The Network Balance Model of Trauma and Resolution—Level I: Large-Scale Neural Networks

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There are three large-scale neural networks in the brain. The default mode network functions in autobiographical memory, self-oriented and social cognition, and imagining the future. The central executive network functions in engagement with the external world, goal-directed attention, and execution of actions. The salience network mediates interoception, emotional processing, and network switching. Flexible, balanced participation of all three networks is required for the processing of memory to its most adaptive form to support optimal behavior. The triple network model of psychopathology suggests that aberrant function of these networks may result in diverse clinical syndromes of psychopathology (Menon, 2011). Acute stress causes a shift in the balance of the large-scale networks, favoring the salience network and rapid, evolutionarily proven survival responses. This shift results in memory being processed by the amygdala and hippocampus, with limited participation of the prefrontal cortex. Typically following the resolution of stress, balance of the three networks is restored, and processing of memory with prefrontal cortex participation resumes spontaneously. The Network Balance Model of Trauma and Resolution posits that failure to restore network balance manifests clinically as posttraumatic stress disorder (PTSD), with inadequately processed and dysfunctionally stored memory (Chamberlin, 2014). Using eye movement desensitization and reprocessing (EMDR) therapy as an example, the model illustrates how the phases of the standard protocol activate specific networks, restoring network balance and the optimal processing of memory. The model offers a physiological mechanism of action for the resolution of psychological trauma in general, and EMDR therapy in particular.

Keywords: neural networks; psychological trauma; PTSD; EMDR therapy; mechanism of action

The Adaptive Information Processing (AIP) model is a theoretical model that guides the development and practice of eye movement desensitization and reprocessing (EMDR) therapy. The AIP hypothesizes that "dysfunctionally stored memory" serves as the foundation of posttraumatic psychopathology. Furthermore ". . . there is a system inherent in all of us that is physiologically geared to process information to a state of mental health . . . by means of this system, negative emotions are relieved, and learning takes place, is appropriately integrated, and is available for future use." EMDR is posited to exert its therapeutic effects through targeted information processing of "dysfunctionally stored memory" (Shapiro, 2018; Shapiro & Laliotis, 2011; Solomon & Shapiro, 2008).

While the clinical effectiveness of EMDR has been well established, the proposed neurobiological mechanisms of EMDR have yet to offer a comprehensive model capable of catalyzing robust targeted biological research (Bergmann, 2008, 2010; Bisson, Roberts, Andrew, Cooper, & Lewis, 2013; Jeffries & Davis, 2012; Rodenburg, Benjamin, de Roos, Meijer, & Stams, 2009; Watts et al., 2013). Without an explicit model of how trauma occurs, these attempts to explain the mechanism of EMDR are limited in their explanatory power.

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The Network Balance Model of Trauma and Resolution

NBMTR Level I

The Network Balance Model of Trauma and Resolution (NBMTR) attempts to explain the development and resolution of psychological trauma at two levels. Originally titled the Network Balance Model Applied to EMDR, the NBMTR (Levels I and II) has been presented at the Eye Movement Desensitization and Reprocessing International Association (EMDRIA) annual conference yearly, beginning in 2014 (Chamberlin, 2014). The NBMTR was developed by combining clinical insights from the practice of EMDR with recent advances in neuroscience. Level I focuses on large-scale neural networks utilizing the core insight of the triple network model of psychopathology (Menon, 2011). The triple network model core insight is that the diverse symptoms of the major clinical syndromes can result from dysfunction of the large-scale networks. Each network has discrete functions, and the optimal processing of experience requires the coordination of these networks interacting repeatedly over time (Barbas, Zikopoulos, & Timbie, 2011; Bressler & Menon, 2010; Kroes & Fernandez, 2012). Under conditions of severe stress, network balance can be compromised or lost (Hermans, Henckens, Joels, & Fernandez, 2014; Hermans et al., 2011). When network balance is lost, critical structures embedded in these networks (e.g., hippocampus, amygdala, and prefrontal cortex) cannot coordinate with each other (Kroes & Fernandez, 2012; Preston & Eichenbaum, 2013). The NBMTR postulates that one result is an inadequately processed and dysfunctionally stored memory, as suggested by the AIP.

The NBMTR posits that restoration of *network balance* in posttraumatic stress disorder (PTSD) is the critical factor in allowing the brain to resume optimal processing of dysfunctionally stored memory. This stands in contrast to the triple network model and its applications to PTSD that emphasize dysfunction within individual networks (Akiki, Averill, & Abdallah, 2017; Lanius, Frewen, Tursich, Jetly, & McKinnon, 2015; Menon, 2011). The emphasis of NBMTR on network balance is driven in part by clinical experience suggesting that restoration of balance may be sufficient to resolve pathology. Network balance may be restored spontaneously, leading to the resolution of PTSD, or as the result of effective trauma treatment, including EMDR therapy. Thus the NBMTR Level I attempts to explain how the dysfunctionally stored memories postulated by the AIP are generated, and then resolved, using EMDR therapy as an example.

NBMTR Level II

The NBMTR Level II (beyond the scope of this article) focuses on the role of memory as the principle substrate for predictions that guide behavior (Bar, 2009; Buckner, 2010). To ensure survival, the brain is constantly making predictions, and then using sensation as feedback to test its predictions (Clark & Clark, 2013). When there is a mismatch between what is predicted and what is currently sensed, the brain registers a "prediction error" (Hohwy, 2013). In response, the brain may update the memory through the process of memory reconsolidation (Dudai, 2006, 2009; Pedreira, Perez-Cuesta, & Maldonado, 2004). The goal of updating the memory is to minimize the prediction error, resulting in more successful behavior in the future. Dysfunctionally stored memories make for poor predictions and result in suboptimal behavior. For example, when a truck backfires in suburbia, it may trigger a veteran's dysfunctionally stored memory so he predicts incoming mortar fire and dives to the ground. The NBMTR postulates that if the networks are balanced, poor predictions based on dysfunctionally stored memories will be mismatched and the memories updated. Furthermore, the NBMTR posits that this process is driven by the thermodynamics of free energy minimization (Friston, 2009; Sengupta, Stemmler, & Friston, 2013). Thus the NMBTR Level II attempts to explain the biological basis of "the system inherent in all of us that is physiologically geared to process information to a state of mental health" postulated by the AIP (Shapiro, 2018 pg. 14).

EMDR therapy is an ideal lens through which to develop and view this model as it is "a comprehensive psychotherapy compatible with all theoretical orientations," and has well delineated clinical interventions (Shapiro, 2018; Shapiro & Laliotis, 2011). In addition, the inclusion of the therapeutic element of eye movements affords the opportunity to appreciate the powerful role that eye movements play in network function (Vernet, Quentin, Chanes, Mitsumasu, & Valero-Cabre, 2014).

Psychopathology and Network Science

Attempts to understand the major clinical syndromes of psychopathology, including PTSD, via reductionist analysis (deconstruct and find the "broken" parts) have not yielded satisfying results. More promising is

analysis applied to the network level of function. With advances in neuroimaging including functional magnetic resonance imaging (MRI) it is now possible to begin to understand brain function through the lens of network science (Bianchi, 2012; Park & Friston, 2013). With these new tools it has become apparent that large-scale networks are a fundamental property of brain organization and architecture (Menon, 2011)—and further, that networks are involved in a dynamic equilibrium characterized by brain wide shifts in neural functioning on a moment-to-moment basis (Bullmore & Sporns, 2012; Menon & Uddin, 2010). A significant advance in understanding the potential role of networks is the triple network model of psychopathology (Menon, 2011). The triple network model suggests diverse syndromes of psychopathology may be understood as a function of the three principle large-scale neural networks. Aberrant functioning within any network can cause dysfunction in the other networks, potentially resulting in a wide range of symptoms involving mood, cognition, and behavior. While the triple network model does not specifically address PTSD, it implies that focusing analysis on the three large-scale networks is sufficient to capture the essential dynamics of clinical psychopathologies. Choosing the correct level of analysis is a critical step in modeling a complex adaptive system like the brain (Bassett & Gazzaniga, 2011).

Large-Scale Neural Networks

The Default Mode Network

The first large-scale neural network to be described was the default mode network (DMN) (Raichle et al., 2001). Functional MRI with a passive subject shows activity in a network that includes the medial prefrontal cortex (mPFC), posterior cingulate cortex, inferior parietal lobule, and hippocampal formation (Buckner, Andrews-Hanna, & Schacter, 2008). The brain appears to "default" to this mode of function in the absence of specific task demands. The DMN appears to function in "internal mentation" including "mind wandering," "daydreaming," or "stimulus independent thought."

Further research on the nature of DMN-mediated internal mentation suggests the functions of this network include episodic memory, self-referential and social cognition, as well as imagining the future (Buckner & Carroll, 2007; Buckner et al., 2008; Spreng & Grady, 2010; Spreng, Mar, & Kim, 2009). So when we remember an event, take another person's perspective, or envision the future, the DMN is active.

The Central Executive Network

In contrast to the DMN stands the central executive network (CEN) or "task positive network" that becomes active when a subject engages in a task with the external world, for example, performing a visual search. A network including the dorsolateral prefrontal cortex (dlPFC), the frontal eye fields, and the posterior parietal cortex becomes active. This network functions in engagement with the external world and execution of actions. Included are the functions of directing eye movements, attention, and cognition, as well as working memory (Corbetta, Patel, & Shulman, 2008; Menon & Uddin, 2010; Seeley et al., 2007).

The Salience Network

The third large-scale neural network is the salience network (SN). This network is anchored by the anterior insular cortex (limbic sensory cortex) and the dorsal anterior cingulate cortex (limbic motor cortex) (Craig, 2009). The SN is notable for its connections to multiple subcortical nuclei involved in emotion, including the amygdala (fear conditioning/behavioral relevance), hypothalamus (regulation of the interior milieu), ventral striatum (reward), and periaqueductal gray (fixed action emotion motor circuits) (Panksepp & Biven, 2012). The SN functions in emotional processing, homeostatic regulation and reward (Seeley et al., 2007). This includes integrating salient input from the body, and from higher-level centers to direct resources (blood, oxygen, glucose) to the most appropriate networks given the current situation (Menon & Uddin, 2010). In effect, the SN acts as a network switch.

