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Research report

Functional retrograde amnesia: A multiple case study

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ABSTRACT

Functional retrograde amnesia (RA) is a rare pathology and has been rarely studied in detail across different patients. We extensively examined five functional RA patients and compared their neuropsychological profile including anterograde and retrograde memory performance, executive functions, emotional processing, and formally assessed psychiatric symptoms. Across patients, neuropsychological deficits beyond RA were most consistently seen in executive functions and attention suggesting that these dysfunctions contribute to the remote memory deficit. In a majority of the patients, problems in social cognition and emotional behaviour were reflected in Theory of Mind deficits and accompanying psychiatric symptoms. Aberrances in a measure of social desirability were detected, pointing to repressive tendencies in three out of the five patients. Future studies of functional RA patients may investigate more specifically which frontal-lobe associated (dys-) functions contribute to the memory retrieval deficit. Moreover, studying more closely the interaction between social cognition, repressive personality style and memory inhibition in this disease seems worthwhile pursuing.

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1. Introduction

Functional retrograde amnesia (RA) refers to a complete or partial loss of remote memories with a primacy of psychological factors in the absence of corresponding structural brain pathology (Kritchevsky et al., 2004). The condition may occur after acute trauma or extremely stressful experiences as in dissociative disorders, for instance, dissociative fugue (Glisky et al., 2004; Markowitsch et al., 1997). The term 'functional' is sometimes used interchangeably with 'psychogenic', suggesting a causal relationship between psychological aetiology and

onset of amnesic symptoms. However, 'functional RA' was also described in neurologically healthy individuals in whom neither psychological precursors nor emotional disturbances were detected (De Renzi et al., 1995; Lucchelli et al., 1998; Sellal et al., 2002). Such cases were sometimes suggested to have functional/metabolic disturbances in memory-relevant brain structures (e.g., De Renzi et al., 1997; De Renzi, 2002) that may have been below thresholds for detection. Alternatively, the possibility of undiscovered emotional problems or previous psychiatric symptoms has to be considered. In this regard, Kopelman (2000) suggested that many RAs of assumed organic

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origin may in fact have been entirely or partly caused by psychological mechanisms. Likewise, [Kapur \(1999\)](#) emphasised that even after significant brain damage, symptoms of RA can result from primary psychological mechanisms and appear disproportionate to the lesion extent and location.

There is no standard approach to distinguish between neurological and psychogenic forms of RA in the absence of unequivocal evidence from either side. Moreover, the fact that almost all previous reports were single cases (for exceptions see [Kritchevsky et al., 2004](#); [Lucchelli et al., 1998](#)) limited the generalizability of previous reports. As a consequence, the idiosyncrasies of the patients in these studies also hampered the construction of precisely demarcated diagnostic criteria. [Kritchevsky et al. \(2004\)](#) convincingly outlined that just this variability in retrograde memory loss and preservation, accompanied by variable degrees of anterograde learning impairment may give important hints of psychogenic causation. Nevertheless, there are questions remaining about how a psychological mechanism so uniformly affects autobiographical-episodic memories while leaving some semantic memories intact, whether other neuropsychological and emotional-motivational factors than memory play a quantifiable role in this disease, and finally whether symptoms of RA can be individually traced back to functional brain activity during remote memory retrieval.

Several neuropsychological characteristics were proposed to differentiate between organic or psychogenic forms of RA. Among these, a dissociation of indirect and direct access to remote memories has been considered. While deliberate cueing failed to evoke past memories in some psychogenic RA cases, more indirect questioning has been successful ([Campodónico and Rediess, 1996](#); [Kopelman et al., 1994](#); [Kritchevsky et al., 2004](#)). Other studies revealed 'reverse' temporal gradients in functional RA – relatively unimpaired retrieval of recent information accompanied by massive deterioration of childhood memories – which is unusual in organic amnesia ([Kritchevsky et al., 1997](#); c.f., [Kopelman and Kapur, 2001](#)). Furthermore, characteristics such as a lack of interest in the symptoms ('la belle indifférence') and secondary gain or benefit from amnesia can indicate psychological mechanisms ([De Renzi et al., 1995](#); [Papagno, 1998](#)). [Kopelman \(2000\)](#) suggested that severe precipitating stress, preceding emotional disturbances (e.g., depression) and past transient organic memory loss (e.g., Transient Global Amnesia), i.e., constituting a preceding 'learning experience' of amnesia, elevate the probability of psychogenic RA. According to [Kopelman \(2000\)](#), this may occur by an interaction with executive functions resulting in inhibition of remote memory retrieval. The clinical picture is further complicated by the possibility of malingering, which is conscious simulation of the symptoms compared to the supposedly unconscious mechanisms in psychogenic amnesia. Assessment of malingering is particularly challenging in individuals with functional RA for several reasons. Firstly, standard instruments of malingering assess anterograde rather than retrograde memory. Secondly, functional RA patients usually re-learn their past very quickly, which can render disentangling of actual and re-learned memories impossible. Thirdly, even with standard procedures for detecting malingering (e.g., symptom validation for assessing below-chance performance), one still does not know whether performance was

consciously aggravated or patients unconsciously 'avoided' correct answers.

Finally, the heterogeneity of functional RA patients reported in the literature is also reflected in functional neuroimaging findings. Resting state monitoring of brain functions, as well as activation paradigms during retrieval of presumably inaccessible information revealed highly individual and inconsistent results. For instance, functional irregularities were observed in temporal regions of the right ([Sellal et al., 2002](#)) and left hemisphere ([Papagno, 1998](#)), bilateral posterior temporal ([De Renzi and Lucchelli, 1993](#); case T.H. from [Nakamura et al., 2002](#)), in frontal or parietal areas of the left ([Stracciari et al., 1994](#)) or right hemisphere ([Starkstein et al., 1997](#)), as well as in posterior cingulate gyrus ([Lucchelli et al., 1995](#)). In other cases, no such pathologies were observed ([De Renzi et al., 1995, 1997](#); [Barbarotto et al., 1996](#)). Summarising these findings, we see thus far limited converging evidence of one crucial brain region via which disturbance of remote memory retrieval necessarily occurs in the absence of structural brain damage.

If psychological factors, in contrast to primarily organic causes, evoke functional RA, then one would predict the syndrome to be characterised by high interindividual variability. As suggested by [Kritchevsky et al. \(2004\)](#), patients' common-sense ideas about memory loss likely determine their clinical presentation of amnesia. From this observation one can speculate that – consciously or not – holding these conceptual ideas online in order to present an internally consistent memory loss over extended periods of time, requires extensive attentional and executive control. Thus, functional RA patients might suffer from diminished attentional and executive functioning in formal neuropsychological testing. For a comprehensive attempt to compare across different patients with functional RA, we studied extensive personal background information, neuropsychological performance, as well as formally assessed current psychiatric symptoms and personality across five patients with functional RA.

2. Case histories

We enrolled two women and three men with an age range of 17–35 years. All patients are right-handed. Except for patient A.B., who at the time of testing was still attending school, all had a 10-year school education, which constitutes the conventional amount of education that nonprofessionals acquire in the countries in which the patients were educated (see below).

Patient A.B. is a 17-year-old schoolgirl. For unknown reasons, she suddenly became unconscious while on an apprenticeship away from home. She fell and struck her head (June 2001). After an unknown period of time (≤ 1 h) she was found lying on the floor. The friends who found her reported that she responded to her name, but she repeatedly stated that she had no memory of where she was and how she happened to be in this situation. Her friends also reported that she seemingly lacked information about herself (e.g., address, recent personal events). Immediately after she was found, A.B. received neurological, neuroradiological, and neuropsychological investigations (encephalogram – EEG, evoked potentials, magnetic resonance imaging – MRI, lumbar puncture, and screening of intelligence, attention, and anterograde memory)

with entirely normal results. A psychiatric report stated hypomania, problems in sexual behaviour and an elevated score in the Minnesota Multiphasic Personality Inventory (MMPI) validity scale indicating exaggeration of psychiatric symptoms. Although not formally documented in the hospital records, her psychologist stated that her friends mentioned a bruise at the right side of her forehead, which she supposedly received from the fall. Following discharge from the hospital after two days, the RA persisted and comprised autobiographical-episodic information as well as some semantic facts covering her entire previous life. It is reported that A.B. was unable to recognise significant others as well as her home and belongings. Anterograde and procedural memory and language were described to be intact (i.e., A.B. was spontaneously able to respond in English and French which she had learned in school). Patient A.B. rapidly re-learned personal and public semantic information. Though few vague images or fragmented personal episodic memories were reported to have returned, re-learning generally did not evoke the actual re-experiencing of these events according to self-report. Interviewing A.B.'s relatives and friends revealed that her personality had not been significantly changed, except that she lost her depressive tendencies (see below). However, several everyday habits were reported to be different compared to the time before the onset of the amnesia (e.g., food preferences).

Medical records revealed that since October 2000 A.B. suffered from major depression until the RA onset. She was treated with a selective serotonin-reuptake inhibitor. The depression was reported to have recovered after the accident. Several paroxysmal states were described preceding and following the accident. These spells were described as brief losses of consciousness during which A.B. fell to the ground. Except for some bruises, none of these incidents caused any injury. To exclude epileptogenic activity, continuous EEG recording was conducted in July 2001, but did not reveal any pathology. Her physicians therefore assumed a psychosomatic origin of her symptoms. Likewise, after the RA onset, several somatic complaints (headache, gastrointestinal pain) emerged whose organic causation remained obscure. Her physician suggested psychogenic/psychosomatic co-contribution. Furthermore, throughout the year preceding the RA onset, there were four documented suicides in her circle of friends. Patient A.B.'s friend reported that before and after the incident, A.B.'s relationships to her mother and younger sister were characterised by recurring conflict and rivalry. When asked directly, A.B. reported that after the onset of the amnesia, her relationship to her sister was "as good as it always was", although she admitted quarrelling with her mother every so often. A.B.'s psychotherapist mentioned that about a year prior to the incident, A.B.'s sister had started becoming friends with some of A.B.'s friends. According to her psychotherapist, this may have been related to A.B.'s behaviour of slowly withdrawing from her friends and developing her depression.

