Differential Impairment of Remembering the Past and Imagining Novel Events after Thalamic Lesions

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Abstract

■ Vividly remembering the past and imagining the future (mental time travel) seem to rely on common neural substrates and mental time travel impairments in patients with brain lesions seem to encompass both temporal domains. However, because future thinking—or more generally imagining novel events—involves the recombination of stored elements into a new event, it requires additional resources that are not shared by episodic memory. We aimed to demonstrate this asymmetry in an event generation task administered to two patients with lesions in the medial dorsal thalamus. Because of the dense connection with pFC, this nucleus of the thalamus is implicated in executive aspects of memory (strategic retrieval), which are presumably more important for future thinking than for episodic memory. Compared with groups of healthy matched control participants, both patients could only produce novel events with extensive help of the experimenter (prompting) in the absence of episodic memory problems. Impairments were most pronounced for imagining personal fictitious and impersonal events. More precisely, the patients' descriptions of novel events lacked content and spatio-temporal relations. The observed impairment is unlikely to trace back to disturbances in self-projection, scene construction, or time concept and could be explained by a recombination deficit. Thus, although memory and the imagination of novel events are tightly linked, they also partly rely on different processes. ■

INTRODUCTION

Mental time travel into the past and the future are sometimes also referred to as episodic memory and episodic future thinking. Although episodic memory was originally defined as memory for what happened in a specific place and at a specific time (what, where, when), it is now regarded as that kind of memory that is accompanied by a certain feeling of re-experiencing an event (autonoetic awareness; Tulving, 2005). We will use the terms mental time travel into the past and episodic memory (as defined by the phenomenological experience of remembering) synonymously in this article and for simplicity, henceforth abbreviate episodic memory to memory.

Memory and future thinking seem to rely on similar neural substrates (Botzung, Denkova, & Manning, 2008; Addis, Wong, & Schacter, 2007; Szpunar, Watson, & McDermott, 2007; Okuda et al., 2003). Investigations with patients suffering from brain lesions show common impairments of both processes (Andelman, Hoofien, Goldberg, Aizenstein, & Neufeld, 2010; Kwan, Carson, Addis, & Rosenbaum, 2010; Rosenbaum, Gilboa, Levine, Winocur, & Moscovitch, 2009; Hassabis, Kumaran, Vann, & Maguire, 2007; Atance & O'Neill, 2001) supporting the constructive episodic simulation hypothesis, which holds that memory is the basis for simulations of the future (Schacter & Addis, 2007; Schacter, Addis, & Buckner, 2007). Only few reports hint at asymmetric impairments of memory and future thinking so far (Maguire, Vargha-Khadem, & Hassabis, 2010; Squire et al., 2010).

There are, however, also profound differences between memory and future thinking (Suddendorf, 2010; Weiler, Suchan, & Daum, 2010), but few published studies have focused on them so far. It has been suggested that future thinking places higher demands on constructive processes (Schacter & Addis, 2007; Schacter et al., 2007) and, therefore, leads to stronger hippocampal involvement (Addis & Schacter, 2008; Addis, Moscovitch, & McAndrews, 2007). Imagination of novel events also requires a process that is not shared by remembering, that is, the recombination of elements stored in memory to generate a truly novel event. Recombination presumably relies on a number of processes that are likely mediated by pFC, for example, the search for details stored in memory and the evaluation whether it is feasible to unify certain details into a single event. Some details may have to be rejected, and additional details are actively retrieved from memory, together with active maintenance of previously retrieved details in working memory. These abilities rely on executive functions mediated by pFC (Moscovitch & Winocur, 2002; Petrides, 2002). Although the above-mentioned processes are also involved in episodic memory, the imagination of novel events presumably requires the retrieval of details from different memory traces and, therefore, entails more effortful

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search mechanisms. It is, thus, likely that frontal cortex control processes are more strongly involved in the generation of novel events compared with simple memory retrieval. In support of this assumption, Addis, Wong, et al. (2007) revealed stronger future-associated activation of several frontal brain areas compared with episodic memory. Furthermore, it was shown that mind wandering into the future decreases when prefrontal resources are used otherwise (Smallwood, Nind, & O'Connor, 2009).

If episodic future thinking or, more generally, imagination of novel events indeed involves additional processes that are not recruited by episodic memory, a selective imagination deficit should emerge if such processes are compromised by lesions. In contrast to previous studies, the current investigation focused on the differences in impairments for memory and imagination to show their asymmetric demands on cognitive processes.

Previous studies focused on patients with profound amnesia (Andelman et al., 2010; Kwan et al., 2010; Rosenbaum et al., 2009; Hassabis, Kumaran, Vann, et al., 2007); the current study applied a new approach by assessing the event generation abilities of patients with only mild or no apparent memory deficits. Patients with lesions in the medial dorsal nucleus (MD) of the thalamus were chosen because it is, due to the tight connection with pFC (Johansen-Berg et al., 2005; Taber, Wen, Khan, & Hurley, 2004; Behrens et al., 2003), critically involved in memory retrieval control processes (Soei, Koch, Schwarz, & Daum, 2008; Carrera & Bogousslavsky, 2006; Schmahmann, 2003; Van der Werf, Jolles, Witter, & Uylings, 2003; Zoppelt, Koch, Schwarz, & Daum, 2003; Van der Werf, Witter, Uylings, & Jolles, 2000). As outlined above, frontal cortex control processes are presumably more important for imagination than for remembering. Even patients with no or only mild memory problems may, thus, show strong deficits in future thinking or similar tasks requiring recombination.

To characterize the potential deficits of patients in detail, the current study assessed mental time travel into past and future along with the imagination of highly unlikely (fictitious) events, imagination of impersonal events (i.e., events happening to another person), recalling facts from public past events, as well as describing likely future developments of public issues (see Table 1). Whereas episodic memory requires scene construction (Hassabis & Maguire, 2007, 2009), episodic future thinking and imagination of fictitious and impersonal events additionally require recombination. Imagination of fictitious events necessitates especially good recombination abilities because highly unlikely impossible scenarios have to be created. Future events, on the other hand, are sometimes only slight variations of past events (thereby minimizing recombination demands). As outlined by Szpunar (2010), the difference in plausibility of episodic future thought and imagination of fictitious events should lead to distinctions at the behavioral and neural levels.

Imagination of impersonal events was included in the current event generation task, because it does not involve self-projection (Buckner & Carroll, 2007) and may, thus, help to disentangle deficits in scene construction, self-projection, and recombination. Descriptions of public past and future events involved stating facts without mentally imagining an event and could presumably be performed by relying on semantic memory alone. Comparison of the performance in these conditions allows the assessment of a general impairment of the concept of time. We hypothesized that patients would be most severely impaired in the fictitious condition because it involves the highest recombination demands. Impairments should also emerge in the other conditions requiring novel event generation (i.e., episodic future thinking and imagination of impersonal events), but to a lesser degree. The mildest deficits should occur for episodic memory, because it does not require recombination of stored details into something novel. Additionally, patients should be able to describe past and future events for the public domain even if they are impaired in the vivid mental imagery conditions.

