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Deficits in Remembering the Past and Imagining the Future in patients with Prefrontal Lesions

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Abstract

Objective: Neuroimaging studies suggest that remembering the past and imagining the future engage a common brain network including several areas of the prefrontal cortex. Although patients with prefrontal damage often are described as blind to the future consequences of their decisions, and inclined to “live in the here and now”, little is known as to how the prefrontal cortex mediates past and future mental time travel. Method: Nine patients with prefrontal lesions and nine healthy controls generated past and future events in response to different time periods. Event transcriptions were scored using the Autobiographical Interview protocol (Levine, Svoboda, Hay, Winocur, & Moscovitch, 2002) which provides a reliable system for categorizing internal (episodic) and external (semantic) information. For each event, participants answered a series of questions to assess self-reported phenomenal characteristics. Results: Patients with prefrontal lesions exhibited deficits in both remembering past events and imagining future events by generating fewer internal details than controls. This effect of group was larger in the past condition than in the future condition. In contrast, no group differences were seen for the number of external details, which were at the same level for patients and controls for both temporal conditions. There were no group differences in ratings of phenomenal characteristics. Conclusion: Our findings suggest that damage to prefrontal structures adversely affects the retrieval of past and the construction of future events. In particular, prefrontal structures are critical for the production of episodic event specific details when engaging in past and future mental time travel.

Keywords: Episodic memory, Episodic Future Thinking, Mental time travel, Prefrontal Cortex, Focal brain lesions.
Deficits in Remembering the Past and Imagining the Future in patients with Prefrontal Lesions

The capacity to imagine or simulate one’s possible future experiences, generally referred to as episodic future thinking (e.g., Atance & O’Neill, 2001; Szpunar, 2010) is pervasive in daily life and supports a range of adaptive behaviors from planning, problem solving, to decision making (Atance & O’Neill, 2001; D’Argembeau, Renaud, & Van der Linden, 2011; Peters & Buchel, 2010; Sheldon, McAdams & Moscovitch, 2011; Suddendorf & Corballis, 2007). From its early conceptualizations (e.g., Tulving, 1985), episodic future thinking has been associated with frontal structures of the brain. Ironically, however, little is known as to how prefrontal lesions impact this capacity.

Prevailing models of episodic future thinking suggest that future event construction relies critically upon episodic memory in order to provide content and details (Atance & O’Neill, 2001; Buckner & Carroll, 2007; Hassabis & Maguire, 2007; Schacter & Addis, 2007; Suddendorf & Corballis, 2007; Tulving, 1985; 2005). This idea rests on neuroimaging studies identifying a common core network underlying both past remembering and future imagining, with several areas of the medial temporal lobes (MTL) and prefrontal cortex (PFC) as key areas of overlap (e.g., Addis, Wong, & Schacter, 2007; Botzung, Denkova, & Manning, 2008; Hassabis, Kumaran, & Maguire, 2007a; Okuda et al., 2003; Szpunar, Watson & McDermott, 2007), as well as on findings of parallel impairments across episodic memory and future thinking in patients with MTL damage (e.g., Hassabis, Kumaran, Vann, & Maguire, 2007b; Kwan, Carson, Addis, & Rosenbaum, 2010; Race, Keane, & Verfaellie, 2011; but see Squire et al., 2010). However, patient studies have suggested that structures beyond the MTL play a crucial role for the capacity for episodic future thinking. For instance, in Alzheimer’s disease, degeneration of the posterior cingulate cortex, appears to be the common underlying neural substrate for impaired episodic memory and future
thinking (Irish, Addis, Hodges, & Piquet, 2012a; Irish, Hodges & Piquet, 2013) and Berryhill and colleagues have shown that posterior parietal lesions also impair this ability (Berryhill, Picasso, Arnold, Drowos & Olson, 2010).

Early theories on human foresight pointed to the frontal lobes as crucial for the ability to engage in mental time travel and to plan for the future (Ingvar, 1985; Tulving, 1985; Wheeler, Stuss & Tulving, 1997). These early observations were based mainly on the apparent inability for patients with PFC lesions to engage in future-oriented cognition, whether as impaired awareness of their continued existence in subjective time (Wheeler et al., 1997; Szpunar, 2011), or as insensitivity to the future consequences when making decisions (Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Damasio, & Damasio, 2000), or as deficient planning and prospective memory (Shallice & Burgess, 1991; Burgess, 2000). However, the question remains whether processes supported by the PFC are necessary for the ability to imagine possible future events and consequently how PFC damage affects past and future event construction.

To date, few studies have directly examined the capacity for episodic future thinking in patients with PFC damage (Berryhill et al., 2010; Irish et al., 2013; Kurczek et al., 2015). Berryhill and colleagues (2010) examined the ability to remember past and imagine future experiences in two patients with posterior parietal lesions and in four patients with dorsomedial and ventrolateral PFC lesions (Berryhill et al., 2010). The authors reported that the PFC patients were impaired in their ability to describe imaginary future events, while the parietal patients were impaired on both autobiographical remembering and future imagining. The fact that the PFC patients were impaired on future thinking was reported to be surprising, because patients had been carefully selected on the basis of not presenting lesions in medial or ventromedial PFC, areas that generally show activation in neuroimaging studies of past and future event construction (Addis et al., 2007; Botzung et al.,
The authors speculated that the results reflected asymmetric demands on cognitive processes, and in particular on executive functions, when constructing past and future events. However, Berryhill et al. (2010) did not employ the same strategies for measuring past and future event construction, making it difficult to compare the two temporal conditions directly.

