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Exploring episodic and semantic contributions to past and future thinking performance in Korsakoff's syndrome

Julie Janssen[1,2] · **Erik Oudman**[1,2] · **Muireann Irish**[3] · **Albert Postma**[1,2]

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Abstract
Korsakoff's syndrome (KS) is a neuropsychiatric disorder characterized by severe declarative memory disruption. While episodic memory deficits and confabulation are well documented, it remains unclear to what extent semantic memory is compromised in this syndrome. Moreover, how such impairments relate to the capacity for future-oriented thinking remains unknown. Here, we sought to determine the extent to which episodic and semantic forms of past and future thinking are impacted in KS and the interrelationship between different classes of memory in this syndrome. Twenty patients with KS and 17 matched healthy controls took part in this study. We included well-established indices of past and future thinking capacity, enabling us to compare episodic (event-based) versus semantic (nonpersonal knowledge) across past and future conditions. We also included a novel event generation task to probe implausible event simulation (i.e., spending a day on the moon). Our findings revealed marked impairments in KS across all forms of past and future thinking, as well as the generation of episodic details on the implausible event simulation task. Correlation analyses revealed significant associations between implausible event construction and episodic and semantic future thinking in KS; however, no significant associations were found between future thinking performance and confabulation. This study is the first, to our knowledge, to reveal striking impairments in the capacity for past and future thinking across episodic and semantic domains in KS. Our findings resonate with current theoretical perspectives in which the lines between episodic and semantic memory systems are viewed as increasingly blurred.

Keywords Imagination · Prospection · Episodic memory · Semantic memory · Dementia · Confabulation

Tulving's influential declarative memory theory proposes that human memory can be divided into at least two subtypes: (i) Episodic memory, referring to memory for personal events embedded in a spatial and temporal context, and (ii) semantic memory, which encompasses a repository of factual and meaning-related knowledge that is not tied to a single event (Tulving, 1972). While Tulving's later writings suggested that episodic and semantic elements likely interact in the service of memory (Renoult & Rugg, 2020), the categorical distinction between these memory systems has largely persisted. In the past decade, however, there has been a shift towards exploring interdependencies between these two systems (Greenberg & Verfaellie, 2010; Irish & Piguet, 2013), moving away from a strict dichotomy (Renoult et al., 2019). While early lesion studies demonstrated a double dissociation between episodic and semantic memory in patients with amnesia (Klein et al., 2002), the advent of sophisticated brain imaging techniques has uncovered considerable overlap between the neural correlates of episodic and semantic forms of memory (Burianová et al., 2010; Rugg & Vilberg, 2013). Use of fine-grained paradigms to probe episodic memory in detail has further demonstrated that the retrieval of past events invariably draws on nonepisodic elements (Strikwerda-Brown, Mothakunnel, et al., 2019b) leading to the proposal that semantic knowledge underlies most, if not all, forms of episodic retrieval (Irish & Piguet, 2013). This resonates with earlier theoretical positions which held that semantic memory is the accumulation of episodic memories

✉ Albert Postma
a.postma@uu.nl

1 Experimental Psychology, Helmholtz Institute, Utrecht University, Utrecht, The Netherlands

2 Korsakoff Center Slingedael, Rotterdam, The Netherlands

3 School of Psychology and Brain and Mind Centre, The University of Sydney, Sydney, Australia

(Squire, 2004), suggesting considerable interdependence between the two systems.

Interest in the potential interactions between episodic and semantic memory has been potentiated by research regarding the cognitive and neural mechanisms of so-called future thinking. Future thinking is the ability to preexperience an event while projecting oneself into that future event, recognizing your own limitations and being able to imagine a noncurrent state that affects you in the future (Atance & O'Neill, 2001). The adaptive value of prospection is now widely established, enabling humans to engage in emotion regulation, affective forecasting, intention formation, planning, and decision-making (Bulley & Irish, 2018; Schacter et al., 2017). Future-oriented cognition can be regarded as a form of self-projection and likely relates to other complex forms of cognition that draw upon mental simulation, including theory of mind, moral reasoning, and prosocial behavior (Buckner & Carroll, 2007; Irish, Piguet, & Hodges, 2012).

Mounting evidence points to a number of shared neurocognitive processes in supporting memory for the past and future-oriented simulation (Schacter et al., 2012). For example, clinical populations characterized by episodic memory impairments, such as temporal lobe epilepsy, Alzheimer's disease, and mild cognitive impairment, display parallel impairments across past and future temporal contexts (Addis et al., 2009; Gamboz et al., 2010; Lechowicz et al., 2016), suggesting disruption of a common core mechanism. Similarly, hippocampal amnesic patients display profound impairments in simulating possible events in the future (Hassabis et al., 2007; Race et al., 2011). More recent findings, however, suggest that an intact episodic memory store may not be entirely sufficient for future thinking. For example, patients with semantic dementia appear unable to envisage their future self, despite retaining an intact memory for their recent sense of self (Duval et al., 2012). Similarly, Irish and colleagues demonstrated an asymmetric impairment in semantic dementia, with impoverished future thinking in the context of relatively intact recent episodic memory (Irish, Addis, et al., 2012a, 2012b). These findings are complemented by observations from developmental amnesics, in whom residual capacity for scene construction has been suggested to rely, in part, upon relatively preserved semantic memory (Hurley et al., 2011). Collectively, these studies suggest that the complex process of imagining the future depends on the interaction between episodic and semantic processes, whereby semantic memory provides the essential scaffold for the simulation (Irish, 2016; Irish & Piguet, 2013), into which contextual details can be bound (Addis, 2018).