Network Switching

Acting as a network switch, the SN is responsible for helping to maintain the balance between the DMN and the CEN called "network anti-correlation" (Goulden et al., 2014; Menon & Uddin, 2010; Sridharan, Levitin, & Menon, 2008). In the mature neurotypical brain, activation of the two networks is like a seesaw. When the CEN is activated by a task, the DMN is deactivated. And when the CEN is inactive, the DMN is activated (Fox et al., 2005). This represents a broad shift from internal to externally directed cognition and vice versa. Such network shifting occurs on the timescale of milliseconds, back and forth, throughout the day. And the steeper the seesaw, that is, the more that one network is strongly activated and the other strongly deactivated, the better the encoding

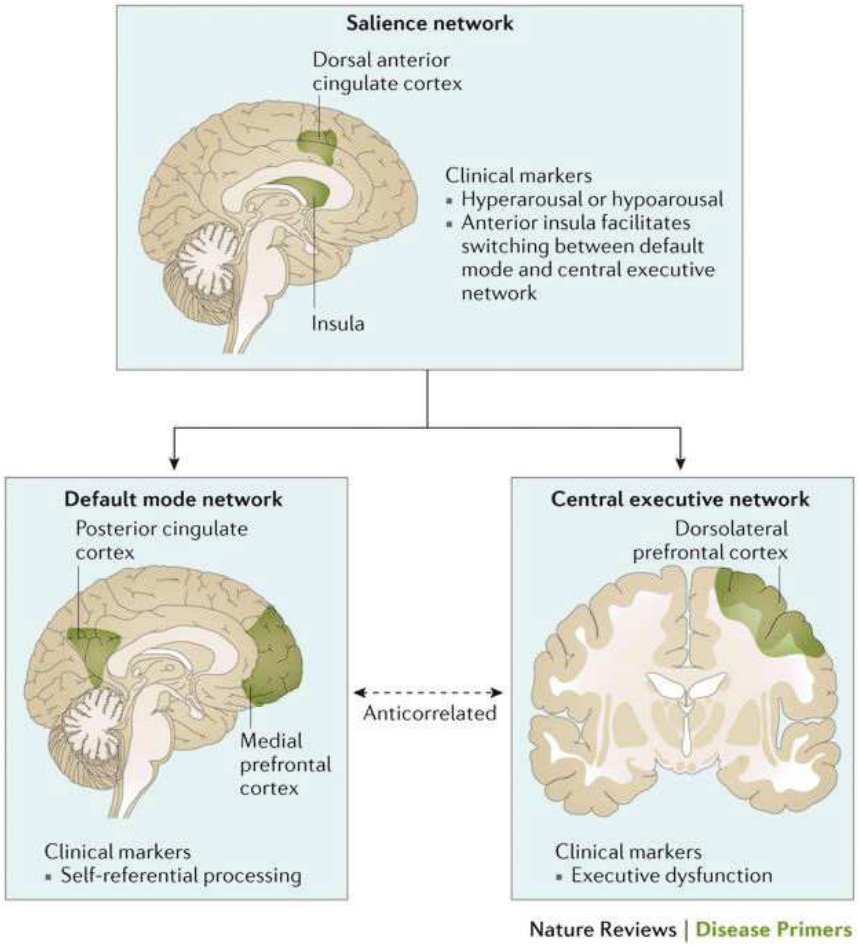

FIGURE 1. The default mode, salience, and central executive networks in PTSD.
Source. Yehuda, R., Hoge, C. W., McFarlane, A. C., Vermetten, E., Lanius, R. A., Nievergelt, C. M.,. . . Hyman, S. E. (2015). Post-traumatic stress disorder. *Nature Reviews Disease Primers, 1*, 15057. doi:10.1038/nrdp.2015.57. Reprinted with permission.

of new memory and executive function (Chai, Ofen, Gabrieli, & Whitfield-Gabrieli, 2013a, 2013b; Kelly, Uddin, Biswal, Castellanos, & Milham, 2008). The following example serves to illustrate how important SN switching can be. If a soldier in a foxhole is "daydreaming" about his wife, his DMN is active and he is in an autobiographical/social cognition mode of processing. If he hears the sound of a sniper's bullet, it is imperative that the SN engages the CEN so he can attend to and engage with the external world and the threat of a sniper. It is equally important to disengage his DMN and turn off "daydreaming." Failure to do so can be lethal. In summary, the SN acts as a network switch orienting the brain to what is most emotionally charged by turning on and off the networks for internally oriented (DMN) and externally oriented (CEN) processing in a reciprocal manner that has important implications for executive function and memory function. Figure 1.

Building on the Triple Network Model

Tests of the Triple Network Model

The triple network model provided a new framework for understanding PTSD beyond the neurocircuitry models of Rauch et al. and others that emphasized exaggerated amygdala responses and deficient frontal cortical function (Rauch, Shin, & Phelps, 2006). The core insight of the triple network model is that the behavior of the three large-scale networks can explain the complex patterns of symptoms observed in the major clinical syndromes. An early meta-analysis by Patel et al. applied this hypothesis to PTSD and found functional alterations in the SN, DMN, and CEN consistent with the triple network model (Patel, Spreng, Shin, & Girard, 2012). They concluded that "individuals with PTSD may over-engage the salience network, while failing to properly recruit the central executive network, and show differential changes in the activation of the default network." Focusing on the function

of the SN and DMN in PTSD, Sripada concluded "disequilibrium between large-scale networks subserving salience detection versus internally focused thought may be associated with PTSD pathophysiology" (Sripada et al., 2012). Taken together, these studies suggested that PTSD could be understood as a "disequilibrium" between the large-scale networks characterized by excessive SN and inadequate CEN activity. This idea formed the foundation of the NBMTR.

NBMTR Adds Complex Adaptive Systems

The NBMTR integrated the core insight of the triple network model with contemporary conceptions of the brain as a "Complex Adaptive System" (Coffey, 1998; Mazzocchi, 2008). Thayer describes the behavior of such physiological systems: "stability, adaptability and health are maintained through variability in the dynamic relationship among system elements . . . however such systems can become unbalanced . . . and a system that becomes 'locked in' to a particular pattern is dysregulated" (Thayer & Sternberg, 2006) In a complex system, it is not necessary to have dysfunctional "parts" to have a dysfunctional system. Dysfunction may arise from disruption in the *patterns of interaction* between the parts. A common example is heart palpitations resulting from stress. An irregular and pathological heartbeat can persist for a period of time without any underlying structural pathology. Most of the time it resolves spontaneously. Healthy balance between cardiac cells is temporarily lost and regained. When PTSD is viewed from this perspective, it is possible that the pathology, at least initially, lies in the dynamic relationship between the parts, not necessarily the parts themselves. This potentially leads to what Merzenich has referred to as a "failure mode in a self organizing system" (Meisel, Storch, Hallmeyer-Elgner, Bullmore, & Gross, 2012; Merzenich, Van Vleet, & Nahum, 2014). (When imbalanced network function is sustained for long periods, it may give rise to structural changes as the system attempts to compensate. Significant evidence of such structural changes has been demonstrated when trauma exposure occurs during brain development [Teicher, Samson, Anderson, & Ohashi, 2016].)

Clinical Evidence of Network Balance

The NBMTR hypothesis of loss of network balance as the critical factor in the pathogenesis of uncomplicated PTSD is supported by several clinical observations. PTSD symptoms generally resolve spontaneously, suggesting a reversible underlying mechanism (Chapman et al., 2011; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). Analogous to the stress-induced palpitations described previously, initially nothing is "broken." Reversibility also suggests that a mechanism of effective treatment will be a mirror of pathogenesis and that insights from one can be used to make inferences about the other and vice versa (Mazzocchi, 2008). The NBMTR was developed using this process of iterative inference that simultaneously generates a model of pathogenesis and a model of treatment as it attempts to complete these partial data sets. The occurrence of spontaneous resolution also reveals a fundamental difference between PTSD and the conditions discussed in the triple network model (Menon, 2011). Frontotemporal dementia and schizophrenia are associated with structural pathology at symptom onset, and are not subject to spontaneous resolution. Thus, it is necessary to go beyond the framework of the triple network model to account for this clinical difference. In models of the pathogenesis of PTSD, the NBMTR is notable in accounting for spontaneous resolution.

Further support comes from the clinical observation that increasing heart rate variability with feedback, thus restoring autonomic balance, can have a profound therapeutic effect on the processing of trauma (Chamberlin, 2011, 2013). Based on the work of Qin et al. and others, this effect can be understood as reversing the loss of network balance between CEN and DMN that occurs with stress and is characterized by decreased heart rate variability (Gillie & Thayer, 2014; Qin, Hermans, Van Marle, Luo, & Fernandez, 2009; Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012). More recent work has suggested that the effect of heart rate variability on network balance is mediated by a region in the mPFC shared by the DMN and SN (Jennings, Sheu, Kuan, Manuck, & Gianaros, 2016; Sakaki et al., 2016).

Taken together these findings provide an important link between autonomic nervous system balance, network balance, and the processing of trauma.

Large-Scale Networks as Modes of Mind

The possibility of network balance being important in PTSD was also inspired by Teasdale's "modes of mind." Specifically, the large-scale networks can be thought of as the biological foundation of the "modes of mind" of the interacting cognitive subsystems framework developed by Teasdale and Barnard (Teasdale, 1999). This model has been invoked to help explain the mechanism of change in EMDR therapy

(Shapiro, 2001). It described three different modes of mind that are involved in the processing of emotional experience: "mindless emoting," "conceptualizing/doing," and "mindful experiencing." Mindless emoting is characterized by immersion in emotional experience with little self-reflection, suggestive of isolated SN functioning. Conceptualizing/doing is characterized by thoughts about the self in the past and in the future with the goal of avoiding discomfort, with little present awareness. This mode is suggestive of isolated DMN functioning. In Teasdale's analysis neither mindless emoting nor conceptualizing/doing lead to a positive psychotherapeutic outcome. In contrast, the mode of mindful experiencing is characterized by integrated affective–cognitive experiencing and inner exploration, with present awareness of felt sense and environment. The mode of mindful experiencing is suggestive of *balanced, flexible functioning of DMN, SN, and CEN networks* and is associated with a positive outcome. From this perspective, the state of "network balance" appears to be important in adaptive emotional processing.

Shifts in Network Balance Induced by Stress

Research has begun to shed light on the dynamic allocation of network resources over time, under conditions of stress. With stress, norepinephrine and dopamine rise rapidly and remain elevated, tapering down quickly following the offset of stress (Hermans et al., 2014). Figure 2. After a short delay following the onset of stress, glucocorticoid secretion increases. The net result of norepinephrine, dopamine, and glucocorticoid release is a shift in resources from the CEN to the SN (Bouret & Sara, 2005; Hermans et al., 2011). This shift in network balance facilitates vigilance, rapid threat detection, and response, at the expense of flexible attention, deliberative thinking, and mnemonic processing (Hermans et al., 2014). Well after the offset of stress, the glucocorticoids previously released begin to exert late effects acting on the cell nucleus. These late effects are thought to be critical in restoring network balance where CEN resumes its baseline level of activity and function (Hermans et al., 2014; Yuen et al., 2009).

Recent experiments have begun to tease out more specifically the nature of the shifts within and between networks that occur under stress as levels of arousal rise.

Within-network cohesion is a measure that reflects coordination of activity within a network. Using heart rate as an index of arousal, the within-network cohesion of the SN steadily increases as arousal increases (Young et al., 2017). In contrast, the between-network cohesion between the SN and CEN peaks at moderate arousal. This suggests that at moderate levels of arousal, corresponding to the clinical concept of being inside the "Window of Tolerance" (Siegel, 1999), the SN is optimally able to engage the CEN to coordinate cognitive activity. At higher levels of arousal the coordination between networks is dramatically reduced, resulting in an effective loss of CEN function (McMenamin, Langeslag, Sirbu, Padmala, & Pessoa, 2014).

Network Imbalance Persists in PTSD

Early neurocircuitry models identified several areas of dysfunction in PTSD. The mPFC and the hippocampus demonstrated hypoactive function (Etkin & Wager, 2007; Shin, Rauch, & Pitman, 2006). The dlPFC was also found to be hypoactive (Bremner et al., 2004; Yan et al., 2013). In contrast the amygdala was found to be hyperactive (Blair et al., 2007; Rauch et al., 2006). Subsequent research identifying network function in PTSD reproduced and extended these findings. Corresponding to mPFC and hippocampal hypoactivity, the network containing these structures, the DMN, was found to be hypoactive (Bluhm et al., 2009; Sripada et al., 2012). Similarly, the dlPFC containing CEN was shown to be hypoactive (Hayes, Hayes, & Mikedis, 2012; Patel et al., 2012). And finally, the amygdala containing SN was hyperactive (Patel et al., 2012; Sripada et al., 2012). In addition, there was evidence of impaired engagement and disengagement of the DMN and CEN (Daniels et al., 2010). Taken together, these findings suggest that the shifts that occur in network function under stress may become stable and persist over time. In other words, the shift in network balance that occurs with stress does not resolve, leaving the individual in a state of network imbalance manifesting as PTSD.

