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By fault or by default

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As we march forward toward newer discoveries in the understanding of the pathophysiology of child psychiatric and neurodevelopmental disorders, questions are often raised regarding the potential "faulty" neural circuits that may be contributory. More recently, many researchers in psychiatry have focused on a newer paradigm that could involve problems in the default mode network (DMN). In this brief submission, we provide a overview of the current understanding of this interesting concept in child psychiatry, and how this may impact our understanding of such disorders, such as attention deficit/hyperactivity disorder (ADHD) and autism spectrum disorders (ASD).

The origins of the DMN can be traced back to incidental findings from early functional neuroimaging studies, which indicated, a consistent network of brain areas which is active when subjects are in a resting state but gets deactivated upon commencement of task related activity. The work of Raichle et al. (2001) is widely accepted as the definitive research which resulted in the emergence of the concept of organized default mode brain function. The last decade has seen a widespread interest in the field of cognitive neurosciences in understanding the intrinsic activity of the brain.

While at rest, the brain continues to be very active and is characterized by multiple, low frequency, resting state neural networks, and one of these is the DMN. Specialized techniques such as resting state functional connectivity MRI (rs fcMRI) are being used to study these networks (Vogel et al., 2010). From a psychiatry standpoint, review papers, such as those by Broyd et al. (2009) and Buckner et al. (2008) explored this fascinating area and provided a detailed introduction to the anatomical and functional aspects of DMN followed by a discussion of the clinical correlation of altered DMN activity with psychopathology seen in conditions such as attention deficit/hyperactivity disorder (ADHD), ASDs, schizophrenia, mood disorders, post-traumatic stress disorder (PTSD), and Alzheimer's disease. The association of DMN with ASD and ADHD makes this a critical neurobiological concept for practitioners in child and adolescent psychiatry to explore and understand. However, it is very important to note that currently, the scientific community considers the concept of DMN to be a work in progress (Raichle and Snyder, 2007) with several challenges hindering the progress, ranging from the technological aspects of functional neuroimaging, to the overall complexity of conducting a study of the functional networks of the brain.

The terms default mode, DMN, and task negative network (TNN) are used interchangeably to describe a network of areas in the frontal, parietal, and temporal lobes which are active at rest but deactivate when the subject is involved in a range of activities which involve focusing on external factors. The medial pre-frontal cortex (MPFC), precuneus, and posterior cingulate cortex (PCC) are considered to be the hubs of this system. Put together, these areas are involved in social cognition, introspective thought process, working memory, and episodic memory. DMN has also emerged as the most likely neural network underlying the concept of stimulus-independent thought sequence (SITS) or "wandering mind," and the sense of self (Gruberger et al., 2011). Wandering mind is thought to occur due to the ability of DMN to continue to process self-referential material at variable levels which is related to the degree of attention required to tend to tasks in external environment. A person who is deeply involved in a task has significant attenuation of DMN with minimal wandering thoughts, whereas a person participating passively in a task has an active DMN giving way to the emergence of activities such as daydreaming, "spacing out," and the opportunity to multi-task. In an interesting paper, Carhart-Harris and Friston (2010) hypothesized that the DMN may be the seat of the ego, which is constantly interacting with the limbic system and other functional networks of the brain through its extensive connections.

Task positive network (TPN) is another resting state network which is believed to be crucial to the ability of the brain to switch from a resting, internally focused state to switching to an active state when dealing with an environmental stimulus. While TPN is constantly running in the background, screening for external factors, the TNN predominates in resting state. Dorsolateral pre-frontal cortex (DLPFC), inferior parietal cortex (IPC), and supplemental motor area (SMA) are considered to be the hubs of the TPN. In fact, TPN and TNN are considered to be "anti-correlated" components of the DMN, very similar to the autonomic nervous system with its parasympathetic and sympathetic components. Overall, DMN plays an important role in constantly processing and responding to the abundant and continuous internal and external signals that our brains and bodies are exposed to.

The DMN goes through a developmental and maturation process. Understanding the role of genetic and environmental factors in the establishment of a fully functional DMN is vital. Gao et al. (2009) demonstrated the presence of DMN in children ranging from the age of 2 weeks to 2 years. In another paper on the topic, Fair et al. (2008) showed that DMN connections are sparse between the ages of 7 and 9, and only develop into a well-connected network in adulthood. Power et al. (2010) stress that the study of the developmental aspects of functional networks of the brain should be done not just at individual network level but also on a much grander scale looking at the developmental aspects of the interconnections between the various resting state networks. Uddin et al. (2010) note that the developmental process of DMN and other resting state networks is characterized by abundant, short range connectivity seen in

children which evolve aided by processes such as pruning to long range functional connectivity seen in adults.

The role of DMN dysfunction in ASD has been demonstrated in multiple studies (Minshew and Keller, 2010). ASD is characterized by reduced interconnectivity between DMN areas especially the MPFC leading to errors in social cognition (Vogel et al., 2010; Stigler et al., 2011). While DMN is considered to underlie the theory of mind, it is also closely involved with the mirror neuron networks. Altered DMN activity in combination with abnormal fronto-striatal-cerebellar networks is considered to be the neurobiological basis for the inattention and hyperactivity of ADHD (Vogel et al., 2010; Liston et al., 2011). Reduced suppression of DMN in the presence of task related activities has been shown to occur in ADHD subjects by using rsfcMRI. This allows the mind to continue to process self-referential activity inspite of the need to focus on external stimuli leading to concentration issues and emergence of ADHD symptoms. Using fMRI in 7–18 years old children with ADHD, Petereson et al. (2009) showed that stimulant medications modulate the suppression of DMN areas during task related activities and improve the attention and decrease hyperactivity. Similarly, Liddle et al. (2011) showed that the "motivation threshold" at which DMN activity is suppressed in response to performance of task was normalized and became comparable to healthy subjects when patients with ADHD are treated with methylphenidate. In a very interesting study, Brown et al. (2011) demonstrated the possible role of DMN in mediating the effects of dopamine transporter protein (DAT) 1 genotype in causing the symptoms of ADHD.

Looking into the future, neuroscientists face the complicated task of integrating and analyzing the information already available from completed studies and to come up with hypotheses looking at the role of genetic, environmental factors in development of normal and aberrant DMN. This could lead to the emergence of novel therapeutic targets in adequately managing complex neuropsychiatric disorders. Several papers are already proposing that functional neuroimaging with focus on DMN be used as a potential diagnostic and even as a therapeutic response monitoring biomarker. As a result, the establishment of specificity, validity, reliability, and use of clinical translational research tools in looking at the feasibility of such options is an exciting challenge for our field.

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