Amygdala Activity and Flashbacks in PTSD: A Review

Tania Storm*[1], Marianne Engberg[2] and Christian Balkenius[1]

[1]Lund University Cognitive Science
[2]DIGNITY – Danish Institute Against Torture

*stormtania@gmail.com

Reliving symptoms and intrusive recollections are core symptoms of Post-Traumatic Stress Disorder (PTSD), one of these symptoms is the flashback. Even though they appear in the PTSD diagnosis, the literature does not clearly define flashbacks. And, even though, flashbacks are well described in PTSD patients, the neuro-cognitive mechanisms underlying them are not well understood and few experimental reports exist on the workings of these memories. Amygdala is one of the brain structures repeatedly targeted in PTSD research due to its involvement in implicit and explicit emotional memory and fear learning. When viewed as an enhancer for survival-related stimuli, the amygdala could theoretically contribute to the generation of flashbacks in several ways. The amygdala modulates hippocampal activity, resulting in enhanced memory for specific details of emotional events of high arousal, it influences visual processing areas during encoding and later retrieval, leading to more vivid memories and, finally, it influences the prefrontal cortex during the stages of retrieval, resulting in a stronger and more vivid reconstruction of memories.

Keywords – memory; flashbacks; PTSD; Post-traumatic stress disorder; amygdala; reliving; emotion; reexperiencing

Introduction

The ICD-10 Classification of Mental and Behavioral Disorders (ICD-10) (WHO, 1992) and The Diagnostic and Statistical Manual of Mental Disorders (DSM-5)(APA, 2013) list persistent reliving/reexperiencing phenomena as one of the diagnostic criteria for Post-traumatic Stress Disorder (PTSD). As described in the manuals, the persistent reliving symptoms include a range of intrusions about the experienced trauma, one of these being the flashback. Flashbacks are accompanied by an intense and convincing 'nowness' (Hellawell and Brewin, 2002; Osuch et al., 2001), meaning that the individual perceives the memory as recurring in the present. The memories are involuntarily triggered, provoked by trauma reminders, often engaging several modalities (Hackmann et al. 2004), they are emotionally intense (Hellawell and Brewin 2002; Osuch et al., 2001) and often cause strong bodily reactions (Osuch et al., 2001).

Even though the flashback is central in the PTSD diagnosis, the literature does not clearly define flashbacks. And even though flashbacks are well described in PTSD patients, the neuro-cognitive mechanisms underlying them are not well understood and few experimental reports exist on the workings of these memories. Accordingly, it is unknown whether flashbacks share any traits with phenomena such as hallucinations and dissociations. The memory of the traumatic event has been suggested to maintain and reinforce the disorder of PTSD (Rubin et al., 2008). The question is why the ability to relive past events, generally considered an important component of episodic memory (Daselaar et al., 2008), in PTSD is amplified to a degree where reliving becomes pathological?

Intrusive trauma memories range from mildly distressing recollections to intense flashbacks. A qualitative ranking establishing the boundaries between the different degrees of intrusive memory has so far not been agreed upon. 'Flashback' is throughout this article defined as the reliving of a past experience, yet, as pertinently pinpointed by Berntsen (2009); *it is unclear exactly how much reliving is required for an ordinary intrusive memory to qualify for flashback* (Berntsen, 2009, p. 174). Intrusive trauma memories bring along a repertoire of sensory impressions from the past. Due to the traumatic nature of the memories, the intrusions are often escorted by a sense of current threat (Hackmann et al., 2004). Even though flashbacks are mostly related to PTSD (Brewin et al., 2010; Bryant 2010 et al., 2010) intrusive memories and nightmares, have been documented in patients suffering from other post-trauma disorders (i.e. depression, phobias and anxiety) (Bryant et al., 2010). Unrelated to trauma, distressing intrusions are found across a wide variety of psychological disorders (including depression, anxiety, obsessive compulsive disorder (OCD) and eating disorders) (Brewin et al., 2010). Flashbacks have the strength to interrupt a person's ongoing mental activity (de Silva and Marks, 1999) and may encompass a physiological response comparable to that of a panic attack (Osuch et al., 2001).

 © 2013 by the authors

Flashbacks (or intrusive trauma memories) have been proposed to rely on a *disintegration* from ordinary autobiographical memory (see e.g. Brewin et al., 2010; Brewin, 2005; Hackmann et al., 2004; Ehlers et al., 2002; Nadel and Jacobs, 1998; Brewin, Dalgleish and Joseph, 1996; van der Kolk and Fisler, 1995) as well as an *enhanced integration* into autobiographical memory (see e.g. Berntsen, 2009; Rubin et al., 2008; Rubin, 2005; Rubin et al., 2004; Berntsen et al., 2003). Whether any of these processes lay the ground for the intrusive flashbacks is yet to be clarified.

Research suggests that brain regions that are activated during encoding are reactivated when the memory is later retrieved (Danker and Anderson, 2010). In the case of PTSD this points to the possible involvement of brain structures such as the amygdala. The amygdala has been repeatedly targeted in the PTSD research and amygdalar hyperactivity has been proposed as one of the underlying neurological mechanisms of PTSD (Shin, 2009; Rainnie and Ressler, 2009), although such hyperactivity has not been consistently documented across studies (Liberzon and Garfinkel, 2009). The amygdala interacts with multiple memory systems and is active in both implicit and explicit memory domains, and well known for its participation in fear learning (Hamann, 2009). In particular, the structure has been associated with the enhancement of emotional memories (McGaugh, 2004; Dolcos et al., 2004). The extreme emotional intensity of the flashbacks in PTSD could point to an abnormality in the enhancement process – and the possibility of an increased facilitation of this process by amygdala. The aim of the current paper is to review the role of amygdala activity in regard to flashbacks.

Emotion, Memory and Amygdala

Stimuli that are emotionally arousing typically leave a more profound and persistent mark in memory than neutral stimuli (Brohawn et al., 2010; Kensinger, 2009; LaBar and Cabeza, 2006; Dolcos et al., 2005; Dolcos et al., 2004; McGaugh, 2004). In addition, the process of retrieving stored information about an emotional event frequently entails *reexperiencing the originally experienced emotional responses* (Hamann, 2009, p. 183), associating the memory with a heightened perception of vividness and confidence relative to a more emotionally neutral memory (Hamann, 2009; Phelps and Sharot, 2008). Whether memory for an emotional event is enhanced is related to the level of emotional arousal, not emotional valence (Hamann, 2009; LaBar and Cabeza, 2006; McGaugh, 2004). And, the degree of amygdala activation during encoding of an emotionally arousing stimulus has been shown to correlate exceedingly with subsequent recall, for aversive as well as attractive stimuli (McGaugh, 2004).