Building on these findings, the present study aimed to further investigate the specific associations between episodic and semantic memory and the capacity for future thinking, in a novel group of neurological patients. Korsakoff's syndrome (KS) is a neuropsychiatric disorder caused by a thiamine (vitamin B_1) deficiency that is often the result of chronic alcohol abuse. KS patients suffer profound retrograde amnesia that extends back over decades (Postma et al., 2006; Race & Verfaellie, 2012). The contextual hypothesis states that the episodic memory deficits found in KS include explicit processing of contextual information and target–context binding (Kessels & Kopelman, 2012). Because of their profound contextual memory deficits, KS patients are typically unable to encode or retrieve episodic information (Kessels et al., 2000).

Conversely, the status of semantic memory in KS remains unclear, with mixed findings reported in the literature. An early study found evidence for intact lexical semantic memory (i.e., the relationship between meaning of words), while conceptual semantic memory (i.e., a combination of features leading to a concept) was impaired relative to healthy controls (Cermak et al., 1978). Later studies exploring performance on tests of cognitive estimation across different dimensions (e.g., size, weight, time) suggested milder deficits in KS relative to an Alzheimer's disease group (Brand et al., 2003), although the task used in these studies was not necessarily a pure measure of semantic processing. On tasks which directly index conceptual knowledge for public facts and general knowledge, KS performance is markedly compromised relative to controls (Fama et al., 2012; Race & Verfaellie, 2012).

To date, only one study to our knowledge has explored the capacity for future thinking in KS. El Haj et al. (2019) asked KS patients to recall two past events and to envisage two possible future events, and reported a significant reduction in event specificity in KS relative to controls, irrespective of temporal condition. This parallel impairment in event specificity was interpreted as reflecting difficulties in extracting and recombining contextual information from past experiences into novel representations of events that may happen in the future. Notably, however, no formal assessment of the level of contextual richness of past or future events was provided. The authors further suggested that a central feature of the KS memory impairment, namely confabulations, might be related to alterations in future thinking in this syndrome (El Haj et al., 2019), although this relationship was not tested. Confabulations are fabricated, or distorted memories about oneself or the world (Borsutzky et al., 2008; Robins, 2019), and could potentially give rise to disordered forms of future thinking, although the relationship between future thinking and confabulations is not clear.

Given the dearth of research on future thinking in KS, the aim of the present study was to chart the capacity for episodic *and* semantic forms of thinking across past and future temporal contexts. We predicted that, relative to controls, KS patients would show marked impairments in the level of contextual detail generated during episodic past and future thinking, while impairments on the semantic measures would be less pronounced. In addition, we included an atemporal condition in which participants were required to mentally construct a novel scenario for which they could not possibly have any direct personal experience (i.e., "imagine spending a day on the moon"; Irish, Addis, et al., 2012a). As such, performance on this task should draw primarily upon semantic knowledge. As a secondary exploratory aim, we sought to examine potential associations between the propensity to confabulate and future thinking performance in KS.

Methods

Participants

Twenty patients diagnosed with KS participated in this study, all of whom were inpatients of the Korsakoff Centre, 'Slingedael' in Rotterdam, the Netherlands. All patients were in the chronic stage of the disorder at the time of testing, and fulfilled the American Psychiatric Association's (2013) *DSM-5* criteria for the Alcohol-induced Major Neurocognitive Disorder, Amnestic Confabulatory type (code: 291.1), and the characteristics of KS described by Kopelman (2002). All patients had been sober for more than 6 months and required intensive sheltered living due to the severity of their amnesia. Other lifetime exclusion criteria were illiteracy, presence of additional neurological disorders (traumatic brain injury, epilepsy, stroke, or brain tumor), or acute psychiatric conditions (psychosis, major depression, etc.). Twenty control participants matched for age and educational level also participated in this study, recruited through acquaintances. Two control participants were excluded because of low MoCA scores (21 and 23) that could reflect mild cognitive impairment. One further control participant was excluded because of highly unusual responses on the moon task, which suggested that his interpretation of task instructions was inaccurate (e.g., "The moon is more of the same reality than what we now live our lives in"). The research was conducted according to the Declaration of Helsinki, and written informed consent was obtained for all participants. Ethics approval for the study was granted by the faculty review board of Utrecht University.