Nonetheless, asymmetric impairments across temporal conditions, with marked deficits in future imagining, despite intact retrieval of personal past events, have also been reported in other populations associated with frontal impairments. This includes two patients with thalamic lesions (Weiler, Suchan, Koch, Schwarz, & Daum, 2011) and in patients with Parkinson’s disease (de Vito et al., 2012). In the latter study, future thinking deficits were found to be associated with impaired executive control. These findings accord with several neuroimaging studies showing increased frontopolar activation during future imagining in healthy individuals (Abraham, Schubotz, & von Cramon, 2008; Addis et al., 2007; Okuda et al., 2003, but see Botzung et al., 2008) and studies showing that more effort appears to be required to bring a future event to mind than to remember a past event (Arnold, McDermott, & Szpunar, 2011). Together these results seem to suggest a differential effect of prefrontal pathology on remembering and imagining, with stronger detrimental effects for the latter, which may reflect that more intensive, or even additional, cognitive operations are required to construct future events.

However, contrary to the above findings, a number of studies have reported symmetrical deficits in past and future event construction in various populations who present with executive or frontal lobe dysfunction (e.g. Abram, Picard, Navarro & Piolino, 2014; Addis, Wong, & Schacter, 2008; Addis, Musicaro, Pan, & Schacter, 2010; Coste et al., 2015; Irish et al., 2012a; Irish, Addis, Hodges, & Piguet, 2012b; Irish et al., 2013; Rasmussen & Berntsen, 2014; Sheldon et al., 2011;
Williams et al., 1996). For instance, Rasmussen and Berntsen (2014) examined a group of traumatic brain injury (TBI) patients, who showed impairments on measures of executive functioning. Using a modified version of the Autobiographical Interview (AI) (Levine et al., 2002), the authors reported that the TBI patients produced significantly fewer episodic details compared with healthy controls for both past and future events with no interaction between group and temporal direction, while there were no differences between patients and controls on the amount of semantic details generated. Relatedly, Coste and colleagues (2015) found TBI patients to show deficits on both semantic and episodic aspects of event construction regardless of the temporal direction. However, in their study, impairments in retrieving past event were mainly predicted by executive deficits (i.e., updating), while impairments in future event construction were predicted by semantic and working memory deficits. These findings illustrate that although impairments are observed across both temporal directions, different neural processes may underlie deficits in past and future event construction. In fact, in a recent study, Irish et al. (2013) reported that although patients with frontotemporal dementia (FTD) showed symmetrical impairments across temporal direction, voxel-based morphometry revealed divergent neural substrates for past and future event construction in these patients. While atrophy in medial prefrontal regions correlated with disruptions in past retrieval, future thinking deficits were associated with atrophy of frontopolar, lateral temporal and medial temporal cortices.

Symmetrical deficits in episodic specificity of past and future events have also been reported in depressed patients (Williams et al., 1996), and Williams and colleagues proposed that such deficits were linked with poor inhibitory control processes (Dalgleish et al., 2007; Williams et al., 2007). Similar findings of symmetrical impairments have also been observed in healthy older adults (Abram et al., 2014; Addis et al., 2008; 2010; Sheldon et al., 2011), and these deficits have been
shown to depend on ageing effects on executive and working memory processes in addition to basic episodic memory processes (Addis et al., 2008; Addis et al., 2010; Abram et al., 2014; Cole et al., 2013; Martinelli et al., 2013; Piolino et al., 2010). Relatedly, episodic memory and episodic future thinking have been found to develop in parallel (Busby & Suddendorf, 2005; Suddendorf & Busby, 2005), and this development seems to progress in conjunction with developmental changes in prefrontal and executive functions (Abram et al., 2014; Atance & Jackson, 2009; Gott & Lah, 2013; Levine, 2004; Picard, Reffuveille, Eustache, & Piolino, 2009). In a recent study, Anderson, Dewhurst and Nash (2012) examined the effect of depleting executive resources on past and future event generation experimentally by employing a dual-task procedure. They found that future thinking was not more affected by dual-task demands than past remembering, suggesting that past and future event generation places equal demands on executive resources. Taken together, these results indicate that episodic memory and future thinking both depend on intact prefrontal/executive functions, although the two constructive processes may rely on somewhat different neural and cognitive substrates.

The suggestion that past and future event construction are critically dependent on prefrontal processes was challenged, however, by a recent study by Kurczek and colleagues (2015) examining past and future event construction in five patients with bilateral medial PFC (mPFC) damage using the modified AI task (Levine et al., 2002). The authors reported that the mPFC patients did not differ from healthy controls in their ability to construct highly detailed episodic past and future events. Instead, the mPFC patients displayed a disruption in self-referential processing, in that they produced fewer self-references during past and future event descriptions than did healthy controls. These results suggest that an intact mPFC is not required to construct highly detailed event
representations regardless of temporal direction, but only to incorporate the self during such event simulations.

The findings reported by Kurczek et al. (2015) are somewhat surprising in light of several studies demonstrating impaired episodic memory with relative sparing of personal semantics in patients with frontal lobe damage (e.g. Della Sala, Laiacona, Spinnler, & Trivelli, 1993; Kopelman, Stanhope, & Kingsley, 1999; Levine, 2004; McKinnon, Svoboda & Levine, 2007; Piolino et al., 2003; Piolino et al., 2007) and neuroimaging findings, that the retrieval of personally relevant, time-specific memories compared with personal semantics shows enhanced medial prefrontal activation (Maguire & Mummery, 1999; Levine et al., 2004). These findings seem to suggest that episodic, but not semantic memory is highly reliant on the integrity of the PFC (McKinnon et al., 2007).