As reported by her physician and relatives after our examination, A.B. gradually started to recover from functional RA after nine months, with no obvious temporal pattern or gradient of complete memory recovery. Following an appendectomy in February 2002, her somatic complaints extinguished and she is reported to be symptom free since then. We saw A.B. four months after the amnesia onset.

Patient C.D. is a 30-year-old engineer. He was born in the UK, married with one child. At the time of his illness he had lived in Germany since 1989. The present condition arose from a car accident during a foreign assignment (June 2001). C.D. reported that he was pinned in a truck for 2 h during which helpers tried to rescue him. Due to high outside temperature and the still strapped seat belt, breathing started to get difficult until he lost consciousness. In our interview, patient C.D. was capable to give a detailed report of the entire injury as well as the sequence of events immediately preceding the injury. In hospital, fractures of the extremities were diagnosed. According to medical records, mild head injury was assumed, but the suspicion was not confirmed due to normal results in EEG and MRI of the head. In contrast to C.D.'s apparently intact memory for the accident and its cause in our examination, he reported that in the hospital he was disoriented to place, time, and person. He stated that he neither remembered his name, nor understood where he was and why he was abroad. In contrast to his own report, medical records mentioned his amnesia for the first time around three weeks after the accident. Patient C.D. reported in our interview that during his stay abroad, though his native English language was unimpaired, he initially did not believe that he could speak and understand German. His deficit extended to knowledge about the usage of common tools (e.g., razors). He further stated that in the weeks and months after the injury, re-learning of formerly known information and activities occurred. Patient C.D. returned to his former occupation in August 2001.

Besides sporadic flashbacks and a few vague feelings of familiarity, he reported being amnesic for all remote memories prior to the incident. In contrast, the acquisition of new information was reported to be spared, permitting him to fill in memory gaps. However, during restoration of his past, no information returned spontaneously and he did not re-experience former events. C.D.'s wife reported that his personality underwent major changes after the accident. She mentioned a general slowing of behaviour and a tendency to misinterpret behaviour of others giving him a distrustful appearance. Due to his behavioural changes, C.D.'s wife initiated a conjoint therapy, but this was terminated after a few sessions by C.D.'s refusal to continue. Furthermore, in the time after he started working again, C.D. reported experiencing several social problems with co-workers and colleagues, which finally led him to quit his job. At the time of our investigation, C.D. was involved in litigation with his former employer. He claimed compensation for his RA emerging from the car accident during his work assignment. It has to be noted that patient C.D.'s cognitive-amnesic symptoms were variable according to reports of different investigators at different times. After our investigation, C.D. was seen by other neuropsychologists for his compensation claim. Interestingly, in the course of this extended testing, he was told that he would get little compensation for his RA, but that his minor executive deficits fitted with the nature of his accident, and would be worthy of compensation. Consequently, by the time of his subsequent neuropsychological testing he was much less concerned about his RA and his results in tests of executive functions were now extremely lowered.

The medical history of C.D. revealed numerous precursory incidents. Besides having been knocked-out during boxing (at

least once in 1991), C.D. suffered from his first closed head injury in November 1993 after an assault. He fell unconscious (<1 day) and later lacked his memory for about 8 h preceding and following the assault. His anterograde memory remained sketchy for about two weeks following the incident. It is further reported that he developed poor distance vision, constant headache, ataxia and right arm hemiparesis. Two days after the assault a suspected cerebrovascular accident was noted. However, EEG revealed no pathological signs and apart from hints for fracture of the right orbit, computed tomography (CT) and MRI of the brain and spinal cord showed normal results. His right arm hemiparesis and ataxia continued for several months and since no organic reason was found, psychogenic causation was suggested. In February 1994, conversion hysteria was diagnosed and a hypnotic procedure was initiated to reduce his hemiparesis, ataxia and the still persisting RA for the assault and assaulters. In the end of March 1994, these symptoms were reported to have recovered due to the hypnotic abreaction. In January 1997, patient C.D. was assaulted again, this time without major consequences. In the years 1997–1998 several incidents of inversion injuries of the extremities, accentuated on the right side, continuing ankle pain and a tendon injury of the right hand's upper limb were reported. Several surgical interventions were followed by wound infections. In November 1999 patient C.D. fell off the stairs in his home and hit the back of his head. For an unknown period of time he went unconscious followed by fatigue and diffuse headache. One day later, he experienced somnolence and possibly a convulsion. He then received intensive care for two days. In hospital he developed paresis of the right arm and shoulder. In the course of trauma diagnosis, a right fronto-parietal venous angioma was detected in angiography. The bleeding risk of the angioma was diagnosed as minimal, and since its location did not correspond to the body side of the motor symptoms its treatment was conservative. Acute CT and MRI as well as a follow-up MRI after one month did not reveal any pathological results and therefore the motor symptoms were suggested to be of psychogenic nature. The right arm weakness continued at least throughout 1999. Furthermore, there are several reports of bilateral knee joint pain, abnormal gait, diffuse abdominal pain, and shortness of breath throughout the same year and later on. In 2000, the patient suffered from diffuse chest pain for which no organic causation could be determined. Therefore, the pain symptoms were suggested being 'most likely of functional origin'.

Under our administration, a resting state ^{18}F -fluoro-2-deoxy-D-glucose (FDG)-PET was conducted to investigate functional/metabolic brain disturbances (March 2002). This examination revealed no pathological signs. Cerebral glucose distribution was within normal range. We saw C.D. eight months after the amnesia onset.

Patient E.F., a married locksmith without children, was 33 years old at the time of his illness. The current condition arose from an incident during a morning shower during which he for unknown reasons went unconscious (January 2002). After an unknown period of time (≤ 4 h) he awoke and was found by his wife arriving at home. She reported that he could remember his name. He acted very agitated and repeatedly asked what had happened. He did not recognise her as his

wife and seemed confused about how to dress when going outside, intending to leave in his bathrobe. He was brought to a nearby hospital where a profound retrograde memory loss was diagnosed in the absence of any pathological signs in CT, MRI, and EEG. Patient E.F. reported that when his mother came to visit him in the hospital after a few hours, her face looked familiar to him although he did not vividly remember who she was. Unlike his continuing lack of memory for his wife, he stated that memory for his parents returned after about 12 h.

In the first 2–3 days he regained memory for childhood and young adulthood whereas he stayed amnesic for personal and semantic information of the most recent 12–14 years. Initially, he reported to have been amnesic for almost everything including also knowledge about objects and common devices and actions (e.g., riding on a tram). Unimpaired anterograde learning abilities enabled him to quickly re-learn recent public facts and events as well as his personal life, though he did not vividly re-experience his autobiography. Specifically, he reported isolated memory fragments of the amnesic period, which, however, did not trigger re-experiencing of the entire autobiographical episodes. Intensive questioning of the patient's relatives and searching medical records did not reveal any past neurological or psychiatric incidents. In the time following the onset of the amnesia, E.F. experienced headaches when starting to work again in his old work place where he had minor contact with chemicals. He successfully changed his position within the same company. E.F. stated that according to his last memories of himself (12–14 years prior to the incident), his personality and cognitive skills did not change to a major degree. His wife confirmed this judgement with regard to the time period from which she knew him (E.F. and his wife had known each other for about 7 years prior to the incident). Under our administration, FDG-PET was conducted to investigate functional/metabolic brain disturbances (March 2002). A slight overall cortical and a significant cerebellar hypometabolism were found. We saw E.F. two months after the amnesia onset.

Patient G.H., a married housewife with three children, was 35 years old at the time of her illness. The present condition arose after anaesthesia for gynaecological surgery (August 2002). While the anaesthesia was reported to have been unproblematic, G.H. awoke disoriented and anxiously started asking the personnel where she was. It was reported that she could remember her name. She experienced herself to be in the year 1989 and was extremely anxious about her current state since she could not remember the reason for her surgery. She reported that her last memory was exactly dated by a day in the end of May 1989, which she could describe in great detail. This day, however, did not appear to bear significant relevance for her life neither before the onset of her amnesia nor – according to her husband – following the amnesia. All episodic and semantic remote memories since then were reported to have vanished. When her husband and eldest child came to the hospital for a visit, she recognised him but was surprised about his seemingly elder appearance. She did not recognise her child who – in her memory – was supposed to be 1.5 years old. Neuroradiological investigation (EEG, CT) did not reveal any brain pathology. In the time after the onset of the amnesia some sporadic flashbacks and vague memory

fragments occurred while she reported to have stayed largely amnesic for the 13 years preceding the incident. G.H. experienced major problems in her social environment after the amnesia started. She reported to often be overwhelmed by the emotional and relational demands of others. She and her husband described her as being extremely sensitive and emotionally unstable since the onset of the amnesia. Due to the fact that she was unable to remember two of her children, she suffered from feelings of guilt regarding her role as a mother and at the same time felt emotionally detached from her family. The psychological strains caused by her situation motivated her to start psychotherapeutic intervention in January 2003.

The medical history of G.H. revealed several incidents. Since her adolescence G.H. suffered from bradycardia and hypotonia. After a series of collapses she started wearing a cardiac pacemaker in 1990. Furthermore, she suffered from various gynaecological and gastrointestinal diseases and complications for which she underwent a considerable number of surgical interventions dated between 1991 and 2002. In addition, since the age of 20 (in 1987) she experienced severe migraine attacks occasionally involving 'altered states of consciousness', during which she was disoriented in time and location. In the context of these attacks she experienced paralysis of one half of the body; G.H. and her husband were unable to remember whether the right or the left body side had been affected. The migraines were successfully treated by acupuncture in 1996. According to information provided by G.H. and by her husband, G.H.'s childhood and young adulthood were extremely stressful. She reported numerous incidents of paternal violence against her mother and the children. Her parents were heavy drinkers and she described incidents when she witnessed and was even supposed to assist in suicide attempts of her mother. According to G.H. and her husband, G.H.'s parents were largely neglecting G.H. as a child, partly because of their alcoholism. As a consequence, G.H.'s current somatic conditions (bradycardia, gastrointestinal and gynaecological conditions) had their precursors in young adulthood due to her parents' refusal to search for medical help on time. She also reported a few insensitive experiences at a gynaecologist whom she saw around the age of 16. In the same year, G.H. met her now husband who finally sent her to a doctor from whom she received appropriate treatment.