Background variables

General cognitive functioning in all participants was measured with the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005). The maximum possible score is 30 points, with a score <26 indicative of cognitive decline. One point was added for persons with the Dutch educational Level 4 or lower (Nasreddine et al., 2005). Additional test results were available for the KS patients on the following tasks: Trail Making Test (TMT), Rey Auditory Verbal Learning Task (RAVLT), and the Zoo Map Test from the Behavioral Assessment of the Dysexecutive Syndrome (BADS). These scores were collated from the clinic's archives or from separate empirical studies that had been completed either before or after the current study. These test scores were not available for controls.

Confabulations were measured using the Nijmegen-Venray Confabulation List-20 (NVCL-20; Rensen et al., 2015), a standardized questionnaire routinely used to assess the propensity for confabulation in KS. Twenty questions were completed by the care staff in the Slingedael Centre, who had regular patient contact. An example question is, "*Does the patient say they have any appointments (with family or a doctor) when they don't?*" Answers are provided on a Likert scale from 1 (*Never*) to 5 (*Always*), leading to a possible score from 20–100. A score >20 is indicative of some form of confabulation.

General test procedure

Participants provided demographic details regarding their age, sex, and educational level. Thereafter, all participants completed the Montreal Cognitive Assessment (MoCA) as a cognitive screening instrument. The experimental tasks were randomly administered according to two possible orders: Order 1: semantic past and future thinking task, episodic past and future thinking task, and novel event generation task last; or Order 2: episodic past and future thinking, novel event generation task, and the semantic past and future thinking task last. These testing schedules ensured that task order was counterbalanced across participants. All responses were recorded digitally for subsequent transcription and scoring. The entire test session was completed within approximately 18 minutes (mean time = 17.4 minutes).

Past and future thinking tasks

Episodic past and future thinking was assessed using a past and future task previously applied in dementia syndromes by Irish, Addis, et al. (2012a), based on the past–future task described by Addis et al. (2008). Participants were instructed to remember a specific event in their lives from the past year, and to imagine a possible personal event that could happen within the next year. There were three trials for each temporal condition (past and future), leading to a total of six events generated. Cue words were provided to assist participants with event generation and were presented on a computer screen along with a corresponding image (*apple, baby, car, oven, toy, wine*). The six cues were randomly assigned to the past or future condition, with past and future trials presented in a random order to participants. Participants were instructed to remember past events in as much detail as possible, and to imagine future events that were plausible relative to their own goals and personal experiences. Importantly, future events were required to be novel, that is they should not have previously occurred in the past. To reduce possible working memory demands a short version of the instructions was presented prior to each experimental trial. General probing questions from the Autobiographical Interview (Levine et al., 2002) were used to encourage participants to generate as much detail as possible (e.g., "Can you tell me more about that? Are there any other details that come to mind?").

Semantic past and future thinking was assessed using a Dutch version of the "Known" (semantic) subscale from the Memory and Temporal Experience questionnaire (Klein et al., 2002). This questionnaire consists of seven questions regarding nonpersonal (i.e., public/semantic) events that have occurred over the past 10 years and seven matched questions regarding the possible occurrence of the same nonpersonal events within the next 10 years. For example, for the past condition, "*Can you tell me what you think were some of the most important political events of the past 10 years*?" is complemented by "*Can you tell me what you think will be some of the most important political issues in the next 10 years*?" for the future condition. To reduce cognitive demands on the KS patients, all "past" items were completed before moving to the "future" condition (as per Klein et al., 2002).

Semantic responses were scored by J.J. in line with the original scoring procedure whereby responses were required to be plausible in the context of past and current world events. Briefly, zero points were given when the participants were not able to provide an answer or gave implausible or inconsistent answers relative to current public events; one point was given for the provision of a plausible and meaningful response that was consistent with current and past world events, and two points were given for two or more correct answers. The maximum score for this task therefore was 14 points for past (i.e., 7 questions $\times$ 2 points max) and 14 points for future (i.e., 7 questions $\times$ 2 points max) conditions.

Novel event generation was assessed using the "moon task," based on Irish, Addis, et al. (2012a), which requires participants to imagine and describe an implausible scenario that they could not have previously experienced (i.e., landing on the moon). Participants were prompted to envisage and describe the scene in as much detail as possible, and the same general probing questions were used as in the episodic past and future thinking task. No picture cues were provided, and there was no time limit imposed.

Scoring procedure for event narratives

All interviews were transcribed by the experimenter (J.J.). The event narratives generated on the episodic past and future thinking task and the moon task were scored in line with the Autobiographical Interview protocol (for full details, see Levine et al., 2002). Briefly, narratives were segmented into information units, which were subsequently classified as internal or external. Internal details are purported to reflect episodic content and relate directly to the main episode, located within a specific spatiotemporal context. Internal details were further subdivided into event, time, place, perceptual, and emotion/thoughts details. In contrast, external details consisted of nonepisodic tangential details, repetitions, semantic facts, or metacognitive statements (see also Strikwerda-Brown, Mothakunnel, et al., 2019b). Where participants were unable to generate any event or provided "empty" responses despite prompting (e.g., "I don't know" or "Nothing"), a score of zero was assigned. All scoring was performed by the experimenter (J.J.). An independent rater, blind to diagnosis and study hypotheses, co-scored all transcripts. Interrater reliability was established using the intraclass correlation coefficient (absolute agreement) and was high across all temporal conditions (past, $r = .9$, $p < .001$; future, $r = .85$, $p < .001$; moon, $r = .8$, $p < .001$). The scores reported in this paper are the means of the scores given by the experimenter and by the independent observer.

