Mediators, mechanisms and moderators of action for EMDR therapy: A review of multiplex effects in modes of bilateral stimulation

Andrew M. Leeds, Ph.D.

Abstract

In “Mediators and mechanisms of change in psychotherapy research” Kazdin states unequivocally (2007, p. 1) that “after decades of psychotherapy research, we cannot provide an evidence-based explanation for how or why even our most well studied interventions produce change…” Despite more than 30 research and review papers and chapters exploring its mechanisms of action, the same conclusion applies to EMDR therapy. To forge a comprehensive framework for understanding EMDR therapy treatment effects, it is essential first to carefully conceptualize differences between mediators, mechanisms and moderators of change in psychotherapy in general (Kazdan, 2007) and in EMDR therapy in particular. Following Kazdan’s guidance (p. 21) – “Looking for one explanation or mechanism for one group, one therapy, or one outcome may yield little” – six primary categories of hypothesized mechanisms of action for EMDR therapy have been examined in careful research or are amenable to direct study. These six distinct hypothesized mechanisms of action appear to provide diverse multiplex effects, sometimes converging and sometimes diverging, leading to various outcomes in different clinical contexts and in different EMDR procedures. This presentation will review the existing laboratory and controlled clinical published research on the specific effects of bilateral eye movements, bilateral tones and bilateral kinesthetic stimulation as used in EMDR therapy to evaluate how these various mediators contribute to EMDR treatment effects in disparate clinical contexts. This analysis will lead to potential implications in EMDR therapy for moderators such as degree of structural dissociation and for mediators including selection of modes of bilateral stimulation.

Mediators, Mechanisms and Moderators of action for EMDR therapy:

A review of multiplex effects in modes of bilateral stimulation

Andrew M. Leeds, Ph.D.

EMDR Europe Conference
The Hague,
June 18, 2016

Acknowledgement

- This presentation is adapted with permission from Chapter 2, pp. 28-48.
- **A Guide to the Standard EMDR Therapy Protocols for Clinicians, Supervisors, and Consultants, 2nd Edition.**
- by Andrew M. Leeds, Ph.D.

2

EMDR therapy "causes" symptom resolution

- "A number of previous meta-analyses have found that EMDR has sustained and lasting treatment effects for Posttraumatic Stress Disorder..."
- "... EMDR ...meet[s] criteria for evidence-based practice in the United Kingdom..., in America..., in Australia ..., and in the Netherlands..."

-- Lee and Cuijpers (2013, p. 231)

3

Causation versus mechanisms

- *"A randomized controlled trial (RCT) may show that that treatment compared to no treatment leads to therapeutic change."*
- *"Demonstrating a **cause** does not say why the intervention led to change or how the change came about."*

Kazdan (2007, p. 3)

4

How does EMDR work?

5

"After decades of psychotherapy research, we cannot provide an evidence-based explanation for how or why even our most well studied interventions produce change…"

"Mediators and mechanisms of change in psychotherapy research"
Kazdin, 2007, p. 1

6

WHY SHOULD IT BE DIFFERENT WITH EMDR THERAPY?

7

Why do we hold EMDR therapy to a different standard?

1. From the start Shapiro proposed EMDR therapy and the AIP model have a neurological basis
2. EMDR treatment effects were claimed – and demonstrated – to be faster than prior therapies
3. Researchers have published extensive neurophysiological and neurological research related to studies of bilateral eye movement, tones and taps and EMDR therapy
4. The subjective experience as client often yields a compelling sense that change is happening deep within the brain

8

Our objectives

9

Four objectives

1. Recognize fundamental differences between mediators, mechanisms and moderators
   a. In psychotherapy in general and
   b. In EMDR therapy in particular
2. Examine research on modes of bilateral stimulation
3. Explore 6 categories of hypothesized mechanisms of action for EMDR therapy
4. Evaluate *interactions* between moderators in EMDR therapy, such as degree of structural dissociation and mediators such as mode of bilateral stimulation

10

What do these terms mean?

- Cause
- Mediator
- Mechanism
- Moderator

11

The search for explanation

- Cause: a variable or intervention that leads to and is responsible for the outcome or change.
- Correlation is not causation.
  - The therapeutic alliance is highly correlated with symptom improvement.
    - Time course studies with multiple measurements show the treatment alliance is strengthened *after* symptom gains.
    - Which is the cause of the other?
  - Similarly time course studies of gains in cognitive therapy (CT) leave the order of change unclear.
    - "whatever may be the basis of changes with CT, it does not seem to be the cognitions…"

(Kazdan, 2007, p. 3)

12

Pre- Post- neurobiological correlates of clinical change do not demonstrate the mechanisms of change

They only show where changes have occurred in the brain

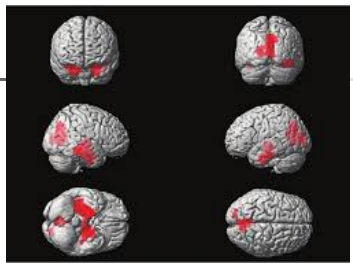
13

Before and after images of EMDR therapy with SPECT and NIRS

- Single photon emission computed tomography (SPECT) and
- Near-infrared spectroscopy (NIRS) imaging
  - before and after effective EMDR treatment for PTSD
- Have identified observable changes in regional blood flow (RBF)
  - when subjects are asked to attend to their standardized trauma scripts

(Lansing, Amen, & Klindt, 2000; Lansing, et al., 2005; Levin, Lazrove, & van der Kolk, 1999; Oh & Choi, 2004; Ohtani, et al., 2009; Pagani et al., 2007; Pagani, et al., 2013).

14



SPECT change pre- to post-EMDR session

"The significant normalization of these activations after the trauma processing can be interpreted as the neurobiological correlate of clinical recovery."

-- Pagani, Hogberg, Fernandez and Siracusano (2013).

15

Definitions in the search for explanation (Kazdan, 2007, p. 3)

- Mechanism: the basis for the effect, i.e., the processes or events that are responsible for the change; the reasons why change occurred or how change came about.
  - By understanding the processes that account for therapeutic change one ought to be better able to optimize therapeutic change.
  - Understanding how therapy works can help
    - identify moderators of treatment, i.e., variables on which the effectiveness of a given treatment may depend.
    - facets that might be particularly influential in treatment outcome and permit better selection of suitable patients.

16

From cause to mechanism: an example with an effective treatment

- Research on SSRIs (e.g. fluoxetine) showed them to be effective, i.e. to **cause** a change in the severity of depressive symptoms.
- The original *proposed* mechanism was by making serotonin more available.
  - Subsequent research ruled this out (Leher, 2011)
    - Depleting serotonin did not cause or worsen depression
  - Then research showed the mechanism to be neurogenesis in the hippocampus (Chang, et al. 2015; Snyder, et al. 2011)
  - Hippocampal neurogenesis is also induced by exercise (van Praag, 2008), another effective treatment for depression.

17

Definitions in the search for explanation (Kazdan, 2007, p. 3)

- Mediator: an intervening variable that may account (statistically) for the relationship between the independent and dependent variable.
  - Something that mediates change may not necessarily explain the processes of how change came about.
  - Also, the mediator could be a proxy for one or more other variables or be a general construct that is not necessarily intended to explain the mechanisms of change.
  - A mediator may be a guide that points to possible mechanisms but is not necessarily a mechanism.

18

Establishing a mediator or mechanism has several requirements

- Strong association.
- Specificity.
- Consistency.
- Experimental manipulation.
- Timeline.
- Gradient.
- Plausibility or coherence.

-- Kazdin, 2007, pp. 4-5

19

Mediators of treatment effects in EMDR therapy

- Mode of bilateral stimulation
  - Eye movements
  - Tactile
  - Auditory
- Speed of bilateral stimulation
- Direction of bilateral stimulation
- Nature of target selection
  - Past, present, future
  - Adaptive or maladaptive memory network
  - Exteroceptive or interoceptive experience

20

Definitions in the search for explanation (Kazdan, 2007, p. 3)

- Moderator: a characteristic that influences the direction or magnitude of the relationship between and independent and dependent variable.
  - If the relationship between variable x and y varies and is different for males and females, sex is a moderator of the relation.
  - Moderators are related to mediators and mechanisms because they suggest that different processes might be involved (e.g., for males or females).

21

Moderators of treatment effects in EMDR therapy

- Age: infant, child, adolescent, adult
- Acute alcohol or drug intoxication
- Degree of structural dissociation
  - Primary (PTSD). See Bae, et al. (2015)
  - Secondary – Disorder of Extreme Stress NOS, Complex PTSD, unspecified dissociative disorder
  - Tertiary – Dissociative Identity Disorder
- Rigid defenses as in personality disorders
  - Idealization, denial, omnipotent control, splitting, projection, dissociation… See Knipe (2014); Mosquera and Knipe (2015)

22

Research on mediators and mechanisms of EMDR therapy

- Over 60 papers have examined
  - Psychophysiological effects
  - Neurological effects
  - Effects of modes of bilateral stimulation
  - Hypothesized mechanisms of action

23

What are the effects of bilateral eye movements?