METHODS

Participants

Two female right-handed patients with thalamic lesions were included in the study. For each patient, 10 healthy

Table 1. Conditions of Event Generation Task and Hypothetically Involved Processes

Condition	*Self-projection*	*Scene Construction*	*Time Concept*	*Recombination*
Episodic memory	o	o	o	x
Episodic future thinking	o	o	o	o
Personal fictitious events	o	o	x	o
Impersonal events	x	o	x	o
Public past events	x	x	o	x
Public future events	x	x	o	x[a]

o denotes that the process is involved in the condition; x denotes that the process is not required to solve this condition.

[a]Public future events do not need to be novel; participants could also state that a certain situation will continue to develop as it does at present and name the reasons for their opinion.

controls matched for age, sex, handedness, education, and intelligence quotient (IQ) were recruited (Table 2; comparison with a *t* test modified for single-case analyses implemented in the program singlims.exe (Crawford & Garthwaite, 2002; Crawford & Howell, 1998), henceforth called modified *t* test: all $|t_9| \leq 1.44$, $p \geq .184$). All participants had normal or corrected-to-normal vision, spoke German fluently, and had no history of psychiatric disorder or substance abuse. Control participants were only included if they had no history of neurological impairment.

Neuropsychological Testing

Visual and verbal short-term and working memory were assessed by the block and digit span subtests of the Wechsler Memory Scale-Revised (Wechsler, 2000). Copy and delayed recall of the Rey–Osterrieth complex figure were used to assess visuospatial processing skills and visual anterograde memory (Osterrieth, 1944). Verbal anterograde memory (recall and recognition) was measured using the Verbal Learning and Memory Test (Verbaler Lern-und Gedächtnistest; Helmstaedter, Lendt, & Lux, 2001), whereas visual recognition was assessed by the Recognition Memory Test (Warrington, 1984). Retrograde memory performance was estimated via the Autobiographical Memory Interview (Kopelman, Wilson, & Baddeley, 1989). Visual imagery abilities were addressed via a subjective rating (Vividness of Visual Imagery Questionnaire; Marks, 1973) and two objective tests similar to those used by Kosslyn, Holtzman, Farah, & Gazzaniga (1985; score: 1 point per correct item): In one test, participants visually imagine 18 animals and judge whether their tails are short or long with respect to the rest of their bodies. In the second test, participants make statements about the shape of orally presented letters. Attention was estimated by the Trail Making Test A (Reitan, 1992). Executive function tests included the Trail Making Test B (Reitan, 1992) and a Word Fluency Test (Regensburger Wortflüssigkeits-Test; Aschenbrenner, Tucha, & Lange, 2000). IQ was estimated by the subtests "Picture Completion," "Similarities," and "General Knowledge" of the German short version of the Wechsler Adult Intelligence Scale (Dahl, 1986).

An impairment is considered significant if the individual score falls below the tenth percentile of the normative sample. Normative data for Wechsler Memory Scale-Revised, Recognition Memory Test, Verbal Learning and Memory Test, Word Fluency Test, and Wechsler Adult Intelligence Scale were derived from the respective test manuals (Helmstaedter et al., 2001; Aschenbrenner et al., 2000; Wechsler, 2000; Dahl, 1986; Warrington, 1984). The Handbook of Normative Data for Neuropsychological Assessment (Mitrushina, Boone, & D'Elia, 1999) was used for the Rey–Osterrieth Complex Figure and Trail Making Tests. No normative data are available for the remaining tests.

The scores of the two patients were additionally compared with the scores of the respective control groups by means of the modified *t* test. Patient 01 (P01) differed significantly from the control group on the phonemic and category switching measures of verbal fluency (both $t_9 \geq -2.37$, $p \leq .042$), immediate recall ($t_9 = -3.24$, $p = .010$), and recognition performance ($t_9 = -3.08$, $p = .013$) in the Verbal Learning and Memory Test and for visual imagery ($t_9 = -4.85$, $p = .005$) in the Animals Test. Patient 02 (P02) differed significantly from her control group with respect to the time needed to complete Trail Making Test A ($t_9 = 6.31$, $p < .001$) and for visual imagery ($t_9 = -9.54$, $p < .001$) in the Letters Test. In all cases, the deviations represented poorer performance by the patients compared with their control groups. All other comparisons did not yield significant differences (all $|t_9| \leq 1.75$, $p \geq .115$).

Structural MRI

MRI was performed on a 3T GE Medical Systems scanner (General Electric Company, Milwaukee, WI). For both patients, high-resolution T_1-weighted images were obtained with 1.2-mm slice sickness. For P01, a T_2-weighted Propeller sequence with 5-mm slice sickness was additionally applied to reduce motion-related artifacts (only T_2-weighted sections are shown for this patient; Figure 1A and B). Lesion localization was performed by an experienced neurologist on the basis of landmarks defined in a stereotactic atlas (Morel, 2007).

P01

P01 was a 57-year-old, right-handed woman (Table 2) with 10 years of school education, who formerly worked as a forwarding merchant and continues working in the electrical engineering office of her husband. Following considerable stress at work, she suffered a bilateral infarct of the paramedian artery 9 years before this investigation, which took place in 2009. Acute symptoms included reduced vigilance, disorientation with respect to time and place, aphasia, apraxia, and severe amnesic syndrome. Neuropsychological deficits improved rapidly during inpatient treatment. However, the patient still suffered from mild aphasic symptoms (occasional phonemic paraphasia and reduced verbal fluency) and impaired anterograde verbal long-term memory (recall and recognition), as revealed by comparisons of the patient scores with normative data (Table 2) and with the control group (see Neuropsychological Testing). Anterograde memory in the visual domain, retrograde memory, and short-term and working memory were in the normal range (Table 2). P01 scored significantly lower than the control group on the Animals Test of visual imagery; however, another objective as well as the subjective measure of imagery did not reveal any abnormalities. The deficit presumably stems from poor knowledge of animal physiology and not from impaired visual imagery. In addition, performance assessed by the Trail Making Tests was in the normal range. At the time of testing, the patient complained about occasional

Table 2. Demographic and Neuropsychological Data of Patients and Control Groups

Demographic Variable/Test	*P01*	*CG01*	*P02*	*CG02*
Demographic Data				
Age (years)	57	57.4 (1.8)	64	64.8 (2.9)
Years of school education	10	10.4 (1.9)	10	10.0 (1.8)
Years of total education[a]	12.5	14.2 (3.7)	12.5	13.4 (2.3)
IQ estimate	106.6	110.5 (5.4)	112.0	119.6 (5.0)
Memory Tests				
WMS-R Digit Span forward[b]	7/12	9.4 (2.0)	7/12	9.3 (1.7)
WMS-R Digit Span backward[b]	5/12	8.3 (2.0)	6/12	7.4 (1.9)
WMS-R Block Span forward[b]	10/12	8.5 (2.0)	7/12	7.5 (1.3)
WMS-R Block Span backward[b]	6/12	7.8 (2.1)	6/12	6.8 (1.2)
Rey Figure copy	35/36	35.4 (1.1)	36/36	34.9 (1.3)
Rey Figure delayed recall	17/36	18.3 (4.9)	13/36	18.5 (4.4)
RMT faces	47/50	42.9 (5.3)	39/50	43.4 (3.3)
VLMT immediate recall	29/75[c]	59.3 (8.9)	40/75	41.9 (7.3)
VLMT delayed recall loss	4/0[d]	0.9 (1.7)	1/0	0.3 (2.1)
VLMT recognition	7/15[d]	13.3 (2.0)	12/15	13.5 (1.1)
AMI semantic[e]	58.5/63	61.4 (2.1)	62.5/63	61.5 (1.6)
AMI episodic[e]	22/27	22.1 (2.4)	18.5/27	20.9 (2.8)
Imagery Tests				
VVIQ[e]	78/80	67.3 (9.6)	72/80	68.6 (7.2)
Animals Test[e]	13/18	17.4 (0.8)	18/18	16.3 (2.0)
Letters Test[e]	20/20	19.7 (0.7)	19/20	20.0 (0.0)
Attention and Executive Function Tests				
Trail Making Test A (time in sec)	53	39.9 (9.5)	58	32.6 (3.8)
Trail Making Test B (time in sec)	131	81.0 (27.3)	86	75.9 (17.7)
RWT phonemic (N. of exemplars)	3[c]	11.7 (3.5)	9	13.9 (3.3)
RWT semantic (N. of exemplars)	11[c]	22.4 (8.3)	17	22.2 (3.3)
RWT category switching (N. of exemplars)	9[d]	15.9 (2.5)	12	14.9 (2.1)