According to G.H.'s husband, her personality underwent major changes since the onset of the amnesia. He described her behaviour as childish and more egocentric than before the amnesia. Her interpretation of other people's reactions and behaviours became erroneous which had led to misunderstandings with others and frustration in herself as well as in the family. Moreover, many of her everyday habits (e.g., choice of clothes, hobbies) were reported to have changed to a major degree. G.H. herself described her relationship to her husband as improved compared to the time before the amnesia onset. She mentioned that he would take care of her more than ever before, and that she was sometimes almost suspicious of his interest and enthusiasm in helping her. We saw G.H. two months after the amnesia onset.

Patient I.J., a salesman working for an import–export company, was 34 years old at the time of his illness. He was

born in Kazakhstan and has lived in Germany since 1993. He is married and father of two children. The present condition arose after he left his home to drive a friend to the airport. On the way back home he intended to visit a former business partner to receive a large amount of money from their corporate business. However, on this day (February 2002) I.J. did not return home and it could not be clarified whether he had ever arrived at his partner's place or not. After three weeks, a train guard found I.J. sleeping in a train in Russia. When the guard woke him up, I.J. was unable to remember any personal information, including his name. He reported that he was not in possession of any of the money that he had intended to receive from his former business partner. Instead, the train guard asked him to pack some clothes scattered around the train cabin in a bag lying near him. He could neither remember the bag nor the clothes. Later he noticed that these clothes were not even approximately his size. According to I.J., the train guard then asked him to leave the train at the next stop and addressed the words to him that 'he would then notice why he had to get off'. After I.J. had left the train he reported to have wandered around the city neither knowing where he was nor who he was. He also experienced severe headache. After about 1 h he returned to the railway station intending to clarify his location. He further reported that at the station, he entered a police compartment where he asked for advice. At this office, he collapsed without losing consciousness. A medical, who had been called by the police, stated that I.J. 'would have died' from high blood pressure if he had not immediately been treated by antihypertensives. As I.J. did not carry any legal documents, his identity was unclear and he was brought to a nearby psychiatric hospital where he stayed the following months. In this hospital, concentration deficits, a 'strong will', the 'ability to suppress feelings and discomfort', and symptoms of Post-Traumatic Stress Disorder (PTSD) were diagnosed. In May 2002, his story was reported in Russian television, which his wife in Germany became aware of. By the end of May 2002, his wife and brother went to Russia to take him home. When they met, I.J. was unable to recognise either his wife and brother or any of the documents they presented to him (e.g., private photos, videos). In June 2002 they returned to Germany. EEG and CT of the head, conducted in the same month, did not reveal any pathological signs. Since I.J.'s anterograde learning abilities were unimpaired, he was able to rapidly acquire remote information, but in the course of this process autobiographical memories did not return spontaneously. It was reported that his remote memory deficit remained basically unchanged. Although he slowly regained his knowledge of the German language, by the time of study he did not speak as fluently as before the onset of the amnesia. Intensive questioning of the patient's relatives and searching medical records did not reveal any precipitating neurological or psychiatric incidents. I.J. reported that besides his RA, he additionally suffered from attentional deficits that prevented him from sustaining concentration over periods longer than 2 h. His wife reported that his personality was unchanged since the onset of the amnesia though some alterations of daily habits occurred (e.g., food preferences). Since the family moved to another town following their return, their former social life has changed to a major degree. Due to these circumstances, however, it was

impossible to clarify to what extent I.J.'s amnesia contributed to these changes. We saw I.J. 13 months after the amnesia onset.

Written informed consent was received from all patients prior to investigation.

3. Methods

3.1. Background evaluation

All patients underwent extensive neuropsychological testing in order to evaluate anterograde memory, intelligence, attention and executive functions, and Theory of Mind. Applied tests can be derived from Table 1 of the results section. Less common tests included the Concentration Endurance Test d2 (Brickenkamp, 1994), subtests Alertness, Divided Attention, and Selective Attention of the Test Battery for the Assessment of Attention (German: Testbatterie zur Aufmerksamkeitsprüfung, TAP; Fimm and Zimmermann, 2001), and the Reading the Mind in the Eyes Test (German adaptation: Fleck et al., 2002 of Baron-Cohen et al., 2001). The Concentration Endurance Test d2 is a speeded letter cancellation task to assess sustained attention and visual scanning abilities. The TAP is a computerised test battery for assessing attentional performance on the basis of reaction times. Its Alertness subtest gives a measure of general slowing. The Divided Attention subtest is a dual-task paradigm and measures the ability to flexibly switch attention between concurrent tasks. The Selective Attention subtest is a go/no-go task in which the subject has to react selectively to one class of stimuli but not to others, inhibiting a dominant response. The Reading the Mind in the Eyes Test measures Theory of Mind abilities and requires self-paced identification of mental states of another person. Subjects are given black and white photographs of the eye region of human adults along with four adjectives describing possible mental states (e.g., 'calm', 'amused', 'cautious', 'sceptical') from which subjects are to choose the most likely state of the person whose eyes are presented in the picture.

Due to cultural and language-related differences in the non-German natives C.D. and I.J., adaptive changes to the test battery were applied where necessary. These included application of the Span Tests from the Wechsler Memory Scale-Revised (WMS-R; German version: Härting et al., 2000), Lexical Fluency (FAS-Test: Spreen and Strauss, 1998; German adaptation: Horn, 1983) and Categorical Fluency (Animal Naming Task: Spreen and Strauss, 1998) in German as well as in C.D.'s and I.J.'s native languages (percentiles are given for the German versions since both patients' results in their native language did not differ substantially from their performance in German), application of Cyrillic letters for Trail Making Test B (TMT-B) in patient I.J., and omission of intelligence screening with the Mehrfachwahl-Wortschatztest (MWT) (German adaptation: Lehrl et al., 1991 of the National Adult Reading Test, Nelson, 1982) in C.D.

Translations were only given to explain instructions for some tests, since both patients were well able to speak and understand German.

3.2. Psychiatric symptoms and personality

Current mood, psychiatric symptoms and personality traits were assessed with three questionnaire measures: Beck Depression Inventory (BDI) (German version by Beck et al., 1995), Symptom Checklist-Revised (SCL-90-R) (Derogatis, 1992; German version by Franke, 1995), and Freiburg Personality Inventory-Revised (FPI-R) (Freiburger Persönlichkeitsinventar-revidierte Fassung Fahrenberg et al., 1989).

The BDI measures current depressed mood and depressive symptoms differentiating between mild to moderate and severe depressive symptomatology. The SCL-90-R assesses psychological stress and psychiatric symptoms with nine different scales including: somatisation, obsession–compulsion, interpersonal sensitivity, depression, anxiety, anger–hostility, phobic anxiety, paranoid ideation, and psychoticism. A Global Severity Index (GSI), derived from all subscales, describes the general psychological stress level. The FPI-R assesses personality on 12 dimensions. These include: life satisfaction, social orientation, achievement motivation, inhibition, excitability, aggressiveness, stress, physical complaints, worries about health, openness, extraversion, and neuroticism. The subscale 'openness' operates as a validity scale. Low results (standard scores one to three) indicate socially desirable response tendencies. If a low result is achieved in this scale, interpretation of all other responses is limited (Fahrenberg et al., 1989).

3.3. Retrograde memory

Retrograde memory was assessed with tests of semantic and episodic remote information. Semantic remote memory tests comprised the Test of Semantic Remote Memory from Schmidtke and Vollmer-Schmolck (1999), ad hoc designed Famous Names Test and Current Words Test, and a Famous Events Test adapted from Leplow and Dierks (1997). Results were corrected for re-learned items after the patients' onset of their amnesia, whenever patients could exactly describe the instance of re-learning (time, context). These re-learning instances were also validated by the patients' relatives. The diverse social–cultural backgrounds challenged the construction of similarly valid measures across patients as well as finding reasonably similar control subjects. Therefore, the ad hoc constructed tests consisted almost exclusively of questions about internationally well-known public events, celebrities and words. We believe that in the case of patient C.D., who was exposed to Western public knowledge throughout his entire life and is married to a German, these items cover remote knowledge that he should be well aware of. Further, we verified the validity of our items with his wife. In contrast, patient I.J.'s wife (who also grew up in Russia) reported that after moving to Germany in 1993, her husband had never been interested in German news or celebrities. Given this fact and the known gag order for Western news in the former Soviet Union, semantic remote memory tests for I.J. comprised different items constructed by two Russians. All of I.J.'s items were validated with the help of his wife who indicated that he would have known the answers to all questions before amnesia onset.

We administered the tests to 10 healthy control subjects (five female, five male subjects; age range: 17–39 years; years

of education: mean = 11.5, SD = 1.5). Since I.J. received different versions of the tests, his performance was compared to that of a single healthy comparison subject with a highly similar personal background (male, 38 years old, 10-year school education, emigrated to the West from Russia in 1992, in no relationship to I.J.).

In the Test of Semantic Remote Memory (Schmidtke and Vollmer-Schmolck, 1999) 81 questions are posed about basic world knowledge usually acquired in or before the first grades of school (e.g., basic biological knowledge, names of car brands, fairy tales, etc.). This test was omitted in patients C.D. and I.J. due to their cultural background. In the Famous Names Test, subjects are asked to choose the correct name of a famous person out of a block of five names, including four fictive names. Further, subjects are asked to provide additional details about the person (e.g., profession, nationality). A total of 20 name blocks were given to all patients except I.J., who received a Russian version with 48 blocks. In the Current Words Test, knowledge of the meaning of 25 words and phrases that became common during roughly the last 25 years is asked for (e.g., 'E.T.', 'snowboard'). Patient I.J. was given a Russian 42-item version. For evaluation of temporal gradients in semantic remote memory, a Famous Events Test adapted from Leplow and Dierks (1997) was administered. In this test, subjects are given verbal descriptions of 24 public news events ranging from years 1980 to 2001 (only items post-1989 were applied in A.B. considering her age). These events have to be free recalled. If an item is not recalled, the subject is given a recognition version with five alternatives, including four fictive answers. Patient I.J. received a Russian 33-item version.