Interestingly, it has been suggested that future events may be constructed by drawing on preserved generalized memory for routinized events or well-established scripts in semantic memory (e.g., Berntsen and Bohn, 2010; D’Argembeau & Mathy, 2011; Rubin, 2013; Szpunar, 2010) and thereby without necessarily relying on episodic memory content. Consistent with the idea that episodic future thinking relies more on schematized knowledge, future events contain fewer sensory details than past events (e.g., Berntsen & Jacobsen, 2008; Berntsen & Bohn, 2010; D’Argembeau & Van der Linden, 2004; 2006; Larsen, 1998) and are rated as both more positive and personally significant (Berntsen & Bohn, 2010; D’Argembeau & Van der Linden, 2004; 2006, Newby-Clark & Ross, 2003).

Suggestive evidence that intact semantic knowledge may be sufficient to imagine future events comes from reports of preserved episodic future thinking in patients with hippocampal amnesia who were free to imagine scenarios of their choice (Squire et al., 2010) and in developmental amnesia (Cooper, Vargha-Khadem, Gadian, & Maguire, 2011; Maguire, Vargha-
Kahdem, & Hassabis, 2010). It has been argued that intact future thinking in such cases may reflect the ability of patients to draw on preserved scripts or generalized knowledge in semantic memory (Cooper et al., 2011; Maguire et al., 2010; Maguire & Hassabis, 2011). In congruence with the notion that semantic memory plays a pivotal role in episodic future thinking, studies of patients with semantic dementia have found that the construction of truly novel events relies critically upon semantic rather than episodic memory (Duval et al., 2012; Irish et al., 2012a; Irish et al., 2012b). Thus, an intriguing possibility is that while PFC damage might impair episodic memory, such deficits will affect future event construction to a lesser extent, when patients are compared with healthy controls, because future thinking to a greater extent draws on schematized and semantic information.

The Present Study

Previous work has demonstrated that frontal/executive processes play a central role in the construction of past and future events. However, the literature is inconclusive as to whether prefrontal damage would impact the construction of past and future events to the same extent, and if not, which of the two temporal directions may show greater impairments, when compared to the performance of healthy controls. While heterogeneity in the lesion profiles and the populations investigated likely explain some of the differences found in prior studies, the divergent findings clearly demonstrate the need for further research to provide insight into the contribution of the prefrontal cortex to past and future mental time travel.

The current study examined the extent to which nine patients with lesions to the PFC could remember past and imagine future autobiographical events. We assessed autobiographical memory and episodic future thinking using an adapted version of the AI scoring procedure (Levine et al., 2002), which has previously been found to be sensitive to impairments in past and future event
construction in healthy older adults (e.g., Addis et al., 2008) and in patient populations (e.g., Race et al., 2011; Rasmussen & Berntsen, 2014). Critically, this scoring method allows for the separation of elements of episodic and semantic autobiographical memory, and makes it possible to compare past and future event constructions directly. In addition, the current study included a series of questions to be rated subjectively regarding the quality of the remembered and imagined events (Rubin, Schrauf, & Greenberg, 2003).

Methods

Participants

Nine patients with focal frontal lesions were recruited from the neurological rehabilitation hospital, Hammel Neurorehabilitation and Research Centre, to which they had been referred for treatment at the time. Nine healthy controls were recruited to match the patient group in terms of age, years of education, gender, handedness and estimated IQ based on performance on the Danish version of the National Adult Reading Test (DART; Dalsgaard, 1998) (Tabel 1). Participants had no prior history of neurological or psychiatric disorder, or substance abuse. There was no clinical evidence of depression among the participants and their scores on the Beck Depression Inventory (BDI-II; Beck, Steer, & Brown, 1996) were within normal range (<10). All participants gave their informed consent to the study after full details had been provided and the procedures were carried out in accordance with guidelines approved by the regional ethics committee.

The PFC patients were selected on the basis that they had damage principally involving cortex anterior to the precentral sulcus. Clinical characteristics as well as neuropsychological tests scores are detailed in Table 2. Structural neuroimaging had been performed with CT or MRI for clinical purposes, and therefore the anatomical delineation of lesions lacked detail. One patient had lesions confined to the right and three to the left cerebral hemisphere, while five patients had lesions
involving the PFC bilaterally. Lesion aetiologies varied and this was not a criterion of inclusion/exclusion in the study. Five patients had lesions due to cerebrovascular accidents, three patients suffered brain contusions and haematomas following closed head injuries, and one patient had damage due to a penetrating head injury. Note that while the patients were selected on the basis of having only frontal pathology, it is possible that especially the patients with closed head injury had undetected lesions in the temporal lobe, as well as diffuse damage. However, excluding these three patients from the analyses did not change the main findings and we therefore chose to include them when reporting the results.

The PFC patients had varying degrees of executive and anterograde memory impairments as assessed by neuropsychological testing (Table 2). In general, patients were at least moderately impaired on one measure of executive dysfunction including phonemic fluency (Jørgensen, 2012), perseverations on the Wisconsin Card Sorting Test (WCST, Nelson, 1976) and set-shifting on the Trail-Making Test (TMT Part B, Reitan, 1985) or on verbal (Verbal Paired Associates and Logical Memory Tests of the Wechsler Memory Scale III (WMS-III, Wechsler, 1997)) or non-verbal (Rey Complex Figure Test (RCFT, Meyers & Meyers, 1995)) episodic memory. However, one patient (P4) showed only mild deficits on phonemic fluency, while another patient (P5) did not show impairments on any of the neuropsychological measures.