Scores of the patients are presented along with the maximum possible score (patient/maximum), where appropriate. AMI = Autobiographical Memory Interview; CG = control group; N. = Number; RMT = Recognition Memory Test; RWT = Regensburger Wortflüssigkeits-Test; VLMT = Verbaler Lern- und Merkfähigkeitstest; VVIQ = Vividness of Visual Imagery Questionnaire; WMS-R = Wechsler Memory Scale-Revised. Raw scores are given for the WMS-R.

[a]School education plus additional formal education, for example, studies and traineeship.

[b]These tests represent also measures of executive function.

[c]Score < 5th percentile. Mean scores of control groups are accompanied by *SD*s in brackets.

[d]Score < 10th percentile of the normative data.

[e]No normative data available.

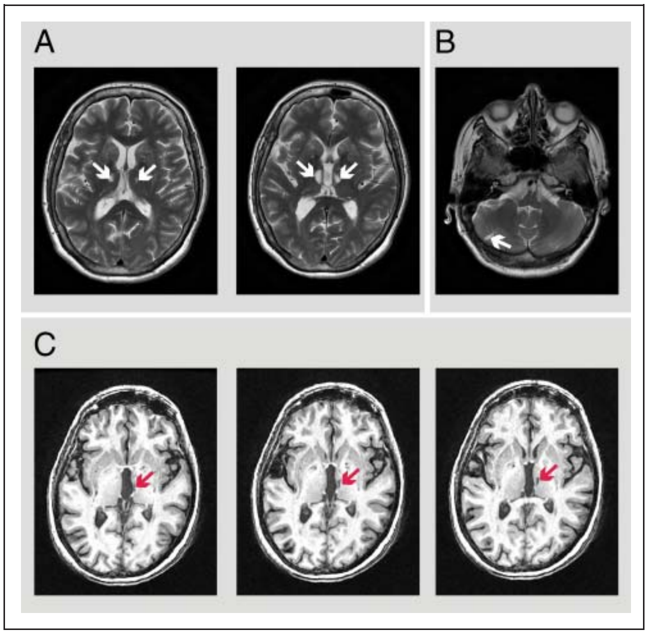

Figure 1. MRI sections of the patients. (A) Axial sections show bilateral lesions of the medial dorsal thalamus (marked by arrows) in T_2-weighted images of P01. (B) T_2-weighted section further reveals a small infarct in the left cerebellum of P01. (C) T_1-weighted axial sections of P02 show a right-sided lesion of the medial dorsal thalamus (marked by arrows). The left hemisphere is represented on the left side of the images.

dizziness, which according to her report usually gets better during summer.

Structural MRI in 2000 revealed bilateral lesions of the MD, which were confirmed by a recent high-resolution scan in 2010 (Figure 1A). MRIs additionally exposed a small left-sided infarct within the cerebellum (Figure 1B) and vascular leukencephalopathy. Although it would be preferable to test patients with lesions to the thalamus only, the main focus of the current study was not to describe the role of the thalamus in mental time travel but to demonstrate the asymmetry between mental time travel into the past and the future.

P02

P02 was a 64-year-old, right-handed woman with 10 years of school education, who formerly worked as a commercial employee and is now retired. She suffered a right-sided infarct of the paramedian artery 5 years before investigation in this study, which took place in 2009. Acute symptoms included left-sided hemiparesis, diplopia, and a depressive syndrome, which was successfully treated with Cipramil 20 but not further documented in the following years. No signs of aphasia were reported; documentation of memory performance in the acute stage is not available. The current memory and verbal fluency scores were all in the normal range (Table 2) and not significantly different from the control group (see Neuropsychological Testing). Consistent with these results, the patient did not report any memory or other cognitive problems in daily life. She only complained about deficits in fine motor skills of her left hand, which, she reported, was caused by a condition of the cervical vertebrae. At the time of testing, P02 was no longer on antidepressant medication; she did, however, receive medication for her elevated blood cholesterol level and for a heart condition.

Comparisons with the control group showed that P02 was significantly slower in Trail Making Test A. Her performance was, nevertheless, still within the normal range of the normative data, and no significant differences emerged for Trail Making Test B. The significant deviation of P02 from controls in the Letters Test for visual imagery is not functionally relevant because P02 still scored high on this test (19/20; all control participants reached the maximum score). Structural MRI in 2004 revealed a right-sided MD lesion, which was confirmed on recent high-resolution scans from 2009 (Figure 1C) along with microangiopathy in the BG and some small white matter lesions.

Event Generation Task

Mental time travel into the past and the future were investigated along with imagination of fictitious and impersonal events as well as description of public past and future events. The first four conditions required vivid mental imagery of events, whereas the public conditions involved the listing of facts only. For each of the six conditions, participants were presented with six cue words (one after the other) and had as much time as needed to remember or imagine an event related to the cue. A maximum of 3 min was then allotted for the verbal description of the event.

Episodic memory: In this condition, participants were required to report a true personal memory of a specific event, that is, an event that only took place once in this form. The events were not to last longer than 1 day and had to be specific in time and place.

Episodic future thinking: Participants were instructed to imagine a personal potential future event, specific in time and place, that was not to last longer than 1 day. The event had to be novel and plausible with respect to the participant's current life circumstances.

Fictitious events: Fictitious events had to be highly unlikely and could be impossible with respect to the laws of nature. The events were not to last longer than 1 day and had to be specific in place. Participants had to imagine themselves acting in the scenario, but they did not have to think about whether the event took place in the past or in the future.

Impersonal events: For the impersonal events, participants had to imagine the German Federal Chancellor Angela Merkel acting in a scenario (similar to Szpunar et al., 2007) that should be plausible or at least follow the laws of nature and was not to involve the participants themselves. The event had to be novel (not known from television) and specific in place and was not to last longer than 1 day. Participants did not have to think about whether it took place in the past or in the future.