Statistical analyses

Data were analyzed using SPSS Version 26. Prior to analyses, data were screened by visual inspection using boxplots and the Shapiro–Wilk test for any major violations of normality, linearity, or outliers. None of the patients or controls were excluded based on these analyses. Multivariate analyses of variance (ANOVAs) with Sidak post hoc tests were conducted to explore group differences (KS, controls) in terms of age, educational level, and MoCA score. Chi-square tests were used to explore group differences in terms of sex distribution.

We started with a $2 \times 2 \times 2$ mixed-model ANOVA to explore main and interaction effects of group (KS, controls), condition (past, future), and type of detail (internal, external). Next, we looked at performance for internal and external details using two separate 2×2 models exploring main effects of group (KS, controls) and condition (past, future), as well as relevant interactions. For the semantic task, a 2×2 mixed-model ANOVA was run to explore main effects of group (KS, controls) and condition (past, future). For the novel event generation task (the moon task), a 2×2 mixed-model ANOVA was run to explore main effects of group (KS, controls) and detail type (internal, external). This was followed by separate analyses for internal and external details. For all models, effect sizes are denoted by η^2. Pearson *r* correlations were run to explore associations between the main outcomes on the experimental tasks and relevant clinical and cognitive variables.

Results

Demographics

Table 1 shows a summary of demographic and clinical variables for study participants ($n = 37$). Groups did not differ significantly for age ($p = .504$), sex ($p = .134$), or level of education ($p = .176$). As expected, KS patients scored significantly lower on the MoCA relative to controls ($p < .001$). Informant responses provided by the primary caretakers on the NVCL-20 indicated that 17 of the 20 Korsakoff patients engaged in confabulations (scores ranging from 25 to 64).

Table 2 Raw performance scores for study participants across the past and future thinking tests

	Korsakoff syndrome (*n* = 20)	Healthy controls (*n* = 17)
Episodic past–future		
Episodic past internal	4.4 (2.9)	5.3 (1.6)
Episodic past external	2.9 (2.2)	3.6 (2.4)
Episodic future internal	2.7 (1.7)	4.5 (1.9)
Episodic future external	2.7 (2.6)	3.3 (2.4)
Novel event—moon		
Moon internal	4.8 (2.5)	6.9 (2.6)
Moon external	3.6 (4.1)	3.1 (2.2)
Semantic past–future		
Semantic past	6.9 (3.1)	12.3 (1.9)
Semantic future	8.5 (3.6)	11.5 (1.8)

Means with standard deviation in parentheses

Table 1 Demographic characteristics for study sample (mean with standard deviation in parentheses)[a]

	Healthy controls (*n* = 17)	Korsakoff's syndrome (*n* = 20)	Group difference
Sex	6:11 (m/f)	12:8 (m/f)	n/s
Age [years]	63.1 (8.7)	64.9 (7.3)	n/s
Level of education[b]	4.8 (1.5)	4.2 (1.3)	n/s
NVCL-20[c] [100]	n/a	38.8 (13.3)	n/a
MoCA [d] [30]	26.8 (2.0)	20.3 (2.7)	***
TMT-A [e] [*T*-value]		37.6 (13.8)	
TMT-B [f] [*T*-value]		37.6 (12.7)	
RAVLT Immediate [g]	[*T*-Value]	27.4 (9.4)	
RAVLT Delayed [h]	[*T*-Value]	22.8 (11.0)	
Zoo Map Test [i](Profile)		1.1 (1.0)	

[a]Unit of measurement and/or maximum test score provided in square brackets where appropriate.

[b]Educational level was classified according to seven categories: 1 = less than primary school (1–5 years of education); 2 = primary school (6 years of education); 3 = prolonged primary school (7–8 years of education); 4 = lower secondary school (7–9 years of education); 5 = secondary school (7–11 years); 6 = higher secondary school and/or university bachelor' sdegree (7–16 years of education); 7 = university master's degree or PhD (17–20 years of education; Verhage, 1964).

[c]Nijmegen-Venray Confabulation List-20 total score, whereby higher scores reflect greater propensity for confabulation. [d]Montreal Cognitive Assessment (MoCA) total score, whereby higher scores reflect better cognitive functioning.

[e]Trail Making Test–A, *T*-value, whereby higher scores reflect better visuomotor attention (Schmand, Houx, & de Koning, 2012).

[f]Trail Making Test–B, *T*-value, whereby higher scores reflect better divided attention (Schmand et al., 2012).

[g]Rey Auditory Verbal Learning Test immediate recall, *T*-value, whereby higher scores reflect better memory encoding (Schmand et al., 2012).

