resources, coordinating efforts, establishing trust within a group) has been shown to be a key factor in prosocial behavior (16). Nevertheless, despite the evidence from real-life settings and neurocognitive correlates, a remaining question is whether prosociality can positively impact brain health outcomes, which refers to measures of cognitive, emotional, motor and neurological well-being, that can be influenced by various factors, including genetics, environment, lifestyle, or access to healthcare.

Could prosocial values play an unrecognized role in brain health?

According to the World Health Organization, brain health refers to the state of brain functioning across cognitive, sensory, social–emotional, behavioral and motor domains, allowing a person to realize their full potential over the life course, irrespective of the presence or absence of disorders (17). Various determinants affect brain development, adaptation, and response to stress and adversity, including physical and mental health, safe environments, security, lifelong learning, social connections, and access to quality services.

Multiple brain diseases (psychiatric and neurological conditions) compromise the core cognitive components of prosociality (18, 19), including empathy (11, 18, 20, 21), moral cognition (18, 22–24), moral emotions (15, 25), and social cooperation (18, 26–29). Conversely, it is not well understood if prosocial habits can induce brain changes. Can prosocial values not only be influenced by brain conditions but also play a crucial, yet overlooked, role in maintaining brain health?

Prosocial behaviors and social cognition have been associated with health in a variety of ways. Engaging in prosocial behaviors has been shown to have a positive impact on mental health (30). Prosocial activities are more likely to experience feelings of happiness, well-being, and social connectedness, which can help to reduce stress and anxiety (31). Even engaging in prosocial behaviors improve mood and reduce symptoms of depression and anxiety. For instance, prosocial behavior mitigates the adverse effects of stressors on emotional well-being, suggesting that it could be an effective stress-coping strategy (32). A statewide population-based study demonstrated that people who engage in volunteer work experience positive impacts on physical health, life satisfaction, social well-being, and reduced depression (33).

At physiological levels, prosociality has been linked with multimodal health. At cardiovascular level and physiological stress responses, prosocial behavior has been linked to improved health (34). For example, prosocial activities are associated with lower levels of inflammation (proinflammatory cytokine activity) (35), which is a risk factor for heart disease and other chronic diseases; and to lower blood pressure (36), which is another important factor for cardiovascular health. The immune system can also be negatively impacted by lack of prosocial behavior (37). Studies have found that individuals who engage in prosocial activities have stronger immune system, which can help to protect against a variety of health conditions (38). Neurohormonal circuitry in caregivers, particularly oxytocin and progesterone, may contribute to the health and longevity benefits associated with helping others due to their stress-buffering and restorative properties (38). Engaging in prosocial activities has been shown to reduce levels of cortisol (39) and inflammation (40), which are key factors in many chronic health conditions. Inflammation protects the overall health as part of the immune response to infection, injury, or harmful substances. While acute inflammation is crucial for protecting the body and maintaining health, chronic inflammation can have detrimental effects on health. Inflammation can cause damage to the body's tissues and contribute to the development of conditions such as heart disease, arthritis, and cancer. By reducing inflammation, prosocial behaviors help to reduce the risk of multiple conditions and improve overall health.

Prosociality-based interventions are designed to enhance empathy, compassion, cooperation, and other prosocial traits that contribute to the well-being of others and foster positive social interactions. Such intervention can take various forms, such as educational programs, group activities, mindfulness practices, or cognitive-behavioral therapies. Some of these prosociality-based interventions have begun to show improvements in brain health (41–43). A longitudinal study (41) found that training in socio-affective and socio-cognitive skills resulted in specific changes in brain morphology among healthy adults, correlating with improvements in cognition and prosociality, and structural plasticity in social brain networks. Socio-affective training reduces experienced negative affect when processing images depicting human suffering and increases activation in the right supramarginal gyrus when confronted with negative stimuli (42). Another study discovered that induced prosocial skills, such as compassion for others and the ability to take another's perspective, are associated with short-term changes in leukocyte telomere length (LTL) and accompanying changes in plasticity of social brain areas (43). Eudaimonic and hedonic lifestyles represent distinct approaches to health and well-being, with eudaimonic well-being focusing on pursuing meaning, personal growth, and self-realization, while hedonic well-being emphasizes seeking pleasure and avoiding pain. Eudaimonic well-being can improve mental health, enhance immune function, and increase longevity, while hedonic well-being can reduce stress, improve cardiovascular health, and enhance social connections (44). In brief, these studies suggest that behavioral changes related to prosociality induce short-term changes associated with improved brain health.

In summary, the available although still emerging indirect evidence suggests that prosocial behavior and social cognition can positively impact health at multiple levels, including behavioral, cardiovascular, immune, stress-related, inflammatory pathways, and brain health (Figure 1). These different effects could be understood as a mechanism for reducing the environmental demands and stress. Allostatic load refers to the cumulative wear and tear on the body's stress systems that occurs over time as a result of chronic exposure to stress and involves a continuous process of energy balance instantiated by the brain to anticipate, regulate, and respond to environmental demands (45, 46). Allostatic overload can lead to alterations in the brain's neural circuitry, neurotransmitter systems, and inflammatory responses, which in turn can impair cognitive functions, emotional regulation, and overall mental well-being. Prosocial behavior has been linked to reduced allostatic overload (39), which can help protect the brain's health against stress and aging and improve overall health.

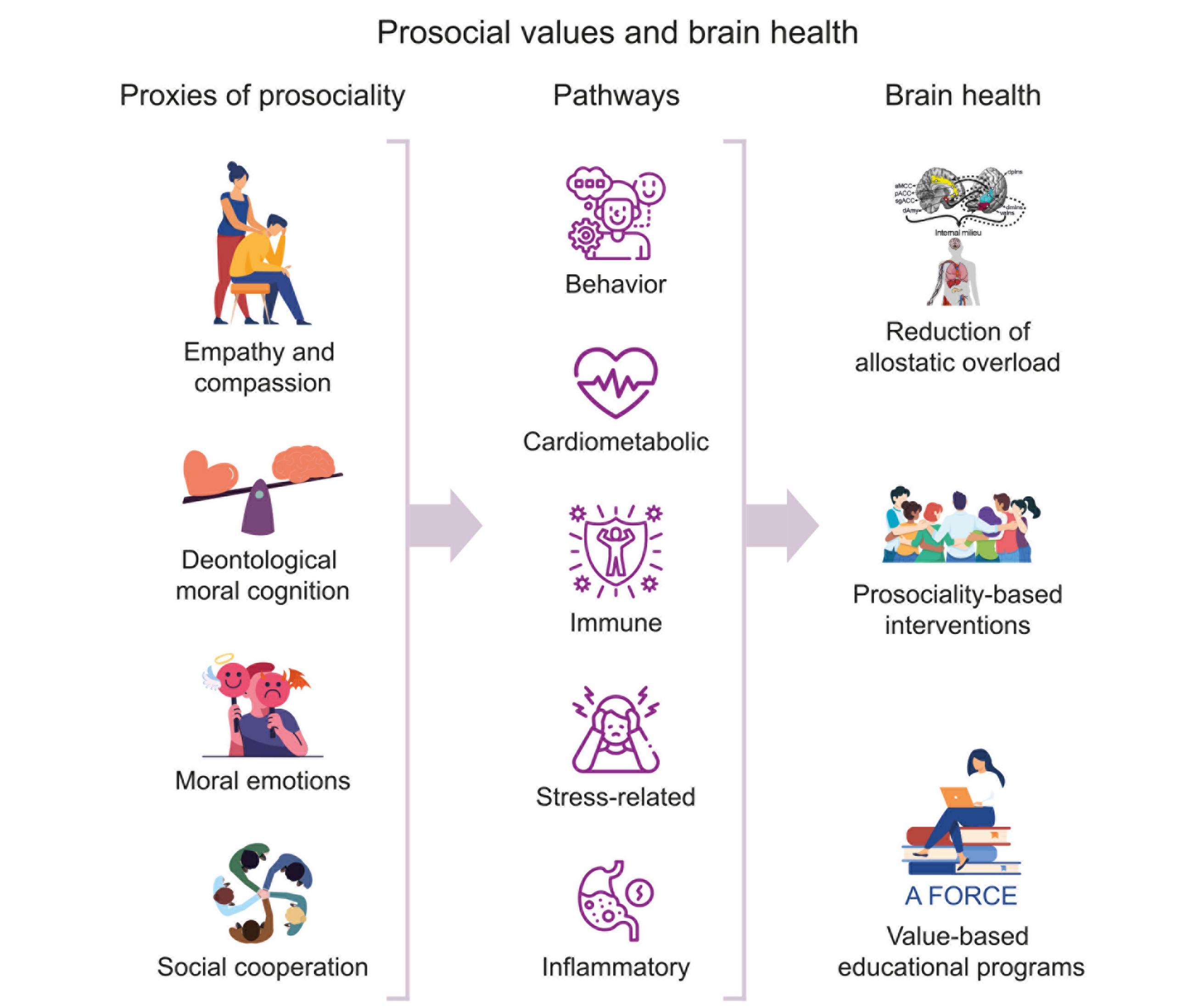

FIGURE 1
The relationship between proxies of prosocial values and brain health through biological pathways. This figure illustrates the proposed hypothesis that proxies of prosocial values, which include social cognitive and affective processes (empathy, deontological moral cognition, moral emotions, and social cooperation), can impact various behavioral and biological pathways. These encompass cardiometabolic, immune, stress-related, and inflammatory processes, which can subsequently enhance brain health by reducing allostatic overload. Integrating prosocial values into educational models (e.g., the A FORCE model), interventions, and public health policies may contribute to improved brain health, particularly in vulnerable populations.

Can prosociality help to improve brain health in populations at risk?

Diverse groups, including individuals affected by negative social or environmental exposures (47), as well as psychiatric (e.g., schizophrenia, anxiety, depression, PTSD) (48), and neurological conditions (e.g., Alzheimer's disease, frontotemporal dementia) (45, 49), constitute populations at risk impacted by allostatic overload. Psychiatric and neurological patients, and individuals exposed to stressful conditions (i.e., poverty or violence) are exposed to allostatic overload (45, 46, 50–53). Prosociality has been linked to allostatic mechanisms (39, 54–56) and prosociality-based interventions have the potential to significantly improve brain health in different populations (41–43). Promoting prosocial values and behaviors can help to reduce allostatic load, improve mood and reduce symptoms of anxiety and depression, improve cardiovascular health, and strengthen the immune system (39, 46) and even directly influence brain health.

Given these potent brain health benefits, in addition to the well know benefic promoting care and concern for the well-being of others, prosociality could be promoted in science, politics, and governmental initiatives. The Global Brain Health Institute (GBHI) has developed "A FORCE" model, a prosociality value-based learning program, which is centered around the six core values of Authenticity, Fairness, Openness, Respect, Courage, and Empathy. A FORCE involves education and training on these values and how they can be applied in daily life and in the context of brain health. Through workshops, discussions, role-playing exercises, and other interactive activities the program help students to internalize these values and understand their importance in promoting brain health. This approach could be the first step for incorporate the value of prosociality into public health policies and programs. Value-based education across the lifespan could be particularly useful in children and adolescents, as well as to understanding how prosociality can improve the long-term cumulative burden across the lifespan.

Conclusion

In this perspective, we linked prosociality with a set of social cognitive processes and proposed that not only is it impacted by various disorders, but it also has the potential to play a role in promoting brain health. Emerging evidence supports this claim, in terms of reducing allostatic overload at behavioral, cardiovascular, immune, stress-related, and inflammatory levels. By incorporating prosocial values into education and public health policies, and developing targeted interventions to support prosocial behavior, we can help to improve brain health in populations that are particularly vulnerable to stress and adverse health outcomes.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

AI conceived this work and prepared the initial draft. DM and BM carefully revised the draft. All authors contributed to the contents of this article and approved the final version.

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Valuing embodiment: insights from dance practice among people living with dementia

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There is a growing appreciation for the ability of person-centered arts-based approaches to extend multiple domains of brain health of people living with dementia. Dance is a multi-modal artistic engagement which has positive impacts on cognition, mobility and the emotional and social aspects of brain health. Although research into multiple domains of brain health among older adults and people living with dementia is promising, several gaps remain, specifically in understanding the benefits of co-creative and improvisational dance practices. Collaborative research between dancers, researchers, people living with dementia and care partners is needed to design and evaluate future research on dance and to determine relevance and usability. Furthermore, the respective praxes and experience of researchers, dance artists and people living with dementia contribute distinctly and uniquely to the identification and the assignment of value to dance in the context of the lives of people living with dementia. In this manuscript the author, a community-based dance artist, creative aging advocate and Atlantic Fellow for Equity in Brain Health, discusses current challenges and gaps in the understanding of the value of dance for and with people living with dementia and how transdisciplinary collaboration between neuroscientists, dance artists and people living with dementia can advance collective comprehension and implementation of dance practice.

KEYWORDS

dance, embodiment, dementia, neuroscience, movement, brain health

Introduction

Dementia is an umbrella term for conditions that affect cognitive function, thinking and social abilities of individuals to the extent that interfere in their daily lives (1). Currently people living with dementia (PLWD) constitute 50 million globally, with projections reaching 153 million by 2050 (2). PLWD experience stigma (3) and multi-layered marginalization that is compounded by the detrimental effects of a progressive chronic illness which can impact affective states (4), mobility and spatial relationships (5, 6), and ability to communicate or follow conversations (7) all of which can hinder meaningful engagement and connection. As a result, PLWD inevitably experience shifts in their modes and capacities for expression which influence their ability to express and feel connected to the communities around them. Reportedly, PLWD and their care partners often experience a reduction in size of their social networks and loss of connection with others as the disease progresses (8). The value and position of the arts as a vehicle for social justice to advance a culture shift toward inclusion, creativity and respect of PLWD at every level of society is increasingly recognized (9), whereas the need for programs that engage and involve people living with dementia as co-creators is apparent (10, 11).

Dance is an art form increasingly recognized for its role to promote brain health (a life-long, multidimensional and dynamic state consisting of cognitive, emotional and motor domains) (12) and wellbeing (13–16) in part through community engagement coupled with physical fitness. Dance, for people living with dementia, centers dignity and meaning and "takes on even greater significance given that corporeality becomes the primary means of engaging with the world and with other." As Kontos states, "Dance provides a unique medium for non-verbal communication, affect and reciprocal engagement which profoundly enables the relational citizenship of persons living with dementia" (17). Nonetheless, compared to other creative practices, the correlation of dance on the physical, cognitive and psychosocial wellbeing of PLWD is under-represented in neuroscience research and understanding of certain types of dance, such as co-creative dance, among PLWD is entirely lacking.

Neuroscientists define dance as a multi-modal activity that couples cognitive tasks with aerobic exercise and social engagement (18). Warburton defines dance as a conscious event, which deploys implicit (procedural) and explicit (declarative) knowledge presenting both neurobiological and phenomenological features (19). Within academic neuroscience research, contradictory, incomplete or over-generalizing representations of dance are common (19). The impact of dance interventions is not reported in a standardized way rendering replicability, relatability to practice and correlation between results of multiple studies challenging (20–25). Often, results from interventions of diverse dance forms are reported together without comprehensive discussion or inference of the findings on their practice (26–29). To map the complex interconnected elements of diverse types of dance practice on multiple domains of well-being, we need trans-disciplinary teams collaborating to design studies, evaluate results and determine implementation. Dance artists bring a specialized skillset to their praxis which is honed through experiential research co-created with their communities of practice. Neuroscientists can help clarify and validate what dancers witness in practice, in turn expanding the resources they have and backing them with evidence. In response, dancers and neuroscientists can work in a mutually beneficial feedback loop of inquiry and application founded in multi-faceted knowledge and evidence. In this manuscript, the author, a community-based dance artist, creative aging advocate and Atlantic Fellow for Equity in Brain Health, discusses current challenges and gaps in the understanding of the value of dance for and with PLWD and how transdisciplinary collaboration between neuroscientists dance artists and PLWD can advance collective comprehension and implementation of dance practice.

Let's get physical: dance, aerobic activity, and the brain

Research has long recognized the positive connection between aerobic exercise and heart and brain health (30). Aerobic exercise increases cerebral oxygenation and blood flow and promotes angiogenesis within the brain in childhood, adulthood and elderhood (31–33). A pooled cohort study evaluating the link between leisure dancing and cardiovascular risk when compared to walking found that moderate-intensity dance activity was correlated to lower cardiovascular disease and mortality over a moderate aerobic-intensity walking (34). Researchers posited this increased protective factor from moderate-intensity dance may be due to higher-intensity bouts within dance. In fact, sports medicine researchers recognize high-intensity interval training as superior in promoting cardiovascular fitness than moderate-intensity continuous aerobic activities (35).

Physical activity in later life was found to increase levels of synaptic proteins in a global (not limited to one region of the brain) and time-dependent fashion (people active up to 0–2 years to end of life have bigger effect). Researchers hypothesize that one reason for this is linked to the cardiovascular connection to brain health (36). As synaptic integrity promotes connectivity in the brain and is seen as a biologic precursor of cognition, this research posits profound implications for physical activity started in later life. When analyzing brain tissue, Casaletto et al. found physical activity provides a powerful neuroprotective factor even in light of existing neuropathologies (36). Although Casaletto's research did not specify a type of physical activity, other research has illustrated how aerobic activity in the form of dance not only supports synaptic integrity but engages circuits that connect regions of the brain (37).

Growing evidence points to forms of dementia like Alzheimer's disease as being related to brain connectivity issues that hinder communication between areas of the brain (38–40). The medial temporal lobe is one of the first networks in the brain to be impacted by neurodegenerative conditions like Alzheimer's disease (41). Sinha et al. tested cognitive flexibility and measured the functional activity within the medial temporal lobes of participants (ages 65+) engaged in moderate aerobic dance and analyzed participants' ability to acquire new information and correlate it to previous knowledge. Those who engaged in the dance program had higher neural flexibility within the medial temporal lobe network which also reflected in cognitive tests and learning new tasks, specifically by learning a new idea and applying it in another context. As a conclusion, the team asserted aerobic dance exerts a rehabilitative and protective effect on medial temporal lobe function (37).

Aerobic activity promotes neurogenesis. Rehfeld et al. matched dance (aerobic dance phrases of increasingly more complex and varying choreography) and conventional fitness training (bicycle ergometer, resistance training and flexibility training) for aerobic exertion. Participants (ages 60+) who joined in the dance program showed a volumetric increase in the medial temporal lobe as well as higher levels of brain derived neurotrophic factor (BDNF) in their plasma (42). BDNF supports synaptic strength as well as neuronal plasticity, specifically through increased neurogenesis by promoting neuronal cell survival and proliferation, and is positively correlated to increases in cognition (43). Rehfeld et al. posit BDNF increase after dance over repetitive fitness training is due to dance coupling aerobic activity with novelty and challenge (42).

Steppin' out: gait as a prodromal marker for brain health

Verghese et al. investigate gait as a prodromal marker for dementia (44). In a study of older adult long-term leisure partner dancers, they observed that compared to non-dancers, they exhibited overall greater balance, which included better gait. However, the dancers did not have greater strength than non-dancers (44). As both sarcopenia and decreased gait are correlated to increased risk of developing dementia (45, 46), this illustrates how dance, when coupled with additional resistance training or specific targeted activities that build muscle strength and endurance could provide a holistic support to functional mobility while off-setting detrimental brain health in advancing age.

I want to dance with somebody: dance enhances mood and social connection

Dance engagement among people living with dementia in residential care settings increases mood and social interaction (47). Engagement in 12 weeks of dance at a residential nursing home reduced the need for depression medication among older adult participants (including people with diagnoses of dementia) (48). Dance-based interventions are significantly beneficial to persons with MCI and dementia in decreasing depression compared with controls, with similar effects in both hospital and community settings (49). This impact on mood may occur due to the aerobic engagement of dance which increases blood flow to the brain (50) as well as from intrinsic reward, which results in neural synchrony, enhanced interpersonal coordination, and an avenue for pro-social behaviors (51).

Dance promotes pro-social behaviors. Dancers and musicians both exhibit higher levels of measures of empathy than controls and consistently higher insular connectivity (52). Researchers posit that this heightened empathetic and insular sensitivity can be attributed to both art forms requiring frequent feedback between internal and external cues. Mirroring is a common practice utilized in dance to promote heightened relational awareness. Engaging in facial mirroring synchronously activates the same areas of the brain, namely, areas that are involved in social connection: the prefrontal cortex, insula and temporo-parietal junction (53). Researchers posit that engaging in physical mirroring, amplifies the practice of empathy (54). Although a definitive theoretical framework explaining mechanisms of empathy in dance mirroring is unclear (55), what is understood is the sensorimotor correlation of empathy and pain (56), which is related to mirror systems (57). Neural synchrony of doctors and patients involved in mirroring resulted in analgesic effects for the patients (53). The extent to which this experience correlates to dance mirroring remains to be discovered, but upcoming research from Emily Cross and team might illuminate this (58).

Dance, specifically co-creative dance improvisation, can be seen as a form of awe, by cultivating an intention and perspective of curiosity, reciprocity, and cooperation. "By shifting attention away from the self and onto the outside world, awe diminishes feelings of self-importance and makes people feel smaller, yet more connected, to a larger community and purpose" (59). Keltner speaks of the ability of engaging in the practice of awe to place individuals neurophysiologically "in sync" with one another, in part through the phenomenon of "Collective Effervescence" or "just moving together, feeling exalted, bubbling, being ecstatic" (60). Dance promotes novelty and a sense of awe within the framework of the quotidian. In application with older adults or PLWD who may find leaving their residence difficult, the value of an approach that cultivates enrichment, awe, and novelty within the ordinary should not be overlooked. Cumulatively, the application of awe and novelty, through the practice of shared dance, has the potential to induce small positive stress resulting in neuroplasticity, while promoting a sense of well-being and belonging. More research is needed to make a direct correlation between mirroring movement, co-creative dance engagement and regions in the brain indicated in social connection, pro-sociality and empathy, but these studies imply promising connection.

Just my imagination? Dance, creativity and improvisation

Neuroplasticity refers to the brain's ability to modify, change, and adapt both structure and function throughout life and in response to experience (61, 62). whereas access to new physical spaces, learning new skills, training memory, playing games, participating in activities associated with spatial learning and motor coordination (i.e., sports, artistic and creative activities,) and a developed social life all constitute an enriched environment (EE) (63). EE benefits global brain health domains resulting in neuroplasticity (64). Per Kempermann, higher physical activity leads to increased proliferation of neurons, synaptogenesis, and more dendritic complexity, while enrichment leads to higher rates of survival of newly formed neuronal cells and recruitment into lasting functional integration. This long-lasting functional integration can be identified as cognitive reserve (65). Robertson argues that the type of positive stress that we experience when we introduce challenge, novelty, and the element of surprise leads to lifelong cognitive reserve (66). Adding an additional task or challenge to an already established task, can add positive stress resulting in increasing noradrenaline, which, can in turn can lead to improved attention and, when sustained, ultimately result in neuronal plasticity (65).

Improvisation in dance is a process-based form of movement inquiry that occurs either individually or in groups and cultivates a "practice of dwelling in possibility" (67). Dance improvisation is experiential by definition and "generates understanding about the phenomena of being through 'presencing' a polyattentive body, conversing with ambiguity, uncertainty, potentiality, and choice" (68). Through this lens, dance improvisation can enrich the environment in a way that cultivates opportunity for challenge and positive stress, with beneficial potential for neuroplasticity and focus.

EE fosters creativity, a multifaceted phenomenon, that uses imagination or original ideas to achieve valued goals (69). One of the dominant ways of evaluating and looking at creativity in neuroscience is by exploring divergent versus convergent thinking. Divergent thinking, which is often classified as playful, self-aware internal rumination, engages the default mode network (DMN), which, among other areas, depend on activation of the medial prefrontal cortex for evaluation of internal stimuli as a core component of the self-awareness network. Convergent thinking depends on the lateral prefrontal and parietal cortices, which are core components of the executive control network (ECN) that supports purposeful use of symbols and intentional inhibition of externally triggered impulses (70). Neuroscience frequently represents divergent and convergent thinking as antagonistic.

Research from Beaty et al. illustrate how among "highly creative individuals" these two ways of thinking and their related brain networks work in concert with one another (71). "Highly creative" individuals exhibit a higher connectivity when performing a creative thinking task between the DMN and the inferior prefrontal cortex, a part of the brain related to the ECN (71) Research from Dr. Charles Limb illuminates potential neurophysiological mechanisms that corroborate this phenomenon through examination of musical jazz solo vs. partners improvisation (72, 73). In comparison to memorized, non-improvised exchange, partner improvised musical exchange was characterized by functional connectivity in the inferior frontal gyrus, the parts of the brain that regulate executive control areas that are linked to cognitive and emotional processing, inhibition, and attention (72). In contrast, solo jazz improvisation resulted in the down regulation of the inhibition network and increased activation in the sensory cortex (73) which correlates to what is recognized during activation of the DMN linked to self-expression and rumination (73). In comparison to solo musical improvisation, there is greater expectation during a musical conversation for relationship and continuity thus increased self-monitoring coupled with rumination is required (72). This data correlates to the research by Beaty and team who recognized that among highly creative individuals, default network engagement was coupled with functional connectivity in the inferior frontal gyrus, an area of the brain involved in inhibition, direction, and executive control.

This research suggests that an improvisational approach invites proficiency in content but trains a flexibility between the global and the local and could offer superior benefits in neuronal engagement and plasticity. Dance improvisation adds the benefits of improvisation to the other emotional, social, physical, and cognitive benefits of dance engagement. Solo dance improvisation, although sometimes responsive to external stimuli is characterized by drawing internally in a ruminative fashion on memory of movement and sensory stimuli with a lack of inhibition of content development. Group dance improvisation and co-creative or collaborative dance making, requires a combination of "in the moment" selective content creation responsive to both external and internal cues, similarly drawing on former embodied knowledge. In this light, a model of both dance and music improvisation might be seen as (1) tapping into a library of accumulated cerebral and corporeal information and reconnecting it in novel ways, (2) training a practice of flexibility and connectivity between areas of the brain, and (3) supporting ease with uncertainty. This is beneficial for supporting brain plasticity and adaptability and has potentially powerful protective brain health implications for diverse ages and abilities. Although research into the specific mechanisms taking place during solo and group dance improvisation is lacking, the similarity in the practice of dance and musical improvisation invites more inquiry into the extent of the neurological similarities and differences between them.

For people living with dementia and care partners, improvisation cultivates engagement (74, 75), but a need persists to understand which brain networks are engaged when they participate in dance improvisation. Future studies should explore functional connectivity among older adults and people living with dementia when engaging in solo and group dance improvisation to establish the extent to which dance improvisation relates to the above noted impact of musical improvisation.

Value of dance for and with people living with dementia

The above review of literature illustrates the benefits of dance for people living with dementia but the value of dance goes beyond what can be quantified through empirical research. Reduction of dance to measurable physiological changes fails to capture its full value to and for people living with dementia. As illustrated by Kontos, adaptation of dance solely for instrumental and therapeutic purposes, impoverishes the understanding of the value of dance for people living with dementia and fails to recognize the ability of dance to promote self-hood, support embodied forms of communication and meaningful collective engagement (17).

A case study of a co-creative dance program for people living with dementia (Supplementary Box 1) emphasizes existing modes of communication by recognizing and coupling verbal and embodied forms of expression. The resulting collaborative dance practices amplify and extend agency, personhood and meaningful connection while building new spaces of belonging and community.

Stories in the Moment™ is a co-creative dance, movement, and storytelling program for people living with dementia and care partners that was developed by the author (76). The intention behind Stories in the Moment™ is to amplify the creative voice of people living with dementia while supporting them and care partners in extending their resources for meaningful communication through individual and collective dance. The class structure balances dance activities led by the facilitator with individual and collective dance improvisation to result in co-created dance stories and miniature dance performances. Activities in the class apply existing evidence-informed benefits of dance on multiple domains of brain health of older adults and people living with dementia but see these as secondary to the primary intention of the program which is to utilize co-creative and improvisation dance to promote agency, personhood and relationality. Frameworks and tools adapted from group dance improvisation support engagement by heightening the awareness of participants' "kinesthetic sense" while encouraging modes of communication most comfortable and accessible to them.

Discussion

Dance is an aesthetic art form that couples beneficial engagement in multiple domains of brain health with relationality and meaning. As we consider the value of dance on health and wellbeing, we need to ensure we include the contributions of the artists and the participants (people living with dementia and care partners) who will be integral to the implementation and growth of this work alongside those of the clinicians, researchers, and policymakers.

Currently, there are gaps in knowledge, and dance continues to be under- and misrepresented in neuroscience research. Without this knowledge, policymakers lack the evidence-base behind which to sponsor and create recommendations for use and clinicians are reticent to prescribe or promote dance practice for their patients. More research is needed to build on preliminary data that is offering promising benefits of diverse forms of dance on multi-modal domains of brain health and well-being. This new research must happen with artists and people living with dementia at the table.

In order to ensure that the knowledge of the lived experience experts (people living with dementia), the applied practice experts (artists) as well as the neuroscientists is acknowledged and leveraged with existing knowledge from empirical, qualitative and experiential research, a horizontal, collaborative and equitable approach, rather than a hierarchical approach is needed (75). If we do not change the systems in which we identify impact and value by expanding and normalizing trans-disciplinary collaborations between dance, neuroscience and the communities they serve, we risk losing the spirit of why these programs actually work – their creativity, their flexibility, their reciprocity, their humanity. At its essence, approaching collaboration from the horizontal allows "for multiple perspectives and recogniz[ing] that making distinctions is a creative act and worth doing in order to understand the nuances of our efforts… [within this approach] many ideas can coexist" (77).

Emily Cross posits what might constitute this horizontal collaborative process between artists and neuroscientists by amplifying a need for a bi-directional listening and cultivating collaborations with the arts that include a two-way communication from the ground up: "arts research is hugely vital in understanding who we are as a human culture and where we come from and where we are going, and science does not really give us that. The value of arts research for arts within itself is tremendous and it does not need science to legitimize itself" (78). In adopting a collective practice of awe and improvisation that invoke deep listening, witnessing and mutual respect, we can build authentically collaborative and mutually beneficial relationships between the arts, research, and the communities we serve.

Author's note

Magda Kaczmarska, MFA is a dance artist, creative aging thought leader and Atlantic Fellow for Equity in Brain Health. She is the Vice President of Foundation Dementia Action Alliance Poland and serves on the board of the Dementia Action Alliance (United States). Kaczmarska founded DanceStream Projects, a creative collective based in New York City, that cultivates transdisciplinary partnerships to provide direct ally-ship and empowerment to communities by bridging arts and health and centering dance as a catalyst for systems change. Kaczmarska mentors future leaders in the creative and health sectors through regular partnership at the Fordham Ailey School of Dance in New York City and the Arts in Medicine Fellowship in Lagos, Nigeria. She served on the National Dance Education Organization (NDEO) Dance and Disability Task Force until 2022 and continues to serve as a representative to the UN with Generations United and is on the executive committee of the UN NGO Committee on Ageing.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

The author confirms being the sole contributor of this work and has approved it for publication.

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Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2023.1174157/full#supplementary-material

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Hope for brain health: impacting the life course and society

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Hope is a cognitive process by which an individual can identify their personal goals and develop actionable steps to achieve results. It has the potential to positively impact people's lives by building resilience, and can be meaningfully experienced at both the individual and group level. Despite this significance, there are sizable gaps in our understanding of the neurobiology of hope. In this perspective paper, the authors discuss why further research is needed on hope and its potency to be harnessed in society as a "tool" to promote brain health across healthy and patient populations. Avenues for future research in hope and the brain are proposed. The authors conclude by identifying strategies for the possible applications of hope in brain health promotion within the areas of technology, arts, media, and education.

KEYWORDS

hope, values, brain health, aging, social brain, scientific education

> *"Even if the hopes you started out with are dashed, hope has to be maintained."*
> *–Seamus Heaney, Poet, Nobel Laureate*

1. Introduction

The story of humanity has always been driven by an innate capacity for resilience. While many factors underpin the individual's ability to face and overcome major obstacles, one has remained universally acknowledged regardless of nation or culture: it is the value of hope.

To hope is to be human, and it has been examined in diverse disciplinary perspectives including theology, philosophy, literature, anthropology, and medical sciences. Although there are several definitions of hope in the literature (Schrank et al., 2008), one of the most widely accepted postulates hope as a psychological construct made up of a set of cognitive mechanisms. Specifically, Snyder (2002), defined hope as "*the perceived capability to derive pathways to desired goals, and motivate oneself via agency thinking to use those pathways.*" Agency thinking embodies motivation to initiate and sustain one's actions to achieve a goal, while "pathway thinking" describes the capacity to find ways to achieve the goal. Simply put, hope is derived from a sense of knowing what one wants to achieve and being able to plan how to get there. While hope overlaps with constructs like optimism and positive thinking, there are subtle differences between these constructs. Optimism is the belief that everything will eventually work out, therefore a passive belief about future outcomes (Alarcon et al., 2013). Positive thinking can be described as a deliberate and conscious effort to manage one's thoughts, emotions, speech, and beliefs so that they focus only on the possibility of good outcomes during challenging or difficult circumstances (McGrath et al., 2006). Hope, by contrast, is an active process that encompasses both an individual's perceptions about their ability to plan and strategize, as well as their motivation to follow through with these strategies in a sustained manner, thereby inspiring confidence and enabling decisive action.

Hope is not just an individual experience, but can also be experienced collectively, i.e., a shared vision and belief that planned efforts can be channelized to reach a goal which is important for change (Braithwaite, 2004; Lueck, 2007). Considering the profound potential for hope on the individual, and the ripple effect on the collective predicated by our innate social interconnectedness, it comes as a surprise that so little research and neuroscientific understanding exists on the subject. While theological and philosophical discourse on hope has largely focused around its value to both the individual and larger society, little has been done to practically study its mechanisms in the brain. Could future research be carried out to explore how to "enhance" hope for functional uses and application in the lives of individuals, as well as greater society?

In this perspective, we highlight why understanding hope as a neurobiological entity is an exciting prospect and possible key to tackling larger systemic issues of brain health, and propose directions for future research on hope and the brain.

2. Brain networks that may contribute to hope

Since hope is considered a cognitive process, it is reasonable to presume that it may be associated with certain brain networks to our knowledge, two studies have explored this to date.

The first used resting state MRI (rsMRI) to investigate the functional brain architecture underlying hope (Wang et al., 2017). Resting state MRI measures spontaneous brain activity at rest. In this study, the correlational relationship between the intensity of spontaneous brain activity and hope (measured using the Dispositional Hope Scale; DHS) was examined. The DHS is a commonly used 12-item questionnaire that assesses both agency thinking and pathway thinking within the concept of hope. The authors found that higher levels of hope (agency thinking and pathway thinking combined) was related to lower spontaneous brain activity in the bilateral medial orbitofrontal cortex (mOFC). This brain region, located in the frontal lobe, is typically involved in motivation and decision-making processes, which are key elements of hope (Snyder, 1999). Agency thinking and pathway thinking were also independently associated with lower spontaneous brain activity in the mOFC in this study.

In a separate study, Wang et al. (2020) assessed the neuroanatomical basis of hope using structural MRI (sMRI). They examined the association between regional gray matter volumes (GMV) and hope as measured via the DHS. Results showed a positive correlation between hope and GMV of the left supplementary motor area (SMA). The SMA is located in the dorsomedial frontal cortex and is responsible for programming complex movements through linking cognition with action (Cona and Semenza, 2017). Further, it forms a conduit between the prefrontal cortex where higher order thinking and planning occurs, and the primary motor cortex, which initiates voluntary movement (Cona and Semenza, 2017). Since the SMA is involved in goal-directed behaviors, it is no surprise that this area is implicated in hope. Interestingly though, Wang et al. (2020) did not find associations between GMV and the individual components of hope (i.e., agency thinking vs. pathway thinking).

Collectively, these two studies suggest that hope may be associated with networks in the frontal cortex. Further, this area, particularly the prefrontal cortex, has been implicated in concepts closely related to hope including optimism and positive thinking. For instance, Dolcos et al. (2016) showed that optimism is associated with increased GMV in the prefrontal cortex.

3. The possible neuromodulation of hope

At the neuromodulator and neurotransmitter level, little is known about hope. However, studies looking at optimism and positive thinking have largely implicated dopamine—a neurotransmitter known to underlie human emotion in the midbrain. Dopamine is important in reward processing and motivation, and may be involved in the anticipation of positive outcomes. One study found that enhancing people's dopamine function increased their prediction bias in an optimistic direction (Sharot et al., 2012). In this study, participants were administered with a drug that enhanced dopaminergic function or a placebo (control group), and were tasked with providing estimates of their likelihood of experiencing various adverse life events. Those in the experimental group were more likely to make optimistic predictions than the control participants. Given the overlapping components of hope with optimism and positive thinking, there is a high probability that dopamine contributes to the expression of hope. The fact that the mesolimbic system of the brain, which regulates motivation for example, is made up of dopamine-producing cells lends credence to this argument (Yin, 2019).

Other neurotransmitters such as oxytocin, serotonin, and norepinephrine have been implicated in experiencing positive emotions and mood regulation, and thus may also underlie hope. Oxytocin, often called the "love hormone," is known to be involved in social bonding, and may be associated with feelings of hope and optimism in the context of social relationships (Alexander et al., 2021). Serotonin is believed to be involved in positive emotions including happiness (Matsunaga et al., 2017), and taking serotonin reuptake inhibitors is an effective medication for depression (Michely et al., 2020). It is thought that it may help individuals maintain a hopeful outlook in the face of adversity (Matsunaga et al., 2017). Additionally, norepinephrine plays a role in feelings of motivation and arousal (Sara and Bouret, 2012). In situations where an individual is faced with a challenge or obstacle, the release of norepinephrine may help to increase their sense of determination and hopefulness.

4. Future research on hope in the brain

Given that there are only two neuroimaging studies assessing the structural and functional underpinnings of hope, and no studies examining hope on a neuromodulatory or even cellular level, more research in these areas is desperately needed. For instance, functional magnetic resonance imaging (fMRI) could examine functional connectivity patterns of brain regions that may underlie hope. Such research could also explore additional brain regions involved in motivation (such as the amygdala and anterior cingulate cortex; Kim, 2013) and planning (such as the superior colliculus and parietal cortex; Mattar and Lengyel, 2022), as these may also be involved in hope.

In addition, since both neuroimaging studies were correlational in design, we are not able to draw causal conclusions about the neurocircuitry of hope. Thus, studies that are longitudinal and interventional in design are needed. Further, these imaging studies evaluated hope using only a questionnaire. An important step for future studies would be to develop research paradigms, such as task-based approaches for hope, and explore more direct measures or biomarkers of hope. This would allow a more objective investigation of the construct of hope and expand application to other areas of research. Understanding the neurobiological basis of hope also becomes critical at this juncture as we conceptualize symptom-based mental illness models to a more dimensional, transdiagnostic understanding of psychopathology. For example, using frameworks like the research domain criteria (RDoC; Hakak-Zargar et al., 2022) and approaches, which embrace advancements in neuroscience and technology. Task-based hope paradigms could also be used in studies measuring neurotransmitter levels to understand how the two may be correlated.

If future research can unravel the mechanisms and circuitry around hope in the brain, could this be leveraged as an intervention more powerful than pharmacological agents? As discussed above, although current evidence in this area is limited, it is an area of scientific inquiry worth considering. Future research to develop evidence-based interventions that specifically target hope across the lifespan could become a powerful intervention. We discuss this in the context of brain health below.

5. Hope to promote brain health

The World Health Organization recognizes brain health[1] as occurring across cognitive, sensory, social–emotional, behavioral, and motor domains (Brain Health, 2022). Irrespective of the presence or absence of brain-related disease, achieving an optimal level of brain health enables success across the life course (Brain Health, 2022). For example, a recent review highlights how specific components of hopelessness could be considered a clinical target for intervention as it improves psychological flexibility and adaptability (Marchetti et al., 2023).

1 Brain Health. WHO (internet). Geneva: 2022. Available from: https://www.who.int/health-topics/brain-health#tab=tab_1

Further, the individual and collective nature of hope makes it worth investigating further for its potential as a wider reaching "tool." Hope as a "tool" could help achieve this objective for individuals, communities, and societies, exercised as a type of cognitive training through use in technology, arts, media, and education.

We postulate that if hope can be developed through the life course, or possibly embedded in consumer products and user-based content for the commercial marketplace, perhaps it can be a large strategic contributor to preventative brain health and better living. For example, patients and their families are often devastated following the diagnosis of brain health conditions like dementia, activating a sense of doom that can lead to anxiety, loss, and despair (Aminzadeh et al., 2007; Lawlor, 2021). Higher mortality rates have been shown among caregivers of elderly individuals with disabling conditions (Sullivan, 2003), and hopelessness has been shown to predict mortality in older adults (Zhu et al., 2017). In these cases, instilling hope could be used to improve patient and family experiences.

While psychological interventions like cognitive behavior therapy and supportive counseling are effective interventions for depression where hopelessness is a common clinical feature, unpacking the mechanisms of hope and neurobiological basis offer potential to develop interventions specifically targeting the use of hope in a clinical setting (Cuijpers et al., 2013; Hernandez and James, 2021; Marchetti et al., 2023). Recent years have seen an abundance of mental health apps for "therapy on-the-go," and while the evidence around their clinical efficacy is limited (Torous et al., 2018; Marshall et al., 2020), they have become incredibly popular among consumers and are increasingly being used as an adjunct. Could future digital applications draw from research on hope in a similar manner to mindfulness and meditation apps, to encourage their users to develop hopefulness? One could envision cognitive training exercises, guided sessions and the accountability of push notifications to encourage regular usage to instill hope and improve a user's brain health. Could hope be something that is improved with daily practice like mindfulness? And if so, would it provide positive emotional and physiological changes in the user's mind over the long-term? At this juncture, future research is required to understand what components could be targeted most effectively to enhance realistic hope, which is the balance between false hope (denial that circumstances have changed with an illness/condition) and false hopelessness (inability to be hopeful about an alternative future; Evans, 2019).

Arts, including visual arts, music, and dance, can be used to cultivate hope, given that it is a powerful way to connect people, heal, and find joy. Through arts, people can express themselves, build resilience, and foster positive change (Dunphy et al., 2019; McCrary et al., 2021). For instance, people with Parkinson's disease experienced benefits in quality of life and well-being after participating in dance classes, and this was associated with improved cognitive function (Hasan et al., 2022). Is it possible that these patients also experienced increased hope and this contributed to the positive changes in brain health? If so, hope through the arts could be used to harness brain health change in patients with neurodegenerative disorders.

Media could also play a larger role in developing hope for brain health. Commercial film and television, print and broadcast journalism, as well as digital or social media are often driven by themes of hope in their narratives. The conflicts within these stories are rife with obstacles that the subjects or protagonists must battle along their journeys, for which hope is a tactical weapon of survival. However, rarely do these industries curate content in a hope-conscious way that encourages viewers to take their lessons learned offscreen and into their own lives. Equipped with greater knowledge of hope's importance on brain health and its potency, these content creators and providers could become more responsible agents of change in the lives of their many global consumers.

Education provides knowledge and skills to pursue goals and overcome challenges, driving neuroplastic changes in the brain that enhance overall connectivity and brain health. Thus, education could be central to first establishing a sense of hope and subsequently building hope within the individual. To achieve this, new hope-focused pedagogies would need to be established and could be used in a number of environments, whether in formal education, vocational training or workplace wellbeing initiatives. Dissemination of hope as an educative tool across all modalities of information exchange could then result in behavior change at the community level, which might then flow into structural changes at the local and national policy level.

6. Final thoughts

In this paper, the authors have described a potential neurobiological basis of hope as a cognitive process, postulated future research directions and, most importantly, explored several strategies for its possible application in brain health. While there is a hypothetical nature to the concept of hope and its uses introduced herein, there is a need to move forward in exploring its actualization regardless of skepticism. An emerging global challenge is upon society in the form of an aging population with increased incidence of dementia and other brain diseases. Public health efforts for earlier detection and research into biomarker-based testing is resulting in more affirmative diagnoses before scalable pharmacological cures are successfully identified. This means there is a need to reframe brain health as soon as possible, and doing so from a perspective of realistic hope can build the resilience necessary for individuals, families, communities and societies to deal with the major challenges ahead.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material; further inquiries can be directed to the corresponding author.

Author contributions

JD, JF, and ZB wrote and edited the final version of the manuscript. JD, JF, ZB, SF, AC, AY-M, SE-J, VU, GM, VC-G, K-HN, BL, and AN contributed to conceptualization of the paper and wrote the initial draft of the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Moral reasoning through the eyes of persons with behavioral variant frontotemporal dementia

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Introduction: Persons with behavioral variant frontotemporal dementia (bvFTD) can exhibit apparently antisocial behaviors. An example is their tendency to adopt utilitarian choices in sacrificial moral dilemmas, i.e. harmful actions to promote overall welfare. Moral cognition models interpret such tendencies as deriving from a lack of emotional engagement and selective impairment in prosocial sentiments.

Methods: We applied a qualitative approach to test those theoretical assumptions and to further explore the emotional experiences and values of people with bvFTD while they contemplate moral scenarios. We conducted semistructured interviews with 14 participants: 7 persons with bvFTD and 7 older healthy controls. Transcripts were coded using ATLAS.ti 5.0.

Results: During the moral reasoning task, persons with bvFTD reported more positive emotions than negative and showed significantly less cognitive precision in their moral reasoning compared to controls. Persons with bvFTD also organized their choices predominantly around kindness and altruism, and their responses reflected higher rule compliance. Our study showed that bvFTD persons' utilitarian responses to moral dilemmas did not arise from an emotionally disengaged or antisocial perspective. Instead, they were underpinned by positive emotionality and prosocial values.

Discussion: These findings enrich current understandings of moral cognition and highlight the importance of incorporating mixed methods approaches in dementia research that take into consideration the viewpoint of cognitively impaired individuals

KEYWORDS

moral reasoning, bvFTD, positive emotionality, mixed method approach, prosocial values

1. Introduction

Moral judgments engage moral cognition, operationalized as the application of cognitive processes to issues we identify as involving "right" and "wrong" behavior (1). Accordingly, models of moral cognition, such as the moral emotion and dual process theory (2, 3), have been developed to explain the cognitive underpinnings of moral judgments and tested in neurological conditions, with a view to determining whether they still hold true in individuals where specific aspects of cognitive processing are impaired. One such condition is the behavioral variant of frontotemporal dementia (bvFTD), a neurodegenerative condition predominantly affecting socioemotional function and, as a result, moral reasoning (4–6). In previous studies, persons with bvFTD have been characterized as individuals who, as opposed to healthy controls, are more inclined to endorse instrumental harm choices so that the greater good is obtained (e.g., being willing to push someone to their death to save five people), a type of choice referred to as "utilitarian." (6, 7) Only a minority of healthy individuals in the population make these choices in moral reasoning scenarios. This expectation that persons with bvFTD will have an abnormally utilitarian outlook works in tandem with a conceptualization of bvFTD as a condition that encompasses a lack of social propriety that is motivated by antisocial traits. Those findings, however, derive from an empirical framework that studies moral reasoning quantitatively and excludes dilemmas that include a dimensional understanding of utilitarianism, where scenarios account for both impartial beneficence (i.e., benefitting strangers equally to close friends and family) and instrumental harm (8). This study aimed to draw a more nuanced picture of moral reasoning in bvFTD via a qualitative approach and the use of dilemmas that examine utilitarianism multi-dimensionally.

Emotions play a major role in the majority of our moral decisions, generating significant tilts to our moral compasses. As proposed by the moral emotion theory, for instance, emotions act as salience messengers to help us distinguish right from wrong, point to moral violations, and motivate moral behavior (2, 9). Because of their associated tone, those "moral emotions" are characterized as self-conscious (e.g., shame, guilt, and pride) and serve as emotional barometers by offering salient feedback on social and moral acceptability (10–12). For example, when individuals do the right thing, positive feelings of pride and self-approval are likely to emerge. Neurological accounts of bvFTD suggest significant impairment within the systems involved in the processing of moral emotions (i.e., medial, orbitofrontal cortex, and superior temporal cortices) (11, 13, 14). As a behavioral sequela, the engagement of prosocial sentiments is hindered. Based on that empirical framework, persons with bvFTD are thought to adopt anti-social decisions and behaviors due to the associated dysfunction of systems subtending moral emotions.

Theoretical accounts that support the role of emotions in moral reasoning are also found in dual-process models (3). While the moral emotion theory focuses on the specific contribution of moral emotions in tagging moral salience, the dual process model highlights two types of processes that subtend decision-making (15). More specifically, the dual-process theory of moral cognition asserts that moral decisions are the product of either one of two distinct mental processes (1, 3, 16): (1) automatic-emotional processes, which are deemed fast and unconscious and promote intuitive judgments (system 1) and (2) conscious-controlled processes, which are slow and deliberative (system 2). Moral decisions drawing from system 2 are less influenced by the immediate emotional features of decision-making (system 1). Instead, they seem to emanate from general knowledge and abstract moral concepts, often accompanied by a more controlled analysis of situational features. Characteristically it is suggested (15) that non-utilitarian judgments are mostly driven by automatic emotional responses, while utilitarian judgments engage controlled cognitive processes.

As emotional disturbances are a cardinal feature of bvFTD, most studies that examine moral reasoning in bvFTD and related neurological conditions contextualize their findings under the prism of dual process models, emphasizing system 1, namely the affective contributions that generate typical moral decisions (17). For example, it has been suggested that when persons with bvFTD, as opposed to healthy controls, are more likely to respond to sacrificial dilemmas by endorsing instrumental harm choices for overall welfare (i.e., utilitarian choices), it is a reflection of their diminished capacity for emotional response (6, 7, 18–20). Similarly, other types of behaviors that are generally deemed immoral (e.g., loss of social tact, unacceptable physical contact, improper verbal or nonverbal communication) are also interpreted under this affective framework. More specifically, the behaviors' occurrence has been attributed to a diminished internal emotional experience, deficits in socioemotional attention, and decreased autonomic responsiveness (21–24).

Earlier studies indicate that the specific mechanism accounting for impairments in emotionally-based moral behavior is a decreased activation of one's representations of the state and situation of others (19, 25). Individuals with bvFTD, for instance, do not seem to understand or embody the mental and emotional state of others due to diminished ability to simulate the same emotional state in themselves. In the case of sacrificial (or "personal") moral dilemmas, a cognitively healthy individual would engage in harm-averse behavior to avoid the negative mental and emotional states brought on by pro-sacrifice responses. With bvFTD, however, the inability to embody and understand these same states may lead to more utilitarian responses, where individuals are more likely to accept harm as a means to promote the greater good. Thus, this lack of embodiment takes the form of an inability to represent the mental ramifications (i.e., the aversive internal experience of employing harm) brought on by adopting pro-sacrifice responses.

