Autobiographical Memory across the Life Span
Brain Imaging and Neuropsychology

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Abstract

Memory is defined as being composed of several systems, each with its distinct neural basis. Of these systems the episodic-autobiographical one is considered to have evolved latest and to be most vulnerable to brain damage or stress conditions. Especially structures of the limbic and the prefrontal cortex are regarded as essential for an appropriate processing of autobiographical events. The importance of these structures is exemplified on the basis of three principle disease conditions: Klüver-Bucy syndrome, Urbach-Wiethe disease and dissociative amnesia. These symptoms also serve to illustrate the vulnerability of autobiographical memory. Furthermore, functional imaging studies in normal subjects of different ages are used to depict the development of autobiographic memory across the life span and to argue for the importance of the ventromedial prefrontal cortex for an integrated binding of memory, based on aspects of time, self, and consciousness.

Keywords: autobiographic memory; limbic system; prefrontal cortex; dissociative amnesia; functional brain imaging; self

Memory Systems

Memory is subdivided according to time and contents. Along the time axis the most frequently used division is that partitioning between short-term and long-term memory, while the division of memory into contents-based systems is much more complex and varies between authors (Conway & Pleydell-Pearce, 2000; Williams et al., 2007; Squire, Knowlton & Musen, 1993; Tulving, 1983). Endel Tulving pioneered research along this line which nowadays progressed to a distinction into five systems (Tulving, 2002, 2005; Markowitsch, 2003; Markowitsch & Welzer, 2009) (Fig. 1). Of these, the episodic-autobiographical memory system is considered to be that one which makes us unique as human beings and which is most closely related to emotions (Markowitsch, 2009). In fact, we consider asynchronous activation of emotion and fact-related components as characteristic for the processing of autobiographical events (Markowitsch, 2008; cf. also LaBar & Cabeza, 2006).

Figure 1: The five long-term memory systems and their assumed brain bases. Procedural memory is largely motor-based, but includes also sensory and cognitive skills (“routines”). Priming refers to a higher likeliness of re-identifying previously perceived stimuli. Perceptual memory allows distinguishing an object, item, or person on the basis of distinct features. Declarative memory is context-free and refers to general facts. It is termed semantic memory or the knowledge systems as well. The episodic-autobiographical memory system is context-specific with respect to time and place. It allows mental time travel. Examples are events such as the last vacation or the dinner of the previous night. Tulving (2005) defined it as the conjunction of autonoetic consciousness, subjective time, and the experiencing self.
Autobiographical memory, is, however, not only defined by the combined activation of affective and cognitive components of information bits, but also by ‘autonoetic consciousness’, as Tulving (2002, 2005) characterized this memory system, when distinguishing it from other systems, which he only considered to be related to noetic consciousness (semantic memory, perceptual memory), or even only to anoetic consciousness (priming, procedural memory) (cf. Fig. 1).

Autonoetic consciousness is considered to develop as a complex interaction of several variables – brain maturation, language development, ability to capture and understand time relations (Markowitsch & Welzer, 2009). Brain damage such as in dementia or psychiatric illnesses may impair or abolish autonoetic consciousness (Markowitsch, 2003a). Autonoetic consciousness is considered to develop in childhood only after the establishment of all other forms of memory, so that it starts to occur not before the fourth year of life (Nelson, 2005). At this time of life, children also start to reflect about themselves (Fig. 2).

Figure 2: Diagram depicting Tulving’s (2002, 2005) assumption of a hierarchical organization of long-term memory systems and demonstrating the developmental aspects in the formation of memory systems.

**Brain and Emotional Memory**

On the brain level, both prefrontal regions (Nauta, 1973; Brand & Markowitsch, 2008) and structures of the expanded limbic system (Nauta, 1979; Nieuwenhuys, 1996; Markowitsch, 2000a, Table 1) – in particular the amygdala and the hippocampal formation, but also orbitofrontal and anterior temporal cortical regions – are considered to be central for the synchronization of the emotional and factual aspects of personal episodes (Fig. 3). Papez (1937) and MacLean (1949, 1970) were the founders of the view that the limbic system is the ‘emotional brain’ (Markowitsch, 1999). MacLean (1970), who coined the term ‘triune brain’ (cf. Fig. 3), considered the limbic system as an interface between neocortex and brainstem. Thereby it would modulate the conscious stream of factual information, processed in the neocortex, and the autonomic, life-supporting functions of the brainstem (Markowitsch, 2009). While the value of the concept of a limbic system was questioned repeatedly, it was always revived again (e.g., Livingston & Escobar, 1971; Isaacson, 1982) and is nowadays even more used than decades ago.