**Materials and experimental procedure**

Participants were asked to recall or imagine a series of eight autobiographical events from four different time periods in their past and future. The procedure was adapted from D’Argembeau and Van der Linden (2004) and from Rasmussen and Berntsen (2014). Participants were instructed to retrieve and imagine personally experienced temporally and contextually specific events. In the future condition, participants were further instructed to imagine and describe events that could
reasonably happen in their personal future. To illustrate the requested level of specificity, participants were given an example of a general and specific past and future event. The type of responses participants were expected to give was clearly stated before each cue was given: ‘You are to describe the event with as much detail as possible, as if you were (re)experiencing it: what you do and feel, the circumstances, with whom, where, and how it happens’. A printed text card of the instructions was placed in front of the participants throughout the experimental task to act as a reminder if needed. It was explained that once an event had been described, they would be asked to rate the phenomenal characteristics of that event.

In the past and future condition, participants were presented with cues in the following formats, respectively: ‘Try to remember an event that has happened to you [specified time period]’ and ‘Try to imagine an event that might happen to you [specified time period]’. In each condition, participants were asked to try to retrieve or imagine events (1) one month into the past/future, (2) one year into the past/future, (3) five years into the past/future, and (4) ten years into the past/future. The order in which the past and future condition were completed was counterbalanced across participants. There were no demands as to the content of the events, only that they should appear clear and vivid to the participant. Once the participants indicated that an event had been retrieved or imagined (there were no time limit for retrieving or imagining an event), they were given three minutes to describe the event in as many details as possible. If participants appeared to struggle to bring to mind a specific event, they were given up to two prompts in the format ‘can you think of a specific incident or episode?’ or ‘can you think of any more details related to the episode?’ Prompts were given until a coherent event was produced or until both prompts were used. All event descriptions were digitally recorded to enable later transcriptions and subsequent scoring of responses.
Subjective ratings

Following the description of each event, participants rated the subjective experience of the events using a subset of scales from the Autobiographical Memory Questionnaire (AMQ, Rubin et al., 2003), which has been applied previously in studies of future thinking (e.g., Berntsen & Jacobsen, 2008). The questions addressed the amount and type of subjective p/re-experiencing associated with the events. Table 3 shows the questions as they were formulated for the past condition. The questions for the future condition were the same, except that the wordings were changed in order to refer to future events. All questions were rated on 7-point scales. The labels before each question in Table 3 indicate the labels used in Table 4 and for the results described in the text.

Scoring of content

Consistent with previous work in this area, event descriptions were assessed using a standardized AI scoring procedure (Levine et al., 2002). For each event descriptions, the central event was identified, if more than one event was mentioned, the one containing most details was selected as the central event. The transcriptions were then segmented into informational bits or details (i.e. unique occurrences observations, or thoughts), and these details were classified into two broad subcategories; internal or external. Internal details were those pieces of information that pertained directly to the main event described, that were specific to time and place, and were considered to reflect episodic p/re-experiencing. Internal details were further separated into five mutually exclusive subcategories: time, place, perceptual, thought/emotion, and event details. External details were those details that pertained to extraneous information that did not require recollection of a specific time or place and that were not uniquely specific to the main event. External details were subdivided into four categories: external event details (specific details
external to the main event), semantic information (facts and extended events/script based knowledge), repetitions, and other (meta-cognitive statements, editorializing).

The event descriptions were scored by two trained raters, who were blind to group membership and the hypotheses of the study. The two raters scored all of the event transcriptions independently of one another. The inter-rater agreement for the composite scores was good as measured by intra-class correlations (two-way random effects model; McGraw & Wong, 1996) of .98 and .90 for internal and external details, respectively.

Results

Analytic strategies

Suitability of variables for parametric analyses was determined using Shapiro-Wilk tests. We found only minor violations of normality in two out of eight variables (future internal and external details in the PFC group). Based on the fact that transforming the data did not correct these violations and that ANOVA is considered quite robust to minor violations when group sizes are equal (Field, 2009), we chose to perform repeated-measures ANOVA with Sidak post hoc tests (Field, 2009) to investigate main effects of group (PFC vs. control), details (internal vs. external) and temporal direction (past vs. future) as well as possible interactions. When appropriate, pairwise comparison of mean differences was also performed using nonparametric Mann-Whitney or Wilcoxon signed ranks tests. Since these analyses yielded similar results with only a few marginal differences, we report the results from the parametric analyses.

First, we examine group differences in the number of internal and external details for past versus future events collapsed across the four temporal distances. Second, we report results regarding group differences in the subjectively rated phenomenal characteristics. Finally, nonparametric correlations (Spearman's rho) were conducted in order to explore the potential
relationship between performance on the event construction task and neuropsychological test measures. Statistical analyses were performed using IBM SPSS Statistics 21.0.

**Group differences on internal and external details for past versus future events**

Both PFC patients and controls were able to generate past and future events to most time periods (PFC, $M = 7.78, SD = 0.44$; controls, $M = 8.00, SD = 0.00$ out of a maximum of 8 events). To determine whether PFC patients’ past and future events differed from those of controls, we collapsed participants’ responses across the four time periods (1 month, 1 year, 5 year and 10 years) and compared the mean number of internal and external details, consistent with analytic strategies used in prior research (e.g., Addis et al., 2008; Rasmussen & Berntsen, 2014).