However, these findings are puzzling both on a conceptual and methodological level. First, utilitarian decisions are thought to reflect care and concern for the good of all sentient beings (26). Indeed, utilitarianism has been coined the "greatest happiness principle," holding that actions are "right" to the extent that they promote happiness for the greatest number of people. Yet, a growing body of research has begun to link these very same 'utilitarian' judgments to antisocial traits like psychopathy and reduced empathic concern (22–24, 27). Hence the connotation of "immorality" associated with utilitarian choices in discussion of persons with bvFTD stands in sharp antithesis to this tenet (i.e., greatest happiness principle). In reviewing the literature on moral cognition, one can see how studies heavily rely on employing moral dilemmas that exclusively measure the instrumental harm tendencies of utilitarianism (i.e., the negative dimension). This might contribute to the characterization of persons with bvFTD as immoral. Impartial and altruistic tendencies (i.e., the positive dimension), in turn, often fall outside of the empirical scope of these studies (8).

Additionally, contemporary studies of moral cognition in bvFTD have tended to frame their understanding of moral reasoning by studying moral dilemmas in a way that generates quantitative outputs, i.e., proportions of utilitarian choices. Such an approach, while arguably permitting more objective understandings of moral cognition, disregards the rich information inherent in associated reasoning and psychological processes (e.g., emotional and cognitive elicitation) that subtend moral choices. In addition, studies rarely collect insights into values and perceptions of rules that could assist in contextualizing morality. This study was designed to bridge these methodological and conceptual gaps by examining moral reasoning qualitatively in healthy older individuals and persons with bvFTD. As such, we examined the psychological processes in moral reasoning through a phenomenological lens, and qualitatively describe morality through the eyes of the individual.

2. Materials and methods

2.1. Study design

This study used a mixed-method design, collecting quantitative (e.g., Mini-Mental State Examination) and qualitative data. The qualitative analysis included both pre-specified (deductive) and emergent (inductive) research questions (28, 29). On the one hand, an inductive design was employed so that participants' responses to moral dilemmas could help generate new, emerging theoretical concepts and patterns (30). On the other hand, deductive approaches served to test theories derived from moral cognition models, and more specifically, to examine the presence of emotion elicitation and prosocial sentiments during moral reasoning.

2.2. Participants

All research participants were recruited at the Memory and Aging Center in the Department of Neurology, UCSF. We utilized purposeful sampling whereby participants were selected explicitly because of an existing bvFTD diagnosis ($N=7$), i.e., met the clinical diagnostic criteria for probable bvFTD (4). For comparison and interpretation of the study results, we recruited healthy controls ($N=7$), consisting of participants without any type of dementia diagnosis. The healthy control sample was drawn from community-dwelling older adults enrolled in a longitudinal study of healthy brain aging at UCSF. Participants in this cohort were verified as neurologically normal following a multidisciplinary assessment including (i) a neurological examination, (ii) in-person neuropsychological testing, and (iii) and an informant interview. A group of multidisciplinary professionals, including neurologists, neuropsychologists, and nurses established individual diagnoses in both the bvFTD and healthy control groups employing neuroimaging, neurological, neuropsychological, and behavioral assessments.

The Committee on Human Research at UCSF approved this study. Before testing, all participants signed informed consent forms, confirming voluntary research participation, and gave permission to use the collected data.

2.3. Moral reasoning task

Participants underwent a semi-structured interview with an embedded moral reasoning task consisting of seven moral dilemmas (see Supplementary Tables S1, S2). Three moral categories were tested, accounting for both positive and negative dimensions of utilitarianism.

2.3.1. Categories falling under the Positive Dimension of Utilitarianism

1. Special obligations dilemmas are composed of three items concerning choices that assess one's attitude toward favoring close others (e.g., family members, friends) at the cost of the greatest expected welfare. An example would be parental choices that prioritize one's own child's well-being over the well-being of other children. Here, utilitarian judgments reflect a disregard for tight social bonds in consideration of the greater good.
2. Agent-centered permissions dilemmas are composed of two items reflecting choices that assess one's attitude toward improving others' welfare at the cost of one's own interests. An example would be whether to donate or keep the money for one's personal use. In this case, the utilitarian choice disregards self-interest for the greater good.

2.3.2. Category falling under the Negative Dimension of Utilitarianism

1. Personal rights dilemmas are composed of two items concerning choices that substantially affect the interests of other people, and in which the best overall outcome could only be produced by violating an individual's rights. For instance, whether to push one person into the path of a runaway trolley that would otherwise kill five people. Here, the utilitarian choice is to sacrifice the individual, so that the greatest welfare is produced.

Additionally, we collected quantitative performance metrics (Likert scale 1–4, definitely/probably, yes/no), with lower scores reflecting higher utilitarian reasoning (max = 28). Additional quantitative scores were calculated for the three moral categories tested: special obligations (SO, max = 12), agent-centered permissions (AP, max = 8) personal rights (PR, max = 8).

2.4. Procedure

2.4.1. Semi-structured interview

A semi-structured interview guide was developed to allow participants to describe their emotions, perceptions, and values as well as their underlying reasoning behind their responses to moral dilemmas (see Supplementary Tables S1, S2). The interview was divided into two main sections: (a) seven moral dilemmas with the option to respond in a utilitarian or non-utilitarian manner on a scale of 1–4 (probably/definitely – yes/no), Two follow-up questions exploring underlying reasoning ("Could you please explain in 2 to 3 sentences why you chose this option?") and emotions involved in each moral decision ("How did you feel when responding to the dilemma?") and (b) Questions contextualizing morality. Participants were asked to provide a wider and deeper understanding of their emotional and cognitive processing by characterizing their experience during moral reasoning. This section of the interview incorporated probe questions about values, rule compliance, and moral flexibility (e.g., Which is the most important value you try to live by?).

2.4.2. Interviewer and interview procedure

The same interviewer (RA) performed all the interviews. Training for the interviews included work with a medical anthropologist (ABS) and sociologist (TH), reading qualitative interviewing technique books (30) and conducting five pilot interviews, followed by minor refinements to the interview guide based on participants' feedback. The interviewer had psychological training with extensive experience working with this older age group. Interviews with the participants were scheduled after obtaining consent and permission to record.

Each interview lasted approximately 40 min and was conducted online, via video conferencing software. It began with a presentation of the general scope of the study, which was portrayed as an invitation to discuss the moral dilemmas. Participants were instructed to provide their initial responses and the interviewer emphasized that there were no expected right and wrong answers. Participants could withdraw from the study at any time.

2.4.3. Qualitative data analysis

Recorded interviews were sent for transcription. Each interview was then reviewed in its entirety against the verbatim transcription, with edits (e.g., corrections and additions) made where necessary. All transcriptions were deidentified. Each transcribed interview received multiple readings to obtain an understanding of each participant's responses. Deductive codes were established according to the purpose of our study (e.g., emotion elicitation), but the codebook allowed for the identification of additional, inductive codes to note concepts that emerged during data review. Lower-order themes (e.g., joy) were used to form the broader scope of higher-order themes (e.g., positive emotion). In an iterative process, themes were refined and checked against the transcripts. Cross-evaluation of the themes was conducted with the consultation of the research team. Analysis was performed via ATLAS.ti software (30, 31).

2.4.4. Rigor

To improve the rigor of the qualitative data analysis process, several validation methods were employed. This included, first, the documentation of the analysis procedure (e.g., codebooks and emerging themes described in detail). Second, regular research team meetings were held during the data collection and analysis process, to provide ongoing transparency and cross-validation of themes. Third, to reduce researcher subjectivity bias, we used the technique of triangulation. Five investigators coded the data independently and subsequently compared and discussed the codes until a consensus was reached. Lastly, divergences in theme categorization were discussed until a consensus was established (32).

3. Results

3.1. Participants' characteristics

The participant sample ($N = 14$) was predominantly white (79%) and consisted of individuals ranging from 52 to 87 years old (M = 68.4 years, SD = 10.4). Participants' general cognitive capacity, functional capacity, and mood were evaluated with a screening battery consisting of the Mini-Mental State Examination (MMSE), the Clinical Dementia Rating (CDR), and the Geriatric Depression Scale (GDS) respectively (see Table 1). For the bvFTD group, we used the CDR plus Behavior and Language domains from the NACC FTLD Module (CDR plus NACC FTLD) as a proxy of disease severity. The measure is an extension of the standard CDR and includes two additional domains that are predominantly affected in FTD: behavior and language. Each patient's CDR plus NACC FTLD global score was calculated based on the scoring rules by Miyagawa and colleagues (32).

Persons with bvFTD's general performance revealed mild impairment in overall cognitive functioning (MMSE; M = 24.5, SD = 3.5), while the average CDR plus NACC FTLD total score was 1.4, indicating that this sample represented the earliest stages of disease progression, at a "mild dementia" level. Scores on GDS suggested significantly more depressive symptoms in the bvFTD group (M = 9.7, SD = 7) than in the healthy controls (M = 2.7, SD = 2.1), though on average the group was below the screening threshold for mild depression on this measure (i.e., scores above 13).

TABLE 1 Participant's general characteristics.

Variables	bvFTD (n=7)	HC (n=7)
Demographics		
Age	63.1 (6.9)	73.7 (9.9)
Education	16.4 (2.9)	17.7 (1.8)
Gender		
Male/Female	4/3	4/3
General functioning		
Mini-mental state examination	24.5 (3.5)	29.3 (0.5)
Clinical Dementia Rating plus NACC FTLD		
Box score	7.2 (3.4)	0 (0)
Global score	1.4 (0.6)	0 (0)
Geriatric depression scale	9.7 (7)	2.7 (2.1)
Moral reasoning		
Special obligations	7.6 (1.5)	7.6 (2.6)
Personal rights	4.3 (1.7)	4.9 (1.7)
Agent-centered permissions	3.3 (1)	3.3 (0.5)
Overall utilitarian	15.1 (2.4)	15.7 (3.6)

Values represent mean (SD), except gender which represents frequency.

In terms of moral reasoning, the healthy control (M = 15.7, SD = 3.6) and the bvFTD (M = 15.1, SD = 2.4) groups' average overall utilitarian scores reflected diverse responses that encompassed both utilitarian and non-utilitarian choices, as both groups scored in the middle range of utilitarian performance. Characteristically, both groups chose more utilitarian responses in the agent-centered permissions moral category, followed by the personal rights and special obligations moral category (see Table 1). In qualitative data analysis, 238 primary codes were extracted and classified as broader themes of emotion elicitation, cognitive elicitation, and contextualization of morality.

3.2. Theme 1: emotion elicitation during moral reasoning

Participants' reasoning across moral dilemmas involved emotion elicitation, revealed by answers to the question following each dilemma: "How did you feel when responding to this dilemma?." Healthy controls and persons with bvFTD were characterized by a different emotional palette, revealing a between-group distinction on the valence of the emotion they reported experiencing while considering their moral responses. Positive emotions, particularly joy were more prevalent when persons with bvFTD contemplated their feelings associated with their reasoning (82% of all joy responses), as opposed to healthy controls, who tended to express more negative emotions, particularly guilt (79% of all guilt responses; see Table 2).

TABLE 2 Across-group comparisons of emotion elicitation during moral reasoning.

Emotion elicitation	bvFTD (*n*=7)		HC (*n*=7)	
	Individuals No (identity)	# of occurrences	Individuals No (identity)	# of occurrences
Negative emotions				
Frustration	2 (1/7)	4 (36%)	4 (3/4/6/7)	7 (64%)
Sadness	4 (1/5/6/7)	12 (44%)	6 (2/3/4/5/6/7)	15 (56%)
Guilt	1 (1)	1 (21%)	3 (2/4/7)	5 (79%)
Positive emotions				
Relief	1 (5)	1 (56%)	1 (5)	1 (44%)
Joy	4 (1/2/6/7)	10 (82%)	2 (6/7)	2 (18%)
Pride	3 (2/5/7)	4 (37%)	4 (1/2/4/5)	7 (63%)

Absolute frequencies and proportions after normalization.

Although emotional blunting constitutes a core diagnostic feature of bvFTD, participants still described feeling an emotional response when the interviewer probed for a description, and some described their response with some emphasis. For instance, when asked whether they would refuse to take money for personal use, to instead donate it to cure HIV, one participant responded:

> *I feel good that I was able to say I do not need the money. I feel good that somebody else is going to do good because I did not take their money. [bvFTD No. 7].*

The same participant – in addition to reflecting on the joy associated with donating money for a good cause – emphasized the positive felt experience of responding in a utilitarian way. They added:

> *It's a good feeling inside. [bvFTD No. 7].*

Along with their felt emotional experience, 5 persons with bvFTD also mentioned the ease associated with the decision-making process. One participant, when reasoning about whether they would undergo repeated blood donations to keep a person from dying, stated:

> *It's, you know, fantastic to save a life. You know and it means nothing to me. I felt great, it was no brainer. [bvFTD No. 2].*

Some participants with bvFTD also expressed a sense of empowerment associated with their utilitarian decisions, as though a sense of self-approval was associated with making the decision, which added to the positive feelings they described. One participant's utilitarian decision (specifically, to personally approve the removal of one's man kidney in order to help a vitamin-deficient family to survive) was accompanied by:

> *I guess I feel empowered to do that. I would feel like, what would be another word? You want one of those feelings words, right? [Interviewer: What do you mean by feeling empowered?] I guess I feel I have the right to make that decision if I had to make that decision. [bvFTD No. 5].*

This more positively valenced emotional outlook stood in antithesis to the healthy controls, more of whom expressed negative emotions associated with their moral responses, sometimes very strongly. Reflecting on their feelings associated with the dilemma of whether they would sacrifice their nephew to save 6 people, healthy-control participants replied:

> *Yes, well there's sadness. There's sadness. There's some frustration because the kid cannot swim. But it's primarily sadness for the fact again of the loss of life. [HC No. 6].*
>
> *Horrified. Absolutely completely horrified. Devastated. Horrified. Super upset. Just horror-stricken. Sort of in shock. Probably would not even feel how truly sad I felt for a while until the shock wore off. It was just absolutely horrible. [HC No. 7].*

When responding to the same dilemma (i.e., sacrificing the nephew for the six strangers) some healthy controls were even able to tap into the bodily dimension of the expressed emotion, articulating visceral sensations, an occurrence that did not explicitly occur in the bvFTD sample. As one participant put it:

> *My stomach is turning inside out. That's my feelings. [HC No. 5].*

In the healthy control group, the majority of participants expressed sadness, frustration, and pride, with three participants expressing guilt, two expressing joy, and one relief as the core emotions accompanying their moral reasoning. Those emotions were often expressed in a more complex, layered manner. Also, self-conscious emotions including guilt and pride were more often expressed by individuals in the healthy control group, while simpler emotions such as joy were less common in this group than in the individuals with bvFTD. This suggests the availability of a more nuanced emotional palette when reflecting on their feelings about their moral responses. Following their response that they would not endure repeated blood donations to prevent a person from dying, one participant described their feelings as follows:

> *Sad and worried about him. And, you know, sort of regretful that I did not feel like I could help him. I feel like a desire to help him and a wish, or her, whoever it is, person. Is it a man? Anyway, whomever it is. A desire to help. And I would feel regretful that I wasn't choosing*

> *to do it. I would feel a loss. A real sadness and regret. Very sad. [HC No. 7].*

3.3. Theme 2: cognitive elicitation during moral reasoning

When contrasting moral reasoning across persons with bvFTD and healthy controls, participants' responses involved a variety of cognitive processes, which we included as an additional core theme of cognitive elicitation (see Table 3). The types of cognitive responses observed appeared to reflect four major categories, two of which reflected positive dimensions (i.e., projection/imagination and insight), and two of which reflected weaknesses in cognitive processing (i.e., cognitive imprecision and poor elaboration). Each of these cognitive elicitation categories differed between the bvFTD and healthy individuals, with responses reflecting projection (82%) and insight (91%) being more common in healthy controls, and responses reflecting cognitive imprecision (67%) and poor elaboration (91%) being more common in persons with bvFTD.

Four individuals in the bvFTD group engaged in projection or imagination, compared to all seven of the healthy controls, and this cognitive process appeared much less frequently in their responses. Specifically, we defined the cognitive process of projection/imagination as the ability to put oneself into the moral scenario as if one was the main character of the dilemma, more richly taking the perspective of the protagonist or recipient by imagining one is giving or experiencing the harms or benefits personally. Given that this cognitive process was seen in 100% of healthy controls, this seems to be an important element of healthy moral reasoning, perhaps providing a deeper experience of the dilemma through the felt experience of its ramifications.

For example, concerning the dilemma of whether they would give the medicine to their own child rather than another child, one participant with bvFTD showed projection in the following manner:

> *Because I would like to help people, but I have [unintelligible thoughts] children and I want to be with them. And if it means I'm going to die, I mean … [bvFTD No. 6].*
>
> *I feel that my … I'm about to. I feel that if I chose to sacrifice six people for the life of one, even though I have a relation to that one, is a selfish thing to do. When in fact, those six people have other people that feel for them. So, why take my feelings out of the equation, it's better to save more than less. [bvFTD No. 7].*

Healthy controls often embedded such cognitive processes in their moral responses. In response to the same dilemma, one participant responded:

> *One of my rules as a parent is to protect my child. So, if there's a choice between my child and another child, I'm always going to pick my child. [HC No. 1].*

In another dilemma, where the participant was asked whether they would save their nephew instead of six strangers, they answered:

> *I mean, I kind of put myself in the place of, like, thinking of it as nephew or even your son, like, also, you know, it's a family member, you know, you'd have to explain it to their family at some point, so – but you would hope that, like, you know, there's six other people that lived, you know, that went on to do their lives. So, yeah, again, it's hard to do it purely on math, but, you know, it's not that strangers have any less value than my nephew. [HC No. 2].*

The degree of insight and awareness underlying the participant's moral responses also differed between the two groups, though this cognitive tendency was seen in fewer participant responses overall (4/14). Only one person with bvFTD expressed metacognitive insight in only one response, while 3 of the healthy controls showed insight on 10 occasions. Healthy controls seemed able to track more accurately their thought and emotional processes accompanying their feelings and reasoning towards moral dilemmas. On the footbridge dilemma, a participant contemplated the reasons for opting to not push a man off the bridge to save the five workers in this way:

> *It's a tough choice. But I went with the first reaction, to the first emotional reaction that I had. I went with that. Because I could sit here for two or three minutes and change my mind back and forth probably. But I think the real true response came immediately for me. And that was I'm not going to push the guy off the footbridge. [HC No.1].*

Metacognitive insight was also observed in the bodily realm. In the same dilemma, a participant expressed insight into how their mind and body could function as a moral compass for their moral judgments:

> *Because – as I said because it would be – I would find it very hard to take affirmative action to do something which causes someone to die. It's much easier – and I think – as I said, I think I would*

TABLE 3 Across-group comparisons of cognitive elicitation during moral reasoning.

Cognitive elicitation	bvFTD (*n*=7)		HC (*n*=7)	
	Individuals No (identity)	# of occurrences	Individuals No (identity)	# of occurrences
Projection/Imagination	4 (1/5/6/7)	7 (18%)	7 (1/2/3/4/5/6/7)	32 (82%)
Insight	1 (7)	1 (9%)	3 (1/2/5)	10 (91%)
Cognitive imprecision	6 (1/2/3/4/6/7)	14 (67%)	1 (4)	7 (33%)
Poor elaboration	5 (1/2/3/4/6)	30 (91%)	2 (6/7)	3 (9%)

Absolute frequencies and proportions after normalization.

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> *be paralyzed, probably, out of, you know, the god awfulness of the situation to do anything. And there's just – I just do not think that I could bring myself to go through – to do that. I do not know if it's a moral dilemma. I think it's more just my mind and body would probably stop me from doing anything – anything, you know, at all. [HC No. 5].*

Another category of cognitive elicitation observed in participant's responses was termed "cognitive imprecision," to describe participants' tendency to reconstruct the premise of the dilemma and fail to approach the dilemma according to its internal logic, showing an underlying resistance to the scenario's structure, and breaking the contractual rules of the posed dilemma. In our sample, the large majority of persons with bvFTD (6 of 7) showed this tendency, compared to only 1 of the healthy controls. Alternating the structure of dilemmas seemed to facilitate decisions and make it easier for participants to respond when the dilemma posed a difficult conflict. For instance, when asked to answer the dilemma that involved pushing a stranger onto the tracks to save five workers, some participants resisted the structure of the dilemma requiring the death of the five workers:

> *Well, even though the way it's worded sounds pretty positive, the death of the five workers is not absolutely known. Maybe they'll look up right away and jump. You know, there are possibilities there, but the – the large person that's right beside me, his – his life is known, and I'd be, you know, sort of the bird in the hand versus the bird in the bush. [bvFTD No.1].*
>
> *I just think it's wrong to do something bad to make something good happen. I think it would be better, for example, for me to jump out there to save all of them. [bvFTD No. 4].*

Similarly, another participant, responding to the dilemma about whether they would give a medicine to their own child or another child, when the medicine was explicitly described as ineffective if the dose was shared, remarked:

> *Well, I'd probably try to split it. [bvFTD No.3].*

An additional category of cognitive elicitation observed in our sample was termed poor elaboration, which was operationalized as providing an inadequate explanation underlying participants' reasoning despite maximal probing by the interviewer. Persons with bvFTD more often failed to elaborate on their responses (making 91% of poor elaborations, with 5 of the 7 bvFTD participants providing 30 poor elaborations, compared to 3 in the healthy controls). This response style was observed to reflect difficulty providing more in-depth, sophisticated reasoning about their moral choices. For example, when asked to contemplate their feelings about why they would agree to give repeated blood donations to save a person from dying, a participant answered:

> *It's always good to help people, but you know. [bvFTD No.6].*

By the same token, another participant when presented with the same dilemma, expressed their feelings with the following short answer:

> *Well, it's a conflict, again. [bvFTD No.3].*

3.4. Theme 3: contextualization of moral reasoning

One of the goals of this study was to also contextualize morality in terms of participants' perception of values and rule compliance. For this reason, after responding to all of the moral dilemmas, participants were asked to openly reflect on the values that they try to live by and their perceptions about rule-breaking. We additionally coded whether participants adhere to philosophical and religious standards, including a frame of reference from which their values seem to emanate.

When asked about the most important value they try to live by, we found that some participants associated their moral reasoning with values reflecting suggesting the presence of a prosocial compass – fairness, kindness, honesty, and the greater good. This tendency spanned both study groups fairly evenly, though more statements of "kindness" as a value were seen in persons with bvFTD, while healthy controls were slightly more likely to espouse the value of fairness (see Table 4). Both groups were equally likely to endorse the greater good as a guiding value. For example, persons with bvFTD responded:

> *Try to be as helpful as I can. [bvFTD No.3].*
>
> *I guess to love the person you are talking to at the time. [bvFTD No.4].*
>
> *To give love and receive love from other people. [bvFTD No.5].*

The values of healthy controls, in turn, focused more on honesty and fairness. Asked to express which values they live by, participants gave the following responses:

> *Honesty is one of them. Being true to myself is another one. [HC No1].*
>
> *I think I try to be I want to be fair and treat everyone equally. That's the most important value to me is that everybody – I do not know if you call that a value in the different types of values, but I guess equality, equal. [HC No2].*
>
> *Do no harm. The golden rule. I mean, however – every different society has a different way of expressing it. But I just think it's do unto others as they would – you would have them do unto you – or do not do to others what you would not like to have them do to you. Yeah. I mean that – the golden rule is – I would not say it's at the front of my consciousness all the time. But I absolutely believe in it. [HC No5].*

Interestingly, while reflecting on their values, more of the persons with bvFTD seemed to base their prosocial compass on philosophical and religious standards than healthy controls (see Table 4). This observation highlighted an external frame of reference around which persons with bvFTD may have constellated their moral beliefs:

> *Well, I think the most important value is I tried to depend on the Lord to help me with things. Sometimes I forget, but real closely related to that is I try to do unto others as – as I think I would feel*

TABLE 4 Across-group comparisons of participants' perception of values and rule.

Contextualization of moral reasoning	bvFTD (*n*=7)		HC (*n*=7)	
	Individuals No (identity)	# of occurrences	Individuals No (identity)	# of occurrences
Prosocial values				
Fairness	1	1 (29%)	3 (1/2/5)	3 (71%)
Kindness	3 (3/4/5)	4 (78%)	1 (7)	1 (22%)
Honesty	1 (7)	1 (38%)	2 (1/2)	2 (62%)
Greater good	2 (2/6)	2 (53%)	2 (3/4)	2 (47%)
Rule perception				
Rule breaking	2 (4/5)	3 (30%)	6 (2/3/4/5/6/7)	6 (70%)
Rule compliance	5 (1/2/3/6/7)	5 (82%)	1 (1)	1 (18%)
Philosophical and religion standards				
Adherence	2 (1/2)	3 (72%)	1 (5)	1 (28%)

Absolute frequencies and proportions after normalization.

> *good if they were doing unto me. That's not necessarily as – as they would treat me but as I would like to have them treat me. But most of them can be related to God. Is that too nebulous? [bvFTD No1].*
>
> *I live by a code, you know, it's the marine code. It's great! it makes me feel alive. Serve and protect, the people of the world [bvFTD No2].*

In terms of rule compliance, a sharp differentiation between healthy controls and persons with bvFTD prevailed. Persons with bvFTD were more rule compliant in their responses, emphasizing the expression of moral facts when dealing with breaking the rules. For example, when asked whether they would break a rule, bvFTD persons were more likely to give broad negations that were lacking in situational nuance, responding:

> *I spent a lot of years as a principal and a teacher and, no, I guess the answer is no. I just would not do it. I would not break a rule in general. [bvFTD No1].*
>
> *No, I would not. no, I would not. Because it's the wrong thing to do. It's totally wrong. [bvFTD No2].*
>
> *I do not think you should. [bvFTD No 3].*
>
> *No. It's not good to break rules. [bvFTD No7].*

On the contrary, healthy controls seemed more willing to break a rule to achieve a goal, reflecting moral flexibility and a tendency to contextualize their behavior. As three participants stated:

> *Yeah. So, for example, in a lot of times in, like, building processes and things that we are doing now, and a lot of the building municipalities just take forever, and there's a lot of red tape and a lot of bureaucracy, and I will not break a rule, per se, but I'll omit steps to get to it, again, if I know the goal is a good one and we had discussions, it's not my own personal goal, yeah, I would do break a rule. I'm not a rule breaker just to do it. If it's around safety for the most part I would not, but, yeah, I would do it in instances. [HC No2].*
>
> *If the goal is to help someone, that's what I was thinking. Yes. Oh, my. But in another situation, if the goal is my goal, you know, I want to win; therefore, I'm going to break a rule, no, I would not do it. But if it's to help someone, yeah, I would break the rule. [HC No 3].*
>
> *Well, there's really no need, no reason not to, and as I get older and as you get older, even in good health you start to contemplate your death, and there's too much that has to happen in the world for me to be satisfied, and I do not like the direction we are going away from what I consider to be necessary. My goals are being more and more ignored and made improbable. And to achieve that goal I would break a law. If I would not get caught. [HC No4].*

4. Discussion

This research is one of the few studies to directly reveal the voices of persons with bvFTD by giving them the opportunity to voice their reasoning, feelings, and values when responding to moral dilemmas. In previous studies, bvFTD has been associated with impairment in socioemotional function, which has been presumed to be the primary reason they are more likely to make utilitarian choices in sacrificial moral dilemmas in which they are willing to endorse harm in service of the greater good. However, our study captured a more holistic understanding of their thought processes by examining moral reasoning qualitatively, and by using a more nuanced measure of utilitarianism. This revealed that some of their utilitarian responses could be characterized as prosocial choices where they sacrificed their own self-interest to support the greater good. Persons with bvFTD were more likely than has previously been reported to endorse prosocial values such as kindness and service to the greater good as important personal values contextualizing their moral choices, and they exhibited significant positive emotionality around even difficult moral decisions.

Our research identified three core themes. The first represents participants' responses to the question, "How did you feel when responding to this moral dilemma?" and thus captures the emerging emotions during the moral reasoning process. In line with previous literature (7, 33), in our study responses of persons with bvFTD were characterized by positive emotionality (e.g., *"I felt great."*), whereas healthy controls were more likely to tag their moral reflections with negative emotions (e.g., *"I felt sad and worried."*). Disrupted experience of emotion, particularly in relation to self-conscious moral emotions such as guilt (12, 17, 34), might account for the different emotional responses between persons with bvFTD and healthy controls. In previous research, this diminishment of self-conscious emotional responses in bvFTD has been predominantly understood in a negative light because it may lead to inappropriate behavior that can be detrimental to their social milieu. In the context of moral reasoning, this lack of self-conscious emotion takes the form of exhibiting not only a lack of guilt but also more positive emotionality when endorsing decisions where harm must be inflicted to ensure the overall welfare of a group or community. Interestingly, we found that in bvFTD prosacrifice and altruistic/impartial choices were accompanied by a more undiluted experience of positive emotion, which participants associated with "doing the right thing." Thus, our study suggests that decreased sensitivity to guilt may be the cornerstone of the overall capacity to be impartially concerned for the greater good (i.e., whether or not some harm infliction is required to achieve overall welfare).

The suggestion that impaired socioemotional function may not hinder, but rather facilitate moral decision-making, has previously been introduced (16, 35). Prinz, for instance, argues philosophically that in certain situations, emotional processes such as affective empathy may actually pose a risk to moral judgment, suggesting that empathy can even have a detrimental impact on the ability to adopt moral judgments that promote overall welfare over the interests of close others. While much attention has been devoted to highlighting the negative aspects of utilitarianism, specifically the inclination to endorse instrumental harm in the context of bvFTD, our findings bring forth a different perspective. Significantly, our research illustrates how impartial tendencies can potentially be attributed to reduced socioemotional responsiveness, as indicated by diminished guilt and a potential lack of affective empathy. This shifts the focus from solely emphasizing negative aspects of loss of empathy to recognizing the underlying mechanisms that contribute to these tendencies and highlighting the retention of prosocial inclinations even in the context of empathy loss.

The second emergent theme, in which participants' cognitive thought processes during moral reasoning were clarified, further elucidates the complex mechanisms embedded in moral reasoning. Our analysis of the responses of persons with bvFTD revealed a quality that we termed "cognitive imprecision." In the context of moral reasoning, this appeared when participants resisted the given structure of the dilemmas, instead circumventing difficult decisions by changing the rules or resisting what the interviewer was asking them to decide (e.g., "*I think it would be better … for me to jump out there to save all of them*"). This observation is in line with previous literature, where this cognitive approach has previously been described in the context of bvFTD as *denkfaulheit* or "mental laziness," (36) operationalized as an inappropriate cognitive shallowness characterized by a lack of depth and drive. In the participants with bvFTD in our study, this imprecision was compounded by poor elaboration, where participants often were unable to clarify or explain their moral reasoning when directly asked. By comparison, healthy controls demonstrated considerably greater cognitive precision and tolerance of nuance in their responses and were able to elaborate their responses more richly. Of note, future studies conjoining qualitative and quantitative measures of metacognition could further shed light on how metacognitive abilities influence moral reasoning in bvFTD and contribute to our overall comprehension of the cognitive processes involved in moral decision-making.

Our data illustrate how moral reasoning engages an interplay between psychological processes, in which emotional and cognitive disruption correlate, and may have important neural interdependencies. Neuroimaging studies of moral reasoning in persons with bvFTD have revealed that a primary source of divergence from healthy controls is altered activation of the salience network (SN) (19). This network is focally affected early in the bvFTD disease process and is pathognomonic to the disease, thus the alterations we observed in metacognitive insight, complex thinking, and elaboration in the bvFTD group, are most probably derived from salience network (SN) dysfunction. Chiong and colleagues (2013) showed that salience-driven attention mediated by the SN can act as a gating mechanism that influences the function of other brain networks and their associated cognitive processes (19). In the context of moral reasoning, when healthy individuals detect moral dilemmas as personally salient, the activation of the SN increases the likelihood of default mode network (DMN) engagement. As a result, autobiographical, self-referential, and perspective-taking processes are employed for more comprehensive and complex reasoning (25, 35, 37). Alternatively, when the SN does not alert the individual that a dilemma has personal relevance (either because it does not involve a personal moral component, or because of dysfunction in the SN), the individual is more likely to approach the dilemma in an impartial manner, activating the adaptive executive control (i.e., frontoparietal) network in the brain instead of the DMN. Our observation that 100% of healthy control participants employed imaginative perspective-taking while contemplating the dilemmas, but this was rarer in persons with bvFTD, is likely related to this lack of activation of the DMN that has resulted from altered SN function.

The third theme we identified in our data involved the contextualization of moral reasoning as a part of one's overarching value system. In our sample, both persons with bvFTD and healthy controls espoused a number of prosocial values that guided their actions, including fairness, kindness, honesty, and the greater good. They also showed roughly equivalent adherence to philosophical and religious standards, though this was slightly greater in persons with bvFTD. Importantly, persons with bvFTD did not show antisocial or cold tendencies in their moral reflections when asked to reflect on their values, suggesting their motives were not as self-centered as implied by existing literature (18, 21, 22). However, we additionally observed the preservation of bvFTD participants' perceptions regarding rules, with bvFTD participants providing many more responses centering around rule compliance than controls (e.g., *"rules should not be broken"*). Healthy controls, in turn, exhibited markedly more rule-breaking tendencies and moral flexibility in their responses (e.g., *"to achieve that goal I would break a law"*). Selective degeneration of neural systems important for mental flexibility could be associated with this increased rule adherence in the participants with bvFTD, and this finding may reflect some mental rigidity (38). Of note, our participants with bvFTD were more likely to actually break the rules of the dilemmas and to resist the interview structure in a cognitively imprecise manner, despite their explicit support of rule compliance when asked to describe their values.

Using a moral reasoning task that accounts for the two-dimensional nature of utilitarianism, along with probing questions regarding values, appeared to be instrumental to understanding moral cognition in bvFTD. For example, bvFTD and HC groups alike responded in a utilitarian way to some of the dilemmas, and this occurred across both personal rights dilemmas (negative dimension) and agent-centered permission and special obligations dilemmas (positive dimension). Importantly, our study challenges existing theories about moral reasoning in bvFTD that recognize utilitarian judgments as stemming from a lack of prosociality (17, 20, 21). Because their utilitarian tendencies span both positive and negative dimensions, and their endorsement of both prosocial values and positive emotions around doing what they believed was right, bvFTD participants' choice to employ harm for the greater good did not appear to reflect a lack of impartial concern. Our findings echo other studies that identified the value of incorporating both positive and negative dimensions of utilitarianism (8, 37).

By leveraging a phenomenological approach, we demonstrate how emotional and cognitive processing interact in the service of moral reasoning. Based on our findings, we propose that knowledge of values and rules is preserved in bvFTD, and to some extent is conveyed in participants' responses to moral dilemmas. One could assume that persons with bvFTD responded in a way that reflected the retention of a moral compass encapsulating both the dimensions of discipline (rule compliance) and prosociality (kindness). It remains of great interest to explore whether, and how, these findings vary across other dementia syndromes, such as Alzheimer's disease syndrome and semantic variant primary progressive aphasia. Finally, despite not being the focus of our study, significant potential scope exists for examining additional processes involved in moral reasoning, such as empathic concern (39), faith (40), and sociocultural background.

Exploring the practical implications of these findings within the context of dementia care, particularly in therapeutics, is an important area for consideration. One notable application lies in the realm of enriching psychosocial interventions between individuals with bvFTD and those in their social environment, wherein cultivating symbolic meaning for careers assumes a central role (41). This enrichment is effectively operationalized through shared activities that serve as a foundation for fostering positive relationship gains. Our research might provide an example of ways to enrich communication by actively engaging persons with dementia to talk about their beliefs and values, and surfacing the prosocial views of individuals with bvFTD. Caregivers, in particular, stand to benefit significantly from this approach by reconnecting with the care recipients' fundamental values, such as kindness, in a deeply meaningful manner. As a result, their caregiving experience may be profoundly reframed as more purposeful and fulfilling.

Our study has several limitations. Foremost, our study examines the responses of a small and somewhat homogenous sample. Participants' responses are grounded on cultural norms and ways of life in the United States, and more specifically the West Coast. Thus, different perspectives and views could emerge from other cultural and research contexts. Expanding the sample size and broadening cultural variation would further elucidate the themes noted in this study and perhaps reveal additional factors. Additionally, our sample represents the earliest stages of bvFTD disease progression, whereas participants at a later stage might show different results. Lastly, this study relies on moral vignettes to measure moral reasoning instead of direct observations of real-life behavior. The dilemmas represent the participants' ideas about hypothetical behaviors rather than observed occurrences. Even though we asked participants to report on their moral reasoning and describe their values, our design did not assess moral behavior in real life. Future studies might achieve greater ecological validity by comparing similar dilemmas to real-world moral behavior. Overall, these results more comprehensively reflect the emotional and cognitive experience of persons with bvFTD by centering their voices, and further highlighting the importance of incorporating qualitative approaches in dementia research.

Data availability statement

Individual-level data presented in this article cannot be made available in a public repository because it consists of raw interview data of a sensitive nature and thus is subject to healthcare privacy regulations. Appropriate sharing of group-level or deidentified aspects of individual-level data will be possible upon request to https://memory.ucsf.edu.

Ethics statement

The Committee on Human Research at UCSF approved this study. Before testing, all participants signed informed consent forms, confirming voluntary research participation, and gave permission to use the collected data.

Author contributions

RA: conceptualization, writing–original draft preparation, resources, methodology, and writing–review and editing. TH and AS: methodology, investigation, resources, and writing–review and editing. KF and PC: methodology and writing–review and editing. BM and JK: resources and writing review and editing. WC: investigation, resources, and writing–review and editing. KR: conceptualization, resources, supervision, project administration, and writing–review and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2023.1197213/full#supplementary-material

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Authenticity and brain health: a values-based perspective and cultural education approach

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This perspective paper discusses the concept of authenticity in relation to brain health and neurodegenerative diseases. We define authenticity as being true to oneself and consider it a social value of relevance to neuroscientists, clinicians, and caregivers. From a biological perspective, behaviors that can be interpreted as expressions of authenticity are produced by distributed brain networks. By understanding it as a dynamic process, we argue that harnessing authenticity across the lifespan can be protective by promoting resilience. We discuss the idea of authentic aging, which appreciates the complexity of human life within the world and can enhance positive views of later life. Authenticity is additionally applicable to caring for people with neurodegenerative diseases, both when understanding the behavior of people with dementia and the response of caregivers. Tailoring care to an individual's personality and strengths may improve their brain health. Finally, we describe an interdisciplinary learning event, themed around masks, designed to engage participants in identifying authenticity in their own work. For scientists, care professionals, and caregivers, reflecting upon authenticity can aid understanding of the person with dementia and therefore improve care.

KEYWORDS

authenticity, resilience, brain health, dementia, values

1. Introduction

Authenticity is a value with direct relevance to brain health. It is defined as the consistency between an entity's internal values and its external expressions or, simply, being true to oneself (1, 2). Brain health is "a life-long, multidimensional, dynamic state consisting of cognitive, emotional, and motor domains underpinned by physiological processes" (3). In neurodegenerative diseases, where brain health is compromised, the whole person is affected. It is therefore relevant to understand a disease's impact on their humanity through a values-based perspective.

There has been little work to date on the application of authenticity to brain health, so we aim to summarize key concepts in this area and highlight the relevance of authenticity to both neurobiology and psychology. We then outline an illustrative educational event designed to stimulate reflection on the practical application of authenticity in brain health.

2. Neuroscience of authenticity

2.1. Authenticity as a social value

Authenticity is primarily a social value. Inherent in its conceptualization are how a person interacts with others, and how authentic others consider their behavior to be (4). In a recent review on authenticity, Dammann et al. summarized the concept in four major categories (4C's): *consistency, conformity, connection, and continuity* (5). The categories are interconnected and relate authenticity to human behavior and interpersonal relationships. When a person is authentic, they naturally exhibit consistency in their behavior. They are true to themselves and consistently act in ways that reflect their genuine beliefs, values, and inner self. Authenticity and conformity can sometimes conflict with each other. In situations where conformity is valued, individuals may feel compelled to suppress their authentic selves to fit in or be accepted by the group. However, maintaining authenticity while navigating social norms is essential for a healthy sense of self. Connection requires genuine communication, empathy, and vulnerability. Authenticity plays a vital role in establishing meaningful interpersonal relationships (6).

Authentic individuals tend to exhibit continuity in their lives by staying true to their core values and beliefs. They navigate changes and challenges while remaining grounded in their authentic selves. In this 4C's model, continuity indicates that authenticity is inherently a non-static value that allows for changes in authenticity over time and places (5). Therefore, we surmise that authenticity is a dynamic process amenable to development. With self-reflection and by discussing important core values with others, we can better understand ourselves and improve our awareness and practice of our own authenticity. To our knowledge this is an area that has not yet been studied but has potential for research with a view to improving resilience.

2.2. Neurobiology of authenticity

To date, most research into authenticity has focused on psychology and individual differences, with little empirical evidence of its localization in the brain, especially in relation to neurodegeneration (7). However, a recent structural magnetic resonance imaging (sMRI) study of 112 healthy young adult volunteers measured trait authenticity using the Authenticity Scale, which contains three sections: self-alienation (awareness of one's physiological states, emotions, and cognitions), authentic living (congruence between one's behavior and one's physiological states, emotions, and cognitions), and accepting external influence (the extent to which one believes they must conform to others' expectations) (7, 8). The investigators found that higher scores on the Authenticity Scale were associated with a larger left precuneus surface area and that lower self-alienation scores (as an indicator of higher authenticity) were associated with smaller volumes of the left amygdala (7). These are key default mode regions for supporting self-awareness (9). The authors also reported that authenticity mediated the relationship between these brain morphological characteristics and self-reported anxiety, suggesting a protective effect of perceived authenticity (how authentic a person feels) (10) on brain health.

2.3. Neurobiology of self-awareness

In the absence of other neurobiological examinations of authenticity, it can be understood through the related concept of self-awareness. As authenticity relies upon the degree of consistency and congruency between the inner self and the projected behavior, it is dependent on self-awareness. Self-awareness is mediated by complex neural circuits that receive both somatic and proprioceptive sensory outputs from the environment (9, 11). It can be divided into two: awareness of the minimal self and of the longitudinal self. The minimal self refers to our physical self in the present moment and includes the current condition of our body, for example our facial features and body position. It also includes the states of our visceral organs and mind and as well as our behavior. Minimal self-awareness is primarily guided by somatic and interoceptive inputs that are represented in brain systems anchored by the somatosensory cortex and insula, respectively. Afferent pathways from the body relay information from the organs and muscles via the laminaI spinothalamocortical tract and vagal afferents to the brainstem, thalamus, and onward to the posterior, mid-, and anterior insula where they are integrated with ongoing contextual details (12). These internal cues color subjective experience and guide decision-making and behavior.

The longitudinal self refers to our continuous existence as a being over time and is primarily built of semantic self-knowledge and autobiographical memories (9). Unlike the minimal self, the longitudinal self is supported by the semantic appraisal network, which has hubs in the anterior temporal lobes and connections to the ventromedial prefrontal cortex, nucleus accumbens, amygdala, and subgenual anterior cingulate cortex, and the default mode network, which includes the ventromedial prefrontal cortex, medial temporal lobes, precuneus, posterior cingulate cortex, and lateral temporoparietal cortex. The semantic appraisal network shows prominent decline in the sematic variant of primary progressive aphasia, a disorder characterized by progressive loss of conceptual knowledge (13, 14). The default mode network is active at rest and during tasks of autobiographic recall and shows selective dysfunction in Alzheimer's disease (9, 11).

The neurobiology of authenticity involves a complex interplay between different brain systems, with the prefrontal cortex playing a central role in self-reflection, self-regulation, and the integration of cognitive and emotional processes (15–18). The neuro-localization of authenticity has been primarily associated with the prefrontal cortex (PFC) and its connections with other brain regions (16). The PFC, particularly the ventromedial prefrontal cortex, as discussed in relation to the longitudinal self, plays a crucial role in social cognition, decision-making, self-representation, and the integration of emotional and cognitive processes. Studies have shown that the ventromedial PFC is involved in self-reflection and self-awareness, which are fundamental aspects of authenticity (15, 16). The ventromedial PFC is also involved in processing and integrating emotional information, which is essential for authentic emotional expression and empathy for others. Therefore, dysfunction in these neural circuits could manifest as impaired self-awareness, or diminished insight, in neurodegenerative syndromes such Alzheimer's disease and frontotemporal dementia (FTD) (15–17).

2.4. Authenticity and resilience

Perceived authenticity, that is how authentic an individual perceives themselves to be, has been associated with mental resilience and has been found to be helpful in recovery from individual and collective trauma in younger adults. In a survey of undergraduate students, Maffly-Kipp et al. assessed the role of perceived authenticity among individuals affected by Hurricane Harvey, which struck Texas and Louisiana in August 2017 (10). The investigators assessed perceived authenticity using the Authenticity Scale (8). The authors found that participants who scored lower on the Authenticity Scale 4 weeks after Hurricane Harvey reported greater levels of stress 9 weeks after the hurricane than individuals with higher scores of perceived authenticity.

Furthermore, authentic living has a positive association with numerous markers of psychological wellbeing such as life satisfaction and self-esteem and a negative association with indicators of psychological distress such as anxiety and depression (5, 19). Goldman and Kernis asked psychology students to respond to questions that measured their authenticity and found strong correlations between authenticity and both self-esteem and a composite measure of subjective well-being (20). The inverse relationship between authenticity and distress may reveal a possible mechanism for enhancing resilience in early and mid-adulthood. It also highlights the applicability of the value of authenticity to lifelong brain health. There is, however, currently a lack of studies on authenticity and wellbeing or resilience in older adults.

3. Application of authenticity to brain health

3.1. Authentic aging and brain health

The relatively new concept of brain health encompasses the bidirectional relationship between the health of the brain and the rest of the body, and the close link between brain health and aging in general (3). The principle of "authentic aging" has been proposed as an alternative to the more biomedical notion of "successful aging" or the potentially loaded "healthy aging" (4). Authentic aging acknowledges the complexity of a human life that is lived within an interconnected world. It allows for growth in later life and accepts that throughout life, including in old age, there are opportunities for increased knowledge and expression of the self (21). Although later life is often considered in relation to its proximity to death, this period can also be a time of wisdom and acceptance (22). If authentic living means being true to oneself and living in accordance with our own values and beliefs, (8) authentic aging encompasses these processes alongside maturity and the richness of life experience. Taking a positive approach to brain aging encourages us to consider the possibility of improving or maintaining brain health by harnessing a person's lifelong strengths when designing person-centered care. Despite a lack of empirical evidence on the overlap between authenticity and brain health, using these conceptual frameworks can aid the understanding of neurogenerative diseases.

3.2. Impairment of self-awareness in neurodegenerative disorders

To live authentically and to be true to ourselves, we first need to know ourselves. Changes in the brain due to aging and neurodegenerative disease can manifest in altered behavior related to reduced self-awareness (23). For some people with Alzheimer's dementia and the people close to them, the loss of autobiographical memories and changes in behavior can feel like losing part of the self (24). If authenticity means being true to oneself and the self is becoming lost, it may seem that people with Alzheimer's dementia can only be authentic to their past self. In addition, in people with dementia who experience depression, low self-esteem is a common symptom (25). Self-esteem is closely linked to self-awareness, with some evidence that increased awareness of the self in people with existing low self-esteem can in fact negatively affect mood (26).

In other types of dementia, such as FTD, reduced inhibition and changes in emotions, behavior, and language can lead to the person expressing themselves in a way they had not done before. Personality change is a central feature of the behavioral variant of FTD, and there is evidence that people with behavioral variant FTD lack insight into their current personality (27). This may reflect a difficulty in updating information about themselves (9). Applying the concept of authenticity can be challenging here, because if the person's new behavior is understood as an expression of their authentic self (i.e., their inner voice without a filter), it may seem inauthentic because it may not reflect how that person has always behaved and seem unfamiliar to people who know them. This conflict has previously been considered in relation to schizophrenia: if an affected individual's personality while ill is seen as not an authentic expression of their self, this discounts the importance of the illness on their life and equally, accepting only their previous personality as authentic discounts their present lived experience (28).

Impaired self-awareness can also be observed in patients with moderate to severe Alzheimer's dementia. This typically takes a form of overestimation of their cognitive performance, functional abilities, and social behavior. In practice, therefore, it is important to integrate reports from people with dementia with a collateral history from a caregiver (16).

3.3. Authenticity and stigma

In some instances, authenticity can lead to stigma, for example when individuals are open about their experience of certain health conditions. Conversely, when a high-profile person feels able to disclose a diagnosis in themselves or their family, their authenticity in doing so can raise awareness of the condition. There is no firm evidence that celebrities talking about personal experiences of dementia reduces stigma and increases diagnosis and treatment rates. However, if a well-known figure publicly accepts and embraces a diagnosis, this may improve perception of the condition (29). Their disclosure can open an opportunity for public education, for example that dementia is not a normal part of aging and that its associated behaviors are due to a physical disease and not personal choice.

3.4. Authenticity in dementia care

Building on the biological framework, the behavior of a person with dementia can be more broadly appraised in the context of their personal history and strengths, and their relationships with other people. In all types of dementia, the concept of authenticity can be employed to help understand the person and to improve care. When there is a perceived loss of contact with the self, recognizing and upholding the person's ability to be authentic can maintain aspects of their personhood (30). For example, especially in residential care settings, where a person may lose touch with tangible aspects of their personal life, supporting their interests can nurture them (31). Regarding the specific symptom of low self-esteem, visual arts

FIGURE 1
Image of the symbolic masks produced in the workshop.

education has been found to be an effective intervention (32). In a qualitative study of art, authenticity, and citizenship, the authors argued that the self persists despite cognitive impairment or dementia and that a participatory artistic intervention may promote authentic living in people with dementia in care homes (33).

Authenticity is relevant in assessing decision-making ability in people with dementia. Although legal frameworks for capacity differ by country, most include guidance about honoring the previous views of a person who has lost capacity. In this context, authenticity can apply to a decision being made that is in keeping with their values, previous decisions, life history, and personality (34, 35). It can mean that even when the person is unable to make their own choices, an authentic decision can still be made with them, or on their behalf.

It may also be helpful for professional and informal caregivers to apply or reflect upon the value of authenticity. The Person-Centered Practice Framework outlines that person-centered healthcare should uphold the patient's own values and also be grounded in professionals' self-awareness (36). Conversely, it has been argued that in certain situations, the caregiver may have to prioritize the authenticity of the person with dementia over their own (37). For example, the person's authentic experience on a given day may be disconnected from the caregiver's reality; they may be waiting or searching for a family member whom the caregiver knows to be deceased. It is common for caregivers in this situation to avoid telling the truth to prevent additional distress (38). Having the ability to discuss challenging ethical questions in relation to authenticity, both before and after they arise, could improve the confidence of professionals and caregivers in coping with these situations.

