EMDR's Neurobiological Mechanisms of Action: A Survey of 20 Years of Searching

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Historically, mechanisms of action have often been difficult to ascertain. Thus far, the definitive discovery of eye movement desensitization and reprocessing (EMDR)'s underlying mechanisms has been equally elusive. We review the neurobiological studies of EMDR, as well as the theoretically driven speculative models that have been posited to date. The speculative theoretically driven models are reviewed historically to illustrate their growth in neurobiological complexity and specificity. Alternatively, the neurobiological studies of EMDR are reviewed with regard to their object of investigation and categorized as follows: findings before and after EMDR therapy (neuroimaging and psychophysiological studies) and findings during the EMDR set (psychophysiological, neuroimaging, and qEEG studies).

Keywords: EMDR; EMDR neural mechanisms; EMDR speculative models; EMDR neurobiological research

Historically, mechanisms of action have often been difficult to ascertain. It was not until 1971 that the mechanisms of aspirin were discovered, although the drug had been in formal use since 1899. Thus far, the definitive discovery and articulation of the underlying mechanisms of eye movement desensitization and reprocessing (EMDR; Shapiro, 2001; Shapiro & Maxfield, 2002) has been equally elusive. Here, we review the neurobiological studies of EMDR, as well as the theoretically driven speculative models that have been posited to date.

The speculative theoretically driven models will be reviewed historically to illustrate their growth in neurobiological complexity and specificity, a development that paralleled the empirical growth and sophistication of numerous allied neuroscience disciplines.

Alternatively, the neurobiological studies of EMDR will be reviewed with regard to their object of investigation. Accordingly, they will be categorized as follows: findings before and after EMDR therapy (neuroimaging and psychophysiological studies) and findings during the EMDR set (psychophysiological, neuroimaging, and qualitative electroencephalography [qEEG] studies). It should be noted that with few exceptions, the majority of these studies have significant methodological limitations. These include sample size, lack of controls, differing neuroimaging paradigms, and inconsistent conceptualization with respect to the parameters measured. Consequently, the research findings should be considered preliminary. They suggest directions for future research and conceptual clarity and consistency.

Posttraumatic Stress Disorder and EMDR: A Brief Overview

The combination of EMDR's complexity and the nature of available neurobiological empirical data have restricted the theoretical speculations to date to EMDR's neural mechanisms of action in the treatment of Type I posttraumatic stress disorder (PTSD).

PTSD has been described as a stress, anxiety, and memory disorder. In the past decade, descriptive and empirical publications have yielded the impression of a disorder manifested by the inability to integrate the totality of a traumatic event into consciousness, thereby causing the intrusion into awareness of fragmented traumatic memories. These intrusive fragments can be visual, olfactory, auditory, kinesthetic, or visceral. Accordingly, PTSD manifests with dramatic symptoms of hyperarousal, intrusive memorial recollections, nightmares, and various modalities of somatosensory flashbacks. These phenomenological responses are often associated with psychophysiological arousal, as evidenced by increased heart rate (HR) and electrical skin conductance, as well as

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decreases in skin temperature. Neuroimaging studies have consistently found hypoactivity in frontal lobe, anterior cingulate, and thalamic areas (reflecting the deleterious effects of PTSD on executive function, attention and cognitive, memorial, affective and somatosensory integration, respectively), as well as temporal/limbic hyperactivation (reflected in hyperarousal, hypervigilance, and the over-consolidation/intrusion of traumatic episodic memory).

Recently, research into exposure to traumatic experiences, in the absence of diagnoses of PTSD, has yielded illuminating data. Exposure to acute stressors has been shown to increase spine synapse formation in the basolateral amygdala (BLA), which may underlie the associated increases in anxiety-like and avoidant behavior (Mitra, Jadhav, McEwen, & Chattarji, 2005; Vyas, Mitra, Shankaranarayana Rao, & Chattarji, 2002). Exposure to repeated/chronic stressors, in the absence of PTSD diagnoses, has been shown to produce anxiety-like behavior in response to standardized nominal stressors (e.g., an open field), increased dendritic growth in the BLA, greater increases in spine density than seen with acute stressors, and dendritic retraction in the hippocampus (McEwen, 2005; Mitra et al., 2005). These changes have been suggested to mediate symptoms of anxiety, avoidance, hypervigilance, and the over-consolidation and intrusion of traumatic memories.

Recently, Ganzel, Casey, Glover, Voss, and Temple (2007) used functional magnetic resonance imaging (fMRI) to assess the impact of proximity to the disaster of September 11, 2001, on amygdala functions in 22 adults who did not meet criteria for any psychiatric disorders, including PTSD. More than 3 years after the terrorist attacks, bilateral amygdala activity in response to viewing fearful faces, compared to calm ones, was higher in people who were within 1.5 miles of the World Trade Center, on September 11, 2001, relative to those who were living more than 200 miles away (all were living in the New York metropolitan area at the time of the scanning). These data suggest that the amygdala and closely related structures are persistently more reactive after trauma exposure (in individuals without a clinical disorder) and that these effects will be observable using mild standardized stressors that do not require traumatic re-experiencing paradigms. Ganzel et al. note that these data are also consistent with a model of amygdala reactivity, following high-intensity trauma exposure, with relatively slow recovery.

With respect to the symptoms of PTSD, EMDR has consistently evidenced the following clinical results: amelioration of symptoms of hyperarousal and hypervigilance; and repair of cognitive, memorial, emotional, and somatosensory fragmentation. The mechanisms of this repair continue to mystify and drive us to search.

The Orienting Response

The notion of the orienting response/reflex (OR; Pavlov, 1927; Sokolov, 1963) acting as an underlying mechanism of EMDR's action appears in a number of the theoretical speculative models and neurobiological EMDR studies. Historically, there has been and continues to be confusion regarding its underlying physiology as well as its differentiation from the startle response/reflex (SR) and defensive response (DR). In many studies, empirical measurements of one have been mistakenly attributed to the other, frequently leading to a view of the OR, SR, and DR as synonymous.

The OR is a physiological process that involves attention directed toward novel and significant stimuli. It is geared toward information processing by comparing novel incoming information and familiar/known information. The OR is differentiated functionally from the SR and DR in that they are geared toward action. The prevailing notion regarding the physiological differentiation between the OR and the SR/DR is regarding their cardio-phasic responses and correlation with respect to information processing (Cook & Turpin, 1997; Graham, 1979; Johnsson, 2006; Sokolov, 1963; Turpin, 2007). Accordingly, the OR manifests in HR deceleration and is input enhancing with respect to attention and information processing. It is, therefore, generally regarded as parasympathetic in nature, promoting habituation. The startle and defensive responses manifest in HR acceleration. They are, therefore, regarded as sympathetic in nature, promoting sensitization and an output enhancing readiness for action.

Although the assertion that cardiac deceleration (parasympathetic functioning) as a major autonomic response component of the OR has been widely cited in the literature, this finding has, nonetheless, attracted controversy. Skin-conductance/electrodermal studies have not been fully consistent. Decreased conductance, with respect to the OR, was noted (Turpin, 1986, 1989), consistent with parasympathetic functioning. Increased conductance/electrodermal response were noted in the DR (Boucsein, 1992; Boucsein, Baltissen, & Euler, 1984); findings that are consistent with sympathetic functioning and differentiating it from the OR. In contrast, findings of

increased conductance, a sympathetic response was found with respect to the OR (Williams et al., 2000).

On the other hand, studies have begun to show a direct relationship between the OR and thalamic activation (Friedman, Goldman, Stern, & Brown, 2009; Menon, Ford, Lim, Glover, & Pfefferbaum, 1997; Minamimoto & Kimura, 2002), findings that are highly consistent with information processing. There are also findings that are inconsistent with sympathetic arousal, a physiological state not consistent with optimal information processing.

This author contends that the failure to accurately differentiate the OR from the SR and/or DR is, at times, a consequence of methodological inconsistency, with respect to the timing intervals of psychophysiological (HR, skin temperature, and/or electrodermal) measures. Therefore, measurements made during an OR study at different intervals (in different studies) could very well yield conflicting results. As will be noted below, continued confusion is promoted with respect to empirical findings regarding consistency or inconsistency with either the subsequent study of OR or startle or defensive responses in relation to other studied phenomena. Therefore, although the issue is not definitively clear, the majority of the findings appear to indicate that the OR is parasympathetic in nature.

Speculative Models of EMDR's Mechanisms

Various theoretical models have been proposed to account for EMDR's underlying physiological mechanisms of action. These speculations have been generated from the perspectives of conditioning, the OR, and from specific neurobiological processes and mechanisms. This article reviews the neurobiological and physiological theories concerning EMDR's possible mechanisms of action. It does not address other proposed mechanisms such as psychological distancing, working memory, and inter-hemispheric communication. For a review of these and other nonbiological theories, see Gunter and Bodner (2009).

Deconditioning Model

Dyck (1993) examined the underlying mechanisms of eye movement desensitization (EMD), the original prototype of EMDR, suggesting that PTSD and EMD be viewed from the perspective of a conditioning model. Accordingly, Dyck proposed that EMD be described as a "stimulus generalization trial in which the original contextual cues have been replaced by new elements that necessarily restrict the extent to which the new buffer contents …" (experiencing the trauma in the EMD treatment setting) "… can be similar to the original buffer contents" (the traumatic experience) (p. 206). Dyck, also, viewed the visual, auditory, or tactile stimulation to be elements of distraction: Therefore, "… the effect of this outcome is that the conditioning trial outcome will constitute an un-reinforced trial and will, thereby, also constitute an extinction trial …" (p. 207).

Orienting Response Models

Denny (1995) suggested an inhibition model wherein an OR suppresses the disturbance of traumatic memories. Central to Denny's proposal is the thesis that EMDR has "embedded at its core systemic methods for solicitation of the (OR) which results in external inhibition, a condition which partially suppresses the conditioned response (CR) of arousal/fear/anxiety to conditioned stimuli (CS) (traumatic memories)" (p. 2). Therefore, according to Denny, repeatedly eliciting the CS (traumatic memory) while simultaneously eliciting the OR, inhibits or suppresses the CR, which permits, after several repetitions of sets of such ORs, alternative responses to the traumatic memory to emerge.

MacCulloch and Feldman (1996) posited that eye movements and alternating audio and tactile stimulation triggered the investigatory components of the OR, representing an evolved safety response to threatening stimuli. They noted further that when external threats are identified in the organism's environment a negative visceral response branch of this investigatory response is triggered, resulting in avoidance responses, such as fight or flight. However, when the investigatory response is activated through active search behavior, yet no danger is identified, a positive visceral branch is activated, leading to a functional reduction in arousal. MacCulloch and Feldman argued that EMDR re-creates this investigatory OR as a result of the combination of EMDR stimulation and the reexperiencing of the traumatic memories and/or flashbacks.