We assessed episodic remote memory with the Autobiographical Memory Inventory (Autobiographisches Gedächtnis-Inventar (AGI); abstract in Fast et al., 2001) developed on the basis of the Autobiographical Memory Interview (Kopelman, 1990). The AGI consists of a semi-structured interview on facts and incidents from the subjects' life regarding specific time periods. Per time period, subjects are required to provide five autobiographical facts, two incidents and details on one of the two incidents. As retrieval help, a list of generic events (e.g., 'first day in school', 'day of graduation', 'first kiss', etc.) is shown throughout the entire length of the interview. Time periods of 0–5 years of age, 6–10 years, 11–17/18 years were tested in all patients. The period from age 18/19 until the onset of the amnesia (age 30 to 34, respectively) was tested in patients C.D., E.F., G.H., and I.J.

4. Results

4.1. Background evaluation

The patients' results in the neuropsychological test battery are shown in Table 1. Unless otherwise stated, scores are given in percentiles derived from normative data.

All patients exhibited normal to above normal intellectual abilities in the verbal and nonverbal intelligence measures.

Anterograde memory assessed with the WMS-R was average to above average in patients A.B., E.F., and G.H., whereas

patients C.D. and I.J. exhibited mild impairment. C.D. showed below average immediate learning with visual memory being weaker than verbal memory. I.J.'s immediate verbal memory index was somewhat low (index = 88), which was mainly due to his weak performance in the subtest Logical Memory. His low 'delayed recall index' (index = 78) also resulted from his low (initial) score in this subtest since all other subtests were within normal range in delayed recall. Furthermore, C.D.'s immediate and delayed memory indices were somewhat unusual showing mild immediate memory impairment but average delayed memory.

We assessed verbal and visual short-term and working memory by Digit Span and Block Span (WMS-R). Working memory was deficient in A.B., C.D. and I.J. Results in these four tests were disparate in patients A.B., C.D. and to a lesser extent also in patient G.H. All patients displayed a preference of verbal over visual material with patient C.D. showing the most pronounced discrepancy between above average verbal (percentile = 92) and impaired nonverbal working memory (percentile = 3). The Rey–Osterrieth Complex Figure revealed no deficits in visual long-term memory. Some of our anterograde memory tests were similar or identical to measures used by Kritchevsky et al. (2004). We provide additional information about our patients' results compared to those of Kritchevsky et al. (2004) in the Appendix.

Whereas some attentional and executive functions were unimpaired, three of four patients, in whom TMT-B was applied, showed deficits (patients A.B., C.D., and I.J.). It has to be mentioned that I.J.'s performance might be underestimated in this test since we could not compare his result to appropriate Russian norms. Patients E.F. and G.H., in whom parts of the Test Battery for the Assessment of Attention were applied, were severely impaired on the Alertness and Divided Attention subtests. G.H. showed similarly weak performance in Selective Attention, whereas E.F. exhibited low average performance. In patient C.D., categorical fluency measured by the Animal Naming Task was impaired. Furthermore, in the Modified Card Sorting Test (MCST) he showed a high number of perseverative errors. G.H. showed elevated interference susceptibility in the Stroop Test.

Three of the four patients, in whom Theory of Mind (ToM) abilities were assessed, exhibited deficits.

In summary, A.B. and I.J. had deficits in visual working memory and mental flexibility; patients E.F. and G.H. showed problems in complex attentional tasks and ToM deficits; patient C.D. exhibited a broader pattern of minor impairment across neuropsychological domains attention/executive functions, anterograde memory and ToM.

4.2. Psychiatric symptoms and personality

Results of the formal assessment of current psychiatric symptoms and personality are summarised in Table 2.

None of the patients showed severe depression in the BDI, although G.H. had a score of 14 points indicating mild depressive tendencies. In the SCL-90-R, deviations from normative data were found in patients A.B., C.D. and G.H. Whereas A.B. showed elevated scores only in subscale 'somatisation' ($T = 73$), C.D. and G.H. exhibited a broader pattern of

Table 1 – Neuropsychological profile of the five patients

| Neuropsychological domain and test | Patients | | | | | |
|---|--|-----------------|------------------|----------------|----------------|-----------------|
| | A.B. | C.D. | E.F. | G.H. | I.J. | |
| <i>Intellectual abilities</i> | | | | | | |
| MWT (German adaptation, Lehrl et al., 1991 of the National Adult Reading Test; Nelson, 1982) | Estimated premorbid IQ | 100 | n.a. | 114 | 91 | 124 |
| Wechsler Adult Intelligence Scale-Revised (WAIS-R; German version: Tewes, 1991) | Verbal-IQ | 118 | 100 | n.a. | 116 | 117 |
| | Performance-IQ | 126 | 110 | n.a. | 103 | 110 |
| | Full-scale-IQ | 124 | 104 | n.a. | 112 | 120 |
| <i>Anterograde memory</i> | | | | | | |
| WMS-R (Wechsler, 1987 ; German version: Härting et al., 2000) | IQ-scaled | | | | | |
| | General memory index | 114 | 83 ^b | 129 | 99 | 91 |
| | Verbal memory index | 115 | 87 | 127 | 90 | 88 |
| | Visual memory index | 104 | 82 ^b | 116 | 119 | 99 |
| | Delayed memory index | 116 | 99 | 124 | 90 | 78 ^b |
| Span Tasks from WMS-R ^a | Digit Span forward | 37 | 87 | 87 | 88 | 68 |
| | Digit Span reversed | 73 | 92 | 56 | 73 | 56 |
| | Block Span forward | 18 | 60 | 97 | 32 | 56 |
| | Block Span reversed | 12 ^b | 3 ^b | 78 | 23 | 13 ^b |
| | Rey–Osterrieth Complex Figure Test (CFT; Osterrieth, 1944) ^a | Copy | 48 | 24 | n.a. | 66 |
| Delayed recall (30 min) | | 82 | 31 | n.a. | 88 | 62 |
| <i>Attention & executive functions</i> | | | | | | |
| TMT (Spreen and Strauss, 1998) ^a | Part A | 73 | 31 | n.a. | 48 | 50 |
| | Part B | 8 ^b | 7 ^b | n.a. | 69 | 1 ^b |
| Concentration Endurance Test d2 (Brickenkamp, 1994) ^a | Error-corrected score | 33 | 16 | n.a. | 21 | 54 |
| Subtests from Test Battery for the Assessment of Attention (Fimm and Zimmermann, 2001) ^a | Simple Alertness | n.a. | n.a. | 0 ^b | 0 ^b | n.a. |
| | Divided Attention | n.a. | n.a. | 0 ^b | 0 ^b | n.a. |
| | Selective Attention | n.a. | n.a. | 21 | 1 ^b | n.a. |
| Stroop-Test (FWIT; German version: Bäumler, 1985) ^a | Word trial | 48 | 51 | n.a. | 24 | 66 |
| | Colour trial | 69 | 71 | n.a. | 24 | 34 |
| | Interference trial | 54 | 46 | n.a. | 1 ^b | 69 |
| Attention/Concentration Index from WMS-R | IQ-scaled | 90 | 113 | 113 | 104 | 94 |
| Lexical Fluency (FAS-Test; Spreen and Strauss, 1998 , German adaptation: Horn, 1983) ^a | | 54 | 50 | 69 | 79 | 27 |
| Categorical Fluency (Animal Naming Task; Spreen and Strauss, 1998) ^a | | 50 | 10 ^b | n.a. | 85 | 93 |
| MCST (Nelson, 1976 ; norms by Obonsawin et al., 1999) ^a | Categories completed | >45 | >45 | >45 | >45 | >45 |
| | Errors | >65 | 35 | >65 | 45–50 | >65 |
| | Perseverative errors | >65 | 10 ^b | >45 | >45 | >65 |
| <i>Theory of Mind</i> | | | | | | |
| Reading the Mind in the Eyes Test (German adaptation, Fleck et al., 2002 of Baron-Cohen et al., 2001) ^a | | n.a. | 1–2 ^b | 0 ^b | 0 ^b | 50 |

n.a.: Not administered.
a Scores are given in percentiles from normative data.
b Deviation from normative data.

deviations. G.H. showed remarkably heightened T-scores in subscales ‘interpersonal sensitivity’ ($T = 80$) and ‘psychoticism’ ($T = 79$), whereas C.D.’s deviations were less pronounced and more evenly distributed across subscales (T-scores between 61 and 68). The GSI clearly indicated moderate current stress in patients C.D. and G.H. In the FPI-R, four of the five patients showed significant deviations in subscale ‘openness’, which operates as a validity scale. Interpretation of all other subscales is compromised if pathologically low openness

scores are obtained ([Fahrenberg et al., 1989](#)). This was observed in C.D., E.F. and I.J. pointing to social desirability in these patients. In contrast, patient A.B. showed highly elevated openness and described herself as being extremely willing to admit minor weaknesses and violations of everyday conventions. Moreover, she showed high ‘neuroticism’ describing herself as suffering from psychosomatic complaints and being emotionally labile, sensitive, and anxious. Patient G.H. described herself as suffering from many physical