PFC "Vicious Cycle" as a Cause of Sustained Network Imbalance

Stress Impairs PFC Function

While it is likely that there are multiple factors contributing to sustained network imbalance, this review will focus on the role of norepinephrine, as it is known to play a significant role in network reset (Bouret & Sara, 2005). Norepinephrine and dopamine neurons arising from the brainstem modulate the function of the PFC (Arnsten, 2009). The "dose–response" curve reflecting the influence of norepinephrine and

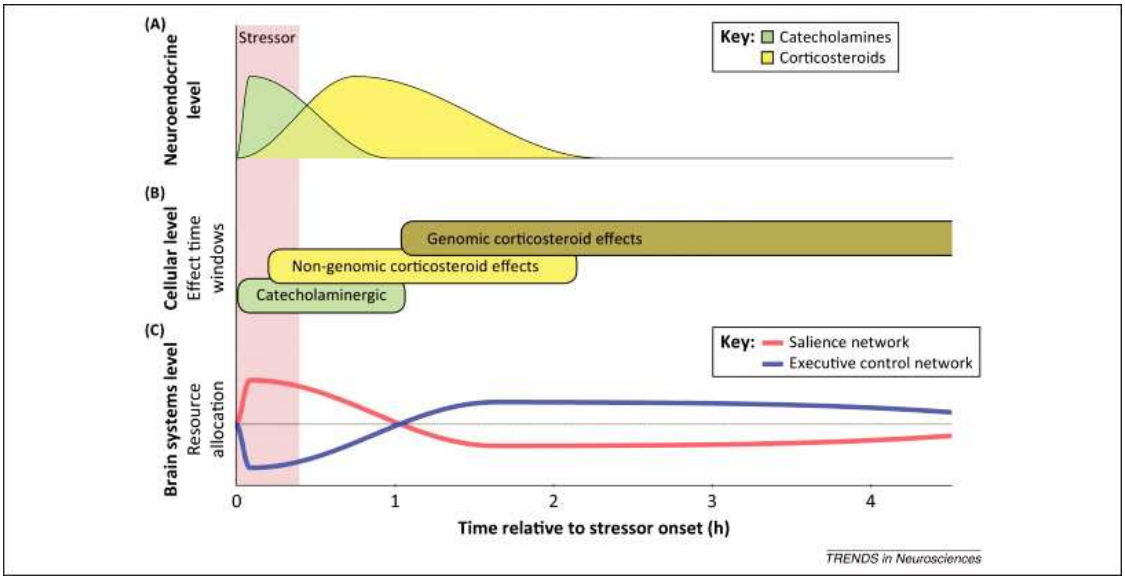

FIGURE 2. Biphasic-reciprocal model of reallocation of neural resources in response to stress. This figure illustrates the link between effects of stress at neuroendocrine (**A**), cellular (**B**), and brain systems (**C**) levels. (A) Neuroendocrine level: following exposure to a stressor, central levels of catecholamines (e.g., norepinephrine and dopamine) increase promptly and normalize not long after stressor offset. Corticosteroid levels in the brain rise more slowly and remain increased for a longer period. (B) Cellular level: cellular effects occur within distinct effect time windows. Catecholamines primarily exert immediate effects through G protein–coupled receptors. Corticosteroids have rapid nongenomic effects that may overlap and interact with catecholaminergic effects in an early time window, but also exert slower genomic effects. (C) Brain systems level: due to local differences in receptor distribution and signaling cascades, opposite effects occur within different neurocognitive systems.

Source. Hermans, E. J., Henckens, M. J., Joels, M., & Fernandez, G. (2014). Dynamic adaptation of large-scale brain networks in response to acute stressors. *Trends Neuroscience, 37*(6), 304-314. doi:10.1016/j.tins.2014.03.006. Reprinted with permission.

dopamine is an "inverted U," such that too little, or too much, of either neurotransmitter impairs PFC function. Even relatively mild stressors e.g. loud noise, public speaking, or watching an upsetting movie, can cause excessive release of noreipnephrine and/or dopamine impairing PFC functions including cognitive flexibility, attention and working memory (Arnsten, 2009; Arnsten & Goldman-Rakic, 1998; Qin et al., 2009). Typically, PFC function is restored shortly after the stressor resolves (Liston, McEwen, & Casey, 2009). Under certain conditions, however, the PFC may enter a prolonged state of diminished function called a "vicious cycle" (Arnsten, 2009).

"Vicious Cycle" of PFC Dysregulation

The PFC may be captured in a "vicious cycle" whereby elevated levels of norepinephrine and dopamine reduce PFC function, including PFC-mediated inhibition of the amygdala. Without inhibition, the amygdala prompts more release of norepinephrine and dopamine, further inhibiting PFC function. This is a positive feedback cycle (more norepinephrine leads to more norepinephrine) that can result in a state of profound dysregulation with sustained loss of PFC function. Per Thayer's description previously noted, this is the type of dysregulation that may occur in complex systems. The NBMTR suggests that the PFC vicious cycle is an important mechanism perpetuating network imbalance, and a prime candidate for the "block" in the information-processing system postulated by the AIP that results in "dysfunctionally stored memories." Indeed, excessive activity of the norepinephrine system resulting from exaggerated response and excessive release is one of the best replicated biological findings in PTSD (Pitman et al., 2012). And this persistence of diminished PFC function can be visualized with brain imaging (Aupperle, Melrose, Stein, & Paulus, 2012; Bergmann, 2010; Rabinak et al., 2011; Francati, Vermetten, & Bremner, 2007; Gilboa et al., 2004; Malejko, Abler, Plener, & Straub, 2017; Pagani, 2015; Patel et al., 2012).

"Vicious Cycle" Compromises PFC Portion of DMN and CEN

The PFC includes regions that are core nodes of the DMN and CEN. Loss of medial PFC function would therefore be expected to result in DMN dysfunction. Similarly, loss of lateral PFC function would be expected to result in CEN dysfunction. As previously noted, dysfunction of both DMN and CEN has

been found in PTSD. Thus the NBMTR postulates that under extreme stress, high levels of norepinephrine and dopamine can drive the PFC into a vicious cycle with prolonged dysfunction of the DMN and CEN, and sustained network imbalance manifesting as PTSD.

Compromised Memory Processing in a State of Network Imbalance

Under extreme stress, network balance shifts to favor SN processing at the expense of the DMN and CEN as previously discussed. Functioning of the amygdala is enhanced, while PFC function is diminished (Arnsten, 2009). This results in significant shifts in the processing of memory. The temporal dynamics model of emotional memory processing attempts to explain the complex shifts in memory function that unfold over time in the PFC, hippocampus, and amygdala under stress (Diamond, Campbell, Park, Halonen, & Zoladz, 2007).

Long-Term Potentiation

Long-term potentiation (LTP) is an established model of memory in which repetitive stimulation of a neuron results in enhanced synaptic transmission (Kandel, Dudai, & Mayford, 2014). As such it can be used to probe the status of the memory forming capacity of a particular brain region, at a particular moment in time. Given the complex alterations in memory resulting from extreme stress, this approach can be helpful in understanding clinical phenomena like "flashbulb" memories, fragmented memories, and amnesia (Zoladz, Park, & Diamond, 2011).

LTP Changes With Stress

Under extreme stress, LTP in the PFC can be inhibited for a prolonged period (Arnsten, 2009; Diamond et al., 2007). In contrast, the hippocampus and amygdala experience an increase in capacity for LTP. In the hippocampus, NMDA receptors become activated. As suggested by Diamond et al., this facilitates the creation of "flashbulb" memories that are vivid, but devoid of context in space and time. This phase of enhanced LTP lasts from seconds to minutes, and creates a simple durable memory near the onset of stress that can enhance survival the next time the situation is encountered. However, the memory lacks a rich contextual representation that helps to localize (and "contain") the memory to a particular place and time. This sets the stage for noncontext-specific cued recall of memories (flashbacks) in PTSD (Packard & Goodman, 2012). After a period of initially enhanced LTP, the hippocampus enters a period of impaired LTP that typically resolves after hours to days.

The amygdala follows a similar pattern to the hippocampus of initially enhanced LTP; however, the duration of enhanced LTP is longer, lasting minutes to hours. An important consequence of this time course is the potential for a prolonged period of learning and memory formation by the amygdala without the coordination or participation of the hippocampus and PFC (Diamond et al., 2007).

Compromised Memory Formation With Stress

Taken together, these complex shifts of enhanced and impaired function unfolding over time, in different structures, result in memory formation that is very different from the long-term memory consolidation that occurs under minimally stressed conditions (Arnsten, Wang, & Paspalas, 2012). In the absence of acute stress, memory formation is characterized by balanced, coordinated action between the PFC, hippocampus, and amygdala that results in the assimilation of experience into the dynamic structures of knowledge called schemas (Preston & Eichenbaum, 2013; Simons & Spiers, 2003). In contrast, as suggested by Diamond et al., under extreme stress memories are characterized by vivid but contextually impoverished "flashbulb" memories, with amnesia for details, and fragmentation—the "dysfunctionally stored memories" of the AIP.

The Role of the PFC in Memory Function

Top-Down Control of Encoding

While the roles of the amygdala and hippocampus in memory function have been well established, understanding the contribution of the PFC is a relatively new development. Early imaging studies found recruitment of the PFC when certain types of information were learned, with evidence of laterality specific to the content (Buckner, Kelley, & Petersen, 1999). Verbal content tended to recruit the left PFC, while nonverbal visual imagery recruited the right PFC. Subsequent work emphasized the role of the PFC in providing "top-down" control of the encoding process with modulation by such factors as current goals and task demands (Simons & Spiers, 2003). In other words, what we remember from an experience is influenced by what is important to us at the time, and how extensively

it is processed ("elaborative encoding") prior to storage. The importance of PFC "top-down" control is reflected in a large body of research that suggests that "brain neuroplasticity is controlled from the top" (Merzenich et al., 2014 pg14). Further work established that interactions between the hippocampus and PFC were mediated by neuronal oscillations that reflect the strength of the connection, which in turn predicts memory performance (Cohen, 2011).

The lateral PFC has been shown to have a role in resolving interference from existing memories that may compete as new experience is encoded (Badre, Poldrack, Pare-Blagoev, Insler, & Wagner, 2005; Thompson-Schill, Bedny, & Goldberg, 2005). This region appears to identify distinctness of new experience, thus driving encoding of a new memory versus assimilation into an existing memory (Kuhl, Bainbridge, & Chun, 2012).