Armstrong and Vaughan (1996) proposed an extinction model whereby the OR is seen to catalyze a new appraisal and change in the neuronal model of the unconditional stimulus. In terms of trauma, they asserted that the UCS contains elements of appraisal, such as "I'm in danger, I'm going to die." Accordingly, prospective reminders of the trauma (CS) precipitate the sequence of experienced fear/terror (CR) and internal appraisal of imminent demise and danger (UCS). Armstrong and Vaughan theorized that EMDR impacts this sequence through two processes. Initially, the individual's arousal system is primed to

respond by instructing the client to focus on elements of the trauma, including the image, physiological sensations, and emotional significance. Subsequently, the EMDR stimulation combined with the trauma elements elicits an intense orienting reaction. They suggested further that as no immediate threat is identifiable in the therapeutic situation, the danger response should rapidly extinguish. Armstrong and Vaughan opined, further, that any form of sensory stimulation results in the OR, although they assign greater significance to eye movements.

Frontal Lobe Activation Model

In 2000, Bergmann suggested that the various sensory modalities of BLS/DAS stimulation facilitated the activation of the lateral cerebellum. This area of the cerebellum was illustrated, utilizing a decade of anatomical and neuroimaging data, to be a complete association area, integrated horizontally and vertically and in both afferent (incoming) and efferent (outgoing) directions, to every major area of the brain. In addition, the cerebellum's dentate output nuclei were shown to project to and activate both the ventrolateral and central lateral nuclei of the thalamus.

The ventrolateral nucleus of thalamus was shown to project to and activate areas of the dorsolateral prefrontal cortex facilitating the integration of traumatic memory into general semantic and other neocortical networks. Although the implications of the central lateral thalamic activation was, at that time, not yet clear with respect to implication, the direct circuitry (cerebellar activation, to thalamic activation, to dorsolateral activation) illustrated a clear blueprint of activation (a possible map of openings for research), illustrating the sequence of neural activation from the inception of EMDR stimulation (BLS/DAS) through the direct circuitry noted above to frontal lobe activation (the most common neuroimaging finding of post-EMDR treatment).

REM-Like Physiological Systems

Stickgold (2002) suggested that the constant reorienting of attention demanded by the alternating, bilateral visual, auditory, or tactile stimuli BLS/DAS mediated a sufficient surge of acetylcholine and an OR, consequently facilitating the activation of REM-like physiological systems that tend to break down as a result of overwhelming trauma and its concomitant brain chemistry. This jumpstart, while awake, of REM sleep-dependent memory processing was hypothesized to promote/facilitate the subsequent reduction in both the strength of hippocampally mediated episodic memories, as well as the amygdaloid-mediated negative affect of PTSD. Accordingly, this was seen to mediate the integration of traumatic memories into general semantic networks. This hypothesis lends support to Shapiro's (1989a; 1989b) suggestion that rhythmic multi-saccadic eye movements represent the brain's automatic inhibitory (or excitation releasing mechanism) and just as unconscious material surfacing during dreaming is partially desensitized by rapid eye movements (REM), it may be possible that anxiety and rapid eye movements are reciprocally inhibitory.

Moreover, in 2008, Stickgold noted that the possibility that bilateral stimulation induces a brain/mind state similar to that of rapid eye movement sleep (Stickgold, 2002) is supported by studies showing that "sleep facilitates forms of memory processing arguably necessary for the resolution of trauma" (p. 289). He reflected, further, that recent research (Rasch, Buchel, Gais, & Born, 2007) had clearly demonstrated that sleep-dependent memory processing results in identification, integration, and enhancement of those aspects of memories calculated to be the most important. In addition, he suggested that it is these more complex forms of sleep-dependent processing that are presumably in play in normal trauma processing. Regarding memory, Stickgold (2007) asserted that memory structures active during encoding are normally reactivated, sometimes with remarkable temporal precision, as they are in waking recall, during subsequent sleep. Accordingly, these findings support the hypothesis that the reactivation of memories during sleep mediates the enhancement of the representation of such memories within the brain. Such enhancement can result from the following: strengthening synaptic connections encoding the original memory; creating similar connections to create alternative representations of the learned information in other brain regions; or connecting the recently learned memory to other related memories. With respect to REM sleep, specifically, he noted that Walker, Liston, Hobson, and Stickgold (2002) tested participants on their ability to solve simple anagrams and found that they performed significantly better after awakening from REM than from non-REM sleep. Hence, these findings suggested that REM sleep facilitates the discovery of previously unrecognized connections between "apparently" unrelated memories. Therefore, Stickgold opined, if EMDR did, indeed, activate REM-dependent brain processes, one would expect to see reflected (in the EMDR process) an increase of unexpected adaptive associative trains of thought.

Reciprocal Suppression/Activation of the Anterior Cingulate Models

Corrigan (2002) posited that auditory, visual, and tactile EMDR stimuli facilitate the bilateral stimulation of relevant thalamo-cingulate tracts, gradually stimulating and deactivating the affective (ventral) subdivision (ACad) of the anterior cingulate gyrus, allowing, then, for the stimulation and activation of the cognitive (dorsal) subdivision (ACcd) and a reciprocal inhibition, within the anterior cingulate. This could be seen to facilitate an increase in affective filtering and a concomitant decrease in affective amplification. This line of reasoning is consistent with Devinsky, Morrell, and Vogt (1995), who suggested that the anterior cingulate cortex (ACC) and its connections provide mechanisms by which affect and intellect can be joined by acting as both an affective amplifier and affective filter, interconnecting the emotional and cognitive components of the mind.

In a similar vein, Kaye (2007) pointed out that the action of eye movements in EMDR is distinctly different from auditory and tactile bilateral stimulation. He noted that the EMDR eye movement procedure is a visual tracking task that demands effortful divided attention, requiring the patient to synchronize his or her gaze on a moving target while concurrently noticing the target memory or its components. This is in obvious contrast to audio and tactile stimulation, which can impact the brain passively. The author suggested that the eye-to-finger tracking task may achieve its therapeutic affect by utilizing error monitoring and/or divided attention to reverse suppression of the upper (dorsal) cognitive subdivision of the anterior cingulate by the lower (ventral) affective subdivision, thereby facilitating the reversal of this reciprocal suppression.

Kaye posited that, during EMDR, there are two routes of influence that stimulate the anterior cingulate to reverse the direction of this reciprocal suppression of cognitive and semantic processing. The first route is error monitoring from the eye-finger tracking task, thereby activating the dorsal/cognitive mediating ACC. He suggested further that this activation may reciprocally suppress the ventral/affect mediating ACC. Kaye suggested that the second route of influence on the ACC may be the pleasurable affect mediating dopaminergic ventral tegmental area (VTA) projections to the ACC that are richly expressed in layer five of the ACC and are activated by such phenomena as resource installation, placebo, approach-oriented, and novelty affects.

Hippocampal Neural Mapping Model

Lister (2003), in an extremely insightful essay, introduced the notion that EMDR's various forms of BLS/DAS facilitate adaptive/reparative changes in the cognitive neural map of the hippocampus, thereby ushering in the beginnings of what we, today, understand to be global neural mapping and thalamocortical-temporal binding. Lister posited that psychic function (perception, motricity, emotion, memory) is organized and executed by the brain in the form of virtual neural maps. Implicit in this article (however more explicit in his talks) is the notion that this virtual neural mapping is comprised of neural networks and organized by alpha, beta, delta, theta, and other wave phenomena.

Lister asserted that the central mediation of cognitive neural mapping resides in the hippocampus and that PTSD disrupts the hippocampal map, producing the concomitant fragmentation of function. Accordingly, he proposed that the action of EMDR be explained by its action on the function of the hippocampus as follows: in conjunction with BLS/DAS, by attending to a particular image/or target, all the associations of that image/target are being made available to the hippocampus via its afferents from the entorhinal cortex. This gathering of the fragments and changing of neural oscillation (muscarinic cholinergic theta waves) is thought to allow for the facilitation of a coherent map/engram of the various neural networks. Since EMDR induces theta waves, Lister hypothesized that it reintegrates the parts of the hippocampal neural map.

Low Frequency Stimulation Model

Rasolkhani-Kalhorn and Harper (2006), in exploring the process of limbic fear memory formation (the potentiation of limbic circuits), noted that the depotentiation of limbic synapses by the induction of low frequency stimulation (LFS) has consistently been shown to lead to erasure or modification of these memories. The authors proposed that LFS could be induced by EMDR stimulation, in that visual, audio, or tactile stimulation tends to be in the range of 1–3 Hz (cycles per second).

Regarding memory traces and circuitry (the trauma/EMDR Target), they argued that memory traces in the hippocampus and amygdala become labile during activation of a trace (target) and it is during such periods of lability (potential malleability) that a memory trace is most easily modified. Accordingly, induction of labile conditions is thought

to occur throughout the period of memory recall during EMDR therapy, as the client focuses on specific memories, experiences, and intense affect while undergoing bilateral brain stimulation (LFS). Therefore, the combination of LFS (BLS/DAS) combined with "noticing" the target or memory can be predicted to mediate the depotentiation of these synapses, resulting in the quenching or modification of fear memory traces.

Thalamic Temporal Binding Model

Bergmann (2008), in considering the thalamus and neural integration, noted that a decade of neuroimaging studies on Type I PTSD had revealed a consistent decrease in thalamic activity. Concurrently, empirical studies of the past decade had shown the thalamus to be centrally involved in the integration of perceptual, somatosensory, memorial, and cognitive processes, a function referred to both as thalamocortical temporal binding and neural global mapping.

Integrating empirical data from the research bases of neural oscillation, perception, memory, and thalamic temporal binding, Bergmann proposed that EMDR's sensory stimulation (BLS/DAS), through its activation of the lateral cerebellum (Bergmann, 2000), facilitated the subsequent activation of the ventrolateral and central lateral thalamic nuclei. These specific and nonspecific, respectively, thalamic nuclei were shown, illustrating decades of research, to comprise the major components of the thalamocortical circuitry that serve to mediate the global mapping and binding of all neural functions.

Accordingly, the activation of this circuitry was hypothesized to facilitate the repair and integration of somatosensory, memorial, cognitive, emotional, and synchronized hemispheric functions that are disrupted in PTSD. In addition, the activation of the ventrolateral thalamic nucleus was shown, illustrated by neural connectivity studies, to facilitate the activation of the dorsolateral prefrontal cortex (the most consistent finding to date of EMDR neuroimaging studies). The findings of Richardson et al. (2009), noted below, although limited to a single case of increased thalamic activation subsequent to successful EMDR treatment, are consistent with this proposed model.

Parietal Lobe Activation Model

Pearson (2009) proposed a spectrum of psychiatric neurological conditions that reflect functional or structural disruption of brain integrity functions, partly subserved by the parietal lobes. In particular, she drew parallels between the neurological syndrome of neglect and the sequelae of psychological trauma. Pearson proposed that the sensory element of EMDR stimulation generates a state of brain plasticity in which parietal operations play a pivotal role.