Table 2 – Results in psychiatric screenings and personality questionnaire

| Test | | Patients | | | | |
|--|---------------------------|-----------------|------------------|------------------|-----------------|------------------|
| | | A.B. | C.D. | E.F. | G.H. | I.J. |
| BDI (German version: Beck et al., 1995) | Cut-offs | | | | | |
| | 12: mild | 2 | 9 | 7 | 14 ^c | 6 |
| | to moderate depression | | | | | |
| | 18: severe depression | | | | | |
| SCL-90-R (German version: Franke, 1995 of Derogatis, 1992) | Cut-off: >60 (T-scores) | | | | | |
| | Somatisation | 73 ^c | 62 ^c | 50 | 56 | 41 |
| | Obsessive–compulsive | 48 | 67 ^c | 57 | 57 | 26 |
| | Interpersonal sensitivity | 33 | 64 ^c | 47 | 80 ^c | 33 |
| | Depression | 46 | 64 ^c | 45 | 66 ^c | 38 |
| | Anxiety | 35 | 60 | 37 | 60 | 38 |
| | Anger–hostility | 56 | 58 | 38 | 70 ^c | 39 |
| | Phobic anxiety | 41 | 61 ^c | 56 | 67 ^c | 53 |
| | Paranoid ideation | 38 | 66 ^c | 53 | 66 ^c | 48 |
| | Psychoticism | 51 | 59 | 50 | 79 ^c | 41 |
| | GSI | 50 | 68 ^c | 48 | 69 ^c | 42 |
| FPI-R (Fahrenberg et al., 1989) | Stanines ^a | | | | | |
| | Life satisfaction | 5 | 4 | 4 | 4 | 5 |
| | Social orientation | 7 | 4 | 8 ^c | 7 | 5 |
| | Achievement motivation | 6 | 4 | 1 ^c | 6 | 2 ^c |
| | Inhibition | 3 | 6 | 4 | 7 | 5 |
| | Excitability | 7 | 5 | 6 | 6 | 2 ^c |
| | Aggressiveness | 7 | 3 | 3 | 4 | 3 |
| | Stress | 6 | 4 | 5 | 5 | 1 ^c |
| | Physical complaints | 6 | 6 | 2 ^c | 8 ^c | 7 |
| | Worries about health | 5 | 2 ^c | 3 | 1 ^c | 2 ^c |
| | Openness ^b | 9 ^c | 1 ^{b,c} | 3 ^{b,c} | 5 | 1 ^{b,c} |
| | Extraversion | 7 | 5 | 3 | 4 | 2 ^c |
| | Neuroticism | 9 ^c | 4 | 5 | 6 | 3 |

a Stanines are standard scores with a maximum of 9. Stanines 1–2 and 8–9 indicate significant deviations from normative data.

b Stanines 1–3 on subscale ‘Openness’ indicate elevated social desirability (e.g., refusal to admit minor weaknesses and everyday violations of conventions) limiting the validity of the responses in the entire questionnaire.

c Deviations from normative data.

complaints but at the same time not at all worried about her health (scales ‘physical complaints’ and ‘worries about health’).

In summary, A.B. showed a tendency for somatisation, extreme openness to admit minor weaknesses in public and signs of emotional lability. C.D.’s general psychological profile was characterised by many psychiatric symptoms combined with lowered openness indicating social desirability. The latter tendency was also seen in patient E.F. Patient G.H. showed mild signs of currently depressed mood. Similar to patient C.D. she presented with numerous psychiatric symptoms wherein interpersonal sensitivity was remarkably elevated. She further described herself as suffering from many physical complaints but not being worried about her health. Finally, similar to C.D. and E.F., patient I.J. showed a tendency for social desirability.

4.3. Remote memory

4.3.1. Semantic memory

In the Test of Semantic Remote Memory patients A.B., E.F., and G.H., in whom this test was applied, scored normal.

Results in the Current Words Test and Famous Names Test are summarised in Fig. 1.

Ten healthy control subjects yielded an average accuracy rate of over 90% in all three measures. The single control person for patient I.J. gave between 71% and 85% correct answers in the Russian test versions. In contrast, in the Current Words Test all patients except for A.B., who gave 100% correct answers, were below the control subjects’ almost perfect performance. Based on 10 control subjects’ results, patient A.B. reached a z-score of $z = .6$, whereas C.D. ($z = -17.8$), E.F. ($z = -25.9$), and G.H. ($z = -17.8$) were clearly impaired. Also I.J., for whom z-scores could not be computed, performed inferior to his control subject in that he reached 51.4% correct answers in contrast to 71.4% scored by his control subject. Name identification in the Famous Names Test was likewise inferior in all patients except A.B. (A.B.: $z = -.3$; C.D.: $z = -10.6$; E.F.: $z = -7.2$; G.H.: $z = -8.8$; I.J. produced 26% correct answers in contrast to 85% scored by his control subject). None of the patients scored below the chance level of 20% in this five-alternative forced choice test. In providing additional information about the celebrities, all patients except A.B. were similarly deficient (C.D.: $z = -6.4$; E.F.: $z = -5.9$; G.H.: $z = -5.3$; I.J. gave 26% correct answers contrasting 81% correct

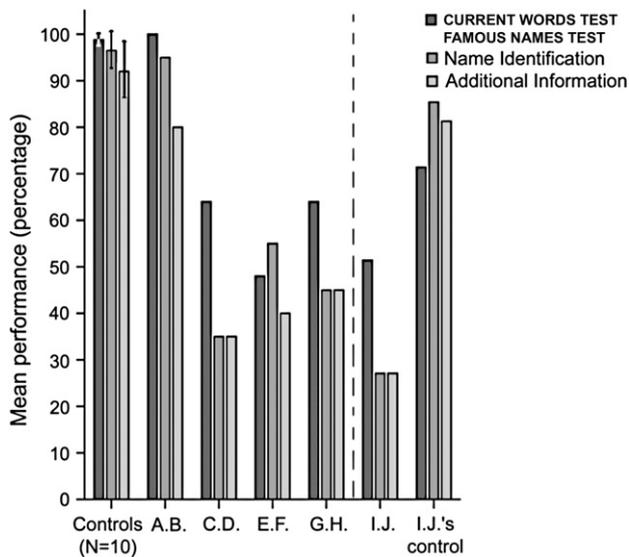


Fig. 1 – Mean performance and standard error of the mean in the healthy control group contrasted with performance of each patient (shown as the percentage of correct answers). The figure displays performance in the Current Words Test and the Famous Names Test with a five-alternative forced choice name identification trial and free recall of additional information. Since I.J. received Russian adaptations of the tests, his performance is contrasted with that of a single control subject originating from the same cultural background (to the right of the dashed line).

responses given by his control subject). Although A.B.'s performance ($z = -1.4$) was somewhat low in this measure, her result might be an effect of her young age in that she was able to recognise names of well-known celebrities, but had not acquired substantial background knowledge about their profession.

In the Famous Events Test (see Fig. 2), 10 control subjects on average recalled 60–80% of the news events. Although not significant, there was a tendency for lower recall of items from earlier compared to more recent time periods ($\chi^2 = 5.5$, $p = .06$). I.J.'s control subject recalled 70–80% of the Russian news events with no differential pattern across time periods ($\chi^2 = 1.1$, $p > .1$).

There was no significant effect of time period and performance in patient A.B. ($\chi^2 = 2.6$, $p > .10$). Recall performance of A.B. was slightly below average in the earliest time period she was tested for (1990–1995: $z = -1.3$), but well within normal range in the most recent time (1996–2001: $z = .4$). Again, one has to keep in mind that she was only 6–11 years old during the earlier time. Patient E.F. showed a significant time period by performance effect ($\chi^2 = 9.6$, $p < .01$). Similarly, though not significant, G.H.'s results across time periods varied ($\chi^2 = 4.4$, $p = .11$). In the early time period (1980–1989), patient E.F. reached normal results ($z = -.6$), whereas patient G.H. was more deficient ($z = -2.0$). Recall of more recent events was impaired in both patients (time period 1990–1995: E.F. $z = -4.0$, G.H. $z = -3.4$; time period 1996–2001: E.F. $z = -4.1$, G.H. $z = -4.1$). We conclude that the temporal gradient in

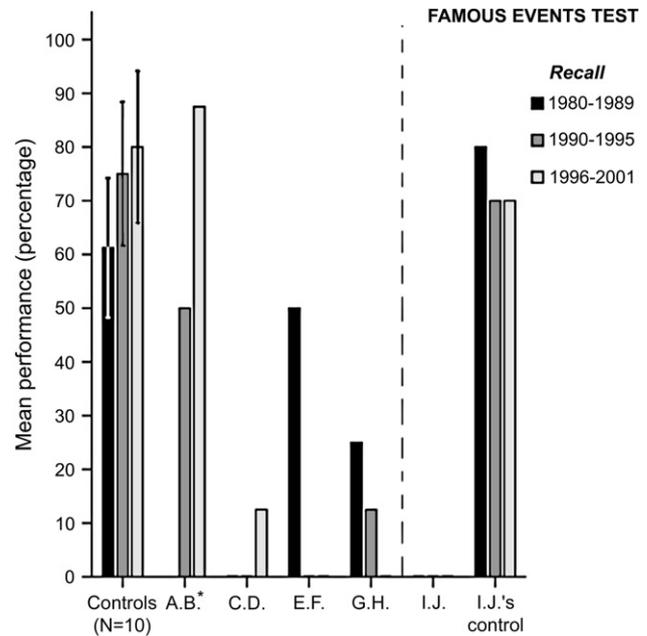


Fig. 2 – Mean performance and standard error of the mean in the healthy control group contrasted with performance of each patient (shown as the percentage of correct answers). The figure displays performance in recall of Famous Events from time periods 1980–1989, 1990–1995, and 1996–2001. Since I.J. received Russian adaptations of the tests, his performance is contrasted with that of a single control subject originating from the same cultural background (to the right of the dashed line). *Due to A.B.'s young age, the time period between 1980 and 1989 was excluded.

remote memory loss reported by patients E.F. and G.H. was reflected in their recall performance in this measure. Performance of C.D. and I.J. was poor. C.D. recalled only 13% of the most recent events with no significant variations across time periods ($\chi^2 = 2.1$, $p > .1$). His performance was below that of controls in all time periods ($z = -3.4$, $z = -4.1$, and $z = -3.4$, respectively). Patient I.J. did not recall any of the public events in question ($\chi^2 = 0$, n.s.).

As can be seen in Fig. 3, recognition of the same events from five alternative choices was between 90% and 100% for 10 control subjects as well as for I.J.'s control person (no effects of time period by performance; control group: $\chi^2 = .1$, $p > .1$; I.J.'s control person: $\chi^2 = 1.1$, $p > .1$).