4. Teaching the value of authenticity: a cultural education approach

We defined authenticity as "being true to ourselves." To explore this in the context of practical application in brain health, we developed a workshop entitled "Behind the Mask." The participants were faculty and fellows in the Atlantic Fellowship for Equity in Brain Health program at the Global Brain Health Institute (GBHI) at the University of California, San Francisco. The workshop was divided into four sections: an introduction to the concept of authenticity, the neuroscience behind it, its cultural background, and an artistic activity to allow creative group reflection. We offer a brief description of this event so that it might serve as a model for teaching about authenticity.

We aimed to encourage discussion about authenticity in dementia, both relating to the experience of the person with dementia and those who interact with them. To stimulate reflection, we posed the question whether it is possible to be authentic while wearing a mask. Throughout the history of human society, masks have been used for celebration, religion, identity, and as a mark of cultural heritage (39). They allow a person to change their outward expression while they remain the same inside. We asked participants to reflect upon the roles played by two fictional characters: a spouse of a person with dementia and a healthcare worker. Attendees were invited to create masks together to express their thoughts about the various masks that these individuals, and each of us, might wear as we navigate our daily lives. Art helped participants move from the abstract of thinking and talking to the concrete nature of a mask as an object full of colors and shapes. Figure 1 is an image of the symbolic masks produced in the workshop.

Our educational event aimed to encourage the diverse attendees to reflect on authenticity as it related to themselves and to the person affected by dementia. Self-awareness and group reflection can enhance resilience and maintain compassion (40). If caregivers of older people apply concepts of authenticity to both understanding the person for whom they care and to their own experience in a caring role, this may improve resilience and prevent burnout.

5. Conclusion

The concept of authenticity encompasses the neurobiological process of self-awareness as well as its psychological manifestations in interpersonal interactions. Adopting a broad translational view of authenticity can offer opportunities for more research on the neurobiological pathways involved, and on potential psychological interventions. We gained value from an educational workshop reflecting on this topic, which would also be of relevance to healthcare practitioners and caregivers of people with dementia.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

LS, BA, and CC-L: conceptualization, writing–original draft, and writing–review and editing. VS: writing–review and editing and supervision. All authors contributed to the article and approved the submitted version.

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Conflict of interest

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Impact of respect, equity, and leadership in brain health

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Respect is a feeling of admiration for someone. It forms one of the core values of the Global Brain Health Institute (GBHI), which strives to protect the world's aging populations from threats to brain health. These values guide us as we advocate for reducing the global impact of dementia. By taking a values-based approach to brain health, we can drive global changes for millions of people. Respect fortifies gratitude and embraces diversity. Philosophical discussions of the ideas support the assertion that respect is crucial in everyday conversations and actions as well as in personal, social, political, and moral spheres. No one can become a leader unless they genuinely respect and care about the success of each team member. Diversity, equity, and inclusivity form the fundamental cornerstones of respect. Understanding this core value of respect will ensure altruistic behavior among the leaders that may help mitigate racism, cultural insults, gender discrimination, stigmatization, religious hatred, and, worst of all, poor leadership abilities that have been the disconcerting examples of disrespect in recent years. We present the underlying neurobiology of respect and its impact on equity and leadership.

KEYWORDS

equity, brain health, leadership, respect, values

1. Introduction

Respect, also called esteem, is a feeling of admiration towards someone. Philosophers define the central concept of respect in various ways as a mode of behavior, a form of treatment, a valuing, a type of attention, a motive, an attitude, a tribute, a principle, a moral virtue, or an epistemic virtue (1). It is one of the core values of the Global Brain Health Institute (GBHI) that strives to protect the world's aging populations from threats to brain health. These values are known by the acronym "A FORCE" and stand for authenticity, fairness, openness, respect, courage, and empathy. These values are connected.

Authenticity assumes a genuine foundation for the initiation of any action. This action may demand fairness in the process, highlighting the need for transparency, equity, and openness. This underlies the curiosity required for evidenced-based change, and this cannot be achieved without respect which fortifies gratitude and embraces diversity. But, to accomplish this, one must be courageous to take risks. And finally, at the heart of community-informed change is the core value of empathy, the ability to feel what others are feeling as if you are feeling it yourself. These values can guide in advocating for reducing the impact of dementia. A transformation may be kindled for millions of people globally by using this values-based approach to brain health.

As we navigate through unprecedented times, human behaviors, like COVID-19 are propagated unpredictably. People's respect can be fickle. "A reputed selfless King was worshipped and respected in a village, and songs were sung in his honor. However, one day everything changed after a young girl in the village became pregnant and gave birth to a child. When asked about the father, she said he was the King's child. How long does it take for respect to become disrespect and admirers to become enemies? The mind waits for a chance; the day admiration ends, condemnation begins. The people of the village attacked the King.[1]"

2. Neurobiology of respect

Respect is central in many disciplines, including biomedicine, ethology, philosophy, and ethics. It has the distinctive property of acting as a "verb and noun," simultaneously activating "action and feeling" in human behavior (2). Respect is a positive social emotion associated with a deep sense of admiration. When recognizing laudatory behavior in another person, Kant suggests (3), "Act in such a way that you treat humanity, whether in your own person or the person of any other, never simply as a means but always at the same time as an end," referring to the inherent worth that shapes our identity and interactions with others.

The complexity of this value can be traced back evolutionarily through dominance hierarchies seen in animal societies, including our closest ancestors, the great apes (4). Related concepts, such as respect for ownership, are lost in young children and only found in children with object-subject conceptualization and theory of mind (ToM) (5, 6). In an experimental study, respect for ownership was found in 4 years-old children in more than 85% of the trials (6), and it is similar across societies in children from 4 to 7 years old (7, 8). Younger children with non-development in ToM and object-subject conceptualization may fall in recognition of ownership and respect. Respect may be supported by the theory of mind, empathy process development, and social hierarchy (9, 10), which may refer to the social brain and prefrontal cortex development (11). Besides, different studies have consistently identified several brain regions as involved in social dominance, including the amygdala, the hippocampus, the striatum, the intraparietal sulcus, and the prefrontal cortex (10) as neuronal networks involved in the social brain, emotional and reward pathways.

Positive feedback activates the ventral tegmental area (VTA) and its projections to the striatum, causing dopamine to be released, which is responsible for positive feelings, optimism, and sociability (12). We are more likely to feel valued and respected with its release. In turn, we become motivated to continue performing/behaving well to gain recognition and to pursue connections with others to achieve common goals (13). Respect and disrespect have distinct components that are cognitive and emotional. At the cognitive level, we construct values we admire in ourselves and others. Simultaneously there are other features that we shun in our semantic appraisal network. The feelings have less to do with rational, cognitive, and higher-level thinking in the neocortex. Instead, these emotions are linked to the limbic system and its connections, including the amygdala, orbitofrontal cortex, hippocampus, striatum, and cingulate—areas involved in emotional, motivational, and reward processes.

Feeling disrespected activates the amygdala, a part of the brain's system that processes strong emotions (14). Even if the person performing the behavior believes they are acting perfectly respectfully, it is perceived as a threat. In contrast to the support received in a social context, the amygdala also mediates the relevance of emotion preceding the significance of the action (15). Aside from this structure, the hypothalamus mediates the self-preservation instincts and the fight-flight-freeze response, which is triggered in the peri-aqueduct grey area and transmitted to the hypothalamus in less than a second. It regulates autonomic function, stress response, temperature, and other essential body processes. When one is respected, hormones such as oxytocin (16, 17) and serotonin are released in the creation of bounding; in contrast, when one is disrespected, hormones such as adrenaline, cortisol, and norepinephrine are released (18). Nonetheless, further research is need to elucidate completely the neurobiology behind values and respect.

2.1. Neuroanatomical localization of respect

So, where in the brain does respect reside? When appreciating exceptional behavior, for example, positive social emotions are typically felt as a way of showing respect. Semantic memory is required for this process. Social semantic information is stored in the anterior temporal lobe (ATL) (19). ATL activity is modulated by semantic knowledge's conceptual features because it necessitates the appraisal of exceptional behavior, as well as the person as a whole; respect activates the ATL. On the other hand, admiration is associated with a person's ideal behavior. In their study, Nakatani et al. (20), observed that appraisal ratings for a person's behavior were higher in admiration-related vignettes. In respect-related vignettes, however, those for the person were higher. The intensities of admiration and respect differentially modulated brain activity in a part of the left ATL. Other significant areas include the medial, orbitofrontal, temporal, and cingulate cortex, which are related to understanding and predicting other people's feelings, ideas, and behaviors, representing the theory of mind (5, 21, 22). This process can potentially alter social interactions by mediating respect behaviors, social needs, emotional reactions, and normative expectations. In another study, Nakatani et al. (20) observed an association of respect and empathic concern with reduced gray matter in the left ATL. Mediation analysis revealed that respect directly affected the gray matter volume when empathic concern was a mediation variable.

On the other hand, is not surprising that prefrontal areas might be involved in respect processing, for example, due to balance decision-making processes through "good or bad" options, representation of reward values, non-rewards and punishment, as well as social relevant information (23, 24). Nonetheless, more research data and new experimental paradigms are needed to completely elucidate brain areas and networks involve in highly hierarchical brain function related to moral values.

3. Diversity in respect

Racism, cultural insults, gender discrimination, stigmatization, religious hatred, and poor leadership abilities have been disconcerting

1 Regional history.

examples of disrespect in recent years. All of these have contributed to inequity in the world's different global communities, integrating disrespect, prejudice, and power, whether expressed quietly or actively, knowingly or unconsciously. Respect is vital in terms of equity and leadership. Unlike egoism, "altruism" is a powerful construct based on a blurred line between the self and the environment, manifesting as a sense of connectedness (25). Altruistic behaviors studied in infants have been shown to maintain and foster future altruistic behaviors throughout development and into adulthood, inadvertently imprinting the moral value of respect globally (26). Altruism appears to be demonstrated through prosocial behaviors, measured using self-reported scales that precisely measure altruistic behavior. The neural correlates of altruistic behavior in the brain include the regions within the mentalizing network, such as the medial prefrontal cortex and temporoparietal junction; reward regions, including the ventral tegmental area, striatum, specifically the nucleus accumbens, and anterior cingulate cortex, and areas of emotional salience network including the dorsolateral prefrontal cortex, insula, and amygdala (27, 28).

When confronted with a predicament, the emotional brain reacts more quickly than the rational brain. This is how humans have evolved and survived, which is critical for leaders to understand. Leaders must proactively aim to rewire their brains to appreciate "others," or those who are not like them, in order to ensure equity among those they lead. Inextricably related are respect and leadership. Altruistic acts foster a sense of respect and equity, both of which are critical elements of good leadership. Outstanding leadership, in turn, generates a climate of respect and high expectations, encouraging everyone to accomplish their best. Leaders must be humble enough to acknowledge that no one has solved the numerous complex problems and that solving them will always be difficult owing to intractable ambiguity. On the other hand, being receptive to novel and unconventional ideas may aid in navigating such problems and identifying the best possible solutions. Recognizing differences, demonstrating cultural humility, and treating others with respect are all essential to achieving objectives.

4. The final verdict

"The girl expressed regret for making false accusations. The villagers questioned the King, 'Why did not he refute this at the outset?' The King said, 'What difference would it have made? The child must belong to someone. People would have relished defaming one more individual if they had the opportunity.' If the King had been concerned about their condemnation, he would also have been concerned about their respect. He had become indifferent to people's behaviors by dropping the idea of good and bad because the thinking makes it so (see footnote 1)."

Indifference to good and bad becomes evident in the activities of real-life practitioners due to the dehumanization in medicine (29). Nonetheless, integrating "A FORCE" concepts in general practice may help "re-humanize" patients (30). Positive psychology and positive psychiatry, as a humanistic movement, could support this process through positive interventions based on the total respect of patient's optimism, wisdom (31), and kindness (32). From our point of view, positive psychology and psychiatry's principles are needed to extend implemented in future practitioners' curricula through promote soft skills sometimes lost in clinic practice. For instance, a humanistic perspective base on values might improve brain health outcomes, even though more research data are needed to validate and extend these practices worldwide to impact overall health care (33). Moreover, these approaches need to be extended even more in society, for example, through regional and global initiatives that impulse multi-level brain health-directed policy agendas, focus to augment sustainability of democratic societies through brain capital, equity, mental health and resilience (34), which not only goes in line with "A FORCE" concepts, but also promotes brain health, altruistic behaviors and democracy (35).

Respect and altruistic behaviors are among the ultimate solutions to global inequity, mediated by selfless leadership skills, one of the core values at the Global Brain Health Institute (GBHI). The acronym for "RESPECT" highlights the construct of altruism: remain calm, encourage others, stay positive, politeness, embrace differences, consider consequences and, more importantly, think before you speak.

5. Limitations and future directions

The study of the neurobiology of values, including respect, faces limitations that must be considered. Firstly, the definition and nature of the respective value can pose challenges when operationalizing the concept and conducting subsequent research. Additionally, incorporating novel methodologies such as neuroimaging (e.g., fMRI, EEG, MEG) holds promise for a deeper understanding of the neurobiological underpinnings of values and respect.

Exploring respect as a value raises intriguing questions from neurobiological and philosophical perspectives that remain open for further investigation. We are still far from obtaining a definitive answer regarding the specific neuronal circuits involved. However, progress can be made by studying human psychology and cognitive neuroscience through experimental procedures and neuroimaging techniques. This interdisciplinary approach will contribute to advancing our knowledge of how different brain areas and neural networks are implicated in the concept of values.

Overall, respect is a complex emotion that allows us to interact in human social situations successfully. But how do we regulate respect in the brain? Is respect influenced subconsciously or consciously by the behaviors of those around us? If so, how much influence does it wield? And how does neural connectivity make this possible? These questions are difficult to fully answer, despite our current understanding of the human brain. The main aim of this manuscript was to generate hypothesis in this field. However, this area is raw, and the summary of the progress needs to be interpreted with caution. Thus, more studies are required for generating evidence with regard to understanding the neurobiology of respect and whether public policy interventions could help boost population respect.

6. Conclusion

In conclusion, integrating cognitive and social neuroscience with new methodologies represents a compelling research area within social cognitive neuroscience. Numerous studies have identified neurobiological markers corresponding to values, but it is not enough. Future research should aim to explore the neurobiological mechanisms underlying values in general, including respect, and investigate specific neural networks associated with these values. Furthermore, understanding the significance of these networks in clinical practice will enhance our comprehension of how social factors impact mental health.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

FA and J-ZV: conceptualization, writing the original draft, reviewing, and edition of final draft. BM, VV, and CP: writing, reviewing, and editing the revised draft. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The neurobiology of openness as a personality trait

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Openness is a multifaceted behavioral disposition that encompasses personal, interpersonal, and cultural dimensions. It has been suggested that the interindividual variability in openness as a personality trait is influenced by various environmental and genetic factors, as well as differences in brain functional and structural connectivity patterns along with their various associated cognitive processes. Alterations in degree of openness have been linked to several aspects of health and disease, being impacted by both physical and mental health, substance use, and neurologic conditions. This review aims to explore the current state of knowledge describing the neurobiological basis of openness and how individual differences in openness can manifest in brain health and disease.

KEYWORDS

Big Five model of personality, openness, dogmatism, cognitive flexibiliity, neurobiology

Introduction

Openness is one of the major personality traits derived from the Big Five model, which is a widely accepted framework for understanding personality that also includes the factors conscientiousness, extraversion, agreeableness, and neuroticism. Openness is characterized by a person's tendency to seek out new experiences and to be willing to explore ideas, values, emotions, and sensations that differ from their previous experience or established preferences (1). This trait has been extensively studied in the field of personality psychology and has been associated with a variety of positive outcomes, such as increased creativity, curiosity, adaptability, mental flexibility, and acceptance of others (2).

For instance, openness can boost creativity because individuals who score high in openness tend to be more imaginative and original in their thinking and, thus, are more likely to be receptive to new and unconventional ideas, which in turn can inspire them to think outside the box and come up with innovative solutions to problems (3). Research has shown that greater openness is directly associated with enhanced creative achievement (4). Openness is also related to mental flexibility, which refers to the ability to adapt one's thinking and behavior to better fit with changing situations and contexts. Individuals who are high in openness tend to be more adaptable, allowing them to navigate uncertain and complex situations with greater ease (5). Trait openness is also connected to more effective, innovative, and ethical leadership because studies have shown that open leaders are more likely to be receptive to feedback and new information, have better critical thinking and quicker problem-solving capabilities, make better decisions, and be more empathically responsive to the needs and mistakes of their followers (6, 7).

Openness as a personality trait has been widely studied in cultural and organizational psychology as well (8). While trait openness correlates with individuals' career advancement into managerial and professional roles (9), studies show that individuals who score high in openness are better able to manage conflicting cultural values and adapt to new cultural contexts, which is a crucial factor underlying success in multicultural organizations and environments. Openness has also been associated with various positive outcomes in professional settings, including better job performance, organizational citizenship behavior (10), and intercultural competence (11).

Measuring openness

Studies have generally used one of two approaches for measuring openness: standardized self- and other-report questionnaires, or direct neuropsychological measures in which openness is conceptualized to overlap with creativity and thus is measured via the volume and quality of creative output.

Typical questionnaire measures of openness ask individuals to rate themselves on a series of items related to their openness to new experiences, ideas, and ways of thinking (12). One of the most comprehensive standard questionnaires for assessing openness is the NEO personality inventory (NEO-PI) (13), which is a popular personality assessment tool that measures the "Big Five Personality Traits" including trait openness. This tool was developed by McCrae and Costa and was first published in 1978 (1). Over the years, they have published three updated versions of the inventory, with the latest being the NEO PI-3 in 2005 (13–15). It measures openness via 68-item subscale facet scores addressing openness to fantasy, aesthetics, feelings, actions, ideas, and values. The fantasy facet refers to the individual's level of imagination, creativity, and tendency to indulge in daydreams. The aesthetics facet assesses the individual's appreciation of art, music, and beauty. The feelings facet refers to the individual's emotional awareness, sensitivity, and tendency to experience deep and intense emotions. The actions facet refers to the individual's level of adventurousness, willingness to take risks, and preference for novelty. The ideas facet assesses the individual's level of intellectual curiosity, open-mindedness, and appreciation for new ideas. Lastly, the values facet refers to the individual's level of openness to alternative belief systems, such as spiritual or religious beliefs (14).

Another commonly used measure of openness is the HEXACO personality inventory (16), developed by Lee and Ashton in the early 2000s as an alternative to the NEO PI-R. It measures six broad dimensions of personality: honesty-humility, emotionality, extraversion, agreeableness, conscientiousness, and openness to experience. The HEXACO model differs from the NEO PI-R in that it includes the honesty-humility dimension and places a greater emphasis on the ethical and moral aspects of openness. The inventory has been revised to improve the psychometric properties of the measure, resulting in the 100-item HEXACO-PI-R in 2018 (4, 17, 18).

The California psychological inventory (CPI) is a personality inventory developed by Gough and Bradley in the 1950s, currently in its most recent version being the CPI-434, which was released in 2005 (19). The CPI is a self-report assessment tool that measures personality traits on 20 scales, including dominance, sociability, responsibility, self-control, and tolerance. The California psychological inventory (CPI) does not have a specific scale for openness; however, the CPI does assess several dimensions investigators have argued are conceptually related to openness, including intellectual efficiency, creativity, and aesthetic appreciation (20).

Another widely used method for measuring openness is through creativity tests that include mental tasks which require individuals to think in unconventional ways. For example, the torrance tests of creative thinking (TTCT) was created by Torrance in the late 1950s and has been studied longitudinally for more than five decades to further validate the test across all age groups (21). This composite test assesses figural and verbal creativity using various subscales such as fluency, originality, elaboration, abstractness of thought, resistance to premature closure, and flexibility, which are based on the performance of different tests that need divergent thinking and other problem-solving skills (22). These tasks are designed to elicit imaginative and original responses from participants, and many of them involve generating alternative uses of objects, making associations between seemingly unrelated items, or imagining hypothetical scenarios (22). Additional examples of these types of "challenge" tasks include the alternative uses task (AUT) (22), the remote associates test (RAT) (23, 24), and the consequence task (25, 26), all of which require individuals to engage in divergent thinking, making distant associations and generating consequences for unlikely or impossible events.

The neurobiological basis of openness in neurologically healthy persons

Studies have used a mixed array of neuroimaging techniques in conjunction with these personality inventories with the goals of localizing the neural networks responsible for shaping openness as a personality trait, and developing better insight into the cognitive mechanisms that anchor openness neurobiologically. The majority of studies have sought to establish a correlation between scores on these measures and different brain regions by examining specific patterns of brain structure and function or neurochemical activity in individuals measured to have different levels of openness. Neuroimaging techniques such as structural magnetic resonance imaging (sMRI), resting-state functional MRI (rsfMRI), magnetic resonance spectroscopy (MRS), single photon emission computed tomography (SPECT), and positron emission tomography (PET) have each provided insights into the neurobiological basis of openness via this group comparison approach. A smaller set of studies have attempted to examine openness through task-based neuroimaging methods such as fMRI, in which participants were asked to perform a task in the scanner that the investigators construed as reflecting cognitive or emotional openness, such as the TTCT, AUT, or RAT. This research design might be less directly applicable to understanding openness as a personality trait but may still shed light on the specific neurobiology of cognitive processes known to contribute to openness, such as creativity and mental flexibility (22, 27–30).

Together, these studies have demonstrated distinct patterns of brain structure, connectivity, and activity, as well as neurochemical correlates, in brain regions known to be associated with creativity, abstraction, and cognitive flexibility. Broadly, the neurobiology of openness seems to be supported by three main functions and their corresponding neural networks: (1) reward processing, including the dopaminergic system along with ventromedial frontal and limbic reward networks, (2) the capacity to identify others' perspectives and distinguish them from one's own, which is supported by the brain's default mode network, and (3) higher-order reasoning and decision-making, which is mediated by the executive frontoparietal control network (ECN). Evidence suggests that higher connectivity and functional integration among these three systems predicts trait openness. A summary of findings from neuroimaging studies across different methodologies is shown in Table 1.

Structural neuroimaging studies

The correlation between regional brain volumetrics and openness in healthy individuals has been examined in several studies with varying results. While some structural neuroimaging studies have found no relationship between openness and cortical brain volume (31), others have implicated a diverse set of structures. DeYoung and colleagues found that individuals who score high in openness tend to

TABLE 1 Summary of neuroimaging studies on trait openness.

Study	Sample	Openness questionnaires/ other tasks	Imaging modality/ network or region analysis methodology	Results summary and interpretation
DeYoung et al. (2010)	116 healthy individuals	NEO-PI-R[2]	sMRI[1] Whole brain volumes and ROIs[3] (voxel-level) expansion or contraction compared to the reference image	There were no discernible correlations between openness and local brain volume One cluster in the right parietal cortex was linked to this feature but was too small to cross the cluster-size criteria (2)
Riccelli et al. (2017)	507 healthy participants from the human connectome study	NEO-FFI[4]	sMRI[1] SBM[5]	Greater area and folding in the prefrontal-parietal regions and a thinner cortex were associated with openness. These results show a relationship between individual variance in the sociocognitive dispositions outlined by the FFM and anatomical variability in prefrontal cortices (30)
Bjørnebekk et al. (2012)	265 healthy individuals	NEO-PI-R[2] BDI[6] WASI[7]	sMRI[1] Multimodal imaging approach: regional analysis of cortical morphometry and white matter DTI[8]	The personality trait most directly connected to brain shape was neuroticism Greater neuroticism was linked to decreased total brain volume, extensive WM microstructure loss, and reduced frontotemporal surface area The inferior frontal gyrus was narrower in people with higher extraversion ratings, and the temporoparietal junction was adversely correlated with conscientiousness There were no conclusive links between agreeableness and openness and brain anatomy (31)
Wenfu Li et al. (2015)	246 college students	NEO-PI-R[2] RAPM[9] WCAT[10]	sMRI[1] VBM[11]	These findings suggest that an individual's trait creativity may be significantly influenced by the specific personality trait of openness to experience and that creativity and the appropriate pMTG volume are related through openness to experience to some extent (34)

(Continued)

TABLE 1 (Continued)

Study	Sample	Openness questionnaires/ other tasks	Imaging modality/ network or region analysis methodology	Results summary and interpretation
Yasuno et al. (2017)	37 healthy participants	NEO-FFI[4]	sMRI[1] VBM[11]	Variations in intra-cortical myelination in the anterior cingulate/medial frontal cortex, posterior cingulate cortex, and posterior insula/adjacent putamen are related to individual differences in openness to experience These results support the theory that myelination serves as a biological underpinning for the trait of openness and plays a role in the relationship between creativity and mental illnesses (32)
Marstrand-Joergensen et al. (2021)	295 unique healthy individuals	NEO-PI-R[2]	[12]rsfMRI Resting-state functional connectivity	Openness, including the fantasy component, was inversely correlated with DMN functional connectivity in the resting state (35)
Wang et al. (2022)	376 healthy participants	NEO-PI-R[2] Creativity tasks: [13]CAQ, [14]CBI, [15]BICB Divergent thinking tasks: [16]PIT, [17]AUT, [18]UST	[12]rsfMRI Specific networks functional connectivity analysis Including the dorsal and ventral attention network, default mode network, limbic network, control network, and two others for somatosensory and visual networks	At the behavioral level, there is a correlation between creative achievement and both experiential openness and diverse thinking. Both openness to new experiences and divergent thinking involves the attentat networks and the default mode network since they both call for focus and the capacity for spontaneous thought (27)
Sun et al. (2019)	29 healthy university students	[2]NEO-PI-R Divergent thinking tasks: [17]AUT, [19]OCT (as a control task)	Task-fMRI Activation functional connectivity analysis	Different combinations of network connectivity patterns predict creativity and openness to experience Positive connections between the precuneus and supramarginal gyrus and the middle frontal gyrus/ superior frontal gyrus were found Individual difference analysis showed a significant correlation between openness to experience and the intensity of functional connectivity between various important default mode, cognitive control, and salience network areas The network-based mechanisms that underlie creativity and the neurological foundation of individual differences in openness to experience were found to be true (54)

(Continued)

TABLE 1 (Continued)

Study	Sample	Openness questionnaires/ other tasks	Imaging modality/ network or region analysis methodology	Results summary and interpretation
Wei et al. (2014)	269 healthy individuals	Divergent thinking: measured by the torrance tests of creative thinking	Pre- and post-task—resting state fMRI Whole-brain voxel-based activity and ROI-functional connectivity	Study findings suggest that increased RSFC between the default mode network's mPFC and mTG may be essential for creativity and that cognitive stimulation can increase RSFC between these two brain regions (reflecting creativity training-induced changes in functional connectivity, especially in the lower creativity individuals who had lower scores of torrance tests of creative thinking) (55)
Beaty et al. (2018)	163 healthy adults	Creative ideation task, alternate uses task (AUT) of divergent thinking	Two task-based fMRI samples and one task-free resting-state sample fMRI during creative ideation task Functional connectivity analysis	Greater default mode network, SN, and ECN functional connectivity are associated with higher creativity and divergent thinking (56)

A summary of findings and methodology from neuroimaging studies showing correlational structural and functional connectivity and activity to variability in openness and creativity and divergent thinking as another aspect of trait openness. We conducted a comprehensive literature search using the PubMed database for studies published from 1979 to 2023 in peer-reviewed journals that investigated the neurobiological correlates of openness. We included original articles that reported brain imaging data or neurophysiological measures of brain function in relation to measures of openness. Here we review the most recent relevant neuroimaging studies. [1]Structural MRI (sMRI), [2]Revised NEO personality inventory (NEO-PI-R) (57), [3]Region of interest (ROI), [4]NEO-five-factors-inventory (NEO-FFI) (13), [5]Surface-based morphometry (SBM), [6]Beck depression inventory (BDI) (58), [7]Wechsler abbreviated scale of intelligence (WASI) (59), [8]Diffusion tensor imaging (DTI), [9]Raven's advanced progressive matrix (RAPM) (60), [10]The creativity assessment packet (WCAT) (61), [11]Voxel-based morphometry (VBM), [12]Resting-state functional magnetic resonance imaging (rsfMRI), [13]The creative achievement questionnaire (CAQ) (62), [14]Creative behavior inventory (CBI) (63), [15]The biographical inventory of creative behaviors (BICB) (64), [16]The product improvement task (PIT), [17]The alternate uses task (AUT) (21), [18]The utopian situations task (UST), [19]Object characteristics task (OCT).

have a larger prefrontal cortex, which is the part of the brain responsible for higher-order thinking, decision-making, and planning (2). They also found an association with the volume of the inferior parietal lobule, which is linked with working memory, attention control, and general intelligence, suggesting that these cognitive processes might be associated with openness (2).

Openness has also been associated with increased gray matter volume in the anterior cingulate cortex (ACC), which is involved in emotion regulation and conflict monitoring (32).

Another neuroimaging study of healthy older adults from the Baltimore longitudinal study of aging found that higher openness was associated with increased gray matter volume in the frontopolar cortex. These regions are involved in cognitive control and executive function (33, 34), and enable individuals with higher openness to hold alternative actions in working memory in order to evaluate new options and ideas (33). The same study showed negative correlations between openness and volume in the right ventromedial prefrontal (vmPFC) and left fronto-insular cortex, regions that are involved in evaluation of negative outcomes and are linked to inhibitory or cautionary reactions to unpleasant or threatening stimuli. These data suggest that people with higher trait openness might be less vulnerable to such inhibitory reactions, while individuals with higher levels of anxiety are less likely to engage in cognitive or behavioral openness due to perceived risk (33, 35).

Functional connectivity studies

Two networks, in particular, appear in the majority of functional connectivity studies of creativity. The first, typically called the default mode network (DMN), includes the posterior cingulate cortex (PCC), dorsomedial prefrontal cortex (dmPFC), lateral parietal cortex, and hippocampal memory regions (33, 36). This network is involved in self-referential processing and social perspective-taking and is thought to be involved in a range of cognitive processes, including interpersonal perspective taking, introspection, and autobiographical memory (37). The second network relevant to trait openness is the executive control network (ECN), which comprises the dorsolateral prefrontal cortex (dlPFC) and the lateral posterior parietal cortex (PPC). It is an externally-oriented network involved in attentional selection, active task control, and executive functions, and is responsible for higher-order reasoning and decision-making. The dlPFC has also been implicated in the regulation of affect via reallocation of attention (36, 38).

Task-free functional imaging studies suggest that openness may be associated with increased functional connectivity *between* brain networks involved in cognitive control (i.e., the ECN) and self-referential processing (the DMN) (27). While higher levels of activity within the DMN have been found to predict lower trait openness, higher levels of connectivity between the DMN and ECN appear to allow individuals with higher levels of openness to better process information, generate new ideas, and approach challenges in creative and innovative ways. This DMN-ECN connectivity pattern in individuals with higher levels of trait openness is also correlated with cognitive flexibility, allowing these individuals to switch between different mental sets and think outside the box (38). Furthermore, evidence from these studies suggests that connectivity of the DMN and ECN networks with the brain's reward regions (including the vmPFC, nucleus accumbens, and head of the caudate) allows individuals with higher trait openness to be better able to integrate diverse sources of emotional and cognitive information, and to have a greater propensity to turn self-reflection and introspection about emotionally salient ideas and experiences into creative action (35).

In otherwise neurologically healthy individuals, certain cognitive and behavioral approaches and personality traits can be maladaptive, even falling on the spectrum of psychopathology. Dogmatism, or fundamentalism, can be understood to represent the opposite of trait openness because it is characterized by rigid adherence to a set of ideas and the intentional exclusion of competing beliefs. Thus, studies of dogmaticism are relevant to the neurobiology of openness, and have important implications for the mechanisms of decision-making, problem-solving, and learning (28). Task-based fMRI studies have shown that individuals with high levels of mental rigidity exhibit lower activation in the vmPFC during tasks that require flexible thinking, such as set-shifting or task-switching, compared to individuals with high levels of mental flexibility (28, 39). Dogmatism has been found to be associated with decreased functional connectivity between the vmPFC and the temporoparietal junction (TPJ) (28), while ideologic openness is associated with increased functional connectivity between the vmPFC and the ACC, regions involved in error monitoring and motivation (28, 40, 41).

Neurochemistry

One of the key neural systems that has been implicated in trait openness is the dopaminergic mesolimbic pathway, which is involved in reward processing, motivation, and novelty-seeking behavior. Several lines of research have demonstrated that individuals high in openness exhibit greater activation in the ventral striatum, a key component of the mesolimbic reward pathway, during tasks that involve processing novel or unexpected information. Other studies showed that individuals who have a particular variant of the dopamine receptor gene (DRD4) tend to score higher in openness (42). The DRD4 gene has also been linked to sensation-seeking behavior and risk-taking (43, 44).

Similarly, the neurotransmitter serotonin is associated with emotion regulation, and individuals who have the long allele variant of the serotonin transporter gene (5-HTTLPR) tend to score higher in openness (45). The short allele variant of the 5-HTTLPR gene has also been linked to anxiety and depression (46), which are negatively correlated with trait openness. Studies have examined the relationship between openness and the serotonergic system using positron emission tomography (PET) with different serotonergic receptor-binding radioligands, but with varied results. Kalbitzer and colleagues showed that participants' scores on the NEO-PI-R openness scale, and particularly the two subscales openness to actions and openness to values, were negatively correlated with the [11C] DASB binding radioligand for 5-HTT in limbic areas including the caudate (47). The authors suggested that because there was less serotonin available in these areas, the action of the remaining serotonin was potentiated, similar to the facilitation caused by antidepressant treatment with selective serotonin reuptake inhibitors (SSRIs). However, other PET studies using different serotonin ligands [5-HT2AR (48) and 5-HT4R (49)] to investigate trait openness found no significant neural associations.

Certain drugs, such as psychedelics (i.e., LSD and psilocybin, which are agonists for the 5-HT2AR serotonin receptor), have been shown to increase openness in some individuals (50, 51). fMRI studies have also shown altered DMN activity and connectivity (52) in individuals during psychedelic use. As described earlier, the DMN is involved in self-referential thinking and introspection, leading to better self-awareness and self-regulation, though heightened DMN activity alone corresponds with decreased openness (36). However, the pattern of brain activity induced by psychedelics is characterized by increased variability and decreased stability, which may in turn result in greater connectivity between the DMN and other networks. The authors posit that this leads to a "liberation" of cognitive and affective processes, allowing for increased creativity and divergent thinking as part of the trait openness (52).

Research using magnetic resonance spectroscopy (MRS) has also revealed that individuals with high levels of openness have higher levels of the neurotransmitter glutamate in anterior cingulate cortex (ACC) regions related to error monitoring and motivation, as well as in vmPFC reward areas (53). Glutamate is a key neurotransmitter involved in synaptic plasticity and learning, and these results suggest that increased glutamatergic activity in these reward and motivation areas in more open individuals may lead to a greater capacity for cognitive flexibility and learning (53).

Trait openness in neurologic disease

While the studies described thus far have included predominantly healthy individuals, additional insights about the neuroanatomical and neurochemical basis of openness can be derived from research models of neurological diseases as well. Lesion studies can shed light on which brain areas are both necessary and sufficient for particular behaviors and thought processes. Studying altered neural activity and connectivity in individuals with brain aging, injury, and disease who also show atypical levels of trait openness can facilitate our understanding of the underlying neural mechanisms.

Age-related cognitive decline

Studies have investigated how trait openness relates to aging as and age-related cognitive decline. Several investigations have found a negative correlation between openness and age (11, 15, 65); however, others showed that openness can have a protective effect against cognitive decline in middle-aged and older adults (66, 67) and correlates with better cognitive performance, social abilities, and well-being in older age (66, 68). Other research has suggested that openness may represent a behavioral channel to cognitive and social engagement, which are linked to a lower risk of dementia and cognitive decline (13, 69, 70).

Traumatic brain injury

Studies of individuals with severe structural brain lesions (28, 71), such as penetrating traumatic brain injury (pTBI) (28), show that they often exhibit an extreme lack of openness in the form of mental rigidity, dogmatism, and ideological or religious fundamentalism. Brain-behavior studies of these individuals' patterns of mental rigidity highlight the role of the vmPFC and its connectivity with other brain regions (28). In a study that included a large sample of patients with pTBI, Zhong and colleagues found that patients with injuries to the vmPFC scored higher than patients with dlPFC lesions on a standardized scale of religious fundamentalism, and that on average both groups showed abnormally high scores compared to neurologically healthy individuals. Analyses adjusting for the size of the lesions in the vmPFC suggested the interaction between vmPFC and dlPFC drove patients to have less cognitive flexibility and openness, again supporting the idea that the connection between reward- and executive-processing areas supports trait openness. This study gives insight into the role of both vmPFC and dlPFC in the revision of religious beliefs, suggesting that loss of cognitive flexibility is linked to an increase in fundamentalist belief adherence and resistance to novel information (28).

Neurodegenerative disease

The neurobiological mechanisms underlying changes in openness in individuals with neurodegenerative brain disease are complex and are still being elucidated. Similar to what has been observed in neurologically healthy individuals, studies in individuals with neurodegenerative disease have suggested that changes in the levels of dopamine, serotonin, and other neurotransmitters may play a role (54, 72). Additionally, the changes in frontal and temporal brain structure and connectivity often observed in patients with neurodegenerative disorders have been repeatedly linked to dysregulation and alteration of previously stable personality traits (73).

Several studies have suggested that individuals with neurodegenerative disorders such as Alzheimer's disease (AD) and Parkinson's disease (PD) may experience a decline in openness, particularly with respect to creativity and decision-making (74). Parkinson's disease is characterized by the degeneration of dopaminergic neurons in the substantia nigra that can lead to both motor and non-motor symptoms. Individuals with PD are more likely to have reduced openness to experience, the degree of which has been associated with the severity of motor symptoms and cognitive decline (75). In PD, atrophy in the vmPFC and dlPFC have been shown to impact both social cognition and decision-making, leading to a decrease in intellectual curiosity (76).

Notably, there is a growing evidence that some personality traits increase the likelihood of developing Alzheimer's disease and other dementias (77, 78). Several studies showed that openness, as a premorbid personality trait, was related to better cognitive outcomes in later life, suggesting that openness to experience contributes to cognitive reserve (79, 80). Openness also correlates with lower levels of aging-related hippocampal volume loss (81), and less Alzheimer's disease-related tau accumulation in the entorhinal cortex in cognitively healthy individuals (82).Tautvydaite and colleagues found that in a mixed group of individuals with and without AD-positive biomarkers, premorbid openness predicted cognitive performance regardless of the individual's cognitive level, demographics, APOEε4 status, or CSF biomarker levels. They found that openness was the only personality domain from the five-factor model that contributed independently to cognitive performance (83). These findings imply that openness as a lifelong personality trait may play a protective role against age-related neuropathological processes (33, 79, 82).

Another neurodegenerative disorder that has been shown to directly impact trait openness is frontotemporal dementia (FTD). FTD is characterized by the degeneration of the frontal and temporal lobes of the brain, leading to changes in behavior, personality, and language (84). Research has shown that individuals with the behavioral variant FTD syndrome (bvFTD) have significantly lower scores on measures of openness compared to healthy controls (85, 86), and that this decline has been linked to neurodegeneration in regions including the vmPFC and ACC (87).

Mental rigidity and dogmatism are common symptoms of FTD, and can manifest in various ways. For example, many individuals with FTD exhibit perseveration, which is the repetition of the same behavior or thought despite changes in the environment. Studies suggest this behavior may be due to atrophy in the dlPFC and ACC, areas involved in cognitive flexibility and inhibitory control (88). Some patients may present with intense resistance to changes in their routine or environment, such as trying new foods, moving to a new residence, or wearing different clothes day to day. Again, studies have linked this with atrophy in the dlPFC and other brain regions that support cognitive flexibility and adaptive behavior (89). Other patients with FTD, particularly those with the right temporal or semantic variant of bvFTD (90), may hold rigid or inflexible beliefs and refuse to consider alternative viewpoints (91, 92). Evidence suggests this may be due to disruptions in the vmPFC, which is involved in making evaluations of rewards during decision-making (93, 94). Furthermore, disruptions in the white matter tracts connecting the dlPFC and other brain regions such as the insula and anterior cingulate cortex, correlate with cognitive inflexibility and dogmatism in FTD (95).

On the other hand, studies of individuals with FTD have also highlighted the relationship between openness and creativity, which can be unleashed in a subset of these patients. For instance, specific patients with bvFTD have been found to display enhanced creativity and divergent thinking in specific contexts such as artistic production (96–98). A subset of individuals with FTD may exhibit dramatically increased engagement in an artistically creative behavior, such as painting, drawing, or composing music, that was not present before the onset of the disease (85, 99). This enhanced creative production is thought to be related to changes in the brain network connectivity between the DMN and the salience network (SN) (95). This phenomenon has been referred to as "unleashed creativity" and may be related to changes in neural networks involved in the processing of semantic and emotional information (96).

An alternate theory to explain this phenomenon is that the loss of inhibitory control that occurs in FTD may release previously suppressed creative tendencies (100). Certain patterns of dysfunction in the vmPFC and dlPFC may lead to a shift in cognitive processing that favors creative thinking over other, more rigorous cognitive processes (99). Persons with FTD who show this unleashed creativity show greater atrophy in the left hemisphere of the brain, particularly in the ventral and dorsolateral frontal and temporal regions associated with social cognition, executive functioning, and semantic processing.

This atrophy appears to release inhibitions in the creative process, allowing for a more free-flowing expression of ideas and emotions (97, 99, 100), and thus, greater openness. Further research into this complex phenomenon in persons with FTD may provide new insights into the neural basis of openness and ultimately inform new strategies for the treatment and care of these individuals.

Conclusion

Openness is a complex construct that encompasses multiple dimensions, but examining the neurobiological basis of openness improves our understanding of the cognitive components of this personality trait. Structural, functional, and lesion studies converge to suggest that connectivity among specific brain networks supports trait openness; specifically, the interaction among (1) reward systems, mediated both by neurotransmitters like dopamine and serotonin and brain structures like the ventromedial prefrontal cortex (vmPFC); (2) frontal and parietal structures in the default mode network (DMN), supporting interpersonal perspective taking, self-reflection, and abstraction; and (3) dorsolateral prefrontal cortex (dlPFC) structures in the executive control network (ECN) that mediate cognitive flexibility and problem-solving. These three brain systems interact synergistically to support openness by increasing mental flexibility, reward responsiveness and novelty-seeking, and the ability to incorporate creativity into thought processes, decision-making, and behavior.

While creativity is typically associated with openness as a positive behavior, in some cases, it can also be associated with dysfunction or pathology. Reductions in openness are often seen in persons with brain disease and injury, particularly those affecting the frontal and temporal lobes. These changes are likely associated with alterations in neurotransmitter levels as well as brain structure and connectivity. The exact neurobiological mechanisms underlying unleashed creativity in FTD remain unclear, though disruptions in the frontotemporal networks critical for the integration of sensory, emotional, and cognitive information may lead to a breakdown in inhibitory processes that normally suppress creative expression, resulting in the emergence of novel and innovative ideas.

Clearly, further research is needed to understand the neuroanatomical basis of openness at a more granular level. With a richer and more precise understanding of the mechanisms underlying openness, better interventions could be developed to augment this highly positive trait, enhancing an individual's receptiveness to new experiences, ideas, perspectives, and values, and thus promoting many aspects of their brain health. From a policy interventional perspective, these links between brain health and openness suggest that fostering openness as a personality trait has the potential for far-reaching benefits across the lifespan on both personal and societal levels. Promoting openness within educational systems and workplaces can shape environments that nurture curiosity, creativity, and a willingness to embrace new ideas. Successful interventions could contribute to the development of individuals who are adaptable, innovative, and open-minded, ultimately leading to better outcomes in education, workforce productivity, social cohesion, and personal brain health and mental well-being.

Author contributions

The manuscript benefited from the collective input of all authors during the conceptualization stage having all authors taking part in developing the ideas for this manuscript. KR and MR played a significant role in designing and structuring the paper. The initial draft was written by MR, who served as the first author, while the other coauthors contributed by reviewing and making edits. KR supervised the work and contributed to the writing, reviewing, and editing processes. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Using personal narrative to promote person-centered values in aging, dementia, and caregiving

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Personal narrative is a powerful way to include people in their care and to understand their values that drive their needs. In this paper, we describe a program designed to teach oral history to clinicians and trainees in the field of aging, dementia and caregiving. The training uses empathic listening, open-ended interviewing, and the discovery of individual values and experience to breakdown stigma and preconceptions of what it means to age with cognitive impairment. Sharing these stories of aging, dementia, and caregiving becomes an important tool to break down stereotypes, promote person-centered care, and advocate for the unheard. The profound impact of the oral history process is felt by the narrator, the interviewer and the listener. Human beings are wired for stories, and oral history taps into that power to connect us and provide better care through better understanding.

KEYWORDS

oral history, personal narrative, values, aging, dementia oral history, dementia

Introduction

Personal stories are a powerful way to share the rich, multi-dimensional nature of people's experiences with aging, dementia, and caregiving. Personal experience offers a bridge to building connection and empathy while breaking down stereotypes and stigma. The Oral History Association defines oral history as the process of eliciting personal narrative by listening to and sharing stories.[1] It involves active listening and the use of open-ended questions that foster sharing of the thoughts, feelings, experiences and values of the narrator. Narrative and personal stories hold a vital place in promoting social justice. The late historian Howard Zinn (1) popularized the practice of "people's history," which creates space for underrepresented accounts from individuals whose stories complicate or contradict dominant narratives. Oral history seeks to turn the microphone from the constantly amplified voices of the powerful and direct it toward ordinary people with stories that need to be heard. These stories become powerful testimonies that help us make sense of our world (2).

In health care, this process is often referred to as narrative medicine with the aim of promoting a deep understanding of the individual values and context that guide a patient's and family's decision-making while fostering a sense of dignity (3, 4). Personal narratives are representative of an individual's experience in life and may be used to relieve

1 https://www.oralhistory.org/about/do-oral-history

psychosocial and existential distress (5). Narrative medicine techniques enhance the collaboration, empathy, and trust between a provider and the patient and help to reduce the perception of a power dynamic (6, 7). While many healthcare providers believe that open-ended interviewing and narrative techniques slow down assessment, almost 80% of patients were able to convey their initial concerns within two minutes when the provider engaged in active listening (8). Telling a personal narrative can be a mechanism for discovering meaning and purpose through a re-evaluation of important life events (5). Personal narratives also have the power to break down stereotypes and othering generalizations that can lump people together into broad categories at the expense of a person's humanity.

Using the oral history process to promote social justice in the arena of aging, dementia, and caregiving brought together two organizations, Voice of Witness (VOW) and the University of California San Francisco Memory and Aging Center (UCSF MAC). VOW fosters an empathy-based understanding of the human experience through an oral history approach. This nonprofit organization promotes social justice and human rights with programs designed to collect stories and amplify the voices of those impacted by, and fighting against, injustice. The mission of the MAC is to provide the highest quality of care for those with cognitive problems and to educate patients, families, the public, and healthcare professionals. The MAC runs the Hellman Visiting Artist Program that brings artists to learn about neurogenerative disorders and foster creative exchange between the artists, clinicians, people living with cognitive impairment, families, and the community. Artists participate for one year and during that time engage in educational opportunities, observe clinical and research encounters, and develop an artistic offering inspired and informed by their experience. The artist presents their creative output with the larger community through a public performance thus raising important awareness about the lived experience of dementia and dementia care. To date, Hellman artists have represented the fields of poetry, dance, music, photography, podcasting, filmmaking, playwriting, comedy, and sculpture.

Out of this shared interest in promoting social justice, VOW became the sixth Hellman Visiting Artist at the MAC. During this residency, VOW staff trained interested MAC staff (physicians, nurses, social workers, research assistants, scientists, and MAC alumni) on conducting oral history interviews, transcription, and the development of a completed "story." Thirty stories were collected, and this launched a permanent and enduring relationship between VOW and the MAC that was named *hear/say*. During the next two years, *hear/say* was incorporated into the annual curriculum of the Atlantic Fellows for Equity in Brain Health at the Global Brain Health Institute (GBHI) due to the shared values in promoting empathy, raising awareness around issues of brain health, and serving vulnerable and underserved populations.

The purpose of this paper is to describe the *hear/say* project that spans several years and leverages a collaboration between academia, health care, and institutions with social justice values. We describe the elements of oral history training, process, and program participants. We share our outcomes relating to the objectives of promoting empathetic listening, open-ended interviewing, discovering individual values and experience, and sharing stories about aging, dementia, and caregiving. We discuss the value and our methodology in forging community partnerships.

Materials and methods

The *hear/say* project team trains participants using an ethics-driven oral history framework developed by VOW (9) and modified to match the needs and experiences of the Atlantic Fellows program. The course gives participants an opportunity to experience every step of the oral history process, including ethics and best practices for building trust between narrators and interviewers, interviewing techniques, recording, transcribing, editing, storytelling, and sharing the stories publicly. The course culminates in an optional public reading (called Readers' Theater) of excerpts from the collected stories, and the stories are added to the ongoing *hear/say* oral history archive.

Participants

In its first year, the *hear/say* participants included physicians, nurses, social workers, research assistants, scientists, and alumni from the MAC. In subsequent years, the participants included the Atlantic Fellows for Equity in Brain Health program at the Global Brain Health Institute (GBHI) based at UCSF MAC and at Trinity College Dublin, the University of Dublin, Ireland. The fellows are a group of interprofessional experts in brain health, aging, and dementia who come from countries around the world and work together to promote brain health and dementia prevention, reduce stigma, and improve the quality of life of people with dementia. Fellows selected for the program represent a wide variety of disciplines including artists, researchers, public health specialists, journalists, health care providers, educators, administrators, and social scientists. Fellowships start in September and last for one year in residence with career-long accompaniment. Components of the fellowships include didactics on a range of topics, (e.g., clinical, ethical, health policy, and leadership) about aging and dementia and leadership development. Each fellow is mentored and asked to develop a project of regional interest that builds on their professional goals and knowledge about dementia. In the fall, the new fellows are invited to participate in an introductory *hear/say* oral history training with a subsequent elective course in the summer. Faculty and staff from GBHI and the MAC are also invited to participate in the course.

