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## The impairment of recollection in functional amnesic states

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#### ABSTRACT

*Introduction*: Functional amnesia refers to various forms of amnesia, which have no direct organic brain basis. Psychological stress and trauma were etiologically linked to its development across various cultures.

*Methods*: We have studied several patients with functional amnesia, employing neuropsychological and neuroimaging methods. Herein we provide a review of the current understanding of the phenomenology, neuropsychology and neurobiology of functional amnesia, which we illustrate by reference to five own case descriptions and other cases presented in the literature.

Results: Functional amnesia is mostly of retrograde nature and presents in the form of a memory blockade or repression to recollect episodic-autobiographical events, which may cover the whole past life. Sometimes, the recollection impairment is localized to certain time epochs. In comparison to functional retrograde amnesia, functional isolated anterograde amnesia is much rarer and data on its neurobiology are scant. In patients with functional amnesia with pronounced retrograde episodic-autobiographical memory impairments, we identified changes in brain metabolism, above all reductions in the temporo-frontal regions of the right hemisphere. Recently, even subtle structural changes in the white matter of the (right) frontal cortex were described in functional retrograde amnesia by other researchers.

Conclusions: The disruption in recollection in functional amnesia is often accompanied by changes in personality dimensions, pertaining to cognition (self-related processing, theory of mind), autonoetic consciousness and affectivity. This suggests that functional amnesia is a multifaceted condition. We hypothesize that the recollection deficit in functional retrograde amnesia primarily reflects a desynchronization between a frontal lobe system, important for autonoetic consciousness, and a temporo-amygdalar system, important for evaluation and emotions. Despite assumptions that functional amnesia can always be reversed, several cases of functional amnesia were found to follow a chronic course, suggesting a need for longitudinal prospective studies to quantify possible global cognitive deterioration over time and its neural underpinnings.

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#### 1. Introduction

Episodic-autobiographical memory (EAM) is characterized by self-referential processes and the qualities of vividness and emotion (Cabeza and St Jacques, 2007). Tulving (2002, 2005; Wheeler et al., 1997) sees recollection of experiences as based on autonoetic consciousness, subjective time experience, and the experiencing self. We have argued that remembering requires conscious recollection embedded in time and space and with an emotional flavoring (Markowitsch and Staniloiu, 2012a). Impairments of recollection have been reported in relationship to various disease conditions, above all to those involving limbic system regions such as the hippocampal formation (for an overview see Markowitsch and Staniloiu, 2012a). Failures of recollection can arise in conjunction with either neurological insults or environmental factors, such as psychological stress or "psychic trauma" (Eulenburg, 1878; van der Hart and Brown, 1990). While forgetfulness as an ailment for traumatic memories is an old motif in the belletristic (Markowitsch, 1992; Staniloiu and Markowitsch, 2012a), some of the most compelling scientific descriptions of failures of recollection linked to environmental influences stem from the last half of the 19th century. At that time the concept of hysteria was popularized by Charcot (e.g., Charcot, 1892), his pupils and collaborators (Bogousslavsky, 2011) and its understanding was further refined by Breuer and Freud (1895) and Janet (1907). Seeds of the still actual debate surrounding the validity of a strict demarcation between organic and psychogenic forms of amnesia (Pommerenke et al., 2012) can also be traced back to the same era. For example in 1878, Bennett had published a "case of cerebral tumour-symptoms simulating hysteria" and had questioned the dichotomy between organic and psychic illnesses. He wrote (p. 120): "In conclusion, there appear to me to be at least two points of interest in this case: 1st, the anomalous symptoms of pressure caused by the tumor; and 2nd, that symptoms of what is called hysteria may co-exist with organic disease of the brain - whether independent of it or the result, being in this patient doubtful. Under any circumstances it serves to indicate what caution should be exercised in diagnosing, and more especially in treating, as hysteria, any nervous affection in women which may appear indefinite or mysterious."

In this contribution we focus on impairments of recollection that are linked to environmental influences and occur in the absence of brain damage as detected by conventional structural imaging techniques or are out of proportion, given the locus and extent of the brain damage (De Renzi et al., 1997; Piolino et al., 2005). It is assumed that recollection requires the synchronous activation of regions engaged in fact-based information processing and regions which give an emotional colorization to the facts, making them unique and personal episodes. We speak of EAMs, instead of episodic or autobiographical memories, as we aim to emphasize that all of the following components - the what, where and when of an event, autonoetic consciousness (Markowitsch, 2003a), selfawareness and capacity for reflection upon the own self in relation to other(s) (Welzer and Markowitsch, 2005) are important ingredients and/or prerequisites of these very personal memories. It is posited that the recollection of personal events requires an integrated activation of several brain hubs, among which the amygdala is a central one (Markowitsch and Staniloiu, 2011a, 2011b, 2012b, in press; Tomasi and Volkow, 2011).

Neither the idea that recollecting recruits several brain areas (e.g., Meynert, 1884), nor the hypothesis that functional amnesic conditions are underlain by physiological abnormalities in the brain is in fact new (Charcot, 1892; Sollier, 1892; Bogousslavsky, 2011; Linden et al., 2012). It took however several decades until these views entered the mainstream of fields, such as psychiatry (Kanaan et al., 2012; Markowitsch, 1996, 2003b; Pietrini, 2003). Herein we repack some of the theoretical frameworks that have guided the understanding of functional amnesia, under the "fresh circumstances" of discoveries in memory research. This process, which might bear comparison to putting new oil into old lanterns, is justified by the resurgence of the interest in the concept of functional neurological symptoms among the working groups for the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) (Kanaan et al., 2012).

After introducing the definitions of functional amnesia and related concepts, we point to relevant aspects of phenomenology, neuropsychology and neurobiology of functional amnesia, by resorting to detailed data from new own case descriptions as well as findings from our previously published research. In this way we provide support for a number of recent recommendations that were advanced for the revision of diagnostic criteria of dissociative amnesic conditions for DSM-V (Spiegel et al., 2011). Additionally, we underline several other aspects, which may need to be taken into consideration for the understanding and final categorizations of these disorders in nosological classifications and future research.

#### 2. Functional amnesia

The citation of Bennett from more than 130 years ago alludes to a still unsolved "riddle" - namely the occurrence of (primarily retrograde) amnesic states which do not correspond to the locus and extent of the brain lesion (Lundholm, 1932; Kapur, 2000, 2002; Kopelman, 2000a, 2000b; Markowitsch, 1996; Fujiwara et al., 2008). This discrepancy was found in a number of patients with so-called functional amnesia (Schacter and Kihlstrom, 1989; Brandt and Van Gorp, 2006). As its name suggests, functional amnesia indicates the block of a function. This block of a function may serve a particular function for the patient, though this might not be (readily) accessible to his conscious awareness, such as it may allow him to refrain from working and taking responsibility or may facilitate his escaping from a situation that had been subjectively perceived as "inescapable" or "intolerable" (Kopelman et al., 1994; Freud, 1956). Given that functional amnesia may be triggered by physical (somatic) factors, psychic factors or a mixture in variable proportions of the two (Markowitsch, 1996; Bogousslavsky, 2011; Pommerenke et al., 2012), the use of this designation may also be functional for the clinician. It may allow the latter to circumvent the ongoing mind-brain debate and facilitate the conveyance of hope for improvement (Kanaan et al., 2012; Stone, 2009). It might furthermore

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