A 2 (Temporal Direction: Past vs. Future) × 2 (Detail: Internal vs. External) × 2 (Group: PFC vs. Control) mixed factorial ANOVA with Temporal Direction and Detail as repeated factors and Group as a between subjects factor (see Figure 1) revealed main effects of both Group, $F(1,16) = 9.74, \eta^2_p = .38, p < .01$, and Detail, $F(1,16) = 18.45, \eta^2_p = .54, p < .001$. Overall, the performances of the PFC patients were poorer than that of the controls, and more internal than external details were produced. The interaction between Group and Detail, $F(1,16) = 7.73, \eta^2_p = .33, p < .05$, was also significant. This interaction reflected, that controls produced more internal details ($M = 36.40; SD = 8.26$) than PFC patients ($M = 16.63; SD = 17.09$), $t(11.54) = 3.13, p < .01$, whereas no differences were found between PFC patients ($M = 11.38; SD = 5.31$) and controls ($M = 11.87; SD = 4.20$) on the amount of external details, $t(16) = 0.22, p = .83$., and that controls produced more internal ($M = 36.40; SD = 8.26$) than external details ($M = 11.88; SD = 4.20$), $t(8) = 7.28, p < .001$, whereas PFC patients produced an equivalent number of internal ($M = 16.63; SD = 17.09$) and external details ($M = 11.38; SD = 5.31$), $t(8) = 0.87, p = .41$. 
A main effect of Temporal Direction was also observed, $F(1,16) = 69.66, \eta^2_p = .81, p < .001$, showing that, overall, participants produced more details in the past than in the future condition. Moreover, a significant Detail and Temporal Direction interaction, $F(1,16) = 27.93, \eta^2_p = .64, p < .001$, reflected that the advantage of the past compared to the future condition was greater for internal ($M = 13.56; SD = 8.99$) than for external details ($M = 2.61; SD = 5.15$), $t(17) = 4.08, p < .01$.

Importantly, the Group × Detail × Temporal Direction interaction was also significant, $F(1,16) = 12.54, \eta^2_p = .44, p < .01$. In order to attain a deeper understanding of this three-way interaction (illustrated by Fig. 1), we conducted two separate follow-up repeated-measures ANOVAs (group x temporal direction), one with internal details and one with external details as the dependent variable. For internal details, the analysis revealed main effects of both Group, $F(1,16) = 9.77, \eta^2_p = .38, p < .01$, and Temporal Direction, $F(1,16) = 71.23, \eta^2_p = .82, p < .001$, reflecting that overall, the PFC patients produced less internal details as compared to controls and that overall more internal details were produced in the past than in the future condition. However, the Group × Temporal Direction interaction was also significant, $F(1,16) = 13.57, \eta^2_p = .46, p < .01$. Here, follow-up post hoc tests showed that although PFC patients produced less internal details than controls to both temporal conditions ($ps < .05$) and both groups produced more internal details in the past than in the future condition ($ps < .05$), this difference was significantly larger for controls ($M = 19.47; SD = 5.37$) than for PFC patients ($M = 7.64; SD = 8.00$), $t(16) = 3.68, p < .01$. In contrast, the result of the ANOVA for external details revealed only a main effect of Temporal Direction, $F(1,16) = 4.73, \eta^2_p = .23, p < .05$, while there were no significant effect of group or interaction.
The results suggest that although PFC patients produced fewer internal details than controls, regardless of temporal direction, this difference was larger in the past condition than in the future condition, due to healthy controls producing more internal details in the past than in the future condition. In other words, the PFC patients did not seem to benefit from events being encoded and stored in memory to the same extent as healthy controls when having to retrieve episodic details.

Profiles of internal detail subcategory are presented in Fig. 2. Significant group differences were found across all detail subcategories (internal event details, time, place, perceptual and thoughts/emotions) in the past condition ($p < .05$). In contrast, there were no significant difference between PFC patients and healthy controls on the amount of event details generated in the future condition ($p = .09$), while patients were impaired on all other internal detail subcategories ($p < .05$).

**Subjective Ratings of Phenomenal Characteristics**

In order to examine whether subjective experience ratings differed between PFC patients and controls, we conducted separate 2 (Group: PFC vs. controls) × 2 (Temporal Direction: past vs. future) mixed-factor ANOVAs for each phenomenal characteristic.

The analyses revealed no main effects of group for any of the variables; that is, PFC patients and healthy controls did not differ on ratings of p/reliving, travel in time, vividness, coherence or valence (see Table 4). Consistent with previous findings, a main effect of temporal direction for valence was observed, reflecting that future events were rated as more emotionally positive than memories for past events, $F(1, 16) = 15.03, \eta^2_p = .48, p < .01$. We did not find effects of temporal direction for any of the other phenomenal characteristics.

The fact that no group differences were found for phenomenal characteristics may suggest that PFC patients inaccurately provided inflated ratings, given the differences observed on the
objective scores. However, it may also be that the AMQ question are less sensitive than the objective measures, and that group differences were not detected due to small sample sizes, numerical differences in the expected direction were observed for ratings of p/reliving (see Table 4).