The amygdala is situated in the anteromedial temporal lobe (Adolphs, 2003) and is connected to a wide range of brain sites including: the sensory and entorhinal cortices, sensory thalamus, the hippocampus, the prefrontal cortex (PFC) and the sensory brainstem. From amygdala projections are sent to, for instance, the PFC, the hypothalamus and polymodal association cortex (LeDoux and Schiller, 2009, plate 2.5 and 2.8). The amygdala is the addressee of exceedingly processed sensory input from all modalities (Aggleton and Saunders, 2000), not least from the visual system (Freese and Amaral, 2009).

By influencing e.g. hormonal and autonomic functions the structure links sensory information with the modulation of the body's physiological state (Aggleton and Saunders, 2000). Via a wide range of structures, including the hippocampus and the PFC, amygdala links sensory input to cognitive processes (Adolphs, 2003) and through connections to cortical areas, the structure modulates memory and attention (LeDoux and Schiller, 2009). In turn, the medial PFC indirectly influences the activity of the amygdala through cortical executive control (LeDoux and Schiller, 2009). Aside from directly influencing the cortical functions, the amygdala modifies cognitive processing by mediating the release of neuromodulators like e.g. norepinephrine and dopamine (LeDoux and Schiller, 2009).

Encoding and Consolidation

According to the memory-modulation hypothesis (McGaugh, 2004), emotionally arousing experiences obtain their privileged status in memory due to amygdala's modulation of the activity in other brain regions during memory encoding and consolidation (Dolcos et al., 2004). The modulation is carried out by mediating the effects of stress hormones, as highly emotional events trigger the release of adrenal stress hormones - a process initiated by the amygdala via the hypothalamic-pituitary-adrenal axis (HPA-axis) resulting in a process of *neurohormonal memory modulation* (LaBar and Cabeza, 2006, p. 55 fig.1). The memory-modulation hypothesis proposes that *amygdala activity should be required for the enhanced long-term memory associated with emotional arousal* (Cahill, 2000, p. 431). Thus, the amygdala is thought to influence memory processes when a situation is adequately rich in emotional arousal (Cahill, 2000). The modulated regions include the hippocampus and parahippocampal areas (i.e. entorhinal, perihinal, and parahippocampal cortices) together with other sites in the medial temporal lobe (MTL) memory system (Dolcos et al., 2004).

The modulation hypothesis has been well confirmed in rat-studies (McGaugh, 2004) and, in particular, the basolateral complex of the amygdala (BLA) is considered a central site with regard to the modulation of emotional memory. Strong evidence for the memory-modulation hypothesis has also been found in studies of the human brain; e.g. in terms of a strong correlation between activity in the amygdala and the MTL memory structures during successful encoding of emotionally arousing, relative to neutral stimuli (Dol-

cos et al., 2004). Interactions between the amygdala and the hippocampal structures are thought to be essential in regard to the processes underlying emotional memory (Brohawn et al., 2010; Phelps, 2004) - specifically, efferent projections from the amygdala to the hippocampus (Brohawn et al., 2010). However, bidirectional interactions, in which the hippocampus modulates the activity of the amygdala, have also been suggested (Hamann, 2009; Phelps, 2004). Where the amygdala is involved in processing the emotional aspects of events (Phelps, 2004) and assignment of emotional importance to stimuli; the hippocampus is associated with explicit memory (Phelps, 2004) and with providing stimuli with contextual meaning (Brohawn et al., 2010). In the terminology of LeDoux (1999) this division is framed as emotional memories (implicit and amygdala-related) versus memories of emotion (explicit and hippocampal-related).

In favor of this partition, lesions to the amygdala have been shown to impair the implicit acquisition of conditioned fear, but not the mechanism related to fear expression and the explicit fear memory (Phelps, 2004; LaBar and Cabeza, 2006). On the contrary, studies of hippocampal lesions have shown the individual's inability to communicate the stimulus-relationship, while not affecting the ability to acquire conditioned fear (Phelps, 2004; LaBar and Cabeza, 2006).

Attention

Emotional arousal and amygdala activity have an adaptive function on memory, in the sense that attentional focus is limited to areas of relevancy for survival. In this manner what is encoded in memory is biologically salient gist information (i.e. few, but crucial details) (Hamann, 2009; Phelps and Sharot, 2008) applicable in future situations. By directing and narrowing attention to biologically salient information, the encoding of emotion-eliciting stimuli is enhanced (Phelps and Sharot, 2008). Some studies suggest that the enhancement of certain details has been more strongly associated with negative experiences than positive ones (Kensinger, 2009). Lesion studies point to a weakening of attention to emotional stimuli as a result of amygdala damage (Phelps, 2004), as well as an impairment of the memory for gist information of emotionally arousing events (Phelps and Sharot, 2008). Aside from strengthening the encoding and consolidation of memories for biologically salient stimuli the structure is involved with the subsequent retrieval.

Retrieval

In the retrieval of emotional memories, contributions from the amygdala have been suggested in regard to the subjective sense of recollection, as well as to the confidence in emotionally arousing memories (Hamann, 2009; Phelps and Sharot, 2008). In addition, the amygdala is believed to facilitate the retrieval of the affective information bound to the time of encoding (Hamann, 2009). This may be even more pronounced for negative than positive or neutral memories (Danker and Anderson, 2010). During the retrieval of emotional memories, many of the brain structures involved in the encoding processes are reactivated (Dolcos et al., 2005), and the remembrance process *involves literally returning to the brain state that was present during that episode* (Danker and Anderson, 2010, p. 87). Yet, during retrieval, the contributions of the different brain structures appear to be *associated more with enhancing the subjective experience of remembering and retrieval of affective characteristics present during encoding than with enhancing accurate retrieval* (Hamann, 2009, p.191). The enhanced recollection and re-experience of emotions associated with the original event during retrieval may, in part, be attributed to the reactivation of amygdala (Hamann, 2009). In fact, subjective ratings of emotional intensity during retrieval have been directly related to activation in temporal lobe structures, including the amygdala and hippocampus (Daselaar et al., 2008). Emotional memories bring along a strong sense of subjective recollection and confidence in their accuracy, even though the details of the memories are often erroneous and inaccurate (Phelps and Sharot, 2008; Kensinger, 2009; Hamann, 2009). Whereas emotional scenes have been shown to elicit activation in the amygdala; neutral scenes activate the posterior hippocampus (Phelps and Sharot, 2008). Accordingly, the subjective sense of recollection is believed to involve amygdala activation in regard to the retrieval of central aspects or details for emotional stimuli; and parahippocampal activation in relation to the retrieval of contextual details for neutral stimuli (Phelps and Sharot, 2008).