Accordingly, she asserted further that

> Recruitment of parietal functions such as attentional and episodic memory processes is consistent with this theory, as is the activation of the parietal functions of reintegration and updating of the individual body schema, relation to extrapersonal space and concept of the self. (Pearson, 2009, p. 44)

This was seen to result in the movement toward a more accurate assessment of the body and self. Pearson (2009) opined that "the resolution of trauma-based symptoms occurs as updated present perceptions and an integrated sense of self replace previously held inaccurate traumatic memories and beliefs which have been stored in separate streams of consciousness" (p. 44). Therefore, she suggested that some trauma-based symptoms may be conceived of as reflecting disruptions in parietal functions and, therefore, will respond to sensory stimulation in a manner similar to neurological syndromes of neglect.

Discussion

Orienting Response Models. The positions of Denny (1995), MacCulloch and Feldman (1996), and Armstrong and Vaughan (1996) differ mainly with respect to the initial effect of the EMDR stimulation. Denny and MacCulloch and Feldman saw the initial reaction as one of de-arousing (parasympathetic), relative to the EMDR stimulation, whereas Armstrong and Vaughan viewed the onset of EMDR stimulation as one of initial (sympathetic) arousal. This proposed model of the OR as an underlying mechanism of EMDR has received empirical support (noted in detail below) by Barrowcliff, Gray, MacCulloch, Freeman, and MacCulloch (2003) and Barrowcliff, Gray, Freeman, and MacCulloch (2004), in their non-EMDR studies of eye movements. On the other hand, the data of Elofsson, von Scheele, Theorell, and Söndergaard (2008) and of Söndergaard and Elofsson (2008), relative to support of the OR, have been noted to be "inconsistent." As will be noted in detail below, Söndergaard and Elofsson, citing the work of Öhman, Hamm, and Hugdahl (2000), viewed the OR as sympathetic in nature. Accordingly, they posited (below) that finger temperature should have dropped (a sympathetic response) if the eye movements caused an OR.

In addition, they noted other findings that contradict the OR hypotheses, such as the decrease in skin conductance and the increase in respiration (parasympathetic responses).

REM System Model—Stickgold, 2002, 2008. To date, no study has, to our knowledge, been undertaken to either directly substantiate or refute this model (Stickgold, 2002, 2008). However, as will be shown below, the findings of Wilson, Silver, Covie, and Foster (1996), as well as those of Elofsson et al. (2008) and Söndergaard and Elofsson (2008), support conclusions that imbue Stickgold's model with explanatory power. Taken together, their data illustrated that eye movements during EMDR activated cholinergic/parasympathetic (decreased cardiac activity, lowered skin conductance/GSR, and increased skin temperature) and inhibited sympathetic systems, indicating similarities to the physiological patterns of REM sleep.

Anterior Cingulate Reciprocal Suppression/Inhibition Model. Although agreeing with MacCulloch and Feldman's (1996) investigatory orienting reflex, Kaye proposed that, rather than attributing the OR to eye movements themselves, the OR should be conceptualized as novelty driven (Kaye, 2007). Therefore, in the second stage of his model, novelty-evoked ORs are resultant from the patients' own newly emerging contextual information, driven by resourcing techniques and/or the use of interweaves. Therefore, rather than the eye movements themselves, Kaye viewed the error monitoring in the finger tracking as facilitating the OR. Although consistent with Corrigan's (2002) speculation with respect to reciprocal suppression of the ACC, this model's focus on visual stimulation limits its explanatory power with respect to tactile and auditory stimulation.

Neurobiological Studies of EMDR

As was noted above, the neurobiological studies of EMDR will be reviewed with regard to their objective of investigation. Accordingly, they will be categorized as follows: findings before and after EMDR therapy (neuroimaging and psychophysiological studies) and findings during the EMDR set (psychophysiological, neuroimaging, and qEEG studies).

Findings Pre- and Post-EMDR Treatment—Neuroimaging

The EMDR neuroimaging studies were undertaken utilizing the following imaging methods: single photon emission computerized tomography (SPECT), magnetic resonance imaging (MRI), and fMRI. SPECT and fMRI examine functional imaging (i.e., which area of the brain is hypo- or hyperactive, as measured by blood flow, oxygenation, metabolism, or tracer perfusion). Imaging with fMRI has also been utilized to examine functional connectivity, wherein, rather than examining activation levels, linkages between different neural systems are studied. MRI is utilized for structural imaging, examining tissue with respect to volume, lesions, or other structural pathology.

With respect to imaging paradigms, the majority of the studies utilized a symptom provocation treatment paradigm, in which the participants were scanned (pre- and posttreatment) during a particular symptomatic state (i.e., after having their symptoms intentionally induced/provoked by traumatic scripts or pictures). Within-group comparisons (in the absence of control groups) could, then, be made to test hypotheses regarding the mediating anatomy of the symptomatic state. The advantage in this paradigm is the ability to examine if traumatic symptoms (in this case) can be externally provoked or triggered. Therefore, the mental state studied is well defined.

One study utilized a neutral state/resting treatment paradigm, wherein participants were studied during a nominal resting state. Thus, within-group comparisons were made to test hypotheses regarding differences in regional brain activity without particular attention to specific neural state variables. The advantage here is to examine the brain without external provocation. On the other hand, examination is being made on an ill-defined mental state, because it may vary from one subject to another and even within the same subject.

One study utilized a cognitive activation treatment paradigm, in which the participants were studied while performing a specifically designed cognitive behavioral task. The advantage to this paradigm is that it more accurately simulates and examines day-to-day functioning (i.e., cognitive functioning and concentration).

With respect to a comprehensive understanding of neural functioning, these various neuroimaging methods and paradigms should be viewed as complementary, allowing for convergent findings across paradigms and laboratories to yield the most cohesive and compelling models of neural functioning and pathology.

Levin, Lazrove, and van der Kolk, 1999. In the first EMDR neuroimaging case study (Levin, Lazrove, & van der Kolk, 1999; van der Kolk, Burbridge, & Suzuki, 1997), Rorschach Ink Blot testing and neuroimaging

utilizing single photon emission computed tomography (SPECT) was administered to six participants with PTSD, prior to and following three sessions of EMDR. Utilizing a symptom provocation paradigm, upon recall of the traumatic memory during SPECT scanning, two areas of the brain evidenced increased activity, post-EMDR treatment relative to pretreatment: the anterior cingulate gyrus and the left frontal lobe.

The authors concluded that activation of these areas may facilitate distinguishing between real threats and traumatic reminders that are no longer relevant to current experience. They propose, further, that activation of the prefrontal cortex may also indicate the assignment of meaning to the emotions associated with traumatic memory via the elaboration of cognitive strategies.

Lansing et al., 2005. In a case series with six participants diagnosed with PTSD, Lansing, Amen, Hanks, and Rudy (2005) utilized psychometric testing (the Posttraumatic Stress Diagnostic Scale) and high-resolution SPECT imaging of EMDR treatment. Imaging was acquired while the participants performed a clinically standardized concentration test, the Connors CPT, as opposed to a script-driven symptom provocation paradigm. Due to the nature of the participants' jobs in law enforcement and their associated risks, the frequency and duration of the treatment sessions were dictated by each subject's individual recuperation time. Consequently, the mean number of EMDR sessions was 3.83 and the mean number of hours was 10.25.

Posttreatment results revealed the following: marked reductions in the Posttraumatic Stress Diagnostic Scale scores; decreased activation in the right occipital lobe [Brodmans Area (BA) 18]; decreased activation in the left parietal lobe [BA 40]; increased activation in the right parietal lobe [BA 4]; and increased activation in the left frontal areas [BA 11, 44, 8, 9]. From a functional neuroanatomy perspective, BA 8 and 9 correspond to the left dorsolateral prefrontal cortex, BA 44 corresponds to the left inferior frontal cortex, and BA 11 corresponds to the left medial frontal gyrus (left orbitofrontal region). These results were reflective of reductions in psychometric measures of PTSD, visual intrusions/flashbacks, physical sensations of hyperarousal, traumatic recall, and grief.

Oh and Choi, 2007. In a controlled SPECT imaging study of EMDR, pretreatment scans of two participants (A and B) diagnosed with PTSD were compared to 10 non-PTSD controls (Oh & Choi, 2007). The participants received six sessions of EMDR during their inpatient hospital stay.

The pretreatment SPECT scans of each PTSD participant were compared to those of the controls. They (A and B) evidenced increased bilateral cerebral blood flow in the limbic parahippocampal areas [left BA 34, right BA 19] and in the parietal areas [BA 6]; the right cingulate gyrus (BA 31); and the right subgyral (BA 40). This comparison also indicated lower cerebral blood flow mainly in the left frontal [BA 9, 10, 46] and parietal areas [BA 3, 4, 40]. These findings of greater blood flow in the limbic areas and lesser blood flow in the prefrontal cortex are consistent with previous PTSD neuroimaging literature and indicative of emotional hyperarousal, hypervigilance, and the over-consolidation and intrusion of episodic memory.

In the analysis comparing participant A and B's pre- and post-EMDR scans, significant activations were observed following EMDR treatment for the right middle frontal gyrus and the right superior frontal gyrus (BA 6, 8, 9, 10, and 46). Significant increases were also observed in the left medial frontal and the right superior frontal gyri (BA 8 and 10). From a functional neuroanatomy perspective, BA 8, 9, and 46 correspond to the dorsolateral prefrontal cortex and BA 10 to the medial prefrontal cortex. Significant deactivation was noted in the right middle temporal and the right subgyral area (BA 20 and 21). The authors concluded that EMDR treatment resulted in the following: (a) emotional regulation due to increased activity of the prefrontal lobe, (b) inhibition of limbic over-stimulation by increased regulation of the association cortex, (c) reduction in the intrusion and over-consolidation of traumatic episodic memory due to the reduction of temporal lobe activity, and (d) the induction of a functional balance between the limbic and prefrontal areas.

The data in this study is limited by the fact that only two participants were studied in comparison to 10 controls.

Pagani et al., 2007. Pagani et al. (2007), in a controlled study utilizing SPECT imaging and a script-driven symptom provocation paradigm, compared the effects of EMDR treatment in 15 participants diagnosed with PTSD. The diagnostic assessment was derived from the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV-TR*) Axis I Disorders (SCID-1). Neuroimaging comparisons were also made with those of a control group of 27 who had been exposed to the same psychological traumas but had not developed PTSD.