Training

The *hear/say* project started outside of the regular GBHI curriculum but in its second year, became a part of the standard educational offerings for the fellows as a summer elective course. Fellows sign up for the elective hear/say course, which consists of a series of workshops to teach the fundamentals of oral history and provide a guided experience through all the steps of the process. The training embodies the collaboration between GBHI and VOW and supplements the goal-oriented interviews (for example, clinical histories) typically employed in clinical settings with training in open-ended, narrator-driven interviews that explore stories and topics meaningful to the narrator. We discuss that the use of the term "narrator" rather than interviewee is deliberate and fosters acknowledgment that the people interviewed have agency and choice in how they relate their story. The course is led by four co-authors and

TABLE 1 Example of story editing.

Transcript excerpt (unedited):
Interviewer (I): taking over some of those tasks?
Narrator (N): yeah, the day to day and such a gradual thing that you do not even notice it. You know it's years before you realize oh, now I'm doing this and oh, now I'm doing this and what is he doing?
I: So, it really creeps up on you?
N: It really creeps up on you. You do not really even notice it because it's just one more thing and you know, as a mother there's always a gazillion things you are doing anyway and you are working and you are just trying to keep everything together and so, if Jim cannot do the dishes now, which was the one thing he loved to do, well then I guess I'll do that too ummm it was yeah, it was so gradual and I think I've told you this before it was like a fog rolling in and rolling in and rolling in and you do not notice it. It just gets thicker and thicker and thicker and then it's so thick and it's been there for so long that you cannot remember what it was like when the sun was out. And you cannot remember what your life was like when you did not have to do everything 'cause you just gradually take it on. Like a sponge I guess. You gradually absorb all the water.
I: was there ever a time that you thought you could not do it?
N: no, I do not think so. I mean, I was always such a competitive person. I mean, and stubborn, so it wasn't an option to not do it. I mean I did try to divorce him (laughs) because his behavior was so bizarre and it just was not, he wasn't living life the way I had imagined we would be living our life and he was pretty unrealistic and unreasonable.
Final (edited) version:
You do not really even notice becoming a caregiver because it's just one more thing. And, as a mother there's always a gazillion things you are doing anyway, and you are working, and you are just trying to keep everything together. And so, if Jim cannot do the dishes now, well then, I guess I'll do that too. It was so gradual, and it was like a fog rolling in and rolling in and rolling in and you do not notice it. It just gets thicker and thicker and thicker and then it's so thick and it's been there for so long that you cannot remember what it was like when the sun was out. And you cannot remember what your life was like when you did not have to do everything, because you just gradually take it on. Like a sponge, I guess. You gradually absorb all the water. And yet, there was never a time that I thought, "I cannot do this." I mean, I was always such a competitive person. And stubborn, so it wasn't an option to not do it.

lead trainers (CM, JM, CP, and EV) with administrative, educational, and technical support from co-author MM. The learning objectives for the course are to increase fellows' capacity for empathy, active listening, and authenticity and to create opportunities for fellows to further their practices and projects by utilizing personal narrative as a tool for positive social change.

Workshops were scheduled at the two founding sites in San Francisco, California and Dublin, Ireland. In the 2018 and 2019 academic years, 10 h of training were provided in person over the course of 5 days at each site. In 2020 and 2021, the training was done in four virtual sessions, each lasting 90 min (6 h total) with participants attending remotely from their home countries.

The workshops begin with an introduction to oral history and the empathy-based and ethics-driven storytelling methodology as practiced by VOW (9). This methodology emphasizes centering the narrator experience, active listening by the interviewer, consent, representation, community relationships, embodying empathy, and learning from first-person narratives. Participants read oral history excerpts from the VOW book series, including the *hear/say* books, and view short video clips from past Readers' Theater events. This contextualizes the oral history techniques and provides participants with a basic road map for their own interviews during the course. The first workshop also includes a former narrator from the *hear/say* series, giving participants the chance to hear from and ask questions of someone who experienced the interview process firsthand.

The second workshop focuses on preparing interviewees for their oral history interviews. This preparation includes practice in crafting open-ended, story-generating questions, and how to create a safe and brave space for the sharing of stories. Participants also engage in practice interviews, taking turns asking each other about a personal artifact or object, to give each person an opportunity to experience the interview process as both narrator and interviewer. Sensitive issues can arise during the interview that can be emotionally distressful for both the narrator and the interviewer. As part of the training, participants are encouraged to share strategies in how to monitor for, and manage, emotional distress (9). The consent process is reviewed (explained in more detail below). The second workshop concludes reviewing the myriad logistics of recording and transcribing interviews in person and virtually. If participants cannot use their smartphone or videoconference software for recording, we provided audio recorders for them. We contracted with an automated transcription service, and we cover how to access and use this service. Participants are given resources to continue their learning by reading full transcripts of official interviews and narratives presented in other mediums, such as animated videos or graphic novels.[2,3] In between the second and third workshops, participants conduct interviews with their chosen narrator(s). If participants do not have access to a narrator, VOW and MAC staff facilitate a connection with one.

The third workshop is an introduction to editing an oral history transcript using the interviews conducted. This process includes acknowledging that people speak differently than they read and write, and that much of the editing process focuses on shaping a narrative that would be clear to a reader yet respects and reflects the voice of the narrator. The VOW methodology takes a literary approach to craft a cohesive and fluid story out of an interview transcript while maintaining the narrator's original words and intent. Narrators are given the opportunity to read their story before publication and consent to sharing or making changes as needed. Participants practice editing in small groups during the workshop to compare different editing choices. Each person gains valuable experience and insight into shaping a story with a clear narrative arc, while honoring the narrator's agency and voice in presenting their story. Table 1 provides an example of story editing from an interview with a family caregiver of a person with dementia: the final edited version appeared in the first *hear/say* book (10).

The final workshop is devoted to sharing brief excerpts of the in-progress oral history narratives. Participants create a "story circle" and celebrate their narrators by bringing their voices into a shared space by reading excerpts aloud. Even in brief excerpts, participants can share moments of joy, pain, struggle, heart, and humor. During this final workshop, the oral history process comes full circle by

2 https://storycorps.org/animation/
3 https://brianfies.blogspot.com/2017/10/a-fire-story-complete.html

hearing from a former hear/say interviewer about how the process has impacted their work beyond the training and how lessons learned around narrator agency, empathy, representation, and active listening have been taken into real-world applications. The session concludes with planning and logistics for the public Readers' Theater event at the end of the course. Before this final event, participants spend more time editing their oral history narratives with guidance from the hear/say team.

Consent

Although Institutional Review Board approval and participant consent are not required for oral history work, all narrators in this project sign a consent form before participating. The form is a "rolling consent" that the hear/say team developed with input from the Atlantic Fellows and other interviewers. It centers on narrator agency and allows the narrator to select a level of sharing they are comfortable with. For example, some narrators may choose to not share their story outside of the interview or they may prefer to not use their full name, and the consent form allows them to make these choices. The consent form allows the narrator to choose how their story can be shared: in a published book, read aloud, and/or filmed, and it allows for the narrator to modify or withdraw their consent at any time during the process. The consent form has been translated into languages used by the *hear/say* participants and has, so far, been translated into traditional and simplified Chinese, French, Portuguese, Romanian, and Spanish.

Ongoing consultation

The *hear/say* team provides follow-up and consultation for participant interviewers on all aspects of the experience including preparation of transcripts and stories, material for the Readers' Theater event, and strategies for incorporating their interview skills and what they had learned from their narrators into project development and future work. Throughout the entire course, the hear/say team is in contact with the participants and hosts drop-in sessions in which the interviewers can show up to ask questions and clarify concepts.

Results

During the first two years of *hear/say*, 13 interviewers that included MAC staff (former and current), Atlantic Fellows, and GBHI faculty and staff collected stories from 31 narrators from five different countries. Four translators and 16 story editors, including the 4 lead trainers, helped finalize the stories. The Readers' Theater event was presented live to about 75 people and followed by a reception. Audience members included interviewers, narrators, colleagues, and the local community. In the third year, training was conducted remotely with 15 fellows and six staff participating. This resulted in ten interviewers who shared eight stories in four languages from five countries during a Readers' Theater with an audience of 80 people. In the fourth year, training was conducted remotely with 9 fellows and six staff participating. This resulted in ten interviewers who shared ten stories in two languages from seven countries during a Readers' Theater with an audience of 106 people. For all the Readers' Theaters, we had the participation of additional readers who read excerpts of the multilingual stories (stories were shared in the narrator's language first, followed by an English translation). During all four years, narrators included people living with cognitive impairment, caregivers, physicians, nurses, scientists, research staff, and artists. Two books have been published (10, 11) and four public Readers' Theater events have been held. Videos of the readings can be seen at memory.ucsf.edu/caregiving-support/caregiver-well-being/hearsay and www.gbhi.org/projects/hearsay.

We include an excerpt from an interview with a man who had been diagnosed with Alzheimer's disease. He participated in our first year of *hear/say* and a portion of his story was read at the Reader's Theater [the complete transcribed story can be found in Prioleau, C. and Merrilees, J., ed. (10)].

> Short of a solving the disease, the best way to help is by teaching people we aren't vegetables yet. Just spreading the word. Because for many people, they think, "Oh my God, it's the end of the world." And it's not the end of the world. It's not great, but it's not the end of the world. And that's important to let people know. That's why having our group is good, being able to teach people who are in the medical profession, and I think advocacy is great… people with the disease talking, telling our story. Sharing our story is so powerful, with any disease. If research needs to be done, we can tell them why by showing our story. And people should also know that you can still have a sense of humor when you have a disease. You live a certain amount of time, and then you plotz. And you do what you can do. I like being a teacher. So, I hope it stays in your head, because I'll probably forget it!

Discussion

The *hear/say* project, by teaching oral history methodology, is a valuable tool for clinical providers, researchers, teachers, and students/trainees in promoting an understanding of an individual's values. Personal stories help to shed light on not only the experience of an individual but can help to forge changes in social policy that impact countless others. Oral history training has helped our staff and trainees to develop tools for building equity and promoting social justice in their work by shedding light on the rarely heard experiences.

In the *hear/say* training programs to date, interviewers and narrators expressed appreciation and gratitude for the opportunity to share their stories, to be heard, and to contribute to knowledge sharing about their experiences. When stories are told and listened to, they become the experience of both the narrator and the interviewer (12). The *hear/say* participants reported this multidirectional benefit: a deeper empathy and mutuality developed as they learned more about their narrators (13). Many reported that the process of conducting an oral history interview gave them new skills in communication and the art and benefits of listening. People have a strong desire to preserve their stories (2) and giving them a safe space to speak their stories is a critical step in forging mutual respect and understanding.

In our situation, exploring shared values among our community partners was a critical bridge to building and sustaining the *hear/say* project. In the first meetings between VOW and the MAC, the four trainers found common ground discussing the potential for blending our areas of expertise: for VOW this was vast experience in the oral history process and for the MAC having access to cohorts whose voices were often not heard or appreciated. We realized that we spoke the same language regarding our shared values of empathy, social justice, and reducing stigma and that each organization brought expertise that the other could grow from. Themes that have been associated with building strong community partnerships include but are not limited to the creation and nurturing of trust, respect for knowledge, community-defined goals, flexibility, compromise, capacity building, and attention to sustainability (14, 15). Values that promote partnerships include respect, communication, mutual benefit, and shared ownership with potential threats including power imbalances, lack of shared vision, and lack of time (16). Throughout the years of collaboration between VOW and GBHI, we continue to nurture these positive values and work on reducing potential threats.

Summary

Aging, threats to brain health, and caregiving can be frightening, isolating, and stigmatizing experiences. Persons living with dementia and their caregivers report that their healthcare providers do not always show respect and knowledge about their culture and their values that drive their decisions (17). Healthcare providers, artists, scientists, and social policy change agents face enormous barriers and challenges in effecting change in this arena and need the tools and strategies necessary to inform change. Personal stories become a strategy for eliciting attention and understanding to these threats to health. The techniques of oral history— interviewing and honoring the agency and primacy of the narrator—are powerful and accessible strategies for understanding the experience and values of an individual whose story can then impact and inform others. In addition, a systematization of the themes within the personal narratives could provide an even more explicit bridge between the values of narrators and the promotion of social justice and healthcare change.

Author contributions

CM, JM, EV, MM, and CP contributed to development of this paper, including the background, results, and discussion. CM and EV wrote the description of the training program. JM supervised all phases of the paper. All authors contributed to the article and approved the submitted version.

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The Black radical imagination: a space of hope and possible futures

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The radical imagination entails stepping outside the confines of the *now* and into the expansiveness of *what could be*. It has been described as the ability to dream of possible futures and bring these possibilities back to the present to drive social transformation. This perspective paper seeks to provide an overview of the radical imagination and its intersections with Afrofuturism, a framework and artistic epistemology that expresses the Black cultural experience through a space of hope where Blackness is integral. In this paper, I propose three processes that comprise the radical imagination: (1) imagining alternative Black futures, (2) radical hope, and (3) collective courage. I consider the neural networks that underlie each process and consider how the Black radical imagination is a portal through which aging Black adults experience hope and envision futures that drive social change. I conclude with considerations of what brain health and healing justice looks like for aging Black Americans— specifically, how invocation of the Black radical imagination may have positive brain health effects for a demographic group at increased risk for Alzheimer's disease and related dementias.

KEYWORDS

imagination, Afrofuturism, alternative futures, health justice, Black aging, neurocognition, values

1. Introduction

> "Colonization of the imagination is the most dangerous and subversive form there is: for it is where all other forms of decolonization are born. When the imagination is unshackled, liberation is limitless."
>
> -Walidah Imarisha.

Our thoughts create our reality. In a world where racism, sexism, homophobia, ageism and other forms of oppression maintain a false social hierarchy and unequal distribution of power, the radical imagination is the foundation to re-envisioning the future and building a new, balanced world. Defined as the "ability to imagine the world, life and social institutions, not as they are but as they might otherwise be," the radical imagination brings "possible futures 'back' to work on the present, to inspire action" (1). To fully unpack the radical imagination requires consideration of its etymology. While the word "radical" in today's day and age often has a negative connotation and is used synonymously with extremism, "radical" is derived from the Latin word, *radix*, which translates to "root." Perhaps not coincidentally, ideas that are deemed "radical" are oftentimes grounded in the understanding and/or identification of systemic inequity, oppression, and power imbalance as root causes of societal problems (2). To be radical, in its truest form, is to get to the root of the problem.

The imagination is the generative foundation for all new ideas and involves the social and cultural creation of meaning (3). Early conceptions of the imagination included the belief that imagining was restricted to solely visual mental imagery (4), but it is now known that the imagination encompasses other perceptual modalities [e.g., auditory, tactile, olfaction; motoric (5, 6)] and underlies prosocial behavior [e.g., empathy (7, 8)] at both the individual and collective levels. As will later be discussed, it is the collective imagination – a group process through which knowledge and new ideas are co-produced (9)– that undergirds many social justice movements toward Black collective liberation. The imagination also exists on a temporal plane in that it can be oriented toward past happenings, alternative presents, or possible futures (3). All three aspects of time are inextricably linked and deeply racialized (10, 11). For example, Black Americans are unjustly cut from accessing all elements of time: (1) they are cut from their past and family lineage via the transatlantic slave trade (11); (2) cut from the present via labor inequities that are rooted in capitalism and the historical commodification of the Black body for capital, which impact access to time, rest, and leisure (12–14) and (3) cut from the future via premature deaths and abbreviated lifespans evidenced by health disparities (15–20), mass incarceration (21, 22), and state-sanctioned violence (23, 24). It is through this intentional manipulation and monopolizing of time that the imagination is squelched, and social and systemic inequities persist. Thus, for Black Americans, the collective invocation of the imagination is a longstanding form of resistance and a critical means of making it to the future. In a society where aging is a privilege, the Black imagination is a tool for survival.

"Any serious motion toward freedom must begin in the mind." (25) The imagination is a mechanism through which we are not only able to envision new, freer worlds, but we can actualize them. To *radically* reimagine requires more than the deconstruction of problematic policies or dismantling existing power structures (although both are important components of it); it additionally encompasses the process of *rebuilding* from a space of possibility. The radical imagination extends beyond mere fantasy. It is a central driver of cognition and perception in that society can only create that which its members can imagine (9, 26). When equipped with deep understanding and acknowledgment of the past, the radical imagination can become a portal to a more just, equitable word (27).

In this perspective paper, I argue there are three components of the Black radical imagination which include: (1) imagining alternative Black futures, (2) radical hope, and (3) collective courage. I explore the neuroanatomical underpinnings of these processes and values, and then consider their relationship to brain health. Lastly, I delineate how the Black radical imagination is a necessary conduit to possible futures rooted in health and healing justice for Black Americans. I reflect on what it means to disrupt existing power imbalances and place Black Americans as the central story writers and designers of an equitable future.

2. Imagining alternative Black futures

People of the African diaspora have long been building new futures to escape trauma and cultivate shared realities. The paradox and illegitimacy of ancient Western criticism was that people from the continent of Africa were considered lacking in imagination and incapable of "true sophistication" required for social evolution, while also, ironically, deemed "too imaginative" in their belief of the supernatural, deities, Dogon myths, and orishas (28). Dating back as far as 500–300 BCE (29), these traditional ideas and belief systems within African societies were the earliest forms of Black imagination and ways of existing that countered the Western gaze.

The term "Black radical imagination," first appearing in Robin D.G. Kelly's, Freedom's Dreams (25), is the process of Black people collectively envisioning a revolutionary and liberated future. Early conjuring of the Black radical imagination is apparent in the kidnapping and forced relocation of ~12.5 million people from the continent of Africa to the Americas via the transatlantic slave trade from 1500 to 1865. This treacherous and inhumane journey overseas required those captured to imagine alternative forms of resistance that ranged from refusing to eat to staged ship revolts. Some even made the difficult decision to jump overboard to cheat the ultimate death: enslavement and control.

Upon arrival to the Americas, through collective struggle and solidarity, those who were Black and enslaved identified ways to undermine slavery and actualize their birthright: freedom. Despite attempts to erase the enslaved of their culture and customs, commodify their labor, and indoctrinate them into Western practices, Black people resisted through subtle acts of defiance (e.g., sabotaging crops, damaging equipment, feigning illness) and through clever communication and escape tactics in this foreign land. For example, the different hairstyles Black women wore contained intricate designs like conrows or Bantu knots and were used as maps hidden in plain sight to escape to freedom (30). Women also hid rice and seeds in their hair to grow once they escaped to a free territory. Songs contained embedded messages for those escaping North to freedom via the secret routes of the Underground Railroad. The spiritual, "Wade in the Water," was sung by enslaved persons to warn those enroute to freedom to avoid trails and use the river to hide their body scent and to evade search dogs (31). Harriet Tubman, an abolitionist and former slave who escaped to freedom, is one of the most widely known conductors of the Underground Railroad. It was her ability to dream of new worlds and incorporate celestial knowledge (using the North Star as a guide) that allowed her to make 13 rescue missions to help others achieve freedom in the North. Although lesser known, Tubman was also a spy in the Union Army and the leader behind the Combahee River raid, freeing 800 enslaved people (32, 33). It was these visions of alternative (free) futures, resourcefulness, and ingenious strategizing that have long carried Black Americans through turbulent times.

The Black radical imagination has been a cornerstone of Black American culture and the social struggle for equity that exists to this day. This collective dreaming of alternative futures is the impetus behind U.S. movements and initiatives for liberation (e.g., Civil Rights Movement, Freedom Riders, March on Washington, Black Lives Matter). Imagining in this context is not a discrete process, but one of co-creation that shapeshifts over time and with the needs of the marginalized community (1). It is shaped by the material and social conditions of society (34). The Black imagination remains a site of resistance to oppression to this day. The process of imagining as a liberation praxis remains integral to the generation of Black possible futures (35).

2.1. Afrofuturism and the imagination

> "The Black voice is forced to be imaginative because otherwise it will be silenced."
> -Jonathan Horstmann

Afrofuturism intersects with the Black imagination to provide a framework for communicating ideas around possible futures and creating spaces of Black empowerment. Afrofuturism is an epistemology and form of artistic expression that explores the African diaspora experience through alternate realities and futures using imagination, technology, and mysticism (36). Coined in 1993 by Mark Dery in his essay "Black to the Future" (37), the practice of Afrofuturism dates to the narrative work of the enslaved and abolitionist discourse of the 18th and 19th centuries (28, 38). Afrofuturism reasserts Black agency in a way that places people of the African diaspora as central storywriters and occupants of past, present, and future. Importantly, the Afrofuturist is not ignorant of historical happenings, but they are not limited by it either (39).

In fact, Afrofuturism has been used by Black American artists, activists, scholars and others as a framework to reclaim and unveil lost histories (40) and reimagine the future through a lens of hope where Blackness is integral and all Black people are safe. It directly counters society's failure to "articulate and witness Black life" free of struggle (41). The creation of counternarratives and counter futures that upend stereotypes and give Black people control over their image is core to Afrofuturism. Thus, Afrofuturists determine *who* is seen and *how* they are seen. From Octavia Butler's pioneering science fiction and speculative writings to Sun Ra and the Arkestra's jazz compilations to the visuals and narrative of the movie Black Panther, Afrofuturism, spans mediums and leans fully into the expansiveness of Black possibility. Existing research denotes the benefit of Black people envisioning possible futures in which they are central (42). Afrofuturism has been utilized as a "praxis for designing equitable futures centered around joy and healing" (43). Because Black bodies are politicized in society, Afrofuturism is political, transformative, and revolutionary (44).

2.2. Cognitive neuroscience of the imagination

A cognitive neuroscience perspective considers imagination to be the representational engagement with that which is absent. Abraham (6) synthesized empirical data and theory from cognitive neuroscience literature which resulted in five ways to categorize the imagination within a single framework: mental imagery (perceptual/motor) imagination, intentionality imagination, novel combinatorial imagination, phenomenology imagination, and altered states of imagination. While these processes are described as distinct, they are not independent of one another.

Mental imagery-based imagination is the representation of a sensory experience without direct external stimulus (45). There is evidence that brain regions responsible for sensory perception or motor generation are also activated when those processes are imagined (45). For instance, imagining the sounds of a song activates the auditory cortex (46) and imagining hand movement activates the premotor cortex (47) which maintains the same somatotopic organization in mental representation (48).

Intentionality imagination encompasses both the recollective and social domains and requires one to make appraisals or some form of judgment about actions or events (that could be geared toward the past or the future). Abraham (6) indicated that this could be imagination involving autobiographical or episodic memory (e.g., remembering high school prom), theory of mind (e.g., considering what another person is thinking), self-referential thinking (e.g., considering your own thoughts), or moral reasoning (e.g., evaluating the acceptability of another's actions). These elements of imagination contain a shared functional neuroanatomical architecture of the default mode network. Specifically, the default mode network consists of the medial prefrontal cortex, retrosplenial and posterior cingulate cortices, anterior lateral temporal cortex, inferior parietal cortex, and mesial temporal lobe (6, 49).

Novel combinatorial imagination consists of the generation of new ideas via creativity, openness, and consideration of the unknown. Abraham (6) noted that key elements of this form of imagination involves extending beyond the status quo, explorative thinking, and combining knowledge in novel ways. Sub-operations of this form of imagination include problem solving and expression, counterfactual reasoning, divergent thinking, hypothesis generation, and hypothetical reasoning (6, 50). Existing data suggests novel combinatorial imagination is also associated with activity in the default mode network. When tasked with the generation of novel open-ended ideas, the medial prefrontal and frontopolar cortex is activated, whereas more lateral aspects of these brain regions are associated with idea selection and determination of relevance (6, 51).

Phenomenology imagination reflects the engagement and response to esthetics that is largely subjective in nature. This form of imagination consists of attentional focus, cognitive engagement/appraisal, and emotional connection in relation to an object (52). Of the existing literature, esthetic appreciation was strongly associated with activity in the anterior insula irrespective of sensory modality (53), consistent with its role in interoceptive states of awareness (54, 55).

Lastly, Abraham (6) defined altered states imagination as those which involve a change in one's awareness or mental state. This diverse range of altered states consist of dreaming, temporary induced states (e.g., use of psychedelics, hypnosis), or states associated with neurological and/or psychiatric symptoms (e.g., delusions, hallucinations, confabulation). Whereas dreaming is associated with activation of default mode network (56, 57) and deactivation of cognitive control networks (58), hypnotic states are associated increased activity in cognitive control networks (i.e., lateral prefrontal regions) and deactivation of the default mode network (59). This dissociation is thought to reflect the distinction between the involuntary vs. voluntary nature of dreaming and hypnosis, respectively. Meditation contains both volitional and nonvolitional elements and therefore includes activation of both the default mode and cognitive control networks (60, 61).

The capacity to imagine the future is a critical element of the human mind. While these processes and neuroanatomical correlates underlying the imagination have been discussed as discrete, the imagination has also been considered a "global emergent process" rather than something localized to a specific brain region (62). The radical imagination may be most consistent with the novel combinatorial form of imagination as it is geared toward the construction of ideas and things that have not yet happened. While there is evidence of the benefits of collectivism and working in community (63), including group wellbeing and support (63, 64), the field of neuroscience has yet to consider the brain health implications of what it means to imagine in connection with others who have a similar lived experience. Further, given the functional activation of sensory and motor cortices without direct sensory input (45), can the imagination initiate neuroplasticity and physiological changes that buffer cognitive decline? In addition to the political nature of the Black imagination, what cognitive health implications does collective dreaming have specifically for Black Americans, who are disproportionately impacted by Alzheimer's disease and related dementias (ADRD) (19, 65)?

2.3. Imagination to promote neuroplasticity

Current evidence indicates Black Americans have approximately a 1.5 to 2 times higher risk of developing ADRD compared to non-Hispanic, white Americans (65–69). A significant proportion of this disparity is likely explained by the social and structural determinants of health (e.g., education, quality healthcare, community, and neighborhood built environment) with racial differences observed across many of these determinants due to historical and contemporary racism as well as unequal distributions of power (70).

For Black Americans, acknowledging the reality of present times while also imagining possible (freer) futures requires the difficult art holding of multiple truths: that racism is insidious and continues to disadvantage racial and ethnic minorities, but change is possible and necessary. Invocation of the radical imagination, through intentional shifts in one's thinking about the construction of the future, may modify ADRD risk via neuroplasticity given the malleable nature of the brain even into late adulthood (71–73).

The concept of neuroplasticity has garnered interest in the field of dementia given the potential to influence cognitive and/or brain reserve (74) and delay clinical symptoms of cognitive decline despite underlying neuropathology. Neuroplasticity is defined as "the ability of the nervous system to change its activity in response to intrinsic or extrinsic stimuli by reorganizing its structure, functioning, or connections." (75) Neuroplasticity can result in changes in neural structure, rewiring of existing neural connections, neurogenesis and synaptogenesis, or neurotransmitter and neurotrophin expression (76–78). Current data suggest external drivers of neuroplasticity are based on the novelty, complexity, and enriching nature of one's environment (78). Thus, experiential exposure to education (79, 80), social engagement (81), and cognitively stimulating activities (82) are thought to support the brain's capacity to resist the clinical manifestation of dementia (83, 84). Lifestyle factors, such as physical exercise and diet, also modulate neuroplasticity (83).

It is possible that one can modify the structural organization of the brain through the act of radically re-imagining an equitable society. Although lesser discussed, several internally-driven factors, related to the process of imagining, induce neuroplastic change. For instance, conceiving new ideas and integrating concepts that are seemingly unrelated requires cognitive flexibility, divergent thinking, and creativity. Routine engagement in these cognitive processes resulted in increased gray matter volume as well as functional changes in brain regions associated with higher level cognitive control (dorsal anterior cingulate cortex, dorsal lateral prefrontal cortex) and posterior brain regions among adults (85). Additionally, thinking about the future requires aspects of both episodic and semantic memory (86, 87) in that imagination requires, to some degree, an extraction of stored information and recombination of that information in new ways, which may also promote neuroplasticity (88). Visualization (i.e., the generation of mental imagery) is a powerful technique associated with neuroplastic change (89) and can be a simple way to tap into the imaginary and, quite literally, "see" ideas of the future. Taken collectively, there is evidence that neuroplasticity can occur in response to different forms of stimulation even if the stimulation is the result of mentally driven efforts as opposed to external ones. Thus, for Black Americans, designing the future and projecting oneself at its center is a revolutionary and necessary act that can also leverage the dynamic nature of the brain. The long-term brain health benefits of what it means to engage the radical imagination and build possible futures remains an area ample for study.

3. From imagination to radical hope

A vision for the future without belief that the outcome is attainable leaves little worth acting upon. Hope is the process of looking to the future with a desired outcome in mind and maintaining belief that the outcome can be actualized. Radical hope specifically adopts a social justice orientation (90) and is considered radical because the hope is driven by the desire for a future rooted in equity and questions of *when* equity will be achieved trumps questions of *how* it will happen. Radical hope is a core tenant of the framework for radical healing for People of Color and Indigenous Individuals (91), and emphasizes Black agency and the design of new futures through a decolonized imagination. Within this framework, radical hope is the fuel that keeps the vision ablaze.

Hope has been instrumental to the livelihood of Black Americans and is described as "a gift from [the] ancestors that fuels [our] will to survive racial trauma." (92) Radical hope carried those kidnapped from the continent of Africa across the Atlantic Ocean to survive the atrocities of the Middle Passage and make it to the Americas. Radical hope is further evidenced in their pursuit of self-taught education and literacy while enslaved, which was key to physical and intellectual emancipation (93, 94) and subverted white domination. The belief that they could achieve freedom in times of precarity and horror exemplifies radical hope. It was the rebuilding of new cultural practices as the old ones were stripped – that is, the development of new traditions, rituals, and narratives that are now cultural staples in present-day Black America – that came from a space of radical hope and possibility (94).

If Black American history has taught us anything, it is that radical hope must not be extinguished or else run the risk of societal stagnation, or even worse, suppression. In author and poet Langston Hughes' Harlem (A Dream Deferred) (95) published in 1951, he raises the important question:

> *What happens to a dream deferred?*
> *Does it dry up*

> *like a raisin in the sun?*
> *Or fester like a sore -*
> *And then run?*

Without having to reference hope directly, Hughes' lines of questioning challenges Black Americans to maintain the collective dream to upend the very real, harrowing happenings of that time: Jim Crow racial segregation, voter suppression, and police brutality. He advocates for Black Americans to have resolve–a steadfast hope–especially in times when the desired outcome is delayed or seemingly out of reach.

Black American hope has often been situated within a religious and/or political context and there are numerous examples in history of the symbiotic relationship between the Black Church and Black political action (96). We experience themes of hope in Martin Luther King, Jr's infamous "I Have a Dream Speech." At the Democratic National Convention in 1988, Reverend Jesse Jackson said, "Use hope and imagination as weapons of survival and progress, but you keep on dreaming, young America […] Keep hope alive!" (97) Hope is also laced throughout Barack Obama's presidency and encapsulated by his campaign slogan, "Yes we can." Radical hope is a throughline of the Black consciousness and imagination that keeps Black Americans afloat in times of precarity.

Most literature approaches the study of hope through a very Western, individualistic lens which emphasizes a bootstrap mentality and belief that the future is shaped exclusively by individual effort and self-determinism. It is important to distinguish this notion from that of radical hope which goes beyond individual desires and actions (98) – radical hope is about committing to a new collective future among a group of people experiencing injustice.

Although new frameworks are emerging that conceptualize hope as a culturally determined value [e.g., see Cherrington's Afrocentric framework (99) and Mosley and colleagues' psychology theory of radical hope (98)], most existing research on hope has come from a Western perspective including Herth's psychological model (100) and Snyder's Theory of Hope (101, 102). According to Synder, hopefulness is a cognitive process comprising three components: (1) *goals thinking* - clear conceptualization of a desired future outcome; (2) *pathways thinking* - the generation of routes and strategies to obtain the outcome; and (3) *agency thinking* - the perception that one can achieve those goals. This theory lends itself to examining potential neuroanatomical and functional correlates of hope.

3.1. Cognitive neuroscience of hope

Prefrontal brain regions likely underlie some components of hope given its emphasis on planning and positing future outcomes (103). Of the few studies examining the neural underpinnings of hope, one study found that higher dispositional hope was associated with lower fractional amplitude of low-frequency fluctuations (fALFF), a measure of fluctuation in resting state BOLD-fMRI signal, in the bilateral medial orbitofrontal cortex (104). Hope was also a significant mediator of the relationship between spontaneous brain activity in the orbitofrontal cortex and symptoms of anxiety. Several studies implicate the orbitofrontal cortex as a region responsible for reward processing and emotion-related learning (105, 106), such that human motivational states (i.e., willingness to act and engage in social behavior) is largely dependent on processing of rewards and punishers. This evaluative process may be closely linked to agency thinking (i.e., belief that one can achieve goals) in Synder's model of hope given the orbitofrontal cortical influence on motivated behavior.

Another study found greater gray matter volume in the supplementary motor area (SMA) was associated with higher hope (107). The SMA, responsible for planning voluntary movements, is also important for mapping cognition to action. This includes inhibiting a response plan, alternating to a new response, and minimizing competing stimuli that interfere with task goals and cause distraction (108). Left SMA lesions are also linked to the executive control (mental manipulation) component of working memory (109) and most closely corresponds to pathways thinking hope.

There is a wealth of positive psychology literature that demonstrates the psychological and physical benefits of hope at the individual level [see (98) and (110) for an overview], which include greater life meaning and satisfaction (111–113), fewer symptoms of anxiety and depression (112, 114–116), less suicidality (112), and feelings of autonomy and purpose (117). Hopefulness is also associated with better recovery from physical illness and injury (116, 118, 119), and positive health behaviors (120).

A large body of work demonstrates that group self-efficacy (i.e., the shared belief that one's group can achieve social change) predicts motivation to partake in collective action (121, 122). Feelings of hope are uniquely associated with Black Americans' collective self-efficacy in that willingness to act on a social matter was present for Black Americans with high hope, but this association was not observed among white Americans in the sample (123, 124). This finding highlights the mobilizing power of hope for Black Americans and how hope is deeply woven into the fabric of Black American existence. Both hope and self-efficacy are necessary antecedents of action toward the future and speak to the unified reclamation of agency that is characteristic of the Black American culture. More studies are needed to understand what it means to hope within a community context and to have a shared sense of purpose.

In sum, radical hope "stretches the limits of what is possible…and belief that it is worth taking the next step" (96, 125). It requires Black Americans' deep examination of our relationship with the past and the future, belief that an alternate future is possible, and a commitment to acting on that future (97, 126).

4. A communal courage

> "I learned that courage was not the absence of fear but the triumph over it. The brave man is not he who does not feel afraid but he who conquers that fear."
> -Nelson Mandela.

The impetus behind any major social justice movement is imagining new ways of being and maintaining hope, but the spark that initiates action and fosters change is courage. Courage is the willingness to act upon imagined possibilities despite fear or possible failure. Asserting one's presence in the future, in a day and age where Black lives are far too often ended prematurely, is a courageous and necessary act.

A core element of courage within a social justice context is that the motivation to act comes from the needs of the community. Most social justice movements have a figurehead who becomes the “face” of the movement, but the work is maintained and propelled forward via on-the-ground mobilization of the community. Thus, it is the collective action — the cooperative behavior of a group to achieve a common goal – that is the backbone of movements for equity. Existing literature suggests that collective action is driven by identity, perceived unfairness, and perceived efficacy (127). There is also alignment of emotions and values across the group which maintains a level of cohesiveness. Amongst the most critical of these shared values is courage. A society, or subgroup, can develop a collective emotional orientation, like communal courage, based on a shared sense of social identity (128). This develops as a byproduct of having shared cultural experiences, processes of socialization, and even racialization.

While there are many different conceptualizations of courage (129), Williams and colleagues (130) delineate the importance of *civil courage* – brave behavior that is specific to social change. This is differentiated from other forms of courage in that civil courage includes indignation about injustice (131). It is also distinguished by the fact that there is a major social cost, or even ostracism, at risk but action is taken regardless due to strong moral imperative (132). This form of courage is exemplified by the Little Rock Nine as the Black teenagers integrated the Arkansas high school in 1957 with escort from the National Guard after being harassed by anti-integrationists. Civil courage was also demonstrated by the four North Carolina A&T students who staged the 1960 Greensboro sit-ins and asked to be served food at a “white-only” Woolworth counter. In both circumstances (and many others), the Black American community moved in solidarity in demonstrating their unwavering support in response to these courageous actions. For example, the college students’ refusal to move and be served food in the Black standing area sparked a wave of 300+ students who joined the protest in solidarity and rippled to other regions around the country to initiate a sit-in movement. This courage in the face of injustice despite huge risk, including the risk of death, remains a testament to the Black American spirit.

Collective courage within a modern-day social justice context may be fostered through: (1) overlap in aspects of identity or lived experience or collective memory, (2) agreement and understanding of the root cause of injustice (e.g., racism), (3) identification of shared goals toward a greater purpose or belief, (4) tolerance of uncertainty and/or risk, and (5) belief that a just and equitable society is possible.

4.1. Cognitive neuroscience of courage

The decision to act in a prosocial manner is a conscious one that requires a specific level of evaluation about the consequences of acting. Civil courage specifically has been noted to rely on (1) internalization of social norms and (2) competency to act when needed (133). There is evidence that the ventrolateral prefrontal cortex plays a role in social reasoning and social norms (134). Additionally, civil courage requires adequate management of fear. Thus, courage is the pursuit of a desired outcome and the willingness to act despite the presence of fear. Fear is an evolutionary safeguard and primary emotion that arises in response to perceived threat or danger (128, 135). It is well established that the amygdala plays a primary role in processing threat and modulates the fear response (136–138). The ventral midline thalamus is additionally critical for one’s response to visual threat in that its nuclei, the xiphoid nucleus and nucleus reuniens, have projections to the basolateral amygdala and the medial prefrontal cortex, respectively (139). Activation of the latter pathway (nucleus reuniens ➔ medial prefrontal cortex) is responsible for the promotion of saliency and arousal. In animal models, activation of this pathway was associated with confrontational responses to threat (139) most consistent with the concept of courage.

One study with a human sample showed fMRI BOLD activity in the subgenual anterior cingulate cortex and right temporal pole was positively correlated with overcoming fear among volunteers who feared snakes but had a live snake moved toward them in an experimental paradigm (140). Somatic arousal (measured by skin conductance level) was attenuated as self-reported fear increased and the participant chose to overcome fear; somatic arousal was elevated in conditions where there was high reported fear and the participant choose to retreat/escape the threat. The subgenual anterior cingulate cortex may be part of the functional neuroanatomical network of courage in that it may inhibit fear-based somatic arousal and increase parasympathetic activity during courageous acts.

Courage operating at the collective level (i.e., communal courage) may have an influence on cognitive health and wellbeing via the social support afforded through ingroup membership, particularly when identifying with a group based on belief in a social justice issue. Social support promotes resilience to stress and adversity (141). Both stress and adversity are factors that have adverse effects on cognitive functioning via hypothalamic pituitary adrenal axis (HPA) dysregulation (142) and inflammation (143), and may increase risk for dementia (144, 145). Lifetime stress is associated with memory decline among middle aged Black Americans (146). In their systematic review of the literature, Kelly and colleagues (147) found higher levels of social support was associated with better general cognitive functioning, and less social support was associated with slower processing speed with a portion of these findings attributable to depression symptoms. Strong social support built through engaging in a collective goal or vision for the future may operate as a buffer against the stress that can come with acting in courageous ways.

5. Toward health and healing justice

The Black radical imagination is a conduit to possible futures rooted in health and healing justice for Black Americans. Both health and healing are liberatory for communities experiencing systemic oppression, which has been described as “society selectively concentrating trauma” (148). For those who are subjects of oppression, this trauma becomes embodied [i.e., integrated at the biological level (149)] and there is a wealth of evidence demonstrating its negative effects on Black bodies (16, 17, 20, 150) and minds (151–156). For example, the detrimental impact of oppression is evidenced in the links between systemic racism and Black women’s higher allostatic load (157) and advanced cellular and biological aging (158, 159). In fact, the weathering hypothesis (i.e., the postulation that Black women’s chronic exposure to stress to accelerates aging and results in health decline) was developed to characterize these environment-biological interactions specific to the intersectional oppression Black women experience (158, 160).

Both chronic stress and trauma contribute to changes at the neuroanatomical and cognitive levels (161–163). However, the neurological and neuropsychological impact of an American history fraught with racism is just now being more deeply explored. Racial discrimination, a direct form of race-based traumatic stress, is associated with lower total brain volume (164), lower fractional anisotropy in the corpus callosum, cingulum, and superior longitudinal fasciculus (165), and heightened activation in brain regions associated with threat vigilance (middle occipital cortex) and threat response (ventromedial prefrontal cortex) (166). There is also evidence that experiences of discrimination are associated with higher levels of spontaneous activity in the amygdala and stronger functional connectivity between amygdala with other neural regions (167) and future work is needed to determine whether this translates to an increase in physiological arousal and/or vigilance. These findings highlight how interpersonal encounters of race and identity-based mistreatment get "under the skin" to influence brain biology.

There is emerging evidence of the links between racism and ADRD among Black Americans (53, 70, 168). Cognitive aging is strongly impacted by the social environment and may be accelerated among Black American by exposures to structural racism across the life course. For instance, laws, public policies, and societal beliefs, shaped by structural racism, differentially allocate health-promoting resources and disadvantage racially and ethnically minoritized populations (169). Manifestations of structural racism can be observed in laws and practices impacting differences in educational quality (170), racial residential segregation (15), access to green space (171), political disempowerment/voter suppression (172), policing (152, 173), and mass incarceration (21, 22), all of which are associated with health inequity (174, 175) and may confer ADRD risk among Black Americans.

Collectively, these findings are confirmation of what Black people have long known – the body keeps the score. The Black body also tells its history. Trauma is transmitted across bodies and over time, and there is evidence that trauma manifests intergenerationally (176). As such, Black healing and health, down to changes initiated at the cellular level, are inextricably linked to Black liberation. Black healing is a liberatory praxis and can be achieved through the radical imagination.

Thus, part of the radical imagination encompasses Black people designing and discovering new ways of being in relation to one's body to facilitate health and healing. This discovery must also center the experiences and desires of young Black girls (177) as well as elders -- those who exist at the margins of society and are overlooked in the process of knowledge production. Importantly, the onus should not be placed on Black people to "fix" a societal problem that was not designed by them; however, Black people deserve to and can live well despite existing injustices. Re-imaging collective wellness is one way of doing so.

The Kindred Southern Healing Justice Collective (178), a grassroots collective of southern healers and health practitioners who address trauma through models of collective wellness, is an excellent example of the radical imagination and healing in practice. Cara Page, one of the founding members of the collective introduced the framework of healing justice (179) – which "identifies how we can holistically respond to and intervene on generational trauma and violence, and to bring collective practices that can impact and transform the consequences of oppression on our bodies, hearts and minds." Healing justice addresses significant gaps in Western medicine through its application of indigenous and ancestral knowledge systems and focus on holistic (mind, body, social, spirit) wellness. Healing within community for Black Americans may look like participation healing circles (180, 181), storytelling or oral tradition practices (182, 183), or engaging in rituals or ceremonies (184), which are culturally-affirming, strengths-based, and empirically supported approaches.

Little academic literature focuses specifically on healing justice as a framework, except for one systematic review (185), likely because "alternative" forms of healing are often overlooked due to epistemic exclusion (186, 187)--a general devaluating and delegitimizing of work that does not fit within Western ways of knowing or healing. However, a great deal of care has been given to healing justice in organizing and social justice spaces.

Extending the Black radical imagination to address issues of cognitive health disparities and the impact of systemic oppression on brain health is critical for Black aging futures and healing justice. Consider: What would it mean for Black Americans to have the space and time to dream of a better future and truly believe the desired outcome is possible? What would it look like for those outcomes to be actualized in this lifetime? What would Black healing look like at the deep cellular level, and what implications would it have for future incidence of ADRD and other physical and mental health conditions? It is through the radical imagination that we create new realities where all have an equal chance of making it to the future.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

The author confirms being the sole contributor of this work and has approved it for publication.

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Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Understanding social attachment as a window into the neural basis of prosocial behavior

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The representation and demonstration of human values are intimately tied to our status as a social species. Humans are relatively unique in our ability to form enduring social attachments, characterized by the development of a selective bond that persists over time. Such relationships include the bonds between parents and offspring, pair bonds between partners and other affiliative contacts, in addition to group relationships to which we may form direct and symbolic affiliations. Many of the cognitive and behavioral processes thought to be linked to our capacity for social attachment—including consolation, empathy, and social motivation, and the implicated neural circuits mediating these constructs, are shared with those thought to be important for the representation of prosocial values. This perspective piece will examine the hypothesis that our ability to form such long-term bonds may play an essential role in the construction of human values and ethical systems, and that components of prosocial behaviors are shared across species. Humans are one of a few species that form such long-term and exclusive attachments and our understanding of the neurobiology underlying attachment behavior has been advanced by studying behavior in non-human animals. The overlap in behavioral and affective constructs underlying attachment behavior and value representation is discussed, followed by evidence from other species that demonstrate attachment behavior that supports the overlapping neurobiological basis for social bonds and prosocial behavior. The understanding of attachment biology has broad implications for human health as well as for understanding the basis for and variations in prosocial behavior.

KEYWORDS

attachment, prosocial behavior, values, comparative neurobiology, pair bonds, oxytocin

Introduction

Social attachments are essential components of human social behavior, forming the basis for relationships between parents and offspring, romantic partners, friends, and even the bonds felt toward ideological or cultural groups. Attachment behavior is often defined by the selective, enduring bonds formed between offspring and a parent or caregiver as well as between unrelated partners or peers in adolescence and adulthood (1–3). A core feature of attachment theory is the existence of a caregiving relationship, typically from adult to child, that is fundamental to guide the development of prosocial behaviors such as empathy, cooperation, reciprocity, and consolation (4–7). Across species, prosocial behaviors are defined by the voluntary actions intended to benefit other individuals (8). In humans, such prosocial behaviors and attitudes are commonly integrated into culturally shaped individual values, defined as the motivations, beliefs, and goals that guide behavior (9). The innate construction of an attachment framework in early development, shaped by learned cultural attitudes and subsequent social experiences, may provide a primary scaffold upon which moral principles and value systems are built.

Early attachment experiences, as formalized by Bowlby and Ainsworth (1, 2, 10), have primarily been described in the relationships between parents and offspring, which are thought to have longstanding effects on subsequent close relationships as well as on broader social development (11–13). Subsequent attachments between mates are typically organized around the formation and maintenance of pair bonds (11, 14). These bonds are also associated with physiological distress upon separation from the pair-mate, and reduced anxiety with reunion (11, 15, 16). Regardless of social, marriage, or mating systems across cultures, pair-bonds are a ubiquitous feature of human relationships (17, 18). Humans are not unique in their ability to form such bonds, but are one of the 3–5% of mammals that form sustained, selective affiliations (19–21). Similarly, prosocial behaviors are identified across species, and in non-human animals may include grooming, support and protection, and food sharing. The neurobiology underlying long-term bonds in both humans and non-human species has been a focus of intense interest and study over the past several decades and is thought to be conserved across species that display attachment behaviors (22–24). The high level of conservation hints at the centrality of these behaviors across phylogeny and indicates that considering the biology of model organisms alongside theories of human social organization may provide powerful entry points into understanding prosocial behavior.

While prior work has explored the link between attachment behavior and the development of prosocial values (4, 6, 25), the perspective that follows suggests that the antecedents to prosocial and ethical behavior exist across species that form long term attachments. This is not to suggest that there is equivalence in the affective and behavioral states experienced, but that there are powerful precursors to prosocial processes present in non-human species. The great apes, some species of monkeys, and birds, among other species, demonstrate behavioral and affective features that approximate those of human social emotions (26–29). Here, I examine two components of prosocial values, social openness (defined as the tendency toward social contact and approach over avoidance or fear) and empathy as examples of constructs that are strongly linked to attachment behavior. I then examine the evidence for conserved underlying neurobiology mediating attachment behavior and prosocial values. Disruptions to these processes play a role in neuropsychiatric diseases that preferentially impair attachment behavior. An understanding of the overlapping neurobiology may have relevance not only to cognitive health but to social health more broadly.

Integrating social attachment and prosocial behavior

The relationship between social attachment and prosocial behavior has been examined previously in the psychological literature (4, 23, 30). Shaver et al. in their Handbook of Attachment put forward that attachment theory, which describes a framework for social-emotional behavior primarily through development (2, 12) is, fundamentally, "a theory of prosocial behavior" (13). Interactions with attachment figures, commonly parental figures, through development shape the mental representations of others. When positive, these attachment relationships provide an enduring sense of safety and security, and the ability to recognize and regulate emotions (7, 13). Studies in adolescents find that secure attachment to parents contributes positively to compassionate, empathic responses to people in need (31, 32). Studies that have directly examined the relationship between the development of social values and adult attachment find that more secure attachments in adulthood are associated with increased prosociality, as measured by social value orientation (the balance of an individual's preference to allocate resources to the self or to others) (33, 34). Similarly, attachment quality and style with a primary caregiver are associated with the degree of altruistic helping seen in adults (35). Attachment style is correlated with the degree of exploration, curiosity, empathy, as well as fear of strangers and openness to others exhibited by adults (5, 36).

Comparative studies across species allow us to observe the "primitive" underpinnings of moral behavior in animals, while also allowing for experimental manipulation of neurobiological mechanisms involved in the representation of constructs such as empathy, fairness, reciprocity, social reward, and social openness (37, 38). A wealth of data from other species suggests not only that there is a neural substrate for attachment and prosocial behavior, but that it also developed by evolutionary selection (19, 39). Across species, social attachments have been defined by similar patterns of behavior, including mate (or pair) bonding, biparental care, and peer affiliation (36, 40). Adult pair bonds are characterized by long-term, preferential mating between two individuals and the active rejection of novel potential mates (14, 17, 41). In non-human primates, prosocial behaviors are present, including reciprocity, mutual assistance, retributive justice, reconciliation, consolation and openness to social engagement and sustained contact (42). Among these, social approach vs. avoidance and empathy and consolation are thought to be shared across species, including in rodents (30, 42, 43).

Our ability to engage in cooperation, sharing, and helping, all key components of prosocial behavior, depends upon a tendency toward social approach as opposed to social threat and fear. However, equally essential to successful social navigation is the selective engagement of such prosocial behaviors within a social network stratified by the strength of attachment relationships (44). The biological function of an innate attachment system is thought to serve to obtain or maintain proximity to significant others and caregivers in times of need or in the presence of threats, and thus to regulate support seeking behavior (4). Across species, social affiliation requires reduced physical distance and reduced threat or fear responses with close contact. In non-human animals, attachment is often measured as selective proximity-seeking and maintenance between individuals. This has been operationalized, for example, in partner-preference tests used to assess pair bonding in prairie voles, socially monogamous species that form long-term attachments (45, 46). The maintenance of proximity by two animals has been conceptualized as a cooperative behavior, one that facilitates and comes to define the pair bond (47). Social engagement and broader prosocial behaviors, including resource sharing, care-taking, and consolation, require a perception of safety, the capacity for which may be established by the nature of early attachment experiences (30).