Similar to her performance in the recall trial, A.B.'s performance in recognition of items from the Famous Events Test did not show a time period by performance effect ($\chi^2 = 1.1$, $p > .1$). Her results were similar to those of the control subjects ($z = -.9$ and $z = -.6$). There were significant effects of time period by performance in E.F. ($\chi^2 = 20.2$, $p < .01$) and G.H. ($\chi^2 = 6.6$, $p = .04$). Events between years 1980 and 1989 were fully (patient E.F., $z = .6$) or partly (patient G.H., $z = -2.6$) recognised, whereas recognition of later dated events was either reduced (1990–1995: $z = -9.4$ for both patients) or not present at all (1996–2001: $z = -10.9$ for both patients). Thus, E.F. and G.H. showed a similar temporal gradient

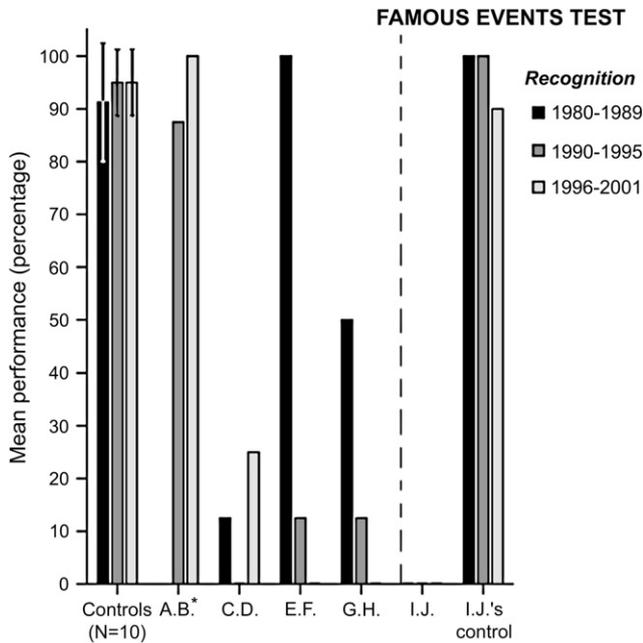


Fig. 3 – Mean performance and standard error of the mean in the healthy control group contrasted with performance of each patient (shown as the percentage of correct answers). The figure displays performance in the five-alternative forced choice recognition of Famous Events from time periods 1980–1989, 1990–1995, and 1996–2001. Since I.J. received Russian adaptations of the tests, his performance is contrasted with that of a single control subject originating from the same cultural background (right to the dashed line). *Due to A.B.'s young age, the time period between 1980 and 1989 was excluded.

in recognition as they did in recall of the events. C.D. recognised 13% of the oldest events ($z = -5.0$) and 25% of most recent events ($z = -8.0$). Further, C.D. did not show an effect of time period by performance ($\chi^2 = 2.3$, $p > .1$). Finally, patient I.J. showed the same temporally ungraded ($\chi^2 = 0$, n.s.) lack of recognition of any of the events as in the recall trial, in stark contrast to the near-perfect performance of his control subject. Recognition of less than 20% in this test indicates below-chance performance (five-alternative forced choice test). In all but patient A.B. this behaviour was observed in at least one time period. In particular, patient C.D. showed below-chance recognition of events from the two earlier time periods (years 1980–1995), E.F. and G.H. showed this pattern in the last two time periods (years 1990–2001) and patient I.J.'s below-chance performance, i.e., 0% recognition hits, affected all time periods.

4.3.2. Autobiographical memory

Remote autobiographical memory performance is summarised in Table 3.

Patient A.B. was able to provide semantic facts about her previous life in a consistent manner (e.g., names of former friends, teachers). All reported episodic events up to the age of 10 years were fragmentary and considerably lacking in

Table 3 – Results in the AGI

| AGI | A.B. | C.D. | E.F. | G.H. | I.J. |
|-------------------------------------|------|------|------|------|------|
| <i>Maximum (raw scores)</i> | | | | | |
| <i>Age 1–5 years</i> | | | | | |
| Facts: 5 | 5 | 0 | 5 | 5 | 1 |
| Episodes: 2 | 2 | 1 | 2 | 2 | 0 |
| Details: 11 | 6 | 2 | 9 | 11 | 0 |
| <i>Age 6–10 years</i> | | | | | |
| Facts: 5 | 5 | 2 | 5 | 5 | 1 |
| Episodes: 2 | 1 | 2 | 2 | 2 | 0 |
| Details: 11 | 8 | 7 | 8 | 11 | 0 |
| <i>Age 11–17/18 years</i> | | | | | |
| Facts: 5 | 5 | 3 | 5 | 5 | 3 |
| Episodes: 2 | 1 | 2 | 2 | 2 | 0 |
| Details: 11 | 11 | 10 | 11 | 11 | 0 |
| <i>Age: 18/19–29/34^a</i> | | | | | |
| Facts: 5 | – | 3 | 2 | 5 | 5 |
| Episodes: 2 | – | 1 | 2 | 1 | 0 |
| Details: 11 | – | 8 | 2 | 5 | 0 |

^a Due to the individual age of the patients and date of the amnesia onset, this age period varied across patients.

detail and contextual embedding. One of the two reported episodes for the age range of 11–17 years was faulty as was confirmed by one of her friends, the other event was provided in a detailed and precise manner (see below). Patient C.D. had difficulties retrieving autobiographical semantic information related to his entire previous life. For instance, he could not provide the address of his home for about the first 14 years of his life, he was unable to name friends or teachers from the time before the age of 10 and he made errors in the temporal sequence and location of former addresses (last 8–9 years). All autobiographical episodes were lacking emotional content and/or episodic details. Despite vivid imagery of single scenes, C.D. was unable to specify temporal and spatial context information of events except for one singular episode that had happened when he was 15 years old. Patient E.F. was able to provide autobiographical semantic and episodic information related to his life up to the age of about 20 years. Retrieval of all later dated facts and events was grossly impaired. The few semantic facts he reported were re-learned after the onset of the amnesia and despite his fragmentary memory for one event (New Year's Eve 2001), he could not remember any further episodes within this time. Patient G.H. provided autobiographical semantic and episodic information about her previous life only until May 1989. Though she mentioned a few later dated semantic facts, she reported that she had re-learned them after the onset of the amnesia. G.H. also reported some episodic information from the amnesic time, but did so in a very fragmentary and emotionally detached manner. During the interview she mentioned several of the aforementioned traumatic childhood events. G.H. described all of them in a consistent manner though she was very distressed by her memories. Thus, her interview had to be interrupted and continued later. Patient I.J. was unable to provide any autobiographical semantic or episodic information concerning his entire previous life. The few semantic facts he

reported were re-learned after the onset of his amnesia and there was no evidence for the retrieval of any episodic information in I.J. However, during a break in the middle of the neuropsychological examination, I.J. mentioned an apparently autobiographical dream he has had during his stay in Russia (c.f., Section 2). In this dream, two small children approached him, which gave him the intensive feeling of being a father. Thus, already in Russia, he had been convinced about this fact of his autobiography. When I.J. became aware of the extent of his RA during the interview, he was very distressed and repeatedly asked for possible explanations for his disease. Thus, the interview had to be interrupted and continued later.

It has to be noted that during the administration of the AMI, patients A.B. and C.D. both recalled one singular event in a vivid and precise manner from the time period between 11 and 17/18 years of age. These memory islands are reflected in the episodic details scores of this time period in Table 3.

Summarising the individual patients' remote memory deficits, it can be stated that A.B. was selectively amnesic for autobiographical-episodic information related to her previous life. Patient C.D. was amnesic for most public and personal facts and events concerning the time prior to the onset of the amnesia. Patient E.F. was amnesic for public and personal facts and events that had happened after about his 20th year of life (last 12–14 years). Similarly, patient G.H. was amnesic for 13 years preceding the onset of her amnesia (21st year of life). She could not retrieve the majority of public and personal facts and events since 1989. As seen in C.D., patient I.J. exhibited extensive semantic and episodic RA for his entire previous life. Although none of the patients performed below chance in the easier semantic remote memory tests (Current Words, Famous Names), all but patient A.B.'s results in the recognition trial of the Famous Events Test point to aggravated memory loss in some or all time periods. Furthermore, all patients remembered at least one fragmentary episode from the amnesic time, though this did never trigger retrieval of complementary context of the memory fragments or retrieval of any further episode from that time.

5. Discussion

In contrast to some previous psychogenic RA patients (e.g., Kritchevsky et al., 2004; Markowitsch et al., 1997; Campodónico and Rediess, 1996; Kopelman et al., 1994), accurate diagnosis of the psychogenic nature of our patients' RA was complicated by various factors. In all but patient I.J. an ostensibly somatic condition marked the beginning of RA including loss of consciousness, a car accident or general anaesthesia. Although most of these instances were later found to bear no actual organic significance, they clearly differ from classical dissociative or other psychiatric symptomology. Furthermore, the psychiatric history of patients E.F. and I.J. was unremarkable (as far as could be assessed). Unlike in classical dissociative amnesia (e.g., Schacter et al., 1982), patients A.B., E.F., and G.H. initially recalled their names when they were found and thus did not suffer from loss of identity. Lastly, patient E.F. exhibited a slight overall cortical and pronounced

cerebellar hypometabolism in resting state FDG-PET pointing to possible diffuse disturbances of brain functions underlying the RA in his case. Nevertheless, we believe that psychological factors contributing to the onset and maintenance of RA were present in all our patients. The major reason for our conclusion is that in none of our patients did we find clear evidence for structural brain damage from history, neurological examinations, or neuroimaging. Even in patients G.H. and I.J., who were unable to undergo high-resolution structural brain imaging, morphological lesions are very unlikely since there was no indication for potential external injury and conventional neuroradiological investigations (CT, EEG) were normal. Secondly, there was a multitude of psychological indications favouring a psychogenic causation. Among these the most obvious were a fugue-like state (I.J.), stressful current events (A.B., G.H.), severe childhood trauma (G.H.), previous experiences of transient memory loss (C.D., G.H.), psychiatric history of depression (A.B.) or conversion symptoms (C.D., G.H.), and previous or current somatic complaints of probable psychogenic origin (A.B., C.D.). Furthermore, formal assessment and other behavioural aberrances observed during and between test sessions give evidence for our reasoning, which will be outlined in the following.