When compared to the nonsymptomatic controls, the PTSD participant showed: increased regional cerebral blood flow (rCBF) in the left and right superior temporal gyri (BA 38); increased rCBF in the

right orbital gyrus (BA 11); increased rCBF in the left and right uncus (BA 36); and increased rCBF in the hypothalamus. The findings of increased rCBF in the limbic temporal area (BA 38) are consistent with previous PTSD neuroimaging literature and indicative of emotional hyperarousal and hypervigilance. The findings of increased rCBF in the left and right uncus (BA 36), an area of the parahippocampal gyrus, are consistent with the over-consolidation and intrusion of episodic memory.

The 15 PTSD participants were then provided with five 90-min sessions of EMDR, and 11 of them showed a positive response, no longer fulfilling the *DSM-IV* criteria for PTSD at posttreatment. The posttreatment findings for all 15 participants (responders as well as nonresponders) were compared to the scans of the non-symptomatic controls that had been taken at beginning of the study. Results were as follows: increased rCBF remained in the orbitofrontal (BA 11) as well as in the temporal (BA 38) cortices; there was decreased rCBF in the uncus (BA 36), an area in the parahippocampal gyrus; increased rCBF in the lateral temporal lobe (BA 21); and rCBF was unchanged in the hypothalamus. The posttreatment findings in the PTSD participants (who responded to EMDR treatment) as compared to the nonresponders were as follows: decreased rCBF in the lower hippocampal, occipito-temporal (BA 37), and visual (BA 17) cortices. The findings of reduced rCBF in the hippocampal temporal area (BA 37) are consistent with and indicative of reduction in the intrusion and over-consolidation of traumatic episodic memory. The finding of reduced rCBF in the visual occipital area (BA 17) is consistent with and indicative of reduced visual flashback symptoms.

Bossini et al., 2007. Bossini, Fagiolini, and Castrogiovanni (2007), utilizing MRI, evaluated hippocampal volumetric changes subsequent to successful EMDR treatment of a 27-year-old man with chronic PTSD related to the suicide of his mother. After 8 weeks of EMDR treatment (one 90-min session per week), the subject no longer met criteria for PTSD, as per measurement by the Clinician Administered PTSD Scale (CAPS) and the Davidson Trauma Scale (DTS). The posttreatment MRI showed an increase of 357.33 mm of the left hippocampus and an increase of 340.40 mm of the right hippocampus.

The authors noted the following in consideration of this data: the inherent limitation of a single case; the relatively short period of time in which the volumetric increase happened poses the question of the possibility that the volumetric growth might be attributable to an increased water and electrolyte content in the hippocampus. However, the magnitude of volumetric increase combined with the documented improvement in the PTSD does, indeed, preclude the dismissal of such data.

Discussion

With respect to functional imaging, the four studies utilized SPECT technology. Levin et al. (1999) and Pagani et al. (2007) utilized symptom provocation paradigms. Lansing et al. (2005) utilized a cognitive paradigm, while Oh and Choi (2007) utilized a resting paradigm. The Bossini et al. (2007) study, examining structural hippocampal volumetric changes, utilized structural MRI technology.

Lansing et al., 2005. Lansing et al. (2005) utilized a cognitive paradigm. This calmer imaging paradigm (in contrast to the more arousing symptom provocation paradigm) may have contributed to the activation of the left orbitofrontal region, an area of activation noted, for the first time in post-EMDR imaging. The authors suggest that increased activity in this area is associated with improvements in depressive symptoms.

Oh and Choi, 2007. In contrast to the imaging studies noted above, posttreatment scans in the Oh and Choi (2007) study showed increased blood flow in the frontal lobes bilaterally (in the left and right dorsolateral prefrontal regions). Brain imaging was acquired, utilizing a resting paradigm, wherein participants were placed in a supine position in a quiet room. Oh and Choi noted that the bilateral frontal findings may have been the result of a quiet paradigm, as opposed to a more activating script-driven symptom provocation paradigm. Nonetheless, numerous studies have recently begun to highlight the role of the right dorsolateral prefrontal cortex in memory retrieval, although it is beyond the scope of this review to explore them.

Pagani et al., 2007. The findings in the Pagani et al. (2007) study require special attention to detail with respect to the conclusions and interpretations. To begin with, comparisons were made between PTSD participants and controls exposed to the same traumas, "without developing PTSD." The use of such a population in contrast to PTSD can be extremely illuminating, given some of the problems of mainstream research data on PTSD. Therefore, taken together, the data in the Pagani et al. study do not illustrate the effects of EMDR on PTSD participants, as compared to nontraumatized controls. Rather, they illustrate a comparison between controls whose nervous systems are kindled (but do not meet criteria for PTSD)

and PTSD participants. As was noted above and illustrated by studies such as Ganzel et al. (2007), such comparisons are extremely informative and indicative, realistically, of the populations that experience traumatic events. Another interesting but unusual aspect of this study is that data is given for responders as well as for nonresponders to EMDR treatment. Even more interesting and informative are the findings that the nonresponders show similar (although not identical) changes in rCBF to the responders.

Psychophysiological Studies

Findings Pre- and Post-EMDR Treatment—Psychophysiology

Lamprecht et al., 2004. Lamprecht et al. (2004), in an electroencephalogram (EEG) study of EMDR, assessed event-related potentials (ERPs), comparing 10 participants diagnosed with PTSD with 10 controls. A modified oddball paradigm was utilized whereby a target auditory stimulus was presented among more frequent standard background and novelty auditory stimuli. The control subjects were treated with a "sham" treatment that consisted of instructions to focus on their worst life event with 10 sets of eye movements, which corresponded to the average number of eye movement sets in the patient group. The participants of the experimental/PTSD group were treated with a single session of EMDR. A comparison of the ERPs revealed a reduction of the P3a component in the posttreatment recording for participants treated with EMDR.

The authors suggested that this finding reflected a reduced orienting to novel stimuli and reduced arousal level. The authors noted that the P3a has been interpreted as an index of automatic allocation of attention toward a source of stimulation and can, therefore, be viewed as a central correlate of the OR. They also reflected that the most interesting finding of the study was that only the participants treated with EMDR evidenced the attenuation of the P3a in the posttreatment session.

Sack et al., 2007. Sack, Lempa, and Lamprecht (2007), in a case series study utilizing a script-driven symptom provocation paradigm, investigated changes in stress-related psychophysiological reactions after treatment of 16 participants diagnosed with PTSD with EMDR. Psychophysiological assessment consisted of measurements of HR and heart rate variability (HRV) during neutral script and during trauma script listening. HRV, a function of respiratory sinus arrhythmia (RSA), is highly correlated with parasympathetic activity.

Simply put, RSA is the body's/brain's ability to utilize breath (nonshallow inhalation and exhalation), to increase parasympathetic tone and, consequently, to enhance affect regulation. Following EMDR treatment, HR acceleration in reaction to the trauma script was significantly reduced at posttreatment and at follow-up. RSA/HRV, indicating parasympathetic tone, increased significantly over the course of treatment, both during the neutral condition script and during the trauma script. Accordingly, participants reported a significant decrease of their subjective distress during the trauma script presentation. The authors noted the following methodological restrictions: the study's relatively small sample size of 16 participants, which was further reduced by two dropouts and partially missing data from three participants, and the absence of a control group precluded the control of the repeated measurements of psychophysiological reactions and the possibility of physiological habituation.

Aubert-Khalfa, Roques, and Blin, 2008. In a study aimed at determining if psychophysiological responses to stress decreased after a single EMDR session, six participants diagnosed with PTSD underwent treatment (Aubert-Khalfa, Roques, & Blin, 2008). Prior to the onset of treatment and 2 weeks subsequent to treatment, participants completed the French versions of The Posttraumatic Checklist Scale (PCLS) and the Impact of Event Scale-Revised (IES-R). Psychophysiological responses (HR and skin conductance) were recorded before and after the EMDR session under two conditions: (a) in a relaxed state and (b) while visualizing their own traumatic event. Subsequent to the EMDR treatment, scores were significantly reduced for the PCLS and the IES-R. Consistent with these changes were reductions in skin conductance and HR, indicative of reduced sympathetic arousal and increased parasympathetic functioning. The authors note that one of the limitations of the study was the small number of participants. They also proposed that, given that the trauma memory was repeated two times (before and after EMDR treatment), the decrease in skin conductance and HR may reflect habituation to the stimulus.

Discussion

Lamprecht et al., 2004. These findings of Lamprecht et al. (2004) are in some ways consistent with the findings of Barrowcliff, Gray, MacCulloch, Freeman, and MacCulloch (2003) and Barrowcliff, Gray, Freeman, and MacCulloch (2004).

Barrowcliff et al. (2003), in a non-EMDR study of eye movements, reported a consistently diminished

level of electrodermal arousal when participants engaged in eye movements, following the presentation of externally generated aversive auditory stimuli, compared to when engaging in an eyes-stationary task. Accordingly, they concluded that eye movements as performed in EMDR, following auditory aversive challenges, resulted in de-arousal, thereby lending credence to the reassurance reflex (OR) models of EMDR proposed by Armstrong and Vaughan (1996), Denny (1995), and MacCulloch and Feldman (1996).

Similarly, Barrowcliff et al. (2004) examined the effects of eye movements on subjective and psychophysiological measures of arousal and distress associated with positive and negative autobiographical memories. Engagement in eye movements, compared to the eyes-stationary condition, resulted in significant reductions on measures of vividness and emotional valence for both positive and negative autobiographical memories. However, reductions in electrodermal arousal were only observed when engaging in eye movements following solicitation of the negative memory. These findings lend further credence to the hypotheses of Armstrong and Vaughan (1996), Denny (1995), and MacCulloch and Feldman (1996).

Sack et al., 2007. The significance of the Sack et al. (2007) study is twofold. First, as the authors asserted, low parasympathetic tone has been identified not only as a risk factor for cardiovascular disease, but also as a concomitant of affect dysregulation in stress-related psychiatric diseases such as depressive and anxiety disorders. Second, there is increasing evidence that low parasympathetic tone may very well be an indicator for frontal cortex hypofunction in association with dominance of amygdala-mediated, sympathetically driven hyperarousal. This will be explored in further detail below with respect to the Sack, Lempa, Steinmetz, Lamprecht, and Hofmann (2008) study.

Aubert-Khalfa, Roques, and Blin, 2008. The findings of increased parasympathetic tone and symptomatic improvement (as measured by psychometrics; Aubert-Khalfa, Roques, & Blin, 2008) are in line with those of Barrowcliff et al. (2003), Barrowcliff et al. (2004), and Sack et al. (2007, 2008). They also lend credence to the reassurance reflex (OR) models of EMDR proposed by Armstrong and Vaughan (1996), Denny (1995), and MacCulloch and Feldman (1996).