Early attachment relationships may also shape our capacity for empathy, an essential component of prosocial values. Empathy comprises both the sharing of emotions between individuals and the adopting of another's point of view. The communication of emotional states ("emotion contagion") as well as consolation behavior and reconciliation are components of empathy that can be examined in non-human animals. The latter two may reflect cognitive processes required for perspective taking (26). Highly social animals, such as humans, apes, corvids, and elephants, show both aspects of empathic response (26, 28, 29, 48). Consolation and reconciliation behavior have been well-characterized in chimpanzees (49, 50). Rhesus monkeys will refuse to pull a chain that delivers food to themselves if doing so shocks a companion (51, 52). Emotion contagion is likely to be present even in rodent species (53, 54). Church (53) found that rats that press a lever to obtain food, stop lever-pressing if that action is paired with delivery of a shock to a neighboring rat. The communication of emotional state is well-described across species and may have a basis in synchronized neural activity between interacting individuals. In a recent study, pairs of socially interacting mice exhibited interbrain correlations of neural activity in prefrontal cortex (PFC) that predicted future social interactions (55). While consolation behavior has not been described in commonly studied rodent species like mice and rats, prairie voles do exhibit consolation behavior characterized by allogrooming of a stressed companion (56). Such findings of shared emotional states and consolation behaviors have supported the view that non-human animals exhibit primitive, but likely neurobiologically conserved, forms of empathy (43, 57).

Overlapping neurobiology of attachment and prosocial behavior

Compared to other species, human and non-human primate maternal and pair-bonding behaviors are more complex and flexible and are likely shaped to a greater degree by early experience. However, the underlying circuitry mediating such bonding behaviors is likely conserved across species. Activity in regions including the amygdala, ventrotegmental area (VTA), hippocampus, anterior cingulate cortex (ACC), insula, and temporal cortex has been implicated in attachment behavior in humans and other species (23). The ACC, in particular, processes information integrating social affective and representational processes (58). The insula, particularly the anterior insula, is thought to encode interoception, as well as affective states associated with physiological processes across species (59). Studies of attachment-related neural responses in humans have commonly examined parents' neural responses to their own infant vs. an unfamiliar infant. Increased connectivity between the ACC and anterior insula is found when parents view their own infant– supporting a hypothesis that synchronized activity across these regions consolidates attachment representations (60). The ACC and anterior insula are also highly implicated in empathic responses in humans, particularly in studies examining empathic pain (61). In comparison to neutral situations, painful conditions elicit significant activation in these regions. The ACC in rats may encode a primitive of fear or pain contagion as neurons in this area respond to both experienced pain and the pain of others (62), and insular cortex in rats mediates age-dependent approach vs avoidance of stressed conspecifics (63). While these regions do not selectively encode attachment and support multiple affective processes associated with social and non-social contexts, research across species has repeatedly implicated these regions in the formation and maintenance of long-term bonds (23, 24).

Work across species has shown that specific neuroendocrine mediators, in particular oxytocin, may act on similar neural circuitry to that described above to mediate many of the correlates to prosocial behavior (64, 65). Oxytocin has been linked to a host of prosocial processes and particularly to attachment behaviors across species. In humans, the oxytocin receptor (OTR) has been associated with empathy, emotion recognition, and socioemotional engagement (66–68). Oxytocin has pleiotropic actions in the brain, but is thought to mediate threat states, somatic and visceral encoding, including pain responses, as well as cognitive processes related to learning and memory and reward as they apply to social behavior (69). The effects of peripheral administration of oxytocin have been described across species with regards to prosocial and cooperative behaviors. In primates as well as monkeys, oxytocin administration facilitates cooperation and pair bonding (70, 71). Marmosets given intranasal oxytocin initiated more bouts of huddling than non-treated animals, and administration of antagonists to OTR eliminated food-sharing between partners (71). In prairie voles, where the oxytocinergic system has perhaps been most extensively studied for its role in attachment, OTR is highly expressed relative to non-monogamous species in the ACC, PLC, anterior insula, and NAc (72, 73). OTR antagonism in the ACC in voles specifically abolished consolation responses toward cagemates that experienced an unobserved stressor (56). In mice, intranasal oxytocin enhances observational fear as well as neural activity within the ACC (74). While it has become increasingly evident that the role of oxytocin in regulating social behaviors is complex and highly context- and stimulus-dependent (75–77), it remains a candidate for coordinating and organizing the underlying components of prosocial behaviors discussed above.

Attachment behavior influences health across the lifespan

It is clear that attachment behavior has profound implications for human health. The development of close relationships early in life is essential for defining one's identity and group affiliations (78, 79) and in surviving to mate and raise offspring. Further, the formation and maintenance of long-term bonds has profound effects on physical and mental health throughout the lifespan (80–82). Intact, close social relationships consistently confer a benefit on diverse health outcomes, while the loss of close relationships and isolation have profound detrimental effects on human health. For example, stronger social relationships, measured by relationship quality, decrease the risk for all-cause morality by 50% (82), similar in effect size to interventions related to diet and physical activity (83). Conversely, decreased social interaction is significantly associated with incident dementia, with a relative risk similar to that of other established risk factors, such as low educational attainment, inactivity, and late-life depression (84, 85).

Data across numerous studies reveal a clear effect of disrupted attachment relationships on all-cause mortality, cardiovascular health, metabolic function, and dementia (86–91).

Interestingly, the same circuits and brain networks implicated in attachment are those commonly disrupted across neuropsychiatric diseases that affect prosocial behaviors, such as behavioral variant frontotemporal dementia (bvFTD) (92–95). bvFTD is characterized by a loss of empathy and often impulsive, disregard for social norms (96), which fundamentally disrupt relationships with attachment figures. These social and emotional deficits correlate with significant degeneration in ACC and orbital frontoinsula (97, 98). The overlap between attachment neurobiology and the circuitry implicated in prosocial deficits in disease highlights the conservation of the underlying processes and their relevance to human health. In this issue Raya et al. propose that the rigidity and perseveration exhibited by patients with FTD reflects a decrease in openness that is linked to atrophy of dlPFC and ACC (99, 100). The deficits in empathy may also involve altered activity in the right anterior temporal lobe and medial frontal regions in FTD patients (101). Such disruptions to the neural circuitry of attachment have profound implications for patient quality of life as well. In dementia patients, and particularly those with bvFTD, decreases in empathy are associated with relationship dissolution and infidelity (102). Further, a rich body of literature has focused on the interactions between caregivers, who are often family or spouses and other attachment figures, and dementia patients and the impact on caregiver wellbeing and health (103–105). While caregivers of those with chronic conditions have been noted to exhibit increased empathy and prosocial behaviors in some studies (106), the ability to maintain attachments with the care recipient may be impacted by conditions like bvFTD with subsequent adverse effects on health outcomes for both the patient and caregiver.

One can also turn to attachment neurobiology to examine deviations from prosocial attitudes that support the values described above of empathy, compassion, reciprocity, etc. Our tendency for inter-group violence, prejudice, and bias may reflect another side of the same attachment biology (107). The development of the circuitry underlying attachment early in life drives the display of culturally normative pro-social values later in life, but may also facilitate tendencies toward out-group bias and persecution. Severe disruptions to attachment development result in profound adult social deficits (3, 108). Neglect from early attachment figures may lead to impaired bond formation later in life, as well as impulsive behaviors including violence (5). Even with typical attachment development, the formation of culturally-derived value systems and intragroup attachment is intricately tied to the neurobiology of human ethnocentrism—the tendency to judge other cultures based on standards of one's own culture (109). Such group-directed prosocial processes may simultaneously promote intergroup "antisocial" tendencies. These processes have relevance in considering care and treatment for dementia patients at both an individual and societal level. It is well documented that conditions like dementia and other neuropsychiatric diseases that may impair attachment behavior continue to be stigmatized (110, 111). This is particularly so for minoritized populations with neurodegenerative conditions, leading to decreased access to and quality of care (112, 113). Deficits in attachment and prosocial behavior that occur in conditions like FTD may further exacerbate stigmatization and ethnocentrism already demonstrated toward patient populations. Understanding these innate tendencies as reactions of the same neural system will help to elucidate both our profound capacity for prosocial and altruistic action as well as the selective withdrawal of such compassionate behaviors toward those of other groups.

The neuroendocrine mechanisms described above may provide insight into the seemingly dichotomous roles of the attachment system in mediating value-based behaviors. One prominent theory regarding oxytocin's effects on behavior suggests that while oxytocin acts to motivate in-group preference and cooperation, it simultaneously promotes out-group "derogation" (77, 109, 114). Several studies in humans have shown that peripheral administration of oxytocin is associated with increased in-group bias and that oxytocin may facilitate the emergence of intergroup conflict and violence (114, 115). In the context of attachment more specifically, the formation of a preference for a partner across species is also accompanied by rejection, often aggressively, of a novel mate (14, 40). Thus, understanding the antisocial correlates of attachment neurobiology may be key to examining the etiology of prejudice, xenophobia, and intergroup violence.

Conclusion

Our unique ability to display selective affiliation not only with other members of our species throughout life but with social constructs such as nationality, religion, and social identity forms the basis for societal values and prosocial ethics. Early relational experiences direct the development and patterning of prosocial motivations and behaviors and have profound effects on brain health later in life (3, 5). The potential for attachment behaviors to serve as proxies in other species for components of value-based behaviors may allow us to examine, manipulate, and causally interpret such behaviors in a way that has previously not been possible in the study of human values. Comparative work on the neurobiology of attachment offers entry points into the circuitry underlying value evolution, formation, and structure as well as the mechanisms underlying disruptions to value systems in disease and common variations of human social behavior. Leveraging such understanding may allow for interventions that facilitate attachment to diverse groups and ideologies, consequently expanding prosocial responses to broader populations while reducing intergroup bias (116). Interventions such as attachment-based family therapy or school-based holistic intervention programs that are focused on early-life interactions between family members and peers have proven beneficial in promoting prosocial behaviors in children and adolescents (117–119). Adapting such programs to other stages of the lifespan may lessen neuropsychiatric symptom burden in certain populations, reduce caregiver burnout, and enhance overall quality of life for both patients and care providers (105, 120–122). Thus, a deeper neurobiological understanding of prosocial thinking and the early attachment experiences that shape it may facilitate our progression toward a more inclusive and global moral position.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

KB conceptualized, planned, and wrote the manuscript.

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Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The reciprocal relationship between openness and creativity: from neurobiology to multicultural environments

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The desire for novelty and variety in experiences, which may manifest in an inclination to engage with individuals from a diverse range of cultural backgrounds, collectively constitutes the personality dimension known as "Openness to Experience." Empirical research has identified a positive correlation between trait openness and various expressions of creativity, such as divergent ideation, innovative problem-solving strategies, and cumulative creative accomplishments. This nexus between openness to interpersonal diversity, as an aspect of the larger personality trait of openness, and creativity has precipitated considerable scholarly interest across the disciplines of personality, social and organizational psychology, and neuroscientific investigation. In this paper, we review the neurobehavioral properties, including the cognitive processes and neural mechanisms, that connect these two constructs. Further, we explore how culture influences levels of openness and creativity in individuals and consider how creativity predisposes individuals toward openness to a plethora of experiences, including those occurring in culturally diverse contexts. This reciprocal entanglement of creativity and openness has been shown to foster a reduction in biases, augment conflict resolution capabilities, and generally yield superior outcomes in multicultural environments.

KEYWORDS

openness to diversity, creativity, multicultural environment, salience network (SN), default mode network (DMN), executive control network (ECN)

Introduction

Openness, as a high-level construct within the Five-Factor Model of personality traits (1, 2), includes various facets such as imagination, perceptiveness, and intellect (3–5). These facets configure a spectrum of cognitive and behavioral patterns and habits (6) associated with various attributes such as broad-mindedness, creativity, intellectual sophistication, curiosity, cognitive flexibility, receptivity to diverse perspectives and cultural practices, desire for novelty, as well as appreciation for varied experiences, values, and beliefs (5, 7, 8).

Openness to experience, a key facet of this broader trait (4, 5), specifically pertains to the degree to which an individual is receptive to novel experiences and divergent forms of thought (5, 9). Individuals who score high on this trait tend to engage in a broad range of interests, are highly imaginative, and typically exhibit a heightened sensitivity to art and beauty. They are prone to introspection and often have an intricate and nuanced emotional life (4, 5, 7). Openness to experience can also specifically entail greater openness to diversity, meaning the predisposition to engage with, appreciate, and respect different perspectives and values, including those coming from other cultures (6). This dimension not only encapsulates a willingness to comprehend and accept cultural differences, but also to adopt new cultural practices and to challenge conventional norms when considering new perspectives and nontraditional values. An individual's capacity for openness, particularly when expressed as an openness to diversity, influences their ability to navigate effectively and thrive in culturally heterogeneous environments, and has been shown to correlate with a reduction of in-group biases, improved intercultural communication, and better conflict resolution skills (6, 10–12).

Creativity, a distinct construct that is nonetheless highly related to the personality trait of openness, describes the mental agility needed to perceive and embrace novel esthetic and intellectual information in order to synthesize it with the goal of generating original ideas, concepts, and works of art (6, 9, 13, 14). While openness does not in itself presuppose generation of novel work but is limited to an attitude of receptiveness toward novelty, creativity by definition involves the production of novel intellectual, esthetic, or physical materials. Silvia and colleagues found that trait openness was a significant predictor of creative achievement across several domains, including writing, visual arts, and music (9). Individuals high in trait openness are more likely to engage in activities that expose them to a broad range of experiences, and this exposure can provide them with a greater repertoire of knowledge and ideas that can be drawn upon during the creative process (15, 16).

Measuring the different facets of openness

The relationship between openness to experience and creativity is intricate, and they share interconnected measurement approaches within the psychological research domain. These measures serve as psychometric lenses, affording researchers nuanced insights into individuals' cognitive and affective orientations toward novelty and diversity.

In psychometric parlance, openness as a personality trait is often assessed through various theoretically grounded behavioral scales that measure different facets by employing standardized self-reported or other-reported questionnaires. For instance, the NEO Personality Inventory is a widely used tool to measure openness. It assesses this trait across six facets: Fantasy, Esthetics, Feelings, Actions, Ideas, and Values (2, 10, 17). The Fantasy facet gauges a person's level of imagination, creativity, and daydreaming tendency. Esthetics measures their appreciation of art, music, and beauty. Feelings examines emotional awareness, sensitivity, and intensity of emotions experienced. Actions evaluates adventurousness, risk-taking propensity, and preference for novelty. Ideas assesses intellectual curiosity, open-mindedness, and appreciation for new concepts. Lastly, the Values facet gauges openness to alternative belief systems, such as spiritual or religious beliefs (10). Additional questionnaire tools include the HEXACO model, which adds an emphasis on the ethical and moral aspects of openness while introducing the Honesty-Humility dimension (18, 19), and the California Psychological Inventory (CPI), which assesses traits that researchers believe are related to openness, such as intellectual efficiency, creativity, and esthetic appreciation (20).

However, openness is also measured via direct neuropsychological assessments where openness is conceived to be reflected by the volume and quality of creative output, conflating the constructs of openness and creativity. One such creativity measure is the Torrance Tests of Creative Thinking (TTCT), which evaluates the performance of tasks requiring divergent thinking and problem-solving skills, and gives examinees higher scores as a result of greater volume and novelty of output (21, 22).

In addition to measures examining openness more broadly, several other tools are used in research settings to explicitly quantify Openness to Diversity and Cultural Openness. The Multicultural Personality Questionnaire (MPQ) (23) assesses seven dimensions, including Cultural Empathy and Open-mindedness, which together gauge an individual's openness to cultural diversity. The Intercultural Sensitivity Scale is another instrument measuring an individual's ability to modify behavior in response to different cultural norms, thus capturing their level of cultural openness (24). The Miville-Guzman Universality-Diversity Scale (M-GUDS) serves as a measure of "universal-diverse orientation," a psychological construct similar to openness to cultural diversity, which quantifies individuals' comfort and interest in interactions with people from diverse cultural, racial, and social backgrounds (25).

Shared cognitive processes and neural mechanisms underlying both openness and creativity

The cognitive processes underlying both openness to diversity and creative thinking involve divergent and convergent thinking, which are distinct but complementary cognitive processes (9, 14). Divergent thinking involves the ability to generate a wide range of possible solutions or ideas to a problem, often through brainstorming or free association. This involves exploring multiple perspectives and possibilities and is often associated with creativity and innovation. It is clear why divergent thinking supports openness to diversity, as it involves being open to a wide range of perspectives, experiences, and ideas from different cultural backgrounds. This can expand the range of possible solutions and approaches to a problem, leading to more creative and innovative outcomes. Openness to diversity can also facilitate divergent thinking by allowing one to make broader associations beyond any stereotypes or biases that may limit the range of ideas generated (14, 16).

However, divergent thinking alone may not lead to effective solutions or choices, as it can result in many possible but often unfeasible ideas. Convergent thinking involves the ability to narrow down a set of options to identify the most appropriate or effective solution to a problem. Yet, this activity is also supportive of both creativity and openness to diversity. This process underpins the drive to actively investigate available options with the goal of finding the most appropriate, often the novel solution in order to resolve a problem or conflict (3, 4, 9, 26), which is an essential component of effective creativity.

Another important promoter of both openness to diversity and creative thinking is the capacity to overcome biases, since implicit biases can act as a barrier to openness to novel cultures and other types of diversity. These biases are unconscious mental shortcuts and stereotypes that individuals use when processing information about others, which can lead to unfair judgments and discrimination against others, particularly when individuals are from cultures and backgrounds with which one has not had extensive experience. Biases can limit the range of perspectives and ideas generated, leading to narrow and uncreative solutions. By being mindful of their biases and actively challenging them, individuals can expand their range of perspectives and ideas, leading to more creative outcomes (14).

The neurocognitive processes underlying both creativity and the capacity for openness rely on an overlapping core of brain networks that include a large set of brain regions, including the amygdala, fusiform gyrus (FFG), insula, ventral striatum, locus coeruleus (LC), anterior cingulate cortex (ACC), posterior cingulate cortex (PCC), and lateral and medial regions of the prefrontal cortex (PFC) (16, 27–32). These structures work together in complex networks to help us perceive and interpret the world around us, consider new ideas and perspectives, draw on our own experiences and beliefs, inhibit biases and automatic responses, and appreciate the perspectives of others. As shown imaginatively in Illustration 1, these structures might be conceptualized as lenses and filters through which we receive and process information about the world, shaping the foundation from which we choose our beliefs and behaviors.

Initially, we perceive the world around us using different brain areas that receive different sensory inputs (visual, auditory, or tactile sensations) via the sensory cortex. An important brain region that is involved in visual perception in interpersonal contexts is the fusiform gyrus (FFG), which is involved in face recognition and therefore contributes to social cognition (29). The FFG is part of a larger network of secondary association cortex that includes the superior temporal sulcus (STS) and other regions that are important for recognizing and processing social information, such as emotional expressions, body language, and features relevant to social hierarchies and status.

Next, this sensory input automatically activates areas that are involved in our emotional reactions and our estimates of reward. Regions of the limbic system, like the amygdala, play a key role in processing emotional information, including fear and aggression, and the ventral striatum and other subcortical regions are involved in reward processing. These regions have also been long understood to directly underpin stereotyping and prejudice, as they contribute to both the negative emotions toward non-native ideas, individuals, and practices that engender exclusionary and antagonistic attitudes, as well as the positive appraisals and reward engendered by in-group individuals and behaviors (26, 29, 33, 34).

Once input passes through the sensory and the limbic systems, in the next stage, attentional and motivational processes engage and modulate the information, mediated by the insula and the dorsal anterior cingulate cortex (dACC), which together comprise the salience network (SN) (35–37). The anterior insula receives multimodal input comprised of a combination of sensory, affective, and visceral afferents, which it rapidly filters to determine what is relevant to the safety, survival, or well-being of the individual, and thus is worthy of additional attention. The dACC plays a role in motivating reactions to these multimodal inputs and modulating autonomic reactivity accordingly.

The SN interacts reciprocally with two other major networks: the default mode network (DMN), which uses internally generated experiences in decision-making, and the adaptive executive control network (ECN), which divides attention and exerts top-down control (16). More specifically, the DMN includes regions such as the medial prefrontal cortex (mPFC), posterior cingulate cortex (PCC), and inferior parietal lobule (IPL) (38). The DMN is the only internally-oriented network in the brain, in the sense that it does not directly respond to or act upon sensory stimuli, but engages in internally generated material such as memories, emotions, and predicted schemas about the world, and is thought to play a role in mind-wandering, introspection, creativity, and interpersonal perspective taking (35, 38). The ECN includes the dorsolateral prefrontal cortex (dlPFC) and the dorsolateral parietal cortex and is active during active thinking, planning, reasoning, and making decisions. While the DMN adds a self-referential, internal dimension to how our sensory and emotional inputs are processed, the ECN exerts top-down control of these inputs by adding the external dimension of conscious planning and reasoning prior to decision-making. The SN also contributes to these processes by monitoring the activity of the ECN and DMN and facilitating flexible switching of attention between the internal and the external streams of thought (26, 36). An important construct that modulates the interactions across those different networks is the noradrenergic system of locus coeruleus (LC) (36). The LC's interactions with the limbic system, SN and DMN exert significant influence on visual and sensory processing by regulating the salience of stimuli, enhancing attention to novel or behaviorally relevant information, and modulating sensory gain, which extends to shaping biased behaviors, attitudes, and responses to novelty (27, 28, 36).

The contribution of each of these brain networks to both openness and creative cognition is summarized in Tables 1, 2.

The reciprocal relationship between openness to cultural diversity and creativity

Several studies suggest a reciprocal relationship in which openness to experience more generally, and openness to cultural diversity more specifically, act to foster creativity by generating greater exposure to new and diverse cross-cultural interactions (9, 15). Multicultural exposure, when facilitated by a habit of openness, encourages individuals to be curious about and investigate novel perspectives, ideas, and beliefs, even when they are different from their own. The process of gaining a deeper understanding of the nuances that make each culture unique provides new knowledge and inspiration for innovative thinking and problem-solving (54). Subsequently, individuals are thereby more likely to creatively incorporate various novel cultural influences into their work, which facilitates cognitive flexibility and the generation of new ideas in a positive feedback loop (15, 55). Moreover, exposure to diverse cultural perspectives has been demonstrated to help individuals to better understand and empathize

TABLE 1 Neural regions and networks associated with openness and creativity.

Brain region	Role in openness and processing of stereotypes	Role in creative processing
Limbic and salience networks		
Ventral Striatum/vmPFC	Involved in reward processing, reinforcement learning, and emotion regulation, which can influence one's openness to diversity and motivation to seek out new experiences and perspectives (39, 40).	Play a role in creative cognition by integrating emotional and motivational factors into idea generation and evaluation. Of potential outcomes of different decisions and choose the most innovative and rewarding option (41).
Amygdala	Provides automatic alerting signals in response to previously learned threats and rewards. This contributes to generating emotional responses associated with stereotypes and biases, which may influence the degree of openness to previously threatening experiences or ideas (29, 33, 42, 43).	Alerts to stimuli that are novel or have emotional valence, allowing attention to novel and stimulating ideas and experiences (29).
Insula	Involved in emotion processing and interoceptive awareness, which can influence one's attention to different experiences and perspectives (42).	Plays a role in the creative process by integrating emotional and bodily signals to guide idea generation and evaluation (44).
dACC	Involved in conflict monitoring and error detection, which can facilitate perspective-taking and overcoming biases in social contexts (29, 43, 45).	Plays a role in the degree to which one is likely to reinterpret novel, complex, or conflicting information as aversive vs. positive. Involved in behavioral motivation, thus can influence the degree to which one seeks out novel experiences and ideas (26, 31).
FFG and other cortical secondary association areas	Involved in the higher-order processing and interpretation of sensory information, including faces, voice prosody, and body postures and gestures, which can influence one's perception of and attitudes toward diversity (29).	May contribute to creativity by facilitating the recognition and association of novel visual or other sensory stimuli in a socio-emotional context (31, 46).
The default mode network		
dmPFC	Involved in aspects of social cognition that rely on perspective-taking and self-referential thought, such as mentalizing about similar and dissimilar others, which is crucial for developing intercultural sensitivity and overcoming stereotypes (47).	Self-awareness, mentalizing, and autobiographical memory allow us to connect emotionally with others as well as draw upon our own experiences and perspectives to generate new and innovative ideas (48).
	Also maintains a schema for predictions and expectations in a social context on the basis of autobiographical experience, which can influence one's cognitive biases and expectations in diverse or novel situations (29, 49).	Plays a role in creative cognition by facilitating the integration of multiple sources of information and experience for predictions and concept generation, supporting the generation of novel solutions and spontaneous ideas (44, 49).
PCC	Involved in self-referential processing and perspective-taking, allows us to see things from different points of view and consider alternative perspectives and be more open-minded when evaluating new ideas (29).	May be involved in divergent thinking and the processing of creative stimuli (26, 44).
IPL	Involved in sensory integration and spatial cognition, which can support perspective-taking and cognitive flexibility (29).	May play a role in the creative process by facilitating the manipulation and transformation of mental representations (44).
The executive control network		
IFG	Involved in inhibiting automatic responses and generating "stop signals," as well as engaging reappraisal of emotions by relabeling emotional experiences, and thus contributes to regulation and moderation of automatic stereotypes and biases (29).	Supports creativity through its function in detecting novelty and redirecting attentional resources toward novel stimuli (31, 50).
dlPFC	Exerts top-down cognitive control, set-shifting, inhibitory processes, and goal-directed behavior, which can support cognitive flexibility and openness to different viewpoints. This contributes to the explicit inhibition of biased thoughts and behaviors and the promotion of flexible and nuanced representations of others (29, 43).	Plays a role in the creative process by facilitating idea generation, evaluation, and selection (44, 50).

vmPFC, Ventromedial Prefrontal Cortex; dACC, Dorsal Anterior Cingulate Cortex; PCC, Posterior Cingulate Cortex; FFG, Fusiform Gyrus; IPL, Inferior Parietal Cortex; IFG, Inferior frontal gyrus; dmPFC, Dorsomedial Prefrontal Cortex; dlPFC, Dorsolateral Prefrontal Cortex.

TABLE 2 Summary of recent studies on openness, bias processing, and creativity.

Study	Sample	Creativity task/questionnaires	Methodology and imaging analysis	Results summary and interpretation
Wei et al. (2014)	*N* = 269 Healthy individuals	Divergent thinking measured by the Torrance Tests of Creative Thinking (TTCT).	Pre and post-task –resting state fMRI Whole-brain voxel-based activity and ROI-functional connectivity	Study findings suggest that increased RSFC between the default mode network's mPFC and mTG, may be essential for creativity and that cognitive stimulation can increase RSFC between these two brain regions (reflecting creativity training-induced changes in functional connectivity, especially in the lower creativity individuals who had lower scores of Torrance Tests of Creative Thinking) (49).
Beaty et al. (2020)	*N* = 23 Healthy individuals	(EI) and semantic (SI) induction tasks, Alternate uses task AUT	fMRI Multivoxel patterns of neural activity	In comparison to episodic induction, semantic induction and subsequent generation were characterized by greater pattern similarity within the left AG, left IPL, and PCC, suggesting that these regions contributed to semantic processing throughout the AUT (51).
Li et al. (2016)	*N* = 304, healthy individuals	TTCT-F, CRT	fMRI Seed-based functional connectivity	Results showed a correlation between higher creativity and reduced RSFC between the mPFC and precuneus and increased RSFC between the left and right dlPFC (46).
Beaty et al. (2018)	*N* = 163 Healthy adults.	Creative ideation task, Alternate uses task (AUT) of divergent thinking	Resting-state and task-based fMRI Two task-based fMRI samples and one task-free resting-state sample fMRI during creative ideation task Functional connectivity analysis	Greater default mode network, SN, and ECN functional connectivity is associated with higher creativity and divergent thinking (44).
Li et al. (2015)	*N* = 246	Raven's Advanced Progressive Matrix (RAPM), Raven's Advanced Progressive Matrix (RAPM, WCAT) (The Creativity Assessment Packet.)	Structural volumetric MRI	These findings suggest that an individual's trait creativity may be significantly influenced by the specific personality trait of openness to experience and that creativity and the appropriate pMTG volume are related through openness to experience to some extent (16).
Marstrand-Joergensen et al. (2021)	*N* = 295	Openness to experience (NEO-PI-R)	Resting-state fMRI Functional connectivity	Resting state connectivity within the DMN was negatively associated with trait openness, including the Fantasy aspect (52).
Wang et al. (2022)	*N* = 39 Healthy individuals	The Creative Achievement Questionnaire (CAQ), Creative Behavior Inventory (CBI), The Biographical Inventory of Creative Behaviors (BICB) To assess divergent thinking: the Product Improvement Task (PIT), The Alternate Uses Task (AUT). Openness to experience (NEO-PI-R)	fMRI functional connectivity	At the behavioral level, there is a correlation between creative achievement and both experiential openness and diverse thinking. Both openness to new experiences and diverse thinking involves the attentat networks and the default mode network since they both call for focus and the capacity for spontaneous thought (53).

(Continued)

TABLE 2 (Continued)

Study	Sample	Creativity task/questionnaires	Methodology and imaging analysis	Results summary and interpretation
Sun et al. (2019)	*N* = 29 healthy adults	Divergent thinking task AUT, control task (OCT-object characteristic task), NEO-Personality Inventory	Resting-state fMRI Activation analysis	Different combinations of network connectivity patterns predict creativity and openness to experience. The results showed that the precuneus and middle temporal gyrus were positively related to the inferior parietal lobule. Positive connections between the precuneus and supramarginal gyrus and the middle frontal gyrus/superior frontal gyrus were found. Individual difference analysis showed a significant correlation between openness to experience and the intensity of FCs between various important default mode, cognitive control, and salience network areas. The network-based mechanisms that underlie creativity and the neurological foundation of individual differences in openness to experience were found to be true (13)
Firat et al. (2017)	*N* = 17 patients with focal brain lesions (vmPFC or amygdala)	The International Affective Picture System (IAPS), the World Wide Web	fMRI Activation analysis	Higher activation of the amygdala in situations individuals had to assess out of group race. These findings show that the amygdala may be encoding other socially valued face characteristics in addition to automatically classifying people into various ethnic groupings. The results suggested a probable involvement of different brain areas in class-based racial assessments: the amygdala for the lower and upper classes and the vmPFC for the middle class (40).
Sakaki et al. (2020)	*N* = 40 Healthy Japanese University Students	Cognitive bias modification for interpretation (CBM-I) tasks, vs. a control group who received positive and negative ending written scenarios. For the assessment test, only the first two sentences were displayed for a total of 10 s. The first two sentences were left up to the participants' interpretation, and they were to think of a possible outcome for the scenario and envision it for 10 s.	Task-based fMRI	Participants perceived novel social scenarios. Whole-brain analysis revealed group-self-awareness interaction, altering brain activity in various areas, including the somatomotor and somatosensory areas, occipital lobe, and Post. Cingulate Gyrus, right amygdala, The hypothesis that the individuals' imagery was altered to be processed as higher social reward may also be supported by the increase in visual cortex activity and reinforced functional connections between the ACC and DLPFC that coincided with SA reduction. Interaction between areas of memory retrieval were also shown by high functional connectivity between IPL PCG, and SFG interact with the ACC, possibly indicates participants' attempts to retrieve and recall positive interpretations for ambiguous social circumstances in a self-referential manner (29).

In curating articles for our review on the relationship between openness and creativity neurobiology, we employed a methodical approach, prioritizing studies with rigorous neuroscientific methodologies, particularly those involving empirical research and neuroimaging techniques.

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with others, which in turn facilitates interpersonal conflict resolution (16, 18).

Reciprocally, creativity leads to greater cultural openness by challenging existing norms and encouraging the exploration of new ideas as a means to resolving conflicts (19, 56). Creativity has the potential to bridge cultural differences and facilitate conflict resolution by generating novel and innovative solutions that are sensitive to diverse cultural perspectives. This may be particularly relevant in situations where traditional approaches have failed. They suggest that a culturally sensitive approach to creativity can promote intercultural understanding and dialog, leading to more effective conflict resolution in multicultural environments (57–59).

The interplay of diversity and creativity in real-world multicultural environments

Globalization has accelerated, and there have been an increasing number of studies examining how cultural differences are managed in light of the internationalization of organizations and, in particular, the rising number of staff members from various cultures. Attitudes toward individualism and conformity changed in the 1980s, at both societal and organizational levels, and this shift has been attributed to several factors that include the impact of multiculturalism and interpersonality (60). Multiculturalism refers to the recognition and celebration of diversity within society, while interpersonality refers to the importance of interpersonal relationships and connections (61–63).

Research by Amabile et al. found that exposure to multiculturalism increased creativity and innovation, as individuals were exposed to new ideas and perspectives. They hypothesized that this, in turn, may have contributed to the growing emphasis on individualism in the 1980s, as individuals were encouraged to pursue their own unique interests and goals in order to boost the success of organizations. Similarly, the importance of interpersonality in the 1980s may have contributed to the shift in attitudes away from conformity. As individuals formed stronger interpersonal connections, they may have felt less pressure to conform to societal norms and expectations, and more empowered to pursue their own goals and interests (60, 64).

In the late 1980s, the theoretical concept of "organizational creativity" was first suggested by Woodmann, who put the term "creativity" in the organizational context in reference to the creative process of individuals who work together in a complex social setting for creating an innovational and useful product (65). One commonly cited model of organizational creativity that has often been used in organizational creativity studies is the Five-Stage Model, developed by Teresa Amabile and colleagues (66, 67). The model includes five stages: Problem Identification, Preparation, Idea Generation, Idea Evaluation, and Outcome Assessment (66, 67). It has been noted that while the first three stages are held in common between individual-level and organizational-level innovation, the remaining two are uniquely related to organizational environment factors such as resources, material systems, and general atmosphere, which may fortify or inhibit creativity in the organizational culture (68). Furthermore, studies have found that organizational diversity was positively related to the generation of new ideas when employees were highly engaged in the creative process. This suggests that organizations must create a supportive environment that encourages employees to engage in the creative process in order to fully benefit from the diversity of their workforce (64, 66).

Studying the collectivistic and individualistic approaches to organizational culture has provided insights into how individual creativity and organizational innovation may interact with each other. The collectivistic approach promotes conformity in a diverse group in service of a common goal, values, or mutual interest, avoiding individualistic values in order to minimize conflicts and opportunism (69). Studies have shown that when a collectivistic orientation is maintained in a diverse organizational culture that shares the common goal of productive, innovative work outcomes, it increases harmony, cooperation, a sense of identification with the work ingroup, and group cohesion (70, 71).

On the other hand, the individualistic approach is more likely to foster creativity on an individual level and is generally associated with a Western cultural mindset about the workspace. Organizational research has indicated that creativity is often an outcome of individuals deviating from consensual normative practices rather than maintaining them, as is more common in collectivistic work cultures (72). Recent research has shown that in order to promote "organizational creativity" in a complex social environment, individualistic values are beneficial, especially when the desired outcome of the work is a creative product (73). Social psychology studies have suggested that another advantage of the individualistic approach is that in a multicultural setting where individuals are accepting of diverse values and perspectives, facilitation of creative performance occurs that is mediated by an increased generation of uncommon and unconventional ideas, as well as by that culture's enhanced receptiveness to ideas that are rooted in non-native cultures (15). Studies have shown that individuals who have experience living in a culture different from their own, and who needed to adapt to that non-native culture, have higher levels of creativity (54).

Additionally, recent studies provide evidence that the likelihood that cultural openness will positively impact creativity and conflict resolution in multicultural environments is mediated by the degree to which the multicultural team feels a sense of psychological safety and inclusiveness (14, 57). Thus, a culturally sensitive approach to creativity can promote intercultural understanding and dialog, fostering a safe and inclusive multicultural environment that facilitates conflict resolution and fosters individuals' creative contributions. Reciprocally, creative thinking helps to generate new and innovative solutions to interpersonal disputes, particularly by seeking resolutions that consider different perspectives and satisfy the needs and interests of all parties involved by going beyond traditional, existing options. The use of creative techniques can help break down communication barriers, enhance collaboration, and promote understanding among conflicting parties as well. This creates a beneficial cycle leading to more positive intergroup attitudes and behaviors (5, 37, 50, 51).

Finding the best approaches to train teams to be more creative has also been a topic of recent investigation (58, 59). Effective training models suggest that it is possible to get positive effects out of diverse teams by building and preparing them systematically for team-driven creative tasks, supporting and preparing them not only cognitively but also motivationally, emotionally, and environmentally to contribute to the teams' creative output (55, 58, 74).

Conclusion

Openness to culturally diverse individuals and ideas is an important behavioral trait that is increasingly necessary for success in today's interconnected world. By promoting inclusivity, individuals can create more diverse and innovative networks that foster creativity, collaboration, and growth in groups and organizations. Implicit biases can act as barriers to openness and inclusivity and reduce the organization's creative output and effective problem solving; thus, it is necessary for individuals and organizations to identify and overcome such biases. Research consistently points to a largely shared neurobiology between creativity and trait openness, where common brain networks (i.e., the reward system, DMN, and ECN) facilitate divergent, convergent, and associative thought processes that play an important role in generating new critical perspectives and getting beyond automatic stereotypes to make further creative associations. While openness to diversity is one aspect of the larger trait of openness, more research with harmonized methodology is needed to directly and explicitly examine the relationship between the two, and to identify factors that may inhibit intercultural openness even in individuals who otherwise show high levels of trait openness. Further research is also needed to clarify the intricate dynamics between openness as a personality trait and the cognitive abilities that comprise it.

In the new era of globalization and multicultural organizational environments, creativity and openness to diversity are important tools when training multicultural groups to collaboratively solve conflicts. The evidence reveals that creativity can help resolve conflicts via the generation of new and innovative solutions, but it also shows that a reciprocal relationship exists in which openness to diversity and multicultural appreciation can enhance group creativity. This highlights the value of including and encouraging a diverse array of individuals within a collective. Supporting "organizational multiculturism" creates an environment that embraces and motivates divergent ideas and diverse individualistic values and creates safety for unconstrained creativity and freedom of thought. Promoting both openness to diversity and creativity can have a significant positive impact on individuals, organizations, and societies as they seek to implement effective solutions and resolve conflicts.

Author contributions

The manuscript benefited from the collective input of all authors during the conceptualization stage having all authors taking part in developing the ideas for this manuscript. KR and MAR played a significant role in designing and structuring the paper. The initial draft was written by MAR, who served as the first author, while AO, VR, JB, MI-M, and KR contributed by reviewing and making edits. In addition, VR contributed to the visual representation of a creative illustration depicting various concepts related to neuroanatomy of creativity and openness. KR supervised the work and contributed to the writing, reviewing, and editing processes. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2023.1235348/full#supplementary-material

ILLUSTRATION 1
An illustrated creative analogy that incorporates the different brain regions and associated networks involved in both openness and creativity, by Veronica Rojas Carstensen, Visual artist, Atlantic Fellow for Brain Health Equity, GBHI, UCSF. This imaginative illustration shows the brain as a complex camera with different lenses and filters that represent the different brain areas involved in creativity and processing of stereotypes and biases. These regions and networks act as lenses and filters that perceive, shape, and project our interpretations and attitudes toward the world around us and act accordingly. dlPFC, Dorsolateral Prefrontal Cortex; ACC, Anterior Cingulate Cortex; mPFC, Medial Prefrontal Cortex; PCC, Posterior Cingulate Cortex; IFG, Inferior frontal gyrus.

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Neuroanatomical and cellular degeneration associated with a social disorder characterized by new ritualistic belief systems in a TDP-C patient vs. a Pick patient

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Frontotemporal dementia (FTD) is a spectrum of clinically and pathologically heterogenous neurodegenerative dementias. Clinical and anatomical variants of FTD have been described and associated with underlying frontotemporal lobar degeneration (FTLD) pathology, including tauopathies (FTLD-tau) or TDP-43 proteinopathies (FTLD-TDP). FTD patients with predominant degeneration of anterior temporal cortices often develop a language disorder of semantic knowledge loss and/or a social disorder often characterized by compulsive rituals and belief systems corresponding to predominant left or right hemisphere involvement, respectively. The neural substrates of these complex social disorders remain unclear. Here, we present a comparative imaging and postmortem study of two patients, one with FTLD-TDP (subtype C) and one with FTLD-tau (subtype Pick disease), who both developed new rigid belief systems. The FTLD-TDP patient developed a complex set of values centered on positivity and associated with specific physical and behavioral features of pigs, while the FTLD-tau patient developed compulsive, goal-directed behaviors related to general themes of positivity and spirituality. Neuroimaging showed left-predominant temporal atrophy in the FTLD-TDP patient and right-predominant frontotemporal atrophy in the FTLD-tau patient. Consistent with antemortem cortical atrophy, histopathologic examinations revealed severe loss of neurons and myelin predominantly in the anterior temporal lobes of both patients, but the FTLD-tau patient showed more bilateral, dorsolateral involvement featuring greater pathology and loss of projection neurons and deep white matter. These findings highlight that the regions within and connected to anterior temporal lobes may have differential vulnerability to distinct FTLD proteinopathies and serve important roles in human belief systems.

KEYWORDS

behavioral variant frontotemporal dementia, primary progressive aphasia, Pick disease, TDP-C, semantic knowledge, social cognition, anterior temporal lobe, cortical layers

Introduction

The neurobiology of cognitive and social impairments in the clinically and pathologically heterogeneous spectrum of frontotemporal dementia (FTD) syndromes is poorly understood (1). The most prominent symptoms of FTD include socio-emotional, language, and motor impairments that occur in various combinations and severity (2). Moreover, the neuropathological substrates for FTD include various subtypes of frontotemporal lobar degeneration (FTLD) proteinopathies, most commonly TDP-43 proteinopathies (FTLD-TDP) and tauopathies (FTLD-tau) (3). FTLD-TDP and FTLD-tau have a similar probability of causing the behavioral variant of FTD (bvFTD), the most common FTD syndrome (4–6). In contrast, variants of primary progressive aphasia (PPA) have some predictive value for specific forms of FTLD (7–11); However, these associations are not absolute, highlighting the clinicopathologic heterogeneity of FTD.

Anatomical patterns of degeneration may help explain clinical and pathologic heterogeneity in FTD (12–14). Neuroimaging studies suggest temporal variants of FTD exhibit early atrophy of the anterior temporal lobes (aTL) linked to either a bvFTD-like syndrome or the semantic variant of PPA (svPPA) depending on the predominant hemisphere involved (15–17). For example, the left temporal variant is most often associated with FTLD-TDP subtype C (TDP-C) pathology and symptoms characteristic of svPPA such as anomia and semantic knowledge loss (15, 18–20). In contrast, the right temporal variant is associated with heterogenous underlying FTLD pathologies and various behavioral and cognitive features including rigid compulsions, goal-oriented rituals, disinhibition, empathy loss, episodic memory loss, topographagnosia, prosopagnosia, depression, somatic complaints, and non-verbal semantic impairments (e.g., biographical person-specific knowledge) (21–30). Moreover, left and right temporal variants of FTD often progress into mixed clinical phenotypes that share similar language and behavioral symptoms within 3–5 years of symptom onset (15, 16, 31), suggesting a clinicoanatomic spectrum of svPPA and bvFTD (30). Interestingly, there also can be an emergence of new artistic creativity and/or new values/beliefs in FTD patients, especially those with predominantly temporal lobe disease (32–34), but the cellular and pathologic correlates of these behavioral symptoms are understudied.

Here, we compare detailed antemortem and postmortem data from one patient with FTLD-tau (Pick disease, PiD) and one patient with FTLD-TDP-C, both of whom developed semantic impairments and social disorders that included complex ritualistic behaviors that manifested as novel and concrete belief systems, to uncover shared and disparate cellular contributions to clinical symptoms in FTD.

Methods

Patients were enrolled in observational research at the Penn Frontotemporal Degeneration Center (FTDC). Clinical diagnoses were established at FTDC consensus meetings using clinical criteria (6, 7). Neuropathologic diagnoses were performed using established methods and current neuropathologic diagnostic criteria (35–37). Patients were genotyped for FTD related genes and were negative for pathogenic mutations in *C9orf72*, *GRN*, *MAPT*, *VCP* and > 20 other genes associated with neurodegenerative disease as described previously (38). Please see Supplementary material for magnetic resonance imaging (MRI) and digital histopathology methods.

Results

FTLD-TDP patient

The first patient was a 67-year-old, right-handed White man with 12 years of education who presented to the Penn FTDC with insidious onset of language problems for 2 years. The patient reported difficulties with naming, understanding the meaning of common words (e.g., deer, acorn), and difficulty spelling, while memory for recent events and conversations was not reported to be problematic. These language changes were accompanied by subtle changes in personality and behavior characterized by reduced social inhibitions (e.g., inappropriate comments about a stranger's body), dysphoria (e.g., crying more often), impatience with his family, and hyperorality for sweets.

On baseline examination, his speech was fluent but featured word-finding pauses, circumlocutions, semantic paraphasic errors (e.g., subordinate substitutions), and semantic knowledge loss (e.g., described a camel drawing as a "European domesticated animal"). He demonstrated worse semantic- than letter-fluency performance and had surface dyslexia. Basic and complex comprehension was intact, and he wrote a complete sentence. He demonstrated retrieval-based verbal memory deficits with relative preservation of visual memory. Set-shifting was weak, but there was no evidence of visuospatial impairment, apraxia, or acalculia. His Mini-Mental State Examination (MMSE) was 24/30, indicating mild impairment. Elemental neurologic examination was unrevealing. At initial visit, he met clinical diagnostic criteria for svPPA, and neuropsychological testing showed relatively isolated semantic loss (Supplementary Table 1).

Within 4 years, a more prominent social disorder emerged featuring a new fixation on pigs, complex goal-directed ritualistic behaviors, and worsening disinhibition (e.g., offering money and food to unfamiliar people/children). His fixation on pigs centered around positive qualities he attributed to them (e.g., intelligence, sensitivity; Figure 1A) and physical characteristics he interpreted as meaningful (Figure 1B). "Keep looking up" became a personal mantra that he readily shared with strangers, and he no longer showed signs of depressed mood. He became increasingly rigid, adhering to a strict exercise routine and hyper-oral diet (i.e., restricted to hamburgers, hot dogs, and cookies eaten in a ritualized manner). Other compulsive behaviors included counting and a specific cleaning routine, with

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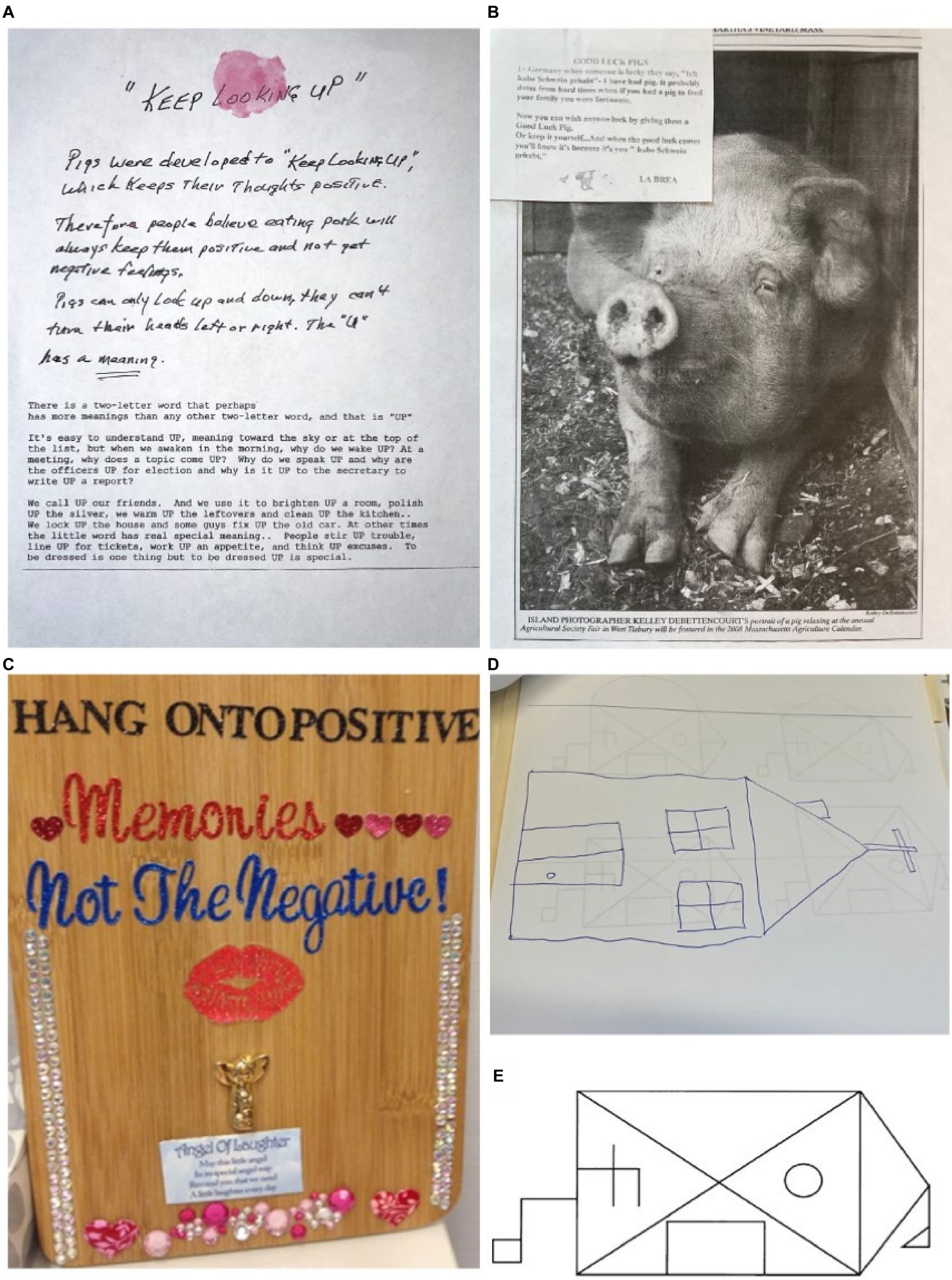

FIGURE 1
Personal items and visual reproductions illustrating evidence of new and rigid belief systems and ritualistic compulsions in both patients. **(A)** A written explication of the FTLD-TDP patient's personal mantra, "keep looking up," which derives positive emotional meaning from the pig's physical characteristic of only being able to look up and down rather than side to side. His belief system featured semantically rich associations of complex and abstract concepts (e.g., intelligence, creativity) with concrete, physical characteristics. **(B)** A sampling of images and written material pertaining to pigs collected by the FTLD-TDP patient, including a German fable and a photo of a pig from an agricultural fair. The fable is titled "GOOD LUCK PIGS" that

(Continued)

FIGURE 1 (Continued)
reads, "In Germany when someone is lucky they say 'Ich habe Schwein gehabt'—I have had pig. It probably dates from a hard time when if you had a pig to feed your family you were fortunate. Now you can wish anyone lucky by giving them a Good Luck Pig. Or keep it yourself... And when the good luck comes you'll know it's because it's you [*sic*] 'habe Schwein gehabt.'" He became obsessive with collecting images and figurines of pigs, and often gave these out to people when discussing his belief system. **(C)** A cutting board that the FTLD-tau patient decorated with messages of positivity, including instructions to "hang onto positive memories not the negative!" and a poem titled "Angel of Laughter" that reads, "May this little angel/In its special angel way/Remind you that we need/A little laughter every day." Her obsessive fixation on positivity was accompanied by compulsive production of positivity-themed visual arts and crafts featuring religious and spiritual iconography. **(D)** Delayed recall trial of the Benson complex figure test showing evidence of enhanced visual artistic creativity despite impaired memory for the target stimulus in the FTLD-tau patient. She continued to ritualistically produce arts and crafts as her disease progressed, but her work became less focused on positivity and reflected semantic knowledge loss (e.g., drawing a turkey with tentacles instead of legs). **(E)** The original Benson complex figure stimulus for reference to the delayed recall copy pictured above.

significant distress if disrupted. His speech became more tangential, and he expressed a wish that he could communicate in numbers instead of words at a late-stage visit. Empathy further reduced, and while frustrated and concerned by his language impairments, he had limited insight into his behavioral changes.