Correlations between past and future event descriptions and neuropsychological test measures

Nonparametric correlations were performed between internal and external details for past and future events for each group separately. In line with prior findings (e.g. Addis et al., 2008; Gamboz et al., 2010; Rasmussen & Berntsen, 2014), strong correlations between past and future internal details were found for both healthy controls ($r_s = .72, p < .05$) and PFC patients ($r_s = .81, p < .01$). For the control group we also found a significant relationship between past and future external details ($r_s = .92, p < .01$), while we did not find a significant relationship in the PFC group, but still a positive correlation in the expected direction ($r_s = .38, p = .32$). Next, we looked at the relationship between the neuropsychological measures and performance on the memory/future thinking task. For the healthy control group, we only obtained measures of verbal fluency (categorical and phonemic). No significant relationship was found between these measures and number of details (internal or external) in the past condition ($r_s = .00 - .61, ns$). In the future condition we found significant correlations between categorical fluency and the number of future internal details ($r_s = .79, p < .05$), while no other significant correlations were obtained ($r_s = -.29 - .61, ns$). The correlational analyses for the PFC patients are displayed in Table 5. Here, past internal details correlated with Part B of the Trail Making Test, while past external details correlated with Digit Span and immediate recall on the RCFT. No other significant relationships were found between the neuropsychological test measures and performance on the memory/future thinking task. However, these correlations were
not statistically significant when correcting for multiple analyses using a more conservative alpha level of $p < .01$. Due to the small sample sizes these correlational analyses should be interpreted with caution.

**Discussion**

Reviewing the literature revealed discrepancies in prior findings concerning prefrontal contributions to past and future mental time travel. While some studies suggest that PFC damage specifically reduces the ability to imagine future events, another part of the literature has found symmetrical impairments across both temporal directions, and a third line of work raises the possibility that PFC damage would affect episodic remembering more than it would affect future imagining. The different findings clearly underscore the need for more systematic studies on PFC involvement in the construction of past and future events.

In the present study, we assessed past and future event construction in PFC patients and healthy controls using a within-subjects design and the same measurements for both temporal directions. Our findings are consistent with the notion that PFC damage affects episodic remembering more than it affects future imagining, in that, although the PFC patients produced fewer internal details than controls regardless of temporal direction, this difference was larger in the past condition than in the future condition. This result reflected that while healthy controls produced more internal details for the past temporal direction as compared with the future temporal direction, PFC patients did not show this effect to the same extent.

This result seems in contrast with a previous study by Berryhill et al. (2010), who found PFC patients to be specifically impaired on the ability to imagine future events, and findings from Kurczek et al. (2015), showing that mPFC patients did not differ from healthy controls in their ability to construct highly detailed episodic past and future events. A number of factors may explain
the divergence with the present study including the use of different methodologies. Most importantly, our patients had less restricted PFC damage, and all presented varying degrees of executive and anterograde memory impairments. In contrast, the PFC patients selected in both the Berryhill et al (2010) and Kurczek et al. (2015) studies were all high functioning and had neuropsychological scores within the normal range.

The presence of executive impairments may play a part in the PFC patients’ deficits in past and future event construction. This suggestion is in line with prevailing models of autobiographical memory, whereby the retrieval of specific past event relies on strategic, elaborative, and evaluative processes mediated by the PFC (Baddeley & Wilson, 1986; Burgess & Schallice, 1996; Cabeza & St Jacques, 2007; Conway & Pleydell-Pearce, 2000; Moscovitch & Melo, 1997). Indeed, in a recent study, examining past and future event generation in a group of TBI patients, Coste et al. (2015) reported a similar pattern of results as in the present study, the effect of group on event information being higher for the past than for the future condition. Similar to our findings, this effect was driven by a difference in performances across temporal direction in the healthy control group, which was not mirrored in the patients group. However, in Coste et al., (2015), this effect was present for both episodic and semantic information in contrast to the present findings. Interestingly, Coste et al. also explored the cognitive mechanisms underlying TBI patients’ deficits and found that past event construction was linked to executive dysfunction specifically related to impaired updating, whereas future event simulation was predicted by working memory binding and semantic impairments, suggesting a greater reliance on semantic information when imagining the future than remembering the past.

In the present study, the PFC patients were particularly impaired in generating episodic details, whereas the semantic aspects of past and future event construction were relatively well-
persevered. These findings accord with previous reports that frontal lobe lesions specifically impair episodic autobiographical memory (Conway & Fthenaki, 2000; Della Sala et al., 1993; Kopelman et al., 1999; Kopelman & Kapur, 2001; Levine et al., 1998; Piolino et al., 2007) and suggest that episodic, but not semantic, autobiographical memory, is highly reliant on the PFC. This is also consistent with studies showing that patients with prefrontal damage often show diminished memory for the context surrounding an event, such as the source and recency of remembered information (e.g. Johnson, Hashtroudi, & Lindsay, 1993; Schacter, Harbluk & McLachlan, 1984; Shimamura, Janowsky, & Squire, 1990; Simons et al., 2002) and are impaired on remember/remember judgments and episodic memory tasks (e.g. Duarte, Ranganath, & Knight, 2005; Wheeler, Stuss & Tulving, 1995; Wheeler & Stuss, 2003), all of which are considered an index of episodic remembering (Wheeler et al., 1997).