Findings During (Within Set) EMDR Treatment—Psychophysiology

Wilson et al., 1996. Wilson et al. (1996) studied 18 traumatized participants who were randomly assigned to a single session of one of three conditions: EMDR, a Time Interval Condition (TIC), or Tapping Alternate Phalanges (TAP). In comparison to the TIC and TAP conditions, autonomic measures showed distinct change during the EMDR treatment as follows: respiration synchronized with the rhythm of the eye movements in a shallow, regular pattern; HR slowed significantly overall; systolic blood pressure increased during early sets, invariably declined during abreactions, and decreased overall; fingertip skin temperature consistently increased; and the galvanic skin response (GSR) consistently decreased in a clear "relaxation response."

Wilson et al. (1996) concluded that the relaxation effect of the eye movements suggests that at least one of the mechanisms operating in EMDR is desensitization by reciprocal inhibition, wherein emotional distress is paired with a learned or "compelled" relaxation response. Wilson et al. concluded that, as proposed by Shapiro (1989a, 1989b), at least one of the mechanisms operating in EMDR is desensitization through an internally generated relaxation response caused by the eye movement, perhaps by processes equivalent to reciprocal inhibition.

Sack et al., 2008. Sack et al. (2008) investigated psychophysiological correlates of EMDR, during treatment sessions. A total of 55 treatment sessions from 10 participants with PTSD were examined. Although, some increases in HR were noted during the session, the onset and the major portions of the EMDR sessions evidenced significant decreases of psychophysiological activity, noted by progressively decreasing HR and increasing HRV. Similarly, these findings suggested that EMDR is associated with an increase in parasympathetic tone, thereby mediating a substantial psychophysiological de-arousal over time.

Elofsson et al., 2008, and Sondergaard and Elofsson, 2008. In a case series study of the physiological correlates of eye movements (Elofsson et al., 2008; Söndergaard & Elofsson, 2008), findings similar to Wilson et al. (1996) were reported. The study explored physiological correlates of eye movements during EMDR treatment in 13 participants diagnosed with PTSD. The investigation was undergone in relation to the current hypotheses of distraction, conditioning, OR activation, and REM-like mechanisms.

During EMDR therapy, fingertip temperature, HR, skin conductance, expiratory carbon dioxide level, and blood pulse oximeter oxygen saturation were measured in the participants. Taken together, the data indicated that eye movements during EMDR activated cholinergic and inhibited sympathetic systems, indicating similarities in the physiological

patterns of REM sleep. The authors argued that Stickgold's (2002) REM systems hypothesis of EMDR contains explanatory power when applied to their data.

Regarding the reciprocal inhibition hypothesis (Wilson et al., 1996; Wolpe, 1990), Elofsson et al. (2008) and Söndergaard and Elofsson (2008) assert supportive consistency with respect to the findings reported above.

Regarding the OR hypothesis, Söndergaard and Elofsson (2008) opined that some of the data were consistent; however, other data were not. As was reflected above, Söndergaard and Elofsson, citing the work of Öhman et al. (2000), appear to view the OR as sympathetic in nature. Consequently, they argued that finger temperature should have dropped if the eye movements caused an OR. They asserted further that other findings that contradict the OR hypothesis were the decrease in skin conductance, denoting relaxation, as well as the increase in respiration.

Discussion

Wilson et al., 1996. The Wilson et al. (1996) data can be seen as somewhat supportive of Stickgold's (2002) REM-related hypothesis. REM sleep has been shown to be a predominantly parasympathetic (vagal) state (Elofsson et al., 2008; Murali, Svatikova, & Somers, 2003; Stickgold, 2002), reflected in decreased cardiac activity, lowered skin conductance/GSR, and increased skin temperature (Kobayashi, Koike, Hirayama, Ito, & Sobue, 2003).

Sack et al., 2008. In addition, the Wilson et al. (1996) and Sack et al. (2008) studies give us another window into EMDR's ability to facilitate the activation of areas of the frontal lobes (the most consistent finding of EMDR neuroimaging). In general, RSA and HRV can be viewed as the functional equivalents of vagal efferent pathways originating in the nucleus ambiguous of the medulla and the myelinated aspect of the vagus nerve. Put another way, the function of the myelinated vagus (ventral vagal complex) is to act as a gentle "brake," thereby fostering calm behavioral states by inhibiting (when necessary) the sympathetic influences (anxiety, fear) on the nervous system. With increasing cortical development, the cortex exhibits greater control over the brain stem via direct (corticobulbar) and indirect (corticoreticular) pathways. This cortical mediation impacts directly on the myelinated ventral vagal complex (Porges, 2001, 2007; Schore, 1994, 2001). Therefore, if one is directly measuring an increase in HRV/RSA, resulting from EMDR treatment, then one may be indirectly measuring increases in frontal lobe activation and mediation.

Elofsson et al., 2008. The data of Elofsson et al. (2008) can also be seen as supportive of Stickgold's (2002) REM-related hypothesis. As was stated above, REM sleep had been shown to be a predominantly parasympathetic (vagal) state (Elofsson et al., 2008; Murali et al., 2003; Stickgold, 2002), reflected in decreased cardiac activity, lowered skin conductance/GSR, and increased skin temperature (Kobayashi et al., 2003). Accordingly, when comparing the typical autonomic pattern for REM sleep with the physiological changes observed in this study, similarities were found in the following measured variables: a vagal shift, indicated by decreased HR and skin conductance; change in the respiratory pattern, with an increased frequency and tendency toward hypercapnic (elevation in CO_2) and hypoxemic (lowered levels of O_2) states and an increase in finger temperature.

Sondergaard and Elofsson, 2008. The conclusions of Söndergaard and Elofsson (2008) with respect to the OR require special attention to detail with respect to the conclusions and interpretations. As was mentioned above, Söndergaard and Elofsson, citing the work of Öhman et al. (2000), appear to view the OR as sympathetic in nature. Therefore, they conclude that their findings of parasympathetic vagal response are inconsistent with the OR.

In a similar vein, Gunter and Bodner (2008) investigated the effects of eye movements on unpleasant memories. This experiment evaluated three theoretical accounts that have attempted to explain how eye movements produce their beneficial effect: the working memory account, the investigatory/orienting reflex, and the increased hemispheric communication (IHC) account. The working memory account and IHC account are not neurobiological theories and thus are beyond the purview of this article. See Gunter and Bodner (2009) for a summary of this research. This article reviews only Gunter and Bodner's (2008) findings regarding the investigatory/orienting reflex.

Gunter and Bodner interpret their finding of increased arousal as an indicative inconsistency with the OR. They note in this and another publication (Gunter & Bodner, 2009) that the bulk of the evidence to date suggests that eye movements are associated with a de-arousal/parasympathetic response during EMDR sessions and question whether the discrepancy in their finding may be due to the populations of study or the procedural or methodological differences between studies (i.e., the timing of arousal measurements). With respect to procedural differences, it should be noted that arousal measurements

were taken at a 96-s interval (as compared to shorter intervals in the Barrowcliff et al., 2004 study) that could account for the finding.

In addition, with respect to comparing OR studies in isolation to within-set or pre–post studies of EMDR, it should be noted again that Sack et al. (2008) found that although some increases in HR were noted during the session, the onset and the major portions of the EMDR sessions evidenced significant decreases of psychophysiological activity, noted by progressively decreasing HR and increasing HRV.

This again illustrates the problem with respect to the influence of the timing of psychophysiological measures (with different studies timing their measures at different intervals) on the data and the conclusions that are derived.

Findings During (Within Set) EMDR Treatment—fMRI

Richardson et al., 2009. In a single-case study, Richardson et al. (2009) assessed the effects of a single session (45 min) of EMDR, utilizing continuous auditory alternating bilateral stimulation (ABS) and fMRI of brain activations. Areas of activation were measured in terms of blood oxygen level dependency (BOLD). The subject was an EMDR therapist suffering from PTSD.

The subject remained in the MR scanner for the entire session, allowing for continuous image acquisitions. Imaging was carried out in four blocks as follows: during "safe place" activity (Block A); during recall of the traumatic event (Block B); during the first 6 min of processing (Block C); and during the remaining 27 min of the session (Block D).

Data acquired during Block A (safe place imagery), in comparison to Block B (trauma memory), revealed the following: increased activation (BOLD signal) in the left caudate and insula (BA 13) and bilaterally within the fusiform gyrus (BA 19, 20, 37) in the temporal lobe. Activation in these areas can be seen as consistent with the internal imaging required in the safe place procedure.

In contrast, the trauma memory, minus the safe place imagery, was associated with clusters of hypoactivation (decreased BOLD signal) mainly in the right superior, middle, and medial frontal lobe (BA 8, 9, 10). Areas of increased activation were noted in the left hemisphere and included the middle and inferior temporal gyri (BA 37, 19), middle occipital gyrus, and cuneus (BA 18, 19). These findings of greater blood flow in the temporal/limbic areas and lesser blood flow in the prefrontal cortex are consistent with previous PTSD neuroimaging literature and indicative of emotional hyperarousal, hypervigilance, and the over-consolidation and intrusion of episodic memory.

As the treatment progressed, in Blocks C and D, the following was noted: increased activation in the right ventromedial prefrontal (orbitofrontal) cortex (BA 11) and hippocampal uncus (BA 28). In addition, the left thalamus and right amygdala were found to have an increased BOLD response. The increase in thalamic activation can be seen as consistent with the repair of thalamocortical temporal binding and the resultant integration of somatosensory, memorial, cognitive, emotional, and synchronized hemispheric functions that are disrupted in PTSD. The ventromedial prefrontal activation might be indicative of the increased RSA/HRV and ventral vagal tone noted in the previous EMDR studies. This will be discussed in further detail below.

This study was limited with respect to being a single case, as well as lacking a control comparison.

Discussion

Richardson et al., 2009. The findings in Block B (pretreatment trauma memory) are consistent with years of neuroimaging data of PTSD, illustrating hypoactivation of the frontal lobes and hyperactivation of the temporal and occipital areas (Richardson et al., 2009). These patterns of activation are indicative of emotional hyperarousal, hypervigilance, flashbacks, and the over-consolidation and intrusion of episodic memory.