24

Two sets of effects from bilateral eye movements

- ***Consistent*** psychophysiological effects
  - de-arousal – a shift from sympathetic to parasympathic activation
- ***Paradoxical*** cognitive effects:
  - *Decreased* **vividness and emotionality** of disturbing memories
  - Enhanced memory processing
  - *Enhanced* memory ***retrieval***
  - Increased ***accuracy*** of memory
  - Induced ***cognitive and semantic flexibility***, and facilitate ***attentional orienting***
    - ***Enhanced executive control processes***, and increased ***metacognitive awareness***

25

Bilateral eye movements produce psychophysiological de-arousal

- Wilson et al. (1996) were the first to show a "relaxation effect" from bilateral eye movements
- Multiple studies confirm decreased sympathetic and increased parasympathetic activity
  - Heart rate significantly decreases within the first 10 seconds
  - Heart rate variability increases
  - Skin conductance decreases
  - Respiratory rate increases during EM, slows after.
- Many scholars propose the orienting response as the mechanism for these effects:

-- Aubert-Khalfa et al., 2008; Elofsson et al., 2008; Sack et al., 2007; Sack et al., 2008; Schubert, Lee & Drummond, 2011

26

Early clinical reports revealed that bilateral EM increase memory retrieval and breach dissociative defenses

- Lipke's (1995) survey of EMDR therapy–trained clinicians identified a greater tendency for forgotten memories to emerge during EMDR reprocessing than in other methods previously used by these clinicians.
- Paulsen (1995) cautioned that the powerful effects of bilateral stimulation are capable of counteracting dissociative defenses, which can lead to significant decompensation in inadequately prepared patients.
  - This lead to a standard of care in EMDR therapy requiring screening for a dissociative disorder and extended preparation for patients with a complex dissociative disorder.
    - International Society for the Study of Trauma and Dissociation, 2011; Shapiro, 1995, 2001.

27

Laboratory studies: paradoxical cognitive effects of bilateral eye movements

- **Decrease** vividness and emotionality of disturbing memories
  - Andrade, Kavanagh, & Baddeley, 1997; Barrowcliff, Gray, Freeman, & MacCulloch, 2004; Gunter & Bodner, 2008; Kavanagh, Freese, Andrade, & May, 2001; Maxfield, Melnyk, & Hayman, 2008; van den Hout & Engelhard, 2012); van den Hout, Muris, Salemink, & Kindt, 2001
- Enhance **memory processing** via interhemispheric interactions
  - Christman et al., 2003; Christman et al., 2004; Christman, Propper, & Brown, 2006
- Enhance memory ***retrieval***
  - Christman, Garvey, Propper, & Phaneuf, 2003; Christman, Propper, & Dion, 2004; Propper & Christman, 2008
- Increase ***accuracy of memory***
  - Christman et al., 2004; Lyle, Logan, & Roediger, 2008; Parker, Relph, & Dagnall, 2008
- Induce ***cognitive and semantic flexibility*** & facilitate ***attentional orienting***
  - Kuiken et al., 2001-2002
- Enhance ***executive control*** processes, and in turn increase ***metacognitive awareness***
  - Lyle and Martin, 2010; Lyle and Orsborn, 2011

28

Bringing order to the research on mechanisms of EMDR therapy

- It is proposed that the various theories on mechanism of EMDR therapy can be organized into six categories.
- These mechanisms produce ***multiplex*** effects leading to ***diverse*** outcomes in ***different clinical populations*** and in ***different clinical applications*** of EMDR therapy procedures.

29

Dual Attention: the primary mediator of EMDR therapy

- Dual attention is not a mechanism
  - It is the primary mediator of EMDR therapy
  - It appears to foster a state of mindfulness, that will be examined as a likely mechanism
    - Mindfulness has been shown to enhance emotional information processing (Rachman, 1980; Teasdale, 1999)

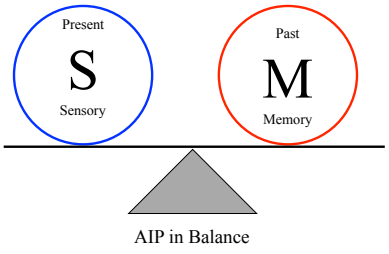
30

Dual Attention – refers to balanced activation

- Dual attention refers to a balance of activation between
  - ***Memory network elements*** ("images") representing "one foot in the past"
  - ***Sensory activation*** (responding to sensory cues) with "one foot in the present"

31

Dual Attention
The Teeter-Totter Model of Consciousness



AIP in Balance

 32

Dual Attention

- Memory elements can be
  - Under activated due to
    - Incorrect target selection
    - Inadequate phase three steps or
    - Dissociative or other defenses
  - Over activated due to
    - Overly intense reliving
    - Inadequate sensory activation

33

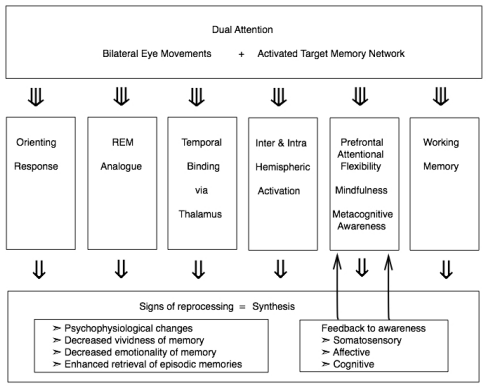
SIX CATEGORIES OF MECHANISMS OF ACTION IN EMDR THERAPY

Multiplex effects

Sometimes converging and sometimes diverging

Leading to various outcomes in different clinical contexts and in different EMDR procedures

34



35

"What is it?"
The orienting response

36

"What is it?" The Orienting response

- The OR first described by Pavlov (1927)
- Sokolov (1963, 1990) proposed that the OR has two distinct phases:
  - first, an alerting reaction in response to a novel stimulus in the environment; and
  - second, habituation that leads to a reduction of the OR with repeated stimulus presentations in the face of no danger or threat.

37

Orienting response and eye movements

- Eye movements associated with the OR are of two types:
  - "One type of eye movement is induced by an external stimulus (*alerting* response);
  - another is induced by an active search of the environment (*investigatory* response)"

Jeffries & Davis, 2012, p. 6

38

Orienting Responses and desynchronization

- Strong OR can produce
  - a broad desynchronization of electrical activity in the brain.
- With milder OR stimuli,
  - there is less intense and
  - cortically more localized desynchronization response
  - that occurs in a specific sensory processing region of the brain.

39

Biphasic orienting responses

- With nonthreatening cues the OR produces a biphasic response
  - first an increase in arousal during the initial orientation to the novel stimulus,
  - then a subcortical appraisal in the limbic system (Siegel, 2012).
  - When the subcortical appraisal indicates the absence of danger, the initial readiness to respond is followed by a dearousal response in the autonomic system.
    - With persistent nonthreatening stimuli, the limbic system rapidly habituates to the stimulation, leading to synchronizing slow waves in the brain and a release of beta-endorphins, which decrease pain and increase feelings of safety and well-being.

40

Early History of the OR with EMDR therapy

- Lipke (1992, 1999) was the first to propose the OR as a mechanism for EMDR treatment effects
- Armstrong and Vaughan (1994, 1996) proposed that an OR triggered by eye movements in EMDR therapy
  (a) prevents avoidance;
  (b) facilitates continued attention to the traumatic memory;
  (c) activates emotional processing (central analyzers);
  (d) facilitates incorporation of new, trauma relevant information; and
  (e) reduces pain via release of beta-endorphins.
- MacCulloch and Feldman (1996) independently proposed the OR as a way to explain EMDR therapy effects with both EM and alternate BLS

41

Data supporting a role for the OR in EMDR therapy -- 1 of 3

- Wilson, Silver, Covi, and Foster (1996)
  - Found OR with EM,
  - but not w/ no-EM, nor w/ self-generated tapping
- Becker, Todd-Overmann, Stoothoff, and Lawson (1998);
  - Confirmed the differential effects of optimal versus insufficient or excessive speed of bilateral eye movements
- Barrowcliff, MacCulloch, & Gray, 2001; Barrowcliff, MacCulloch, Gray, MacCulloch, & Freeman, 2001; MacCulloch & Barrowcliff, 2001
  - Concluded that cognitive load (i.e., distraction) was **not** the mechanism behind these psychophysiological effects;
  - This was disputed by the proponents of the working memory hypothesis.

42

OR and working memory in EMDR

- Later, Barrowcliff, Gray, MacCulloch, Freeman, and MacCulloch (2003) proposed in actual clinical settings both the OR and working memory effects function in parallel.
- Sondergaard and Elofsson (2008) concluded that the physiological data supported
  - reciprocal inhibition and the REM hypothesis,
  - not the OR, which they believed should quickly habituate.
  - They minimized the biphasic nature of the OR and the difference between
    - The initial stimulus (alerting response) with sympathetic arousal
    - And the active search of the environment (investigatory response) finding neutral data and a shift to parasympathetic tone.