Public past events: Following Klein, Loftus, and Kihlstrom (2002), participants did not have to mentally imagine a scenario in public conditions but had to state facts of an event that truly happened and was important for the public (e.g., a description of World War II). These events were typically known from the news or general knowledge learned in school. Participants hypothetically could solve the condition by relying on semantic memory alone; however, healthy participants may use different forms of memory for reciting facts about past events (e.g., recalling overlearned facts about World War II vs. recalling a single television report about the Afghanistan crisis vs. vividly remembering how one learned about the September 11th terrorist attacks). Description of personal experiences or opinions was not allowed.

Public future events: The same constrictions as for public past events applied (facts only, no personal information). Participants had to predict how current situations important for the public could develop in the future on the basis of what they know about the world now (e.g., how unemployment will develop).

Each condition required a combination of scene construction, self-projection, concept of time, and recombination (Table 1). For all conditions involving scene construction, participants were asked to produce a vivid mental image and describe it in as much detail as possible. Participants could close their eyes if it helped in generating the image.

Prompting

Participants were encouraged to talk freely and give all required information by themselves. However, if they stopped before reaching the time limit and left out important aspects, they were prompted to add this information following a fixed prompting scheme: (a) Could you describe the place where the scenario takes place? (b) Could you describe what you/Angela Merkel are/is doing in the scenario? (c) Could you describe this event in more detail (if only one to two sentences were given)?

If all required information were given, the trial was considered complete, even if the time limit had not been reached. For the first event of each condition, however, participants were asked if they completely described all details or whether they could still add something, even if the event already met all criteria. If participants responded to a prompt by stating that they could not answer this question, they were encouraged to try again until the time limit was reached or they attempted a response. In case participants did not adhere to the criteria of the conditions, they were interrupted and made aware which rule they broke. Errors made by the participants comprised descriptions longer than 1 day, adding personal information in the impersonal condition (e.g., participant meets Angela Merkel), choosing probable events in the fictitious condition, describing a general event instead of a specific moment, recasting past events as future events, switching between different events, and stating personal experiences, opinions, and wishes in the public conditions.

Stimulus Material

Cue words were comparable across conditions with respect to frequency in the German language (measures derived from an on-line dictionary, dict.uni-leipzig.de/), familiarity, valence, and context availability (rated by 58 participants via questionnaires). For the mental time travel and public conditions, three of six cue words were shared between past and future conditions to increase the difficulty of inventing a new event in the future condition.

Subjective Ratings

Similar to the study of Hassabis, Kumaran, Vann, et al. (2007), participants had to rate each event on a number of phenomenological characteristics immediately after describing the event. Both mental time travel conditions and fictitious condition were rated for perspective, valence, personal significance, emotionality, richness of detail, spatial coherence, and feeling of presence. Additionally, occurrence probability was judged for episodic future events. Impersonal events involving Angela Merkel were only rated on richness of detail and spatial coherence. For public events, participants rated how much general knowledge they possessed about the issue they talked about (richness of detail). Judgments were made based on a 7-point scale, with 7 being the highest rating. For all events involving a concept of time (see Table 1), the temporal distance of the event to the present had to be stated.

Procedure

All six trials of one condition were executed before the next condition was started. Cue words within each condition were presented in a fixed order, but the order of conditions was pseudorandomized across participants. At the start of each condition, participants received written instructions along with an event example. Instructions were discussed until fully clear. Cue words were presented on cards that were placed on the table and remained visible throughout the trial, together with a summary of the instructions. Subjective ratings were carried out after each verbal description. Depending on the participant's speed, the event generation task lasted between 2 and 3.5 hr. Neuropsychological tests were completed afterwards (1.5–2 hr). Participants could take breaks whenever necessary, and the whole experiment could be split on several days (in most cases, two sessions on different days).

Participants signed informed written consent before participation and were reimbursed for participation and travel expenses. Assessment took place either at the Ruhr

University Bochum or at the Klinikum Dortmund. The study was approved by the ethics committee of the medical faculty of the Ruhr University Bochum, and all experiments were carried out in accordance with the Declaration of Helsinki.

Interview Analysis

Interviews were recorded digitally and later transcribed verbatim. The descriptions were segmented into statements belonging to four different categories for the vivid imagery conditions (similar to Hassabis, Kumaran, Vann, et al., 2007; categories were modified on the basis of the analysis of 21 pilot data sets): category "content" comprising present entities, thoughts, emotions, actions, and sensorial descriptions; category "spatio-temporal" including spatial and temporal references; category "description" comprising intentions, explanations, and other descriptions; category "uninformative" including repetitions, uncertainty statements, and irrelevant information. (The categories "content" and "spatio-temporal" map onto the "internal details score" introduced by Levine, Svoboda, Hay, Winocur, and Moscovitch, 2002, for the analysis of the Autobiographical Interview, whereas the categories "description" and "uninformative" broadly map onto the "external detail score." The focus of the current analysis was, however, not on separating episodic and semantic details.) For the public conditions, data were only divided into uninformative information and correct facts. All events were rated by two independent judges, the author and a second person blind to group membership and the aims of the study, and both judges trained the procedure with several pilot data sets. For each event description, the number of statements belonging to each category was determined and compared between judges. If the counts of both judges differed by more than 1, a consensus rating was achieved: Both ratings were compared word by word to find the deviations, and each judge explained the reasons why she had assigned a statement to a certain category. It was then discussed which category better described the statement until consensus was achieved. If category counts differed only by 1, the mean value of both counts was calculated. Interrater reliability was generally high (average Cronbach's $\alpha = .84$). Finally, counts of the consensus ratings were summed across all events of one condition.

Statistical Analysis

Statistical analysis was performed using PASW Statistics 18 (IBM Corporation, Armonk, NY), Matlab 7.3 R2006b (The MathWorks, Inc., Natick, MA), and singlims.exe (modified *t* test; Crawford & Garthwaite, 2002; Crawford & Howell, 1998). Significance threshold was set to $p < .05$ (two-tailed).

For each of the four vivid imagery conditions, scores of the patients separate for all four categories (content, spatio-temporal, description, uninformative) were compared with the average scores of the respective control groups by means of the modified *t* test. For the public conditions, the number of facts and uninformative statements were subjected to *t* test analysis. For all six conditions, an additional comparison was made between patients and controls for the number of prompts given by the experimenter to achieve an event description meeting the protocol guidelines (see Prompting).

Because the verbal output of the participants differed in speed and because P01 had reduced verbal fluency compared with controls (Table 2), the data were scaled by the number of words: The number of statements for a certain category was multiplied by 100 and divided by the number of words used to describe the event in that trial. Only the scaled data entered the statistical comparison. For each significant difference between patient and associated control group, the magnitude of the patients' impairments was quantified as the number of *SD*s by which the patient score deviated from that of the control group (z score).

Analysis of Subjective Ratings and Temporal Distance

Scores for subjective ratings of phenomenological properties and judgments of temporal distance were averaged across trials for each participant and subsequently averaged across all control participants of one group, separately for each condition. Scores of patients were compared with the means of the respective control groups using the modified *t* test.

Correlations

To establish whether there was a link between the objective and subjective measures in the current study, Pearsons's correlation coefficients (r) were calculated for the subjective ratings of phenomenological properties and the number of statements determined by the judges (objective measure). Most of the phenomenological ratings did not have a direct correlate in the objective measures (e.g., feeling of presence, personal significance); richness of detail, however, could be inferred from the ratings of the judges as well: Objective richness of detail in the vivid conditions was calculated as the sum of all content and spatio-temporal statements, whereas the number of facts served as objective measure for the public conditions. Correlations were calculated separately for both control groups; patient data were not included.