As stated above, emotion and cognition interact most closely in autobiographic memory (Williams et al., 2007; Pessao, 2008; Markowitsch & Welzer, 2009; Reinhold & Markowitsch, 2009). If a structure within the expanded or greater limbic system is inactive or functions in a maladaptive way, neither a proper encoding nor a proper retrieval of autobiographical information will be possible (Markowitsch, 2003b). This interruption of synchronized affect–memory processing can be seen in patients in whom fiber tracts are damaged, disconnecting an interchange between relevant regions. One such fiber tract is the uncinate fascicle whose ventral branch interconnects and who apparently is the only fiber tract growing and

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**Figure 3:**

Top: Schematic sagittal section through a mammalian brain, illustrating MacLean’s (1970) idea of a triune brain in which the limbic system works as an interface between the neocortex (controlling intellectual functions) and the brainstem (controlling basic physiological functions). Bottom: Schematic sagittal section through the human cerebrum, showing the main structures of the expanded limbic system.
expanding lifelong (Lebel, Walker, Leemans, Phillips & Beaulieu, 2008). Furthermore, it is asymmetric in that way, that it is larger in the right hemisphere and contains 33% more fibers in the right compared to the left hemisphere (Highley, Walker, Esiri, Crow & Harrison, 2002) (Fig. 4).

As Figure 4 shows the uncinate fascicle bidirectionally connects those portions of the temporal and frontal lobes which are considered as essential for the retrieval of memories – either autobiographical, when predominantly the right hemisphere is involved, or semantic memories, when predominantly the left hemisphere is engaged (Kroll, Markowitsch, Knight & von Cramon, 1997; Markowitsch, Calabrese, Neufeld, Gehlen & Durwen, 1999).

Figure 4: The location of the ventral branch of the uncinate fascicle, interconnecting the inferior lateral prefrontal cortex and the temporopolar cortex. It is assumed that these regions are essential for triggering the retrieval of semantic (left hemisphere) and episodic-autobiographical information (right hemisphere) (cf. Markowitsch & Welzer, 2009).

Another structure which is important for autobiographical memory across the life time is the amygdala. Bilateral damage to this region apparently interferes with autobiographic memory processing. Two syndromes supporting its central role in autobiographic memory encoding and therefore its role in binding emotions to remembered events are the Klüver-Bucy-syndrome and the Urbach-Wiethe disease (Markowitsch, Calabrese, Neufeld, Gehlen & Durwen, 1999; Siebert, Markowitsch, Bartels, 2003). Klüver-Bucy syndrome is a complex syndrome which initially appeared in monkeys after bilateral lesions of the anterior temporal lobes (Klüver & Bucy, 1937; Klüver, 1955; Lilly, Cummings, Benson & Frankel, 1983). It is characterized by amnesia – the most frequently and consistently described symptom – as well as by affective disturbances, hypersexuality, agnosia, hyperorality, and hypermetamorphosis (a tendency to attend obsessively to everything appearing in the patient’s close proximity. Urbach-Wiethe disease as well is a complex syndrome primarily resulting from a genetically caused calcification of the amygdala. In this disease patients are not amnesic, but they have problems in selecting the proper (emotional) aspects of new information as was demonstrated in the study of Cahill, Babinsky, Markowitsch, and McGaugh (1995). In this study we showed that patients with Urbach-Wiethe disease whom a story was told, later reproduced to a high extent neutral, but not (the more important) emotional parts of the story. This example indicates that the amygdala is indeed necessary for an integrated autobiographical memory.