43

Data supporting a role for the OR in EMDR therapy -- 2 of 3

- Elofsson, von Scheele, Theorell, and Sondergaard (2008); Sack, Lempa, Steinmetz, Lamprecht, and Hofmann (2008)
  - An initial increase in RR could be related to either the initial OR or to increased accessing of memories as described previously by Christman, et al., 2003; Christman, et al., 2004; Propper & Christman, 2008.

44

Data supporting a role for the OR in EMDR therapy -- 3 of 3

- Schubert, Lee & Drummond (2011)
  - "Heart rate decreased significantly when eye movements began; skin conductance decreased during eye movement sets; heart rate variability and respiration rate increased significantly as eye movements continued; and orienting responses were more frequent in the eye movement than no-eye movement condition at the start of exposure." (p. 1)
- Propose parallel modes of action:
  - Direct physiological shifts -> cognitive re-appraisals
  - Dual attention task-> reduces distress
    - "Through the process of reciprocal inhibition, in which a relaxation response is paired with exposure to distressing memories, negative appraisals of distressing memories weaken, and avoidance of trauma memory processing decreases. Eye movements, as a dual-attention task, may also reduce distress to a tolerable level and create a cognitive and physiological state in which effective processing of trauma information can occur. The relaxation response associated with EMs in EMDR is clinically meaningful as it may serve to moderate arousal throughout treatment sessions. Thus, EMDR may be particularly suitable for patients who cannot tolerate the high stress associated with exposure." (p. 8)

45

The OR supports a role for EM in standard EMDR and RDI

- Rachman (1980) proposed that relaxation (de-arousal) is central to "emotional processing"
- Bilateral eye movements, tones, or kinesthetic stimulation,
  - to different degrees
- reliably trigger a "compelled relaxation response" (Wilson et al., 1996)
- By activating the investigatory response to neutral stimuli
- This helps to explain the observed efficacy of BLS with both standard EMDR reprocessing and RDI.

46

REM Analogue Hypothesis

47

REM Analogue

- As early as her seminal paper 1989 on EMD, Shapiro suggested
  - the reciprocal inhibition observed in the EMD[R] process could be related to
  - the body's natural excitation releasing mechanism that occurs in REM sleep.
- In 2001 she noted the lack of direct support for this hypothesis.

48

Stickgold (2002, 2008)

- EMDR therapy activates a form of memory processing
- that is normally sleep dependent, and
- that is more than simple "memory consolidation" as
  - [REM] "sleep-dependent memory processing also results in the identification, integration, and enhancement of those aspects of memories calculated to be most important" (2008, p. 290).
  - "REM sleep appears to facilitate the activation of more distant associations than seen either in non-REM sleep or in the normal wake state" (2008, p. 295)
- During EMDR therapy:
  - "This REM-like state permits the integration of traumatic memories into associative cortical networks *without interference from hippocampally mediated episodic* recall." (2002, p. 71)

49

Saccadic EM versus smooth pursuit tracking EM

- Saccadic eye movement — Saccades
  - are rapid, ballistic movements of the eyes that
  - abruptly change the point of fixation
  - They typically take place while reading, gazing around a room, and during REM sleep.
  - can be voluntary, but are often made unconsciously.
  - called ballistic because
    - the saccade-generating system cannot adjust to changes in position of the target during the 15 to 100 ms required for the eye movement (Purves et al., 2001).
- Smooth pursuit eye movement are
  - much slower (than saccadic EM), than voluntary tracking movements of the eyes
  - designed to keep a moving stimulus on the fovea.
  - Only highly trained observers can make smooth pursuit EM without tracking a moving target.
  - Other observers generally make saccadic EM (Purves et al., 2001).

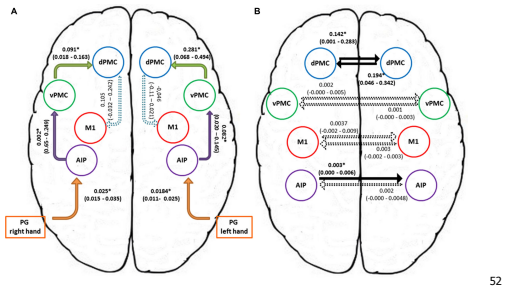
50

Saccades EM, tracking EM REM and the OR

- Stickgold
  - Noted that **smooth pursuit EM** generally used in EMDR therapy differ from
  - the **saccadic EM** found in REM sleep
    - (and in alternate eye gaze procedures used in the laboratory studies described later in presentation).
  - He proposed the leading candidate for such a mechanism is the OR and described research models to test this hypothesis (2002, p. 72).
    - He cautioned against the use of an eye fixation control condition to avoid confounding variables.

51

Inter- and Intra- Hemispheric Activation



52

Inter- and Intra-hemispheric activation

- Initially proposed by Russell (1992) and later by
- Servan-Schreiber (2000, p. 38), who suggested EMDR therapy may
  - "induce a background of synchronous neural activity across cerebral hemispheres and perhaps within each hemisphere."

53

Early interhemispheric QEEG data from Nicosia (1994)

- an unpublished single-case EMDR treatment report with quantitative electroencephalographic (QEEG) data
- a rapid elimination in psychogenic amnesia occurred with an increase in delta and theta band coherence in homologous areas of the left and right hemisphere from 4.99 to 0.1 standard deviations out of phase

54

Early interhemispheric QEEG data from Nicosia (1994)

- He proposed the increase in inter-hemispheric delta and theta band coherence was partly due to the effect of EM in generating synchronizing (theta) pacemaker signals arising in and ascending from the lateral pontine region of the reticular formation.
- He referenced REM sleep and theta rhythm activation of the N-methyl-d-aspartate (NMDA) receptors of the hippocampus
- He hypothesized that EMDR therapy activated a REM-like system for memory reorganization.

55

Bergmann (1998, 2001)

- Bergman proposed that the repetitive (bilateral) redirection of attention in EMDR therapy turns on the brain's REM sleep system,
  - which leads to the integration of the traumatic memory into general semantic networks by activating
    - (a) a filtering function in the cingulate gyrus,
    - (b) cognitive and language functions supported by the lateral cerebellum, and
    - (c) integrative functions in the left dorsolateral prefrontal cortex.

56

Mixed laboratory findings on the Inter-hemispheric hypothesis (IhC)

- Two studies failed to support the IhC
  - But there were significant design issues
- Propper, Pierce, Geisler, Christman, and Bellorado (2007)
  - Failed to control for EM-related electrical artifacts
- Samara, Elzinga, Slagter, and Nieuwenhuis (2011)
  - Failed to include a true episodic memory recall condition

57

Keller et al.'s (2014, p. 116) review concluded that

- "Until IhC is measured during or immediately following bilateral stimulation while the participant is contemplating personally meaningful episodic memories, the IhC model for the effects of EMDR on the reprocessing of traumatic memories remains untested".

58

Retrieval of episodic memories and hemispheric communication

- Christman, Garvey, Propper, and Phaneuf (2003) found that ***retrieval of episodic memories was facilitated when preceded by bilateral horizontal saccadic eye movements***.
- This supports clinician observations first reported in a survey by Lipke (1995)
- Christman et al. suggested that bilateral saccadic eye movements ***enhance interhemispheric interaction*** and may help EMDR patients retrieve episodic memories of traumatic experiences.

59

Memory accuracy and saccadic EM Propper and Christman (2008)

- Propper and Christman summarized a series of studies on the effects of bilateral saccadic eye movements, similar to those employed in EMDR therapy,
- Found significant improvement in episodic memory across a wide range of memory tests
  - more accurate recall of word lists and
  - personal journal entries with fewer false recollections.
- Based on Compton and Mintzer (2001, p. 276), they suggested
  - "interhemispheric interaction served to reduce stress and worry"
  - and that EMDR might reduce distress associated with recalling traumatic memories.

60

Memory accuracy and saccadic EM Lyle and Jacobs (2010, p. 581)

- Reported two experiments showing improved memory with saccadic EM in which
  - "Participants viewed slideshows depicting crimes, and received contradictory and additive misinformation about event details."
- Compared with an eye fixation condition
  - "Saccades increased discrimination between seen and unseen event details regardless of whether or what type of misinformation was presented."

61

Earlier offset of childhood amnesia with saccadic EM

- Christman, Propper, and Brown (2006) found that following saccadic horizontal EMs, subjects recalled earlier episodic memories from childhood than in a no-EM condition.

62

Saccades – not tracking EM – used in laboratory studies

- These memory retrieval effects were not produced by the *smooth pursuit EM investigated in other studies and more commonly used in EMDR therapy*.
- "participants watched a dot appear alternately on the left and right sides of a computer screen for 30 seconds, with dots alternating left–right position every 500 milliseconds".
  (Propper & Christman, 2008, p 269)
- Jeffries and Davis (2012) in reviewing the role of EM in EMDR therapy called for more research to investigate the differences between the effects of
  - saccadic (as in reading, REM sleep, and in watching alternate left–right dots) and
  - the smooth pursuit tracking EM commonly used in EMDR therapy.