His longitudinal cognitive profile (Supplementary Table 1) reflected progressive semantic knowledge loss and eventually impaired episodic memory and attention, with mild global cognitive impairment (CDR = 1, MMSE = 23, 8 years after onset). He became more globally and functionally impaired (CDR = 2, MMSE = 19) 12 years after onset and died with end-stage dementia after 15 years.

Neuropathologic examination found TDP-43 pathology in the form of mostly dystrophic neurites consistent with a primary neuropathologic diagnosis of FTLD-TDP-C. Co-pathologies included limbic stage Lewy Body Disease and low Alzheimer disease neuropathologic change [Thal: A1, Braak: B1 (Stage II), CERAD: C0], and severe arteriolosclerosis.

FTLD-tau patient

The second patient was a 57-year-old, right-handed White woman with a nursing degree who presented to the Penn FTDC with a 2–3 year history of slowly progressive memory problems and behavioral disinhibition. She initially reported somatic complaints of sensory changes and déjà vu phenomena that were initially evaluated for epilepsy, but a workup was unrevealing, and she was referred for a cognitive evaluation.

The patient reported mild memory problems, but her family reported significant personality changes, including a new obsession with positivity and spirituality. She began to dress and dye her hair in bright colors and got a tattoo with a positive slogan which became a personal mantra. She exhibited disinhibition (e.g., approaching strangers with messages of positivity), impulsivity (e.g., attempting to sell her house suddenly without notifying her family), poor judgment (e.g., authoring a book on positivity that lost significant money to a predatory publisher), and reduced empathy (e.g., lacking appropriate concern following the death of a loved one). She became compulsive about creating artwork, including making frequent trips to buy large quantities of art supplies to make crafts that often conveyed positive messages with themes of spirituality (Figure 1C). She showed limited insight into these behavioral changes.

On examination, she had fluent speech and child-like affect. Confrontation naming was impaired despite relatively preserved object knowledge. Comprehension was intact, but she had surface dyslexia. Verbal memory showed retrieval-based impairment and visual recall was preserved. She had a poor mental search strategy, low letter fluency, and significant set-shifting difficulties. Despite problems with memory, executive functioning, and language, her MMSE was 30/30 at the initial visit. Elemental neurologic examination was unrevealing. Neuropsychological testing showed a pattern of prominent executive dysfunction with naming and semantic deficits and poor face recognition (Supplementary Table 2), and she met clinical criteria for bvFTD.

Within 4 years, her behavioral symptoms progressively worsened. She spent a large sum of money to buy a used car in poor condition despite having her driver's license revoked, continued compulsively shopping and creating art, and obsessively recorded food and water intake. Her speech became more stereotypic (e.g., "Handsome boy brings me joy"), and she became agitated if ritualistic behaviors were disrupted. Her art and visual reproductions showed evidence of continued visual artistic creativity (Figure 1D); however, over time her artwork for animals were reported to show signs of degradation of semantic knowledge (e.g., turkey drawing with tentacles). Six years after symptom onset, she became dependent for self-care (CDR = 3, MMSE = 12) with significantly impaired comprehension (Supplementary Table 2), increasing apathy, and hyperorality with weight gain. She passed away with end-stage dementia 11 years after onset.

Neuropathologic examination found frequent tau pathology in the form of Pick bodies and ramified astrocytes, characteristic of PiD without co-pathology other than severe arteriosclerosis.

Comparative antemortem MRI

Baseline MRI within 2 years of symptom onset in each patient found a similar predominance of aTL atrophy in each patient, but with opposing hemispheric asymmetry (i.e., left > right in FTLD-TDP; right > left in FTLD-tau), consistent with initial clinical diagnoses (Figure 2A). Additionally, FTLD-TDP showed leftward asymmetry in the insula and anterior cingulate, whereas FTLD-tau showed rightward asymmetry in the insula and inferior frontal lobe.

Follow-up MRIs were acquired ~63% into clinical progression for the FTLD-TDP patient (i.e., 8 years after baseline MRI) vs. ~36% into clinical progression for the FTLD-tau patient (i.e., 2 years after baseline MRI) when both had mixed clinical features of bvFTD and svPPA (Figure 2B). In FTLD-TDP, cortical atrophy worsened but remained asymmetric in left frontotemporal regions with spread to left posterior orbitofrontal cortex, peri-genual cingulate cortices, and ventrolateral temporal cortices. In contrast, cortical atrophy remained rightward asymmetric in the FTLD-tau case and spread into the right

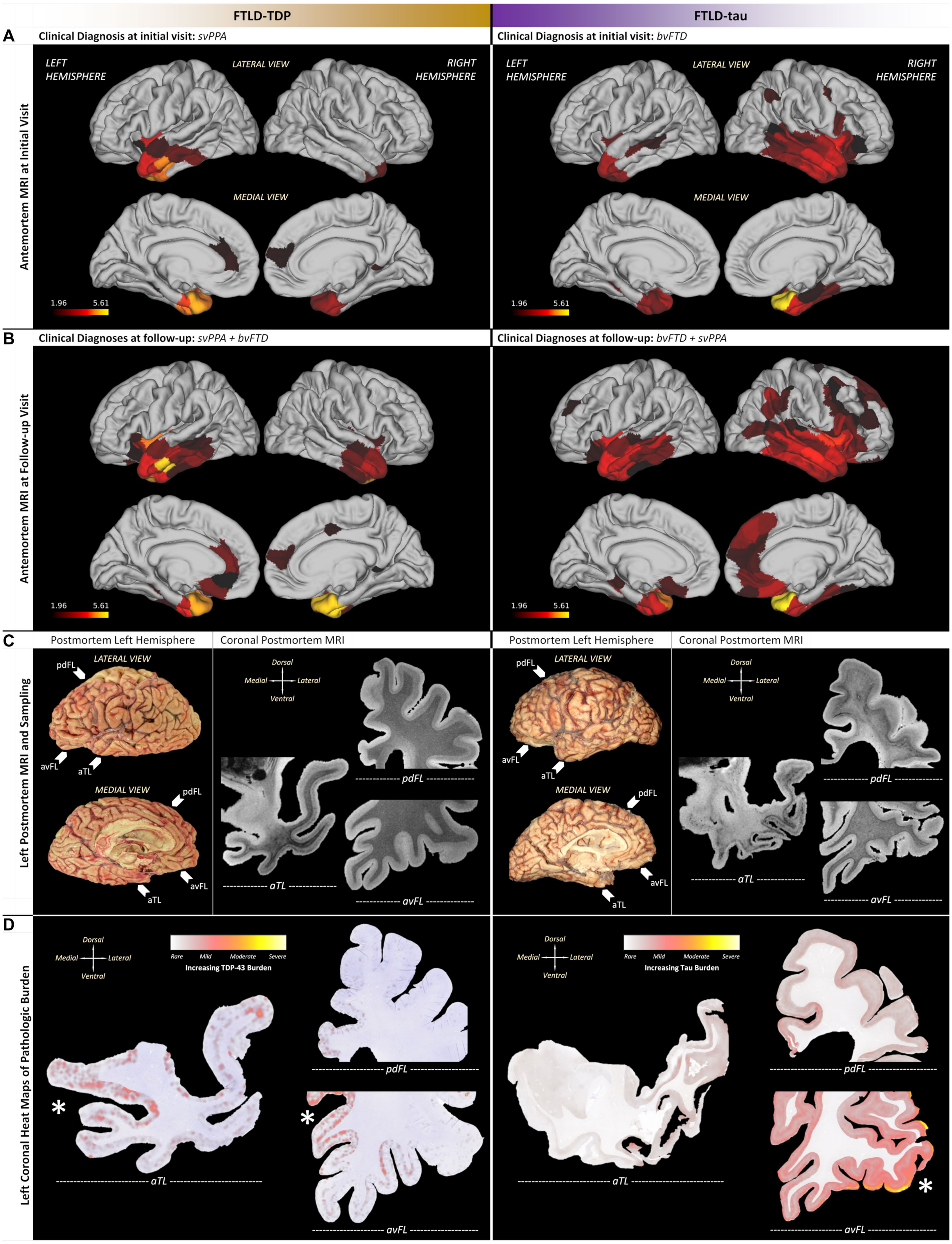

FIGURE 2
Patient-specific macroscopic patterns of cortical atrophy and neuropathologic changes using antemortem T_1-weighted MRI and postmortem T_2*-weighted MRI. **(A)** Initial MRI revealed a similar predilection for aTL but with opposing hemispheric asymmetry, including leftward asymmetry in the insula and anterior cingulate for FTLD-TDP, in contrast to rightward asymmetry in the insula and inferior frontal lobe for FTLD-tau. **(B)** Follow-up MRI in both patients showed spread and worsening of atrophy with preserved asymmetries observed in initial MRI, but the FTLD-tau patient showed greater spread in medial frontal and dorsolateral cortices throughout frontal, temporal, and parietal lobes. **(C)** In the left hemisphere of each patient, postmortem MRI helped identify aTL-predominant pathology and neurodegeneration that guided histopathology (arrows next to photographs of

(Continued)

FIGURE 2 (Continued)
autopsied brains point to whole hemisphere coronal sections used in subsequent comparative examinations of histopathology). **(D)** Quantitative heat maps of areas occupied by pathology identified patient-specific regions of peak pathology (denoted by asterisks near regions with greater red/yellow), including the FTLD-TDP patient accumulating greater TDP-43 burden in medial limbic/paralimbic regions with greater neurodegeneration, while the FTLD-tau patient accumulated greater tau burden in ventrolateral regions with relative neuronal preservation. Note that tau burden was consistently more frequent than TDP-43 burden; thus, scales of pathologic burden are distinct and specific to each molecular pathology due to normalization within each patient. aTL, anterior temporal lobe; pdFL, posterior dorsal frontal lobe; avFL, anterior ventral frontal lobe. All scale bars = 20 μm.

medial frontal regions and dorsolateral cortices throughout frontal, temporal, and parietal lobes.

Comparative postmortem MRI and histopathology

Postmortem T_2*-weighted MRI contrast is sensitive to iron in healthy myelin (39) and iron-rich gliosis (40), revealing neurodegenerative patterns to guide histopathologic sampling (Figures 2, 3). Hypointensity from intracortical and deep myelin loss was most pronounced in the aTL (i.e., predominantly ventral temporal gyri) for both patients, but extended into dorsolateral frontal regions in PiD (Figure 2C). The FTLD-TDP patient displayed bands of upper layer hypointensity more concentrated to ventral isocortices, while the FTLD-tau patient showed variable laminar banding including mid and lower layer bands of hypointensity in more dorsolateral isocortices. These bands corresponded to iron-rich gliosis with hypertrophic, dystrophic, or amoeboid morphologies in both patients, including frequent iron-rich astrocytes near microvessels (Figure 3A).

To identify macro- (regional) and mesoscopic (laminar) patterns of histopathology, digital heat maps depicting the area occupied by pathologic inclusions found mild, patchy deposits of TDP-43 and tau pathology in the ventral aTL where atrophy was greatest (Figure 2D). In fact, the FTLD-TDP patient showed more (i.e., moderate-to-severe) TDP-43 pathology in regions with relatively less MRI-based atrophy than the ventral aTL, including the superior temporal gyrus, amygdala-hippocampal complex, peri-genual cingulate, and medial orbital gyri. Similarly, the FTLD-tau patient showed reduced tau burden in the severely atrophied aTL and the greatest tau burden in relatively less atrophied regions but in regions distinct from the FTLD-TDP patient, including pars orbitalis and Broca's area.

Consistent with macro- and mesoscopic patterns reported above, microscopic patterns revealed a combination of shared and patient-specific laminar distributions of pathology and loss of projection neurons and axons. In the aTL, there was greater upper layer TDP-43 inclusions and loss of myelin and projection neurons in both upper and lower layers of medioventral gyri compared to relatively spared dorsolateral gyri in the FTLD-TDP patient (Figures 3B–D). In contrast, the FTLD-tau patient consistently showed severe tau pathology in layers II and IV-VI which corresponded to more severe and widespread loss of myelin and projection neurons in all layers and greater vacuolation/neuropil disintegration in lateral vs. medial regions. Moreover, deep white matter rarefaction and pathology was unique to the FTLD-tau patient and corresponded to hyperintense signal on postmortem MRI (Figures 3A–D).

In the frontal lobe, the FTLD-TDP patient accumulated more TDP-43 pathology in medial and ventral frontal regions (e.g., peri-genual cingulate and medial orbital gyri) comparable to the severity and layer involvement found in medioventral aTL (Figures 2D, 4A,B). Moreover, dorsal and lateral frontal regions with minimal neuron loss accumulated rare-to-mild TDP-43 inclusions in upper and lower layers. In contrast, medial and dorsolateral frontal regions of the FTLD-tau patient featured moderate-to-severe loss of projection neurons despite lower tau burden (Figures 4C,D). In both patients, loss of projection neurons and myelin were strongly concordant, especially the vertically oriented fibers traversing layers IV–VI (Figures 4E,F). However, the FTLD-tau patient displayed greater myelin loss in both gray and white matter, which corresponded to the overall greater loss of projection neurons and widespread tau pathology. In addition to myelin loss, the FTLD-tau patient displayed greater axonal loss most evident by the atrophied corpus callosum compared to the FTLD-TDP patient.

Comparison of available contralateral homologs found inconsistently greater TDP-43 pathology and neurodegeneration in left regions of the FTLD-TDP patient, while tau pathology and neurodegeneration were inconsistently greater in the right regions of the FTLD-tau patient (Supplementary Figure 1).

Discussion

We present a detailed macro- and microanatomical investigation of two FTD patients with distinct FTLD proteinopathies that shared aTL-predominant atrophy associated with new onsets of compulsive and rigid belief systems. While their belief systems both centered on themes of positivity, the FTLD-TDP patient developed a complex schema of abstract concepts such as "intelligence and sensitivity" linked to pigs. In comparison, the FTLD-tau patient had a more generalized belief system of positivity with hyper-religious features that manifested in new artistic creativity. By pairing longitudinal clinical assessments with antemortem MRI and postmortem MRI-guided histology rarely collected in the same individuals, our multi-modal investigation revealed an early and shared susceptibility to aTL neurodegeneration concentrated to ventral aTL isocortices. However, divergent patterns of neurodegeneration between patients included disproportionate involvement of dorsal and lateral isocortex in the FTLD-tau patient, which corresponded to more prominent loss of projection neurons and long-range axons in infragranular layers and deep white matter. We hypothesize that early and severe degeneration of aTL and frontotemporal paralimbic regions contributed to semantic knowledge loss and the emergence of new belief systems. Moreover, we speculate that degradation of abstract concepts in the FTLD-tau patient was related to reduced integration of semantic concepts due to their severe frontoparietal degeneration compared to the FTLD-TDP patient. These data provide a unique view into the potential neural substrates of complex human value systems and FTD clinical symptomatology.

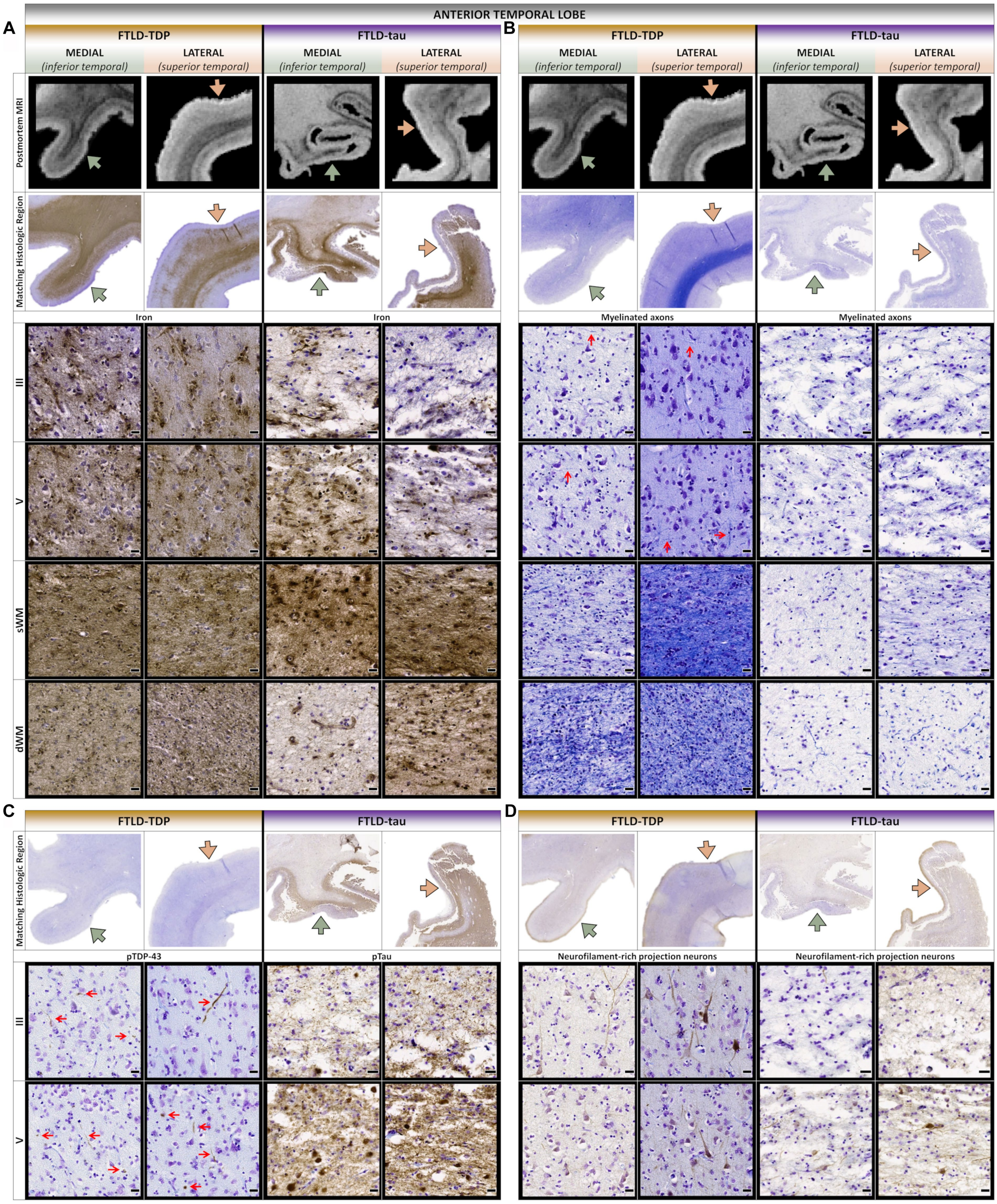

FIGURE 3
Comparative postmortem T_2*-weighted MRI and histopathology of the anterior temporal lobe. **(A)** While iron frequently accumulated in lower layers and superficial white matter in both patients, the FTLD-TDP patient often displayed greater upper layer iron more concentrated to medioventral isocortices with greater atrophy and hypointensities. **(B)** Both patients showed severe loss of interlaminar and white matter myelin in medioventral isocortices, but the FTLD-tau patient showed more widespread and severe myelin loss, especially in dorsolateral isocortices and deep white matter. Red arrows point to examples of horizontally and vertically oriented myelinated fibers across cortical layers. **(C)** The FTLD-TDP patient accumulated TDP-43 inclusions in upper and lower layers throughout medial and lateral isocortices, but the FTLD-tau patient accumulated more tau inclusions in lower layers throughout medial and lateral isocortices. Red arrows point to examples of TDP-43 inclusions across cortical layers. **(D)** Both patients showed severe loss of projection neurons in upper and lower cortical layers, but the FTLD-tau patient displayed more severe neurodegeneration with more prominent vacuolation and neuropil disintegration. sWM, superficial white matter; dWM, deep white matter; all scale bars = 20 µm.

We found hemispheric and regional patterns of disease consistent with the initial clinical diagnoses of svPPA in the FTLD-TDP patient and bvFTD in the FTLD-tau patient (1, 10, 41). Initial MRI found left-predominant aTL atrophy in the FTLD-TDP patient and right-predominant frontotemporal atrophy in the FTLD-tau patient (Figure 2). Furthermore, these observations were confirmed

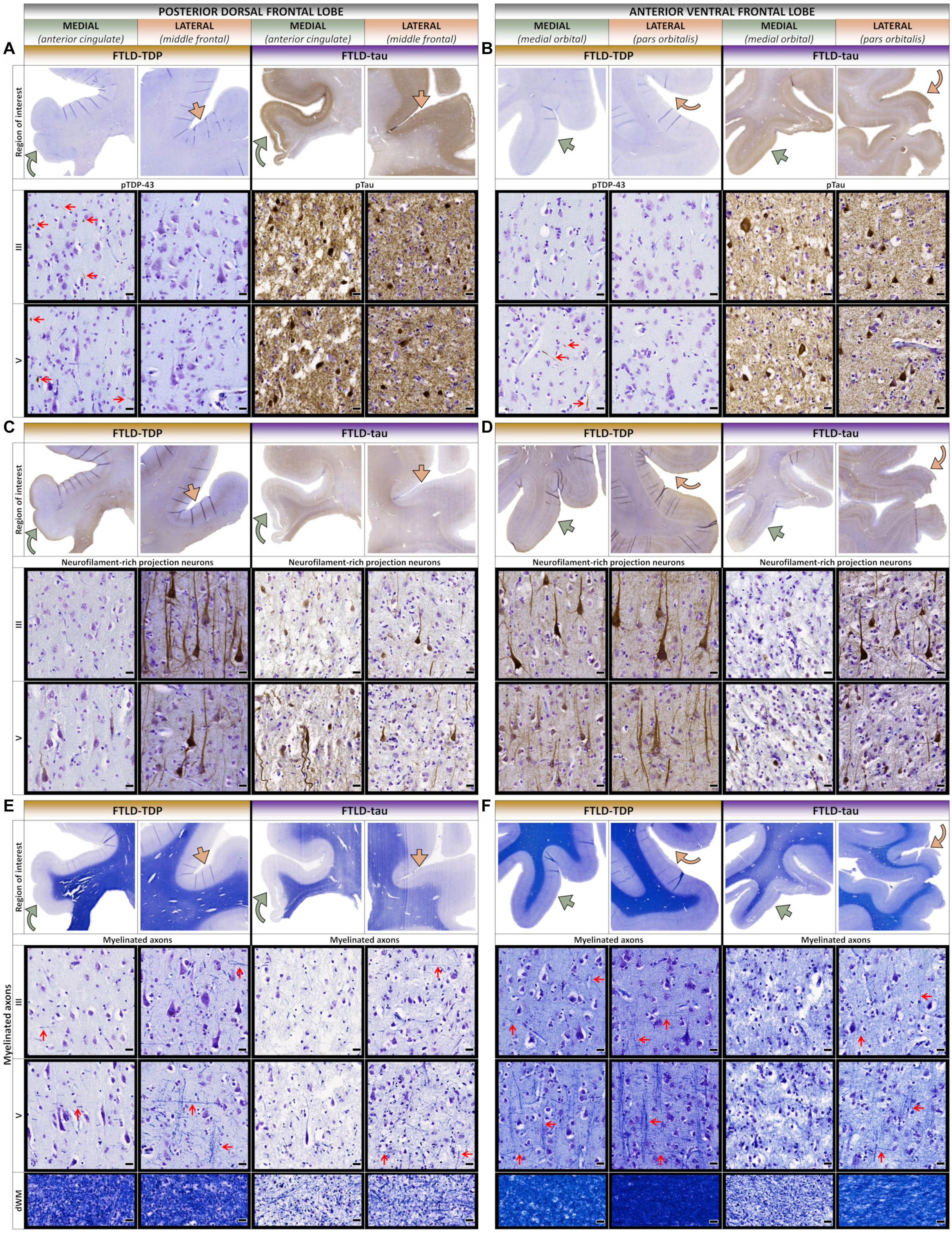

FIGURE 4
Comparative histopathology of the frontal lobe. **(A)** In the posterior dorsal frontal lobe (pdFL), the FTLD-TDP patient accumulated more TDP-43 pathology in upper and lower layers of medial proisocortical regions (e.g., anterior cingulate) compared to lateral isocortical regions (e.g., middle frontal). In contrast, the FTLD-tau patient accumulated severe pathology in both upper and lower layers consistently between medial and lateral regions. Red arrows point to examples of TDP-43 inclusions across cortical layers. **(B)** In the anterior ventral frontal lobe (avFL), the FTLD-TDP patient accumulated more TDP-43 pathology in predominantly lower layers of medial regions (e.g., medial orbital) compared to lateral regions (e.g., pars orbitalis). In contrast, the FTLD-tau patient accumulated severe pathology in both upper and lower layers consistently between medial and lateral regions. Red arrows point to examples of TDP-43 inclusions across cortical layers. **(C)** In the pdFL, the FTLD-TDP patient showed greater loss of

(Continued)

FIGURE 4 (Continued)
projection neurons in all layers of medial proisocortical regions compared to lateral isocortical regions. In contrast, the FTLD-tau patient showed a similar severe loss of projection neurons in all layers between medial and lateral regions. **(D)** In the avFL, the FTLD-TDP patient showed a slightly greater loss of projection neurons in all layers of medial regions compared to lateral regions. In contrast, the FTLD-tau patient showed greater loss of projection neurons in medial regions compared to lateral regions. **(E)** In the pdFL, the FTLD-TDP patient showed greater loss of interlaminar myelin in medial proisocortices, especially vertical myelinated fibers denoted by sideways-pointing red arrows compared to relatively preserved horizontal myelinated fibers denoted by red arrows pointing up. In contrast, the FTLD-tau patient showed overall greater myelin loss, particularly vertical myelinated fibers. Red arrows point to examples of horizontally and vertically oriented myelinated fibers across cortical layers. **(F)** In the avFL, the FTLD-TDP patient showed a slightly greater loss of myelin in medial regions compared to lateral regions, while the FTLD-tau patient showed more severe and widespread myelin loss between regions, with relatively rare preservation of myelinated fibers in lateral regions. Red arrows point to examples of horizontally and vertically oriented myelinated fibers across cortical layers. All scale bars = 20 μm.

postmortem in bilaterally sampled tissue (Supplementary Figure 1). The disproportionate involvement of the left aTL in the FTLD-TDP patient corresponds to the initial presentation of classic svPPA-related language symptoms (18–20, 41, 42). Accompanying these language changes were early behavioral features of dysphoria, impulsivity, and social disinhibition, which may be related to the patient's additional atrophy of limbic and paralimbic hubs of the salience network, such as the frontoinsula and anterior cingulate (30, 43). In contrast, the FTLD-tau patient began with typical bvFTD symptoms including disinhibition, impulsivity, loss of empathy, and poor judgment consistent with their pronounced atrophy of right paralimbic regions (30, 44). However, there was also evidence for prosopagnosia and semantic language deficits that corresponded to the severe and extensive involvement of the bilateral temporal lobes. Her initial behavioral changes and subsequent language impairments are also largely consistent with the recently proposed criteria for the "semantic/right temporal" bvFTD phenotype (30). The FTLD-tau patient additionally had early somatic symptoms, hyper-religiosity, and episodic memory loss which are linked to right temporal disease (21, 23). In summary, both patients presented with a mix of language and behavioral features at the earliest clinical visits that were associated with early MRI-based atrophy of aTL and insula with more contralateral spread over time in both patients (Figure 2). Together our findings are consistent with previous literature (1, 16, 24) and suggest that hemispheric asymmetries of aTL disease likely influence the clinical features across the spectrum of bvFTD and svPPA.

Both patients also developed prominent complex rituals centered around their new belief systems that manifested in different ways. Specifically, the FTLD-TDP patient developed a new obsessive fixation on pigs early into disease course that eventually became the foundation of a broader belief system that supported an optimistic outlook and positive affect. Indeed, there was a temporal association between the onset of his pig obsession and improvement in mood symptoms that was stable until death (Supplementary Table 1). This new belief system featured new associations between concepts of intelligence and positivity with concrete anatomy or customs associated with pigs (Figure 1). The FTLD-tau patient developed a similarly intense fixation on positivity and happiness with spiritual overtones, but this manifested differently and more broadly by way of her artwork, personal appearance, and social behaviors. She also developed hoarding behavior in combination with rituals centered on shopping and daily production of visual artwork (Figure 1). The presence of complex rituals in both patients and artistic creativity in the FTLD-tau patient is consistent with data suggesting aTL atrophy contributes to complex goal-directed compulsive behavior (45, 46) and emergent visual creativity in FTD (33). Subcortical structures with dense connections to the aTL and regional hubs of the salience network have also been implicated in ritualistic and impulsive behavior in FTD, with evidence for basal ganglia involvement in aberrant reward processing (47) that may contribute to symptoms of excessive spending in the FTLD-tau patient and giving away money to strangers in the FTLD-TDP patient. These behaviors are consistent with existing reports of dissociable impairments in loss aversion (i.e., bias in decision making for avoidance of loss regardless of the potential gains or risk) and delayed discounting (i.e., perception of a greater value to immediate rewards than future rewards) in bvFTD and svPPA, respectively (48). Abnormal reward processing in FTD can resemble the impulse control phenomenon of reckless generosity previously described as a side effect of dopamine replacement therapy in Parkinson's disease (49). However, unlike reckless generosity, which is due to hypersensitivity of the dopaminergic system and often reversible after reducing dopaminergic therapy in PD (50, 51), deficits in delayed discounting in svPPA appear driven by reduced valuation of future rewards leading and are linked to reduced connectivity of the anterior cingulate and medial temporal lobe (52) and atrophy in the dorsomedial prefrontal cortex, orbitofrontal cortex, subgenual anterior cingulate cortex, and ventral striatum that includes the dopaminergic system (53). Thus, a complex interaction of subcortical dopaminergic and cortical frontal and anterior temporal brain connectivity likely contributes to the observed symptoms of aberrant reward processing in FTD; however, the relatively selective degeneration of the aTL and paralimbic regions in the FTLD-TDP patient may have driven his impulsive generosity with strangers (54).

Differences in their new-onset belief systems may be explained in part by relatively unique anatomical involvement between patients. While semantic knowledge and social cognition are critically dependent on the integrity of the aTL, there are also contributions from connected regions. Indeed, a large body of literature supports a conceptual model in which bilateral aTL are neural hubs that integrate modality-specific inputs from distributed neocortical regions to generate generalizable semantic representations (55–58). Integration includes visual and auditory features from posterior temporal and occipital cortices, emotional valence from medial temporal and basal forebrain structures, and interoceptive cues from posterior frontal regions (55). In addition to the aTL, inferior parietal regions including the angular gyrus may contribute to semantic knowledge and integrative aspects of semantic processing to facilitate generalization of objects within a category (59–62). The FTLD-tau patient showed overall greater and more widespread neurodegeneration compared to the FTLD-TDP patient with a prominent loss of projection neurons and myelin/axonal loss associated with long-range tracts including severe atrophy of the corpus callosum and interlobar fiber bundles such as the uncinate and longitudinal fasciculi known to contribute to a multitude of language and behavioral impairments in FTD (63–66). In contrast, projection neuron loss and deep white matter changes were largely confined to the aTL in the FTLD-TDP patient. Moreover, these findings align with previous work demonstrating that white matter and projection neuron-rich lower layers accumulate severe tau pathology relatively spared by TDP-43 pathology (67, 68). We hypothesize these laminar distributions may also influence the more widespread spread of tau pathology to dorsolateral cortices across frontal, temporal, and parietal lobes typically associated with PiD (38, 69, 70) in contrast to the relatively focal involvement of left medial and ventral frontotemporal regions characteristic of TDP-C pathology (19, 31, 71, 72). One interpretation of these data is that the relatively focal left aTL disease in the FTLD-TDP patient may have led to a disconnection from temporoparietal areas and other integrative semantic hubs, resulting in inappropriate associations between concrete pig features (e.g., looking up) and less concrete concepts (e.g., positivity) relatively spared in svPPA (73). Despite the decline in semantic knowledge, the FTLD-TDP patient interestingly expressed the desire to communicate in numbers, possibly representing relative spared numeric comprehension subserved by posterior temporoparietal areas (59, 60, 74). He additionally showed improvement over time on several tests of executive functioning (i.e., Trail Making Test Part B, Letter Fluency) that may reflect relative sparing of prefrontal cortical regions and frontostriatal white matter connections that support executive processes (75). In contrast, the FTLD-tau patient developed a more generalized schema of positivity and had more diffuse cognitive impairment secondary to widespread disease across integrative hubs (76, 77).

Our ultra-high-resolution iron-sensitive MRI approach to guide histopathological sampling led to additional observations. While hypointense signal and iron-rich gliosis were predominantly found in the aTL of both patients, we found somewhat different laminar patterns. Similar to previous work (40, 78), select ventral aTL showed bands of upper layer hypointensity alongside variable mid and lower layer hypointense signal in the FTLD-TDP patient, while the FTLD-tau patient had more prominent but variable mid and deep layer bands of hypointensity in the aTL. These imaging findings corresponded to iron-rich gliosis, raising interesting questions about the potential role of non-cell autonomous neurodegeneration in FTLD. The localization of iron-rich gliosis to aTL epicenter regions may suggest this process occurs early in disease, or alternatively, is a later-occurring phenomenon associated with advanced neurodegeneration. PET imaging for microglial activation in living FTD patients suggests the former (79, 80), but further work is needed with autopsy confirmation.

The observed differences in macro-, meso-, and microscopic distributions of pathology between patients may suggest differences in the rate of neurodegeneration between proteinopathies and laminar patterns of cellular spread. Indeed, the FTLD-tau patient with 11 years of symptoms accumulated more severe and widespread pathology compared to the FTLD-TDP patient with a longer symptom course of 16 years. It is possible that the more extensive tau accumulation in all cortical layers for PiD (68, 69, 81–84) and concordant severe neurodegeneration of long-range projection neurons responsible for intra- and interhemispheric connections contributed to the more widespread neuropathologic changes in the FTLD-tau patient. In contrast, TDP-43 mediated neurodegeneration was relatively focal and most prominent in upper layers I-II consistent with previous work (19, 31, 68, 72, 85, 86), but unexpectedly frequent in additional layers V–VI. The cells bearing TDP-43-positive dystrophic neurites are currently understudied, but one possibility is that upper layer TDP-C pathology may originate from layer V/VI projection neurons whose distal ends of apical and basal dendrites are enriched in layers I–II and V–VI (87). The most severely degenerated regions of the aTL corresponded to relatively low accumulations of tau and TDP-43 pathology, consistent with previous findings in the aTL of patients with TDP-C or familial tauopathies (19, 72, 88). While TDP-43 burden and neurodegeneration were both greater medially than laterally in the FTLD-TDP patient, tau burden was higher in ventrolateral frontal isocortex with mild neurodegeneration compared to medial and dorsolateral frontotemporal cortices with peak neurodegeneration in the FTLD-tau patient. These patterns of partial overlap and divergence suggest a dynamic process of protein aggregation and neurodegeneration likely influenced by multiple factors, including regional-, cell-, and proteinopathy-specific mechanisms that contribute to variable rates of progression, duration, and clinical manifestations.

We find both convergent and divergent patterns of comparative neurodegeneration between FTLD proteinopathies that highlight potential mechanisms of selective vulnerabilities in FTD and neural substrates for complex human behavior. However, these observations will need to be confirmed in larger patient cohorts using methods integrating antemortem and postmortem neuroimaging with digital histopathology and antemortem behavioral assessments. While assessment of complex behavioral and neuropsychiatric symptoms in FTLD is methodologically challenging, advancements such as digital monitoring and event sampling using wearable devices and smartphones (e.g., activity tracking, psychophysiological monitoring) have the potential to capture more objective and ecologically valid metrics of behavioral disturbance (89, 90). These limitations notwithstanding, these illustrative descriptions can guide future large-scale, multi-modal studies of selective vulnerability in anatomic variants of FTD to further understanding of human values and belief systems.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Institutional Review Board of the University of Pennsylvania. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

DO, ER, and DJI contributed to the conception and design of the study. DO, ER, and DJI contributed to the first draft of the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2023.1245886/full#supplementary-material

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Economic and social values in the brain: evidence from lesions to the human ventromedial prefrontal cortex

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Making good economic and social decisions is essential for individual and social welfare. Decades of research have provided compelling evidence that damage to the ventromedial prefrontal cortex (vmPFC) is associated with dramatic personality changes and impairments in economic and social decision-making. However, whether the vmPFC subserves a unified mechanism in the social and non-social domains remains unclear. When choosing between economic options, the vmPFC is thought to guide decision by encoding value signals that reflect the motivational relevance of the options on a common scale. A recent framework, the "extended common neural currency" hypothesis, suggests that the vmPFC may also assign values to social factors and principles, thereby guiding social decision-making. Although neural value signals have been observed in the vmPFC in both social and non-social studies, it is yet to be determined whether they have a causal influence on behavior or merely correlate with decision-making. In this review, we assess whether lesion studies of patients with vmPFC damage offer evidence for such a causal role of the vmPFC in shaping economic and social behavior.

KEYWORDS

reward value, social value, ventromedial prefrontal cortex, orbitofrontal cortex, lesion studies, decision-making

1. Introduction

Throughout the history of neurology, individual patient cases have played a major role in deepening our understanding of brain-behavior relationships. Among these cases, Phineas Gage and patient EVR, have generated enduring interest in the role of ventral areas of the prefrontal cortex, including the ventromedial prefrontal cortex (vmPFC, Figure 1). These two prototypical cases triggered a paradigm shift in neurology, from an era where the vmPFC was considered as a silent or less prominent cortex, to the view that the vmPFC plays a pivotal role in shaping human behavior. Following brain damage in ventromedial and orbital prefrontal areas, both patients displayed striking changes in personality and manner, despite seemingly preserved basic intellectual abilities (1–4). The story of these famous cases and their behavioral impairments have been documented in great details over the years. Here, we just briefly outline two aspects of the behavioral changes of these patients that appear relevant for the purpose of this review. First, both patients seemed impaired in value-based decision-making. Gage's initial description stated that he "*does not estimate size or money accurately, though he has memory as perfect as*

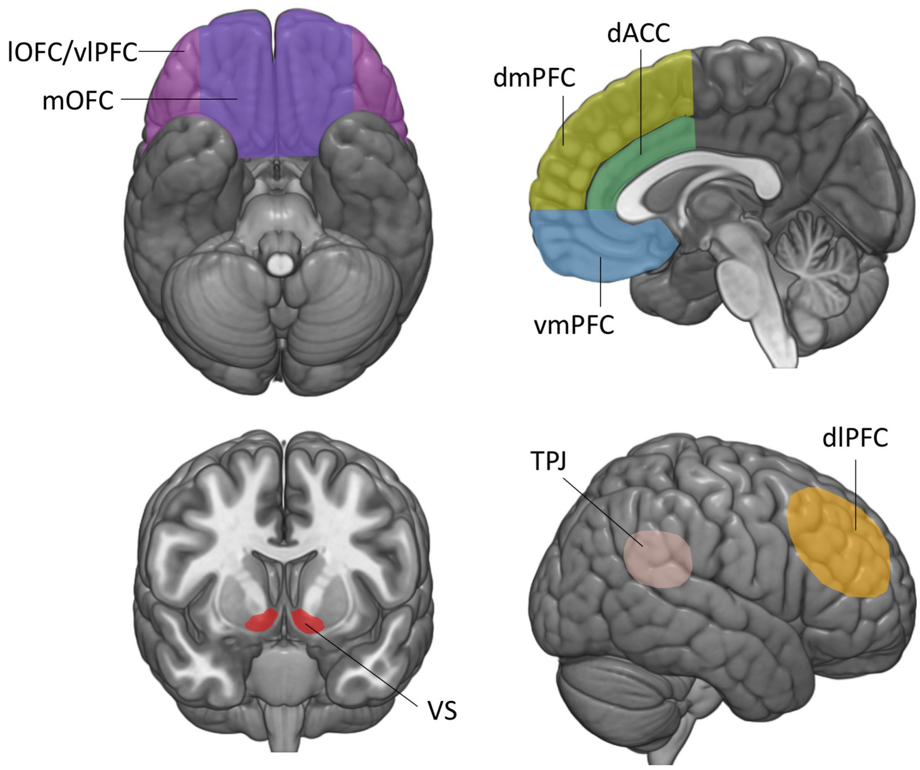

FIGURE 1
Brain regions involved in the construction of economic and social value. The vmPFC is defined here as the medial orbitofrontal cortex and lower portions of the medial prefrontal cortex and anterior cingulate cortex, below the genu of the corpus callosum. mOFC, medial orbitofrontal cortex; lOFC, lateral orbitofrontal cortex; vmPFC, ventromedial prefrontal cortex; vlPFC, ventrolateral prefrontal cortex; dmPFC, dorsomedial prefrontal cortex; dlPFC, dorsolateral prefrontal cortex; dACC, dorsal anterior cingulate cortex; *VS*, ventral striatum; TPJ, temporo-parietal junction.

ever. He would not take $1,000 for a few pebbles which he took from an ancient river bed where he was at work" (4). Similarly, for EVR, "*deciding where to dine might take hours, as he discussed each restaurant's seating plan, particulars of menu, atmosphere, and management. He would drive to each restaurant to see how busy it was, but even then, he could not finally decide which to choose. Purchasing small items required in-depth consideration of brands, prices, and the best method of purchase*" (2). Second, Gage and EVR also demonstrated impaired abilities in social decision-making. While Gage showed suspected impairments in social norm compliance and empathy, being described as "*irreverent, indulging at times in the grossest profanity (which was not previously his custom) … manifesting but little deference for his fellows*" (3), EVR showed poor judgment in choosing valuable social partners. For example, he began a short-lived relationship with a disreputable woman, and became "*involved in a home-building partnership with a former coworker, a man of questionable reputation who had been fired from the company. Despite warnings by family and friends, EVR invested all his savings in the partnership. The business failed and he had to declare bankruptcy, losing his entire investment*" (2).

Although Gage and EVR cases pointed to a fundamental role of the vmPFC in social and non-social decision-making, the precise nature of the function(s) supported by this region has been long debated. Several theories have been put forward to propose a unified function of the vmPFC, including the somatic marker (5) and the affective meaning hypotheses (6). More recently the "cognitive map" hypothesis postulated a role for the vmPFC in learning the structure of the world by representing the relationships between its different states (7–10). Another theoretical framework, the "extended common neural currency" hypothesis, suggests that identical neural processes in the vmPFC assign values, or the motivational relevance, to social and non-social factors (11). This framework builds on theories proposed in the field of non-social decision-making. Empirical studies in that field have identified a set of brain regions, including the vmPFC and the ventral striatum, as part of a brain valuation system. Neural activity in these regions is thought to encode a "common neural currency," allowing the value of different rewards or actions to be compared on a common scale, which is essential for guiding decision-making across different contexts (11). Recent observations showing the involvement of the brain valuation system during social decision-making have suggested extending the "common neural currency" hypothesis to social factors (11). In that schema, identical neurons in the vmPFC would process social and non-social value signals, although they may incorporate inputs from different brain regions that process information relevant for social or non-social contexts (11). By contrast, a "social valuation specific schema" assumes the existence of a distinct population of neurons, that may or may not be located in the vmPFC, dedicated specifically to computing values in social contexts (11).

Note that functional imaging studies implicating the vmPFC in reward valuation (12, 13) provide correlational, not causal, evidence for its role in value processing. Demonstrating the causal role of the vmPFC with non-invasive brain stimulation techniques is difficult as current methods mostly target brain areas at the cortical surface.

Human lesion studies provide an alternative method to demonstrate the critical role of damaged regions.

Here, we aimed at assessing whether human vmPFC lesion studies support a causal role for the vmPFC in both social and non-social decision-making. We define social decisions as choice situations involving more than one person. We chose to focus this review on published works that could address the "extended common neural currency" hypothesis and establish whether the vmPFC represents the values of both social and non-social factors. We searched for vmPFC lesion studies spanning from 1990 to 2023 by querying the MEDLINE database with the following terms: ('vmPFC' OR 'ventromedial prefrontal' OR 'orbitofrontal' OR "medial prefrontal') AND ('patients' OR 'lesion' OR 'damage'). We only included group studies that used social or value-based decision-making tasks in patients with focal lesions in the vmPFC. We excluded clinical case studies, studies involving only patients with non-focal lesions such as neurodegenerative diseases or non-penetrating traumatic brain injuries, and studies that did not employ behavioral tasks addressing either social or non-social decision-making (for reviews on the effect of vmPFC damage on all cognitive domains, see (14, 15)).

This review is structured as follows. First, we provide an overview of lesion studies implicating the vmPFC in representing the economic value of various goods during non-social decision-making. We then review lesion studies that have examined the role of the vmPFC in assigning values to the diverse contexts and interactions during social decision-making. For both economic and social values, we start off by summarizing key results from functional imaging studies identifying value signals in the vmPFC, and then outline the impairments in decision-making that result from vmPFC damage. Note that the functional imaging studies presented here are intended to provide a summary of the main findings related to each decision-making task, not to provide a comprehensive review on brain activations in social and non-social decision-making, which would fall beyond the scope of this review. We group the presentation of lesion studies by the type of valuation process or social situation they address. Note that in this review, we refer to the vmPFC as the medial orbitofrontal cortex (OFC) (Figure 1, area 14) and lower portions of the medial prefrontal (mPFC) and anterior cingulate cortex (ACC) below the genu of the corpus callosum (Figure 1, areas 24, 25, 32) (16), since imaging and lesion studies hardly dissociated these regions. Finally, we discuss open questions that could contribute to a more comprehensive understanding of the function of the vmPFC in shaping social and non-social behavior.

2. Economic values in the vmPFC

Dysfunction of the vmPFC has been associated early with abnormal goal-directed behaviors, including apathy, lack of initiative, poor judgment, indecisiveness and defective decision-making in particular in the economic domain. Later work led to the hypothesis that the vmPFC might represent the economic value of different goods in a common neural currency. In this section, we refer to economic values as the motivational and hedonic relevance of non-social options, such as material goods, monetary rewards, food etc. Economic value signals have been examined in the brain at three distinct stages of the decision-making process: during the receipt and consumption of rewards, when learning from obtained rewards, and when choosing rewards. These different stages involve distinct types of value signals: experienced value, anticipated value and decision value. We therefore group the presentation of studies on economic values according to these three types of neural value processes.

2.1. Experienced values

Experienced values signals correspond to the neural activity associated with the immediate hedonic aspects of receiving or consuming a reward, for example the outcome of a choice. Such value signals have been found in a set of brain regions that constitute the brain valuation system, including the ventral striatum (*VS*) and the vmPFC. In the vmPFC, neural activity has been associated, for example, with the subjective pleasantness of receiving monetary rewards, different types of food (e.g., snacks, juices, milkshakes, wine, etc.), or various goods (e.g., trinkets, pieces of music, movies, etc.) (13, 17–20). A causal role of the vmPFC in hedonic responses would therefore predict reduced expression of pleasure, i.e., anhedonia, after vmPFC damage. Few studies, however, have examined this prediction. Damage to the vmPFC was found to reduce self-reported happiness compared to prefrontal lesions outside of the vmPFC (21). However, in a larger population of combat veterans with penetrating brain injuries, bilateral lesion to the vmPFC was not associated with higher anhedonia in self-reported scales and clinical interviews (22). Moreover, in a behavioral gambling task, patients with vmPFC damage showed preserved pleasantness ratings and emotional autonomic responses when experiencing monetary gains (23, 24). Although these patients experienced weaker disappointment and no regret in the task (i.e., the effect on hedonic experience of unobtained outcomes and unchosen gambles, respectively), further studies suggested that those impairments reflected ventrolateral rather that ventromedial damage (24). Lesion studies therefore provide little evidence for a causal role of the vmPFC in hedonic experience. This is consistent with the idea that the vmPFC is involved in "*coding*" but not in "*causing*" pleasure (25), in the sense that it encodes a signal that correlates with hedonic experience without underlying this mental experience. However, such a signal that scales with the hedonic experience of reward might constitute a prerequisite to learn to anticipate future rewards and later guide decision-making.

2.2. Anticipated values

Anticipated values signals reflect the prediction of the experienced value associated with the different options under consideration. These signals have been observed in functional imaging studies in the *VS*, the OFC and the vmPFC (26–29). During value learning, anticipated value is thought to be dynamically updated based on "reward prediction error" (RPE) signals. Prediction errors measure deviations from individuals' reward expectancies: they are positive when experienced value is greater than anticipated, and negative otherwise. Such RPE signals have been identified in midbrain dopaminergic neurons and have also been consistently measured in the *VS*, to which these neurons project (30–32). Hence, dopaminergic projections could facilitate value learning by gating plasticity between sensory information and anticipated value representations in the *VS* and the

BOX 1 Economic and social games.