RESULTS

Vivid Imagery Conditions

Patients exhibited marked impairments during the vivid imagination of novel events, whereas they were well able to recall episodic memories (see Supplementary Data for exemplary transcripts of event descriptions). The deficits are obvious in the number of prompts that the experimenter needed to encourage the participants to describe the events with all necessary information. Both patients needed significantly more prompts than the respective control group in every condition (P01: all $t_9 \geq 4.41$, $p \leq .002$; P02: $t_9 \geq 2.37$, $p \leq .042$) except for episodic memories (P01: $t_9 = 1.79$, $p = .108$; P02: $t_9 = 0.67$, $p = .522$; see Figure 2, left).

Comparison of the number of statements produced in the different categories between patients and control groups did not reveal any significant deviation for episodic memories (all $|t_9| \leq 0.16$, $p \geq .139$; see Figure 3). For episodic future thoughts, a trend toward fewer content statements of P01 compared with controls emerged ($t_9 = -2.06$, $p = .070$; all other comparisons: $|t_9| \leq 0.14$, $p \geq .208$). Patients' impairments were most obvious in the impersonal and fictitious conditions. Even with extensive prompting (see Figure 2), P01's impersonal events had significantly less spatio-temporal information than those of controls ($t_9 = -3.19$, $p = .011$) and by trend fewer content statements ($t_9 = -2.20$, $p = .055$). Similarly, P02 produced significantly fewer content information than controls ($t_9 = -2.37$, $p = .042$) and by trend fewer spatio-temporal statements ($t_9 = -2.00$, $p = .076$). For fictitious events, P01 produced significantly more uninformative statements ($t_9 = 2.70$, $p = .025$) and by trend less content statements ($t_9 = -2.18$, $p = .057$) than controls. Results of P02, on the other hand, only revealed a weak trend toward significantly less content statements compared with controls ($t_9 = -1.85$, $p = .098$; all other comparisons: $|t_9| \leq 1.71$, $p \geq .121$).

The above-reported data suggest that the impairments of both patients are stronger for the fictitious and impersonal conditions compared with the episodic future thinking condition, because impairments in the latter mainly manifested themselves in an increased need for intervention by the experimenter (prompting) to achieve complete event descriptions. This asymmetric deficit pattern was confirmed by a quantitative analysis of impairment magnitude. P01's scores were, on average, 4.5 *SD*s below the control group scores for both fictitious and impersonal events. For episodic future events, on the other hand, the difference was only 3.4 *SD*s. Similarly, P02's scores fell 3.1 and 3.6 *SD*s below the control group scores for impersonal and fictitious events, with a milder impairment of 2.5 *SD*s for future events.

Public Conditions

The analysis of the public conditions showed a dissociation between both patients' performance. Although no significant differences emerged between P02 and her control group (all $|t_9| \leq 1.03$, $p \geq .331$), P01 listed significantly fewer facts than controls for public past ($t_9 = -3.66$, $p = .005$) and future events ($t_9 = -2.80$, $p = .021$), and, at the same time, tended to produce more uninformative statements in the past condition ($t_9 = 2.11$, $p = .064$; see Figure 4). For two of the past events, P01 was unable to produce an event at all.

As can be seen in Figure 2 (right), a similar pattern emerged for the number of prompts: Whereas P02 tended to differ from controls for public past events only ($t_9 = 2.21$, $p = .054$; future: $t_9 = -0.07$, $p = .949$), P01 needed significantly more prompts than healthy matched participants in both conditions (both $t_9 \geq 4.44$, $p \leq .002$).

Subjective Ratings

The analysis of the richness of detail ratings in public conditions (i.e., the subjective estimate of general knowledge for the described topics) did not reveal any significant deviation of the patients' scores from the scores of their respective control groups (all $|t_9| \leq 1.28$, $p \geq .234$; see Figure 5). Although this is in line with the good performance of P02 in the public conditions, it does not match with P01's impairments on the objective measures (see Public Conditions).

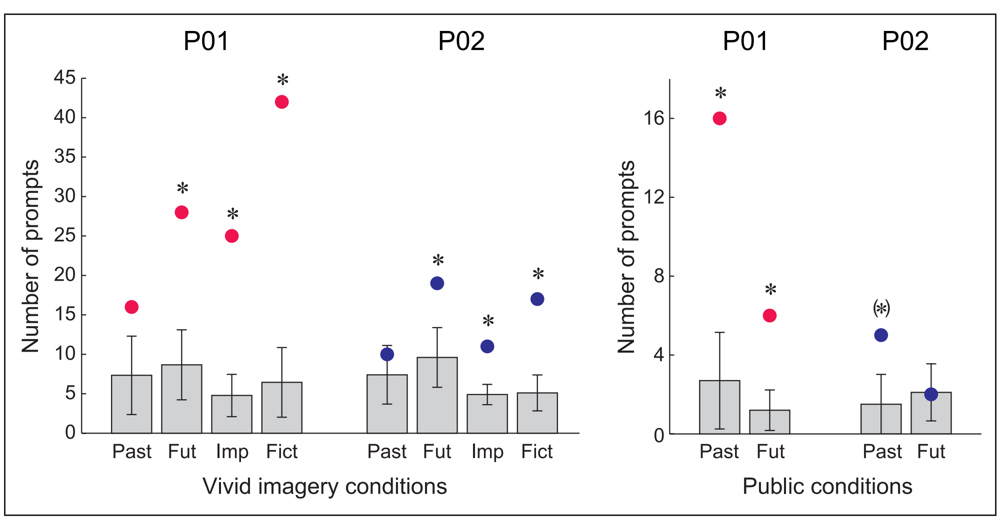

Figure 2. Number of prompts in vivid imagery and public conditions. Bars represent means of the control groups; error bars denote *SD*s. Dots show the number of prompts for patients. The number of prompts represents the sum over all trials of one condition. Fut = future; Imp = impersonal; Fict = fictitious. $^*p < .05$; $^{(*)}p < .1$.