Assimilation Into Schemas

A significant conceptual breakthrough occurred with research supporting the role of the PFC in the assimilation of new memories into "schemas" or preexisting networks of knowledge (Preston & Eichenbaum, 2013). As humans develop, memories rapidly accumulate and new experience needs to be integrated into existing schemas (Piaget, 1952). The contemporary conception of schemas is as "superordinate knowledge structures that reflect abstracted commonalities across multiple experiences, exerting powerful influences over how events are perceived, interpreted, and remembered" (Gilboa & Marlatte, 2017). Different processes participate in the creation, maintenance, and function of schemas. According to Gilboa and Marlatte, "assimilation" refers to *adapting incoming information* to fit into existing schemas and reflects how existing knowledge can influence perception and encoding. "Gist extraction" is a process whereby essential elements of an experience, absent which meaning would be changed, are elaborated and incorporated into schemas. "Accommodation" refers to a process of *modifying schemas* in response to new information, reflecting the fact that schemas are active knowledge structures. The schema-linked interactions between medial prefrontal and medial temporal regions model attempts to explain the interactions between the medial PFC and the hippocampus (Van Kesteren, Ruiter, Fernandez, & Henson, 2012). These interactions are complex with the two regions competing or cooperating with each other under different circumstances and at different points in time. Imaging results suggest that memory integration is a unique PFC-dependent state that is widespread and requires a balance between memory retrieval and encoding (Richter, Chanales, & Kuhl, 2015). In summary, given its role in the assimilation and accommodation of experience into schemas, the PFC is critical in the integration of memory into an adaptive form to guide behavior as postulated by the AIP.

The Role of Networks in Attention

While we are awake, there is an unceasing competition for our attention. Internal and external stimuli, as well as self-directed goals, vie for our attention and the associated cognitive processing resources. Right now your attention is "goal directed" toward reading this article. Your attention is not directed toward how your face feels. Oops, now it is directed toward your face. Come on back. Similarly, your attention is not directed toward the sounds around you. Now it is. Come on back. The ability to stay on task and filter out task-irrelevant stimuli, while simultaneously retaining the ability to respond to task-irrelevant but important stimuli, for example, a fire alarm sounding, is the product of a delicately balanced competition. Elucidating the nature of this competition has been a major challenge for cognitive neuroscience research.

Attention Is Linked to Eye Movements

Through analysis of psychological, anatomical, and physiological data Corbetta concluded that "attentional processes are tightly linked to oculomotor processes" (Corbetta, 1998). In "dual task" experiments, where the eyes are drawn to one location and attention is cued by sound to a different location, the focus of processing is obligatorily linked to the eye movement. In other words, we tend to process where we look, even if there are other competing stimuli in the environment. Physiologically, voluntary movement of the eyes is driven by a region of the PFC called the frontal eye fields that is a major node in the CEN (Hermans et al., 2014; Vernet et al., 2014). When we perform voluntarily saccadic eye movements we are activating the CEN.

Competition Between Attention Networks

Subsequent research identified networks involved in the orienting of attention, and shed light on the competitive, and coordinated relationship of these networks. Corbetta and colleagues identified a network corresponding to the CEN that was associated with "goal-driven," "top-down" attention (Corbetta et al.,

2008). In addition, a network corresponding to the SN was associated with "stimulus-driven" or "bottom-up" attention. In their analysis, the SN is responsible for interrupting ongoing activity in the CEN in order to reorient to a behaviorally relevant stimulus. Thus, the SN is postulated to act as a "circuit breaker" for CEN processing. In contrast, the CEN is responsible for identifying, selecting, and linking relevant stimuli in the pursuit of a goal, while suppressing the activity in the SN to prevent reorienting to distracting events. Thus, the SN and CEN are in competition for the orientation of attention.

"Top-Down" Control of Attention by Frontal Eye Fields

A study by Wen and colleagues, using behavioral measures and network causality analysis, concluded that the CEN controls goal driven top-down deployment of attention, while the SN mediates bottom-up stimulus-driven reorienting. In addition, the stronger the causal influence from CEN to SN (inhibition of the reorienting signal) the better the behavioral performance on a visual attention task (Wen, Yao, Liu, & Ding, 2012). Buschman and Miller confirmed the role of the CEN and SN in regulating attention while demonstrating that the frontal eye fields direct shifts of attention when the eyes move, but also direct shifts of attention when the eyes do not move, so-called covert orienting (Buschman & Miller, 2009). This finding supports the role of the frontal eye fields in "top-down" control of attention more broadly. In fact, using tactile and visual stimuli, Macaluso demonstrated that the attentional networks are "supramodal," that is, not simply yoked to vision but incorporating other sensory modalities as well (Macaluso, Frith, & Driver, 2002). That the attentional networks respond to tactile as well as visual stimuli may help to explain the efficacy of tactile bilateral stimulation (BLS) in EMDR therapy as conceived by the NBMTR.

Cooperation Between Attention Networks

Thus research supports two major networks that compete for capture of attention. The SN facilitates "bottom-up" stimulus-driven attention that drives orientation to what is *most emotionally charged*. The CEN facilitates "top-down" goal-directed attention to what is *most relevant*. Following competition for attention one network will prevail, either the SN driving reorientation, or the CEN driving sustained goal-directed attention. After one network prevails, both networks cooperate in a "super-network," working together to attend and process (Menon, 2015; Niendam et al., 2012; Parks & Madden, 2013; Vossel, Geng, & Fink, 2014). A recent study of cognitive control has characterized this "super-network" as the coordinated activity of the SN and CEN (Cai et al., 2016). Like team members who compete to lead a project, once a leader is determined, the members work together on the project, until a new project arrives, and the competition to lead begins again. The networks supporting attention have distinct but complementary roles, and continuously engage in cycles of competition and cooperation.

Compromised Attention in PTSD Resulting From Network Imbalance

Attention Bias Variability

A recent meta-analysis found that attention and working memory were among the most severely compromised neurocognitive functions in PTSD (Scott et al., 2015).

Early investigators characterized the abnormalities in attention seen in PTSD as a bias toward threatening stimuli (Fani et al., 2012). While this is frequently demonstrated in clinical populations, there is also a high incidence of bias *away* from threat, for example, ignoring threat (Bar-Haim et al., 2010; Sipos, Bar-Haim, Abend, Adler, & Bliese, 2014). This observation led to the recognition that the abnormalities in attention seen in PTSD are characterized by an increase in attention bias variability (ABV). PTSD sufferers are biased toward the extremes of attention, that is, excessive attention *toward* threat at times, and excessive attention *away* from threat at other times (contributing to reckless behavior) (Iacoviello et al., 2014; Naim et al., 2015). In PTSD, the deployment of attention is not balanced. Control of attention is compromised. And there is evidence that this compromise may precede trauma exposure in PTSD-susceptible individuals, and that it is further exacerbated by trauma exposure (Aupperle et al., 2012).

Failure to Recruit CEN Compromises Attention

The difficulty regulating attention seen in PTSD is believed to result from deficits in the recruitment of lateral prefrontal regions (Aupperle et al., 2012; Aupperle et al., 2012; Blair et al., 2013; Pannu Hayes, Labar, Petty, McCarthy, & Morey, 2009). More broadly, the deficits are thought to reflect a network imbalance between the SN and the CEN, with impaired recruitment of CEN compromising goal-directed attention and working memory (Daniels

et al., 2010; Esterman et al., 2013; Patel et al., 2012). Given that impaired regulation of attention appears to be a core deficit in PTSD, interventions have been attempted to directly ameliorate this deficit. Attention control training requires subjects to ignore irrelevant threatening stimuli to more successfully complete the goal-directed task at hand. In so doing, subjects are balancing attention allocation between irrelevant threatening stimuli, and goal-directed neutral stimuli on a moment by moment basis. Implicit in attention control training is the need to balance the SN and CEN. Initial results are promising demonstrating a reduction in ABV and in PTSD symptoms (Badura-Brack et al., 2015).

Once again a critical function in PTSD, control of attention, is caused by a sustained imbalance of large-scale neural networks. How might the brain be prodded to tip the balance back to CEN engagement with normalization of the multiple functions disrupted in PTSD? One way to attempt to answer this question is to reverse engineer effective clinical treatments of PTSD through the lens of large-scale neural networks (Csete & Doyle, 2002). In other words, how do the clinical interventions impact network function and promote the reestablishment of dynamic large-scale network balance?

How EMDR May Activate and Balance Large-Scale Networks

EMDR is an integrative psychotherapy utilizing eight phases. Based on current knowledge regarding neural network function, it is possible to hypothesize network activation/activity engendered by particular phases. This process is facilitated by the fact that the activity of the large-scale networks is associated with clinically observable behavior. In the assessment phase, identification of a specific image that represents the traumatic event serves as a cue to activate the DMN as it performs its function of autobiographical memory retrieval (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010; Buckner et al., 2008; Spreng et al., 2009). Within the DMN, the hippocampus uses a partial cue of the memory, for example, an image, to activate the entire neocortical ensemble that represents the memory (Teyler & Rudy, 2007). Identifying a particular image versus a supraordinate category, that is, the image of my car accident versus "car accidents," encourages activation of the unique episodic memory network corresponding to that experience. The requirement of specifying "the worst part of the experience" likely engages the SN, particularly the anterior insula, in its integrative role of "valuation" of different elements within an experience (Craig, 2009).

Negative and Positive Cognition

Elicitation of the negative cognition by asking, "What words go best with that picture that express your negative belief about yourself no?" or "How do you define yourself?" attempts to capture beliefs or judgments about the self that are related to the traumatic experience. Self-referential beliefs such as "I have a quick temper" or "I forget important things" have been shown to result from activation of the mPFC and posterior cingulate cortex, core nodes of the DMN (Buckner et al., 2008; Buckner & Carroll, 2007; Johnson et al., 2002; Northoff & Bermpohl, 2004; Spreng & Grady, 2010). Elicitation of the positive cognition by asking "What would you like to believe about yourself? " activates the DMN in a slightly different way harnessing the role of DMN in prospective cognition, that is,predicting the future (Bar, 2009; Spreng et al., 2009). To the extent that the positive cognition is realized through processing, the individual has created what pioneering neuroscientist David Ingvar referred to as a "Memory of the Future" (Ingvar, 1985).

Initiation of Reexperiencing

After activating the DMN by eliciting the memory and negative cognition, asking for the associated emotion and the location of the sensation in the body may activate the SN. The anterior insula is a critical node in the SN and is thought to support subjective awareness of emotions (Craig, 2009). The posterior insula, also part of the SN, is the structure responsible for the highest level of representation of internal sensation in the body (Craig, 2009; Uddin, 2015). Recently it has been demonstrated that interoceptive recall activates the posterior insula (DeVille et al., 2018). With activation of the DMN and the SN with respect to the traumatic memory, the memory has been brought "online," and the client is in a state of reexperiencing. Processing has begun. The level of arousal may rise precipitously. In fact the level of arousal, mediated by norepinephrine, may rise sufficiently to induce the "vicious cycle" of network imbalance described previously. The PFC is inhibited and information processing is blocked. Outside of the treatment setting, precipitation of the "vicious cycle" can reinforce the original experience and thus be retraumatizing. As a result, PTSD sufferers learn to not activate the DMN by avoiding cues that trigger the memory (Aupperle

et al., 2012). And they also learn to avoid activating the SN by suppressing awareness of bodily sensation. Taken together, these adaptive responses may minimize retraumatization in the short term, while simultaneously precluding the opportunity for a more adaptive response of fully processing the memory so that it no longer has the power to induce a "vicious cycle."