63

Handedness, EM and support for intra-hemispheric effects

- During saccades or an eye fixation control condition, arrays of letter matching targets and probes were presented to
  - The same hemisphere (within-hemisphere trials)
  - Or separate hemispheres (across-hemisphere trials)
- For strongly right handed subjects, saccades increased match-detection accuracy on *within-hemisphere trials only*, suggesting that… ***saccades enhance intrahemispheric processing*** but not inter-hemispheric interaction.
- *Except for subjects* who were not strongly right-handed who showed ***higher across-hemisphere accuracy*** which may reflect *greater interhemispheric interaction*.

-- Lyle and Martin (2010, p. 128)

64

Positive memories + EM support for intra-hemisphere coherence model

- A laboratory EEG study by Keller et al. (2014) on the effects of BL EM on ***positive memories*** found
  - No support for an interhemispheric model,
  - **Data supporting an intrahemispheric coherence model** for EMDR therapy effects
  - Increased memory strength and vividness for all three conditions
    - eye fixation, a blinking colored dot, and BL EM.
    - Recall Stickgold's (2002) cautions on confounding effects of eye fixation vs. no eye direction instructions
    - Their data supports a role for bilateral stimulation with RDI
- They observed "a marginally nonsignificant increase in Frontal Beta interhemispheric coherence" in the BL EM condition,
  - A larger sample size would be needed to achieve sufficient statistical power to clarify.

65

Intra-hemispheric EEG coherence support from a clinical case series

- Farina et al. (2014) investigated the integration of traumatic memories
  - measured EEG coherence and heart rate variability (HRV)
  - before and after actual EMDR therapy sessions
  - during recall of six patients' traumatic memories.
- During trauma memory recall after EMDR therapy
  - No evidence of interhemispheric connectivity.
  - "increase of left intra-hemispheric EEG coherence, between fronto-parietal and temporal cortical areas, in the beta frequency band"
  - increase in the high-frequency component of HRV, known to reflect vagal activity
  - changes in the intrahemispheric coherence values
    - directly correlated with changes in HRV and
    - inversely related to decreases in subjective disturbance (SUD) scores.

66

Research issues with Saccadic EM and tracking EM

- Both normal subjects and patients receiving EMDR therapy display a certain number of catch-up saccades when attempting to engage in smooth pursuit tracking eye movements.
- Patients receiving EMDR therapy display greater difficulty in maintaining smooth pursuit eye movements early in the session and display some catch-up saccadic eye movements.
- As the session progresses and reported level of SUD decreases, these saccadic eye movements appear less frequently (Kapoula, Yang, Bonnet, Bourtoire, & Sandretto, 2010).
- Therefore, patients receiving EMDR therapy with smooth pursuit tracking eye movements are also engaged in saccadic eye movements, which cross the midline.

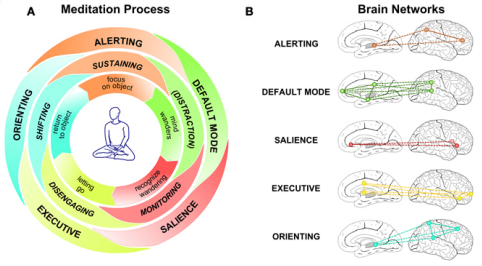
67

Summary of inter- and intra-hemispheric EM research

- Horizontal EM
  - May increase episodic memory retrieval by promoting interhemispheric and/or intrahemispheric interaction and
  - May increase attentional control processes by enhancing functioning in the anterior cingulate and the PFC,
    - leading to increased mindfulness and metacognitive awareness.
- See reviews in Jeffries and Davis (2012); Parker, Parkin, and Dagnall (2013); Keller et al. (2014); and Yaggie et al. (2015).

68

Mindfulness, prefrontal attentional flexibility, and metacognitive awareness as a mechanism for the effects of EMDR therapy



69

Mindfulness, prefrontal attentional flexibility, metacognitive awareness

- Mindful awareness has a long tradition in Buddhist meditation practices (Goldstein, 1994; McMahan, 2008).
- Teasdale (1999) operationalized a cognitive model of *mindfulness* and proposed it as central to fostering ***emotional processing*** as originally described by Rachman (1980).
- Attentional flexibility and executive functioning are central to mindful noticing.
- Left frontoparietal areas are activated in mindfulness-based meditation (Raffone et al., 2007)

70

EMDR therapy instructions support mindfulness and "bare attention"

- The steps of the Assessment Phase alternate between
  - Evocative awareness of sensory, affective, and somatic perceptions mediated in the right hemisphere and
  - Evaluative and narrative processes mediated in the left hemisphere and prefrontal orbital cortex
  - This sequence helps ensure whole brain activation and helps set the stage for mindful awareness.
- Mindful awareness and free association are fostered by specific instructions given
  - In the Preparation Phase – the train metaphor
  - Before each EMDR therapy session – "*sometimes things will change and sometimes they will not, just notice without judging…*"
  - Between sets of bilateral eye movements – "*notice that and continue*"
- These instructions support
  - the state of "mindful experience/being" described by Teasdale (1999)
  - encourage the state of mindful awareness known as "bare attention" (Goldstein, 1994)

71

Brain structures associated with mindfulness, attentional flexibility, metacognitive awareness

- The dorsolateral prefrontal cortex (DLPFC)
  - Verbal fluency, ability to maintain and shift set, planning, response inhibition, working memory, organizational skills, reasoning, problem solving and abstract thinking
- The anterior cingulate cortex (ACC)
  - Emotional drives, integration, inhibition of inappropriate responses, decision making
- The orbitofrontal cortex (OFC)
  - Impulse control, maintenance of set, monitoring socially appropriate behaviors, evaluating subjective emotional experiences.

72

ACC/PFC coupling model and Two-stage cortical coherence models

- Neurobiological studies show that the bilateral eye movements employed in EMDR therapy directly contribute to improvements in attentional flexibility and executive functioning, which are central to mindful noticing.
- Keller, Stevens, Lui, Murray, and Yaggie (2014, p. 114) refer to this as the
  - Amygdala-anterior cingulate (ACC)/prefrontal cortical (PFC) coupling model
- Yaggie et al. (2015) expanded the ACC/PFC to
  - A two-stage cortical coherence model for EMDR
  - suggesting an integrative, multi-stage, multi-phase model
  - with preliminary data
  - parallel to the TCB model of Lanius and Bergmann (2014)

73

Research shows bilateral EM enhances executive function

- Edlin and Lyle (2013) studied undergraduates exposed to 30-second sets of bilateral eye movements
- "*The simple act of repeatedly looking left and right can **enhance subsequent cognition**, including **divergent thinking**, detection of matching letters from visual arrays, and **memory retrieval**. . . . These findings suggest that saccades are an effective means of **improving attentional control**. Of greater theoretical importance, the study establishes attentional enhancement as a potential mechanism by which saccades enhance other aspects of cognition.*" (p. 345)
- They found that "*saccades increased the operation of the executive function network, which encompasses attentional control*" (p. 349).

74

SPECT: EMDR therapy normalizes function in the ACC and PFC

- Levin et al. (1999) reported on a single case SPECT study
  - SPECT images showed normalization of activity in both
    - the anterior cingulate gyrus and
    - the left frontal lobe
  - These changes were corroborated by Rorschach data, which showed
    - Decreases in the Hypervigilance Index, and
    - Increases in available ego resources as measured by the Experience Actual variable (p. 159)

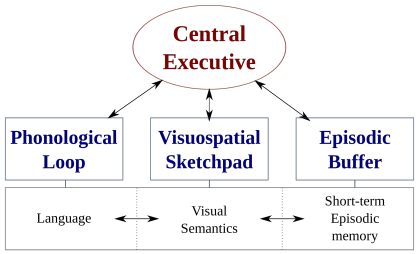
75

NIRS: EMDR therapy normalizes function in the PFC

- Ohtani et al. (2009) used near-infrared spectroscopy (NIRS)
  - 13 patients with PTSD received EMDR treatment over the course of several weeks
  - They found direct correlations between
    - the degree of clinical improvement as assessed with the clinician-administered PTSD scale (Blake et al., 1995)
    - and reductions in over activity in the lateral PFC.

76

Working memory model



77

Elements of the working memory model

- The working memory model describes a central executive and three subsystem "buffers" where the central executive can hold information for later use.
  - The phonological loop stores verbal and auditory information.
  - The visuospatial sketchpad (VSSP) stores visuospatial information.
    - (Baddeley, 1986, 2000; Baddeley & Hitch, 1974)
  - The episodic buffer links information across domains to form integrated units of visual, spatial, and verbal information with time sequencing (or chronological ordering), such as the memory of a story or a movie scene.
    - (Baddeley, 2000)
- These are short term memory systems.

78

Taxing limited working memory resources

- Andrade, Kavanagh, and Baddeley (1997) suggested that during EMDR reprocessing sessions, memories are held in the VSSP, and that the disturbing images become less vivid when eye movements make use of the limited processing resources in the VSSP.
- "…working memory becomes less efficient when doing two tasks at once. Thus benefits occur when the client is forced to divide their attention between the traumatic memory and another competing task.

  Jeffries and Davis (2012, p. 8)

79

Are EM more more taxing than other modes of BL stimulation?