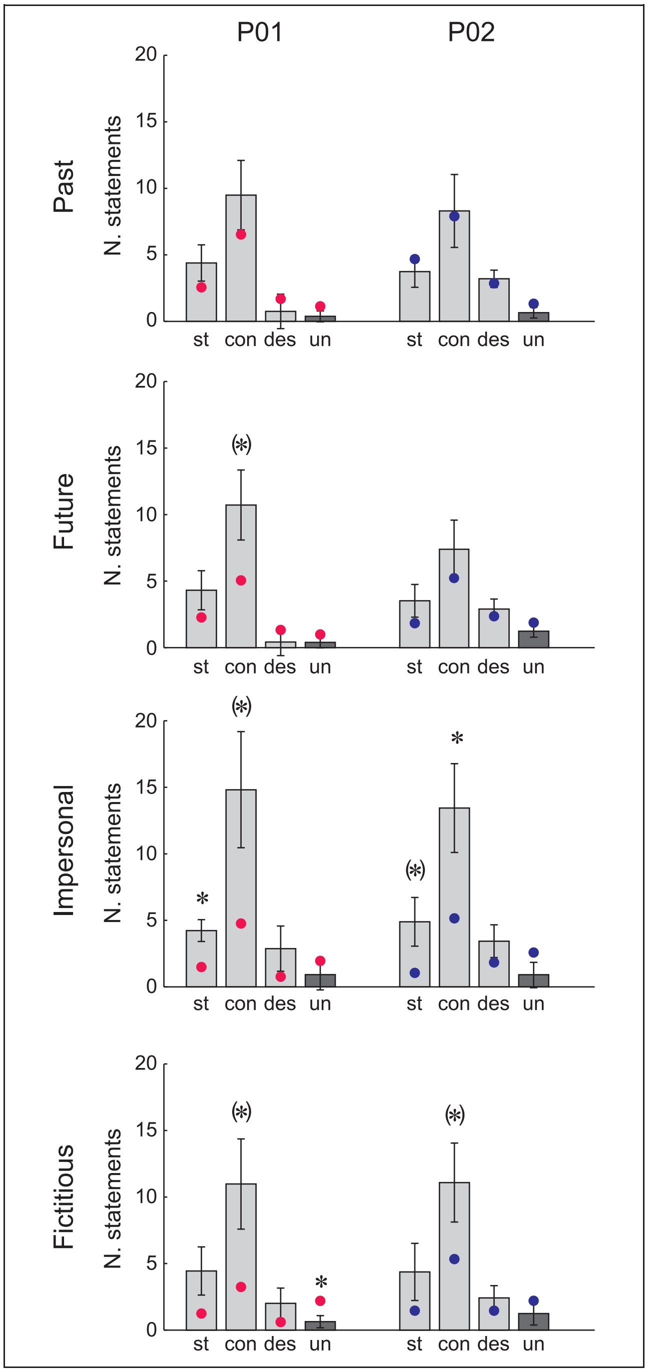

Figure 3. Comparison of number of statements generated by patients and controls in the four categories of the vivid imagery conditions. Bars represent means of the control groups; error bars denote *SD*s. Dark bar color indicates that higher scores for these variables represent worse performance. Dots show results of the patients. The number (N.) of statements represents the sum over all trials of one condition, scaled by the number of words. con = content; des = description; st = spatio-temporal; un = uninformative. $*p < .05$; $^{(*)}p < .1$.

Unlike objective measures (Vivid Imagery Conditions), subjective variables of the quality of vivid imagination showed only few significant deviations between patients and their control groups (see Figure 6). P01 rated the richness of detail of fictitious events significantly lower than the

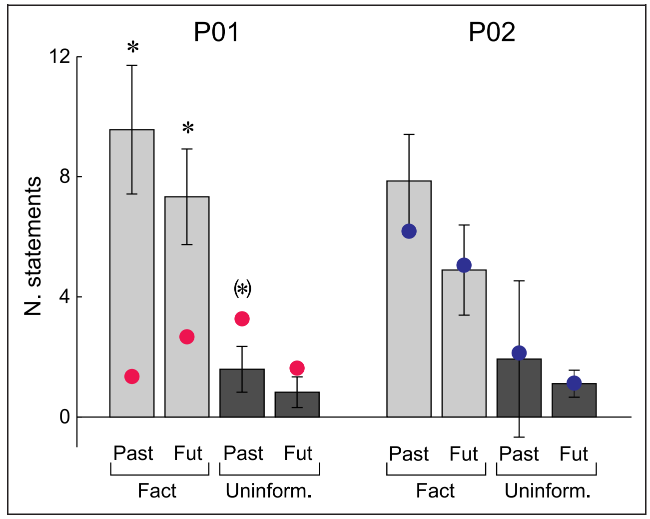

Figure 4. Comparison of number (N.) of statements generated by patients and controls in the two public conditions. Bars represent means of the control groups; error bars denote *SD*s. Dark bar color indicates that higher scores for these variables represent worse performance. Dots show results of the patients. The number of statements represents the sum over all trials of one condition, scaled by the number of words. Fut = future; Uninform. = uninformative. $*p < .05$; $^{(*)}p < .1$.

control group ($t_9 = -3.01, p = .015$). Additionally, a trend emerged for lower richness of detail ratings of P01 in the episodic memory condition ($t_9 = -2.06, p = .070$). Significant differences between the ratings of P02 and her control group were observed in the impersonal event condition only, with P02 assigning lower richness of detail ($t_9 = -6.04, p = .003$) and spatial coherence scores ($t_9 = -6.04, p < .001$) to her imagination. No other comparisons reached significance (all $|t_9| \leq 1.59, p \geq .146$).

There was no significant correlation between subjective and objective richness of detail in any of the six conditions in the control group of P02 (all $p \geq .107$, $|r| \leq 0.54$). In the

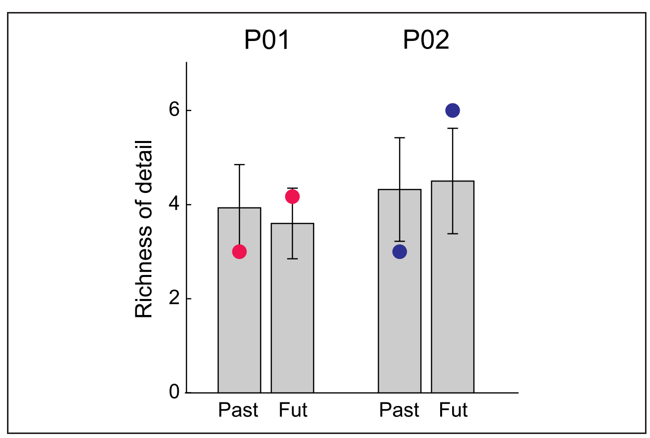

Figure 5. Subjective ratings of the richness of detail in the public conditions. Bars represent means of the control groups; error bars denote *SD*s. Dots show the patients' scores. Maximum richness of detail score was 7. Fut = Future.