### Autobiographic Memory – Data from Patients

Deficits in autobiographical memory and its continuity from the past to present and future are particularly evident in patients with rare psychiatric disease conditions, subsumed under the heading of dissociative amnesias. Particularly evident are these deficits in patients with ‘mnestic block syndrome’, a term created by us (Markowitsch, 1998, 2000b, 2002, 2003b; Markowitsch, Kessler et al., 1999), and used by other investigators as well (e.g., Stracciari, Fonti & Guarino, 2008). We and other groups have also used the terms ‘psychogenic amnesia’ or ‘functional amnesia’ for these patients (Markowitsch, 2003b; Brandt & Van Gorp, 2006; Stracciarì et al., 2008). It is assumed that in such patients after a significant emotional event – such as a major stress or psychic traumatic condition – a coordinated action of limbic and neocortical structures becomes disturbed. Patients with mnestic block syndrome lose access to their autobiography – either totally or for a certain time epoch. The syndrome may pass with reinstatement of the personal past, or may persist over years – probably even life-long. It is characterized by a loss of access to the own biography and – in most instances – a preservation (or relatively quickly regain) of semantic memory and of the other, “lower” memory systems; cf. Fig. 1) (Markowitsch, 2003, 2008) (but see for a more cautious note van der Hart & Nijenhuis, 2001). The patients are able to read, write, calculate, and behave appropriately in social situations, and they are able to acquire and store new memories, however, frequently not with the same degree of emotional embedding as in normal subjects. Frequently, they are less concerned about their impaired state than their immediate partners or relatives, a phenomenon described already by Janet (1907) as “belle indifférence”. It is assumed that the binding or synchronization between facts and their emotional attachment is blocked. This holds especially for material which is threatening, sad or otherwise attached to negative emotions as in conditions of posttraumatic stress disorder (Driessen et al., 2004). It may, however, generalize the story...
to all personal memories or to personal memories from a certain epoch. Sometimes, especially at the onset of the functional amnesic condition, it may extend to semantic material (e.g., the ability to speak a foreign language) or even to non-declarative (procedural; cf. Fig. 1) forms of memory. These extended amnesic conditions are usually transient in nature.

This syndrome may occur after minor accidents or after particularly stressful events. It is assumed that the underlying causes are, however, much deeper and have to be traced to a stressful or traumatic childhood or youth (Markowitsch, 2008) (cf. the model on its etiology given in Table 23.2, p. 325, of Markowitsch, 2000). Interestingly, we quite consistently found neural correlates of their amnesia when scanning their brains with FDG-positron emission tomography (Markowitsch, Kessler, Van der Ven, Weber-Luxenburger & Heiss, 1998; Markowitsch, Kessler, Weber-Luxenburger, Van der Ven & Heiss, 2000; Reinhold, Kühnel, Brand & Markowitsch, 2006). Regions with reduced metabolism were found in the temporo-frontal junction area, particularly of the right hemisphere, and therefore in that area, where most receptors for stress hormones are found (O’Brien, 1997; Sapolsky, 2000; de Kloet, Joels & Holsboer, 2005; Yehuda, Blair, Labinsky & Bierer, 2007).

When re-analyzing the brains of 14 patients with psychogenic amnesia, we found that fronto-temporal regions of the right hemisphere, in particular the inferior lateral prefrontal cortex, was hypometabolic, indicating that a reinstatement of a normal metabolism in this region might probably lead to reinstatement of their autobiographical memories (Brand et al., 2009) (Fig. 5).

These data are furthermore in close agreement with our data on brain-damaged patients with autobiographical retrograde amnesia (Calabrese et al., 1996; Markowitsch et al., 1993; Kroll et al., 1997), as well as with the results of functional imaging studies, pointing to the central importance of the right fronto-temporal region for autobiographical memory retrieval (Fink et al., 1996).

Our data in these patients consequently show that environmentally induced stress situations may change brain activity and cerebral metabolism persistently and may therefore disturb the required synchrony necessary to bind affective and cognitive portions of episodic-autobiographical memories and to keep track of relations between episodes across time (Markowitsch, 2005; Suddendorf & Corballis, 2007; Roberts & Feeney, 2009).

They also indicate that the brain’s circuitry in getting access to previously stored information is altered and that especially fronto-temporal regions of the right hemisphere may be sensitive to autobiographical old memory processing. Finally, these data demonstrate that autobiographical memory is vulnerable to brain damage as well as to stressful or psycho-traumatic life situations that may occur during life time.