- From the perspective of WM theorists,
  - BL EM include both a visual and a spatial component
  - BL taping and auditory tasks only have a spatial component.
- Andrade et al. (1997) and Kavanagh, Freese, Andrade, and May (2001) proposed that EMs may be more effective (i.e., more taxing on the central executive) than other dual-attention tasks.
- This was tested by Van den Hout, Muris, Salemink, and Kindt (2001) who replicated Andrade et al.'s (1997) working memory experiment with longer dual attention tasks.
  - EMs reduced vividness of memories; tapping did not.
  - However they used a less taxing form of taping than Andrade et al.

80

Is BL stimulation more effective when it matches the modality of the memory?

- Lilley, Andrade, Turpin, Sabin-Farrell, and Holmes (2009) suggested working memory effects might be most effective if they match the modality of the trauma memory
  - bilateral sounds might better disrupt disturbing auditory memory
- However, research by Kristjánsdóttir and Lee (2011) found that EM led to greater decrease in vividness than listening to counting irrespective of the modality of the memory
  - supporting a role for the working memory hypothesis
  - but not for mode-specific effects.

81

WM versus inter-hemispheric communication

- Gunter and Bodner (2008) tested the WM hypothesis against
  - The investigatory reflex and
  - Inter-hemispheric communication (IHC).
- They concluded their experiments provided more support for a WM hypothesis than either the investigatory reflex or the IHC hypotheses
- However
  - They used non-clinical subjects
  - They did not replicate standard EMDR therapy procedures.
    - For example, in the investigatory response test, they had subjects engage in EM while not holding their disturbing memory in mind during bilateral EM.
    - Instead they asked subjects to access the target memory only after engaging in bilateral EM.

82

What speed is best?

- While holding a disturbing memory in mind, Maxfield, Melynk, and Hayman (2008) asked nonclinical subjects to engage in no EMs, slow EMs, or fast EMs.
- They found
  - Larger decreases in vividness and emotional intensity of disturbing memories from both slow and fast EMs than from no EMs
  - Larger decreases from fast EMs than slow EMs.
- They suggested this was due to fast EMs being harder to perform than slow EMs and therefore more taxing on the VSSP.
- Van Veen et al. (2015) also showed fast EM had a significantly stronger effect on vividness and emotionality of disturbing autobiographical memories than either slow EM or no EM.

83

Fast enough but not too fast

- Research by Maxfield (2004) and by Becker et al. (1998) showed that eye movements need to be sufficiently distracting by being fast enough to disrupt the VSSP without being too fast.
- We should keep in mind that other neurological mechanisms examined in this presentation could account independently and/or concurrently for speed specific effects.

84

WM and reaction times

- Van den Hout et al. (2010a) studied both reaction times and vividness of negative memories in healthy volunteers in response to EM and to auditory beeps.
  - EM slowed reaction times to auditory tasks
  - beeps did not slow reaction times to visual tasks.
- Both EM and beeps decreased vividness of negative memories, but the effect was larger for EM.

85

Mode preferences versus effectiveness of BL stimulation

- De Jongh, Ernst, Marques, and Hornsveld (2013) studied individuals with PTSD and other disorders
  - Tones were less effective than EM in diminishing the emotionality of disturbing autobiographical memories.
  - Paradoxically, they noted that 64% of subjects preferred to continue the study with tones.

86

Time course changes in vividness and emotionality - 1

- Unpleasant autobiographical memories in healthy subjects were studied in both EM and eye stationary (ES) conditions.
- Compared to the ES condition, EM led to
  - decreased vividness within 2 seconds; emotionality began to decrease only after 74 seconds.
- Smeets, Dijs, Pervan, Engelhard, and van den Hout (2012, p. 355) suggest "The finding that emotionality reductions lag behind those of vividness implies a causal relation"
- But acknowledge "an appropriate evaluation of such a causal relation would require an experimental approach."

87

Time course changes in vividness and emotionality - 2

- However in a more recent WM study by van Veen et al. (2015)
  - image vividness did not correlate with observed decrease of emotionality over time,
  - inconsistent with the Smeets et al. experimental prediction, and
  - not supporting the earlier finding of Smeets et al. (2012).
  - Van Veen et al. did find that fast EM led to less emotional, less vivid, and more difficult to retrieve images than did slow EM.
- Although it is possible that a WM effect on vividness of visual images could causally lead to decreases in emotionality, the van Veen et al. finding make this less likely.
- It is equally plausible that other mechanisms (such as the OR and others discussed in this presentation) lead to decreases in emotionality by independent pathways.

88

A significant role for the working memory hypothesis

- A growing body of laboratory research by Andrade et al. (1997), Gunter and Bodner (2008), van den Hout et al. (2001), and others demonstrates that elements of the working memory hypothesis contribute to EMDR therapy treatment effects.
- Phenomenologically, patients treated with EMDR therapy routinely report difficulty in maintaining all the elements of the selected target memory in mind during bilateral eye movements, and that the sensory aspects of their memories become less vivid.

89

Support for multiple mechanisms in addition to WM

- Multiple laboratory studies including Christman et al. (2003); Christman and Propper (2001); Lyle and Jacobs (2010); and Propper and Christman (2008) among others discussed previously, found that EM enhance recall of autobiographical memories.
  - Note the intriguing title of Lyle and Jacobs (2010) article: Is saccade-induced retrieval enhancement a potential means of improving eyewitness evidence?
- Nieuwenhuis et al. (2013) found that bilateral saccadic EM and tactile stimulation, but not auditory stimulation, enhanced memory retrieval.
- They concluded, "it is unclear how this working- memory account can explain the beneficial effect of horizontal eye movements on normal memory retrieval."

90

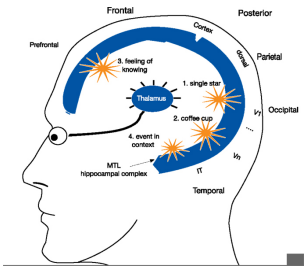
Limitations of existing WM studies

- Nearly all of the research on the working memory hypothesis uses
  - (a) subjects who do not meet the criteria for PTSD,
  - (b) conditions that do not fully match those used in the standard EMDR therapy protocol, and
  - (c) designs that do not explicitly rule out the contributions of other mechanisms,
- the existing working memory studies fail to resolve the degree to which alternate mechanisms contribute to EMDR treatment effects.

91

Information processing via temporal binding:

The effects of EMDR therapy on thalamic function

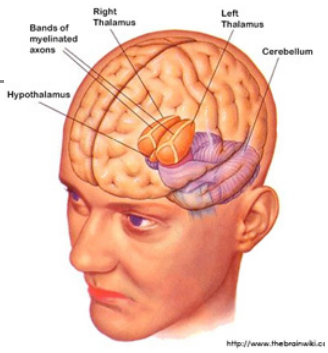


92

The central role of the thalamus in sensory integration and consciousness

A major relay center capable of synchronizing neural structures throughout the brain

- The thalamus consists of a pair of bilateral brain structures near the center of the brain, just above the brain stem.
- It is reciprocally interconnected with many areas of the brain.



93

The thalamocortical binding hypothesis (TCB)

Lanius and Bergmann (2014)

- Alternating bilateral sensory stimulation plays an important role in AIP
  - By directly affecting thalamic activity
  - By modulating oscillatory activity in the brain and
  - Contributing to the synchronization of dynamic neuronal networks across multiple brain subsystems

See foundational material in Joliot, Ribary and Llinás (1994)

94

Lanius and Bergmann (2014)

Top-down, bottom-up, back-front integration

- "The thalamus is not only a relay station mediating both top-down (information from the cortex) as well as bottom-up processing (information from the brain stem; afferent input to the cortex), but it is also involved in integration of information.
- It is reciprocally interconnected with the PFC, the basal ganglia, the somatosensory cortex, the association areas, the auditory cortex, the visual cortex, the motor cortex, the cerebellum, brainstem, and limbic structures." (p. 218)

95

Lanius and Bergmann (2014)

The synchronization of dynamic neuronal networks across multiple brain subsystems

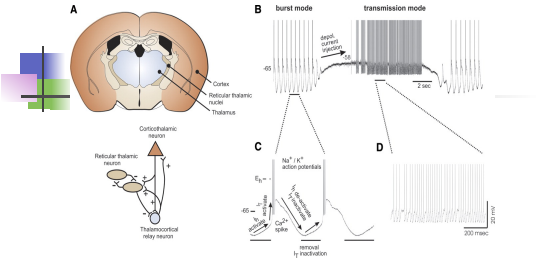
- "This is referred to as temporal binding. This process conjoins the fractured aspects of internal and external reality in the time domain, counteracting the effects of dissociation. This process not only affects hemispheric laterality but also memorial, somatosensory, emotional, and cognitive integration." (p. 217)

96

Overwhelming experiences lead to hyperpolarization in the thalamus

- Aversive experiences lead to excess sympathetic arousal
  - via excess release of dopamine, nor-epinephrine, and epinephrine.
- With insufficient relational engagement and insufficient tone in the phylogenically newer ventral vagal system (found in mammals)
- Inhibitory neurotransmitters are released
  - (endogenous opioids and endogenous cannabinoids)
- This triggers the older, more primitive dorsovagal system that counteracts the excess sympathetic arousal.
- Simultaneous excess sympathetic combined with dorsovagal parasympathetic arousal lead to
  - Hyperpolarization of the thalamus and
  - An effective disconnection (dissociation) among critical cortical areas involved in the sensory processing of the overwhelming experience.

