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Functional amnesia: the mnestic block syndrome

Hans J. Markowitsch

Abstract

The roots of the expression "functional amnesia" are discussed with particular reference to the old concept of hysteria. The more recent assessment of the existence of memory subsystems is used to demonstrate contents-related selective amnesias. The increasing number of patients with lasting amnesic conditions, particularly in the domain of episodic or autobiographic memories without concomitant brain damage provoked the postulation of the existence of a syndrome called "mnestic block syndrome". This syndrome can be visualized as a kind of disconnection which undermines the access to the engrams or storage places. As long as there are no clearer or more straightforward possibilities to explain the multitude of suddenly occurring and globally acting amnesias without manifest brain tissue damage, the assumption of a mnestic block condition can be taken as a preliminary model to attack the multitude of manifestations of functional amnesia.

Mots clés : Mémoire, autobiographie, hystérie, dépression.
Key words: Memory, autobiography, hysteria, depression.

Address for correspondence: Hans J. Markowitsch, Physiological Psychology, University of Bielefeld, P.O. Box 10 01 31, 33501 Bielefeld, Germany (e-mail: hjmarkowitsch@uni-bielefeld.de).

INTRODUCTION

Memory is a universal function in the animal kingdom which has its likely origin in its survival value for both individual and species. Individuals remembered where food and fellow partners were situated, which food was tasteful and which one poisonous. Survival of the species was promoted when an individual memorized the smell of a sexually available partner. The sense of smell was most intimately affixed to memory and the smell processing brain regions - principally situated in the limbic system (Markowitsch, 1999a; Nauta, 1979) - became the closest targets for memory processing.

A regular human life without memory cannot be imagined and the importance of memory has been stressed by various celebrities: Napoleon said "A head without the power of memory is like a fortress without a garrison", and Hering (1921) wrote "Memory connects innumerable single phenomena into a whole, and just as the body would be scattered like dust in countless atoms if the attraction of matter did not hold it together so consciousness - without the connecting power of memory - would fall apart in as many fragments as it contains moments" (p. 12). These examples can be related to the Janus head-like appearance of memory - looking back from the present into the past and at the same time attests the passing of time from the present to the future (Figure 1).

The causes of the fragility of memory likewise have been studied with numerous approaches since centuries (Clarke & Dewhurst, 1972; Markowitsch, 1992). The most obvious explanation for amnesia - the severest version of a memory disturbance - is brain damage at a strategic locus. Bilateral damage of a number of circumscribed regions can result in permanent amnesia, and it is assumed that these regions are bottlenecks for information transfer. Most well-known are examples of patients like HM (Scoville & Milner, 1957) with bilateral damage to the medial temporal lobe and life-long amnesia, or patients with Korsakoff's syndrome, who in spite of preserved intelligence, remain unable to acquire long term information. Regions in the limbic system are crucial for the transfer of information from short-term to long-term memory (Markowitsch, 2000 a & b).

Figure 1. Possible consequences of brain injury on old and new memories.

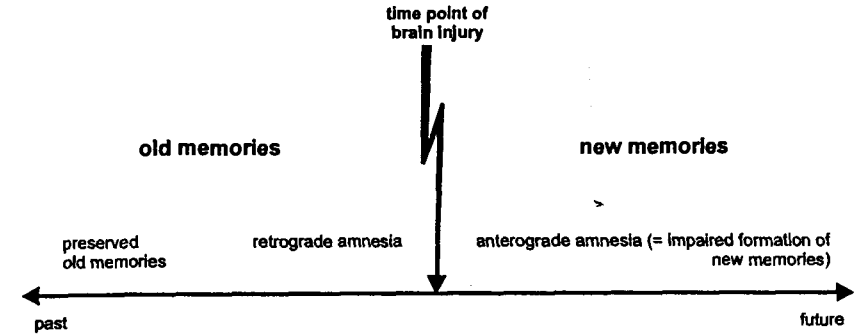

Figure 1. Conséquences possibles de lésions cérébrales sur les mémoires ancienne et récente.