The findings in Blocks C and D also illustrate similarities as follows: Lansing et al. (2005) noted a posttreatment increase of the left orbitofrontal (ventromedial prefrontal) cortex. Although the Richardson et al. (2009) study found posttreatment increased activation in the right ventromedial prefrontal cortex, the pattern of both findings is theoretically consistent with two decades of empirical studies that illustrate the orbitomedial prefrontal cortex [composed of the lateral orbitofrontal cortex (OFC) and the medial ventromedial prefrontal cortex (vmPFC)] as both the apex and executor of the rostral limbic (emotion mediating/affect regulating) system. From that perspective, this data is also consistent with the findings of Elofsson et al. (2008), Sack et al. (2007, 2008), and Wilson et al. (1996). As was noted above, each of those studies illustrated a posttreatment, parasympathetic (vagal) shift. Both the amygdala and the orbitomedial prefrontal cortex (OMPFC) have connections with the lateral hypothalamus, an area known to activate

parasympathetic responses through interconnections with the vagus nerve in the medulla. Accordingly, the OMPFC system enhances its inputs into the nucleus ambiguous, of the medulla, allowing it to engage the ventral vagal complex, thereby expanding its affect regulatory capacities (Porges, 1997, 2001, 2007; Schore 1994, 2001). In addition, the finding of increased thalamic activation subsequent to EMDR treatment, noted for the first time, is consistent with the research as follows: Lanius, Williamson, and Densmore (2001) and Lanius, Williamson, and Hopper (2003) identified reduced thalamic activation in patients who suffer from PTSD, replicating similar findings by Bremner, Staib, and Kaloupek (1999) and Liberzon, Taylor, and Amdur (1999). Given the thalamus' pivotal role in temporal binding and neural mapping, the consequences of this lowered thalamic activation are impairments in the functional connectivity of various dynamic neuronal networks, evidenced by failures in cognitive, memorial, affective, somatosensory, and interhemispheric integration. The thalamic finding is also consistent and supportive of a theoretical model (Bergmann, 2008), wherein alternating bilateral stimulation/dual attention stimulation (BLS/DAS) is predicted to activate areas of the thalamus (reduced in activation by PTSD), thereby repairing failures in cognitive, memorial, affective, somatosensory, and interhemispheric integration. This study also appears to be the first to examine the use of continued BLS/DAS throughout the session.

Findings During (Within Set) EMDR Treatment—qEEG

Harper et al., 2009. Harper, Rasolkhani-Kalhorn, and Drozd (2009), in a study designed to investigate their previously postulated synaptic-depotentiation speculations of EMDR's mechanism of action (Rasolkhani-Kalhorn & Harper, 2006), examined evidence based primarily on qEEG studies of PTSD and EMDR treatment. The EEGs of six participants, all exhibiting symptoms of PTSD, were recorded during the experimental procedure. The authors note that the principal aim of this study was to determine the reaction of the brain to the part of the EMDR protocol that includes bilateral stimulation (phase 4).

Prior to the experiment, each participant was given a clinical interview to determine trauma history and general appropriateness for the procedure. A Personality Assessment Inventory (PAI) was administered, along with the Foa Posttraumatic Stress Diagnostic Scale (Foa PDS) and the Dissociative Experience Scale (DES).

During phase 4 of the EMDR protocol, the authors note that the application of the BLS/DAS caused an immediate slowing of the depolarization rate of neurons in the frontal lobes, from the dominant waking state frequency of approximately 7 Hz to about 1.5 Hz. Harper et al. (2009) hypothesized that this evoked response may result from the intrinsic properties of principal cells in the memory networks of the neocortex and limbic system, or to a thalamocortical rhythm, associated with slow wave sleep. The DAS/BLS also generated a several-fold increase in wave power. The authors note that the high power of the induced waves tends to ensure that all synapses mediating the memory, held in attention, become synchronously active. Accordingly, the noted change in high power and low frequency waves of the neuronal depolarizations is seen to denote a change from conditions favorable to synaptic potentiation (increases in anxiety) to one of depotentiation (reduction in anxiety).

Discussion

Harper et al. (2009) note that BLS/DAS during EMDR "significantly increases the power of a naturally occurring low frequency rhythm in memory areas of the brain, binding these areas together and causing receptors on the synapses of fear-memory traces to be disabled" (abstract, p. 81). This study illuminates a number of issues in our EMDR puzzle: it sheds light on the paucity of information that we have on the effect of EMDR treatment on the rostral limbic system by giving us data on the depotentiation of limbic circuits; it yields data that will, quite possibly, augment the speculations regarding the reciprocal inhibition of the anterior cingulate (Corrigan, 2002; Kaye, 2007) and open windows into their research; and further study of the data regarding depolarization may shed light on thalamocortical rhythms and neural binding, noted in Bergmann (2008) and noted briefly in the findings of Richardson et al. (2009), vis-à-vis their findings of increased thalamic activation subsequent to EMDR treatment.

Synthesis

The theoretically driven speculative models, EMDR neurobiological studies, related neurobiological studies, and their interrelationship are summarized in Table 1.

Examination of the theoretical models illustrates similarities and complementarities, as well as differences.

TABLE 1. Theoretical Models and Related Empirical Studies

Theoretical model	Proposed areas of neural involvement	Proposed physiological changes	Research support	Research contradiction
Conditioning model (Dyck, 1993)	None	Deconditioning, reciprocal inhibition, distraction	Relaxation response–reciprocal inhibition (Wilson et al., 1996) Increased HRV/parasympathetic tone (Sack et al., 2007, 2008) Increased vagal parasympathetic function (Elofsson et al., 2008; Söndergaard & Elofsson, 2008)	None to date
Orienting response model (Armstrong & Vaughan, 1996; Denny, 1995; MacCulloch & Feldman, 1996)	None	Inhibition of the conditioned response by the repetition of the orienting response	Reduced electrodermal arousal (Barrowcliff et al., 2003, 2004) Reduction of P3a—correlate of orienting response (Lamprecht et al., 2004) Increased vagal parasympathetic function (Elofsson et al., 2008; Söndergaard & Elofsson, 2008)	Increased sympathetic response (Gunter & Bodner, 2008)
Frontal lobe activation model (Bergmann, 2000)	Cerebellum, thalamus, and frontal lobes	BLS-induced sequential, activation of the cerebellum, ventrolateral and central lateral thalamic nuclei, and frontal lobes	Increased thalamic activation (Richardson et al., 2009) Increased dorsolateral cortex activation (Lansing et al., 2005; Levin et al., 1999; Oh & Choi, 2007) Increased HRV/parasympathetic tone (Sack et al., 2007, 2008)	None to date
REM systems activation model (Stickgold, 2002, 2008)	Brainstem, hippocampus, and semantic cortex	BLS-induced activation of REM sleep systems, thereby integrating traumatic memories into general semantic networks	REM-induced adaptive associations and memories (Walker et al., 2002) Decreased cardiac and skin conductance (Elofsson et al., 2008; Söndergaard & Elofsson, 2008) Increased skin temperature, hypercapnia, and hypoxia (Elofsson et al., 2008; Söndergaard & Elofsson, 2008) Sleep dependent memory processing (Rasch et al., 2007)	None to date

Anterior cingulate reciprocal inhibition/ suppression model (Corrigan, 2002; Kaye, 2007)	Anterior cingulate cortex (ACC)	BLS-induced deactivation of the ventral ACC and eventual activation of the dorsal ACC	None to date	None to date
Hippocampal remapping model (Lister, 2003)	Hippocampus	BLS-induced reintegration of the hippocampal cognitive map	None to date	None to date
Limbic circuit depotentiation model (Rasolkhani-Kalhorn & Harper, 2006)	Amygdalo-hippocampal limbic circuits	BLS-induced LFS facilitates depotentiation of limbic circuits, resulting in quenching or modification of fear traces	Slowing of the depolarization rate of neurons in the frontal lobes, from 7 Hz to 1.5 Hz (Harper, Rasolkhani-Kalhorn, & Drozd, 2009) Decreased temporal lobe activation (Oh & Choi, 2007; Pagani et al., 2007)	None to date
Thalamic temporal binding model (Bergmann, 2008)	Cerebellum, thalamus, and frontal lobes	BLS-induced activation of the ventrolateral and central lateral thalamic nuclei, facilitating repair of thalamic hypoactivation, impaired temporal binding, and frontal lobes activation	Increased thalamic activation (Richardson et al., 2009) Increased dorsolateral cortex activation (Lansing et al., 2005; Levin et al., 1999; Oh & Choi, 2007) Increased HRV/parasympathetic tone (Sack et al., 2007, 2008)	None to date
Parietal lobe activation model (Pearson, 2009)	Parietal lobes	BLS-induced stimulation of the parietal lobes, facilitating the reintegration and updating of body schema, and concept of self	None to date	None to date

In the conditioning/reciprocal inhibition model (Dyck, 1993), BLS is seen to constitute a parasympathetic/inhibitory effect. Empirically, this model is supported by similar findings of "compelled" parasympathetic/relaxation response (Wilson et al., 1996), increased HRV/parasympathetic tone (Sack et al., 2007, 2008), and increased parasympathetic/vagal function (Elofsson et al., 2008; Söndergaard & Elofsson, 2008).

The OR models (Armstrong & Vaughan, 1996; Denny, 1995; MacCulloch & Feldman, 1996) differ as follows: MacCulloch and Feldman view BLS as parasympathetic in origin, whereas Armstrong and Vaughan view it initially as sympathetic. Denny's position, albeit implicit, seems to view BLS as parasympathetic in origin. Empirically, these models are supported by findings of reduced electrodermal arousal (Barrowcliff et al., 2003, 2004) and reduction of the P3a component (correlate of the OR; Lamprecht et al., 2004). The OR models are also supported by the findings of decreased HR and increased RSA/HRV, indicators of increased parasympathetic effects (Aubert-Khalfa, Roques, & Blin, 2008; Sack et al., 2007, 2008). The contradictory findings of Elofsson et al. (2008) are indicative of the preliminary nature of all these studies and the need for future research.

The frontal lobe activation (Bergmann, 2000) and the thalamic temporal binding (Bergmann, 2008) models are similar theoretically in that both predict a sequential BLS-induced activation of the cerebellum, ventrolateral and central lateral thalamic nuclei, and dorsolateral cortex. Both are tentatively (a single-case study) supported by a finding of increased thalamic activation (Richardson et al., 2009). Both models are also supported by findings of increased dorsolateral activation (Lansing et al., 2005; Levin et al., 1999; Oh & Choi, 2007). In addition, the findings of increased HRV (Sack et al., 2007, 2008) can be interpreted as indirect evidence of increased frontal lobe activation. The thalamic temporal binding model and the hippocampal remapping model (Lister, 2003) are similar in that both predict aspects of neural/network remapping.

The REM systems activation model (Stickgold, 2002, 2008) predicts BLS-induced activation of an OR and REM sleep systems, thereby repairing REM system impairment, facilitating the integration of traumatic memories into general semantic networks. Empirically, the model receives indirect support from findings of decreased cardiac and skin conductance, as well as increased skin temperature, hypercapnia (increased CO_2), and hypoxia (decreased O_2; Elofsson et al., 2008; Söndergaard & Elofsson, 2008): findings that are consistent with REM sleep physiology. It also receives support from findings of increased REM-induced adaptive associations in a non-EMDR study (Walker et al., 2002) and sleep-dependent memory processing in a non-EMDR study (Rasch et al., 2007).

The limbic circuit depotentiation model (Rasolkhani-Kalhorn & Harper, 2006) predicts that BLS-induced LFS facilitates depotentiation of limbic circuits, resulting in quenching or modification of fear traces. Empirically, the model receives support from findings of slow depolarization rates of frontal lobe neurons (Harper et al., 2009) and, indirectly, from findings of decreased temporal lobe activation (Oh & Choi, 2007; Pagani et al., 2007).