97



Thalamocortical neurons fire in two distinct firing modes called transmission mode and burst mode

Transmission mode: During wakefulness and REM sleep, thalamocortical neurons are depolarized by afferent inputs and switch to the transmission or "single spike" mode in which information is gated through the thalamus and forwarded to the cortex.

Burst mode: During non-REM sleep and epileptic discharges thalamic networks display a monotonous repetitive firing pattern at hyperpolarized membrane potentials. Thalamocortical neurons enter the burst mode and decrease transfer of sensory information to the cortex.

Biel, et al. (2009)

98

Reversing the dissociation of thalamocortical dysrhythmia

- "deactivation of specific thalamic nuclei by increased arousal interferes with the integration of sensory components of an experience into an integrated memory" leading to the dissociation of memory elements."

  Lanius and Bergmann (2014, p. 214)

- This failure of integration is known as thalamocortical dysrhythmia (TCD)
- Llinás and Ribary (2001) suggested TCD may underlie many neurological and psychiatric conditions.
- A therapy process that corrects and reverses TCD would be applicable to a range of conditions (not merely PTSD).

99

Sensory stimuli produce phase locking and temporal binding

- "In alert subjects continuous 40-Hz oscillations can be recorded over large areas of the surface of the head… not in phase.. but [with] a 12- to 13—msec phase shift between the rostral and caudal parts of the brain…
- On presentation of sensory stimuli, the oscillations show phase locking which is proposed to be related to cognitive processing and to the temporal binding of sensory stimuli."

Llinás and Pare (1996, p. 9)

100

Restoring temporal binding and thalamocortical dialogue

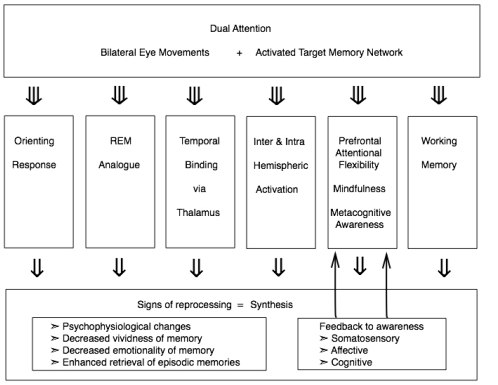
- Lanius and Bergmann (2014) propose that the alternating bilateral stimulation used in EMDR therapy reverses the deactivation of thalamic nuclei.
- "We hypothesize that this process is at the basis of information processing and a sense of self." (p. 228)
  - See discussion in Engel and Singer (2001).

101

The thalamocortical binding hypothesis

- Provides a neurobiological foundation for Shapiro's (1995, 2001) physiologically based AIP model
- Is consistent with Shapiro's (1995, 2001) proposal that visual, auditory, and tactile BLS can all be effective modalities (Servan-Schreiber, Schooler, Dew, Carter, & Bartone, 2006)
- Is parallel to and may serve as an integrative framework for other neurobiological models
  - TCB is consistent with the OR, prefrontal (mindfulness) and the inter- and intra-hemispheric hypotheses (as well as top-down, bottom-up, and front-back) models of neural integration.
- When TCD brain rhythms are reset, they led to synthesis, integration, and mindful noticing.
- Both laboratory and clinical studies are needed to demonstrate that BL sensory stimulation enhance TCD in human subjects.

102



103

Summary

- Rather than a single mechanism, a review of the literature leads to a proposal for a comprehensive framework of six hypothesized mechanisms of action for EMDR therapy that together yield multiplex effects.
- These different mechanisms of action sometimes converge and sometimes diverge, leading to various outcomes in different clinical contexts and in different EMDR procedures.

104

Example- divergent responses due to moderator – structural dissociation

- In simple PTSD (primary structural dissociation), bilateral EM (reprocessing) can lead to:
  - Initially increased retrieval of maladaptive memory (inter-, intra-hemispheric; thalamocortical binding: TCB) and briefly increased subjective disturbance,
  - Quickly followed by a de-arousal response (OR, REM) and disruption of memory vividness (WM)
  - A new perspective on the memory and self (PFC, metacognitive awareness, TCB).
- In (unrecognized and unprepared) secondary and tertiary structural dissociation, bilateral EM (reprocessing) can lead to:
  - Increased associative processes (inter-, intra-hemispheric; thalamocortical binding)
  - Breaching primitive dissociative defenses and
  - Triggering metacognitive awareness of conflicted self-states
  - This quickly overwhelms the current integrative capacities of the patient
  - Leading to emergence of a defensive action system (ranging from shutdown, to flight urges, to an anger state)
  - Subsequent decompensation in the patient
- See Bae, Kim and Park (2015); Gonzalez and Mosquera (2012); Lanius, Paulsen and Corrigan (2014).

105

Future directions

- Laboratory and clinical research have identified multiple potential mechanisms.
- Some past research has been organized around attempts to demonstrate the superiority of one theory of mechanism over others using overly reductionistic interpretations of data.
- The full breadth of the data supports the existence of converging and diverging multiplex effects of the bilateral stimulation used in EMDR therapy.
- Future research should be directed toward exploring the diverse, multiplex nature of responses to EMDR therapy and laboratory bilateral stimulation procedures taking into account moderator variables such as age (child or adult) and presence or absence of rigid personality or dissociative defenses.

106

Specific future research

- Yaggie, et al. (2015) should be replicated as they recommended with
  - Larger sample size
  - Males and females carefully lateralized for handedness
  - With denser EEG electrode arrays or with MEG
  - Using clinical populations with severe trauma experiences
  - Comparing all three types of bilateral stimulation
  - Examining inter- and intra-hemispheric interactions
  - Incorporating all essential components of standard EMDR reprocessing
  - With EEG or MEG and memory vividness and valence measures at multiple time points in the process, including before and after free association processing

107

thank you!

108

Mediators, mechanisms and moderators of action for EMDR therapy: A review of multiplex effects in modes of bilateral stimulation

Andrew M. Leeds, Ph.D.

References

Alvarez, J. A., & Emory, E. (2006). Executive function and the frontal lobes: A meta-analytic review. *Neuropsychology Review*, *16*(1), 17-42. doi:10.1007/s11065-006-9002-x

Andrade, J., Kavanagh, D., & Baddeley, A. (1997). Eye-movements and visual imagery: A working memory approach to the treatment of post-traumatic stress disorder. *British Journal of Clinical Psychology, 36*, 209–223.

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

Armstrong, N., & Vaughan, K. (1994, June). *An orienting response model for EMDR*. Paper presented at the meeting of the New South Wales Behaviour Therapy Interest Group, Sydney, Australia.

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, 51-56.

Baddeley, A. D. (1986). *Working memory*. Oxford, UK: Oxford University Press.

Baddeley, A. (2000). The episodic buffer: A new component of working memory? *Trends in Cognitive Sciences*, *4*(11), 417-423.

Baddeley, A. D., & Hitch, G. J. (1974). Working memory. In G. A. Bower (Ed.), *The psychology of learning and motivation* (pp. 47–89). New York, NY: Academic Press.

Bae, H., Kim, D., & Park, Y. C. (2015). Dissociation predicts treatment response in eye movement desensitization and reprocessing (EMDR) for post-traumatic stress disorder. Journal of Trauma & Dissociation : The Official Journal of the International Society for the Study of Dissociation (ISSD), 17(1), 112-130. doi:10.1080/15299732.2015.1037039

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*, 325–345.

Barrowcliff, A. L., Gray, N. S., MacCulloch, S., Freeman, T. C., & MacCulloch, M. J. (2003). Horizontal rhythmical eye movements consistently diminish the arousal provoked by auditory stimuli. *British Journal of Clinical Psychology, 42*(Pt. 3), 289–302.

Barrowcliff, A. L., MacCulloch, M. J., & Gray, N. S. (2001). *The de-arousal model of eye movement desensitization and reprocessing (EMDR), Part III: Psychophysiological and psychological concomitants of change in the treatment of post-traumatic stress disorder (PTSD) and their relation to the EMDR protocol*. Paper presented at the EMDR Europe 2nd Annual Conference on EMDR Innovations in Theory and Practice, London, UK.

Barrowcliff, A. L., MacCulloch, M. J., Gray, N. S., MacCulloch, S., & Freeman, T. C. A. (2001). *The de- arousal model of eye movement desensitization and reprocessing (EMDR), Part II: An investigation of the mechanisms underlying treatment effects in EMDR*. Paper presented at the EMDR Europe 2nd Annual Conference on EMDR Innovations in Theory and Practice, London, UK.

Becker, L., Todd-Overmann, T., Stoothoff, W., & Lawson, P. (1998). *Ironic memory, PTSD and EMDR: Do eye movements hinder the avoidance process leading to greater accessibility of traumatic memories?* Paper presented at the EMDRIA Annual Conference, Baltimore, MD.