Box 1

Influences from Amygdala on Emotional Memory

Amygdala-related factors include:

- Enhanced encoding and consolidation of emotionally arousing memories
- Increased attention to and perception of survival-related aspects of the scene
- Enhanced encoding of gist information
- Facilitated retrieval of emotionally arousing memories
- Enhanced vividness and re-experience of emotions related to the original event
- Boosted confidence in the retrieved memory
- Intensification of the recollective experience

Even though emotion in general benefits memory, *long-lasting detrimental consequences are sometimes observed, particularly after severe or prolonged stress* (LaBar and Cabeza, 2006, p.54). This is the case in PTSD, where memories of exceedingly emotional events become intrusive and critically distressing (Brohawn et al., 2010). The involvement of the amygdala in the processes reviewed so far offer interesting aspects in regard to PTSD as the disorder arises from the exposure to an extremely emotionally stressful event. It is therefore interesting to explore how the amygdala-dependent mechanisms reviewed may be linked to flashbacks.As summarized in Box 1, the research reviewed indicates a relation between amygdala activity and some of the known features of flashbacks, for instance the high degree of vividness, strong sense of current threat, emphasis on certain details opposed to contextual details, lack of spatio-temporal information, distortion of subjective time, and confidence in the accuracy of the memory to an extent where it is believed to be happening in the present.

Amygdala and PTSD

The limbic structures (Liberzon et al., 1999) and, particularly, the amygdala, hippocampus and PFC (Rainnie and Ressler, 2009) have, due to their involvement in memory, stress, emotion and fear, continuously been addressed in the PTSD research. In this context several imaging studies have found amygdala activity in relation to PTSD symptom provocation (Liberzon and Garfinkel, 2009). PTSD studies have pointed to a positive correlation between amygdala activation and symptom severity, suggesting amygdalar hyperresponsitivity to trauma reminders as well as trauma-neutral stimuli (Shin et al., 2006; Shin 2009). However, findings of increased amygdala responsivity or involvement are not concordant across studies (Liberzon and Garfinkel, 2009) and exactly how the amygdala is involved in the PTSD pathology remains unclear.

Liberzon et al. (1999) found evidence of increased Regional Cerebral Blood Flow (rCBF) in the area of the left amygdala in individuals suffering from PTSD during exposure to traumatic stimuli. However, Liberzon et al. do note that the activation of the area of the amygdala could be a consequence of arousal and not the traumatic memory as such. Exaggerated amygdala activity has also been documented in the recall of negative relative to neutral pictures (Brohawn et al., 2010) and increased activity in both the amygdala and hippocampus during the construction of negative episodic memories, relative to positive memories, has been found in PTSD (St. Jacques et al., 2010).

The amygdala is exceedingly involved with fear conditioning (Dębiec and LeDoux, 2009) as well as fear extinction (Francati et al., 2007). It has been suggested that PTSD symptoms (such as hyperarousal and intrusive memories) result from alterations in the fear response system, in that safe stimuli are paired with the traumatic experience and thereby perceived as dangerous (Francati et al., 2007). This would support the notion that a dysfunction in the amygdala or any of the regions participating in the fear network (i.e. the medial PFC, the thalamic and sensory cortical areas, the hippocampus etc) may result in exaggerated response to neutral or weak conditioned stimuli (Rainnie and Ressler, 2009). The amygdala's role in mediating autonomic responses as well as in associating conditioned and unconditioned stimuli offers an obvious target for investigation.

PTSD has been hypothesized to develop as a consequence of the individual's failure to extinguish learned fear responses (Rogers et al., 2009; Koenigs and Grafman, 2009). This model might be too simplified and not capture all aspects of the disorder (Gilboa et al., 2004) yet some aspects of this representation may be useful. Targeting structural abnormality, a magnetic resonance imaging (MRI) study by Rogers et al. (2009) suggest a positive correlation between reduced density of the anterior cingulate cortex (ACC) (a medial PFC structure) and decreased left amygdala volume in PTSD. Both structures are associated with fear extinction (Rogers et al., 2009). It should be noted that acute and chronic stress exposure may have affect the structures differently. Whereas only one of the subjects was suffering from PTSD at the time of the study (the other eight had a PTSD history), all participants had been exposed to acute stress – chronic stress exposure has, on the contrary, been associated with an increase in amygdala volume (Rogers et al., 2009). And, more specifically, studies in rodents have associated the effects of chronic stress with increased density in the BLA of the amygdala – and only reticent changes after acute stress exposure (Roozendaal et al., 2009).

Functional imaging studies point to a dysregulation of emotional responses due to a decrease or hypoactivity of the PFC, combined with hyperactivity of the amygdala as one of the underlying mechanisms of PTSD (Koenigs and Grafman, 2009; Shin, 2009; Francati et al., 2007; Shin et al., 2006). The PFC is generally believed to regulate and inhibit the activity of the amygdala in regard to emotion regulation and fear extinction. Hypoactivity of the PFC would result in defective inhibition and thereby account for some of the characteristics of PTSD (Koenigs and Grafman, 2009). Even though imaging studies have supported this standpoint, in particular one lesion study suggest otherwise.

Koenigs et al. (2008) carried out a large study based on The Vietnam Head Injury Study (VHIS) - consisting of 193 combat veterans with lesions in different parts of the brain and 52 veterans with no brain injury but matched prevalence of PTSD. Isolated amygdala lesion

accounts for only 15 of cases; still, the results are interesting: prevalence of PTSD matched with amygdala lesion was 0%. Moreover, PTSD prevalence matched with ventromedial PFC (vmPFC) lesion (n=40) was 18% – considerably lower than in subjects with no brain damage (48%) or lesion in other brain sites (40%) (Koenigs et al., 2008, p. 234). The results indicate a causal relation between the development of

PTSD and the involvement of the vmPFC and amygdala. This study suggests that damage to the vmPFC, does not entail a higher prevalence of PTSD - even though its executive function is severely diminished.

Koenigs et al. (2008) suggest that the vmPFC has a causal role in PTSD, associated with self-reflective processes and the reactivation of emotional states of the past. In healthy individuals, the medial PFC is associated with emotion regulation as well as the experience of emotion as such (St. Jacques et al., 2010) and with the interpretation of the self-relatedness and contextualization of stimuli (Liberzon and Garfinkel, 2009). Contextualization refers to the evaluation of a situation and selection of appropriate response, and a deficit in these processes could underlie core aspects of PTSD (Liberzon and Garfinkel, 2009) – for example hypervigilance. Finally, and of outmost importance to our argument, the PFC is suggested a role in reliving (Daselaar et al.,2008).

The hypothesized hypofunction of the PFC combined with amygdalar hyperactivity in PTSD is challenged also by the outcome of a functional connectivity analysis by Gilboa et al. (2004). Results from the study indicate a correlation in the activity of the ACC and the amygdala during exposure to trauma scripts in PTSD. Greater co-activation of the amygdala and the vmPFC in PTSD during retrieval of emotionally negative episodic memories relative to positive or neutral memories has also been documented (St. Jacques et al. 2010), implying a particular enhancement of vivid re-experiencing of negative autobiographical memories. Finally, a lack of PFC influences on the visual cortex has been documented in PTSD patients exposed to trauma scripts, together with increased amygdala influences on these same visual processing areas (Gilboa et al., 2004). These processes may contribute to vivid re-experiencing phenomena, as a lack of PFC influences may lead to a lack of discrimination of the activity in the visual areas.