HYSTERIA

Though the knowledge that focal brain damage to bottleneck structures of the brain can result in amnesia was available since the last century (Bechterew, 1900; Gudden, 1896), memory research of this time was dominated by psychiatric influences - Charcot's hysteric patients being famous examples (e.g., Charcot, 1892; see also Janet, 1894). Relations between hysteria and brain damage were common (Bennett, 1878; Gordon, 1927; Krafft-Ebing, 1898; Read, 1923; Thyssen, 1888). Indeed, the examples of religiously motivated (Hoche, 1933) and war related hysterias (Bauer, 1917) were frequent, and prisoners sometimes presented with the so-called Ganser syndrome (Ganser, 1898, 1904), a well-known (transient) amnesic state which consisted of a hysterical semi-trance or twilight state and could be characterized by the tendency to give only approximate reactions, and to deny things under high pressure. Impairments of consciousness, amnesia, and the existence of hallucinations were prominent features.

Already in 1878, Bennett published a "case of cerebral tumour-symptoms simulating hysteria" and 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 tumour; 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."

Especially retrograde amnesia was frequently considered to be of hysteric origin, even in the presence of brain damage, and indeed – seen for example from a psychoanalytic perspective (Breuer & Freud, 1895) – the altered life perspective after brain injuries may produce psychic symptoms, including the psychologically motivated forgetting of the better premorbid life. Vice versa, psychogenic amnesia, which is most likely observed in subjects with an unfriendly childhood or youth, or with prolonged difficult life conditions in their past, may be described as a mechanism of protection from an "unfavorable past" (Schultz, 1924; Markowitsch, 1996).

Seen in this context, organic and psychogenic forms of amnesia may be interdependent and the likeliness of this possibility will be discussed in the following. First, however, a short recapitulation of prerequisites for discussing amnesic states will be presented.

MEMORY AS A NON-UNITARY PHENOMENON

While the term "global amnesia" has found widespread use in the past and still is used at present, either per se (Seger, Rabin, Zarella, & Gabrieli, 1997; Vaidya, Gabrieli, Verfaellie, & Fleischman, 1998; Welch et al., 1996) or within the expression "transient global amnesia" (Markowitsch, 1990), the work of Tulving (1983) and its application to neuropsychology demonstrated that there are several forms of memory, some of which may be severely impaired after a given brain damage while others may be principally preserved (Markowitsch, 2000a). Four subsystems of long-term memory are of especial interest: "episodic

memory", "knowledge" (or semantic memory), "procedural memory", and "priming" (Figure 2). This sequence can be seen as a hierarchical one (Tulving, 1995) with episodic memory being the most advanced system (Tulving & Markowitsch, 1998) and that which is most vulnerable to brain damage (with the exception of basal ganglia damage).

Figure 2. Content-based subdivisions of memory.

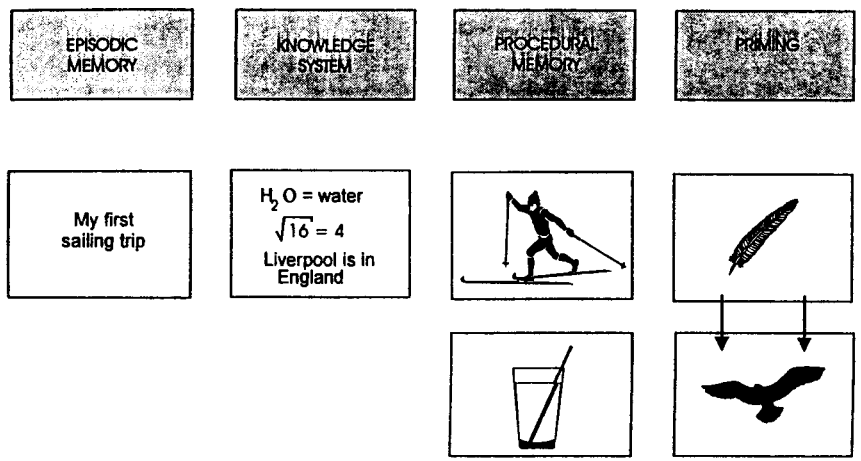

Figure 2. Organisation de la mémoire en subdivisions.