[h]Rey Auditory Verbal Learning Test delayed recall, *T*-value, whereby higher scores reflect better memory retention and retrieval (Schmand et al., 2012).

[i]Zoo Map Test of the BADS, profile score.

Episodic past and future thinking

Overall performance

A 2 × 2 × 2 mixed-model ANOVA was used to explore main effects of group (KS, controls), condition (past, future) and detail type (internal, external) as well as relevant interactions on the episodic task (see Table 2). A significant main effect of condition signaled that more details were generated for past relative to future thinking, $F(1, 35) = 6.81$, $p = .013$, $\eta^2 = .16$. Importantly, the main group effect was not significant, $F(1, 35) = 3.03$, $p = .090$, $\eta^2 = .08$, suggesting comparable overall performance. There was a significant effect of detail type, $F(1, 35) = 10.86$, $p = .002$, $\eta^2 = .24$], suggesting overall more internal details were provided relative to external details, irrespective of group or condition. The condition by detail type interaction was significant, $F(1, 35) = 5.73$, $p = .022$, $\eta^2 = .14$, indicating greater provision of internal and external details in the past relative to the future condition. None of the other interaction effects was significant.

Internal details on the episodic task

A separate 2 × 2 mixed-model ANOVA was used to explore main effects of group (KS, controls) and condition (past, future) for internal details on the episodic task (see Table 2). The main effect of group was significant, $F(1, 35) = 5.23$, $p = .03$, $\eta^2 = .13$, indicating that control participants provided significantly more internal details than KS in both the past and future conditions. A significant main effect of condition was also found, $F(1, 35) = 10.57$, $p = .003$, $\eta^2 = .23$, reflecting the provision of fewer internal details in the future compared with the past condition, irrespective of group. The Group × Condition interaction was not significant, $F(1, 35) = 0.99$, $p = .33$, $\eta^2 = .03$.

External details on the episodic task

The 2 × 2 mixed-model ANOVA revealed no significant main effect of group, $F(1, 35) = 0.78$, $p = .38$, $\eta^2 = .022$, indicating comparable levels of external details generated in the KS and control groups. Further, no significant main effect of condition was found, $F(1, 35) = 0.51$, $p = .48$, $\eta^2 = .014$, suggesting a comparable level of external details across past and future conditions. The Group × Condition interaction was also not significant, $F(1, 35) = 0.01$, $p = .93$, $\eta^2 < .001$.

Total amount of probes given

Next, an independent-samples t test was performed to determine whether the number of probes provided on the episodic task differed between KS and control participants. A significant group difference was found, $t(1, 35) = 10.57$, $p < .001$, indicating that more probes were provided to KS ($M = 19.6$, $SD = 4.7$) compared with control ($M = 6.1$, $SD = 2.5$) participants.

Novel event generation—Moon task

A 2 × 2 mixed-model ANOVA was run to explore main effects of group (KS, control) and detail type (internal, external) on the moon task (see Table 2). The main effect of group was not significant, $F(1, 35) = 1.094$, $p = .30$, $\eta^2 = .030$, suggesting that, overall KS patients and controls generated comparable narrative lengths on the moon task. The main effect of detail type, however, was significant, $F(1, 35) = 14.66$, $p < .001$, $\eta^2 = .30$, showing that the number of internal details was higher than that of external details, irrespective of group. The Group × Detail Type interaction was found to approach statistical significance, $F(1, 35) = 3.96$, $p = .06$, $\eta^2 = .10$.

Separate analyses for the internal and external details revealed that controls generated significantly higher levels of internal details on the moon task relative to KS patients, $F(1, 35) = 6.16$, $p < .05$, with no group differences observed for external details ($p = .649$). Representative examples of participant responses on the moon task are provided in Supplementary Material.

Semantic forms of past and future thinking

A 2 × 2 mixed-model ANOVA was used to explore main effects of group (KS, controls) and condition (past, future) on the "Known" subscale of the Memory and Temporal Experience questionnaire (see Table 2, Figs. 1 and 2). A significant main effect of group was found, $F(1, 35) = 23.98$, $p < .0001$ $\eta^2 = .41$, whereby KS participants were significantly impaired relative to controls, irrespective of condition. No significant main effect of condition was found, $F(1, 35) = 1.703$, $p = .20$, $\eta^2 = .05$, suggesting comparable semantic performance across past and future contexts, irrespective of group. The Group × Condition interaction was significant, $F(1, 35) = 15.252$, $p < .001$, $\eta^2 = .30$, with KS patients generating significantly less detail in both semantic past, $F(1, 35) = 40.04$, $p < .001$, and semantic future, $F(1, 35) = 9.42$, $p < .01$, conditions relative to controls. Moreover, within group performance was significantly better in the future relative to the past condition in KS ($p < .01$) , whereas the converse pattern was marginally significant in controls (i.e., past > future; $p = .054$). Representative examples of participant responses are provided in the Supplementary Material.