Deactivation of Amygdala

As the study of Koenigs et al. (2008) points toward, disrupting the activity of the amygdala may offer a possibility for alleviating PTSD. Targeting the amygdala (more precisely the BLA) via Deep Brain Stimulation (DBS) in traumatized rats has been associated with a reduction in PTSD symptoms (Langevin et al., 2010) as well has pharmacological treatment of the rat amygdala (Dębiec and LeDoux, 2006). By targeting the lateral nucleus of the amygdala subsequent to fear conditioning, Dębiec and LeDoux (2006) found that memory consolidation was impaired – and that the procedure had the same effect on memory reconsolidation if applied after retrieval, thereby offering a possibility for disrupting fear memories during the reconsolidation process. Evidently, these studies only address limited aspects of the human PTSD symptomatology, yet they may offer valuable insights into the disorder.

All in all evidence does point to the possibility of amygdalar involvement in the PTSD pathology. Intrusive memories are one of the key symptoms of PTSD and amygdala's participation in many aspects of emotional memory has been asserted. Intrusive recollections (here: (*recurrent and intrusive distressing recollections of cancer-related events* (Matsuoko et al., 2003, p. 737)) has been suggested to be related to smaller amygdala volume in cancer survivors (Matsuoko et al., 2003). However, amygdala's direct involvement in PTSD and full-blown flashbacks still needs to be addressed.

Flashbacks

By examining the rCBF related to flashback intensity in individuals suffering from chronic PTSD, Osuch et al. (2001) found a positive correlation between flashback

intensity and rCBF in the left hippocampal regions (involved in memory) as well as in the putamen, cerebellum and somatosensory cortex – all associated with motor control. An inverse correlation between rCBF and flashback intensity was found in the prefrontal, the medial temporal and the right fusiform cortices (the two latter associated with complex visual or spatial processing). Osuch et al. suggest that an increase in flashback intensity may be related to a loss of higher-order executive functioning normally carried out by the PFC encompassing *the temporary loss of present-reality orientation* (Osuch et al., 2001, p. 251). Liberzon et al. (1997) described one subject experiencing a flashback, exhibiting an altered cortico-thalamic rCBF pattern and propose that the increased cortico-thalamic activity may bear witness of a *shift of attention away from external stimuli and toward the internal stimuli of the flashback* (Liberzon et al., 1997, p. 149). Altered thalamic activity has been theorized to be one of the mechanisms triggering the generation of flashbacks (Lanius et al., 2001) in accordance with propositions that the thalamus has a function in regard to consciousness, and in the binding of external and internal 'reality' into one (Lanius et al., 2005). A hyperactive thalamo-cortical 'closed loop' network resulting in *direction of the attention to internal imagination and temporary functional withdrawal from the external world* (Huber et al., 2001, p. 134) has also been suggested as the basis for flashback experiences by Huber et al. (2001). Additionally Huber et al. (2001) note that the medial dorsal thalamus is involved in gaze control, as well saccades and eye-following movements. The authors hypothesize that one of the consequences of the treatment method Eye Movement Desensitization and Reprocessing (EMDR) (Shapiro 1989) is a temporary interruption of the closed thalamo-cortical loop, redirecting attention to reality.

Results from a functional connectivity analysis of traumatic memory (Lanius et al., 2004) point to a difference in the activity patterns of subjects with a PTSD diagnosis and a group of non-PTSD controls. During retrieval the PTSD group showed activity in

brain areas related to non-verbal memory; whereas non-PTSD subjects showed activity in areas associated with the retrieval of verbal episodic memory. Lanius et al. (2004) note that all PTSD subjects experienced the traumatic memories as flashbacks, however, it should be noted that the definition of flashbacks is somewhat vague.

In regard to structural abnormalities, a recent study (Kroes et al., 2011) found that specifically the severity of reexperiencing - and in particular flashback symptoms, correlated with reduced brain volume in a number of areas. Principal areas were the inferior temporal gyrus, associated with the ventral stream of visual processing and the parietal operculum and the insula – areas associated with somatosensory processing (Kroes et al., 2011).

Few experimental reports exist on the neurological processes activated during flashbacks in PTSD and the findings do not suggest direct involvement of the amygdala during the flashback experience. Yet, amygdala may participate in a wide range of processes ultimately causing past experiences to intrude as flashbacks. The following sections outline a review of findings on the interplay of emotion, memory, stress and amygdala activity and suggests critical links between flashbacks generation and amygdala.

Flashbacks and Amygdala

Stress

Generally, stress facilitates the formation of long-term adaptive responses and enhances memory for emotionally arousing or stressful events so that important information is stored and easily recalled (Roozendaal et al., 2009). In PTSD these processes have been proposed to be permanently altered due to persistent activity in the amygdala (Roozendaal et al., 2009). Basically, a traumatic event is inherently extremely stressful and emotional which logically influences the memory-encoding processes. Rodent studies suggest that the BLA of the amygdala (contrary to e.g. the hippocampus and the PFC) increases its density following the exposure to chronic stress (Roozendaal et al., 2009) indicating that stress has a positive effect on the structure. Amygdala-related memory processes may as a consequence be enhanced by high levels of stress.

Gist-information and De-contextualization

Flashbacks have been described as highly emotional and de-contextualized. Directing attention to gist information is believed to be facilitated by amygdala activity (Phelps and Sharot, 2008), giving emotional arousal a *memory-narrowing effect* (Kensinger, 2009, p.101). As amygdala directs attention to biologically salient aspects of emotionally arousing situations (Hamann, 2009) – other aspects are necessarily neglected. This effect may be even more pronounced in negative experiences, with an even stronger focus on vivid details (Kensinger, 2009). The content of the flashbacks may therefore arise from an extreme memory narrowing effect onto biologically salient information. The result of which is that the memories are high in emotional content and low in contextual detail.

Hippocampus and Stress

The de-contextualized nature of trauma memories in PTSD has been suggested to result from dys- or hypofunction of the hippocampus, as a consequence of the effects of stress and arousal mediated by the amygdala. Contrary to the amygdala, the hippocampus is exceedingly sensitive to stress (Kim and Diamond, 2002). A U-shaped relation between stress (and the release of stresshormones like corticosterone) and hippocampal function has been suggested (Nadel and Jacobs, 1998; Kim and Diamond, 2002). According to this relation, hippocampal function may be impaired by both abnormally high and low levels of cortisol. Moreover, chronical hyperarousal has been found to affect the hippocampus negatively (Hayes et al. 2010). Kim and Diamond (2002) suggest a differentiation in the ways stress affects hippocampal activity; *stress enhances hippocampus-dependent fear-related learning and memory, and impairs the processing of spatial information that is acquired outside the fear-conditioning context* (Kim and Diamond, 2002, p. 456) – a delineation that corresponds well with the flashback characteristics.