The Role of Dual Attention in Restoring Network Balance

In the context of EMDR therapy, activation of the DMN and SN into a state of reexperiencing sets the stage for processing of the memory with the aid of "dual attention" and eye movements. As the level of arousal and norepinephrine rises beyond moderate levels, the circuit-breaking, reorienting function of the SN interrupts coordinated activity with the CEN. The capacity for flexible and sustained deployment of attention is lost. Per the NBMTR, the individual is in a state of continuous reorienting to the threatening stimuli of the dysfunctionally stored memory. It is impossible to orient and sustain attention on anything else, including neutral stimuli. This is essentially a state of "safety blindness," with an inability to "see now." This is reflected in deficits in safety learning characteristic of PTSD (Jovanovic, Kazama, Bachevalier, & Davis, 2012; Sijbrandij, Engelhard, Lommen, Leer, & Baas, 2013,).

Dual Attention Recruits CEN Overriding the SN

"Dual attention" is a therapist-directed task that attempts to compel simultaneous attention to the internal state of reexperiencing of the traumatic memory, and to the external environment. The NBMTR posits that this externally oriented task activates the CEN "manually," thus compensating for the demonstrated failure to recruit lateral prefrontal regions in PTSD (Aupperle et al., 2012; Blair et al., 2013; Pannu Hayes et al., 2009; Patel et al., 2012; Rabinak et al., 2014). Activating the CEN may then suppress activity in the DMN through the previously described phenomenon of network anticorrelation (Chen et al., 2013; Fox et al., 2005; Spreng, Stevens, Chamberlain, Gilmore, & Schacter, 2010). This is a good candidate mechanism for the "desensitization" that often occurs quite rapidly in clinical practice, given that the CEN has minimal connectivity to the principal subcortical nuclei involved in emotional processing (Seeley et al., 2007). Success in activating the CEN can be monitored by the therapist in real time. Is the client following instructions, engaging in the task, showing evidence of external orientation? and so forth. If the client is not externally orienting, the therapist may invoke prompts, for example, "over here . . . follow my fingers . . . that's good" to "pull" attention to the external world, and to bring the CEN online. The net effect of "dual attention" may be to activate the CEN, tipping the balance back toward external orientation, and overriding the sustained reorienting signal of the SN. With CEN activation two functions become possible. The first is the resumption of competition between CEN and SN, whereby the CEN is able to exert inhibitory control signals on the SN to prevent orienting to irrelevant stimuli (Corbetta et al., 2008; Vossel et al., 2014; Wen et al., 2012). For example, there is no need to orient to a memory-driven reexperiencing of a bomb exploding, when in the present there is no bomb exploding. Second, there is the possibility of cooperation between SN and CEN necessary for cognitive control operations (Cai et al., 2016; Menon, 2015; Vossel et al., 2014). This includes the critical role of the CEN in stimulus evaluation during orienting, that is, what is the behavioral significance of the current stimulus (Han & Marois, 2014)? Therapist-guided "dual attention" is a critical intervention that may facilitate restoration of dynamic large-scale network balance. In doing so, dual attention may restore network competition–cooperation cycles that underlie the flexible and sustained deployment of attention and other higher-level cognitive processes, including processing of memory. In principal, dual attention can be achieved by a variety of tasks that require CEN/executive function; however, the empirically supported, preferred task in EMDR therapy is utilizing eye movements.

The Role of Eye Movements in Restoring Network Balance

Eye movements have a variety of biological effects relevant to the resolution of trauma (Chamberlin, 2014). These effects include resetting the theta rhythm and increasing sensory sampling, thus driving mismatch, memory reconsolidation, and prediction error minimization (Friston, Adams, Perrinet, & Breakspear, 2012; Jutras, Fries, & Buffalo, 2013). Eye movements also increase the generation of associations linking disparate networks (Johansson & Johansson, 2014). The NBMTR Level II will discuss these important effects of eye movements that are beyond the scope of the present article. The current discussion will be limited to the effects of eye movements on large-scale network function.

Multiple subcortical and cortical nuclei participate in the orchestration of eye movements. Central to the movement of the eyes and the deployment of attention is a region known as the frontal eye fields, a core node in the CEN (Corbetta et al., 2008; Hermans et al., 2014; Vernet et al., 2014). While subcortical nuclei are capable of generating reflexive saccadic eye movements, voluntary "goal-directed" saccadic movements of the type used in EMDR therapy require participation of the frontal eye Fifld̀s (Schall, 2004, 2009; Vernet et al., 2014).

Eye Movements Activate CEN Restoring Network Balance

As previously postulated, prompted by the emotionally charged dysfunctional memory, the SN drives orientation toward the memory, interrupting orientation toward anything else. Therapist-guided saccadic eye movements may activate the CEN and compel attention to the external world in the present, momentarily overriding the SN signal. This appears to allow the individual to briefly orient to the present and "see safety." The more the orientation to a safe present is achieved, the weaker the SN drive to reorient to the dysfunctionally stored memory—and the greater the restoration of the CEN ability to inhibit the SN signal to reorient to the dysfunctional memory. Typically, this is achieved progressively with repeated sets of subjective reports followed by eye movements. Gradually, CEN function may be restored and network balance reestablished so that it is self-sustaining.

As the desensitization phase proceeds, reports of self-experience that activate DMN- and SN-mediated internal attention alternate with sets of eye movements that activate CEN-mediated external attention. Such repeated switching from internally biased to externally biased modes of processing is believed to drive learning and the updating of internal models (Honey, Newman, & Schapiro, 2018).

The Role of the Therapist in EMDR Therapy

From the NBMTR perspective, the role of the therapist in EMDR therapy can be thought of as orchestrating the activation and balance of large-scale neural networks. Contemporary network science is embedded in the standard protocol, and each phase activates specific neural networks in a particular order. The therapist guides the process by attempting to optimize network activation and balance at each step by attending to, and accommodating individual variation. This includes a broad range of activities from case conceptualization and target selection, to monitoring and coregulation of arousal. Because neural networks are dynamic and constantly changing, the therapist must maintain an awareness of network activation and balance throughout processing. The therapeutic goal is to support a state of network balance that is necessary for widespread, flexible, dynamic cooperation of disparate brain regions and the processing of memory. Loss of activation and therefore balance will result in a failure to sustain processing. Thus, the interventions for blocked processing include changing direction or speed of eye movements (activate CEN), attending to particular sensations (activate SN), or return to target (activate DMN), in order to try to reestablish network balance. From the perspective of the NBMTR, the rule of thumb is straightforward: "If the networks are balanced, the memory will process."

The Effect of EMDR Therapy on Network Balance

The NBMTR model awaits research testing the hypothesis of resolution of network imbalance with successful treatment of PTSD. However, there are several existing network studies using EMDR that are relevant. Landin-Romero found significantly improved task-induced DMN deactivation in a patient with bipolar disorder and subsyndromal PTSD (Landin-Romero et al., 2013). At baseline the patient failed to appropriately deactivate the DMN while performing the n-back working memory task. Following 14 sessions of EMDR therapy with significant symptomatic improvement, there was a corresponding improvement in the deactivation of the DMN. This is consistent with the NBMTR suggesting restoration of network balance reflected by significantly improved "network anticorrelation."

Jung et al. studied nine firefighters (vs. eight healthy controls) with subsyndromal PTSD using functional magnetic resonance imaging (fMRI) (Jung, Chang, & Kim, 2016). They found abnormal values in several network measures reflecting "disturbances in the optimal balance between the functional segregation and integration within the networks." Each firefighter received three sessions of EMDR with symptomatic improvement. The authors concluded "sub-threshold manifestations of PTSD may be due to a disruption in the optimal balance in the functional brain networks, and that this disruption can be ameliorated by psychotherapy."

Conclusion

The NBMTR posits that extreme stress causes an imbalance of large-scale neural networks that may persist, compromising the processing of experience and leading to dysfunctionally stored memories. Network balance may be restored spontaneously or through effective trauma treatment like EMDR therapy, resulting in resolution of PTSD symptoms.

REFERENCES

Akiki, T. J., Averill, C. L., & Abdallah, C. G. (2017). A network-based neurobiological model of PTSD: Evidence from structural and functional neuroimaging studies. *Current Psychiatry Reports, 19*(11), 81. doi:10.1007/s11920-017-0840-4

Andrews-Hanna, J. R., Reidler, J. S., Sepulcre, J., Poulin, R., & Buckner, R. L. (2010). Functional-anatomic fractionation of the brain's default network. *Neuron, 65*(4), 550–562. doi:10.1016/j.neuron.2010.02.005

Arnsten, A. F. (2009). Stress signalling pathways that impair prefrontal cortex structure and function. *Nature Reviews Neuroscience, 10*(6), 410–422. doi:10.1038/nrn2648

Arnsten, A. F., & Goldman-Rakic, P. S. (1998). Noise stress impairs prefrontal cortical cognitive function in monkeys: Evidence for a hyperdopaminergic mechanism. *Archives of General Psychiatry, 55*(4), 362–368.

Arnsten, A. F., Wang, M. J., & Paspalas, C. D. (2012). Neuromodulation of thought: Flexibilities and vulnerabilities in prefrontal cortical network synapses. *Neuron, 76*(1), 223–239. doi:10.1016/j.neuron.2012.08.038

Aupperle, R. L., Allard, C. B., Grimes, E. M., Simmons, A. N., Flagan, T., Behrooznia, M., . . . Stein, M. B. (2012). Dorsolateral prefrontal cortex activation during emotional anticipation and neuropsychological performance in posttraumatic stress disorder. *Archives of General Psychiatry, 69*(4), 360–371. doi:10.1001/archgenpsychiatry.2011.1539

Aupperle, R. L., Melrose, A. J., Stein, M. B., & Paulus, M. P. (2012). Executive function and PTSD: Disengaging from trauma. *Neuropharmacology, 62*(2), 686–694. doi:10.1016/j.neuropharm.2011.02.008

Badre, D., Poldrack, R. A., Pare-Blagoev, E. J., Insler, R. Z., & Wagner, A. D. (2005). Dissociable controlled retrieval and generalized selection mechanisms in ventrolateral prefrontal cortex. *Neuron, 47*(6), 907–918. doi:10.1016/j.neuron.2005.07.023

Badura-Brack, A. S., Naim, R., Ryan, T. J., Levy, O., Abend, R., Khanna, M. M., . . . Bar-Haim, Y. (2015). Effect of attention training on attention bias variability and PTSD symptoms: Randomized controlled trials in israeli and U.S. Combat veterans. *American Journal of Psychiatry, 172*, 1233–1241. doi:10.1176/appi.ajp.2015.14121578

Bar, M. (2009). The proactive brain: Memory for predictions. *Philosophical Transactions Royal Society London B, Biological Sciences, 364*(1521), 1235–1243. doi:10.1098/rstb.2008.0310

Barbas, H., Zikopoulos, B., & Timbie, C. (2011). Sensory pathways and emotional context for action in primate prefrontal cortex. *Biological Psychiatry, 69*(12), 1133–1139. doi:10.1016/j.biopsych.2010.08.008

Bar-Haim, Y., Holoshitz, Y., Eldar, S., Frenkel, T. I., Muller, D., Charney, D. S., . . . Wald, I. (2010). Life-threatening danger and suppression of attention bias to threat. *American Journal of Psychiatry, 167*(6), 694–698. doi:10.1176/appi.ajp.2009.09070956

Bassett, D. S., & Gazzaniga, M. S. (2011). Understanding complexity in the human brain. *Trends in Cognitive Sciences, 15*(5), 200–209. doi:10.1016/j.tics.2011.03.006

Bergmann, U. (2008). The neurobiology of EMDR: Exploring the thalamus and neural integration. *Journal of EMDR Practice and Research, 2*(4), 300–314. doi:10.1891/1933-3196.2.4.300

Bergmann, U. (2010). EMDR's neurobiological mechanisms of action: A survey of 20 years of searching. *Journal of EMDR Practice and Research, 4*(1), 22–42.