Another division of importance is that between explicit, or consciously aware and reflected, and implicit or automatic, non-reflected forms of memory (Eustache et al., 1997; Gabrieli, Fleischman, Keane, Reminger, & Morrell, 1995; Rugg et al., 1998; Winocur, Moscovitch, & Stuss, 1996). Explicit memory processing is closely bound to the episodic memory system, while the other three systems predominantly process information implicitly (Tulving, 1995).

Episodic memory is the only memory system that deals with the past and makes the personally experienced past accessible through autonoetic

awareness. It allows mental "time travel" through subjective time, from the present to the past and to the future (Tulving & Markowitsch, 1998). Episodic memory has to do with conscious recollection of previous experiences of events, happenings, and situations. The important word in this context is "experience", which indicates the emotional embedding of episodic memories and their usual connection with or reference to the own person. The knowledge system on the other hand deals with (neutral) facts without referring to their context in time. These two systems are of primary importance for the following discussion.

BRAIN - MEMORY INTERACTIONS

The sequence of information processing naturally engages wide neural networks. Most forms of information are first perceived via the sensory organs, and then are transmitted to uni- and polymodal cortical areas. After short-term storage an important selection process occurs in regions of the limbic system which filter, synchronize, associate, assimilate, and finally transmit successfully pre-processed information for long-term storage (Markowitsch, 2000a). Affect-related processing is of particular importance within this stage and amygdaloid and septal regions contribute to this substantially (Markowitsch, 2000a).

Cortically stored information from the knowledge and the episodic systems apparently needs anterior temporal and infero-lateral prefrontal regions for retrieval or ecphory (Markowitsch, 1995, 1997, 2000a). (Tulving, 1983, used the term "ecphory" to describe the process by which retrieval cues interact with stored information so that an image or a representation of the information in question appears.) A hemispheric specialization has been found which links the right hemisphere to the retrieval of episodic (or autobiographic), and the left hemisphere to the retrieval of semantic information or knowledge facts (Fink et al., 1996; Markowitsch, 1995; Tulving, Kapur, Craik, Moscovitch, & Houle, 1994). Damage to the temporo-frontal junction area of (predominantly) the right hemisphere leads to an inability to ecphorize episodic-autobiographic information (Calabrese et al., 1996; Kroll, Markowitsch, Knight, & von Cramon, 1997; Markowitsch et al., 1993; Markowitsch & Ewald, 1997), and predominantly damage to the left hemisphere to an inability of fact recall (De Renzi, Liotti, & Nichelli, 1987; Markowitsch, Calabrese, Neufeld, Gehlen, & Durwen, 1999a).

FUNCTIONAL AMNESIA AND THE MNESTIC BLOCK SYNDROME

Most interestingly, we recently found the brain loci implicated in autobiographic memory retrieval to be similarly hypometabolic in a patient with a clear organic basis of her brain damage (herpes simplex encephalitis) (Calabrese et al., 1996), and in another one for whom such an organic basis could be excluded or at least was found to be very unlikely (Markowitsch et al., 1997a; Figure 3) - a patient diagnosed as having a psychogenic amnesia. (Similar findings of changes in cerebral blood flow have recently been reported by Yazící & Kostakoglu, 1998, for patients with conversion disorders.)

This observation brought us to compare the memory disorders in patients with organic retrograde amnesia and with psychogenic (retrograde) amnesia in more detail. The pattern of deficits was found to be closely similar in patients of either etiology (Markowitsch, 1996). Adding functional imaging techniques as diagnostic tools confirmed the hypothesis that the right temporo-frontal junction area, which is bilaterally connected via the uncinate fascicle, is engaged in the retrieval of episodic-autobiographical information (Fink et al., 1996; Markowitsch et al., 1999b), and that failure of such retrieval - as in psychogenic amnesia or psychogenic fugue conditions - also failed to activate this junction area of the right hemisphere (Markowitsch, Fink, Thöne, Kessler, & Heiss, 1997b).