That the hippocampus may participate in enhancing certain memory aspects is further supported by Dolcos et al. (2005) suggesting a *synergistic mechanism in which emotion enhances recollection and recollection enhances emotion* (Dolcos et al., 2005, p. 2631) and in which *processing of emotional cues related to traumatic events may trigger recollection of traumatic memories, which is accompanied by HC* [hippocampus] *activity. This, in turn, may intensify AMY* [amygdala] *activity associated with emotional (e.g. fear-related) responses* (Dolcos et al., 2005, p. 2631). Basically, during retrieval the hippocampus may emphasize the effects originally orchestrated by amygdala. Co-activation of the amygdala and hippocampus during emotional arousal has been related to increased plasticity for memory – believed to be reenacted during retrieval (Hamann, 2009). Increased connectivity between the amygdala and hippocampus during retrieval of emotional information has been associated with an enhanced ability to retrieve specific details of a situation (Kensinger, 2009). Moreover, increased activation of the hippocampus and amygdala in regard to the construction of negative autobiographical memories relative to positive has been found in PTSD, thereby indicating that enhanced activity may be associated with negative valence in PTSD (St. Jacques et al., 2010).

PFC and Retrieval

Dysregulation of emotional responses due to amygdala hyperactivity resulting from PFC hypoactivity, has been suggested as one of the components of the PTSD pathology (Koenigs and Grafman, 2009; Shin, 2009;

Francati et al., 2007; Shin et al., 2006). Aside from the results of Koenigs et al. (2008)'s lesion study, this theoretical standpoint is challenged by other findings suggesting greater co-activation of the amygdala and the PFC in PTSD (Gilboa et al., 2004) and in particular during memory retrieval (St. Jacques et al., 2010), suggesting a somewhat causal role of the PFC in PTSD – possibly in boosting emotional reliving (Koenigs and Grafman, 2009; Koenigs et al., 2008).

Daselaar et al. (2008) suggest a spatiotemporal separation of the subjective ratings of reliving and emotional intensity during the retrieval of autobiographical memories. This could mean that the respective contributions of amygdala and the PFC to flashbacks are temporally dissociable. In the study by Daselaar et al. (2008), the actual reliving experience is understood as occurring *after* emotional information has been retrieved. The different temporal stages are believed to be associated with different brain sites, i.e.: the amygdala, hippocampus, somatosensory cortex etc with emotion intensity; and the right and medial PFC, thalamus, cingulated gyrus etc with reliving (Daselaar et al., 2008). Daselaar et al. (2008) outline that the involvement of amygdala, hippocampus, somatosensory cortex etc before the memory is fully formed indicates that an *early detection of high arousal during retrieval may spur and guide efforts at event reconstruction* (Daselaar et al., 2008, p. 226). Thereby supporting an interpretation of emotion as an early warning system (Daselaar et al., 2008, p. 219) preparing the individual for action before more conscious processing begins, as well as amygdala's engagement in the intensification of the recollective experience and confidence in the retrieved memory.

During memory retrieval in PTSD, the activity of the PFC, and thereby reliving, may be affected by an extreme enhancement of the amygdala-related processes surrounding emotional responses and danger detection. St. Jacques et al. (2010) found evidence for greater amygdala and hippocampal activity during the construction stages relative to the elaboration stages of memory retrieval in a PTSD group compared to a group of controls – indicating an enhancement of emotional intensity in PTSD early in the retrieval process. In the same study negative memories elicited greater amygdala-PFC coupling in PTSD – indicating an enhancement of reliving of these memories in PTSD in particular.

One reason why not all studies report amygdala hyperactivity in PTSD or engagement during the flashback experience could be ascribed this temporal division. Even though amygdala activity is not reported during the flashback; amygdala may actually enforce its occurrence. By enhancing emotional intensity via interactions with the PFC the experience of reliving is most likely up-regulated, consistent with the suggestion that one of the key ways in which emotion modulates the memory processes is by intensifying the recollective experience (Phelps and Sharot 2008). Moreover, exaggerated emotional information sent from amygdala to the PFC may result in deficient discrimination by the PFC. As mentioned; the PFC plays a role in contextualization and appropriate response to stimuli - deficient contextualization may therefore entail a de-contextualization of trauma cues (Liberzon and Garfinkel, 2009) and possibly *lead to the inappropriate expression of trauma-related memories and emotions* (Liberzon and Garfinkel, 2009, p. 313). Ultimately, the PFC participates in up-regulating reliving of the inappropriate and emotionally intense experience.

Thus, as some theories propose (Shin, 2009; Francati et al., 2007; Shin et al., 2006), one may understand the activity of the amygdala as uninhibited, as signals from the amygdala are not critically evaluated by the PFC. However, the reason is not necessarily PFC hypoactivity, but possibly deficient discrimination – in the sense that the PFC works to reinforce the uninhibited amygdala signal.

Visual Imagery and Reliving

Studies have found that visual imagery and the degree of experienced reliving are strongly associated factors (Daselaar et al., 2008). Generally, visual information has been suggested as an important component of autobiographical memory (Rubin, 2005). Even though flashbacks have been found to intrude in many different modalities, vision seems to be one of the most prominent (Hackmann et al., 2004). As stronger visual imagery as well as emotionality lead to enhanced recollection (Rubin, 2005), the vividness of flashbacks may, in part, be attributed these processes.

Amygdala interacts strongly with the visual processing areas (Brewin, 2005) and may be involved with the activity of these areas regarding encoding as well as retrieval. Amygdala directs attention to biologically salient stimuli, and is also believed to enhance sensory and thereby visual perception of these stimuli (Hamann, 2009). In this sense, an enhanced amygdala response to fear-provoking or emotional stimuli may enhance processing in the visual cortex (Phelps 2004; Phelps and Sharot, 2008). Taken that the areas that are active during encoding are, in part, reactivated during retrieval (Danker and Anderson, 2010; Hamann, 2009), enhanced processing in the visual areas during encoding results in a similar enhancement during retrieval. As activity in the visual processing areas of the brain is associated with the reliving experience of autobiographical memories (Daselaar et al., 2008) it can be related to the elaboration stages of retrieval. The amygdala is, as mentioned, associated with the earlier retrieval stages (Daselaar et al., 2008) and may be theorized to enhance processing in the visual areas during retrieval, thereby up-regulating the experience of reliving. The enhanced activity during retrieval is bound to the initial encoding, and, due to the attention-narrowing effects of the amygdala, the memories are accompanied by a limited amount of accessible visual imagery. It should be noted that the amygdala may interact in similar ways with other modalities, as the structure interacts with all (Aggleton and Saunders,

2000). Amygdala might enhance the contribution of all senses to the vivid flashbacks, making the flashbacks rich in perceptual content.