The distinction between episodic versus semantic information may also explain why the difference between PFC patients and healthy controls was smaller in the future condition than in the past condition. There is a growing agreement that imagining the future relies more on semantic and schema-based knowledge than remembering the past (Abraham & Bubic, 2015; Anderson & Dewhurst, 2009; Berntsen & Bohn, 2010; D’Argembeau & Mathy, 2011; Irish & Piguet, 2013; Klein, 2013; Rubin, 2013; Szpunar, Spreng, & Schacter, 2014). Evidence that semantic memory is critically involved in the construction of future events comes from patients with semantic dementia whose loss of semantic knowledge severely affects the ability to construct future events, despite their relatively intact retrieval of recent episodic events (Irish et al., 2012a; Irish et al., 2012b). Moreover, several studies have provided suggestive evidence that preserved semantic memory may be sufficient to support episodic future thinking in patients with hippocampal amnesia (Cooper et al., 2011; Hurley, Maguire, & Vargha-Khadem, 2011; Maguire et al., 2010). For instance, Cooper et
al. (2011) found that children with early hippocampal damage and developmental amnesia were able to successfully imagine novel events, and speculated that early damage may have allowed these children to rely on preserved semantic information during event construction. Squire et al. (2010) reported intact future thinking in a group of patients with hippocampal amnesia using the AI scoring procedure (Levine et al., 2002). However, in this study the future thinking task differed from those employed in other studies, by the tasks being less constrained, in that the patients were free to imagine past and future events of their choice in response to cue-words (the events did not have to directly relate to the cue-words). These patients not only displayed intact future thinking, but were also less impaired on the memory task, compared with previous findings, indicating that placing less constraints on the task may have allowed patients to draw more on generic knowledge (Maguire et al., 2010), which may have benefitted episodic future thinking to a higher degree than episodic memory. In line with this suggestion, Race et al. (2011) found that amnesic patients produced a greater number of details, when imagining more familiar and scripted events than imagining less familiar events.

The task used in the present study has several similarities to the one employed by Squire et al. (2010), in that there were no demands as to the content of the events, only that they should be plausible and specific. This raises the possibility that the greater effect of group on episodic details for the past than for the future condition reflected that the future thinking task, to a greater extent than the episodic memory task, could be solved by relying on semantic representations.

However, the picture is far from clear and unequivocal; patients with prefrontal lesions have been shown to perform at near-normal levels during more structured tasks. For instance, several studies have reported that PFC patients are more impaired on free recall than cued recall tasks (Dimitrov et al., 1999; Stuss et al., 1994) and that recall can be improved by externally provided
strategies at retrieval (Gershberg & Shimamura, 1995; Kopelman & Stanhope, 1998). Thus, it is possible that using more specific probes than the ones used here would have benefitted PFC patients’ performance.

**Phenomenological experience**

Contrary to the objective measures of episodic details (Levine et al., 2002), there were no significant differences between PFC patients and controls on the subjective ratings, derived from the AMQ (Rubin et al., 2003). The PFC patients did not report a diminished sense of re-/pre-experience or of travelling in time, during remembering and imagining. Nor did they report that their event representations were less vivid or coherent than the control participants. Although these null findings in part may be due to the lack of power because of the small sample size, our results are in line with previous studies reporting a striking dissociation between subjective and objective measures in this particular patient population. For instance, Duarte et al. (2005) found that while the subjective experience of recollection (remember judgments) was not reduced in patients with left lateral PFC lesions, objective recollection (source memory accuracy) was. Similarly, in their study, Berryhill et al. (2010) reported that the PFC patients overestimated the quality of their imagined events compared with their actual performance on the constructive experience task, indicating a lack of insight into own impairments commonly associated with PFC damage. Duarte et al. (2005) suggested that a possible explanation for the observed dissociation between objective and subjective measures in PFC patients is that the two processes are dependent on different PFC subregions. Indeed, one study has found that whereas subjective reports of remembering in patients with dorsolateral PFC lesions were intact, patients with frontopolar lesions gave fewer remember responses to recognized items than did healthy controls (Wheeler & Stuss, 2003).

**Limitations**
The present study has several limitations, which need to be taken into account when interpreting the results. Firstly, the small sample sizes mean that conclusions should be drawn only tentatively. In particular, any null findings should be interpreted with caution, it therefore may be important to focus on the reported effect sizes rather than on significance levels. A second limitation is the heterogeneity and lack of anatomical detail of the PFC patients’ lesions, which prevent any conclusions as to the effect of lesions to different PFC subregions on past and future event construction. Finally, we did not interview relatives or close others, and we were therefore unable to assess whether memories and future imaginings were more accurate or plausible among controls than PFC patients. Frontal lobe damage, in particular to the ventromedial PFC, has been associated with memory distortions and confabulation (Burgess & Schallice, 1996; Gilboa & Moscovitch, 2002).

Conclusion

In conclusion, this study examined autobiographical memory and episodic future thinking in patients with PFC lesion using a within-subjects design and the same tasks and scoring methods for both temporal directions. We demonstrated that damage to the PFC can cause impairments in the ability to reconstruct experienced past events and to construct future personal events, PFC patients producing fewer episodic details than controls regardless of temporal direction. Importantly, this group difference was larger in the past condition than in the future condition. This result reflected that while the PFC patients did not produce more episodic than semantic information for any of the temporal directions, the controls produced more episodic details for both temporal directions and even more so for the past relative to the future condition, causing a larger group difference in the past condition. Our results suggest that PFC processes are critical for strategic processes involved in the retrieval of episodic event specific details, and the differential effect of group on temporal
direction may reflect that episodic future thinking relies more on schemata or scripts and other forms of semantic knowledge and less so on episodic memory. An important question for future research is to determine the contribution of specific PFC regions to cognitive processes involved in past and future mental time travel. Medial prefrontal regions have been linked to self-referential aspects of past and future event construction (Abraham et al., 2008; Kurczek et al., 2015), while the ventrolateral and dorsal PFC have been linked with strategic processes involved in the selection and organization of information during episodic retrieval (Badre & Wagner, 2007; Blumenfeld & Ranganath, 2007). Future work should aim at providing a finer-grained understanding of the possible contributions of these regions to event construction.
References