Furthermore, patients with psychogenic or functional amnesia appear emotionally flattened. The same reduction in affect expression appears in patients with selective or largely selective retrograde (or anterograde) amnesia of an organic basis appear (Table 1).

Figure 3. Horizontal SPECT-images through the brains of two patients with selective retrograde amnesia for autobiographical information. The section on the left is from a patient with a probable organically based amnesia (herpes simplex encephalitis; Calabrese et al., 1996). It was done three years post-infection and demonstrates the area of hypoperfusion in the right temporo-frontal region. The section on the right shows the brain of a patient with probable psychogenic amnesia (Markowitsch et al., 1997a). Again, a significant metabolic reduction is visible in the right temporo-frontal junction zone. (After Calabrese et al., 1996, and Markowitsch et al., 1997a.)

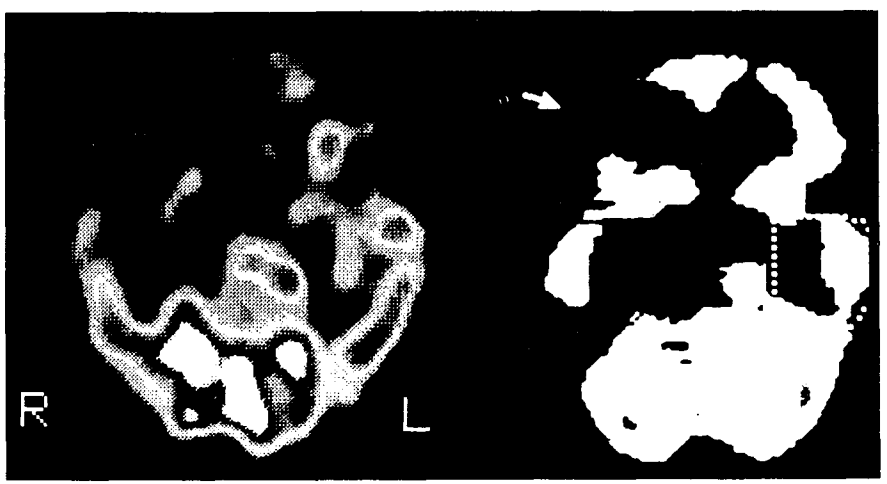

Figure 3. Coupes horizontales, en SPECT, des cerveaux de deux patients présentant une amnésie rétrograde autobiographique sélective. L'image de gauche est celle d'un patient présentant une probable amnésie organique à la suite d'une encéphalite herpétique (Calabrese et al., 1996). Elle a été réalisée 3 ans après l'infection et montre une hypoperfusion dans la région temporo-frontale droite. L'image de droite est celle d'un patient présentant une probable amnésie psychogène (Markowitsch et al., 1997a). On retrouve un hypodébit significatif dans la région temporo-frontale droite.

Table 1
Examples of descriptions of patients with organic or functional amnesia indicating emotional flattening

Study	Remarks on the patient's affective behavior
Wechsler (1973)	"... cerebral dysfunction due to organic disease results in a comparatively selective inability to recall emotionally charged, ... material" (p. 134) [various kinds of brain damage]
Markowitsch et al. (1993)	"The quite constant mood of the patient underlined the impression of somnambulism." (p. 648) [diencephalic infarct]
Calabrese et al. (1996)	"Emotional flattening is a frequent concomitant in patients with retrograde amnesia, both of organic and psychogenic origin" (p. 309) [encephalitis]
J. Kessler et al. (1997)	"During the interviews [with a psychiatrist], his retreat from social bonds was reflected by his keeping a certain distance, only occasionally entering into a more warm and emotional conversation" (p. 609) [functional amnesia]
Markowitsch et al. (1997b)	"... he repeatedly mentioned that life events were apparently of much less importance to him than to his wife and children." (p. 152) [psychogenic fugue]
Kroll et al. (1977)	"His memories seem 'flat'" (p. 1380) [traumatic organic retrograde amnesia]

Tableau 1
Exemples de descriptions de patients souffrant d'amnésie d'origine organique ou fonctionnelle.