Reconsolidation

Another aspect of importance is the consequences of repetitively retrieving and thereby reconsolidating a memory – a process involving amygdala activity (La-Bar and Cabeza, 2006). The reactivation of memories is strengthened as a consequence of repeated retrieval (Danker and Anderson, 2010) and in PTSD the constant rehearsal of trauma memories is believed to sustain the disorder (de Quervain and Margraf, 2008). In regard to flashbacks, amygdala may increase the accessibility of the memories by enhancing their survival-related value, leading to more frequent activation and subsequent reconsolidation. The memory trace is then constantly rehearsed and difficult to forget. Finally, the nowness of the flashbacks may cause an even stronger reaction from the amygdala, as if the experience was actually happening in the present – ultimately commingling consolidation and reconsolidation and enhancing both.

Discussion

The interplay of emotion and memory is a complex one and amygdala is a multifaceted structure. The paper at hand only addresses limited aspects of this complexity. Within the restrictions that this entails we have examined how the amygdala could contribute to the phenomenology, the intensity and extreme reliving qualities of flashbacks. By understanding the amygdala as a catalyst for the encoding, consolidation and retrieval of emotionally arousing survival-related information, flashbacks are theorized to partly result from an extreme enhancement of these processes. This enhancement is hypothesized to originate from the exceedingly stressful, emotional and fear-eliciting circumstances at the time of trauma.As summarized in Box 2 the amygdala is suggested to contribute to flashback occurrence in a number of ways. Through influences on the MTL memory system, in particular the hippocampus, the sensory processing areas – especially the visual cortex, and the PFC, the amygdala facilitates the encoding and consolidation of highly emotional, vivid, de-contextualized memories for specific, biologically salient details of the event. The re-experience of the memory during retrieval is then up-regulated due to amygdala reinforcement of the emotional importance of the memory. As many of the structures engaged during encoding are reactivated, increased processing occurs in the visual areas, enhancing vividness and adding to an up-regulation of the reliving experience. In addition, the hippocampus assists the amygdala in retrieving the highly emotional (but somewhat de-contextualized) memory. In that the amygdala enhances the emotional relevancy of the memory in the early stages of the retrieval process, the result is a stronger and more vivid reconstruction of the memory by the PFC – and again an increase in reliving. Moreover, the signal from amygdala of the memory's extreme survival-relevancy may result in deficient discrimination from the PFC and the retrieval of the memory in inappropriate or unrelated situations, and thereby the somewhat involuntary retrieval of these memories. Finally, the memories are believed to be easily triggered due to the fact that certain processes work in favor of their relevancy and preservation. The constant reactivation of the memories, also partly orchestrated by the amygdala, lead to their ongoing reconsolidation. In sum, the amygdala may contribute to the intensity of flashbacks, the experience of reliving and thereby the distortion of the individual's spatiotemporal perception via an up-regulation of emotional relevancy.

For the time being, reports on experienced flashbacks, and thereby their occurrence, rely largely on subjective ratings and self-report, the neural underpinnings are not agreed upon and even though bodily reactions have been measured during reliving, no pattern (e.g. a raise in heart rate) has been directly related to flashback experience. In general, experimental research on flashbacks and intrusive trauma memories is limited. Most often, theories on how the initial memory is encoded in PTSD rely on deductions from how memory, stress and fear interact in general, together with reports on animal models of fear learning. Aside from studies in rodents, the encoding processes have been observed in the laboratory in humans, testing

Box 2

Amygdala's Possible Contributions to Flashbacks

Encoding:

Interactions with hippocampus → enhanced plasticity for the memory trace + decreased encoding of contextual details

Interactions with PFC → attention narrowing to gist-information

Interactions with the visual processing areas → enhanced visual perception of survival-related stimuli

Retrieval:

Interactions with the hippocampus → enhanced retrieval

Interactions with PFC → up-regulation of reliving + more vivid reconstruction of the retrieved memory

Interactions with the visual processing areas → enhanced vividness + intensification of the experience of reliving

memory of e.g. neutral, negative and positive stimuli. The laboratory setting is, however, far from similar to reality, and the effects of emotion on memory cannot be sufficiently simulated experimentally, even less for traumatizing experiences, as these entail a level of survival-related relevancy that cannot (or should not) be imitated in a laboratory setting.

In accordance with The Dual Representation Theory (Brewin, Dalgleish and Joseph, 1996; Brewin et al., 2010) the paper at hand suggests, enhanced amygdala modulation of hippocampal activity may result in a lack of encoding and consolidation of hippocampal-dependent peripheral/contextual details, combined with an enhancement of the encoding of amygdala-dependent emotional aspects. In addition, the differentiating impact of stress on amygdala and hippocampal activity, respectively, has been reviewed, supporting the theory originally presented by Nadel and Jacobs (1998). It is, however, not necessarily a question of lack of integration, but could as well be ascribed a shift in attention, resulting in the formation of memories containing emotionally relevant information.

The flashback-memories are of high survival-related value, emotional in content and, partly, due to amygdala activity, easily triggered as well as strengthened during retrieval.

Even with the limitations that that the results from one study alone entails, the lesion study by Koenigs et al (2008) does strongly associate amygdala activity with the development of PTSD. Koenigs et al. (2008) found 0% PTSD prevalence in Vietnam veterans with amygdala damage, underlining the importance of considering the role of the structure in the PTSD pathology. Additionally, the same study points to the significance of vmPFC activity in PTSD. PFC activity – and not hypoactivity - has been reported in several of the studies reviewed and the paper at hand suggests a crucial role for this structure especially in relation to flashback-phenomena. Even though the few experimental studies examining flashbacks do not report amygdala activity during its occurrence, the structure may in large part participate in and contribute to the processes finally resulting in flashbacks. The study by Daselaar et al. (2008) suggests the possibility of temporally dissociating the retrieval of emotional information from the later, conscious, experience of reliving, thereby offering a possible explanation as to why amygdala activity is not captured by imaging studies. The amygdala may, however, contribute to the earlier stages of memory retrieval – as well as encoding.

The current paper suggests the amygdala as an enhancer of emotional relevancy contributing to the intensity and experience of reliving characteristic of flashbacks. Future efforts should be made to examine the neurological activity associated with flashbacks. Moreover, efforts should be made to examine flashbacks in relation to other dissociative states, and comparable phenomena such as hallucinations.

References

Adolphs, R. (2003). Amygdala. In L. Nadel (Ed.), *Encyclopedia of Cognitive Science* (pp, 98-105). London, England: Nature Publishing Group.

Aggleton, J.P. & Saunders, R.C. (2000). The amygdala – what's happened in the last decade? In J.P. Aggleton (Ed.), *The Amygdala: A functional analysis* (pp 1-30). Oxford, England: Oxford University Press.