5.1. Neuropsychological and psychiatric assessment

Overall, our patients performed disproportionately better in all neuropsychological tests other than the remote memory evaluations. Similar to the previous case series of Kritchevsky et al. (2004), our patients' anterograde memory deficits were variable and – if present – more dominant in verbal memory. Patient C.D. further showed impaired immediate memory contrasting intact delayed memory, a pattern that was also observed in 6 out of 10 functional RA patients reported by Kritchevsky et al. (2004).

Moreover, although the sheer quantity of tests per patient might exaggerate positive findings, neuropsychological assessment clearly pointed to some disturbances normally associated with frontal-lobe function in all our patients. Attentional problems were detected in patients E.F. and G.H. tested with the more challenging tasks of the Test Battery for the Assessment of Attention. However, also the more basic Concentration Endurance Test d2 revealed low performance in C.D. (16th percentile) and G.H. (21st percentile). Moreover, in patients (A.B., C.D., I.J.), in whom the RA was not temporally graded and covered the entire life, span tasks that are usually characterised as measures of attention and working memory were impaired. Thus, a general attentional deficit appears to be present in most of the patients. In the same patients (A.B., C.D., I.J.), cognitive flexibility (TMT-B) was deficient and further, executive functions set-shifting (MCST), and inhibition of interference (Stroop Test) were deteriorated in G.H. and/or C.D., raising the question whether these disturbances are related to the failure of remote memory retrieval. Consistent with our observation, a few previous studies of functional RA patients that assessed these functions in detail, found attentional deficits (Campodónico and Rediess, 1996; Stracciari et al., 1994) or executive dysfunctions (Glisky et al., 2004) in their cases. In the context

of most our patients' psychological background and their current situation, we suggest that these dysfunctions are due to stress-related factors rather than direct organic causation. In this regard, Raskin (1997) previously observed working memory deficits and executive dysfunctions in patients suffering from mild head trauma accompanied by former psychological trauma compared to patients without such psychological precursors. Similarly, Stein et al. (2002) found that victims of violence, regardless whether they had a clinical expression of PTSD or not, have a heightened probability for deficits in attention, working memory, set-shifting and response inhibition, all of which point to frontal-lobe associated dysfunctions after experience of stress. Impaired executive control, in turn, has been associated with dysfunctional autobiographical retrieval (Kopelman, 2000). Note that even in the absence of obvious psychological factors in the aetiology of RA (i.e., in patient E.F.), the current situation is likely to exert a considerable everyday stress on our patients. This was particularly obvious during interviews with the patients' relatives. Such persistent stress may yield attentional/executive dysfunction, contributing to retrieval deficits and eventually leading also to the maintenance of RA.

Interestingly, impaired Theory of Mind (ToM) abilities were observed in three of the four patients (C.D., E.F., G.H.) in whom the ToM test was applied. ToM performance was not reported in earlier work on functional RA and we suggest that our patients' RA and ToM deficits share a common basis. Previously, Corcoran and Frith (2003) observed a correlation between impairment in ToM abilities and autobiographical-episodic retrieval deficits in individuals with schizophrenia. Thus, patients with autobiographical disturbances may be less able to resort to contextual knowledge such as one's own previous feelings, intentions and thoughts necessary for the retrieval of specific autobiographical (personal events) or social information (ToM). Further, more indirect evidence comes from Klein et al. (1996). Their functional RA patient experienced transient and selective autobiographical-episodic RA after mild traumatic brain injury. Although autobiographical-episodic memory retrieval during her amnesic time was vastly deficient, she was well able to judge her general personality traits, a measure of self- and social knowledge, and her judgements did not change after recovery from the RA. The patients from our sample who exhibited ToM deficits showed RA for autobiographical-episodic memories and personal semantic knowledge. It might be that their loss of personal semantics (e.g., "How do I look like when I am angry?") together with their deficient autobiographical-episodic memory (e.g., "How did person XY look like when she was angry at me at my sister's wedding?") contributed to their problems in judging other persons' mental states. It has to be noted at this point that in all our cases remote memory testing was conducted in the end of the entire examination. With this sequence, it is unlikely that the ToM test, somewhat resembling the Famous Faces Test, created the impression of measuring the patients' remote memory loss and therefore possibly inducing attempts to lower their performance. Given that all patients gave the impression of being very motivated to perform well in general neuropsychological testing,

including the ToM test, our observation of ToM deficits, although preliminary, appears to be valid. Certainly, ToM functions should be studied in more detail in future investigations with functional RA patients.

Turning to the assessment of psychiatric symptoms and personality, the SCL-90-R seemed to show current psychological stress in patients C.D. and G.H. and to a lesser degree also in A.B. One of the most interesting results, however, was that four out of the five patients had abnormal scores on the openness dimension of the Freiburg Personality Inventory, a validity scale indicating socially desirable behaviour. In the three patients with unusually low scores, this points to self-repressive tendencies in social situations, whereas A.B., showing a heightened score, may overly disregard social norms and values. Nevertheless, in all of them an ongoing difficulty in social contexts can be assumed. Again, also this type of behaviour may follow the logic of the individually perceived remote memory deficit; lacking knowledge of oneself in general, semantic terms and in specific social situations, a coarse reference to commonsense 'good manners' might have been preferable for C.D., E.F., and I.J. In contrast, patient A.B., whose semantic knowledge about herself was intact, may have used that knowledge and exaggerated her disregard of social norms. In fact, when we checked A.B.'s self-judgement with her best friend's and mother's help, they both stated that her character and attitude were rather opposite of what she had answered in the questionnaire. Therefore, we conclude that her judgement about her own openness might be more an idealisation than the truth. Note that given these tendencies, one can also doubt the patients' responses in other questionnaires. In detail, the only patient who did not show any aberrance in FPI-R openness was G.H. whose responses in the SCL-90-R might properly reflect current psychological complaints. In the case of C.D., however, the results may indicate exaggerations. Also, given their reduced openness, we cannot be sure whether patient E.F. and I.J. correctly negated current psychological symptoms in the SCL-90-R.

Concerning our observation of impairment in measures of frontal-lobe functions together with repressive tendencies, Anderson and Green (2001) revealed that also healthy subjects might repress unwanted memories by executive inhibitory control. Though it can be questioned whether motivated forgetting of personally irrelevant information as in Anderson and Green (2001) parallels the unconscious inhibition of one's own past in functional RA (Kihlstrom, 2002), Anderson and Green's results give hints for possible cognitive mechanisms underlying repression (c.f., Conway, 2001).

5.2. Remote memory testing

Central to our patients' symptoms was the complete loss of autobiographical-episodic memories from the entire life or certain time periods. Most interestingly and consistent with former investigations of functional RA patients (Barbarotto et al., 1996; Campodonico and Rediess, 1996; Kopelman et al., 1994), we observed implicit use of 'forgotten'

information, particularly obvious during semantic remote memory testing. As suggested by Kritchevsky et al. (2004), the less explicitly a memory test appeared to measure the symptoms in functional RA, the more likely information is retrieved that is inaccessible through direct questioning. Accordingly, in the easier semantic remote memory tests (Current Words, Famous Names), although all patients but A.B. scored lower than controls, they did not show zero- or below-chance performance. In contrast, the more direct Famous Events Test, sometimes explicitly including the year of the event in its questions, revealed below-chance performance in some (C.D., E.F., G.H.) or all (I.J.) time periods. This kind of behaviour is usually taken as proof of simulation (e.g., Lezak, 1995), and therefore we can assume conscious contributions to aggravation of the deficits. However, although malingering cannot be ruled out, there are numerous indications of less deliberate factors to the deficit (e.g., psychiatric symptoms, personality characteristics, premorbid psychiatric history), so that our patients' neuropsychological presentation is most probably a combination of both, conscious and unconscious aspects. Further anecdotal evidence for implicit use of 'forgotten' memories through more indirect access was observed in A.B. and G.H. Although being almost entirely amnesic for any personal episode in the autobiographical interview, A.B. involuntarily recalled fragments of former autobiographical events during the Famous Events Test. Similarly, in the same test G.H. misunderstood a question as if it was referring to an incident that had happened in 1988, prior to the time period covered by amnesia. In fact, the incident had happened in 1990; that is, within the amnesic time interval. She performed perfectly on this item and could even provide considerable details on the public event in question. When she noticed that she had misjudged the date, she instantly refused to answer the next questions so that the test had to be interrupted and continued later. We consider two interpretations of this behaviour: G.H. might have deliberately avoided correct answers of all items within her amnesic time period, we caught her making a mistake and she became emotionally upset about this fact. Alternatively, G.H. might have unconsciously avoided correct answers within her amnesic time period, we confronted her and she became upset after realising that she indeed was able to remember information from that time. Given that a highly emotional reaction would be an ill suited attempt to cover deliberate malingering and considering the multitude of her additional psychiatric symptoms, we favour the psychogenic rather than conscious alternative. Although malingering might seem likely, we cannot conclude simulation without confession of the patient.

The temporal gradient of the amnesia in G.H. invalidates any direct organic causation as the beginning of her amnesia was exactly pinpointed to a day in May 1989. Though steep temporal gradients can also occur in organic RA (Albert et al., 1981), it is not common for the amnesia onset to be as precise as a single day. To a lesser degree also patient E.F.'s graded remote memory loss is unusual, since it was contrasted with remarkably unimpaired memory for all information prior to 12–14 years. An interesting case in this context is patient P.N. studied by Costello et al. (1998). P.N. suffered from 'isolated RA' after left anterior dorsomedial prefrontal brain damage, but he also showed a sharp

temporal gradient of remote memory loss (19 years) precisely covering a stressful time period in his life. Finding diminished left and right prefrontal brain activity during autobiographical memory retrieval as measured with PET, the authors suggested that their patient's lesion interrupted prefrontal trigger mechanisms necessary for autobiographical memory retrieval. Nevertheless, given the definite psychological co-contribution it might still be that his prefrontal functional disturbances were due to stress-related factors. Another psychogenic RA patient (Kapur, 1996), showed a strikingly similar temporal gradient of 14 years as was seen in E.F. and G.H. (see also patient A.M.N. studied by Markowitsch et al. 1998, 2000).