Finally, it was found that exposure to major stress conditions – either long-lasting, continuous stress, or the repetition of single, significant stress event after a long time gap, or the interaction of physical and psychic stress conditions – resulted in amnesia. This form of amnesia was

termed "mnestic block syndrome" (Markowitsch, 1998) and was observed in patients after whiplash injury (Markowitsch, Kessler, Kalbe, & Herholz, 1999b), after a frightening experience (Markowitsch, Kessler, van der Ven, Weber-Luxenburger, & Heiss, 1998), and after chronic subjectively inescapable stress (Markowitsch et al., 1999b). Furthermore, we observed in a patient who most likely had been sexually abused during her childhood a selective block for the retrieval of autobiographical events from the episode between her 10th and 16th years (Markowitsch, Thiel, Kessler, & Heiss, 1997c).

Interestingly, there is a variance in the affection of anterograde and retrograde amnesia with single patients showing pure anterograde (J. Kessler et al., 1997), pure retrograde (Markowitsch et al., 1997b,c), or a mixture of anterograde and retrograde amnesias (Markowitsch et al., 1998, 1999b). And also of interest, metabolic brain changes in memory processing are for some, but not all cases detectable. For one patient a strong correlation between cognitive and brain metabolic activations could be detected: he initially manifested a severe hypometabolic state in memory processing regions of the brain and was anterogradely and partly also retrogradely amnesic (Markowitsch et al., 1998); after one year, his brain metabolism had returned to normal conditions and his cognitive status had significantly improved, though he still showed impairments in remembering or retrieving information after a long delay (Markowitsch et al., 2000).

BRAIN MECHANISMS POSSIBLY UNDERLYING THE "MNESTIC BLOCK SYNDROME"

All mental activities require brain activity. Consequently, it is assumed – in line with the evidence from the patients studied so far – that in patients with continuing autobiographic encoding or retrieval impairments certain regions of the brain are blocked from engaging in their usual or natural activity. That is, a kind of disconnection syndrome hinders the neural nets to contribute in a way to information processing (either encoding or retrieval) which occurs in a normally performing brain (Markowitsch, 1998).

It is proposed that the disconnection or mnestic block is provoked by an inappropriate processing of stress hormones – glucocorticoids – on the brain level. It is known that especially affect and memory processing regions of the medial and anterior temporal lobe (amygdala, hippocampus) possess a high number of glucocorticoid receptors (Fuchs & Flügge, 1998; Roozendaal & McGaugh, 1997; Roozendaal, Portillo-Marquez, & McGaugh, 1996; Watanabe, Yamaguchi, & McEwen, 1996). Furthermore, there is now increasing evidence for interactions between stress hormones and neurotransmitters (Joëls & de Kloet, 1992; Lupien & McEwen, 1997; Majewska, 1992). Serotonin, for instance, plays a central role in stress coping and its lack may induce depression (Bell & Nutt, 1998; Chaouloff, 1993; Davis, Suris, Lambert, Heimberg, & Petty, 1997; Southwick et al., 1997a). And even in patients with obsessive-compulsive disorder retrieving of autobiographical memory was demonstrated to be deficient and the deficiency was attributed to a co-morbid diagnosis of major depression (Wilhelm, McNally, Baer, & Florin, 1997). Southwick, Morgan, Nicolaou, and Charney (1997b) found distortions and omission of trauma-related events in soldiers from the Kuweit war and Sutker, Winstead, Galina, and Allain (1991) reported cognitive deficits in prisoners of war and participants of the Korean war. Stress hormones seem also to have a major impact on brain aging (Porter & Landfield, 1998) and are intimately related to post-traumatic stress disorder (PTSD) (Heim, Ehlert, Hanker, & Hellhammer, 1998).