American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders, DSM-V* Washington: American Psychiatric Publishing Group

Berntsen, D., Willert, M. & Rubin, D.C. (2003). Splintered Memories or Vivid Landmarks? Qualities and Organization of Traumatic Memories with and Without PTSD. *Appl Cogn Psychol:* 17, 675-693

Berntsen, D. (2009). *Involuntary Autobiographical Memories, An Introduction to the Unbidden Past.* UK: Cambridge University Press

Brewin, C.R., Dalgleish, T. & Joseph, S. (1996). A dual representation theory of post traumatic stress disorder. *Psychol Rev* 103(4), 670–686

Brewin, C.R. (2005). Encoding and Retrieval of Traumatic Memories. In J.J. Vasterling & C.R. Brewin (Eds.) *Neuropsychology of PTSD, Biological, Cognitive, and Clinical Perspectives* (pp. 131-152). New York: The Guilford Press

Brewin, C.R., Gregory, J.D., Lipton, M. & Burgess, N. (2010). Intrusive Images in Psychological Disorders: Characteristics, Neural Mechanisms, and Treatment Implications. *Psychol Rev* 117(1), 210-232

Brohawn, K.H., Offringa, R., Pfaff, D.L., Hughes, K.C. & Shin, L.M. (2010). The Neural Correlates of Emotional Memory in Posttraumatic Stress Disorder. *Biol Psychiatry* 68, 1023-1030

Bryant, R.A., O'Donnell, M.L., Creamer, M., McFarlane, A.C. & Silove, D. (2010). Posttraumatic intrusive symptoms across psychiatric disorders. *J Psychiatr Res* 45, 842-847

Cahill, L. (2000). Modulation of long-term memory in humans by emotional arousal: adrenergic activation and the amygdala. In J.P. Aggleton (Ed.) *The Amygdala: A functional analysis* (pp. 425-446). Oxford, England: Oxford University Press.

Danker, J.F. & Anderson, J.R. (2010). The Ghosts of Brain States Past: Remembering Reactivates the Brain Regions Engaged During Encoding. *Psychol Bull* 136(1), 87-102

Daselaar, S.M., Rice, H.J., Greenberg, D.L., Cabeza, R., LaBar, K.S. & Rubin, D.C. (2008). The Spatiotemporal Dynamics of Autobiographical Memory: Neural Correlates of Recall, Emotional Intensity, and Reliving. *Cereb Cortex* 18, 217-229

Dębiec, J. & LeDoux, J. (2006). Noradrenergic Signaling in the Amygdala Contributes to the Reconsolidation of Fear Memory, Treatment Implications for PTSD. *Ann NY Acad Sci* 1071, 521-524

Dębiec, J., LeDoux, J. (2009). The Amygdala and the Neural Pathways of Fear. In P.J. Shiromani, T.M. Keane & J.E. LeDoux (Eds) *Post-Traumatic Stress Disorder, Basic Science and Clinical Practice* (pp. 23-38). New York: Humana Press

De Silva, P. & Marks, M. (1999). Intrusive thinking in post-traumatic stress disorder. In W. Yule (Ed.) *Post Traumatic Stress Disorders Concepts and Therapy* (pp 161-175). England: John Wiley and Sons Ltd

De Quervain, D.J.F. & Margraf J (2008). Glucocorticoids for the treatment of post-traumatic stress disorder and phobias: A novel therapeutic approach. *Eur J Pharmacol* 586, 365-371

Dolcos, F., LaBar, K.S. & Cabeza, R. (2004). Interaction between the Amygdala and the Medial Temporal Lobe Memory System Predicts Better Memory for Emotional Events. *Neuron* 42, 855-863

Dolcos, F., LaBar, K.S. & Cabeza, R. (2005). Remembering one year later: Role of the amygdala and the medial temporal lobe memory system in retrieving emotional memories. *PNAS* 102(7), 2626-2631

Ehlers, A., Hackmann, A., Steil, R., Clohessy, S., Wenninger, K. & Winter, H. (2002). The nature of intrusive memories after trauma: the warning signal hypothesis. *Behav Res Ther* 40, 995–1002

Francati, V., Vermetten, E. & Bremner, J.D. (2007). Functional Neuroimaging studies in posttraumatic stress disorder: review of current methods and findings. *Depress Anxiety* 24, 202-218

Freese, J.L. & Amaral, D.G. (2009). Neuroanatomy of the Primate Amygdala. In P.J. Whalen & E.A. Phelps (Eds.) *The Human Amygdala* (pp 3-42). New York, USA: The Guilford Press

Gilboa, A., Shalev, A.Y., Laor, L., Lester, H., Louzoun, Y., Chisin, R. & Bonne, O. (2004). Functional Connectivity of the Prefrontal Cortex and the Amygdala in Posttraumatic Stress Disorder. *Biol Psychiatry* 55, 263-272

Hackmann, A., Ehlers, A., Speckens, A. & Clark, D.M. (2004). Characteristics and Content of Intrusive Memories in PTSD and Their Changes With Treatment. *J Trauma Stress* 17(3), 231-240

Hamann, S. (2009). The Human Amygdala and Memory. In P.J. Whalen & E.A. Phelps (Eds.) *The Human Amygdala* (pp. 177-203). New York, USA: The Guilford Press

Hayes, J.P., LaBar, K.S., McCarthy, G., Selgrade, E., Nasser, J., Dolcos, F., VISN 6 Mid-Atlantic MIRECC Workgroup & Morey, R.A. (2010). Reduced hippocampal and amygdala activity predicts memory distortions for trauma reminders in combat-related PTSD. *J Psychiatr Res* 45, 660-669

Hellawell, S.J. & Brewin, C.R.(2002). A comparison of flashbacks and ordinary autobiographical memories of trauma: cognitive resources and behavioural observations. *Behav Res Ther* 40, 1143–1156

Huber, M., Siol, T., Herholz, K., Lenz, O., Köhle, K. & Heiss, W.D. (2001). Activation of Thalamo-Cortical Systems in Post-Traumatic Flashbacks: A Positron Emission Tomography Study. *Traumatology* 7(4), 131-141

Kensinger, E.A. (2009). Remembering the Details: Effects of Emotion. *Emot Rev* 1 (2), 99-113

Kim, J.J. & Diamond, D.M. (2002). The stressed hippocampus, synaptic plasticity and lost memories. *Nat Rev Neurosci* 3, 453-462

Koenigs, M., Huey, E.D., Raymont, V., Cheon, B., Solomon, J., Wassermann, E.M. & Grafman, J. (2008)

Focal brain damage protects against post-traumatic stress disorder in combat veterans. *Nat Neurosci* 11 (2), 232-237