Biel, M., Wahl-Schott, C., Michalakis, S., & Zong, X. (2009). Hyperpolarization-Activated cation channels: From genes to function. *Physiological Reviews*, *89*(3), 847-885. doi:10.1152/physrev.00029.2008

Blake, D. D., Weathers, F. W., Nagy, L. M., Kaloupek, D. G., Gusman, F. D., Charney, D. S., & Keane, T. M. (1995). The development of a clinician-administered PTSD scale. *Journal of Traumatic Stress, 8*(1), 75–90.

Chang, H. K., Kim, K. H., Kang, K. W., Kang, Y. J., Kim, T. W., Park, H. K., . . . Kim, C. J. (2015). Antidepressants modulate glycine action in rat hippocampus. *Journal of Exercise Rehabilitation*, *11*(6), 311-9. doi:10.12965/jer.150263

Christman, S. D., Garvey, K. J., Propper, R. E., & Phaneuf, K. A. (2003). Bilateral eye movements enhance the retrieval of episodic memories. *Neuropsychology, 17*(2), 221–229.

Christman, S. D., & Propper, R. E. (2001). Superior episodic memory is associated with interhemispheric processing. *Neuropsychology, 15*, 607–616.

Christman, S. D., Propper, R. E., & Brown, T. J. (2006). Increased interhemispheric interaction is associated with earlier offset of childhood amnesia. *Neuropsychology*, *20*(3), 336-345. doi:10.1037/0894-4105.20.3.336

Compton, R. J., & Mintzer, D. A. (2001). Effects of worry and evaluation stress on interhemispheric interaction. *Neuropsychology, 15*, 427–43

de Jongh, A., Ernst, R., Marques, L., & Hornsveld, H. (2013). The impact of eye movements and tones on disturbing memories involving PTSD and other mental disorders. *Journal of Behavior Therapy and Experimental Psychiatry, 44*(4), 477–483. doi:10.1016/j.jbtep.2013.07.002

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

Engel, A. K., & Singer, W. (2001). Temporal binding and the neural correlates of sensory awareness. Trends in Cognitive Sciences, 5(1), 16– 25.

Goldstein, J. (1994). *Insight meditation: The practice of freedom*. Boston, MA: Shambhala Publications.

International Society for the Study of Trauma and Dissociation. (2011). Guidelines for treating dissociative disorder in adults, third revision. *Journal of Trauma & Dissociation, 12*(2), 115–187.

Jeffries, F. W., & Davis, P. (2012). What is the role of eye movements in eye movement desensitization and reprocessing (EMDR) for post-traumatic stress disorder (PTSD)? A review. *Behavioural and Cognitive Psychotherapy*, *41*(3), 1-11. doi:10.1017/S1352465812000793

Joliot, M., Ribary, U., & Llinás, R. (1994). Human oscillatory brain activity near 40 hz coexists with cognitive temporal binding. *Proceedings of the National Academy of Sciences of the United States of America*, *91*(24), 11748-51.

Kapoula, Z., Yang, Q., Bonnet, A., Bourtoire, P., & Sandretto, J. (2010). EMDR effects on pursuit eye move- ments. *PLoS ONE, 5*(5), e10762. doi:10.1371/journal.pone.0010762

Kavanagh, D. J., Freese, S., Andrade, J., & May, J. (2001). Effects of visuospatial tasks on desensitization to emotive memories. *British Journal of Clinical Psychology, 40*(Pt. 3), 267–280.

Kazdin, A. E. (2007). Mediators and mechanisms of change in psychotherapy research. *Annual Review of Clinical Psychology*, *3*, 1-27. doi:10.1146/annurev.clinpsy.3.022806.091432

Keller, B., Stevens, L., Lui, C., Murray, J., & Yaggie, M. (2014). The effects of bilateral eye movements on EEG coherence when recalling a pleasant memory. *Journal of EMDR Practice and Research*, *8*(3), 113-128. doi:10.1891/1933-3196.8.3.113

Knipe, J. (2014). An adaptive information processing model for treating psychological defenses. In *EMDR toolbox: Theory and treatment of complex PTSD and dissociation* (pp. 39-58). New York: Springer Publishing Company.

Kristjánsdóttir, K., & Lee, C. W. (2011). A comparison of visual versus auditory concurrent tasks on reduc- ing the distress and vividness of aversive autobiographical memories. *Journal of EMDR Practice and Research, 5*(2), 34–41. doi:10.1891/1933-3196.5.2.34

Lanius, U. F., & Bergmann, U. (2014). Dissociation, EMDR, and adaptive information processing: The role of sensory stimulation and sensory awareness. In U. F. Lanius, S. L. Paulsen, & F. M. Corrigan (Eds.), *Neurobiology and treatment of traumatic dissociation: Towards an embodied self* (pp. 213–242). New York, NY: Springer.

Lanius, U. F., Paulsen, S. L., & Corrigan, F. M. (2014). *Neurobiology and treatment of traumatic dissociation: Towards an embodied self*. New York: Springer Publishing Company.

Lansing, K. M., Amen, G. G., & Klindt, W. C. (2000, November). *Tracking the neurological impact of CBT and EMDR in the treatment of PTSD*. Paper presented at the Annual Meeting of the Association for the Advancement for Behavior Therapy, New Orleans, LA.

Lansing, K., Amen, D. G., Hanks, C., & Rudy, L. (2005). High-resolution brain SPECT imaging and eye movement desensitization and reprocessing in police officers with PTSD. *The Journal of Neuropsychiatry and Clinical Neurosciences, 17*(4), 526–532.

Lee, C. W., & Drummond, P. D. (2008). Effects of eye movement versus therapist instructions on the processing of distressing memories. *Journal of Anxiety Disorders*, 22, 801-808.

Leher, J. (2011) How does Prozac work? Wired. http://www.wired.com/2011/11/how-does-prozac-work/

Levin, P., Lazrove, S., & van der Kolk, B. (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(1–2), 159–172.

Lilley, S. A., Andrade, J., Turpin, G., Sabin-Farrell, R., & Holmes, E. A. (2009). Visuospatial working memory interference with recollections of trauma. *British Journal of Clinical Psychology, 48*(3), 309–321.

Llinás, R. R., & Pare, D. (1996). The brain as a closed system modulated by the senses. In R. Llinás & P. Churchland (Eds.), The mind-brain continuum (pp. 1– 18). Cambridge, MA: MIT Press.

Llinás, R., & Ribary, U. (2001). Consciousness and the brain. The thalamocortical dialogue in health and disease. *Annals of the New York Academy of Sciences*, 929, 166–175.

Lipke, H. (1992). *Manual for the teaching of Shapiro's EMDR in the treatment of combat-related PTSD*. Pacific Grove, CA: EMDR Institute.

Lipke, H. (1995). EMDR clinician survey. In F. Shapiro (Ed.), *Eye movement desensitization and reprocessing, basic principles, protocols and procedures* (1st ed., pp. 376–386). New York, NY: The Guilford Press.

Lipke, H. (1999). *EMDR and psychotherapy integration: Theoretical and clinical suggestions with focus on traumatic stress*. Boca Raton, FL: CRC Press.

Lyle, K. B., & Martin, J. M. (2010). Bilateral saccades increase intrahemispheric processing but not inter- hemispheric interaction: Implications for saccade-induced retrieval enhancement. *Brain and Cognition, 73*(2), 128–134. doi:/10.1016/j.bandc.2010.04.004

Lyle, K. B., & Jacobs, N. E. (2010). Is saccade-induced retrieval enhancement a potential means of improving eyewitness evidence? *Memory, 18*(6), 581–594. doi:10.1080/09658211.2010.493891

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

Maxfield, L. J. (2004). A working memory analysis of the dual attention component of eye movement desensitization and reprocessing (Doctoral dissertation, Lakehead University). Dissertation Abstracts International, 64(10-B).

Maxfield, L., Melnyk, W. T., & Hayman, G. C. A. (2008). A working memory explanation for the effects of eye movements in EMDR. *Journal of EMDR Practice and Research*, *2*(4), 247–261. doi:10.1891/1933-3196.2.4.247

McMahan, D. L. (2008). *The making of Buddhist modernism*. Oxford, UK; New York, NY: Oxford University Press.

Mosquera, D., & Knipe, J. (2015). Understanding and treating narcissism with EMDR therapy. *Journal of EMDR Practice and Research*, *9*(1), 46-63. doi:10.1891/1933-3196.9.1.46

Gonzalez, A., & Mosquera, D. (2012). *EMDR and dissociation: The progressive approach*. Charleston, SC: Amazon Imprint.

Nicosia, G. (1994, March). *A mechanism for dissociation suggested by the quantitative analysis of electroencephalograpy*. Paper presented at the International EMDR Annual Conference, Sunnyvale, CA.