Iowa gambling task	In this task, participants choose cards from four different decks. Each card provides either a gain or a loss. Two decks are "good decks," providing small gains but also smaller losses, leading to a net gain overall. The two others decks are "bad decks," providing big gains but even bigger losses, leading to a net loss overall. The goal is to earn as much money as possible.
Dictator game	In this game, one participant decides how to share a monetary amount with an anonymous partner. The recipient only plays a passive role. The amount of money allocated to the partner serves as a measure of the dictator's deviation from self-interest and provides evidence of the influence of fairness and altruism in social behavior.
Ultimatum game	In this game, a proposer, who is endowed with a sum of money (the stake), must suggest a way to split it with another player, the responder. The responder may accept or reject the offer. If the responder rejects the offer, neither player receives any money. The behaviors of both the proposer and the responder can serve as a measure of fairness preferences.
Trust game	In this game, an investor is endowed with a sum of money and decides how much money to send to a trustee. The amount transferred is then multiplied (e.g., by a factor > 1), and the trustee must decide how much to return to the investor. In single-shot versions of this game, the investor's behavior is a measure of trust, while the trustee's behavior is a measure of trustworthiness and social-preferences.
Prisoner's dilemma game	In this task, two anonymous participants independently decide whether to cooperate or to defect. Each player is paid according to the combination of the two decisions. The payoffs are arranged such that each player will earn the most by defecting, but the team will collectively earn the highest earning if both participants cooperate. Behavior in this task is taken as a measure of social cooperation.
Public good game	In this game, several participants decide how much to contribute to a group pot (i.e., maximizing joints payoffs), which is multiplied and split equally amongst all participants, and how much to keep for themselves (i.e., maximizing individual payoffs by free-riding). Single-shot versions of this game measure social cooperation.
Moral dilemma	In the classic 'trolley problem', a trolley is hurtling down a track toward five people who are tied to the rails and cannot move. A lever is within reach that can switch the trolley to a different track where there is only one person tied up. Participants must decide whether to sacrifice one person by pulling the lever in order to save the lives of five others. In the 'Footbridge' variation of this dilemma, the person deciding the fate of the individuals must physically push someone off a bridge to stop the trolley and save the others.

vmPFC. To establish the causal role of the vmPFC in supporting value learning and anticipation, lesion studies have used different learning paradigms.

The critical role of the vmPFC in learning the rewarding outcome associated with a stimulus was first suggested after seminal work that employed the Iowa gambling task [IGT, Box 1; (33)]. Poor performance in the IGT, however, is not specific to vmPFC damage (34–36). Performance in the IGT is also difficult to interpret, in part because the task involves both deterministic and probabilistic aspects, meaning that stimuli may predict rewarding outcomes either with certainty or a certain degree of probability, as well as apparent reversals in stimulus-value contingencies (37). In tasks involving only deterministic associations between stimuli and reward values, damage to the vmPFC was not found to significantly impair reward learning (38). Tasks involving probabilistic contingencies demonstrated inconsistent impairments and suggested that bilateral vmPFC lesions may be required to reliably affect reward learning (39–42). Furthermore, the vmPFC was shown to be specifically critical for learning the value of stimuli but not for learning the value of actions (39, 43). Instead, successful action-value learning was found to depend on the integrity of the dmPFC, although the vmPFC may be necessary for awareness about action-value relationships (39, 43). In a changing environment, stimulus-value associations can evolve over time, for example when discovering that a previously liked food is toxic, requiring individuals to update the learned value. Deficits in reversal learning tasks have been demonstrated consistently after vmPFC injury (21, 38–40, 42, 44) [but see (41)]. Moreover, reward value can also change as a result of a change in individuals' internal states, for example when satiated with a particular food. In devaluation tasks, patients with focal damage to the vmPFC demonstrated impaired devaluation, persisting in selecting conditioned stimuli associated with food that had been devaluated through selective satiation (45). Consistent evidence therefore supports the causal role of the vmPFC in the flexible updating of anticipated or learned reward values, which can then be used to guide behavior and decision-making.

2.3. Decision values

Decision values signals are thought to measure the difference between the considered option value and another option value, and are used to guide decisions toward the option with the largest benefit. They rely on the net value of options, integrating the anticipated values and costs of each option. Functional imaging studies have identified such value signals at the time of decision in a network of regions, including the vmPFC, during simple binary decisions, for example when choosing between two different food items, drinks, monetary rewards, products, artworks, etc. (12, 13). Decision value signals in the vmPFC have also been shown to integrate the different costs, such as the delay, the effort, or the uncertainty associated with the options of a choice (27, 46–48). The vmPFC has, therefore, been hypothesized to be critical for economic rationality and utility maximization. Damage to the vmPFC has been shown to induce choice inconsistency and choice intransitivity. Choice inconsistency consists in not choosing the same option during repeated choices, or not choosing the option that was given the best rating. Choice intransitivity consists in choosing A over B, B over C, but C over A (39, 49, 50) although not always (51). Yet, when present (but see (51)), these effects are small and vmPFC patients can still make decisions readily. This led to the hypothesis that the vmPFC may not be necessary for rational decision-making *per se*, but rather may promote preference stability by reducing variability in valuation across time (52). In repeated choices, individuals with vmPFC damage express preferences that are indeed more variable, but fundamentally transitive (52). Therefore, vmPFC may not be the only critical structure supporting rational value-based choices, which may rely instead on distributed areas, including the *VS*, that can compensate for damage in the vmPFC (52). Increased choice variability may also participate to explain inconsistent results observed in tasks that assess cost-related preferences. In intertemporal choices that involve choosing between smaller immediate rewards and larger delayed rewards, some studies reported greater temporal discounting of delayed rewards after vmPFC damage (53–57), while others reported no difference compared to controls (58, 59). Similarly, lesions to the vmPFC have been suggested to affect decision-making under uncertainty. Yet, although increased risk-taking has been reported in vmPFC patients (54, 56, 60–62), some studies found no effect (24, 59), one study reported higher risk-taking in the loss-domain but lower risk-taking in the gain-domain (63), and another found increased risk-taking only while receiving dynamic feedback (64). Little data exist on the impact of vmPFC damage in humans on effort- and reward-based decision-making, that involve deciding to make an effort to obtain a reward, but preliminary results suggests that vmPFC may not be critical for such decisions (65). In closely related incentive motivation tasks, that involve effectively producing effort to obtain a reward, damage to the vmPFC reduced the vigor of effort (saccade velocity) produced in response to different reward levels (66). However, here again, the magnitude of this deficit was moderate, in particular in comparison to that observed after lesion to the ventral striato-pallidal complex which completely abolishes effort modulation (67, 68). This series of lesion studies therefore suggest that, at the time of decision or action, the vmPFC may not be critical, but may play a modulating role in shaping value-based behavior. Interestingly, recent findings on valuation about multidimensional options could shed light on the specific role of the vmPFC in decision-making. When value has to be inferred from the multiple attributes of a stimulus, vmPFC patients differ from prefrontal lesioned and healthy control individuals in how they weight the different attributes in certain choices, for example when choosing artworks based on their perceptual, conceptual and affective characteristics (69), but not in other, for example when choosing potential houses based on their features (70). Recent work suggested that vmPFC damage might specifically affect decision-making when value must be inferred from the unique combination of attributes, in other words their interaction, and not when value can be inferred from the sum of independent attributes (71). Such a role could potentially account for why vmPFC patients are not incapable of making choices, but systematically deviate from healthy individuals in their decisions.

3. Social values in the vmPFC

Beyond its role in economic valuation, the vmPFC has been implicated early in shaping social behavior. In the 1970s and 1980s, the terms "pseudopsychopathy" (72) and "acquired sociopathy" (2) were coined to describe the dramatic personality and behavioral changes in the social realm observed in patients with vmPFC damage: blunted affect, lack of empathy, poor tolerance to frustration and irritability, social inappropriateness and antisocial behaviors (73–78). However, the precise cognitive mechanisms underlying these social deficits have remained elusive. In the following sections, we review the lesion studies that have examined the role of the vmPFC in supporting social value signals and which may support the "extended common neural currency" model. To simplify the wide range of contexts and decision types encountered in these studies, we group them into three classes of social values: the value that one assigns to other individuals, the value of outcomes that benefit others, and the value of outcomes that conform to social norms (11).

3.1. Value assigned to others

Most people tend to pursue social interactions that offer some form of gratification or benefit. The first class of social valuation therefore concerns situations in which individuals assess the personal value of another person, for example when judging the attractiveness or trustworthiness of a person, or situations in which they assess the value of another person's actions to themselves, for example when being applauded by someone or when having trust reciprocated by someone. Functional imaging studies have found neural activation in the vmPFC when receiving, or anticipating rewarding social outcomes, such as viewing faces with positive affects (79), attractive faces (80), erotic photos (81), or when receiving social approval or romantic interest from others (82–84). Neural activity in the vmPFC also predicts subsequent decisions about liked others, such as the willingness to pay to view attractive faces (85) or to donate to preferred charities (86). BOLD activity in the vmPFC is also associated with learning about moral values of others, such as their honesty and trustworthiness (87, 88) and with the willingness to reciprocate trust (89). Consistent with imaging studies, lesion studies support the causal involvement of the vmPFC in the valuation of others. First, vmPFC damage reduces the tendency to approach positive and avoid negative emotional faces, particularly for negative affect, while preserving the ability to recognize facial expressions (90–92). Similarly, patients with vmPFC lesions have lower inter-personal disgust, showing less reluctance to interact with unsavory others or with individuals described as socially deviant (93). They also show lower consistency when choosing between potential spouses, based on non-physical attributes (94). Additionally, vmPFC damage affects social judgment about others, decreasing for example the perceived trustworthiness of unknown individuals (95, 96), and impairing the ability to revise these judgments based on the individuals' observed social and moral conducts (97). These findings demonstrate consistent impairment in behaving according to the value attached to other individuals after damage to the vmPFC.

3.2. Value of outcomes benefiting others

People are not always driven by their own self-interest and frequently take into account the well-being of others. Thus, a second class of social value signals correspond to the vicarious valuation of outcomes that are rewarding for others, adopting their perspective, for example when rejoicing in someone's victory, or when choosing to cook for someone his or her favorite food. Empirical studies have found that experiencing reward when directly receiving positive outcomes, or when observing others receiving such outcomes, activated the same regions of the brain valuation system, in particular the vmPFC (98). Experiencing reward for others also consistently recruit the *VS* (99, 100), although this structure may be preferentially activated in response to personal as compared to vicarious reward (98). Importantly, vicarious value signals in the vmPFC have been shown to predict choices during decisions that result in benefits for others, such as purchasing DVD movies or selecting monetary rewards for others (101–103). Additionally, the vmPFC encodes reward prediction error signals that support learning about another person's preferences (104, 105). By contrast, bilateral damage to the vmPFC reduces empathic tendencies toward others in clinical questionnaires (76). In economic games, such as the dictator and the ultimatum game (Box 1), patients with focal vmPFC lesions showed impaired concern about payoff to others, giving less money to anonymous strangers (95), even to individuals who are suffering (106). In the trust game (Box 1), when they are endowed from an investor with a sum of money that is later tripled, patients with vmPFC damage make lower back transfer to the investor than healthy controls (96). Taken together, these results therefore provide support for a critical role of the vmPFC in other-regarding preferences. *Empathy*, the ability to share another person's feelings, has been conceived as an initial step that can motivate such other-regarding motivation, or *sympathy,* and is considered one of the fundamental motives driving altruistic acts, which entail personal costs for the benefit of others (107).

3.3. Value of social norms and principles

People's behavior is not solely determined by their own interest or by the interest of specific others, but is also shaped by the collective welfare. A third class of social value signals therefore consists in the valuation of options or outcomes according to their conformity with normative social principles, for example when rejoicing in a fair distribution, or when turning down a bribe. Functional imaging studies have consistently reported neural value signals in reward-related brain regions in relation to social principles, such as fairness, cooperation or morality. For example, in economic exchange tasks such as the ultimatum game (Box 1), a fair distribution of money among players is perceived as rewarding and is associated with neural activation in the ventral striatum and vmPFC (108, 109). By contrast, inequality has been associated with activation of neural networks involved in conflict and aversive outcomes, including dorsal ACC and anterior insula (110). When given the opportunity, people tend to punish norm violators who propose unfair distributions, even when this is costly for them (111). Punishing defectors is thought to promote social norms enforcement (112), and is perceived as rewarding and elicits activation in the vmPFC (111). Another example of social principle eliciting neural value signals is cooperation. Research using the Prisoner's Dilemma game (Box 1) has shown that mutual cooperation is associated with increased activation in reward-related brain regions, including the vmPFC (113). These results have been proposed as evidence of the intrinsic value of cooperation, which can motivate individuals to engage in prosocial behavior and collective action. Finally, value signals have also been reported in the vmPFC during moral dilemmas (Box 1), for example when judging the moral acceptability of sacrificing a single life to save a larger group of dying (114). These findings suggest that normative social principles have inherent values that are encoded in the vmPFC. Damage to this region may therefore impact on how such principles shape human behavior. Lesion studies have, however, provided conflicting results on the antisocial or prosocial effects of vmPFC damage. In the ultimatum game (Box 1), vmPFC patients were initially reported to reject unfair offers at a higher rate than healthy controls, although showing normal levels of anger following unfair offers (95, 115, 116). These patients would also demand, as responders, the same amount that they offered as proposers, whereas controls generally offer more than they demand (95). This result has been interpreted as reflecting an insensitivity to guilt in vmPFC patients, defined as the aversion for advantageous inequity (95). This finding was replicated in another study, but only when monetary gains were presented as abstract amounts to be received later (117). When offers were readily available in cash, vmPFC patients showed normal rejection rate of unfair offers. Inconsistently, a recent study found that vmPFC patients showed diminished sensitivity to unfairness and were more willing to accept unfair offers than control participants (118). Research on the impact of vmPFC damage on cooperation is more limited, but one study reported that vmPFC patients were more likely to cooperate in a public good game (Box 1), with the opposite being true for dlPFC patients who cooperated less than control patients (94). These preliminary results challenge the view that vmPFC is a necessary component for cooperative behavior. By contrast, the impact of vmPFC damage on moral judgments is well-established. In moral dilemmas that involve causing the death of one person to save several lives, patients with vmPFC damage are more likely to choose the utilitarian option, that consists in sacrificing one person, than control individuals (116, 119–122). Although early works suggested that vmPFC patients might be especially impaired in personal versus impersonal moral dilemmas, when directly versus indirectly causing harm, further work showed that they endorsed utilitarian actions more often than healthy individuals, regardless of the situation (122). This utilitarian behavior has been interpreted as reflecting a lack of automatic affective response to moral transgressions in vmPFC patients, which was supported by the absence of autonomic skin response prior to such violations (120). Consistently, when judging the morality of actions made by others, vmPFC patients relied more on the outcome of the actions (i.e., whether they were harmful or not) than on the intention with which the actions were pursued (i.e., whether they were intentional or accidental), suggesting that vmPFC is necessary for integrating both intention and outcome into a moral value (123, 124). Although the impact of damage to the vmPFC on decision-making based on social principles, such as fairness, cooperation and morality, is often reported, it is not yet fully understood why such damage can result in both prosocial and antisocial behaviors.

4. Discussion and open questions

Most of the findings discussed above support the notion that the vmPFC represents neural value signals both in social and non-social contexts, consistent with the "extended common neural currency" hypothesis. However, the extent to which the vmPFC is critical for value processing may depend on the specific stage of the decision-making process or the nature of the rewarding outcome. In the economic domain, while the vmPFC may not be strictly necessary for experiencing the hedonic value of rewards, its integrity seems essential for learning and flexibly updating reward value. By contrast, empirical studies have produced mixed results regarding the effects of vmPFC damage on choices: some studies demonstrated deficits or biases that were moderate or restricted to certain types of decisions, while others showed preserved abilities to make consistent choices. In the social domain, lesion studies support the critical role of the vmPFC in assigning a subjective value to other individuals. They also support its necessary role in vicariously representing the benefits obtained by others. Damage to the vmPFC also demonstrated its critical role in moral judgments but showed inconsistent deficits in decision-making based on other normative social principles such as cooperation and fairness. The inconsistent effects of vmPFC's lesions on choices in certain social and non-social contexts suggest that the vmPFC may exert a modulatory rather than a necessary role at the time of decision. Alternatively, it is possible that the vmPFC is involved in certain types of valuation more specifically, for example when an option's value can only be determined by the interaction between its attributes and not by attributes independently (71).

The common involvement of the vmPFC in both social and non-social contexts raises the question of whether valuation in these contexts relies on the same neurons, or on distinct sub-regions or populations of neurons within the vmPFC. Meta-analyses have suggested a possible posterior-to-anterior gradient of value representations corresponding to concrete-to-abstract rewards (13). Yet, only few imaging studies have directly compared social and non-social value signals using the same experimental design (81, 104, 125–127). One of these studies observed a ventral-to-dorsal gradient in the processing of self- vs. other-regarding value signals (127). While lesion studies do not provide the necessary anatomical specificity to dissociate the roles of distinct areas within the vmPFC, single-unit recordings studies have started to identified neurons that may selectively encode social vs. non-social aspects of rewards both in non-human primates (128, 129) and in humans (130). However, it is worth noting that a clear distinction between social and non-social decisions can be subject to debate. Many decisions in people's lives, which may not involve another person at first glance, may, in fact, carry a social component. Consider, for example, the strong social influence that can impact the value people assign to material goods, such as when they decide to eat a vegetarian meal or buy a luxury car. Further works will help clarify whether the valuation of stimuli associated with social versus non-social contexts is implemented by common or overlapping but specialized neuronal populations.

The inconsistent effects observed after damage to the vmPFC, both in social and non-social decision-making, also question the influence of the heterogeneity of lesions across patients (Figure 2). A first factor that may contribute to these inconsistencies is the variability in the nature of the lesions across different studies (Figure 2). Ischemic, hemorrhagic, traumatic, or surgical causes can lead to different distributions of lesions and varying degrees of functional impairment. Samples consisting primarily of orbital meningioma cases involve more bilateral and anterior lesions, while vascular lesions often

FIGURE 2
Heterogeneity of vmPFC lesions in human studies. **(A)** Etiology of vmPFC lesions among cited studies with individual lesion data. **(B)** Location of lesions among cited studies with individual lesion data. Each column represents a patient. Green and red rectangles represent preserved and damaged areas, respectively. Brain areas are represented from top to bottom in the following order: right dmPFC/ACC, right vmPFC, right OFC, left OFC, left vmPFC, left dmPFC/ACC. SAH, subarachnoid hemorrhage. TBI, Traumatic brain injury. dmPFC, dorsomedial prefrontal cortex. ACC, anterior cingulate cortex. vmPFC, ventromedial prefrontal cortex. OFC, orbitofrontal cortex.

concern more posterior and unilateral lesions (14). Moreover, although surgical resection of brain tumors can lead to a greater degree of functional impairment compared to vascular lesions or traumatic brain injuries, the slow progression of tissue damage, as the tumor expands, may allow for brain plasticity and functional compensation over time (131). The age of lesion onset may also significantly influence the degree of functional impairment. Early-onset lesions that impact neurodevelopment tend to lead to more pronounced deficits (132–134). The age of lesion onset may also interact with changes in brain plasticity across the lifespan, and thus condition functional recovery. Thus, an important guideline for future studies would be to report the nature and the location of individual lesions, as well as the age of lesion onset when describing vmPFC patients (14). Finally, the variability in the impact of vmPFC damage raises the question of possible hemispheric specialization or functional redundancy between left and right vmPFC. Bilateral lesions in the vmPFC are rare and most of the patients included in the lesion studies mentioned above had unilateral lesions (Figure 2). Thus, it remains possible that compensation from the preserved vmPFC masked the effects of unilateral vmPFC damage. However, the limited sample size of vmPFC studies, which classically include only a tenth of patients or fewer, hinder the ability to compare the effects of bilateral and unilateral damage to the right or left vmPFC. Small samples also limit our ability to investigate deficits that arise from the interaction of lesions in the vmPFC and another region. Therefore, future research should aim to include larger samples of patients, possibly through multicenter collaboration, with a sufficient number of bilateral lesions, to investigate the potential effects of laterality, redundancy, and interactions following vmPFC damage.

Another question that remains is how specific the role of the vmPFC is in social and non-social decision-making, as such complex behaviors are likely to involve a network of multiple brain regions. While lesion studies shed light on the contribution of the vmPFC, few of them directly compared the effects of damage to the vmPFC to damage in other parts of the prefrontal cortex. Therefore, including control patients with prefrontal lesions outside the vmPFC in future studies would be essential to gaining a more comprehensive understanding of the unique role of the vmPFC in decision-making. Moreover, there is also evidence that the vmPFC receives specialized inputs from specific brain regions when constructing values in social and non-social contexts. For example, structures outside the classical reward circuitry and typically associated with social cognition, such as the dmPFC, dlPFC and TPJ, have been shown to be preferentially engaged in response to vicarious as compared to personal reward (98), and are thought to provide information that are relevant for the construction of social values through their connectivity with the vmPFC (11, 86). Further research is needed to provide a more comprehensive understanding of how remote cortical areas provide inputs for the computation of values in both social and non-social contexts. Additionally, investigating the impact of lesions in these structures and in the subcortical and white matter pathways that convey specific information to the vmPFC could shed light on diverse biases in decision-making.

In this review, we hope to have summarized the evidence supporting the notion that the vmPFC encodes value signals at different stages of the decision-making process, when receiving, learning and deciding about valued outcomes, both in the economic domain and in various social contexts, for example when valuating other individuals, others' benefit, or social normative principles. In the modern era, non-invasive brain stimulation techniques, such as Transcranial Magnetic Simulation (TMS) and Transcranial Direct Current Stimulation (tdCS), are classically used to demonstrate causality in brain functions. Yet, these methods can hardly modulate neural activity in subcortical structures or medial cortical areas as they primarily target brain areas at the cortical surface. Here, we have therefore also tried to emphasize the invaluable contribution of lesion studies in establishing or challenging causal brain-behavior relationships, particularly in reward-related brain areas, like the vmPFC or the ventral striatum. Overall, neuroimaging and lesion studies support an "extended common neural currency" schema, where the vmPFC serves as key motivational node that shapes both social and non-social human behaviors, but flexibly integrates inputs specific to the decision-making context.

Author contributions

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Fairness: from the guts to the brain – a critical examination by Atlantic fellows of the Global Brain Health Institute

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In January 2023, the Global Brain Health Institute (GBHI) at UCSF hosted an online salon to discuss the relationship between fairness and brain health equity. We aimed to address two primary questions: first, how is fairness perceived by the public, and how does it manifest in societal constructs like equity and justice? Second, what are the neurobiological foundations of fairness, and how do they impact brain health? Drawing from interdisciplinary fields such as philosophy, psychology, and neuroscience, the salon served as a platform for participants to share diverse perspectives on fairness. Fairness is a multifaceted concept encompassing equity, justice, empathy, opportunity, non-discrimination, and the Golden Rule, but by delving into its evolutionary origins, we can verify its deep-rooted presence in both human and animal behaviors. Real-world experiments, such as Frans de Waal's capuchin monkey study, have proven enlightening, elucidating many mechanisms that have shaped our neurobiological responses to fairness. Contemporary cognitive neuroscience research further emphasizes the role of neuroanatomical areas and neurotransmitters in encoding fairness-related processes. We also discussed the critical interconnection between fairness and healthcare equity, particularly its implications for brain health. These values are instrumental in promoting social justice and improving health outcomes. In our polarized social landscape, there are rising concerns about a potential decrease in fairness and prosocial behaviors due to isolated social bubbles. We stress the urgency for interventions that enhance perspective-taking, reasoning, and empathy. Overall, fairness is vital to fostering an equitable society and its subsequent influence on brain health outcomes.

KEYWORDS

fairness, equity, social justice, brain health, neurobiology

Introduction

Fairness plays a vital role in shaping human experiences across various aspects of life (Scarpa et al., 2021). Recognizing its importance, the Global Brain Health Institute (GBHI) has identified fairness as one of its core values, emphasizing its significance in creating a just and equitable society. In this context, fairness is defined as the just and unbiased treatment of all individuals, regardless of their background, guided by principles of justice and equality. Our activities were framed within the theoretical understanding of social justice theories, which emphasize the role of fairness in equitable resource distribution and social inclusion.

In January 2023, three Atlantic Fellows from the GBHI at the University of California San Francisco (UCSF) organized an online salon titled "Fairness: from the guts to the brain," which aimed to explore and critically assess the value of fairness and its relation to brain health and equity. An online salon refers to a virtual gathering of individuals who engage in intellectual discussions and exchange ideas on a specific topic. This format enables participants from various locations to come together, fostering a diverse and inclusive environment for deep and meaningful conversations.

In the online salon, participants critically examined the concept of fairness, discussing its primal component and exploring the instinctive, visceral reactions to unfairness. However, the salon also emphasized that promoting fairness requires more than just gut feelings. Immediate reactions can lead to biased or unfair actions, necessitating active reflection on fairness as a concept and intentional efforts to cultivate it as a value. Throughout the salon, the value of fairness was analyzed in depth, considering its manifestation within various cultural and community contexts and delving into the science behind it. By engaging in this critical examination, participants gained a deeper understanding of the complexities surrounding fairness and its role in fostering a more just and equitable society.

In the following sections, we first investigate personal views on fairness. Then, we examine its evolutionary roots in humans and animals. We move on to its neurobiological basis, guided by cognitive neuroscience research. We also discuss its vital role in healthcare equity and brain health, incorporating diverse cultural insights. Finally, we consider the future of fairness in a polarized world.

Exploring the multifaceted concept of fairness: insights from public opinion

Fairness is a concept that pervades various aspects of human life and is deeply ingrained in our moral, social, and political values (Schroeder et al., 2019). To understand what people think about fairness, we conducted a two-step investigation, collecting word cloud responses during our online session and taking to the streets of San Francisco to gather first-hand opinions.

To gain an initial grasp of people's thoughts on fairness, we asked our 40 salon participants (Atlantic Fellows for Equity in Brain Health, GNBHI, and UCSF professionals) to provide one or a few words that they associate with the concept. The resulting word cloud revealed four prominent terms: equity, justice, empathy, and opportunity (Figure 1). These findings suggest that fairness, in the public's perception, revolves around the ideas of equal treatment, the application of just principles, the ability to understand and share others' feelings, and the provision of chances for individuals to succeed.

To further explore public opinion on fairness, we also approached eight anonymous individuals of different ages and backgrounds in the streets of San Francisco to capture more nuanced and diverse perspectives. The responses were varied but revealed some recurring themes:

1. Fairness as non-discrimination: Participants emphasized the importance of not judging people based on race, gender, religion, or other traits but instead on their character.
2. Fairness as enabling opportunity: Respondents noted that fairness meant giving everyone opportunities and helping people explore those opportunities, including having a political voice and access to education, jobs, and housing.
3. Fairness as emotional warmth: Some interviewees highlighted the emotional aspect of fairness, associating it with feelings of warmth and kindness.
4. Fairness as social justice: Many responses pointed to broader social issues, such as the Black Lives Matter movement, indicating that fairness is closely connected to the pursuit of social justice.
5. Fairness as the Golden Rule: A particularly poignant testimony from a formerly homeless individual emphasized the importance of treating others as one would like to be treated (i.e., the Golden Rule, an ethical principle found in many cultures and religions), encapsulating the essence of fairness.

It is important to note that the activities described were not designed as formal research with systematic methods and analysis plans. Rather, they were illustrative activities aimed at enriching an educational discussion on fairness. As our interviews were conducted in San Francisco, United States, one must consider that perceptions of fairness may vary based on demographic factors such as cultural background, age, and socioeconomic status. Our observations, therefore, may not be universally applicable and could differ in other settings. Properly designed research studies could explore how these demographic variables influence public perceptions of fairness. Even so, our exploration has suggested a multifaceted concept encompassing equity, justice, empathy, opportunity, non-discrimination, and the Golden Rule. By understanding these diverse dimensions of fairness, we can better engage in meaningful conversations and strive to create a more just and equitable society.

The evolutionary origins of fairness

Building upon this multi-dimensional understanding of fairness, as reflected in public opinion, we delve deeper into the evolutionary origins of this essential concept. The perception of fairness is not limited to humans but is also observable in certain animal species, particularly those that engage in collective hunting. Once the target is achieved, rewards, typically in the form of food, should be distributed proportionally to the effort each individual has contributed. This equitable share is vital for replenishing energy and maintaining group harmony. Failure to distribute rewards fairly may lead to aggressive behavior or the death of individuals who have exerted significant

FIGURE 1
Word Cloud on the salon participants' responses to "What words come to your mind when thinking on the concept of Fairness?". The size of each word in the cloud represents its frequency as a response. Larger words were mentioned more often in the public opinion survey (created using mentimeter.com).

effort. Moreover, unfair distribution of rewards may lead to the exclusion of individuals from the group (Brosnan and De Waal, 2014).

In the human context, the development of language has further refined our ability to make fairness-related decisions over the long term (Brosnan and De Waal, 2014; McAuliffe et al., 2017). Language has empowered societies to achieve more complex goals and has allowed the integration of community values, such as charity, into the decision-making process. While further research is needed to fully comprehend the impact of language on fairness, charitable actions are not only morally commendable but can also carry economic incentives, such as tax benefits. These economic factors can further influence decision-making, thereby emphasizing the societal importance of fairness.

Incorporating abstract thinking into decision-making processes has been pivotal in understanding fairness as a form of secondary compensation (Brosnan and De Waal, 2014; McAuliffe et al., 2017). Imagine a local community organizer who advocates for the creation of a community garden in a low-income neighborhood. The immediate costs and labor involved might seem like a burden to some community members. However, employing abstract thinking allows the group to consider secondary compensations: the garden could serve as a source of fresh produce, a learning environment for children, and a communal space that fosters neighborhood cohesion. Over time, these benefits could even contribute to lower crime rates and improved mental health among residents. In this example, abstract thinking enables individuals to weigh the immediate costs against a broader range of long-term benefits, thereby promoting fairness in the form of secondary compensation. Abstract thinking enables the evaluation of even more intricate cost–benefit scenarios, taking into account local, regional, or even global objectives such as those outlined in the sustainable development goals agenda.

The neurobiology of fairness

Exploring parallels between human and animal reactions to inequity

The neurobiology of fairness has become a subject of interest among researchers, as understanding the biological basis of our reactions to unfairness may provide valuable insights into human behavior and social structures. With that in mind, we conducted an experiment with our salon participants to explore their reactions to unfair situations. We then drew parallels between these human reactions and those observed in animals, specifically by examining Frans de Waal's famous study involving capuchin monkeys receiving unequal pay (Brosnan and de Waal, 2003).

In our social experiment, salon participants were electronically grouped with two non-player characters and assigned unique avatars (Supplementary Appendix A). The objective was to reach the end of a designated path, with the first two players securing job opportunities while the third remained unemployed. Participants answered questions related to fairness at each step, which allowed them to move forward. The game was designed to simulate real-world unfairness, incorporating challenges such as unequal starting positions, limited access to quality food and transportation, and appearance-based discrimination. All real-life participants were covertly set up to experience the series of unfair disadvantages, although they were unaware of this manipulation. For example, they started the game four positions behind due to 'bonus' points arbitrarily given to non-player characters. Additionally, they lost a turn because of abdominal pain caused by eating at a low-quality restaurant and not having medical care, thereby spotlighting the issue of healthcare inequities. These intentionally engineered setbacks led participants to report feelings of frustration and irritation, allowing them to empathize with individuals who face similar systemic barriers in real life.

To draw parallels between human and animal reactions to unfairness, we showed an excerpt from Frans de Waal's TED Talk (De Waal, 2011). The talk featured a capuchin monkey experiment where unequal rewards led to visible agitation. In the experiment, the monkeys were placed in separate but adjoining cages, visible to each other, and trained to exchange a small stone for a cucumber slice as a reward. Both monkeys willingly performed the task when they were rewarded equally. However, when one monkey was given a more desirable grape as a reward instead of a cucumber slice, the other monkey, who continued to receive a cucumber, quickly became agitated. This monkey refused to accept the cucumber and sometimes even threw it back at the experimenter. The demonstration of agitation and refusal to accept the unequal reward showcased the innate sense of fairness in these primates, highlighting a deep-rooted biological reaction to unfairness.

The social experiment conducted with our salon participants and the comparison to Frans de Waal's capuchin monkey experiment highlight the similarities between human and animal reactions to unfairness. Like the monkeys, our participants displayed emotional responses when faced with unfair situations, highlighting the deeply ingrained neurobiological basis for fairness that transcends species boundaries.

Other studies have shown that humans are not the only species to display complex prosocial behaviors like helping and sharing. Empathy and satisfaction often motivate such actions in humans, and previous research has shown similar behavior in chimpanzees. In a study conducted by Horner et al. (2011), researchers investigated the prosocial choices of chimpanzees using a token-based experimental setup. The chimpanzees were tasked with selecting tokens, with each color representing a different outcome. When the chimpanzees chose one color, they alone received a reward, while selecting the other color resulted in both themselves and their partner receiving a reward. The results demonstrated that when a partner was present, the chimpanzees were more inclined to choose the token that benefited both parties, showcasing their prosocial behavior. This study highlights the connection between negative responses to inequity and cooperation levels across various species. The ability to detect and react to unfairness, or inequity aversion, may have provided an evolutionary advantage by enabling individuals to assess the value of their cooperative partners more accurately.

In summary, both humans and chimpanzees have been observed to respond negatively when they receive more than their partners, suggesting that they are capable of prioritizing long-term cooperative relationships over immediate gains. By adopting a comparative approach, researchers have gained valuable insights into the origins of inequity responses, which in turn deepens our understanding of the human perception of fairness. However, it is worth noting that these observations are generally made within small, cohesive groups. In larger societal contexts where different groups compete for limited resources, survival instincts and competition may take precedence (Lee et al., 2018). While there is limited research on this specific aspect, it raises important questions about the scalability of these prosocial behaviors in more complex social structures.

The neural basis of fairness

Cognitive neuroscience research has begun to explore how the human brain encodes fairness-related processes. Most research in this area falls under the umbrella of Decision Neuroscience, an interdisciplinary field that aims to understand the fundamentals of human decision-making (Li and Tracer, 2017). Within this approach, tasks are often designed to prompt participants to decide about monetary divisions in interactive settings, balancing rewards and cooperation with partners. Combined with brain imaging methods, these tasks lead to numerous findings on the neural underpinnings of fairness behavior.

There are several neural mechanisms involved in these complex abstract analyses. For instance, the anterior insula plays a significant role in monitoring fairness or unfairness, becoming more active when someone is faced with an unfair situation (Li and Tracer, 2017). Other brain regions, such as the anterior cingulate cortex and dorsolateral prefrontal cortex, are crucial in monitoring conflicting information and expectation discrepancies, ultimately influencing future decisions (Li and Tracer, 2017). Fair behavior can be satisfying, activating our brain's reward networks. Studies have found that neural activity in the ventromedial prefrontal cortex and ventral striatum increases when a participant donates money to their preferred charity. Additionally, some researchers argue that the Theory of Mind – the ability to maintain a mental model of others' thoughts – also plays a role in fair behavior (Takagishi et al., 2010). To guide decision-making, the medial prefrontal cortex is proposed to integrate emotional, deliberative, and social information, especially when social interests conflict with self-interest. Fairness may thus be a strategic choice influenced by understanding others' reactions to our behaviors.

In a series of studies conducted by Crockett and colleagues, the role of serotonin in shaping our reactions to fairness was investigated (Crockett et al., 2008, 2010a,b, 2013). The researchers found that participants with depleted serotonin levels were more likely to reject a greater proportion of unfair offers but not fair offers without showing changes in mood, judgment, basic reward processing, or response inhibition. On the other hand, enhancing serotonin levels made participants more likely to judge harmful actions as forbidden, but only in cases where the harms were emotionally salient. Furthermore, increasing serotonin levels in participants resulted in a decreased likelihood of rejecting unfair offers (i.e., the decision to decline a resource allocation they find inequitable, even if it comes at a personal loss; this action serves as a social deterrent against the proposer's unfair behavior in future interactions). This implies that serotonin plays a crucial role in modulating specific retaliation rather than general norm enforcement. Participants with depleted serotonin were more inclined to punish unfair behavior directed toward themselves but not unfair behavior directed toward others. These findings highlight the significant influence of serotonin on our behavioral reactions to fairness and retaliation, shedding light on the complex neurobiological mechanisms that underlie our sense of justice and moral decision-making. This is especially relevant in the context of a growing mental health crisis, where disorders like depression, often linked to serotonergic dysfunction due to chronic stress, are increasingly prevalent. The implication is that individuals suffering from such disorders may be more sensitive to perceived injustices directed toward them but less responsive to unfairness affecting others.

At UCSF, a team of researchers led by Virginia Sturm has been investigating the impact of behavioral variant frontotemporal dementia (bvFTD) on prosocial choices and fairness behavior. BvFTD is a neurodegenerative disease characterized by atrophy in the frontal and temporal lobes, leading to significant changes in social and emotional functioning. In a study by Sturm et al. (2017), the researchers examined the relationship between prosocial deficits in bvFTD patients and the degree of atrophy in brain regions associated with reward processing. Utilizing a task that required participants to allocate money between themselves and others, the authors observed that bvFTD patients exhibited reduced prosocial behavior compared to healthy controls. Furthermore, this reduction in prosocial behavior was associated with atrophy in the ventromedial prefrontal cortex and the ventral striatum, both of which are key components of the brain's reward network.

In a subsequent study, Sturm et al. (2018) explored the link between resting parasympathetic dysfunction and prosocial helping deficits in bvFTD patients. They found that bvFTD patients with decreased resting parasympathetic activity, as indicated by respiratory sinus arrhythmia, showed reduced prosocial behavior. This suggests impaired parasympathetic regulation might be linked to diminished prosocial tendencies in bvFTD patients. Moreover, these results align with research on heart rate variability (HRV) as a measure of parasympathetic activity. Notably, studies have shown a correlation between HRV and altruistic, prosocial behavior in the general population (Fooken, 2017). The findings suggest that HRV could serve as a modifiable biomarker for prosocial tendencies. Intriguingly, HRV can be improved through regular exercise and physical training, opening the door for potential interventions to enhance prosocial behavior. The implications of these findings could be far-reaching, warranting further research to explore HRV as a modifiable biomarker for prosocial behavior.

These studies provide insights into the neurological basis of "clinical unfairness" and highlight the need to understand bvFTD's impact on brain areas related to social cognition and decision-making. This knowledge could guide the development of targeted interventions to address prosocial behavior deficits in such populations.

Fairness and equity in brain health

Equity and fairness in healthcare are interconnected concepts that significantly contribute to advancing social justice and improving health outcomes for all, not just for specific subsets of individuals. This perspective is underscored by the research conducted by Dr. Ivan Arroyave, a notable contributor in the field and professor at the University of Antioquia, Colombia. In his research, Dr. Arroyave, who lectured in our salon, scrutinized the disparities in premature adult mortality in Colombia from 1998 to 2007, focusing on the correlation with educational attainment (Arroyave et al., 2014). The results indicated that individuals with only primary education were at a higher risk of premature death than those with post-secondary education. This study underscored the necessity for multi-sectoral policies to address these issues, especially among less educated populations, to enhance health equity.

Salon participants and hosts further reflected on the concept of brain health equity. The consensus was that fairness, when applied as a societal construct, could facilitate access to resources and opportunities that foster optimal brain health. The insights of Dr. Kai Kennedy, an Atlantic Fellow for Health Equity, Associate Professor, and Vice Chair of Equity at UCSF, further corroborated this viewpoint.

In a Q&A session during our salon, Dr. Kennedy highlighted strategies to address health disparities by promoting fairness and brain health equity. When asked about actions to prioritize in communities to address health inequity in relation to brain and mental health, Prof. Kennedy emphasized the importance of soliciting community perspectives, especially when forming partnerships with authoritative or external entities. She also stressed the need to understand local values, knowledge, and practices related to health and healthcare. Furthermore, she advocated for upholding sustainable collective self-determination as a goal, where community members can determine their ideal outcomes and play a significant role in defining interventions and assessing progress. When asked about a superpower that could address brain health inequity, Dr. Kennedy expressed a desire to see the invisible, illuminate issues in communities, and identify potential problem-solving resources and strategies. She noted that this superpower should not be exclusive; many people could have it and contribute unique perspectives to inform a collective consciousness and move toward community-identified solutions to relevant issues.

Equity and fairness in healthcare are interconnected concepts that significantly contribute to advancing social justice and improving health outcomes for all. While Dr. Kennedy's insights provide a valuable framework for understanding the role of fairness in brain health equity, it is crucial to delve deeper into how fairness, as a societal construct, can translate into practical measures for equitable access to resources and opportunities for optimal brain health. Policy-making can be one of the most direct ways fairness impacts brain health equity, such as policies that ensure equitable access to healthcare resources like neuroimaging technologies or specialized neurological care. Fairness also extends to addressing the social determinants of health, like education, housing, and employment opportunities, which have a cascading effect on brain health. Community-based interventions, such as localized mental health programs, can be instrumental in promoting brain health equity, especially when they are culturally sensitive and tailored to meet the specific needs of a community. The advent of telemedicine and mobile health apps offers a unique opportunity to promote brain health equity by making healthcare more accessible, but it is crucial to ensure these technologies are equally accessible to all. Ethical considerations, particularly in the context of medical research, also play a role in ensuring that clinical trials for neurological conditions are inclusive and representative. By adopting a multifaceted approach that incorporates policy changes, addresses social determinants, and leverages community and technological resources, we can translate the societal construct of fairness into practical measures that promote brain health equity.

Cultural perspectives on fairness and brain health equity

Our salon was conducted at UCSF, primarily involving a United States-based, highly educated, and possibly privileged demographic. However, it is crucial to note that the salon moderators and authors of this perspective come from diverse backgrounds, including Africa and Latin America. Moreover, Atlantic Fellows for Equity in Brain Health, most of whom hail from developing countries, participated in our activities, enriching the discussions with their personal and professional experiences.

One of the authors, an African-born, British-trained scientist, presented a compelling case study during the salon. She highlighted the stark disparities in brain health equity in Sub-Saharan Africa, a region often overlooked in global discussions. The case study touched upon the "Haves and Have Nots" in low- and middle-income countries, emphasizing the socioeconomic disparities within such nations. It also discussed the AFRICA-FINGERS project, aimed at addressing brain health inequity in low resource settings such as in Africa through a precision prevention framework (Kivipelto et al., 2020). The presentation described the African concept of Ubuntu, which emphasizes the interconnectedness of humanity, suggesting that fairness and equity are not just individual but collective responsibilities.

By incorporating these diverse viewpoints, we can better understand how fairness as a societal construct can translate into practical measures that promote equitable access to resources and opportunities for improving brain health globally. This inclusion of cultural perspectives also advances our understanding of fairness and its implications for brain health equity, thereby strengthening the overall impact of our work.

The future of fairness

In today's rapidly evolving and polarizing social landscape, concerns have arisen over the potential decline in fairness and prosocial behaviors. Prosocial tendencies, which involve acting in the best interest of others, are generally stronger with increased social closeness and tend to diminish as social distance grows. The rise of isolated social bubbles and echo chambers in contemporary society sparks concern regarding the implications for fairness and social cooperation. Social bubbles refer to the phenomenon in which individuals primarily associate with others who share similar values, beliefs, and opinions (Arguedas et al., 2022). This can result in a lack of exposure to diverse perspectives and reinforcement of existing biases. Additionally, echo chambers are environments where people are repeatedly exposed to the same viewpoints, causing a confirmation bias and an amplification of those opinions (Brugnoli et al., 2019). Both social bubbles and echo chambers can be perpetuated by social media algorithms that prioritize content that aligns with users' preferences, further exacerbating the issue.

The social consequences of social bubbles and echo chambers can be detrimental to fairness and cooperation. As individuals become more entrenched within these environments, they may increasingly perceive those outside their social circles as strangers or even as adversaries. Consequently, empathy, understanding, and concern for the well-being of others may decline, resulting in decreased motivation to treat others fairly. In a more divided society, this trend can contribute to increased polarization, reduced tolerance, and heightened intergroup conflicts.

The possibility of declining fairness in society raises essential questions about whether we can reverse this trend. As discussed above, if heart rate variability (HRV) is a biomarker for prosocial behavior, interventions aimed at improving it could have broader societal implications. For instance, regular exercise has been shown to improve HRV, suggesting a hypothetical strategy for fostering prosocial behavior (De Couck et al., 2019). This aligns with the holistic notion of "healthy body, healthy mind, healthy societies." While this is admittedly a long shot and requires further empirical validation, the idea presents an intriguing avenue for future research and potential community-based interventions.

Another approach might be trying to effectively enhance empathy, a critical factor in promoting fairness. Empathy is a complex construct, encompassing affective, cognitive, and intentional components (Decety and Yoder, 2016). While modifying affective empathy may be challenging, research suggests that cognitive empathy and empathic concern could be more promising targets for intervention. A study by Decety and Yoder (2016) examined the relationship between different aspects of empathy and sensitivity to justice for others, as well as the endorsement of moral rules. They found that cognitive empathy and empathic concern, rather than emotional empathy, predicted participants' sensitivity to justice and moral rule endorsement. Cognitive empathy involves the ability to understand another person's perspective and feelings, while empathic concern is the capacity to feel concern and compassion for others. On the other hand, emotional empathy refers to sharing another's emotional experience.

These findings, coupled with the overall contributions from the GBHI Fairness Salon 2023, suggest that to foster fairness in society that could have a direct impact and/or lead to equitable brain health outcomes, efforts should focus on promoting perspective-taking, reasoning, and empathic concern, rather than solely emphasizing emotional sharing with those experiencing misfortune. In other words, to enhance fairness, we must actively reflect on the concept and intentionally cultivate it as a core value.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2023.1241125/full#supplementary-material

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One step beyond the lab and clinic: "walking the dementia conversation"

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Millions of dollars have been lost in dementia research over the last 30 years owing to unsuccessful clinical trials aimed at finding an effective treatment for the condition. Although two promising drugs have been identified, the research effort is insufficient. The dehumanization of patients and the pressure to publish have led to a decline in the quality and usefulness of scientific research. One way to tackle these problems is establishing close contact with those who put their faith in researchers. Fine-tuning the participation of patients with dementia and caregivers in research design and improving their connection and communication with researchers could positively contribute to enhancing the perspectives and designing strategies for scientists in order to generate a new and enriching vision. The Walking the Talk for Dementia event showed that people can still live with dementia despite their condition. Approximately 300 people participated in the all-week "Santiago's Camino" symposium. People living with dementia, caregivers, healthcare professionals, activists, clinicians, and researchers participated in this event. The "Walking the Talk for Dementia" (WTD) event vividly demonstrated a strong commitment to upholding Global Brain Health Institute's (GBHI) core values of Authenticity, Fairness, Openness, Respect, Courage, and Empathy (A FORCE) to advance equity in brain health. These values provide clear guidance for their advocacy initiatives aimed at mitigating the global impact of dementia. Research and development are essential across scientific fields, especially in clinical contexts where involving patients and caregivers is critical. The WTD initiative exemplifies this aspect by bringing together researchers, caregivers, and dementia patients on the Camino de Santiago in Spain.

KEYWORDS

patients, dementia, empathy, openness, research participation

Introduction

Dementia is an advanced state of cognitive and functional deterioration often associated with advanced age (1), but it can also affect a large, relatively young population under 60 years (2). Although some types of dementia, such as Alzheimer's, Parkinson's, or others, are well-known, there are many causes of dementia and even intermediate phases between the condition and cognitive and functional normality (3). It is known that the prevalence of dementia is increasing worldwide, and according to the World Health Organization (4), more than 55 million people currently suffer from it, with an increase of 10 million cases annually. By 2050, an additional 152 million people are estimated to be affected by dementia (5). Out of those affected, nearly 60%—70% of cases are associated with Alzheimer's disease (4).

Although a vast amount of preclinical research has been carried out to elucidate causes, mechanisms, and therapeutic approaches, and hundreds of clinical trials have been carried out in search of specific treatments, few results have been genuinely fruitful but have been abandoned (6). There are currently two drugs that the scientific community and the US Food and Drug Administration (FDA) have paid attention to for the treatment of Alzheimer's dementia: lecanemab (7, 8) and aducanumab (9–11). In this context of initial FDA-approved treatments, and despite controversies (9), several questions arise for the researchers. To what extent is researchers' knowledge of patients established? To what extent does the medical professional know the individuals being treated? What are patients' feedback regarding the study conducted and the allocation of funding and resources?

Walking the talk for dementia conversation

We recently had the opportunity to participate in an event called "Walking the Talk for Dementia." In this event, participants worldwide were invited to walk the Camino de Santiago, with the aim of raising funds for dementia research and care, and the event managed to attract more than 300 participants. The event featured an information fair on dementia, providing knowledge about the disease and ways to support individuals with dementia and their families. This pilgrimage route spanned several paths, leading to the city of Santiago de Compostela, located in the northwest of Spain. Pilgrims travel to this city in search of the tomb of the Apostle Santiago. In this event, different world-class researchers in dementia, including Spanish researchers, caregivers, and even patients living with dementia were invited to follow this path over 4 days (see Figure 1).

Methodology

The necessary logistics for conducting the WTD (ambulances, paramedics, caregivers, transport buses, and other necessary equipment) was arranged by two Brazilian organizations, Instituto Vovó Nilva and Associação Crônicos do Dia a Dia (CDD), a Brazilian NGO focused on chronic patients. CDD predominantly funded the project with the support and collaboration of the Alzheimer's Disease International (12), Global Brain Health Institute (13), Atlantic Fellows, and others. This event culminated in a 2-day symposium, where the experiences of various patients and researchers were presented.

This event saw 300 participants (from 25 countries, spanning five continents) walking through the "Camino de Santiago" for 4 days and attending the final 2-day symposium. Regarding patients with dementia, 10 of them participated through the week from six countries with diverse cultural backgrounds (United States, Ireland, England, Singapore, Spain, and Namibia). Otherwise, a majority of dementia patients participated for only 1, 2, or 3 days.

The objective of the event was to establish an atmosphere conducive to open and non-judgmental dialogues among individuals living with dementia, caregivers, healthcare professionals, and policymakers. Those living with dementia and their caregivers, after providing consent, openly shared their individual experiences with the intent to raise awareness. No formal clinical assessment, neuroimaging, or treatment (specific clinical data) was shared during the symposium by the organizers. A signed speaker release form for the recording was obtained and the event was then podcasted.

A different staging

Contrary to the formality of symposiums and scientific events, WTD was an event for all those involved in dementia care. The openness in communication, the dialogue, the straightforward explanations, and the interactions were a rare occurrence but provided rich experiences for the participants, among whom patients with Alzheimer's dementia and those with lewy body dementia (14) were present. The 2-day symposium began with presentations by some researchers, moderated by other attendees, who often turned out to be patients invited by the organizers. The presentations also included exhibiting patients, during which the attendees were seated on round tables so that everyone's voice was heard. This event demonstrated a practical way of fostering patient and public involvement (PPI), a growing methodology for inviting patients and the public to participate in research, its implementation, planning, and active participation (15). Although the traditional way of implementing a PPI goes hand in hand with committees organized by the investigators, the staging was practically driven by patients and their caregivers. As GBHI fellows, we aspire to improve brain health and reduce the global impact of dementia by reaching out to the local communities and worldwide networks. Our core values at GBHI are symbolized by the acronym "A FORCE," which signifies Authenticity, Fairness, Openness, Respect, Courage, and Empathy. Therefore, we embrace these values to ensure brain health equity. These values guide us as we advocate for reducing the global impact of dementia. By adopting these value-driven approaches to brain health, science, arts, humanities, and advocacy, we can drive change for millions of people with dementia. "Walking the Talk for Dementia" as a novel event exemplified this transformation and displayed our core values.