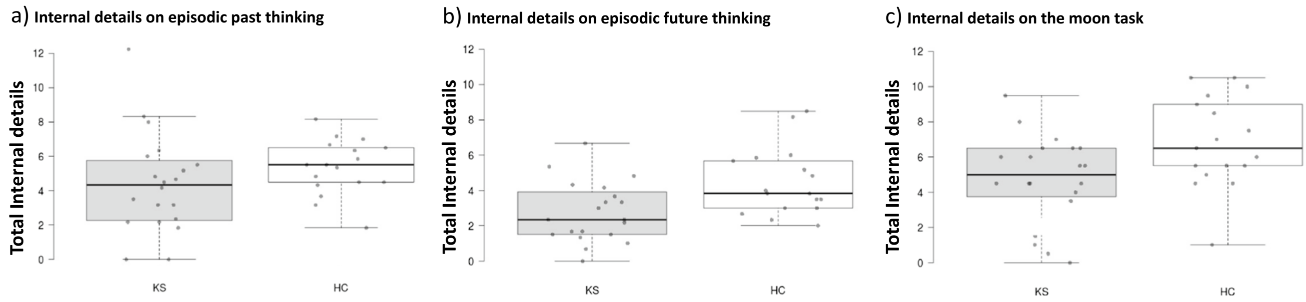

Fig. 1 Box plots presenting total number of internal details generated on the episodic past–future task (Panels **a**, **b**) and the moon task (Panel **c**) for Korsakoff patients (KS) and healthy controls (HC). Boxes represent the upper and lower quartiles; vertical line represents the median; whiskers represent the highest and lowest observations; dots represent individual data points in each group

Correlational analysis

Pearson's correlations were run to explore associations between clinical variables and performance on the experimental tasks, focusing on internal details in the episodic past and future thinking task, internal details in the moon task, and semantic past and future thinking scores. Considering first the control group, a significant association was observed between semantic past and semantic future scores on the semantic task, $r(17) = .61$, $p < .01$. No other significant associations were observed between past and future thinking performance on the experimental tasks in controls.

In the KS group, a significant association was observed between semantic past and semantic future thinking performance on the semantic task, $r(20) = .81$, $p < .001$. Internal details on the moon task correlated positively with semantic future thinking, $r(20) = .52$, $p = .019$, while an association on the threshold of significance was observed between internal details on the moon task and internal details on the episodic future thinking task, $r(20) = .44$, $p = .051$.

Correlations between past–future thinking and clinical variables in KS

No significant correlations were observed between the experimental tasks (episodic past–future; semantic past–future; moon task) and overall cognitive impairment as indexed by the MoCA or executive function as measured by the Trail Making Test–Part B in the KS group. Similarly, no significant associations were found between informant-rated confabulation scores on the NVCL-20 and any of the experimental tasks in KS (all p values $> .09$).

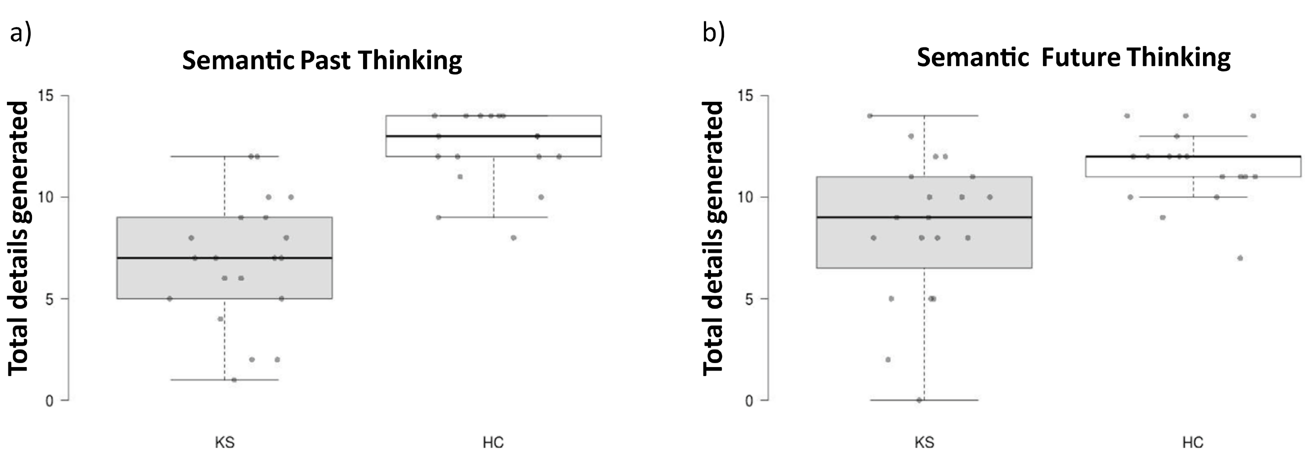

Fig. 2 Box for total number of details generated on the (**a**) semantic past and (**b**) semantic future thinking conditions for Korsakoff patients (KS) and healthy controls (HC). Boxes represent the upper and lower quartiles; vertical line represents the median; whiskers represent the highest and lowest observations; dots represent individual data points in each group