**The Development of Autobiographical Memory Binding**

As stated before, autobiographic memory develops over time (Fig. 2). We have studied the retrieval of autobiographical memories in adolescents and young adults (Oddo et al., 2010).

Adolescents were around 16 years and young adults around 22 years of age. Similar to our previous studies (e.g., Fink et al., 1996; Piecke, Weiss, Markowitsch, Zilles & Fink, 2003) we asked subjects to retrieve specific life episodes while their brain was scanned with functional magnetic resonance imaging. The life episodes were subdivided into four age ranges. These were for the older group: (P1) age 3 until the beginning of school, (P2) beginning of school until age 15, (P3) age 15 to age 18, (P4) recent memories from the last year before the interview. For the younger groups, the age ranges were the following: (P1) age 3 until the beginning of school, (P2) beginning of school to age 10, (P3) age 11 to age 14, (P4) recent memories from the last year before the interview. Similarly, we studied brain activations towards general life events (e.g., “Right after the start, an Air France Concorde plane crashes into a hotel”), divided into the same time epochs. The results revealed that in both groups especially the ventromedial prefrontal cortex was active (cf. Fig. 6, and Fig. 2 for its location) when the interaction between time and memory was analyzed (that is, when the activations of all four semantic memory epochs were subtracted from all four autobiographic memory epochs and the combined late autobiographic and semantic from the combined early
autobiographic and semantic memory activations). It was also found that autobiographical events resulted in a higher signal change in brain blood flow than semantic memories and that within the autobiographical memory domain signal changes increased from the early years of development to the presence (Fig. 6).

Consequently, we assume that the ventromedial prefrontal region, which since several years has been regarded to be central for the self, but also to theory of mind functions (e.g. Johnson et al., 2002; Schulte-Rüther, Markowitsch, Fink & Piefke, 2007) constitutes the core region for self-reflection of own memories across time.

As flexible mental time travelling constitutes a unique attribute of autobiographic memory (Markowitsch, 2005), these results highlight again the importance of well-developed frontal lobes for integrating and binding memory, time, consciousness and the self. These results were underlined by the finding that the older group showed a stronger ventromedial prefrontal activation than the younger one, indicating that attributes of an integrated self are more firmly established in young adulthood than during adolescence. Neuroanatomical tracing data, done with diffusion tensor magnetic resonance imaging, confirm the view that the prefrontal cortex is more than other brain regions dependent on a proper input from the environment in order to myelinate and therefore interconnect with other brain structures properly (Klingberg, Vaidya, Gabrieli, Moseley & Hedehus, 1999; Sowell et al., 2003; Powell, 2006).

These data on adolescents and young adults are complemented by functional imaging studies in middle-aged (Piefke, Weiss, Zilles, Markowitsch & Fink, 2003) and aged individuals (Markowitsch & Welzer, 2009).

All of these studies demonstrate that autobiographical memory retrieval engages a common network of prefrontal and limbic brain structures and that compared to the later age, the episodes learned in childhood and youth still are represented most distinctly and with the strongest emotional flavor until the end of life or – in cases of dementia – until the full-blown symptomatology of dementia are apparent (Markowitsch & Welzer, 2009).

**Conclusions**

A broad range of studies in normal, non-brain damaged subjects, in patients with brain damage and in patients with psychiatric disorders all indicate that human autobiographical memory is a complex phenomenon that requires a unique and highly synchronous pattern of binding processes in order to become successfully encoded, stored, and retrieved. Modern brain imaging techniques allow following and tracing the networks implicated in these processes. They furthermore – together with data from brain-damaged individuals – allow tracing the development and establishment and deterioration of autobiographical memory over time.

Figure 6: TOP: The interaction between time and memory type leads to a strong activation in the ventromedial prefrontal cortex, especially for recent autobiographical episodes. (Data from young adults.) BOTTOM: Plots of percentage signal change in the maximally activated voxel within the ventromedial prefrontal cortex in relation to the experimental conditions semantic memory (SM), time epochs P1 – P4, and autobiographical memory (AM), time epochs P1 – P4. The signal change increases across time periods only for autobiographical memories. Displayed are means and standard errors of the mean. (After Fig. 2 of Oddo et al., 2010.)

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