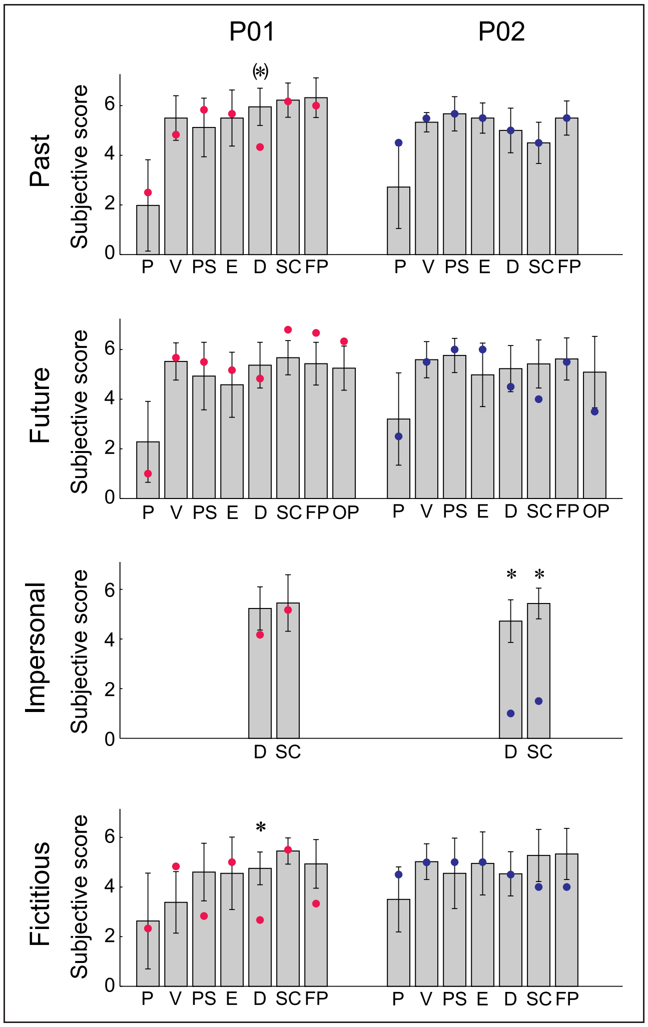

Figure 6. Subjective ratings of the phenomenal properties in the vivid imagery conditions. Bars represent means of the control groups; error bars denote *SD*s. Dots show the patients' scores. Maximum score was 7. Scores for perspective and valence ratings have been recoded from a scale ranging from −3 to 3 into a scale ranging from 1 to 7 for better comparison with other scores. High perspective scores indicate high frequency of observer perspective; high valence scores indicate high frequency of positive events. P = perspective; V = valence; PS = personal significance; E = emotionality; D = richness of detail; SC = spatial coherence; FP = feeling of presence; OP = occurrence probability. $^{*}p < .05$; $^{(*)}p < .1$.

control group of P01, only the correlation in the impersonal condition reached significance ($p = .018$, $r = 0.72$; all other $p \geq .128$, $|r| \leq 0.51$).

Temporal Distance

The temporal distance of events to present did not significantly differ between patients and controls in the episodic and public conditions (all $p \geq .161$, $|t_9| \leq 1.53$; see Table 3). Both patients recalled events from periods before and after the stroke: Half of P01's episodic memories stemmed from the past year (stroke 9 years before this investigation); half of P02's episodic memories dated back no further than 2 years (stroke 5 years before this investigation).

DISCUSSION

The present study aimed to further characterize mental time travel into the past and the future as well as other forms of imagination with respect to their asymmetric recruitment of subprocesses. The data of two patients with lesions in MD of the thalamus did not yield significant deficits for episodic memory but prominent impairments during imagination of fictitious and impersonal events as well as milder deficits during episodic future thinking. Compared with controls, the patients' problems manifested themselves in reduced content and spatio-temporal information (fictitious and impersonal events) and an elevated need for prompting (all three novel event types). The deficit pattern for fictitious and impersonal event imagination was partially underlined by the self-reported problems of the patients (subjective ratings of phenomenological properties; see Subjective Ratings). The results, thus, corroborated the hypothesis that lesions in a brain region linking frontal cortex control mechanisms with medial-temporal lobe memory processes would significantly affect tasks that require the recombination of stored information into a novel event. In general, P01 was more strongly impaired than P02 in the event generation task and in neuropsychological tests (Table 2). These results may relate to the larger and bilateral lesion

Table 3. Temporal Distance Ratings for Episodic and Public Conditions

	Public Conditions				*Episodic Conditions*			
Temporal Direction	*P01*	*CG01*	*P02*	*CG02*	*P01*	*CG01*	*P02*	*CG02*
Past	27.8	18.1 (9.3)	0.1	18.8 (11.6)	16.8	16.6 (11.5)	21.4	22.3 (7.4)
Future	9.2	27.1 (52.1)	4.0	189.1 (522.1)	0.6	3.0 (3.2)	3.1	4.7 (5.3)

Temporal distance is given in years. Means across all members of a group with *SD*s in brackets are given for control groups. The temporal distance for public events differs qualitatively from that of episodic events in that it can transcend the participant's life span. Especially in the public future condition, participants considered very large time spans. CG = control group.

of P01 and are in accordance with the assumption that lesions have to encompass a substantial portion of MD to cause memory problems (Kritchevsky, Graff-Radford, & Damasio, 1987).

Novel Event Generation Deficits

Previous studies with brain-lesioned patients led only to preliminary evidence for imbalances in impairments of mental time travel into the past and the future (Andelman et al., 2010; Maguire et al., 2010; Squire et al., 2010). However, remembering and imagining are not uniform capacities but include various components (Suddendorf & Corballis, 2007), which are likely to be differentially recruited for both processes.

In line with our hypotheses, both patients were strongly impaired in imagining novel events (Figure 2), which require scene construction and recombination (Table 1). Scene construction was previously held responsible for imagination deficits in patients with hippocampal lesions (Hassabis, Kumaran, Vann, et al., 2007), but patients in the current study had no problem during episodic memory, which requires scene construction as well. Additional analyses confirmed that deficits extended across different statement categories and were not disproportionally pronounced for spatial references. It would, nevertheless, be interesting to assess the spatial coherence of events by the questionnaire used by Hassabis, Kumaran, Vann, et al. (2007), which would yield a more thorough subjective measure of spatial coherence as the rating scale used in the present study.

Thus, deficits may stem from a recombination deficit, more specifically from a deficient search of details stored in memory. As outlined in Introduction, recombination comprises several subprocesses, for instance, the searching of details in memory and the evaluation of these details. Searching several memory traces for appropriate details (novel event conditions) presumably requires more prefrontal resources than searching one memory trace (episodic memory condition), thus potentially explaining the deficits observed in the present study. It has, however, also been suggested that imagination of novel events may require more constructive resources and, thus, more binding than remembering (Addis, Wong, et al., 2007), which poses an alternative explanation for the here-reported deficits.

Self-projection impairments can be ruled out as the underlying deficit because gross impairments in the patients' performance occurred in the impersonal condition, which did not require such processes (Figure 2; see also Table 1), and patients had no problems with projecting themselves backward in time.

Furthermore, the results do not suggest a general disturbance of the time concept, as both patients had the most pronounced problems in those conditions that did not involve a concept of past and future and P02 was additionally unimpaired in the public conditions. Taken together, the empirical evidence is in accordance with a recombination deficit, which matches with the recently reported link between creativity and thalamic gating mechanisms that regulate the filtering and flow of information (de Manzano, Cervenka, Karabanov, Farde, & Ullen, 2010). In line with this, patients exhibited increasing impairments with increasing recombination demands, that is, deficits were larger in the fictitious than in the future thinking condition. The strong deficits for imagining Angela Merkel were unexpected, because participants should be able to use common knowledge and routine scenarios to fulfill this task. However, the instructions stressed that a novel event was to be generated and cue words forced private contexts (e.g., garden). This transfer of Angela Merkel into a context that was usually only known from personal experiences may have been equally difficult for the patients as transferring themselves into a completely new context in the fictitious condition.

In summary, although a recombination deficit could explain the observed impairments, the data are open to other interpretations as well: Patients could, for instance, be more impaired in gaining access to nonepisodic representations or show a binding deficit, which is especially pronounced for new events, because those require more binding than episodic memories. Testing the patients with the recombination task recently invented by Addis et al. (Addis, Musicaro, Pan, & Schacter, 2010; Addis, Pan, Vu, Laiser, & Schacter, 2009) would be an interesting endeavor for the future to clarify this issue.