Discussion

This is the first study, to our knowledge, to compare past and future thinking performance across episodic and semantic conditions in Korsakoff's syndrome (KS) relative to matched healthy controls. Our objective was to determine the extent to which episodic and semantic forms of past and future thinking are impacted in KS and the interrelationship between different classes of memory in this syndrome. Overall, we found widespread difficulties in the KS group for episodic and semantic past and future thinking, accompanied by an impaired capacity to construct novel events. Correlation analyses revealed significant associations in the KS group between semantic past and future thinking, while novel event construction was found to relate to semantic and episodic future thinking, but not overall cognitive impairment or executive function. We discuss these findings in the context of current theoretical frameworks regarding episodic–semantic interactions, as well as posing some novel future directions for understanding the nature of memory dysfunction in KS.

The most striking finding in the current study was our demonstration of significant disturbances in past and future thinking across episodic and semantic domains. Considering first the episodic task, we found that KS patients generated significantly fewer internal details across past and future temporal contexts compared with control participants. This is in line with our original hypotheses and converges with the extant literature on episodic memory deficits in KS (Kessels & Kopelman, 2012; Postma et al., 2006; Race & Verfaellie, 2012). The past–future task has been used widely used to document impairments in the retrieval of past events and the simulation of possible personal future events across a range of populations including older adults (Addis et al., 2008), mild cognitive impairment (Gamboz et al., 2010), semantic dementia (Irish, Addis, et al., 2012b) and frontotemporal dementia (Irish, Hodges & Piguet, 2013). Only one previous study to our knowledge, however, has explored the capacity for future thinking in KS. El Haj et al. (2019) demonstrated that KS patients could generate plausible events in the past and future, albeit of lower specificity and reduced quality relative to controls. We extend these findings using a detailed measure of event construction to demonstrate that past and future narratives are grossly impoverished in KS. One aspect which remains unclear is the origin of these disturbances in terms of the specific profile of contextual details which make up the overall internal detail score. Due to time constraints, it was not possible to rigorously probe past and future thinking using the full Specific Probing schedule of the Autobiographical Interview. Future studies will be important to identify the contextual details most vulnerable to disruption in KS. Likewise, the provision of specific probes during autobiographical narration has been shown to reliably improve the level of contextual detail produced by healthy older adults and patients with dementia (Levine et al., 2002; Ramanan et al., 2021). While KS patients required significantly more general probing relative to controls, it remains unclear whether the full Specific Probing schedule of the Autobiographical Interview might ameliorate strategic retrieval deficits in these patients. Future research will be required to explore these issues in more depth.

Turning our attention to the semantic task, we found evidence of marked difficulties in generating past and future semantic forms of information in KS. This finding suggests that future thinking impairments are not confined to the domain of episodic memory, but encompass the nonpersonal/semantic domain as well. To date, the status of semantic memory in KS has remained unclear, with a mixed profile of loss and sparing reported in the literature. For example, early studies suggested intact lexical memory but compromised cognitive estimations, as well as compromised memory for semantic facts (Brand et al., 2003; Cermak et al., 1978; Race & Verfaellie, 2012). We extend these findings to suggest a gross incapacity to generate semantic information regarding past and future occurrences in KS relative to controls. While KS patient performance was better in the future relative to the past semantic condition, we note that this may reflect a practice effect on the task, as we did not counterbalance across past and future conditions. Previous studies exploring the capacity for semantic forms of future thinking in clinical populations have revealed variable profiles of impairment, whereby semantic prospection is not as deleteriously affected as that of episodic simulation (Irish et al., 2016). A recent study by Race et al. (2013), however, suggests that elaboration may play an important role in this context, as MTL patients were found to generate a comparable number of semantic events relative to controls, yet could not elaborate on these occurrences in detail. We tentatively suggest a similar underlying mechanism here, whereby KS patients may be able to generate a limited number of nonpersonal future occurrences yet would be markedly impaired if asked to embellish or describe these in detail.

On the novel event construction task, participants were required to envisage an event of which they had no prior episodic experience—namely, spending a day on the moon. The rationale for including the moon task was to probe improbable forms of event simulation, highly unlikely to occur within the participant's timeline, which would be predicted to rely more heavily on semantic contributions (Abraham & Bubić, 2015; Irish, 2020). Complementing our findings of semantic past and future thinking impairments, KS patients were found to generate significantly fewer internal, but not external, details compared to controls when envisaging a day on the moon. These findings demonstrate that, in concert with an impaired capacity for plausible event simulation, implausible event construction is also markedly compromised in KS. Interestingly, we did not find any evidence of bizarre or unusual event descriptions that might suggest confabulation on this measure in the KS group. Rather, KS patients adhered to task instructions and provided an appropriate description of the moon condition, but one which was markedly divested of contextual detail.