Table 1. Demographics of PFC patients and healthy controls

<table>
<thead>
<tr>
<th></th>
<th>PFC patients (n=9)</th>
<th>Healthy controls (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male/female)</td>
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<td>6/3</td>
</tr>
<tr>
<td>Handedness (right/left)</td>
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<td>9/0</td>
</tr>
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<td>Age in years</td>
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<td>43.44 (15.88)</td>
</tr>
<tr>
<td></td>
<td>(18-64)</td>
<td>(20-65)</td>
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<tr>
<td>Education in years</td>
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<td>13.11 (1.96)</td>
</tr>
<tr>
<td></td>
<td>(11-16)</td>
<td>(10-16)</td>
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<td>31.89 (7.66)</td>
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<tr>
<td></td>
<td>(20-36)</td>
<td>(20-45)</td>
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<tr>
<td>Time since brain insult in months</td>
<td>2.67 (0.87)</td>
<td>(2-4)</td>
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Note: Numbers in parentheses to the right of the mean are SDs; numbers in parentheses below the mean and SD are ranges.
Table 2. Clinical characteristics and neuropsychological performance of patient with PFC damage.

<table>
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<tr>
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<th>P1</th>
<th>P2</th>
<th>P3</th>
<th>P4</th>
<th>P5</th>
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<th>P7</th>
<th>P8</th>
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<td>H</td>
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<td>CHI</td>
<td>H</td>
<td>CHI</td>
<td>PHI</td>
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<td>L-F</td>
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<td>LR-F</td>
<td>LR-F</td>
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<td>Phonemic (Z)</td>
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<td>-1.07</td>
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<td>Immediate (Z)</td>
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<td>-0.91</td>
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<td>Delayed (Z)</td>
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<td>-0.83</td>
<td>0.68</td>
<td>-1.44</td>
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</tbody>
</table>

*Note. Aetiology: I = infarct, H = hemorrhage, CHI = Closed Head Injury, PHI = Penetrating Head Injury; Lesion site: F = frontal; Lesion side: L = left, R = right. The normative data for the tests were taken from the original manuals or from the sources referenced below: Fluency, Verbal Fluency Task; RCFT, Rey’s Complex Figure Test; Stroop, The stroop color and word test; TMT, Trail Making Test; WAIS, Wechsler Adult Intelligence Scale IV; WCST, Wisconsin Card Sorting Test; WMS, Wechsler Memory Scale III; LM1, logical memory immediate; LM2, logical memory delayed; VPA1, verbal paired associates immediate; VPA2, verbal paired associates delayed; SS, scaled score (cutoff for abnormal, ≤ 4); Z, Z score (cutoff for abnormal, ≤ -2); T, T-score (cutoff for abnormal < 30). Jørgensen (2012); Gade & Mortensen (1994).
Table 3. Questions and answering options asked for the events in the study shown for the past condition (translated from Danish)

<table>
<thead>
<tr>
<th>Variable and Question</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>P/reliving:</td>
<td>While remembering the event, it feels as though I relive it in my mind. (1 = not at all, 7 = to a very high degree)</td>
</tr>
<tr>
<td>Travel in time:</td>
<td>The memory made me feel as if I traveled back in time to the actual situation. (1 = not at all, 7 = to a very high degree)</td>
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<tr>
<td>Vividness:</td>
<td>As I recall the event, it appears vivid and clear (1 = not at all, 7 = to a very high degree)</td>
</tr>
<tr>
<td>Coherence:</td>
<td>As I recall the event, it seems to come to me as a coherent story (as opposed to incoherent or fragmented). (1 = not at all, 7 = to a very high degree)</td>
</tr>
<tr>
<td>Valence:</td>
<td>The feelings I experience, as I recall/imagine the event are (-3 = extremely negative, 3 = extremely positive)</td>
</tr>
</tbody>
</table>
Table 4. Mean ratings (and standard deviations) as a function of Group (PFC and controls) and Temporal Direction (past and future).

<table>
<thead>
<tr>
<th></th>
<th>PFC patients</th>
<th>Controls</th>
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<tr>
<td></td>
<td>Past events</td>
<td>Future events</td>
</tr>
<tr>
<td>P/reliving</td>
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<td>4.89 (1.33)</td>
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<td>Vividness</td>
<td>5.25 (1.76)</td>
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<tr>
<td>Coherence</td>
<td>4.94 (1.80)</td>
<td>4.39 (1.78)</td>
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<tr>
<td>Valence</td>
<td>0.31 (0.96)</td>
<td>1.83 (1.10)</td>
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Table 5. Spearman’s rho correlations between neuropsychological test measures and performance on the memory/future thinking task in the PFC group.

<table>
<thead>
<tr>
<th>Test variable</th>
<th>Past internal</th>
<th>Past external</th>
<th>Future internal</th>
<th>Future external</th>
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<td><strong>Working memory/ executive function</strong></td>
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<td>.70*</td>
<td>.04</td>
<td>.44</td>
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<tr>
<td>Digit span (backward)</td>
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<td>.25</td>
<td>.37</td>
<td>.33</td>
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<td>-.05</td>
<td>-.03</td>
<td>.36</td>
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<tr>
<td>TMT Part B</td>
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<td>-.52</td>
<td>.22</td>
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<td>Verbal fluency (phonemic)</td>
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<td>.53</td>
<td>.08</td>
<td>.13</td>
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</table>

*p < .05
Figure Caption

Figure 1. Mean number of internal and external details generated for past and future events by PFC patients and healthy controls. Error bars represent standard errors of the mean.

Figure 2. Profiles of internal detail subcategory for past and future events in PFC patients and healthy controls. Error bars represent standard errors of the mean.
Fig. 1.
Fig. 2.