Koenigs, M. & Grafman, J. (2009). Posttraumatic Stress Disorder: The Role of Medial Prefrontal Cortex and Amygdala. *Neuroscientist* 15 (5), 540-548

Kroes, M.C.W., Whalley, M.G., Rugg, M.D. & Brewin, C.R. (2011). Association between flashbacks and structural brain abnormalities in posttraumatic stress disorder. *Eur Psychiatry* 26, 525–531

LaBar, K.S., & Cabeza, R. (2006). Cognitive neuroscience of emotional memory. *Nat Rev Neurosci* 7, 54-64

Langevin, J., De Salles, A.A.F., Kosoyan, H.P. & Krahl, S.E. (2010). Deep brain stimulation of the amygdala alleviates post-traumatic stress disorder symptoms in rat model. *J Psychiatr* Res 44, 1241-1245

Lanius, R.A., Williamson, P.C., Densmore, M., Boksman, K., Gupta, M.A., Neufeld, R.W., Gati, J.S. & Menon, R.S. (2001). Neural Correlates of Traumatic Memories in Posttraumatic Stress Disorder: A Functional MRI Investigation. *Am J Psychiatry* 158 (11), 1920-1922

Lanius, R.A., Williamson, P.C., Densmore, M., Boksman, K., Neufeld, R.W., Gati. J.S. & Menon, R.S. (2004). The Nature of Traumatic Memories: A 4-T MRI Functional Connectivity Analysis. *Am J Psychiatry* 161, 36-44

Lanius, R.A., Williamson, P.C., Bluhm, R.L., Densmore, M., Boksman, K., Neufeld, R.W.J., Gati, J.S. & Menon,

R.S. (2005). Functional Connectivity of Dissociative Responses in Posttraumatic Stress Disorder: A Functional Magnetic Resonance Imaging Investigation. *Biol Psychiatry* 57, 873-884

LeDoux, J. (1999). *The Emotional Brain*. London, UK: *Phoenix – Orion Books Ltd*

LeDoux, J.E. & Schiller, D. (2009). The Human Amygdala: Insights from Other Animals In P.J. Whalen & E.A. Phelps (Eds.) *The Human Amygdala* (pp. 43-60). New York, USA: The Guilford Press

Liberzon, I., Taylor, S.T., Fig, L.M. & Koeppe, R.A. (1997). Alterations of corticothalamic perfusion ra-

tios during a PTSD flashback. *Depress Anxiety* 4, 146-150

Liberzon, I., Taylor, S.F., Amdur, R., Jung, T.D., Chamberlain, K.R., Minoshima, S., Koeppe, R.A. & Fig,

L.M. (1999). Brain Activation in PTSD in Response to Trauma-Related Stimuli. *Biol Psychiatry* 45 (7), 817-826

Liberzon, I. & Garfinkel, S.N. (2009). Functional Neuroimaging in Post-Traumatic Stress Disorder. In P.J. Shiromani, T.M. Keane & J.E. LeDoux (Eds) *Post-Traumatic Stress Disorder, Basic Science and Clinical Practice* (pp. 297-317). New York: Humana Press

Matsuoko, Y., Yamawaki, S., Inagaki, M., Akechi T. & Uchitomi, Y. (2003). A Volumetric Study of Amygdala in Cancer Survivors with Intrusive Recollections. *Biol Psychiatry* 54, 736-743

McGaugh, J.L. (2004). The amygdala modulates the consolidation of memories of emotionally arousing experiences. *Ann Rev Neurosci* 27 (1), 1-28

Nadel, L. & Jacobs, J. (1998). Traumatic Memory Is Special. *Curr Dir Psychol Sci* 7 (5), 154-157

Osuch, E.A., Benson, B., Geraci, M., Podell, D., Herscovitch, P., McCann, U.D. & Post, R.M. (2001). Regional Cerebral Blood Flow Correlated with Flashback Intensity in Patients with Posttraumatic Stress Disorder. *Biol Psychiatry* 50, 246-253

Phelps, E.A. (2004). Human emotion and memory: interactions of the amygdala and hippocampal complex. *Curr Opin Neurobiol* 14, 198-202

Phelps, E.A. & Sharot, T. (2008) How (and Why) Emotion Enhances the Subjective Sense of Recollection. Curr Dir Psychol Sci 17 (2): 147-152

Rainnie, D.G. & Ressler, K.J. (2009). Physiology of the Amygdala: Implications for PTSD. In P.J. Shiromani, T.M. Keane & J.E. LeDoux (Eds) *Post-Traumatic Stress Disorder, Basic Science and Clinical Practice* (pp. 39-78). New York: Humana Press

Rogers, M.A., Yamasue, H., Abe, O., Yamada, H., Ohtani, T., Iwanami, A., Aoki, S., Kato, N. & Kasai, K. (2009). Smaller amygdala volume and reduced anterior cingulated gray matter density associated with history of post-traumatic stress disorder. *Psychiatr Res: Neuroimaging* 174, 210-216

Roozendaal, B., McEwen, B.S. & Chattarji, S. (2009). Stress, memory and the amygdala. *Nat Rev Neurosci* 10, 423-433

Rubin, D.C., Feldman, M.E. & Beckham, J.C. (2004). Reliving, Emotions, and Fragmentation in the Autobiographical Memories of Veterans Diagnosed with PTSD. *Appl Cogn Psychol* 18, 17-35

Rubin, D.C. (2005). A Basic-Systems Approach to Autobiographical Memory. *Curr Dir Psychol Sci* 14 (2), 79-83

Rubin, D.C., Boals, A. & Berntsen, D. (2008). Memory in Posttraumatic Stress Disorder: Properties of voluntary and involuntary, traumatic and non-traumatic autobiographical memories in people with and without PTSD symptoms. *J Exp Psychol Gen* 137 (4), 591-614

Shapiro, F. (1989). Eye movement desensitization: A new treatment for post-traumatic stress disorder. *J Behav Ther Exp Psychiatry* 20 (3), 211-217

Shin, L.M., Rauch, S.L. & Pitman, R.K. (2006). Amygdala, Medial Prefrontal Cortex, and Hippocampal Function in PTSD. *Ann NY Acad Sci* 1071, 67-79

Shin, L.M. (2009). The Amygdala in Post-Traumatic Stress Disorder. In P.J. Shiromani, T.M. Keane & J.E. LeDoux (Eds) *Post-Traumatic Stress Disorder, Basic Science and Clinical Practice* (pp. 319-336). New York: Humana Press

St. Jacques, P.L., Botzung, A., Miles, A. & Rubin, D.C. (2010). Functional neuroimaging of emotionally intense autobiographical memories in post-traumatic stress disorder. *J Psychiatr Res* 45, 630-637

Van der Kolk, B.A. & Fisler, R. (1995). Dissociation and the Fragmentary Nature of Traumatic Memories: Overview and Exploratory Study. *J Trauma Stress* 8 (4), 505-525