A secondary aim of this study was to explore potential associations between task performance across episodic and semantic domains. Importantly, our correlation analyses revealed significant associations between reduced internal details on the moon task and episodic and semantic future thinking deficits in the KS group, suggesting the interplay of episodic and semantic memory in the origin of constructive simulation impairments in this syndrome. Previous studies have suggested that difficulties in contextual memory formation represent a candidate mechanism for episodic amnesia in KS (see Kessels & Kopelman, 2012, for a review). In this light, lesions to diencephalic structures, predominantly the thalamus and mammillary bodies, likely disrupt not only the relational binding of content from episodic experiences but also the capacity to make associative links between semantic concepts, all of which are essential for generating creative and novel responses (see Paulin et al., 2020). Future studies exploring the capacity for relational binding of episodic and semantic content in KS are required to test this proposal.

Finally, we sought to explore the potential relationship between confabulation and future thinking performance in KS. Confabulations often evoke bizarre and improbable reports, where the person giving the report is completely unaware of the fact that these events never happened (Dalla Barba & Boissé, 2010). While the KS group comprised a high number of confabulators, in line with a recent study (Oudman, Rensen, & Kessels, 2021), we did not find significant associations between performance on any of the experimental tasks and the frequency of confabulations on the NCVL-20. While the NCLV-20 holds good reliability and validity, we note that as a proxy-based measure it captures the frequency, but not necessarily the severity, of confabulation in the patient's daily life. Future studies should try to tease apart the potential relationship between confabulation and future thinking in KS by using more targeted instruments to provoke confabulation such as the Dalla-Barba confabulation scale (Dalla Barba et al., 2018). Importantly, a qualitative review of the KS transcripts suggested that patients successfully adhered to the task instructions and provided plausible responses on all of the experimental tasks. It may be that the constrained nature of the tasks used here limited the opportunity for confabulation in KS patients, and we suggest that exploring unconstrained forms of spontaneous cognition using minimally cognitively demanding tasks (e.g., O'Callaghan et al., 2019) might prove fruitful. Moreover, it would be informative to collect data across a larger sample of KS patients enabling us to stratify by confabulation severity.

From a clinical perspective, it is important to consider our findings in relation to the everyday experience and behavior of KS patients. Previous studies have suggested that loss of the future may potentiate feelings of depression, apathy, or anhedonia in clinical populations (Hsiao et al., 2013; Shaw et al., 2021). As such, impaired future thinking abilities in KS may have marked repercussions for many aspects of daily life. If patients cannot form a proper image of forthcoming social situations and of the effects of their behaviors in these scenarios, problems may arise in domains such as moral decision-making, emotion regulation, planning, and theory of mind. These self-projection and emotional functions are crucial for human communication and interaction, enabling us to form an enduring sense of who we are as individuals across subjective time (Strikwerda-Brown, Grilli, et al., 2019a). While not a focus of the present study, we propose that loss of future thinking capacity may be closely related to affective and motivational changes in KS (Brion et al., 2016). During testing, the experimenter noted that KS patients often seemed disengaged from current events, with high levels of apathy and social withdrawal. Indeed, some patients stated that none of the events being discussed interested them, because they were living in a chronic care facility and presumably sheltered from world events (see the Supplementary Material). While intuitive, it remains unclear how prospection relates to motivation and goal-directed behavior. From a clinical perspective, addressing these questions can potentially inform the development of future thinking training interventions to bolster foresight capacities and thereby improve engagement of the individual living with KS.

A number of methodological considerations warrant discussion. Firstly, our sample sizes are relatively small, reflecting the rarity of the KS syndrome and the challenges in accessing protected patient groups of this nature. We note that our findings are preliminary and require replication in a larger cohort, ideally stratified by disease severity. Secondly, our ability to explore potential cognitive mechanisms of past and future thinking performance was limited by our access to appropriate clinical data for the KS sample. Only the MoCA scores were collected at the same time as the experimental tasks and other neuropsychological tests stemmed from routine clinical testing or other studies that did not overlap in time. As such it is difficult to determine the extent to which the past and future thinking impairments observed here were driven by specific cognitive impairments. Thirdly, in order to stay faithful to previous testing protocols, we used the same cue words and images as previous studies (Addis et al., 2008; Irish, Addis, et al., 2012a); however, the nature of the residential care setting may have placed the KS patients at a disadvantage. For example, by virtue of their living in sheltered accommodation, KS patients are less likely to experience salient or personally significant events from their recent past. Thus, even though we used commonplace, frequently encountered cue words, the KS patients likely have a less rich pool of experiences from which to draw upon. Finally, as mentioned above, we did not include a formal measure of motivation in the current study, and we suggest that this will be important for future studies to establish the relationship between apathy and future thinking in this population.

In summary, this study is the first, to our knowledge, to probe episodic and semantic forms of past and future thinking in the clinical syndrome of KS. Our findings suggest marked past and future thinking deficits across semantic and episodic tasks that cannot be understood in terms of a strict episodic–semantic dichotomy. These findings resonate with a shift towards conceptualizing episodic and semantic memory as interacting components along a continuum (Irish & Vatansever, 2020), and point towards the need for further empirical study in this unique patient population.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.3758/s13421-021-01262-2.

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