Bianchi, M. T. (2012). Synchronizing bench and bedside. In M. T. Bianchi, V. S. Caviness, & S. S. Cash (Eds.), *Network approaches to diseases of the brain*. (pp. 3–12). Sharhah, UAE: Bentham.

Bisson, J. I., Roberts, N. P., Andrew, M., Cooper, R., & Lewis, C. (2013). Psychological therapies for chronic post-traumatic stress disorder (PTSD) in adults. *Cochrane Database of Systematic Reviews*,2013 Dec 13; (12), Cd003388. doi:10.1002/14651858.CD003388.pub4

Blair, K. S., Smith, B. W., Mitchell, D. G., Morton, J., Vythilingam, M., Pessoa, L., . . . Blair, R. J. (2007). Modulation of emotion by cognition and cognition by emotion. *Neuroimage, 35*(1), 430–440. doi:10.1016/j.neuroimage.2006.11.048

Blair, K. S., Vythilingam, M., Crowe, S. L., McCaffrey, D. E., Ng, P., Wu, C. C., . . . Blair, R. J. (2013). Cognitive control of attention is differentially affected in trauma-exposed individuals with and without posttraumatic stress disorder. *Psychological Medicine, 43*(1), 85–95. doi:10.1017/s0033291712000840

Bluhm, R. L., Williamson, P. C., Osuch, E. A., Frewen, P. A., Stevens, T. K., Boksman, K., . . . Lanius, R. A. (2009). Alterations in default network connectivity in posttraumatic stress disorder related to early-life trauma. *Journal of Psychiatry Neuroscience, 34*(3), 187–194.

Bouret, S., & Sara, S. J. (2005). Network reset: A simplified overarching theory of locus coeruleus noradrenaline function. *Trends in Neurosciences, 28*(11), 574–582. doi:10.1016/j.tins.2005.09.002

Bremner, J. D., Vermetten, E., Vythilingam, M., Afzal, N., Schmahl, C., Elzinga, B., . . . Charney, D. S. (2004). Neural correlates of the classic color and emotional stroop in women with abuse-related posttraumatic stress disorder. *Biological Psychiatry, 55*(6), 612–620. doi:10.1016/j.biopsych.2003.10.001

Bressler, S. L., & Menon, V. (2010). Large-scale brain networks in cognition: Emerging methods and principles. *Trends in Cognitive Sciences, 14*(6), 277–290. doi:10.1016/j.tics.2010.04.004

Buckner, R. L. (2010). The role of the hippocampus in prediction and imagination. *Annual Review of Psychology, 61*, 27–48, c21–c28. doi:10.1146/annurev.psych.60.110707.163508

Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain's default network: Anatomy, function, and relevance to disease. *Annals of the New York Academy of Sciences, 1124*, 1–38. doi:10.1196/annals.1440.011

Buckner, R. L., & Carroll, D. C. (2007). Self-projection and the brain. *Trends in Cognitive Sciences, 11*(2), 49–57. doi:10.1016/j.tics.2006.11.004

Buckner, R. L., Kelley, W. M., & Petersen, S. E. (1999). Frontal cortex contributes to human memory formation. *Nature Neuroscience, 2*(4), 311–314. doi:10.1038/7221

Bullmore, E., & Sporns, O. (2012). The economy of brain network organization. *Nature Reviews Neuroscience, 13*(5), 336–349. doi:10.1038/nrn3214

Buschman, T. J., & Miller, E. K. (2009). Serial, covert shifts of attention during visual search are reflected by the frontal eye fields and correlated with population oscillations. *Neuron, 63*(3), 386–396. doi:10.1016/j.neuron.2009.06.020

Cai, W., Chen, T., Ryali, S., Kochalka, J., Li, C. S., & Menon, V. (2016). Causal interactions within a frontal-cingulate-parietal network during cognitive control: Convergent evidence from a multisite-multitask investigation. *Cerebral Cortex, 26*(5), 2140–2153. doi:10.1093/cercor/bhv046

Chai, X. J., Ofen, N., Gabrieli, J. D., & Whitfield-Gabrieli, S. (2013a). Development of deactivation of the default-mode network during episodic memory formation. *Neuroimage, 84c*, 932–938. doi:10.1016/j.neuroimage.2013.09.032

Chai, X. J., Ofen, N., Gabrieli, J. D., & Whitfield-Gabrieli, S. (2013b). Selective development of anticorrelated networks in the intrinsic functional organization of the human brain. *Journal of Cognitive Neuroscience, 26*(3), 501–13. doi:10.1162/jocn_a_00517

Chamberlin, D. E. (2011). Physiological psychotherapy: Opening the "Trauma Window" in high achievers. *Biofeedback, 39*(1), 21–26.

Chamberlin, D. E. (2013). *Physio-logical psychotherapy: The integration of heart rate variability feedback into EMDR*. Paper presented at the 18th EMDR International Association Annual Conference, Austin, TX.

Chamberlin, D. E. (2014). *The network balance model applied to EMDR*. Paper presented at the 20th EMDR International Association Annual Meeting, Denver, CO.

Chapman, C., Mills, K., Slade, T., McFarlane, A. C., Bryant, R. A., Creamer, M., . . . Teesson, M. (2011). Remission from post-traumatic stress disorder in the general population. *Psychological Medicine, 42*(8), 1695–1703. doi:10.1017/S0033291711002856

Chen, A. C., Oathes, D. J., Chang, C., Bradley, T., Zhou, Z. W., Williams, L. M., . . . Etkin, A. (2013). Causal interactions between fronto-parietal central executive and default-mode networks in humans. *Proceedings of the National Academy of Sciences of the United States of America, 110*(49), 19944–19949. doi:10.1073/pnas.1311772110

Clark, A., & Clark, A. (2013). Whatever next? Predictive brains, situated agents, and the future of cognitive science. *Behavioral and Brain Sciences, 36*(03), 181–204. doi:10.1017/S0140525X12000477

Coffey, D. S. (1998). Self-organization, complexity and chaos: The new biology for medicine. *Nature Medicine, 4*(8), 882–885.

Cohen, M. X. (2011). Hippocampal-prefrontal connectivity predicts midfrontal oscillations and long-term memory performance. *Current Biology, 21*(22), 1900–1905. doi:10.1016/j.cub.2011.09.036

Corbetta, M. (1998). Frontoparietal cortical networks for directing attention and the eye to visual locations: Identical, independent, or overlapping neural systems? *Proceedings of the National Academy of Sciences of the United States of America, 95*(3), 831–838.

Corbetta, M., Patel, G., & Shulman, G. L. (2008). The reorienting system of the human brain: From environment to theory of mind. *Neuron, 58*(3), 306–324. doi:10.1016/j.neuron.2008.04.017

Craig, A. D. (2009). How do you feel–now? The anterior insula and human awareness. *Nature Reviews Neuroscience, 10*(1), 59–70. doi:10.1038/nrn2555

Csete, M. E., & Doyle, J. C. (2002). Reverse engineering of biological complexity. *Science, 295*(5560), 1664. doi:10.1126/science.1069981

Daniels, J. K., McFarlane, A. C., Bluhm, R. L., Moores, K. A., Clark, C. R., Shaw, M. E., . . . Lanius, R. A. (2010). Switching between executive and default mode networks in posttraumatic stress disorder: Alterations in functional connectivity. *Journal of Psychiatry & Neuroscience, 35*(4), 258–266.

DeVille, D. C., Kerr, K. L., Avery, J. A., Burrows, K., Bodurka, J., Feinstein, J., . . . Simmons, W. K. (2018). The neural bases of interoceptive encoding and recall in healthy adults and adults with depression. *Biological Psychiatry: Cognitive Neuroscience Neuroimaging, 3*(6), 546–554. doi:10.1016/j.bpsc.2018.03.010

Diamond, D. M., Campbell, A. M., Park, C. R., Halonen, J., & Zoladz, P. R. (2007). The temporal dynamics model of emotional memory processing: A synthesis on the neurobiological basis of stress-induced amnesia, flashbulb and traumatic memories, and the Yerkes-Dodson law. *Neural Plasticity, 2007*. doi:10.1155/2007/60803

Dudai, Y. (2006). Reconsolidation: The advantage of being refocused. *Current Opinion in Neurobiology, 16*(2), 174–178. doi:10.1016/j.conb.2006.03.010

Dudai, Y. (2009). Predicting not to predict too much: How the cellular machinery of memory anticipates the uncertain future. *Philosophical Transaction of the Royal Society of London. Series B, Biological Sciences, 364*(1521), 1255–1262. doi:10.1098/rstb.2008.0320

Esterman, M., DeGutis, J., Mercado, R., Rosenblatt, A., Vasterling, J. J., Milberg, W., . . . McGlinchey, R. (2013). Stress-related psychological symptoms are associated with increased attentional capture by visually salient distractors. *Journal of the International Neuropsychological Society, 19*(7), 835–840. doi:10.1017/s135561771300057x

Etkin, A., & Wager, T. D. (2007). Functional neuroimaging of anxiety: A meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. *American Journal of Psychiatry, 164*(10), 1476–1488. doi:10.1176/appi.ajp.2007.07030504

Fani, N., Tone, E. B., Phifer, J., Norrholm, S. D., Bradley, B., Ressler, K. J., . . . Jovanovic, T. (2012). Attention bias toward threat is associated with exaggerated fear expression and impaired extinction in PTSD. *Psychological Medicine, 42*(3), 533–543. doi:10.1017/s0033291711001565

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D.C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences of the United States of America, 102*(27), 9673–9678. doi:10.1073/pnas.0504136102

Francati, V., Vermetten, E., & Bremner, J. D. (2007). Functional neuroimaging studies in posttraumatic stress disorder: Review of current methods and findings. *Depression and Anxiety, 24*(3), 202–218. doi:10.1002/da.20208

Friston, K. (2009). The free-energy principle: A rough guide to the brain? *Trends in Cognitive Science, 13*(7), 293–301. doi:10.1016/j.tics.2009.04.005

Friston, K., Adams, R. A., Perrinet, L., & Breakspear, M. (2012). Perceptions as hypotheses: Saccades as experiments. *Frontiers in Psychology, 3*, 151. doi:10.3389/fpsyg.2012.00151

Gilboa, A., & Marlatte, H. (2017). Neurobiology of schemas and schema-mediated memory. *Trends in Cognitive Sciences, 21*(8), 618–631. doi:10.1016/j.tics.2017.04.013

Gilboa, A., Shalev, A. Y., Laor, L., Lester, H., Louzoun, Y., Chisin, R., . . . Bonne, O. (2004). Functional connectivity of the prefrontal cortex and the amygdala in posttraumatic stress disorder. *Biological Psychiatry, 55*(3), 263–272.