5.3. Further behavioural observations

The question of whether our RA patients gained a secondary benefit from their amnesia should be considered. In general, the sheer fact of receiving increased attention for themselves due to their deficit, including our research interest in their condition, might have been triggering and/or reinforcing their pathology. In patient A.B. secondary gain can be seen in the fact that she lost her depressive symptoms. Concomitantly, she was reported by others to have extensively changed her everyday mood, and she herself described her present situation as satisfying. Also, we observed personal benefit from the amnesic state in patient C.D. Over and above, he quit his job a while after the accident and was involved in a major compensation case with his former employer giving him a direct interest in maintaining or aggravating his pathology. His change of focus on executive dysfunctions instead of RA when seemingly more advantageous with regard to his compensation claim (see Section 2) can be seen in the same light. Furthermore, C.D. gave interviews for several news magazines and TV stations, a circumstance, which demonstrates that he received increased attention for his condition even from the public. Some evidence of secondary gain was also obvious for G.H. Her husband reported that after the onset of amnesia, she started to behave in a childish and egocentric way, which initially enabled her to avoid most of her daily duties. In addition, she herself reported a vast improvement in the way her husband took care of her after amnesia onset. Given her background, issues of personal care might have been a critical topic throughout her entire life. Moreover, the time period for which G.H. became amnesic included numerous surgeries, which left her unable to become pregnant. Her husband reported that approximately six months after the RA onset she started to vehemently express the wish to have another baby and even following clarification by her husband she kept denying her sterility. Thus, her amnesia may have yielded a secondary gain in terms of forgetting a currently stressful autobiographical actuality. We could not see any secondary gain from the RA in patient E.F. Finally, the onset of patient I.J.'s amnesia requires specific attention. He was found disoriented and amnesic three weeks after he had disappeared from home and these symptoms are commonly labelled as dissociative fugues. However, the exact circumstances of his disappearance remained unclear. Though his

wife did not report any preceding stressful life event, the possibility that he experienced a precursory psychological or organic trauma has to be considered for several reasons. Firstly, he was diagnosed suffering from symptoms of PTSD during his initial stay in Russia. Secondly, when he was found in the train, he reported not having been in possession of a large amount of money he had intended to receive from his former business partner. Instead, he carried a bag of clothes which were not even approximately his size. It can be hypothesised that he did not buy these clothes himself – though this possibility cannot be excluded either – but instead was given the bag by a potential assaulter. From this course of events, it may seem justified to reason that there was an immediately preceding stressful event. When we asked I.J. and his wife about possible legal actions to regain the money he had lost during or before his fugue, their answers were very evasive. They both emphasised their current demand for a peaceful life in their new neighbourhood where they had moved almost immediately after I.J.'s return, all of which may point to attempts to obscure the course of events. The reasons of this secrecy remained unclear but could indicate fear of the potential assaulter. Unfortunately, it was impossible to identify the former business partner's name or address since I.J. himself did not remember either and I.J.'s wife claimed not to have known him.

Although aspects of malingering seem likely in most of our cases, especially in patient C.D., again, as none of the patients confessed malingering, the proportions of conscious and unconscious contributions to the memory loss remain unclear.

6. Conclusion

Since unequivocal evidence of either psychological or organic evidence is often difficult to gather in patients with functional RA, sufficient background information about the patients' current and previous personal background is absolutely essential to reach a conclusion. In our sample of five patients, the condition was most consistently accompanied by attentional and executive dysfunctions rather than anterograde learning problems that were previously reported. Moreover, other commonalities were detected in Theory of Mind deficits and aberrances in conforming with social norms, the latter of which resembled repressive tendencies in three of the five patients. Semantic remote memory tests showed implicit usage of overtly inaccessible information and pointed to aggravated memory loss. Future studies may investigate in more detail how social phenomena such as Theory of Mind, or a repressive coping style and (inhibitory) frontal-lobe associated processes such as selective attention interact with functional remote memory loss.

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Appendix

We observed similar performance in our patients in some of the anterograde memory tests when contrasted with previous results reported by Kritchevsky et al. (2004). However, it has to be noted that we used different versions of the verbal memory tests. As such, story recall in Kritchevsky et al. comprised memory for 10 story segments, WMS-R Logical Memory applied in our group requires recall of 50 story segments; Kritchevsky et al.'s (2004) word pair learning comprised 10 word pairs, whereas Verbal Paired Associates of the WMS-R consists of eight word pairs. Finally, some cases of Kritchevsky et al. received the Rey–Osterrieth Complex Figure, whereas others were given the Taylor Complex Figure. Nevertheless, in order to provide approximate comparisons, we rescaled Kritchevsky et al.'s data of story recall, word pair learning trials and copy/delayed recall of a complex figure and contrasted these scores with our patients' percentage-scaled results in WMS-R immediate and delayed Logical Memory, the first three trials in the Verbal Paired Associates and copy/delayed recall of the Rey–Osterrieth Complex Figure. As can be seen in Figs. A1–A3, we observed similar,

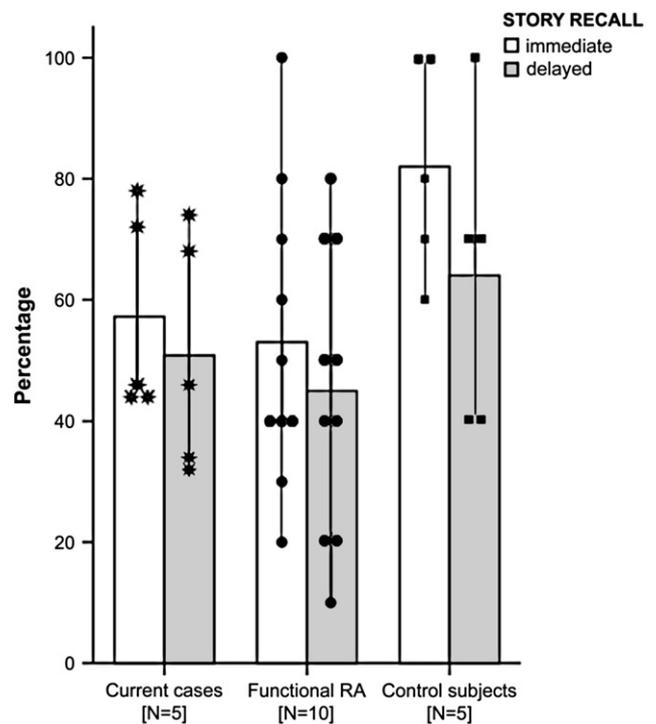


Fig. A1 – Story recall performance of the current five cases compared to functional RA patients and control subjects reported by Kritchevsky et al. (2004). Test scores are scaled as percentages from a total number of 10 story segments in Kritchevsky et al. (2004) and 50 story segments in our testing with Logical Memory of WMS-R. Recall was tested immediately and delayed after 20 min in our sample. In Kritchevsky et al. (2004) immediate testing was followed by delayed testing after 10–20 min.

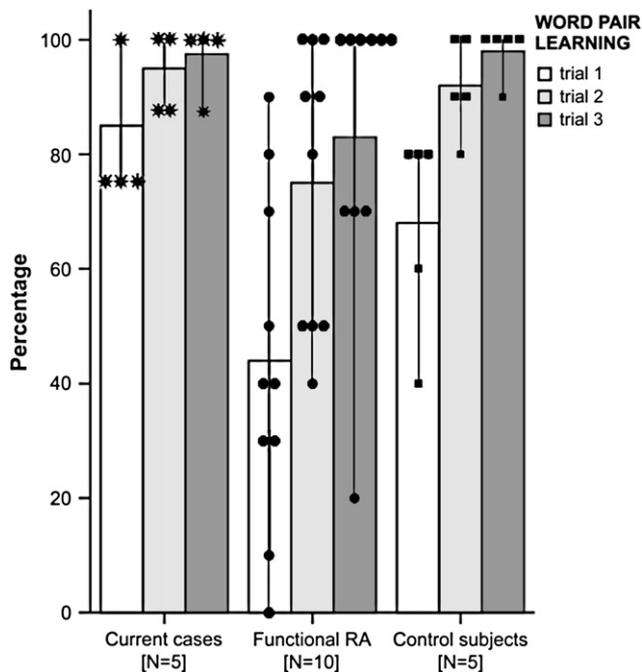


Fig. A2 – Word pair learning performance of the current five cases compared to functional RA patients and control subjects reported by Kritchevsky et al. (2004). Test scores are scaled as percentages recalled from a total of 10 word pairs in Kritchevsky et al. (2004) and eight word pairs in our testing with Verbal Paired Associates of WMS-R. Recall was tested immediately over three consecutive study trials.

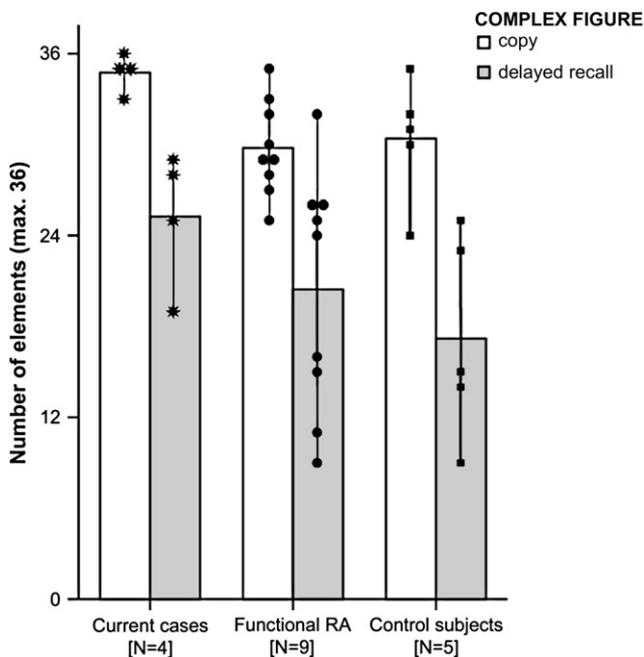


Fig. A3 – Figure copy and figure recall performance of the current five cases compared to functional RA patients and control subjects reported by Kritchevsky et al. (2004). Recall was tested immediately and delayed after 30 min in our sample. In Kritchevsky et al. (2004) immediate testing was followed by delayed testing after 10–20 min.

though less variable results in our patients compared to Kritchevsky et al. (2004).

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