Nieuwenhuis, S., Elzinga, B. M., Ras, P. H., Berends, F., Duijs, P., Samara, Z., & Slagter, H. A. (2013). Bilateral saccadic eye movements and tactile stimulation, but not auditory stimulation, enhance memory retrieval. *Brain and Cognition, 81*(1), 52–56. doi:10.1016/j.bandc.2012.10.003

Oh, D.-H., & Choi, J. (2004). Changes in the regional cerebral perfusion after eye movement desensitization and reprocessing: A SPECT study of two cases. *Korean Journal of Biological Psychiatry*, 11(2), 173–180.

Ohtani, T., Matsuo, K., Kasai, K., Kato, T., & Kato, N. (2009). Hemodynamic responses of eye movement desensitization and reprocessing in posttraumatic stress disorder. *Neuroscience Research, 65*(4), 375–383. doi:10.1016/j.neures.2009.08.014

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

Pagani, M., Hogberg, G., Fernandez, I., & Siracusano, A. (2013). Correlates of EMDR therapy in functional and structural neuroimaging: A critical summary of recent findings. *Journal of EMDR Practice and Research*, *7*(1), 29-38. doi:10.1891/1933-3196.7.1.29

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

Paulsen, S. (1995). Eye movement desensitization and reprocessing: Its cautious use in the dissociative disorders. *Dissociation*, *8*(1), 32-44.

Pavlov, I. P. (1927). *Conditioned reflexes: An investigation of the physiological activity of the cerebral cortex*. New York, NY: Dover Publications, Ind.

Propper, R. E., & Christman, S. D. (2008). Interhemispheric interaction and saccadic horizontal eye movements implications for episodic memory, EMDR, and PTSD. *Journal of EMDR Practice and Research, 2*(4), 269–281. doi:10.1891/1933-3196.2.4.269

Propper, R. E., Pierce, J., Geisler, M. W., Christman, S. D., & Bellorado, N. (2007). Effect of bilateral eye movements on frontal interhemispheric gamma EEG coherence: Implications for EMDR therapy. *Journal of Nervous and Mental Disease, 195*(9), 785–788.

Purves, D., Augustine, G. J., Fitzpatrick, D., et al. (2001). *Neuroscience. 2nd edition. Types of eye movements and their functions*. Sunderland, MA: Sinauer Associates. Retrieved March 20, 2015, from http://www.ncbi.nlm.nih.gov/books/NBK10991

Rachman, S. (1980). Emotional processing. *Behaviour Research and Therapy*, *14*, 125-132.

Raffone, A., Manna, A., Perrucci, G. M., Ferretti, A., Del Gratta, C., Belardinelli, M. O., & Luca Romani, G. (2007). Neural correlates of mindfulness and concentration in buddhist monks: A fMRI study. *IEEE Xplore,* 242–244. doi:10.1109/NFSI-ICFBI.2007.4387740

Russell, M. C. (1992). *Towards a neuropsychological approach to PTSD: An integrative conceptualization of etiology and mechanisms of therapeutic change*. Unpublished doctoral dissertation, Pacific Graduate School of Psychology, Palo Alto, CA.

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, 15-23.

Sack, M., Lempa, W., Steinmetz, A., Lamprecht, F., & Hofmann, A. (2008). Alterations in autonomic tone during trauma exposure using eye movement Desensitisation. *Journal of Anxiety Disorders*, 22, 1264-1271.

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

Schubert, S. J., Lee, C. W., & Drummond, P. D. (2011). The efficacy and psychophysiological correlates of dual-attention tasks in eye movement desensitization and reprocessing (EMDR). *Journal of Anxiety Disorders*, 25(1), 1 - 11. doi:10.1016/j.janxdis.2010.06.024

Servan-Schreiber, D. (2000). POINT: Eye movement desensitization and reprocessing: Is psychiatry missing the point? *Psychiatric Times, 17*(7), 36–40.

Servan-Schreiber, D., Schooler, J., Dew, M. A., Carter, C., & Bartone, P. (2006). Eye movement desensitization and reprocessing for posttraumatic stress disorder: A pilot blinded, randomized study of stimulation type. *Psychotherapy and Psychosomatics, 75*(5), 290–297.

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

Shapiro, F. (1995). *Eye movement desensitization and reprocessing, basic principles, protocols and procedures*. New York: The Guilford Press.

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

Siegel, D. J. (2012). *The developing mind: How relationships and the brain interact to shape who we are* (2nd ed.). New York, NY: Guilford Press.

Snyder, J. S., Soumier, A., Brewer, M., Pickel, J., & Cameron, H. A. (2011). Adult hippocampal neurogenesis buffers stress responses and depressive behaviour. *Nature*, *476*(7361), 458-61. doi:10.1038/nature10287

Sokolov, E. N. (1963). *Perception and the conditioned reflex* (S. W. Waydenfeld, Trans.). Pergamon Press, Oxford (Original work published 1958).

Sokolov, E. N. (1990). The orienting response, and future directions of its development. *Pavolovian Journal of Biological Sciences, 25*(3), 142–150.

Sondergaard, H. P., & Elofsson, U. (2008). Psychophysiological studies of EMDR. *Journal of EMDR Practice and Research*, *2*(4), 282–288. doi:10.1891/1933-3196.2.4.282

Teasdale, J. D. (1999). Emotional processing, three modes of mind and the prevention of relapse in depression. *Behaviour Research and Therapy*, *37 Suppl 1*, S53-77.

Tzan-Fu, S., Ching-Kuan, W., & Nien-Mu, C. (2004). Mindfulness meditation training combined with eye movement desensitization and reprocessing in psychotherapy of an elderly patient. *Chang Gung Medical Journal, 27*(6), 464–469.

van den Hout, M. A., Engelhard, I. M., Rijkeboer, M. M., Koekebakker, J., Hornsveld, H., Leer, A.,...Akse, N. (2010a). EMDR: Eye movements superior to beeps in taxing working memory and reducing vividness of recollections. *Behaviour Research and Therapy, 49*(2), 92–98. doi:10.1016/j.brat.2010.11.003

van den Hout, M. A., Engelhard, I. M., Smeets, M. A. M., Hornsveld, H., Hoogeveen, E., de Heer, E., . . . Rijke- boer, M. (2010b). Counting during recall: Taxing of working memory and reduced vividness and emotionality of negative memories. *Applied Cognitive Psychology, 24*(3), 303–311. doi:10.1002/acp.1677

van den Hout, M., & Engelhard, I. (2012). How does EMDR work? *Journal of Experimental Psychopathology*, *3*(5), 724-738. doi:10.5127/jep.028212

van den Hout, M., Muris, P., Salemink, E., & Kindt, M. (2001). Autobiographical memories become less vivid and emotional after eye movements. *British Journal of Clinical Psychology, 40*(Pt. 2), 121–130.

van Veen, S. C., van Schie, K., Wijngaards-de Meij, L. D., Littel, M., Engelhard, I. M., & van den Hout, M. A. (2015). Speed matters: Relationship between speed of eye movements and modification of aversive autobiographical memories. *Frontiers in Psychiatry/Frontiers Research Foundation, 6*, 45. doi:10.3389/ fpsyt.2015.00045

van Praag, H. (2008). Neurogenesis and exercise: Past and future directions. *Neuromolecular Medicine*, *10*(2), 128-40. doi:10.1007/s12017-008-8028-z

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

Yaggie, M., Stevens, L., Miller, S., Abbott, A., Woodruff, C., Getchis, M., . . . Daiss, S. (2015). Electroencephalography coherence, memory vividness, and emotional valence effects of bilateral eye movements during unpleasant memory recall and subsequent free association: Implications for eye movement desensitization and reprocessing. *Journal of EMDR Practice and Research, 9*(2), 78–97. doi:10.1891/1933-3196.9.2.78

Photo and Figure Credits

Slide 1 from https://www.coursera.org/course/brainspace

Slide 5 from https://www.newearth.media/wp-content/uploads/sites/9/2014/01/Silhouette_man_woman_2-300x172.png

Slide 6 from https://www.coursera.org/course/brainspace

Slide 9 from http://isc.jcu.cz/wp-content/uploads/seminarsdotusbdotacdotir.gif

Slide 15 from Pagani, Hogberg, Fernandez & Siracusano (2013).

Slide 18 from http://isc.jcu.cz/about-us/

Slide 24 from http://funkymangosmusings.blogspot.com/2011/04/ms-research-roundup-april-2011-part-1.html

Slide 32 from Leeds (2016, p. 30, Figure 2.6)

Slide 35 from Leeds (2016, p. 29, Figure 2.5)

Slide 52 from http://journal.frontiersin.org/article/10.3389/fnins.2013.00008/full

Slide 70 from http://journal.frontiersin.org/article/10.3389/fpsyg.2013.00200/full

Slide 78 from https://en.wikipedia.org/wiki/Baddeley%27s_model_of_working_memory

Slide 93 from http://www.frontiersin.org/files/Articles/40168/fpsyg-04-00200-HTML/image_m/fpsyg-04-00200-g001.jpg

Slide 94 from http://www.itg.kit.edu/img/Fig-1_human_thalamus_s.jpg

Slide 99 from Biel et al., (2009) http://physrev.physiology.org/content/89/3/847

Slide 104 from Leeds (2016, p. 29, Figure 2.5)