Authenticity

The event was initially conceived by a Brazilian individual, Fernando, who at present is deeply immersed in dementia research due to his professional background. However, it all began when he decided to drop his philosophy studies and dedicate himself to caring for his grandmother with Alzheimer's for over 6 years. Fernando and his partners did not want to create something for people with dementia but rather to work with people with dementia, which is why Laureen Waters, a person living with Alzheimer's in South Carolina, United States, was invited to join

FIGURE 1
The "Walking the Talk for Dementia" event, held on April 2023 in Santiago de Compostela, was a 5K walk organized by the Spanish Association of Family Members of People with Dementia (AFA) and the Spanish Association of Alzheimer's (AE Alzheimer), Global Brain Health Institute (GBHI), and other institutions. Drawing over 300 participants, the WTD aimed to raise funds for dementia research and care. The event featured an information fair on dementia, providing knowledge about the disease and ways to support individuals with dementia and their families.

the board and take part in organizing the event. Her presence ensured that the perspective of individuals with dementia would be represented and influence important decisions regarding the WTD.

Fairness

In PPI committees, participants are often invited to help in different phases of the investigation, such as selecting instruments that the investigator will need to assess other patients with the same disease, and that will serve to address problems with which they live on a day-to-day basis. The patients' approach can generate a completely new vision with a different and enriching interpretation for researchers (15).

Openness

Experiencing dementia within the closest family circle is a profoundly transformative journey filled with dramatic life changes and ever-changing emotions. It is only natural that this experience shapes our perception of people with dementia, extending beyond our immediate family. Fortunately, not all professionals dedicated to developing diagnostic alternatives, treatments, and care for people with dementia have had the opportunity to personally experience it within their own families. Therefore, it is of the utmost importance to foster experiences that can, in some way, recreate these relationships, forging strong bonds between both sides of this complementary universe formed by the diagnosed individuals and those seeking solutions to facilitate or improve their lives within this context.

Courage

Regarding this practice, we consider that the primary use is the humanization of the patient, contrary to dehumanization in medicine and other professions related to patient care (16). Dehumanization, which in many countries is increased by the protocol or policies of the ministries of health that impose a limit of patients added to the administrative burden that they may have, cut the time of patient care, and thereby limit the listening to the patient part. In WTD, being able to talk informally with patients, the fact that they go on stage and present their experiences and their needs or that caregivers talk about the importance of the perception of signs, which is different for caregivers and also for people who take care of these caregivers showed the importance of returning to a fundamental question in bioethics for researchers: For whom do we do what we do?

Respect

Taking a broader perspective, and, in this section, from the point of view of clinicians rather than researchers, the interaction with individuals diagnosed with dementia is part of their daily lives but in a different context than what was experienced during the WTD. In clinical roles, we are accustomed to evaluating capabilities and constantly searching for markers that indicate when it may be time for individuals to stop driving, traveling, or taking risks. However, the WTD provided a unique and transformative experience far removed from our usual clinical practice. It allowed us the space to witness the element of surprise and be genuinely impressed by the determination of individuals living with lewy body dementia. Many of them, who were once limited to walking just a block and doubted by their doctors, defied expectations by walking 5 km or more each day.

Empathy

We believe that the WTD has introduced an innovative approach to scientific conferences, emphasizing genuine, deep, and enriching exchanges among professionals, researchers, and individuals living with dementia. Over 4 days, walking 10 km daily, this experience creates a unique environment where personal and professional experiences, expertise, knowledge, vulnerability, emotions, and expectations can be shared. Through the choice of walking companions and engaging in meaningful conversations about dementia, participants have the opportunity to step out of their laboratories and "walk in each other's shoes," resulting in a profound and impactful transformation.

When Kevin Quaid, living with lewy body dementia and Parkinson's dementia, from Ireland, was invited by Fernando to join the WTD, his initial reaction was, "Do you think I can? Do you think I'm capable?" Fernando responded, "I think enough people are telling you what you can or cannot do, should or should not do. So, I want to hear from you. Do you believe you can? And more importantly, do you want, dude?" Kevin replied that it would be a dream come true but not without shedding a few tears. The overwhelming emotion was not solely about the imminent journey to Spain or the adventure itself, but the first profound impact for Kevin realized that someone genuinely valued his voice and opinion himself.

We agree that the basic answer would be by and for the patients. However, in the current research context, researchers often develop their work in a rush and under pressure to publish because of incentives and recognition, often leaving scientific quality aside (17). It is where the researcher's bioethical principles are lost.

The interaction with patients who live with the disease day-to-day allowed them to develop empathy; the shared environment and the stories sharpened assertiveness, and their coexistence promoted understanding. We believe that these aspects were central to this event, which united all those involved in dementia and glorified new ties.

In this manner, the PPI shows its importance and use in research; however, it has not been implemented in several Latin American countries; on the contrary, it entails using resources that are often unavailable (18). In addition to this fact, the dehumanization of patients and the immediate search for the publication of scientific texts (16, 17), without taking care of the quality, is generating excessive publications without scientific impact and, above all, without clinical utility. Many problems in bioethics, research, development, innovation, and clinical, social, and technological usefulness may be in decline because those who live with dementia or those who care for them are not being considered. After all, the researchers are dehumanizing those suffering from the disease or for not listening to those who know the most about the condition they live with.

The stigma problem

The problem of stigma in dementia is that patients and relatives can perceive the social, family, and work effects of a diagnosis (19). However, the lack of knowledge in society about these disorders often erroneously stigmatizes patients in relation to the factors that they have been traditionally associated with.

In the case of dementia, it is believed that patients are completely unaware of the disease or of the cognitive or functional deficit they suffer from, or on the contrary, these deficits are normalized with comments such as: "It's part of old age," "It's/you are old," and "It is normal for you to forget," among others. It is believed that aging is necessarily related to a loss of cognitive processes, normalizing the presence of signs and symptoms associated with various pathologies associated with dementia or age [Alzheimer's disease (20), frontotemporal dementia (21), vascular dementia (22), and others] being, on the contrary, characteristics that appear at the beginning of these pathologies. By normalizing them, we only accentuate the progression of these disorders by avoiding their early diagnosis and treatment; thus, the stigma in dementia and other diseases often promotes ignorance and fear while exacerbating the chronicity and accentuation of deficits.

Thus, researchers must consider their work's ethical implications, behavior, and disclosure to society, considering their work's clinical utility and impact. A prevailing need is to be clear about national and international regulations when planning their investigations, the consideration and involvement of patients and the public in the different phases of the research, and adherence to clear ethical rules.

The confidentiality and privacy granted to the patient, the simple communication with them, or the review that the protocols are irrefutably followed is not enough for adequate ethics, but, on the contrary, it is necessary to add the search for the scientific, social, and clinical impact of our work, by and for patients and their families, and it should be the common goal to develop replicable, verifiable, and helpful research. In this way, we not only avoid potential damage to the study (for example, in its verifiability) or to the patients but, on the contrary, in relevant emotional damage to the family, the patient, society, and the scientific community.

It is also necessary for researchers to consider the possible social and cultural implications of their research, its credibility with society, and the educational impact on the training of new researchers; this is particularly relevant since university students see research as a complicated, inaccessible, complex topic that adds to university difficulties and impairs their development (23, 24).

The road does not end in Santiago. It begins there

Implementing a novel methodology for the participation of patients, caregivers, and researchers left memorable experiences. It reaffirmed the fundamental ethical aspects to continue to be focused on patients and their families, such as assertive communication by clinicians, empathy by scientists, the development that integrates patients and caregivers, and above all, the redirection of funds to better-designed jobs involving all participants in an inclusive, diverse, and equitable way.

The failure of many clinical trials has been due to several factors. We wish to emphasize the inadequate characterization of patients with dementia, such as Alzheimer's, as there are multiple types of dementia. This is due to the syndromes generated, whether typical or atypical (25), brain regions affected, and unknown interaction of factors in these disorders, and could have been avoided in many instances with the formal involvement of caregivers and patients in the investigations through the PPI, in addition to supporting personnel who report information and researchers who collaborate in the design and identification (15).

When you bring together such contrasting and distinct cultures in the same environment, representing all continents but fostering a conducive space for exchanging experiences, you become acutely aware of the research world's entrenched racial and social inequities. While some communities do not feel adequately represented by research groups advancing studies that fail to involve their members inclusively, the campaigns and well-known figures participating in the PPI panels are typically white individuals from developed countries. Low- and middle-income countries (LMICs) face significant challenges in finding appropriate representation and embodiment of dementia experiences within their nations. These challenges stem from numerous intertwined problems, including stigma, delayed diagnoses, and low scientific literacy. These aspects feed into one another, preventing the voices of these communities from being heard and their needs from being effectively addressed.

All the reflections heard at the symposium allowed a genuine renewal of the interests of researchers and renewed the expectations of patients and their families, but above all, it allowed them to talk about issues that are often not talked about, to listen to those who are not heard too, and also encouraged them to think from divergent perspectives, all with a common goal, to face dementia.

Conclusion

Research, innovation, and development are necessary for all branches of science. However, in those that involve the clinical context, it is even more critical to apply the patients themselves and their caregivers, learn about their perspectives in research, and conduct research in ways that humanize the patients. However, we must consider how science is communicated and how learning and sharing transfer spaces have been built. This step is beneficial and enriching. The experience of "Walking the Talk for Dementia," an event that brought together researchers, caregivers, and patients with dementia and allowed them to walk together on the Camino de Santiago in Spain, has opened the possibilities for various purposes and perspectives. In this manner, we would like to highlight that the launch of this event was a practical way of proposing "patient and public involvement" (PPI), a growing methodology of inviting patients and the public to participate in research and implementation of the design of clinical trials. This would ensure that the voices of caregivers and patients are heard, and an enriching vision can be achieved for researchers.

The "Walking the Talk for Dementia" initiative served as a platform to raise awareness and funds for dementia research and care, bringing together patients, attendees, participants, clinicians, researchers, caregivers, and family members. Their dedication paves the way for impactful collaborations in the future, contributing to improving the lives of individuals affected by dementia and their families.

Limitations

Within the parameters of the event, several limitations were discerned. First, the event's funding was limited, which would limit the number of participants, precedence, and location. The program's relatively brief duration restricted its capacity to encompass the full spectrum of experiences among individuals living with dementia and their care partners on a global scale. While we secured some funding to diversify participant representation, the event primarily relied on voluntary participation contributions contingent upon the availability of participants' time and resources. The reliance on voluntarism may have constrained both the event's outreach and its potential impact, potentially compromising the richness of participant diversity and experiences.

The event was organized primarily by Brazilians and Spaniards and took place in Spain. Still, in order for it to be a global event and bring multiple perspectives, English was adopted as the official language for the event. This decision limited our reach significantly, especially considering that individuals from disadvantaged social backgrounds in Latin America were unable to attend. Finding ways to overcome this challenge should be further explored in future events, ensuring more diversity and inclusion; for example, the incorporation of online language translation services, although beneficial, necessitated additional funding.

It is noteworthy that, with regard to data collection, the event organizers did not acquire any formal or clinical data from participants. In future events, the inclusion of qualitative methodologies and orientation toward focus groups for initial public and patient involvement (PPI) activities could prove advantageous.

By addressing these limitations in upcoming dementia-related events, there is a significant potential to augment their effectiveness in the ongoing battle against these debilitating diseases.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

JZ-V: Conceptualization, Funding acquisition, Writing – original draft, Writing – review & editing, Validation. FA-P: Conceptualization, Writing – original draft, Writing – review & editing. AK: Writing – original draft, Writing – review & editing. FA: Writing – original draft, Writing – review & editing. CP-M: Writing – original draft, Writing – review & editing.

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Walking the Talk for Dementia in Santiago de Compostela demonstrated that we can create a significant impact when we come together for a common purpose. Every shared story, every step taken, and every conversation held during this event will resonate through time, reminding us that dementia does not define the individuals who experience it nor their loved ones. Ultimately, our gratitude extends to all those involved in this transformative initiative: patients, caregivers, family members, clinicians, researchers, and attendees; your participation has left an indelible mark on our hearts and has strengthened our commitment to continue working together toward a more understanding and supportive world for all those affected by dementia.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Empathy as a crucial skill in disrupting disparities in global brain health

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Brain health refers to the state of a person's brain function across various domains, including cognitive, behavioral and motor functions. Healthy brains are associated with better individual health, increased creativity, and enhanced productivity. A person's brain health is intricately connected to personal, social and environmental factors. Racial, ethnic, and social disparities affect brain health and on the global scale these disparities within and between regions present a hurdle to brain health. To overcome global disparities, greater collaboration between practitioners and healthcare providers and the people they serve is essential. This requires cultural humility driven by empathy. Empathy is a core prosocial value, a cognitive-emotional skill that helps us understand ourselves and others. This position paper aims to provide an overview of the vital roles of empathy, cooperation, and interdisciplinary partnerships. By consciously integrating this understanding in practice, leaders can better position themselves to address the diverse challenges faced by communities, promote inclusivity in policies and practices, and further more equitable solutions to the problem of global brain health.

KEYWORDS
empathy, brain health, cultural humility, disparity, equity, leadership, value

Introduction

In today's interdependent world, prioritizing and improving brain health becomes a vital goal in advancing the collective health of populations across the globe (1, 2). The term "brain health" is not a standardized one. According to the World Health Organization (WHO), brain health is "the state of brain functioning across cognitive, sensory, social–emotional, behavioral and motor domains, allowing a person to realize their full potential over the life course, irrespective of the presence or absence of disorders" (3). There is heterogeneity among institutions and researchers on how brain health is defined, a recent literature review on definitions of brain health revealed that, despite these differences, the common thread is the conceptualization of brain health as dynamic and multidimensional, encompassing both objectively measured and perceived components (4).

Progressively realizing the global right to brain health and global interdependence (i.e., worldwide mutual dependence between countries) allows systematically identifying and eliminating inequities stemming from social processes. Global leaders need to appreciate the effects of culture on dynamics between people and communities and to consciously commit to developing cultural humility. Cultural humility involves recognizing the values and perspectives of different cultures, advocating for inclusive and culturally sensitive approaches, and identifying the unique barriers that contribute to health and other social disparities. Empathy, a fundamental aspect of social interaction, a construct that accounts for a sense of similarity in feelings experienced by oneself and others, is essential to truly acknowledging the needs of others, for open conversation around challenging topics and for creative problem solving (Figure 1).

In this position paper, we argue that empathy, cultural humility and cooperation as fundamental for eliminating disparities and achieving global equity in brain health. We start by explaining inequalities and demonstrating disparities in global brain health. Then we identify cultural humility and emphasize its role in dealing with the global health problems. We focus on empathy and discuss how empathy and cooperation can challenge the biases and assumptions that underpin brain health disparities. Finally, we envision how art and science collaborations can remove barriers between individuals, institutions, and nations, and improve the prospects for equity in brain health across the world.

Global inequalities affect the most vulnerable social groups

Health inequalities and health inequity have been defined in various ways with overlapping use (5). According to the World Health Organization (WHO), health inequalities are measurable differences in health across population subgroups, and health equity is defined as the absence of unfair, avoidable or remediable differences in health among population groups, defined by social, economic, demographic or geographic characteristics (6, 7). Different theories were developed to explain health inequalities. The inequalities might be associated with the differences based on culture, health behaviors, social mobility or genetics; however the main causal factor for the differences in health outcomes is suggested to be the differences in socioeconomic status of social groups, as proposed by the structural theory (8). This understanding calls for a more systematic way of approaching the concern of brain health inequalities for individuals and communities, as they perpetuate cycles of disadvantage and contribute to broader health inequities. The 2021 Global Health Security Index, an indicator of health security and related capabilities across 195 countries, analyzing experience from the COVID-19 pandemic, concluded that most countries came unprepared maintaining a capable accessible health system, where preparedness needs of vulnerable populations were most often neglected (9). Examples of vulnerable populations include people with cognitive and physical disabilities, chronic health conditions (e.g., diabetes, heart disease), and mental health issues (10). These vulnerabilities are also known risks for brain health across the world, including high, middle- and low-income countries.

Understanding brain health disparities

Disparities in brain health are evident in different facets. Take the resource aspect as an example. The number of specialists and healthcare workers, the number of facilities per individual, and their resources respecting brain health widely vary across the globe. There is a clear lack of brain health workforce particularly in Africa and South East Asia (11, 12). This discrepancy remains when the workforce is classified by income level; low and lower-middle-income countries are in a very disadvantageous position. Disparities are overwhelming for brain health risk factors, which include but are not limited to education (13), smoking (14), diabetes (15), and hypertension (16). A brief survey on disparities in dementia among the authors of this paper from 17 countries and 5 continents displayed the existence of apparent inequalities in access to assessment and treatment [unpublished data, presented at the Global Brain Health Institute (GBHI) Annual Meeting 2022]. The surveyors found such disparities also existed within the countries and varied with social and economic factors.

Wealth, education, occupational status, race/ ethnicity or gender predict variations in health status on an individual level, these factors converge with a dynamic interdependent process influencing the health outcomes (17). Wealth disparities, measured according to the distribution of wealth from economic activity through jobs and demands, income, and pollution levels, exist both between and within countries (18). Disparities in the distribution of wealth across the globe are reflected in global peace (19). The 2021 Global Peace Index highlighted the connection between peace and health, emphasizing the role of disparities within and between nations associated with domestic and international conflicts, respectively (19). A responsible, ethical, and inclusive global health approach constitutes a genuine foundation to take action to promote brain health across the globe

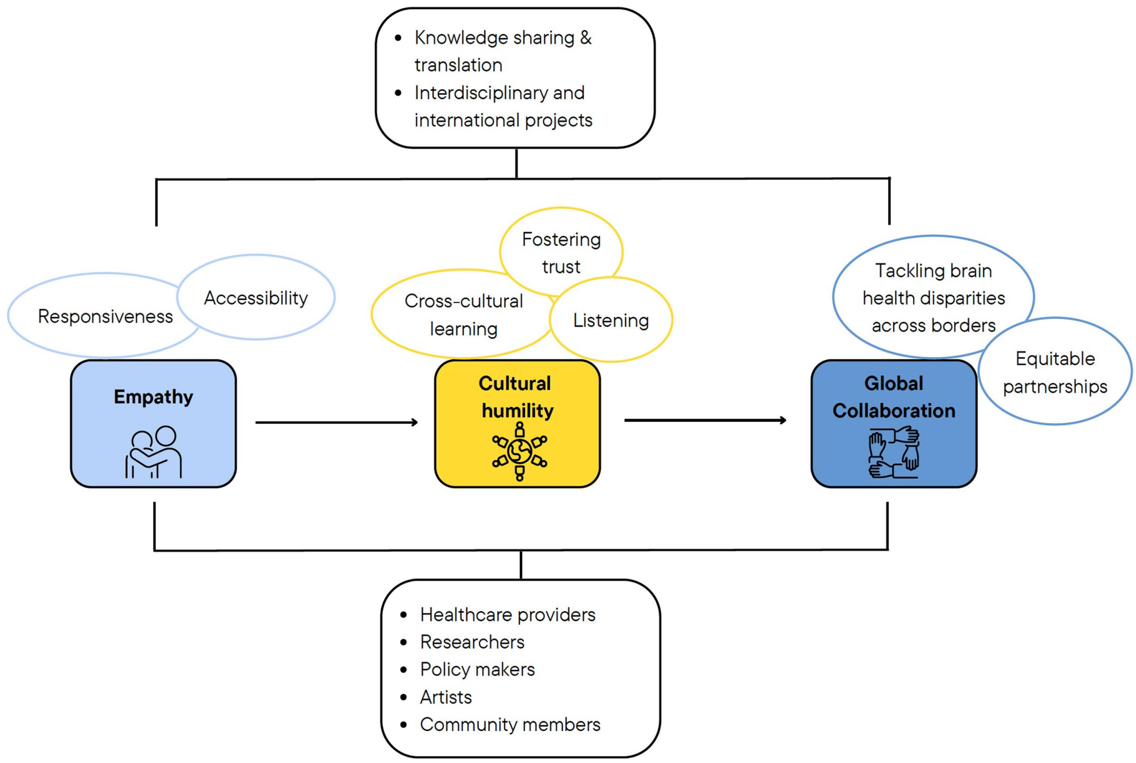

FIGURE 1
Framework outlining the position advanced in the paper. The value of empathy in tackling disparities in brain health by encouraging more responsive and accessible services, fostering trust among and between diverse populations through cultural humility, and pursuing collaborative interdisciplinary efforts to create responsive, accessible, and effective systems of care.

(20). The aim remains to disrupt disparities in brain health within and between countries. It is hard to imagine a more significant challenge for the leaders than to combat disparities.

Disparities display the existence of global inequities in health

Disparities among different social groups remain a problem for brain health across the globe as exemplified in dementia. In the US, even though there is an overall decline in the disparities trend in dementia prevalence (21), racial and ethnic disparities remain significant (22–25). The annual incidence of dementia among African American and Hispanic American populations was significantly higher as compared to Caucasian population (26), and the burden of known risk factors for dementia differed among ethnic groups (27). The Global Council on Brain Health, a collaboration of experts convened by the AARP emphasizes the role of social determinants of health and identifies health disparities as a policy imperative (10, 28). The US National Plan to Address Alzheimer's Disease (29) includes efforts to address inequities in dementia risk factors among vulnerable populations, based on needs assessment and developing targeted plans addressing any system gaps that stand in the way of such efforts. In Canada, the rates of dementia and its modifiable risk factors started to decrease, and protective factors increase, according to the 2021 annual report to Parliament on Canada's national dementia strategy, A Dementia Strategy for Canada: Together We Aspire (30). The progress is attributed to collective aspirations embedded in the strategy's national objectives including advancing knowledge of Canadians about modifiable risks of dementia, access to quality care, and raising awareness of, and elimination of stigmatizing behaviors. Despite these collective efforts, some populations within Canada have been identified as more likely to face barriers to equitable care and/or are at higher risk of developing dementia, including transgender and non-binary adults living with dementia, Indigenous people, and people from ethnic populations and those living in rural and remote communities (31, 32).

In the low – and middle income countries, socioeconomic factors including indices of poverty were associated with increased dementia rates in South Africa (33), Colombia (34), Chile (35), and Brazil (36). While dementia rates are exponentially growing in all countries of the world, and projections display that almost 150 million individuals will be affected by dementia by 2050 (37, 38), the estimations rates are disproportionately high for low to middle-income countries as compared to high income countries (39).

Unjustified and avoidable differences in race/ethnicity, gender, and class-based socioeconomic differences exist in many other neurological and mental health disorders across the globe (40–43), with disparities started to emerge during early stages of brain development (44). The effects of these individual factors on brain health may be distinct and particularly robust on individuals with intersectional identities. This is alarming and calls for action of global leaders for equity in brain health. It also recognizes the importance of investing in efforts to identify and discuss challenges related to disparities, identify opportunities for global collaboration and action, and share ideas for a global strategy.

Overcoming disparities requires respectful dialog, and its essence is cultural humility

Effectively addressing global disparities in brain health requires collaboration among diverse groups of people from different cultural backgrounds. To ensure successful interactions, it is crucial to appreciate the cultural constructs and history of partners (45, 46).

Cultural humility refers to a more thoughtful and substantive understanding of other cultures and people which are unlike our own, and application of such understanding in practice. Tervalon and Murray-Garcia first coined the term "cultural humility" as a corrective to cultural competence, a skill that can be taught, acquired, and achieved, and it is frequently referred to as a necessary and sufficient condition for working effectively with diverse groups of people possessing ethnic, racial, and class differences (47). Cultural humility involves actively engaging in the process of learning about other cultures, their worldview, and any oppression or discrimination that they may have historically experienced, while also being mindful of our thoughts and feelings regarding those cultures. This includes overcoming any preconceived assumptions, prejudices, and biases people carry (45, 46).

Cultural humility calls for application in various aspects of life, including clinical work, education, and research. The need for cultural humility is particularly important in clinical practice, where clinicians are working with people from widely diverse cultural backgrounds. Putting aside their own belief systems and considering patients' and caregivers' perspectives is an essential skill for clinicians when developing a patient-centered treatment or care plan (48, 49). Inquiring about patients' backgrounds, practices, religion, and culture, is essential to avoid stereotyping and in determining individual patient's needs, goals, and preferable treatment options, to be in line with the paradigm of person-centered care. Cultural humility helps to create deeper connections and understanding between patients and care providers, which may increase patient satisfaction and care outcomes for vulnerable groups/minorities.

It is important to emphasize the role of cultural humility in identifying, addressing, preventing, and eliminating racism and discrimination in healthcare institutions (50–53). Racism in healthcare politics was suggested as a root cause of racial health inequities in the US (51). Discrimination may also be evident based on religion or other social factors. Historical attitudes toward the health care institutions, especially among marginalized communities, can shape their perceptions and health-related decisions (54, 55). Understanding and resolving underlying factors affecting trust in medical institutions play a crucial role in moderating the likelihood of individuals pursuing medical care (56, 57).

In research, especially in health research, the application of cultural humility allows the researchers to generate culture-sensitive hypotheses, apply culturally-neutral methods, and analyze the results with an appreciation of the influence of their own culture (58). Multicultural projects having a common goal but different resources in executing the same mutual interests have challenges. Each party has inherent differences, differing values, methods and rewards. Understanding the basic motivations, values, and sensitivities of each party in multicultural projects is crucial, as it lays the foundation for proper recognition and acknowledgment of their independence. This is essential because it fosters an environment of respect and inclusivity, allowing diverse groups to collaborate effectively toward a common goal. Acknowledging and respecting cultural differences becomes pivotal in international collaboration, as such recognition paves the way for meaningful communication and conflict resolution, promoting successful outcomes for all parties involved.

A troubling aspect in research is funding disparity for ethnic and racial minorities and women, and non-English speaking countries. Cultural humility allows us to reflect on the ways global funding and publishing agencies impact scientific research, and how scholars with cultures and languages other than English are frequently excluded due to biases or language barriers, and limited access to funding (58, 59).

Cultural humility is also essential in education, especially in disciplines emphasizing professional training and tied to a patient or client (e.g., nursing, medicine, and counseling). Humanities-based disciplines (e.g., art, music, literature, film, and theater) are well-positioned to incorporate cultural humility by addressing the perspectives of people in ways that encourage critical reflection, empathy, and appreciation for diversity in human artistic creativity (60).

Art as a manifestation and media of cultural humility

Artistic manifestations are the fingerprints of a culture. Whether it is a painting, a dance, or a novel, artistic works are shaped by the character and the history of the culture in which they are created (61). Therefore, being exposed to artistic expressions can help us to understand a different culture and its particular perspective of the world (62). While this can help us recognize and embrace our own culture's uniqueness, it can also help us appreciate others and embrace diversity. In the global health scenario, this means that art can be a tool to promote respectful intercultural dialog.

But, also importantly, art reflects our cultural past. In traditional artistic expressions, we can recognize the diverse influences that have carved a culture across time. We can also identify some of the same features in other - separated- cultures, realizing that they are not watertight compartments throughout history. This way, barriers between cultures begin to blur, our cultural arrogance smooths because we are aware of how much we share, and we start to recognize ourselves as habitants of one unique world, and not so different from our pairs.

Embracing cultural humility offers a valuable approach to navigating diversity and counter impediments to disparities that emerged from marginalization and stigmatization of disadvantaged communities. In light of disparities in brain health, cultural humility can foster empowerment, inclusivity, and respectful global collaborations.

The role of empathy in brain health leadership

Leadership skills are required to promote public health changes to protect and promote brain health (63). Leaders must profoundly understand their own and global community (64–66), including cultural beliefs, practices, and political views, to create and implement reproducible, sustainable, and scalable interventions to protect brain health. Leaders need to create cross-culture connections to navigate global landscape, and to be in a position to influence people from diverse backgrounds. No problem will be solved without being connected with those who struggle, and a meaningful connection is impossible without empathy and cooperation (67).

Empathy is essential for lasting social change and sustainable collaborative actions to disrupt disparities. Empathetic traits are predictors of conflict-free decision-making and interpersonal cohesion that help to accept and integrate social changes (68). In this section, we will briefly introduce the concept of empathy including its biological underpinnings as it relates to the topic of the current issue.

The fundamentals of empathy

Empathy is considered the capacity to understand, feel and assess what other individuals experience in its context (69). Empathy encompasses many motor, affective-emotional, social, cognitive, and behavioral processes which are mediated by the activity in a set of neural areas, including the temporal pole, the precuneus, the ventromedial prefrontal cortex, the bilateral angular gyrus, the amygdala, the insula, and the sensorimotor cortices (69).

A primer on empathy in the context of social interactions

Success in social interactions is critical for promoting leadership in improving health (70). Social interactions in humans are rooted in different implicit and intrapsychic social cognitive skills (69). Social cognition studies have explored the processes that underlie social and emotional perception and their integration (71): the processes that allow humans to have empathy for others, including the capacity to mimic others' motor behaviors (motor resonance processes) (72), sharing the emotional and painful experiences of others (affective sharing) (73, 74) and understanding others´ intentions, mental and emotional states (perspective taking) (75); as well as the processes that lead to increased drive and motivation for helping others and behaving in a cooperative manner (cooperative behavior or compassion) (76).

Empathy is so essential for human communication that the lack or loss of empathy are not variants in the human behavioral repertoire; they are symptoms. Two conditions that prominently affect the ability to empathize are psychopathy and behavioral variant frontotemporal dementia (bvFTD). The harmful actions and violation of the rights of others in psychopathy is associated with a lack of empathy (77). In bvFTD, the loss of empathy results in severe problems in close relationships (78). These display that the empathic ability is crucial for our most basic human connections.

In relation to empathy, humans can also behave in cooperative and altruistic forms in certain situations (68, 79–81). Cooperation is an organizing principle in human societies (82, 83). Evolutionary explanations of cooperation were proposed including kin selection, reciprocity and group selection; the extent of the use of these mechanisms and the ability to learn from the others are suggested to be different in humans than other organisms (83). Cooperation is dependent on empathy where individuals' cooperative capacity are affected by whether they recognize the moral view of the others (84, 85), but empathy is not the sole decisive factor (86). These behaviors are represented in a set of brain areas, including the orbitofrontal cortices and ventral striatum. Moreover, cooperation is determined by other psychological traits including motivation, drive and positive affect all of which promote well-being (87, 88).

Empathy and cooperative behaviors (sometimes referred as compassion behaviors) (76) are crucial skills for promoting leadership in brain health. Public health leaders must understand health disparities, recognize the suffering, and share an urgency to intervene. The impact of actions on improving brain health are highly determined by the level of understanding of individuals to be served. That understanding requires empathy and cooperation (87, 88).

The role of empathy and cooperation in brain health leadership

Measuring an individual's ability to read the emotional state of others, to be empathetic with their affective states, to infer their mental states and cooperation are vital steps in the development of adaptive forms of leadership. Individuals with high social cognitive skills can use these skills to nurture positive relationships with others. If brain health leaders can reflect on the level of empathy in their leadership decisions, they can succeed in improving the performance of their teams.

One principal form of leadership that relies on empathy and cooperative skills is the servant leadership approach (64). Understanding the emotions, actions and decisions of the people being served is crucial in the operational process of this leadership and this information is used to deploy the team in the most effective way as well as to develop strategies that best fit the target population. This approach helps the leaders elevate non-privileged staff members' efforts (65).

In brain health, as the suffering of the patients may involve a dehumanizing process in which the patients lose their autonomy; empathy and cooperation become essential features of the medical management. Most of the time, families and close relatives are responsible for the care of the patients, which also puts family members in a vulnerable situation. In those scenarios, empathy is crucial for fitting more humanistic interventions, focused on promoting autonomy and participation, so as the cooperation skills, the ability of behaving to cover for and favor others´ needs.

Empathy and cooperation are both critical to promote brain health changes. However, those processes do not always interact in a parsimonious manner, rather paradoxical interactions may occur. Although some aspects of empathy such as the empathic concern are positively associated with motivation and orientation to help others, different domains of empathy could attenuate prosocial behaviors (89). Notably, personal distress experienced by individuals with high empathy when seeing others' suffering could sometimes reduce their cooperative skills (90). The emotional responses (i.e., heightened sensitivity and compassion, affective empathy), may reduce the capacity to trigger behavioral motivation to cooperate and to mobilize appropriate actions for helping others (89, 91). The mentioned effect has been previously reported in health settings in which physicians and nurses could

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be affected by their capacity to help when they experience a high degree of distress toward other's needs (92–94). High personal distress could affect leaders' capacity to cope with emotional demands and organize and implement concrete actions for promoting positive changes. Considering that empathy and cooperation are critical processes to initiate actions and promote changes, leaders working in community should be prepared to deal with emotional load.

Empathy and cooperation align with radical collaboration

For successful leadership in global brain health, we find radical collaboration essential. Radical collaboration is a term coined by Tamm and Luyet over 20 years ago, which refers to "an animated network of actors working toward a shared frame of collective action" (95). Its importance is emphasized particularly for global problems where the efforts of single entities do not suffice to overcome the depth of the problem. Radical collaboration settings leverage individuals' interests and intrinsic motivations while grounding collaboration in freely made commitments between peers (95). By grounding themselves in partnership, peers anchor with empathetic, cooperative, and equitable scenarios, featuring a fluid approach to leadership granted by the trust. These facets of radical collaboration paint a striking alternative to the traditional corporate model by providing more opportunities for the less-privileged actors (96). Radical collaboration has been applied on a global scale by the United Nations General Assembly during the COVID-19 pandemic when responding to global crises and reaching sustainable development goals (97).

Radical collaboration could also be beneficial to tackle brain health challenges particularly in low-income countries in which specific social disparities might play a significant role in brain health (98). Leaders in brain health should establish dialog with local leaders based on empathy and cultural humility to understand the social, medical and cultural conditions that regionally determine brain health. Leaders can then draw, coordinate, and build structured plans. It is essential to recognize the unique challenges faced by each community and to address systemic issues, to effectively promote equity in access to resources and opportunities, and responsive care (99, 100).

Radical collaboration principles have also been applied to resolve issues related to global disparities in brain health. The Atlantic Fellowship for Equity in Brain Health at the GBHI is located in UCSF Memory and Aging Center and Trinity College, Dublin, and offers a year-long fellowship program to professionals including clinicians, scientists, artists, art producers, and economists from around the world (101). The program is sponsored by the Atlantic Institute and run in collaboration with other programs that promote fairer, healthier, and inclusive societies. By embracing diverse perspectives of fellows coming from high-, middle-, and low-income countries within the processes of problem-solving including idea generation, solution finding, and innovation, and practicing empathy and cultural humility, future leaders for equity in brain health facilitate equitable and non-hierarchical interactions, which are critical to overcome misunderstanding, low trusts, interpersonal and political conflicts, facilitate active and lasting collaborations, and stimulate positive societal change.

Conclusion

Disparities exist on different levels between and within countries, affecting brain health from birth to death. Cultural humility is essential in addressing disparities across populations, given their diverse needs and access and the impact that bias and lack of understanding can have on systems and the consequent perpetuation of inequalities. Empathy and its conscious utilization in daily interactions and collaborative models are required for cultural humility, cooperation, and collaboration. It may appear straightforward in the era of globalization but the recorded persistent and growing health and social disparities tell a different story and call for a more active approach.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

This manuscript was prepared as a statement paper following the authors joint presentation at the GBHI Annual Meeting at 2022. All authors contributed to the design and the content of the above mentioned presentation and the manuscript. FF, CL, TM, HS, and YA wrote the first draft. YA wrote the first draft and edited the final manuscript. YA supervised the authorships and the writing of the manuscript. All authors revised the working drafts. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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The neuroscience of respect: insights from cross-cultural perspectives

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Cultural values such as respect influence cognition, emotion, and behavior by modulating brain functioning. This mini-review discusses the cultural differences of respect as an essential human value, and the neural underpinnings accompanying them. Although neuroscientific studies are limited, we outline potential brain structures and networks that contribute to respect and use clinical examples to illustrate how behavior changes when these neural systems fail. A better understanding of the neuroanatomical basis of respect and its neural manifestations across cultures will help to advance current conceptualizations of the biology of human values.

KEYWORDS

cultural values, neuroscience, respect, neuroanatomical, neurodegenerative disorders

Introduction

The human brain is biologically prepared to acquire culture (Fiske, 2002). By shaping our identities, perceptions, and behaviors, culture provides a framework for understanding and navigating the world around us and shapes our brain activity (Han and Humphreys, 2016). Culture is a complex concept that encompasses a myriad of practices including language, dress, food, and music. Shared values, beliefs, and behaviors are also central elements of culture that bond people together and create a common identity that sets them apart from other groups.

Respect is a fundamental human value that refers to the consideration and admiration that one shows for oneself, others, and the environment (Li and Fischer, 2007). As respect motivates people to validate and acknowledge the feelings of others, it has a crucial role in human relationships, one facet of which is empathy, the ability to feel and comprehend the experiences of others (Decety and Jackson, 2004). The association between respect and empathy is likely bidirectional; when individuals respect others, they are more likely to feel empathy for them, and when they feel respected, they may express their emotions more openly and honestly, and elicit greater empathy. Feelings of mutual respect, therefore, can lead to better emotional connection and understanding between individuals (Li and Fischer, 2007).

While the value of respect may be universal, its specific manifestations differ across cultures (Mackenzie and Wallace, 2011). Therefore, the way in which respect influences the brain in people across cultures may also vary. Cultural neuroscience is an interdisciplinary area of study that combines theories and methods from the fields of cultural psychology and neuroscience (Han and Northoff, 2009; Ames and Fiske, 2010; Chiao et al., 2013; Han et al., 2013; Kim and Sasaki, 2014). This approach explores how culture shapes brain functioning and, conversely, how neural processes influence cultural values, beliefs, and practices (Nisbett et al., 2001; Nisbett and Masuda, 2003; Chiao et al., 2010; Kitayama and Park, 2010; Park and Huang, 2010; Rule et al., 2013; Han and Humphreys, 2016). Although relatively little is known about how cultural differences concerning respect influence brain functioning (Li and Fischer, 2007), prior studies can enlighten our understanding of the neural basis of respect and help to elucidate its varying role in cognition, emotion, and behavior across cultures (Mesquita and Walker, 2003).

Cross-cultural displays of respect

Cultures around the world hold the value of respect in high regard, but social norms that guide demonstrations of respect vary from one culture to the next (Mackenzie and Wallace, 2011). While many cultures encourage respect for elders and those of higher social status, collectivist and individualistic societies have notable differences in cultural norms surrounding respect (Ingersoll-Dayton and Saengtienchai, 1999). Here we describe some cultural practices to illustrate commonalities and differences in the practice of respect across cultures, but it is important to note that these are generalizations and that demonstrations of respect can also differ between individuals in the same culture.

In collectivist societies, respect is deeply ingrained in traditional customs and norms that guide social interactions. Collectivist societies tend to emphasize the wellbeing of the group over the needs and desires of individuals, and conveying respect is an integral part of verbal and non-verbal communication. In Asian cultures, people communicate respect and honor for their parents through filial piety practices such as bowing, using honorific titles, speaking politely, maintaining harmony, and avoiding actions that may cause their parents "loss of face" or embarrassment (Ingersoll-Dayton and Saengtienchai, 1999). Elders in Latin American cultures are also addressed with formal titles, and people maintain adequate personal space during social interactions to show deference. Using greetings and expressions of politeness, such as "please" and "thank you," as well as appropriate body language and gestures, is crucial for demonstrating respect (Calzada et al., 2010). In African cultures, respect is also expressed through greetings and gestures as well as attentive listening. Respect is extended to all members of the community, irrespective of age or social status, but elders are highly revered and considered to be a source of wisdom, guidance, and experience. Younger individuals, therefore, are expected to obey the older members of the community (Idang, 2015). In Middle Eastern and Indian cultures, respect is often linked to hospitality, honor, and family and underlies one's sense of duty toward elders. Most widely spoken Indian languages, for example, have a system of honorifics that conveys the degree of familiarity and formality within relationships (Bhatt, 2012). Respect for guests, elders, and those in positions of authority is demonstrated by using formal titles (Qidwai et al., 2017; Memon et al., 2021).

Individualistic societies, in contrast, prioritize values, norms, and practices that promote personal autonomy and independence. In these societies, individuals are encouraged to express their unique identities and to pursue their own goals. Independence is highly valued, and personal achievements, skills, and talents are key priorities (Hsieh, 2011; Grossmann and Santos, 2016). People in individualistic societies are expected to take responsibility for their lives, and their success is often measured on an individual basis. As equality and the protection of personal choices and rights are central tenets of individualistic societies, fostering environments with fair treatment of all is of paramount importance. Unlike collectivist societies, which focus on larger communities, individualistic societies focus on the nuclear family and emphasize the importance of self-sufficiency within a smaller family unit. While Western countries including Australia, Canada, Germany, the Netherlands, and the United States (Grossmann and Santos, 2016) often prioritize principles of individualism, there are still expectations and standards for showing respect to others. For example, using good manners and respecting personal space, privacy, personal boundaries, and consent are highly valued in Western cultures regardless of a person's gender, race, ethnicity, religion, social status, or other characteristics (Hsieh, 2011).

Neuroanatomical basis of respect

Respect is a multifaceted value and so, too, are its neuroanatomical underpinnings. While there are no specific brain structures solely dedicated to respect, certain neural regions and networks may have crucial roles in the cognitive, emotional, and behavioral processes that foster respect (Etkin et al., 2015). To show respect in social contexts, one must first know the pertinent rules to follow (Memon et al., 2021). In the brain, the anterior temporal lobes contain all types of semantic knowledge and may be important for storing semantic knowledge about respect. The left anterior temporal lobe holds information about verbal concepts and objects and, thus, might create associations among words, facts, and social rules that are relevant to respect (Joyal et al., 2017). Although research on the neural basis of respect is limited, one previous study found that the left anterior temporal lobe participates in determining the extent to which one feels respect and admiration for others in various situations (Nakatani et al., 2019). The right anterior temporal lobe, in contrast, is essential for representing non-verbal concepts and socio-emotional information. By helping people to understand others' voice prosody, bodily movement, and facial behavior, the right anterior temporal lobe is important for understanding emotions and social information which may foster respect in interpersonal contexts (Rosen et al., 2005; Rankin et al., 2006).

Respect invokes feelings of admiration and appreciation (Nakatani et al., 2019), and brain networks that support emotions are also likely important for this other–oriented value (Etkin et al., 2015; Nakatani et al., 2019; Sander and Nummenmaa, 2021). Through connections with the ventral striatum, amygdala, hypothalamus, and periaqueductal gray, the anterior cingulate cortex and ventral anterior insula are critical for generating and sensing internal changes in the body that arise during emotions, empathy, and reward (Seeley et al., 2012; Vogt, 2014; Etkin et al., 2015). Working together, this system allows people to detect salient information in the environment, to produce and experience emotions, and to nurture feelings of social connection (Decety, 2015). These regions may also contribute to the positive feelings that arise as people value the worth and dignity of others and admire their skills or virtues (Immordino-Yang et al., 2009). Feeling respected by others may elicit similar warm feelings. With close connections to admiration, gratitude, and elevation—prosocial emotions that people feel when witnessing others' exemplary behavior (Algoe, 2009)—respect may foster mutually enjoyable experiences (Algoe, 2019).

One must know the social rules that guide respectful behavior, but interpersonal interactions are dynamic, and social rules can change in an instant. In South Korean culture, for example, humor is often a part of social interaction, but what one person finds funny, another might find offensive. Understanding the appropriateness of humor requires constant awareness of the current context and the people involved. A joke that is acceptable in one setting may be inappropriate in another, and what was considered funny yesterday may not be perceived the same way today (Kim and Plester, 2019). To ensure that one acts in a respectful manner, one must track ongoing situations and adjust behavior as needed. The successful navigation of complex social situations, therefore, requires flexibility in cognition and behavior. The orbitofrontal cortex is an area in the ventral frontal lobes that guides decision-making and helps people to modify their actions and adapt to changing social environments (Kringelbach and Rolls, 2004). By allowing people to monitor and adjust their thoughts, actions, and emotions to each dynamic context, the orbitofrontal cortex is critical for fostering displays of respect during ongoing social interactions.

Brain damage can disrupt respect

Neuroimaging studies of healthy individuals can elucidate the neural networks that promote respect, but clinical studies have revealed how respect can decline when there is dysfunction in these brain systems. Perhaps the most well-known person who lost respect for social norms was Phineas Gage, a railroad worker who suffered a terrible injury to his orbitofrontal cortex when an iron rod shot through his skull and brain. Although Gage survived this horrific accident, his behavior after brain injury altered radically. Prior to the accident, he had been a well-respected man who adhered to typical social norms. But after his orbitofrontal cortex injury, Gage began to swear and drink to excess. He was no longer the man he had been, and his social interactions were often problematic as he could no longer control his behavior or show respect for others (O'Driscoll and Leach, 1998).

In certain neurodegenerative disorders, respectful behavior also declines when atrophy progresses through the orbitofrontal cortex and connected neural networks. The behavioral variant of frontotemporal dementia (bvFTD) is a neurodegenerative disorder in which there is selective tissue loss in the orbitofrontal cortex as well as the ventral anterior insula, anterior cingulate cortex, amygdala, and anterior temporal lobes (Seeley et al., 2012). In bvFTD, changes in social behavior, personality, and emotion (e.g., apathy, loss of empathy, and compulsivity) are common (Rosen et al., 2005; Rankin et al., 2006; Sturm et al., 2006, 2016). As people with bvFTD may defy social norms and hurt other people's feelings, their behavior may also be considered disrespectful. Atrophy in the orbitofrontal cortex and connected brain networks, may contribute to loss of respect in bvFTD because patients are no longer able to abide by the social rules that are necessary in showing respect.

Cultural influences on brain functioning

Although much remains unknown about how culture shapes brain functioning, a growing body of research suggests that activity patterns in the brain allow people to think and behave in culturally appropriate ways (Nisbett et al., 2001; Domínguez et al., 2009; Kitayama and Park, 2010; Park and Huang, 2010; Rule et al., 2013; Han and Humphreys, 2016). By repeatedly engaging in cultural perspectives and practices, people may shape their own brain network in specific ways that allow them to think and act according to cultural norms without much deliberation or effort (Kitayama and Uskul, 2011). How a culture influences brain functioning may vary, however. People from collectivist societies, for example, focus more on context and relationships and tend toward a more holistic (interdependent) cognitive style that is characterized by thematic categorization of objects, a focus on contextual information and relationships in visual attention, an emphasis on situational causes in attribution, and dialecticism (Nisbett et al., 2001; Varnum et al., 2010; Han and Humphreys, 2016). People from individualistic societies, in contrast, focus more on objects and attributes and tend toward a more analytic (independent) cognitive style that is characterized by taxonomic and rule-based categorization of objects, a narrow focus on visual attention, and the use of formal logic in reasoning (Nisbett et al., 2001). Consistent with these differences, people from Western cultures tend to remember more details of objects and events in autobiographical memory than people from Eastern cultures (Wang, 2001).

Neuroimaging studies have also found distinct patterns of neural activation in people from different cultures (Rule et al., 2013; Zhang et al., 2022). One study compared brain activity in participants from the United States and Japan in response to affectively laden stimuli and found cultural differences in reward system activity (Freeman et al., 2009). While in the scanner, participants viewed images that depicted dominance (e.g., power, control, and authority) or subordination (e.g., inferiority, submissiveness, or feeling being controlled by others). While the American participants—who are encouraged to be independent, assertive, and skeptical of authority—showed increased activity in the medial prefrontal cortex and caudate to the stimuli that elicited feelings of dominance, the Japanese participants—who are encouraged to be deferent, cooperative, and mindful of their social obligations—activated those same areas in response to the stimuli that elicited feelings of subordination (Freeman et al., 2009). These results suggested that culturally-preferred social information elicited greater activity in reward systems in each group.

In another study, European Americans and East Asians completed simple visuospatial tasks that required them to make absolute judgments (ignoring visual context) or relative judgments (taking visual context into account) while in the scanner (Hedden et al., 2008). As European Americans tend to make absolute judgments, and East Asians tend to make relative judgments, the researchers hypothesized that overriding these culturally-based tendencies would require greater effort and cognitive control.

Consistent with their expectations, the results showed that activity in frontoparietal regions that support attention and cognitive control was greater when the participants in each group made judgments that were not culturally preferred (Hedden et al., 2008). Other studies have found these cultural differences in neural activity also extend to other areas of cognition including visual perception (Gutchess et al., 2006; Goh et al., 2010; Rule et al., 2013), causal attribution (Han et al., 2011), mental calculation (Tang et al., 2006), and self-reflection (Zhu et al., 2007).

Respect and cultural neuroscience

Cultural practices and values can modulate brain functioning and influence how people process social, emotional, and cognitive information (Etkin et al., 2015; Nakatani et al., 2019; Sander and Nummenmaa, 2021). Much remains unknown, however, about how specific values such as respect, shape neural processes in various cultures. Although it is an important area of research, there are many factors that make the neuroscience of respect a challenging topic to study. Social norms and expectations surrounding respect are not fixed or static but change and evolve across time, people, and situations. As technological advancements and globalization continue to develop, intercultural interactions and social norms also continue to change. With an increasingly connected world, individuals may inhabit multiple cultures and hold multiple cultural identities (Nisbett et al., 2001). Their ability to shift flexibly between different modes of thinking and acting may make it difficult to determine which cultural values shape brain functioning in a given setting. A more sophisticated conceptualization of the neural underpinnings of respect will require the identification of common brain networks that support respectful behavior across cultures and differences in brain activity that contribute to culturally-specific manifestations of respect.

Conclusions

The neuroscience of respect is a complex and evolving field that remains replete with unanswered questions. By integrating the study of culture and neuroscience, however, we can gain important insights into the complex interplay between human values and the brain. A better understanding of respect has the potential to promote cross-cultural understanding and foster more inclusive and harmonious societies. The value of respect is already recognized as a core value in diversity, equity, and inclusion frameworks across sectors (Kiradoo, 2022), but leaders and co-workers from different cultures may communicate about or process information differently, as detailed in this review. More research is needed to elucidate how knowledge about the biological basis of respect can inform interventions and strategies that promote respectful behavior and reduce conflict in diverse cultural settings.

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