Gillie, B. L., & Thayer, J. F. (2014). Individual differences in resting heart rate variability and cognitive control in posttraumatic stress disorder. *Frontiers in Psychology, 5*, 758. doi:10.3389/fpsyg.2014.00758

Goulden, N., Khusnulina, A., Davis, N. J., Bracewell, R. M., Bokde, A. L., McNulty, J. P., . . . Mullins, P. G. (2014). The salience network is responsible for switching between the default mode network and the central executive network: Replication from DCM. *Neuroimage. 99*:180–90. doi:10.1016/j.neuroimage.2014.05.052

Han, S. W., & Marois, R. (2014). Functional fractionation of the stimulus-driven attention network. *Journal of Neuroscience, 34*(20), 6958–6969. doi:10.1523/jneurosci.4975-13.2014

Hayes, J. P., Hayes, S. M., & Mikedis, A. M. (2012). Quantitative meta-analysis of neural activity in posttraumatic stress disorder. *Biology of Mood & Anxiety Disorders, 2*(1), 9. doi:10.1186/2045-5380-2-9

Hermans, E. J., Henckens, M. J., Joels, M., & Fernandez, G. (2014). Dynamic adaptation of large-scale brain networks in response to acute stressors. *Trends in Neurosciences, 37*(6), 304–314. doi:10.1016/j.tins.2014.03.006

Hermans, E. J., Van Marle, H. J., Ossewaarde, L., Henckens, M. J., Qin, S., & . . . Fernandez, G. (2011). Stress-related noradrenergic activity prompts large-scale neural network reconfiguration. *Science*, *334*(6059), 1151–1153. doi:10.1126/science.1209603

Hohwy, J. (2013). *The predictive mind*. New York, NY: Oxford University Press.

Honey, C. J., Newman, E. L., & Schapiro, A. C. (2018). Switching between internal and external modes: A multiscale learning principle. *Network Neuroscience, 1*(4), 339–356. doi:10.1162/NETN_a_00024

Iacoviello, B. M., Wu, G., Abend, R., Murrough, J. W., Feder, A., Fruchter, E., . . . Charney, D. S. (2014). Attention bias variability and symptoms of posttraumatic stress disorder. *Journal of Traumatic Stress, 27*(2), 232–239. doi:10.1002/jts.21899

Ingvar, D. H. (1985). "Memory of the future": An essay on the temporal organization of conscious awareness. *Human Neurobiology, 4*(3), 127–136.

Jeffries, F. W., & Davis, P. (2012). What is the role of eye movements in eye movement desensitization and reprocessing (EMDR) for post-traumatic stress disorder (PTSD)? A review. *Behavioural and Cognitive Psychotherapy*, *41*(3), 290–300. doi:10.1017/s1352465812000793

Jennings, J. R., Sheu, L. K., Kuan, D. C., Manuck, S. B., & Gianaros, P. J. (2016). Resting state connectivity of the medial prefrontal cortex covaries with individual differences in high-frequency heart rate variability. *Psychophysiology, 53*(4), 444–454. doi:10.1111/psyp.12586

Johansson, R., & Johansson, M. (2014). Look here, eye movements play a functional role in memory retrieval. *Psychological Science, 25*(1), 236–242. doi:10.1177/0956797613498260

Johnson, S. C., Baxter, L. C., Wilder, L. S., Pipe, J. G., Heiserman, J. E., & Prigatano, G. P. (2002). Neural correlates of self-reflection. *Brain, 125*(pt. 8), 1808–1814.

Jovanovic, T., Kazama, A., Bachevalier, J., & Davis, M. (2012). Impaired safety signal learning may be a biomarker of PTSD. *Neuropharmacology, 62*(2), 695–704. doi:10.1016/j.neuropharm.2011.02.023

Jung, W. H., Chang, K. J., & Kim, N. H. (2016). Disrupted topological organization in the whole-brain functional network of trauma-exposed firefighters: A preliminary study. *Psychiatry Research, 250*, 15–23. doi:10.1016/j.pscychresns.2016.03.003

Jutras, M. J., Fries, P., & Buffalo, E. A. (2013). Oscillatory activity in the monkey hippocampus during visual exploration and memory formation. *Proceedings of the National Academy of Sciences of the United States of America, 110*(32), 13144–13149. doi:10.1073/pnas.1302351110

Kandel, E. R., Dudai, Y., & Mayford, M. R. (2014). The molecular and systems biology of memory. *Cell, 157*(1), 163–186. doi:10.1016/j.cell.2014.03.001

Kelly, A. M., Uddin, L. Q., Biswal, B. B., Castellanos, F. X., & Milham, M. P. (2008). Competition between functional brain networks mediates behavioral variability. *Neuroimage, 39*(1), 527–537. doi:10.1016/j.neuroimage.2007.08.008

Kessler, R. C., Sonnega, A., Bromet, E., Hughes, M., & Nelson, C. B. (1995). Posttraumatic stress disorder in the national comorbidity survey. *Archives of General Psychiatry, 52*(12), 1048–1060.

Kroes, M. C., & Fernandez, G. (2012). Dynamic neural systems enable adaptive, flexible memories. *Neuroscience and Biobehavioral Reviews, 36*(7), 1646–1666. doi:10.1016/j.neubiorev.2012.02.014

Kuhl, B. A., Bainbridge, W. A., & Chun, M. M. (2012). Neural reactivation reveals mechanisms for updating memory. *Journal of Neuroscience, 32*(10), 3453–3461. doi:10.1523/jneurosci.5846-11.2012

Landin-Romero, R., Novo, P., Vicens, V., McKenna, P. J., Santed, A., Pomarol-Clotet, E., . . . Amann, B. L. (2013). EMDR therapy modulates the default mode network in a subsyndromal, traumatized bipolar patient. *Neuropsychobiology, 67*(3), 181–184. doi:10.1159/000346654

Lanius, R. A., Frewen, P. A., Tursich, M., Jetly, R., & McKinnon, M. C. (2015). Restoring large-scale brain networks in PTSD and related disorders: A proposal for neuroscientifically-informed treatment interventions. *European Journal of Psychotraumatology, 6*. doi:10.3402/ejpt.v6.27313

Liston, C., McEwen, B. S., & Casey, B. J. (2009). Psychosocial stress reversibly disrupts prefrontal processing and attentional control. *Proceedings of the National Academy of Science of the United States of America, 106*(3), 912–917. doi:10.1073/pnas.0807041106

Macaluso, E., Frith, C. D., & Driver, J. (2002). Supramodal effects of covert spatial orienting triggered by visual or tactile events. *Journal of Cognitive Neuroscience, 14*(3), 389–401. doi:10.1162/089892902317361912

Malejko, K., Abler, B., Plener, P. L., & Straub, J. (2017). Neural correlates of psychotherapeutic treatment of post-traumatic stress disorder: A systematic literature review. *Frontiers in Psychiatry, 8*, 85. doi:10.3389/fpsyt.2017.00085

Mazzocchi, F. (2008). Complexity in biology. Exceeding the limits of reductionism and determinism using complexity theory. *EMBO Reports, 9*(1), 10–14. doi:10.1038/sj.embor.7401147

McMenamin, B. W., Langeslag, S. J., Sirbu, M., Padmala, S., & Pessoa, L. (2014). Network organization unfolds over time during periods of anxious anticipation. *Journal of Neuroscience, 34*(34), 11261–11273. doi:10.1523/jneurosci.1579-14.2014

Meisel, C., Storch, A., Hallmeyer-Elgner, S., Bullmore, E., & Gross, T. (2012). Failure of adaptive self-organized criticality during epileptic seizure attacks. *PLOS Computational Biology, 8*(1), e1002312. doi:10.1371/journal.pcbi.1002312

Menon, V. (2011). Large-scale brain networks and psychopathology: A unifying triple network model. *Trends in Cognitive Sciences, 15*(10), 483–506. doi:10.1016/j.tics.2011.08.003

Menon, V. (2015). Large-scale functional brain organization. In A. W. Toga (Ed.), *Brain mapping* (pp. 449–459). Philadelphia, PA: Elsevier.

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: A network model of insula function. *Brain Structure Function, 214*(5-6), 655–667. doi:10.1007/s00429-010-0262-0

Merzenich, M. M., Van Vleet, T. M., & Nahum, M. (2014). Brain plasticity-based therapeutics. *Frontiers in Human Neuroscience, 8*, 385. doi:10.3389/fnhum.2014.00385

Naim, R., Abend, R., Wald, I., Eldar, S., Levi, O., Fruchter, E., . . . Bar-Haim, Y. (2015). Threat-related attention bias variability and posttraumatic stress. *American Journal of Psychiatry, 172*(12), 1242–1250. doi:10.1176/appi.ajp.2015.14121579

Niendam, T. A., Laird, A. R., Ray, K. L., Dean, Y. M., Glahn, D. C., & Carter, C. S. (2012). Meta-analytic evidence for a superordinate cognitive control network subserving diverse executive functions. *Cognitive Affective Behavioral Neuroscience, 12*(2), 241–268. doi:10.3758/s13415-011-0083-5

Northoff, G., & Bermpohl, F. (2004). Cortical midline structures and the self. *Trends in Cognitive Sciences, 8*(3), 102–107. doi:10.1016/j.tics.2004.01.004

Packard, M. G., & Goodman, J. (2012). Emotional arousal and multiple memory systems in the mammalian brain. *Frontiers in Behavioral Neuroscience, 6,14*.

Pagani, M. (2015, August). *Imaging EMDR related neurobiological changes.* Plenary presented at the 20th EMDR International Conference, Philadelphia, PA.

Panksepp, J., & Biven, L. (2012). *The archaeology of mind: Neuroevolutionary origins of human emotions* (1st ed.). New York, NY: W.W. Norton.

Pannu, Hayes., J, Labar., S., K., Petty, C. M., McCarthy, G., & Morey, R. A. (2009). Alterations in the neural circuitry for emotion and attention associated with posttraumatic stress symptomatology. *Psychiatry Research, 172*(1), 7–15. doi:10.1016/j.pscychresns.2008.05.005

Park, H. J., & Friston, K. (2013). Structural and functional brain networks: From connections to cognition. *Science, 342*(6158), 1238411. doi:10.1126/science.1238411

Parks, E. L., & Madden, D. J. (2013). Brain connectivity and visual attention. *Brain Connectivity, 3*(4), 317–338. doi:10.1089/brain.2012.0139

Patel, R., Spreng, R. N., Shin, L. M., & Girard, T. A. (2012). Neurocircuitry models of posttraumatic stress disorder and beyond: A meta-analysis of functional neuroimaging studies. *Neuroscience Biobehavioral Reviews, 36*(9), 2130–2142. doi:10.1016/j.neubiorev.2012.06.003

Pedreira, M. E., Perez-Cuesta, L. M., & Maldonado, H. (2004). Mismatch between what is expected and what actually occurs triggers memory reconsolidation

or extinction. *Learning Memory, 11*(5), 579–585. doi:10.1101/lm.76904

Piaget, J. (1952). *The origins of intelligence in children*. New York, NY: International Universities Press.