The multiple nature of stress makes a concise definition impossible. Already Selye (1956) pointed to the subjectivity in the treatment of stimuli within and between individuals: what is stressful for one person on one occasion may not be so on another. Similarly, what one person considers stressful, another needs not. Furthermore, the consequences of stress may differ over time: in the short-term, stress may induce positive, adaptive changes, and in the long-term it may become maladaptive. There exist physical, psychic, and social stressors (stress-evoking agents). The most widely accepted definition of stress relies on a person's response and takes the activation of the pituitary-adrenal axis as measure of stress (Akil et al., 1999; Dunn, 1987).

Inappropriate action of stress hormones on the brain level and all along the hypothalamo-hypophyseal-adrenocortical axis (HHA) was proposed to be central for these kinds of impairments (Herman & Cullinan, 1997; Holsboer, 1989). Failure of successful coping with intense stress situations was hypothesized to lead to up to 25% reduction of the hippocampal volume in combat veterans (Gurvits et al., 1996). Most likely these reductions are due to a shrunken hippocampal neuropil (Magariños, McEwen, Flügge, & Fuchs, 1996; Magariños, Verdugo, & McEwen, 1997).

Results of studies by Bremner, Sapolsky, and others suggest that excessive stress may induce lasting memory disturbances as well as permanent changes on the brain level (Bremner, Krystal, Southwick, & Charney, 1995a; Bremner et al., 1993, 1995b, 1995c, 1997; Sapolsky, 1994, 1996a, 1996b; Barrett, Green, Morris, Giles, & Croft, 1996; Carlier, Lamberts, Fouwels, & Gersons, 1996; Elder, Shanahan, & Clipp, 1997; Layton & Wardi-Zonna, 1995; Skodol et al., 1996; Van der Kolk, 1994). Within this context a predisposition in childhood has been frequently suggested to enhance the likeliness of an outbreak of stress-related cognitive deteriorations in adulthood (Aldenhoff, 1997; Liotti, 1992; Schacter, Koutstall, & Norman, 1996) and even to hinder the development of the limbic system (Teicher, Glod, Surrey, & Swett, 1993).

A number of reports propose that a predisposition for the development of stress-related cognitive changes in adulthood is enforced by mechanisms present in childhood (Aldenhoff, 1997; Kuyken & Brewin, 1995; Liotti, 1992; Parks & Balon, 1995; Schacter et al., 1996; Teicher et al., 1993). Teicher et al. (1993), for instance, showed that early physical or sexual abuse hinders the development of the limbic system highly significantly. The case history of our patient AMN, who had seen the outbreak of an open fire as an adult and had seen a person burning to death at age four, is another example (Markowitsch et al., 1998).

Depressive states likewise change the glucocorticoid feedback on brain level (Young, Haskett, Murphy-Weinberg, Watson, & Akil, 1991) and induce changes in the cellular immune response (Dorian & Garfinkel, 1989; Herbert & Cohen, 1993; O'Leary, 1990). In a comprehensive survey, Aldenhoff (1997) discussed relations between glucocorticoids

and depression. He indicated that there is an "overdrive" in the cortisol response in depression while there is a suppression under the condition of PTSD. He concluded that the time point of the stress reaction and the state of the organism will control the reaction form of the organism. Aldenhoff's scheme of the development of depression implies the existence of an early trauma state and a (re-)activation via psychological mechanisms or biological events, which after a latency phase will lead to a vegetative-emotional cognitive dissociation, a psychobiological stress reaction and depression. Similarly, though with much closer links to animal research, Lupien and McEwen (1997) presented with their review on the acute effects of corticosteroids on cognitions an impressive insight into endocrinological modulations of complex behavioral states.