The anterior cingulate reciprocal suppression models (Corrigan, 2002; Kaye, 2007) are similar in that both predict BLS-induced lowered activation of the ventral/affective ACC and eventual increased activation of the dorsal/cognitive ACC. They differ in that Kaye's model is articulated specifically to the effect of eye movements and the visual tracking task, while Corrigan's views these mechanisms as a result of BLS in general. Neither model is, as yet, supported directly by empirical findings. The findings of increased anterior cingulate activation (Levin et al., 1999; van der Kolk et al., 1997) may provide indirect support; however, the lack of specificity with respect to Brodmann's areas precludes the identification of dorsal, medial, or ventral loci of activation.

The parietal lobe activation model (Pearson, 2009) predicts that BLS-induced stimulation of the parietal lobes facilitates the reintegration and updating of body schema and the concept of self. To date, neither direct nor indirect empirical support is available. Lansing et al.'s (2005) findings of decreased parietal activation [BA 40, 4] are inconsistent with this model, but not necessarily contradictory, given the size the parietal area.

Summary

Theoretical Models. The majority of the speculative models can be seen from a theoretical perspective to possibly dovetail with each other. The underlying physiologies of temporal binding, neural mapping, hippocampal remapping, limbic depotentiation, frontal lobe activation, reciprocal ACC suppression, and REM systems activation are sufficiently interrelated with respect to the OR and neural systems linkage as to preclude mutual exclusion. Future findings will, undoubtedly, shed increasing light on their interrelationship. Our knowledge of parietal functioning is still limited, but will continue to grow.

The OR models, the earliest in our evolution of theorizing, do appear to relate to the facilitation of information processing and, therefore, to models of temporal binding, REM systems activation, and increased RSA/HRV vagal tone. There are, however, problems with consistency in their conceptualization. Notwithstanding that many of these studies require repetition in order to codify consistent data, it certainly begs the question as to the influence of the timing of psychophysiological measures (with different studies timing their measures at different intervals) on the outcomes. Until this problem is remedied, one would wonder how there could be consistencies within OR studies, let alone in comparing OR studies in isolation to EMDR studies of complete sessions.

Neuroimaging Studies. A similar pattern can be seen in our neurobiological studies. Similar neuroimaging post-EMDR findings have been noted with respect to left frontal lobe activation (Lansing et al., 2005; Levin et al., 1999; Oh & Choi, 2007), decreased occipital activation (Lansing et al., 2005; Pagani et al., 2007), and decreased temporal lobe activation (Oh & Choi, 2007; Pagani et al., 2007). These findings are indicative of the following: (a) emotional regulation due to increased activity of the prefrontal lobe, (b) inhibition of limbic over-stimulation by increased regulation of the association cortex, (c) reduction in the intrusion and over-consolidation of traumatic episodic memory due to the reduction of temporal lobe activity, (d) the reduction of occipitally mediated flashbacks, and (e) the induction of a functional balance between the limbic and prefrontal areas.

Recent modifications in neuroimaging paradigms have illustrated findings of bilateral dorsolateral prefrontal activation (Oh & Choi, 2007), as well as left orbitofrontal (Lansing et al., 2005) and right ventromedial prefrontal activation (Richardson et al., 2009). The implications of these findings have yet to be fully understood, but suggest repair in memorial function, working memory/concentration, and affect regulation, respectively. In addition, the finding of increased thalamic activation following successful EMDR treatment (Richardson et al., 2009) was noted for the first time. The consequence of such a change suggests the repair of failures in cognitive, memorial, affective, somatosensory, and interhemispheric integration, which are disrupted in PTSD.

The Pagani et al. (2007) study compared PTSD participants to controls exposed to trauma (who did not meet criteria for PTSD). As was noted above, the use of such a population in contrast to PTSD can be extremely illuminating, given the fact that the PTSD literature consistently states that few people (~12%–16%) actually meet criteria for PTSD after exposure to trauma. Therefore, taken together, the data in the Pagani et al. study do not illustrate the effects of EMDR on PTSD participants, as compared to nontraumatized controls. Rather, they illustrate a comparison between controls whose nervous systems are kindled (but do not meet criteria for PTSD) and PTSD participants. As was noted above, such comparisons are extremely informative, and indicative, realistically, of the populations that experience traumatic events.

Psychophysiology Studies. Similarly, consistencies have been seen in our psychophysiological studies, manifested by findings of parasympathetic relaxation responses, increased HRV parasympathetic tone, reduced electrodermal function, reduced EEG P3a function, and increased vagal parasympathetic function. These findings suggest that EMDR mediates directly on affect regulatory systems, inducing an initial "compelling" parasympathetic state change that facilitates information processing and neural linkage repair and the eventual stable trait change that is seen as a result of successful EMDR treatment.

Concluding Speculation

Combining the patterns found in the speculative models and empirical findings allows us to make a collective speculation regarding the nature of EMDR stimulation (visual, auditory, and tactile) and its relationship to the neural circuitry underlying EMDR's mechanism of action.

EMDR's sensory stimulation appears to mediate the OR, facilitating parasympathetic, cholinergic, and information processing mechanisms. In the form of repetitive sensory stimulation and repetitive OR, it appears to activate cerebellar, hypothalamo, medullary (vagal), pontine, thalamic, and orbitomedial/prefrontal cortices in the following ways: (a) Repetitive ORs are proposed to mediate the activation of the ventral vagal complex, located in the nucleus ambiguous, of the medulla, promoting increases in RSA/HRV, a resultant increase in parasympathetic functioning and the facilitation of information processing. (b) Repetitive ORs are hypothesized to mediate cholinergic mechanisms, leading to pontine-geniculate-occipital (PGO) activation, leading to the activation of REM systems. This may facilitate, through REM-like information processing, the subsequent reduction in both the strength of hippocampally mediated episodic memories, as well as the amygdaloid-mediated

negative affect of PTSD and the subsequent integration of traumatic memories into general semantic networks. (c) Repetitive sensory stimulation and repetitive ORs are predicted to activate the lateral cerebellum, facilitating through its output dentate nuclei the activation of the ventrolateral and central lateral thalamic nuclei. Comprising the major components of the thalamocortical circuitry that mediates the binding and integration of neural functioning, its activation may facilitate the repair and integration of somatosensory, memorial, cognitive, emotional, and hemispheric functioning. In addition, the activation of the ventrolateral thalamic nucleus (through its projections) may activate the prefrontal cortices, the most consistent finding of EMDR neuroimaging studies.

Conclusion

The search for EMDR's mechanisms of action began in the early 1990s, initially proceeding slowly and tentatively. As we entered the new millennium, the pace quickened. Theoretically driven speculative models, grounded in empirical findings from related neurobiological research bases, became more detailed and prevalent. Similarly, neurobiological studies became increasingly widespread, utilizing psychophysiological and neuroimaging examinations of EMDR treatment. Given the profound complexity of EMDR, it is imperative that this balance of inquiry and research continue. Ultimately, only empirical technologies and methodologies can definitively provide the windows of observation into underlying mechanisms of action. However, models and theories that organize knowledge and generate plausible explanations inform and drive research. Without theoretically driven models, which synthesize information from various related disciplines, it would be difficult to generate and empirically test hypotheses that link autonomic function, neurobiological theory, and clinical phenomena.

References

Armstrong, M. S., & Vaughan, K. (1996). An orienting response model of eye movement desensitization. *Journal of Behavior Therapy & Experimental Psychiatry, 27*, 21–32.

Aubert-Khalfa, S., Roques, J., & Blin, O. (2008). Evidence of a decrease in heart rate and skin conductance responses in PTSD patients after a single EMDR session. *Journal of EMDR Practice and Research, 2*(1), 51–56.

Barrowcliff, A. L., Gray, N. S., MacCulloch, S., Freeman, T. C. A., & MacCulloch, M. J. (2003). Horizontal rhythmical eye movements consistently diminish the arousal provoked by auditory stimuli. *British Journal of Clinical Psychology, 42*, 289–302.

Barrowcliff, A. L., Gray, N. S., Freeman, T. C. A., & MacCulloch, M. J. (2004). Eye movements reduce the vividness, emotional valence and electrodermal arousal associated with negative autobiographical memories. *Journal of Forensic Psychiatry and Psychology, 15*(2), 325–345.

Bergmann, U. (2000). Further thoughts on the neurobiology of EMDR: The role of the cerebellum in accelerated information processing. *Traumatology, 6*(3), 175–200.

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

Bossini, L., Fagiolini, A., & Castrogiovanni, P. (2007). Neuroanatomical changes after EMDR in Posttraumatic Stress Disorder. *Journal of Neuropsychiatry and Clinical Neuroscience, 19*, 457–458.

Boucsein, W. (1992). *Electrodermal activity*. New York: Plenum Press.

Boucsein, W., Baltissen, R., & Euler, W. (1984). Dependence of skin conductance reactions and skin resistance reactions on previous level. *Psychophysiology, 21*, 212–218.

Bremner, J. D., Staib, L., & Kaloupek, D. (1999). Neural correlates of exposure to traumatic pictures and sound in Vietnam combat veterans with and without posttraumatic stress disorder: A positron emission tomography study. *Biological Psychiatry, 45*, 806–816.

Cook, E., & Turpin, G. (1997). Differentiating orienting, startle and defense responses: The role of affect and its implications for psychopathology. In P. Lang, R. Simons, & M. Balaban (Eds.), *Attention and orienting: Sensory and motivational processes*. Mahwah, NJ: Lawrence Erlbaum; 137–164.

Corrigan, F. (2002). Mindfulness, dissociation, EMDR, and the anterior cingulated cortex: A hypothesis. *Contemporary Hypnosis, 19*(1), 8–17.

Denny, N. R. (1995). An orienting reflex/external inhibition model of EMDR and Thought Field Therapy. *Traumatology, 1*(1), 1–6.

Devinsky, O., Morrell, M., & Vogt, B. (1995). Contributions of anterior cingulate cortex to behavior. *Brain, 118*, 279–306.

Dyck, M. J. (1993). A proposal for a conditioning model of eye movement desensitization treatment for posttraumatic stress disorder. *Journal of Behavior Therapy and Experimental Psychiatry, 24*(3), 201–210.

Elofsson, U. O. E., von Scheele, B., Theorell, T., & Söndergaard, H. P. (2008). Physiological correlates of eye movement desensitization and reprocessing. *Journal of Anxiety Disorders, 22*(4), 622–634.

Friedman, D., Goldman, R., Stern, Y., & Brown, T. (2009). The brain's orienting response: An event-related functional magnetic resonance imaging investigation. *Human Brain Mapping, 30*(4), 1144–1154.