Pitman, R. K., Rasmusson, A. M., Koenen, K. C., Shin, L. M., Orr, S. P., Gilbertson, M. W., . . . Liberzon, I. (2012). Biological studies of post-traumatic stress disorder. *Nature Reviews Neuroscience, 13*(11), 769–787. doi:10.1038/nrn3339

Preston, A. R., & Eichenbaum, H. (2013). Interplay of hippocampus and prefrontal cortex in memory. *Current Biology, 23*(17), R764–773. doi:10.1016/j.cub.2013.05.041

Qin, S., Hermans, E. J., Van Marle, H. J., Luo, J., & Fernandez, G. (2009). Acute psychological stress reduces working memory-related activity in the dorsolateral prefrontal cortex. *Biological Psychiatry*, *66*(1), 25–32. doi:10.1016/j.biopsych.2009.03.006

Rabinak, C. A., Angstadt, M., Welsh, R. C., Kennedy, A., Lyubkin, M., Martis, B., . . . Phan, K. L. (2011). Altered amygdala resting-state functional connectivity in posttraumatic stress disorder. *Frontiers in Psychiatry, 2:62*. doi:10.3389/fpsyt.2011.00062

Rabinak, C. A., MacNamara, A., Kennedy, A. E., Angstadt, M., Stein, M. B., Liberzon, I., . . . Phan, K. L. (2014). Focal and aberrant prefrontal engagement during emotion regulation in veterans with posttraumatic stress disorder. *Depression Anxiety, 31*(10), 851–861. doi:10.1002/da.22243

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences of the United States of America, 98*(2), 676–682. doi:10.1073/pnas.98.2.676

Rauch, S. L., Shin, L. M., & Phelps, E. A. (2006). Neurocircuitry models of posttraumatic stress disorder and extinction: Human neuroimaging research—past, present, and future. *Biological Psychiatry, 60*(4), 376–382. doi:10.1016/j.biopsych.2006.06.004

Richter, F. R., Chanales, A. J. H., & Kuhl, B. A. (2015). Predicting the integration of overlapping memories by decoding mnemonic processing states during learning. *Neuroimage*, *124*(Pt A), 323–335. doi:10.1016/j.neuroimage.2015.08.051

Rodenburg, R., Benjamin, A., de Roos, C., Meijer, A. M. & Stams, G. J. (2009). Efficacy of EMDR in children: A meta-analysis. *Clinical Psychology Review, 29*(7), 599–606. doi:10.1016/j.cpr.2009.06.008

Sakaki, M., Yoo, H. J., Nga, L., Lee, T. H., Thayer, J. F., & Mather, M. (2016). Heart rate variability is associated with amygdala functional connectivity with MPFC across younger and older adults. *Neuroimage*, *139*, 44–52. doi:10.1016/j.neuroimage.2016.05.076

Schall, J. D. (2004). On the role of frontal eye field in guiding attention and saccades. *Vision Research, 44*(12), 1453–1467. doi:10.1016/j.visres.2003.10.025

Schall, J. D. (2009). *Frontal eye fields. In L. Squire (Eds.), Encyclopedia of neuroscience* (pp. 367–374). London: Academies Press.

Scott, J. C., Matt, G. E., Wrocklage, K. M., Crnich, C., Jordan, J., Southwick, S. M., . . . Schweinsburg, B. C. (2015). A quantitative meta-analysis of neurocognitive functioning in posttraumatic stress disorder. *Psychological Bulletin, 141*(1), 105–140. doi:10.1037/a0038039

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., Kenna, H., . . . Greicius, M. D. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *Journal of Neuroscience, 27*(9), 2349–2356. doi:10.1523/jneurosci.5587-06.2007

Sengupta, B., Stemmler, M. B., & Friston, K. J. (2013). Information and efficiency in the nervous system—a synthesis. *PLOS Computational Biology, 9*(7), e1003157. doi:10.1371/journal.pcbi.1003157

Shapiro, F. (2001). *Eye movement desensitization and reprocessing (EMDR): Basic principles, protocols, and procedures* (2nd ed.). New York, NY: Guilford.

Shapiro, F. (2018). *Eye movement desensitization and reprocessing (EDMR) therapy: Basic principles, protocols, and procedures* (3rd ed.). New York, NY: Guilford.

Shapiro, F., & Laliotis, D. (2011). EMDR and the adaptive information processing model: Integrative treatment and case conceptualization. *Clinical Social Work Journal, 39*(2), 191–200. doi:10.1007/s10615-010-0300-7

Shin, L. M., Rauch, S. L., & Pitman, R. K. (2006). Amygdala, medial prefrontal cortex, and hippocampal function in PTSD. *Annals of the New York Academy of Sciences, 1071*, 67–79. doi:10.1196/annals.1364.007

Siegel, D. J. (1999). *The developing mind: Toward a neurobiology of interpersonal experience*. New York, NY: Guilford.

Sijbrandij, M., Engelhard, I. M., Lommen, M. J., Leer, A., & Baas, J. M. (2013). Impaired fear inhibition learning predicts the persistence of symptoms of posttraumatic stress disorder (PTSD). *Journal of Psychiatric Research, 47*(12), 1991–1997. doi:10.1016/j.jpsychires.2013.09.008

Simons, J. S., & Spiers, H. J. (2003). Prefrontal and medial temporal lobe interactions in long-term memory. *Nature Reviews Neuroscience, 4*(8), 637–648. doi:10.1038/nrn1178

Sipos, M. L., Bar-Haim, Y., Abend, R., Adler, A. B., & Bliese, P. D. (2014). Postdeployment threat-related attention bias interacts with combat exposure to account for PTSD and anxiety symptoms in soldiers. *Depression and Anxiety, 31*(2), 124–129. doi:10.1002/da.22157

Solomon, R., & Shapiro, F. (2008). EMDR and the adaptive information processing model. *Journal of EMDR Practice and Research, 2*(4), 315–325.

Spreng, R. N., & Grady, C. L. (2010). Patterns of brain activity supporting autobiographical memory, prospection, and theory of mind, and their relationship to the default mode network. *Journal of Cognitive Neuroscience, 22*(6), 1112–1123. doi:10.1162/jocn.2009.21282

Spreng, R. N., Mar, R. A., & Kim, A. S. (2009). The common neural basis of autobiographical memory, prospection, navigation, theory of mind, and the default mode: A quantitative meta-analysis. *Journal of Cognitive Neuroscience, 21*(3), 489–510. doi:10.1162/jocn.2008.21029

Spreng, R. N., Stevens, W. D., Chamberlain, J. P., Gilmore, A. W., & Schacter, D. L. (2010). Default network

activity, coupled with the frontoparietal control network, supports goal-directed cognition. *Neuroimage, 53*(1), 303–317. doi:10.1016/j.neuroimage.2010.06.016

Sridharan, D., Levitin, D. J., & Menon, V. (2008). A critical role for the right fronto-insular cortex in switching between central-executive and default-mode networks. *Proceedings of the National Academy of Sciences of the United States of America, 105*(34), 12569–12574. doi:10.1073/pnas.0800005105

Sripada, R. K., King, A. P., Welsh, R. C., Garfinkel, S. N., Wang, X., Sripada, C. S., . . . Liberzon, I. (2012). Neural dysregulation in posttraumatic stress disorder: Evidence for disrupted equilibrium between salience and default mode brain networks. *Psychosomatic Medicine, 74*(9), 904–911. doi:10.1097/PSY.0b013e318273bf33

Teasdale, J. D. (1999). Emotional processing, three modes of mind and the prevention of relapse in depression. *Behaviour Research and Therapy, 37*(Suppl. 1), S53–S77.

Teicher, M. H., Samson, J. A., Anderson, C. M., & Ohashi, K. (2016). The effects of childhood maltreatment on brain structure, function and connectivity. *Nature Reviews Neuroscience, 17*(10), 652–666. doi:10.1038/nrn.2016.111

Teyler, T. J., & Rudy, J. W. (2007). The hippocampal indexing theory and episodic memory: Updating the index. *Hippocampus, 17*(12), 1158–1169. doi:10.1002/hipo.20350

Thayer, J. F., Ahs, F., Fredrikson, M., Sollers, J. J., 3rd, & Wager, T. D. (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neuroscience Biobehavioral Reviews, 36*(2), 747–756. doi:10.1016/j.neubiorev.2011.11.009

Thayer, J. F., & Sternberg, E. (2006). Beyond heart rate variability: Vagal regulation of allostatic systems. *Annals of the New York Academy of Sciences, 1088*, 361–372. doi:10.1196/annals.1366.014

Thompson-Schill, S. L., Bedny, M., & Goldberg, R. F. (2005). The frontal lobes and the regulation of mental activity. *Current Opinion in Neurobiology, 15*(2), 219–224. doi:10.1016/j.conb.2005.03.006

Uddin, L. Q. (2015). Salience processing and insular cortical function and dysfunction. *Nature Reviews Neuroscience, 16*(1), 55–61. doi:10.1038/nrn3857

Van Kesteren, M. T., Ruiter, D. J., Fernandez, G., & Henson, R. N. (2012). How schema and novelty augment memory formation. *Trends in Neurosciences*, *35*(4), 211–219. doi:10.1016/j.tins.2012.02.001

Vernet, M., Quentin, R., Chanes, L., Mitsumasu, A., & Valero-Cabre, A. (2014). Frontal eye field, where art thou? Anatomy, function, and non-invasive manipulation of frontal regions involved in eye movements and associated cognitive operations. *Frontiers in Integrative Neuroscience, 8*, 66. doi:10.3389/fnint.2014.00066

Vossel, S., Geng, J. J., & Fink, G. R. (2014). Dorsal and ventral attention systems: Distinct neural circuits but collaborative roles. *Neuroscientist, 20*(2), 150–159. doi:10.1177/1073858413494269

Watts, B. V., Schnurr, P. P., Mayo, L., Young-Xu, Y., Weeks, W. B., & Friedman, M. J. (2013). Meta-analysis of the efficacy of treatments for posttraumatic stress disorder. *Journal of Clinical Psychiatry, 74*(6), e541–e550. doi:10.4088/JCP.12r08225

Wen, X., Yao, L., Liu, Y., & Ding, M. (2012). Causal interactions in attention networks predict behavioral performance. *Journal of Neuroscience, 32*(4), 1284–1292. doi:10.1523/jneurosci.2817-11.2012

Yan, X., Brown, A. D., Lazar, M., Cressman, V. L., Henn-Haase, C., Neylan, T. C., . . . Marmar, C. R. (2013). Spontaneous brain activity in combat related PTSD. *Neuroscience Letters, 547*, 1–5. doi:10.1016/j.neulet.2013.04.032

Yehuda, R., Hoge, C. W., McFarlane, A. C., Vermetten, E., Lanius, R. A., Nievergelt, C. M., . . . Hyman, S. E. (2015). Post-traumatic stress disorder. *Nature Reviews Disease Primers, 1*, 15057. doi:10.1038/nrdp.2015.57

Young, C. B., Raz, G., Everaerd, D., Beckmann, C. F., Tendolkar, I., Hendler, T., . . . Hermans, E. J. (2017). Dynamic shifts in large-scale brain network nalance as a function of arousal. *Journal of Neuroscience, 37*(2), 281–290. doi:10.1523/jneurosci.1759-16.2016

Yuen, E. Y., Liu, W., Karatsoreos, I. N., Feng, J., McEwen, B. S., & Yan, Z. (2009). Acute stress enhances glutamatergic transmission in prefrontal cortex and facilitates working memory. *Proceedings of the National Academy of Sciences of the United States of America, 106*(33), 14075–14079. doi:10.1073/pnas.0906791106

Zoladz, P. R., Park, C. R., & Diamond, D. M. (2011). Neurobiological basis of the complex effects of stress on memory and synaptic plasticity. In D. Mostofsky & C.D. Conrad (Eds.), *The handbook of stress* (pp. 157–178). Hoboken, NJ: John Wiley & Sons.

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