Public Event Generation Deficits

Deficits for public event generation only emerged for P01 (Figure 4). Similarly, Rosenbaum et al. (2009) reported that K. C. cannot recall nonpersonal semantic narratives because of a binding problem. Although binding was intact in P01, neuropsychological background testing revealed a verbal anterograde memory impairment (Table 2), and encoding of public events may more heavily rely on verbal information than encoding of episodic memories: Whereas the latter are experienced in a multimodal fashion, public events come to our attention from printed media or by listening to descriptions. Deficits in the public condition may, thus, be linked to P01's specific deficit in the verbal domain. P01 was additionally impaired during forecasting the future, which is not surprising, given that knowledge about public developments in the past is the basis for reasoning what might happen in the future.

In contrast to the marked impairment in the objective measures of public event generation (Vivid Imagery Conditions), P01's subjective assessment did not significantly differ from that of controls (Subjective Ratings). P01 stated on several occasions that she was aware of her memory problems, but she may have adjusted the rating scale to her own abilities, meaning that a maximum score of 7 represented her best possible performance and not the best possible performance of any other person.

Subjective Ratings

For vivid imagery, P02's subjective assessment of her event generation abilities matched with the analysis of objective measures (compare Figures 3 and 6). P01, on the other hand, had pronounced problems in generating impersonal, fictitious, and future events (see Figures 2 and 3) but only assigned lower scores to the richness of detail for fictitious events. Additionally, she tended to express lower detail scores for episodic memories compared with controls (Figure 6). It was previously shown that patients with hippocampal damage are unable to accurately evaluate their memory and future thinking performances (Kwan et al., 2010; Addis, Moscovitch, et al., 2007; Banos et al., 2004), and the same may be true for patients with other lesion locations.

There were further no correlations between subjective and objective measures of richness of detail in healthy controls (except for the impersonal condition in the control group of P01; see Subjective Ratings). Several explanations exist for this finding. First, the sample size was small, and correlations may not have reached significance because of missing statistical power. Second, participants indicated that they often had more details in mind than they expressed in words, and instructions were to rate the richness of detail in the mental image. Third, correlations were computed for the average richness of detail scores of each healthy participant (not for single trials), and interindividual differences may exist in interpreting the rating scale, thus blurring potential effects. Finally, it may be that what is termed "objective detail score" here may not capture the same elements that participants considered for rating subjective richness of detail. The analysis of subjective measures was, however, not the main focus of this study.

Contribution of MD to Mental Time Travel

MD has a dense connection to pFC (Klein et al., 2010; Johansen-Berg et al., 2005; Taber et al., 2004; Behrens et al., 2003), and symptoms accompanying lesions in this brain area often resemble those found after frontal lobe damage (Carrera & Bogousslavsky, 2006; Schmahmann, 2003; Van der Werf et al., 2000; Bogousslavsky, Regli, & Uske, 1988). The pFC seems to be of special importance for the simulation of novel events (Addis, Wong, et al., 2007; Ingvar, 1985), potentially by mediating strategic retrieval (Petrides, 1996, 2002). For mentally traveling into the past, strategic retrieval is—if at all—engaged to select one memory among the others matching the cue word; details can then presumably be activated via associative mechanisms (Simons & Spiers, 2003; Moscovitch & Winocur, 2002; Petrides, 2002). For the imagination of a novel event, on the other hand, parts of different episodic memories as well as semantic knowledge are combined, thereby placing strong demands on prefrontal resources.

Neuroimaging studies have revealed a core network for mental time travel and other forms of imagination (Botzung et al., 2008; Addis, Wong, et al., 2007; Hassabis, Kumaran, & Maguire, 2007; Szpunar et al., 2007; Okuda et al., 2003), but activation of the thalamus has not been discussed so far. Electrophysiological investigations in animals suggest that inputs from MD modulate the activity of neurons that connect the hippocampus with pFC (Floresco & Grace, 2003) and that MD is partially involved in mediating behavioral flexibility (Block, Dhanji, Thompson-Tardif, & Floresco, 2007). Van der Werf et al. (2003) concluded from their analysis of human patients that the MD seems to play a role in adjusting prefrontal executive processes during memory depending, for instance, on the plans and intentions of the organism. In addition, a recent study highlighted the potential importance of the thalamus for creativity (de Manzano et al., 2010), which might be essential for the generation of truly novel events. Further behavioral studies in patients and investigations using functional MRI, linking recombination with other measures of divergent thinking, will be needed for elucidating the exact role that the MD plays for mental time travel.

Influence of Recovery and Other Brain Abnormalities

It has to be noted that both patients in the present study were assessed long after suffering the infarct and some recovery processes have presumably taken place. Whereas no information on acute memory function is available for P02, P01 was initially characterized by a severe amnesic syndrome, which had declined to a verbal anterograde memory impairment at the time of assessment for the present study. Andelman et al. (2010) recently described an asymmetric recovery of memory and future thinking abilities, and patients in the current study may have undergone similar developments. It would, thus, be interesting for future studies to compare remembering and imagining in the acute stage and several years later. Although we cannot rule out that the persisting verbal fluency impairment of P01 partially contributed to her deficits, it importantly cannot explain the differential impairment for memory and imagination.

Apparently in contrast with the observed executive dysfunction in the event generation task, both patients were unimpaired in standard tests of executive functions. Because of time constraints, only few of these tests were administered, which may have been too easy to detect the deficit.

P01 and P02 showed further brain abnormalities outside the thalamus, which may have contributed to the patients' impairments, and further investigations with patients suffering from lesions in the MD are necessary to confirm the here-presented findings. The consistent recombination impairment in both P01 and P02 nevertheless matches well with the presumed role of MD and pFC in memory and prediction.

During the acute stage of the infarction, P02 had suffered from a depressive syndrome, which was successfully treated by antidepressant medication. Depression was shown to reduce the specificity of episodic memories and future thoughts (Williams et al., 1996) but would be unlikely to explain the asymmetric impairment of imagination and memory, which is the main finding of the current study.

Conclusion

The present study showed for the first time that impairments in imagining novel events can occur in the absence of measurable impairments for mental time travel into the past. Two patients with lesions in MD exhibited deficits when attempting to imagine potential future events, and even more pronounced problems occurred during imagination of impersonal and fictitious events. These problems are unlikely to be caused by deficits in self-projection, time concept, or a general failure to bind event details but could be linked to a recombination impairment. In contrast to previous reports of patients with lesions in the hippocampus who seemed to suffer from a general scene construction deficit, patients with lesions in the thalamus appear to be impaired in the executive aspects of imagination mediated by the connection between MD and pFC. The results clearly demonstrate that asymmetries exist between mental time travel into the past and the future: Although episodic memory seems to be the basis for episodic future thinking, future thinking draws on additional processes. It does, however, become clear from the pronounced impairments in the fictitious and impersonal conditions that the asymmetry reported herein is not specific for a distinction between past and future events but applies more broadly to the distinction between remembering and imagining novel events. The results nevertheless corroborate a distinction between plausible and implausible imagined events as recently proposed by Szpunar (2010). It will be of considerable interest in future studies to investigate subprocesses of recombination, that is, search for details, evaluation of details, and binding, and to explore the relation between recombination and creativity.

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