Ganzel, B., Casey, B. J., Glover, G., Voss, H. U., & Temple, E. (2007). The aftermath of 911: Effect of intensity and recency of trauma on outcome. *Emotion, 7*(2), 227–238.

Graham, F. (1979). Distinguishing among orienting, defense, and startle reflexes. In H. Kimmel, E. van Olst, & J. Orlebeke (Eds.), *The orienting reflex in humans* (pp. 137–167). Hillsdale, NJ: Lawrence Erlbaum.

Gunter, R. W., & Bodner, G. E. (2008). How eye movements affect unpleasant memories: Support for working memory account. *Behavior Research and Therapy, 46*, 913–931.

Gunter, R. W., & Bodner, G. E. (2009). EMDR Works . . . But How? Recent progress in the search for treatment mechanisms. *Journal of EMDR Practice and Research, 3*(3), 161–168.

Harper, M., Rasolkhani-Kalhorn, T., & Drozd, J. F. (2009). On the neural basis of EMDR therapy: Insights from qEEG studies. *Traumatology, 15*(2), 81–95.

Johnsson, P. (2006). Respiratory sinus arrhythmia as a function of state anxiety in healthy individuals. *International Journal of Psychophysiology, 63*(1), 48–54.

Kaye, B. (2007). Reversing reciprocal suppression in the anterior cingulate cortex: A hypothetical model to explain EMDR effectiveness. *Journal of EMDR Practice and Research, 1*(2), 88–99.

Kobayashi, R., Koike, Y., Hirayama, M., Ito, H., & Sobue, G. (2003). Skin sympathetic nerve function during sleep—a study with effector responses. *Autonomic Neuroscience: Basic and Clinical, 103*(1–2), 121–126.

Lamprecht, F., Kohnke, C., Lempa, W., Sack, M., Matzke, M., & Munte, T. (2004). Event-related potentials and EMDR treatment of post-traumatic stress disorder. *Neuroscience Research, 49*, 267–272.

Lanius, R. A., Williamson, P. C., & Densmore, M. (2001). Neural correlates of traumatic memories in posttraumatic stress disorder: A functional MRI investigation. *American Journal of Psychiatry, 158*, 1920–1922.

Lanius, R. A., Williamson, P. C., & Hopper, J. (2003). Recall of emotional states in posttraumatic stress disorder: An fMRI investigation. *Biological Psychiatry, 53*, 204–210.

Lansing, K., Amen, D. G., Hanks, C., & Rudy, L. (2005). High resolution brain SPECT imaging and EMDR in police officers with PTSD. *Journal of Neuropsychiatry and Clinical Neurosciences, 17*, 526–532.

Levin, P., Lazrove, S., & van der Kolk, B. A. (1999). What psychological testing and neuroimaging tell us about the treatment of posttraumatic stress disorder (PTSD) by eye movement desensitization and reprocessing (EMDR). *Journal of Anxiety Disorders, 13*, 159–172.

Liberzon, I., Taylor, S. F., & Amdur, R. (1999). Brain activation in PTSD in response to trauma-related stimuli. *Biological Psychiatry, 45*, 817–826.

Lister, D. (2003). Correcting the Cognitive Map with EMDR: A Possible Neurological Mechanism. *The EMDR Practitioner.* Retrieved April 1, 2009, from http://www.emdr-practitioner.net/practitioner_articles/lister_02_2003.html

MacCulloch, M. J., & Feldman, P. (1996). Eye movement desensitization treatment utilizes the positive visceral elements of the investigatory reflex to inhibit the memories of post-traumatic stress disorder: A theoretical analysis. *British Journal of Psychiatry, 169*, 571–579.

McEwen, B. (2005). Glucocorticoids, depression and mood disorders: Structural remodeling in the brain. *Metabolism: Clinical and Experimental, 54*, 20–23.

Menon, V., Ford, J. M., Lim, K. O., Glover, G. H., & Pfefferbaum, A. (1997). Combined event-related fMRI and EEG evidence for temporal-parietal activation during target detection. *Neuro Report, 8*, 3029–3037.

Minamimoto, T., & Kimura, M. (2002). Participation of the thalamic CM-Pf complex in attentional orienting. *Journal of Neurophysiology, 87*(6), 3090–3101.

Mitra, R., Jadhav, S., McEwen, B. S., & Chattarji, S. (2005). Stress duration modulates the spatiotemporal patterns of spine formation in the basolateral amygdala. *Proceedings of the National Academy of Sciences USA, 102*, 9371–9376.

Murali, N. S., Svatikova, A., & Somers, V. K. (2003). Cardiovascular physiology and sleep. *Frontiers in Bioscience, 8*, 636–652.

Oh, D.-H., & Choi, J. (2007). Changes in the regional cerebral perfusion after Eye Movement Desensitization and Reprocessing: A SPECT study of two cases. *Journal of EMDR Practice and Research, 1*(1), 24–30.

Öhman, A., Hamm, A., & Hugdahl, K. (2000). Cognition, and the autonomic nervous system: Orienting, anticipation, and conditioning. In J. Cacioppo, L. Tassinary, & G. Berntson (Eds.), *Handbook of Psychophysiology* (pp. 533–575). Cambridge, England: Cambridge University Press.

Pagani, M., Hogberg, G., Salmaso, D., Nardo, D., Sundin, O., Jonsson, C., et al. (2007). Effects of EMDR psychotherapy on 99m Tc-HMPAO distribution in occupation-related post-traumatic stress disorder. *Nuclear Medicine Communications, 28*(10), 757–765.

Pavlov, I. P. (1927). *Conditions reflexes: An investigation of the physiological activity of the cerebral cortex*. London: Oxford University Press.

Pearson, H. J. (2009). Present and accounted for: Sensory stimulation and parietal neuroplasticity. *Journal of EMDR Practice and Research, 3*(1), 39–49.

Porges, S. W. (1997). Emotion: An evolutionary byproduct of the neural regulation of the autonomic nervous system. *Annals of the New York Academy of Sciences, 807*, 62–77.

Porges, S. W. (2001). The polyvagal theory: Phylogenetic substrates of a social nervous system. *International Journal of Psychophysiology, 42*, 29–52.

Porges, S. W. (2007). The Polyvagal perspective. *Biological Psychology, 74*(2), 116–143.

Rasch, B., Buchel, C., Gais, S., & Born, J. (2007). Odor cues during slow-wave sleep prompt declarative memory consolidation. *Science, 315*, 1426–1429.

Rasolkhani-Kalhorn, T., & Harper, M. (2006). EMDR and low frequency stimulation of the brain. *Traumatology, 12*(1), 9–24.

Richardson, R., Williams, S. R., Hepenstall, S., Gregory, L., McKie, S., & Corrigan, F. (2009). A single-case fMRI study EMDR treatment of a patient with posttraumatic stress disorder. *Journal of EMDR Practice and Research, 3*(1), 10–23.

Sack, M., Lempa, W., & Lamprecht, F. (2007). Assessment of psychophysiological stress reactions during a traumatic reminder in patients treated with EMDR. *Journal of EMDR Practice and Research, 1*(1), 15–23.

Sack, M., Lempa, W., Steinmetz, A., Lamprecht, F., & Hofmann, A. (2008). Alterations in autonomic tone during trauma exposure using eye movement desensitization and reprocessing (EMDR)—results of a preliminary investigation. *Journal of Anxiety Disorders, 22*(7), 1264–1271.

Schore, A. N. (1994). *Affect regulation and the origin of the self: The neurobiology of emotional development*. Hillsdale, NJ: Lawrence Erlbaum.

Schore, A. N. (2001). The effects of a secure attachment relationship on right brain development, affect regulation and infant mental health. *Infant Mental Health Journal, 22*(1–2), 7–66.

Shapiro, F. (1989a). Efficacy of the eye movement desensitization procedure in the treatment of traumatic memories. *Journal of Traumatic Stress, 2*, 199–223.

Shapiro, F. (1989b). Eye movement desensitization procedure: A new treatment for post-traumatic stress disorder. *Journal of Behavior Therapy and Experimental Psychiatry, 20*, 211–217.

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

Shapiro, F., & Maxfield, L. (2002). EMDR: Information processing in the treatment of trauma. *In Session: Journal of Clinical Psychology, 58*, 933–946.

Sokolov, E. N. (1963). *Perception and the conditioned reflex*. New York: Pergamon Press.

Söndergaard, H. P., & Elofsson, U. (2008). Psychophysiological studies of EMDR. *Journal of EMDR Practice and Research, 2*(4), 282–288.

Stickgold, R. (2002). EMDR: a putative neurobiological mechanism of action. *Journal of Clinical Psychology, 58*(1), 61–75.

Stickgold, R. (2007). Of sleep, memories and trauma. *Nature Neuroscience, 10*(5), 540–542.

Stickgold, R. (2008). Sleep-dependent memory processing and EMDR action. *Journal of EMDR Practice and Research, 2*(4), 289–299.

Turpin, G. (1986). Effects of stimulus intensity on autonomic responding: The problem of differentiating orienting and defense reflexes. *Psychophysiology, 23*, 1–14.

Turpin, G. (1989). An inadequate test of the habituation of the cardiac decelerative response component of the orienting reflex: Necessary conditions and sufficient evidence. A comment on Vossel and Zimmer. *Journal of Psychophysiology, 3*, 129–140.

Turpin, G. (2007). Orienting response. In D. Sander & K. Scherer (Eds.), *Oxford companion to the affective sciences*. Oxford: Oxford University Press; 292–293.

van der Kolk, B., Burbridge, J., & Suzuki, J. (1997). The psychobiology of traumatic memory: Clinical implications of neuroimaging studies. *Annals of the New York Academy of Sciences, 821*, 99–113.

Vyas, A., Mitra, R., Shankaranarayana Rao, B. S., & Chattarji, S. (2002). Chronic stress induces contrasting patterns of dendritic remodeling in hippocampal and amygdaloid neurons. *Journal of Neuroscience, 22*, 6810–6818.

Walker, M. P., Liston, C., Hobson, J. A., & Stickgold, R. (2002). Cognitive flexibility across the sleep-wake cycle: REM sleep enhancement of anagram problem solving. *Cognitive Brain Research, 14*, 317–324.

Williams, L. M., Brammer, M. J., Skerrett, D., Lagopolous, J., Rennie, C., Kozec, K., et al. (2000). The neural correlates of orienting: An integration of fMRI and skin conductance orienting. *Brain Imaging, 11*(13), 3011–3015.

Wilson, D. L., Silver, S. M., Covi, W. G., & Foster, S. (1996). Eye movement desensitization and reprocessing: Effectiveness and autonomic correlates. *Journal of Behavior Therapy and Experimental Psychiatry, 27*(3), 219–229.

Wolpe, J. (1990). *The practice of behavior therapy* (4th ed.). New York: Pergamon Press.

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