There are also intimate relations between stress, depression and an increased risk to suffer PTSD (Bleich, Koslowsky, Dolev, & Lerer, 1997; Breslau, Davis, Peterson, & Schultz, 1997; Fawzi, Murphy, Pham, Lin, Poole, & Mollica, 1997; R. C. Kessler, 1997; O'Brien, 1997; Peck, Robertson, & Zeffert, 1996; Silove, Sinnerbrink, Field, Manicavasagar, & Steel, 1997). Yehuda, Giller, and Mason (1993) emphasized the similarities between PTSD and depression (insomnia, concentration disturbances, social retreat, loss of interests), but discussed the opposite activity changes in the HHA-response as well. All these data suggest that the memory disorders observed in cases with functional amnesia may at least in part be due to a changed glucocorticoid metabolism, and that in some cases this change may cause irreversible brain damage (cf. Bremner et al., 1993, 1995a, b, c, 1997; Gurvits et al., 1996) while in others it may lead to temporary blocking mechanisms (Horton, 1993; Markowitsch et al., 1998). Recently, altered brain metabolic states have been found with PET in response to both psychogenic (fugue caused) amnesia (Markowitsch et al., 1997b) and hysterical paralysis (Marshall, Halligan, Fink, Wade, & Frackowiak, 1997).

From the review presented above, it follows that the distinction between organic and psychogenic amnesias may in fact be more likely one between direct, massive neuronal damage due to a known and obvious cause (e.g., infarct, traumatic brain injury, neurodegenerative or neoplasmic change) and one between indirect, environmentally (or even internally, i.e., "thought") induced metabolic damage (Markowitsch,

1996; Markowitsch et al., 1999c), most likely via excitotoxic mechanisms (Whetsell, 1996). Both forms certainly have neuronal changes as common denominator and their comparison may result in a more integrative view of the causes of memory (and other mental) disturbances (Alexander, 1996; Andreasen, 1997).

Using functional imaging, we demonstrated a positive correlation between the metabolic activation of the bottleneck structures of the medial diencephalon and the medial temporal lobe – which are necessary for successful initial encoding of information – and cognitive, in particular memory performance (Markowitsch et al., 1998, 1999b). We proposed that a block via stress-induced biochemical alterations may lead to temporary anterograde amnesia and that de-blocking over time and with the help of drug and psychotherapeutic treatment may reinstate more appropriate memory performance. Similarly, a blocking of the anterior temporal polar region (which together with infero-lateral prefrontal regions is necessary for ecphorizing old memories (Fink et al., 1996; Markowitsch et al., 1997c), may lead to temporary retrograde amnesia.

We do not know whether these still somewhat simplistic models will hold, but the documented evidence from numerous single cases suggests that we have to refine or even abandon current views on neurology- vs. psychiatry-based memory disturbances with the aim of establishing more unitary models of information processing in healthy and affected brains. There may be various stages between organic and psychic disease conditions, including psychogenic and somatopsychic ones (Alexander, 1996; Kisely, Goldberg, & Simon, 1997; Radanov, Di Stefano, Schnidrig, & Sturzenegger, 1994; White & Moorey, 1997).

As long as there are no clearer or more straightforward possibilities to explain the multitude of suddenly occurring and globally acting amnesias without manifest brain tissue damage, the assumption of a mnestic block condition can be taken as a preliminary model to attack the multitude of manifestations of functional amnesia.

RÉSUMÉ

Les origines du concept d'amnésie fonctionnelle sont discutées en référence à l'ancien concept d'amnésie hystérique. La connaissance récente des sous-systèmes de mémoire permet d'isoler des amnésies rétrogrades sélectives. Le nombre croissant de patients avec des amnésies durables, en particulier dans les domaines épisodique et autobiographique sans lésion visible sur l'imagerie, permet de définir le syndrome de "blocage fonctionnel de la mémoire". Ce syndrome peut être envisagé comme une sorte de dysconnexion qui bloque l'accès à certains sites de stockage. Tant qu'aucune explication convaincante n'existera pour ces amnésies persistantes massives et de début brutal, ce blocage de mémoire pourra être proposé comme modèle d'approche des multiples symptômes de l'amnésie fonctionnelle.

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