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Route learning in Korsakoff's syndrome: Residual acquisition of spatial memory despite profound amnesia

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Korsakoff's syndrome (KS) is characterized by explicit amnesia, but relatively spared implicit memory. The aim of this study was to assess to what extent KS patients can acquire spatial information while performing a spatial navigation task. Furthermore, we examined whether residual spatial acquisition in KS was based on automatic or effortful coding processes. Therefore, 20 KS patients and 20 matched healthy controls performed six tasks on spatial navigation after they navigated through a residential area. Ten participants per group were instructed to pay close attention (intentional condition), while 10 received mock instructions (incidental condition). KS patients showed hampered performance on a majority of tasks, yet their performance was superior to chance level on a route time and distance estimation tasks, a map drawing task and a route walking task. Performance was relatively spared on the route distance estimation task, but there were large variations between participants. Acquisition in KS was automatic rather than effortful, since no significant differences were obtained between the intentional and incidental condition on any task, whereas for the healthy controls, the intention to learn was beneficial for the map drawing task and the route walking task. The results of this study suggest that KS patients are still able to acquire spatial information during navigation on multiple domains despite the presence of the explicit amnesia. Residual acquisition is most likely based on automatic coding processes.

Korsakoff's syndrome (KS) is a chronic neuropsychiatric disorder caused by thiamine deficiency typically following prolonged excessive alcohol abuse and self-neglect. KS is characterized by severe anterograde amnesia affecting all domains of explicit memory (Kopelman, 1995). There is, however, evidence that KS patients have even more pronounced problems in remembering contextual information, such as spatial memory

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for coordinate (exact locations of objects in space) as well as categorical (relative) object to location binding (Kessels, Postma, Wester, & de Haan, 2000). Also, forming associations between temporal order information and spatial information is severely hampered (Postma, Van Asselen, Keuper, Wester, & Kessels, 2006). Although the syndrome is characterized by severe impairments in learning and remembering contextual information explicitly, implicit learning of contextual information seems relatively preserved in KS (Hayes, Fortier, Levine, Milberg, & McGlinchey, 2012). It has, for example, been shown that patients with KS show intact ability to acquire contextual information after repeated presentation, resulting in faster localization of a target in the environment (Oudman, Van der Stichel, Wester, Kessels, & Postma, 2011). Moreover, Postma, Antonides, Wester, and Kessels (2008) illustrated that KS patients demonstrated unconscious influence of spatial configurations on a subsequent task in an object-location memory paradigm. Both studies indicate that despite the severity of cognitive deterioration in KS, patients are still able to retrieve some contextual information implicitly.

A daily activity which requires processing of temporal and spatial information is spatial navigation. Although several studies have been performed on learning of computerized spatial tasks in KS patients, surprisingly little research has been performed on actual spatial navigation (see Kessels & Kopelman, 2012 for a review). Spatial navigation concerns remembering where things are, and applying this information to get from one location to another, for example, while walking or driving from one place to another (Postma, van Oers, Back, & Plukaard, 2012). Automatic processing of spatial information would be advantageous in such complex daily activities. Hasher and Zacks (1979) made the distinction between automatic and effortful processing of spatial information. The authors argued that because of its ecological significance, spatial memory operates mainly or even fully automatically, that is, without direct attention and intent. Several studies have supported that at least some information is automatically encoded during spatial navigation. For example, when not paying any attention to a new environment, we will most likely still be able to remember, or at least recognize some familiar landmarks and remember the temporal position of the landmarks along the route (Cornell, Heth, & Alberts, 1994). Moreover, a global sense of direction does not necessary require effort (Postma *et al.*, 2008). Others, however, have found better performance on spatial navigation when locations were encoded intentionally (Light & Zelinski, 1983). Recent studies on spatial navigation emphasized different aspects of route learning in the light of automaticity. Van Asselen, Fritschy, and Postma (2006) showed that without the instruction to remember a route, participants performed equally compared to those who were instructed to remember the route on tasks involving landmark information and route knowledge, such as landmark recognition and landmark ordering. Survey knowledge, such as drawing a map-like presentation and walking the route in reverse was hampered. The results of this study suggest that some aspects of spatial navigation are automatically coded, but some others are not.

Not only has the topic of route learning and navigation rarely been investigated in KS, the issue of automatic acquisition is still largely unexplored. This is remarkable because automatic navigation is relevant in everyday life for both healthy persons as patients with KS. The finding that some aspects of spatial navigation are processed automatically is of interest since this could suggest that despite the presence of amnesia in KS residual acquisition of information relevant to spatial navigation might still be available. To our knowledge, however, this has never been the topic of investigation. To date, there has been only one study on repeated route walking in KS (Kessels, van Loon, & Wester, 2007). The primary goal of this study was to evaluate the effectiveness of the errorless learning teaching technique in KS, showing no beneficial effect compared to trial-and-error learning with respect to taking the correct turns on the route. The study did not involve a healthy control group. Moreover, a recent study suggested that errorless learning could in fact be beneficial for skill learning in KS, dependent on the task at hand (Oudman *et al.*, 2013).

In light of the foregoing, the main objective of this study was to examine whether KS patients still have some potential for acquisition of specific spatial information during spatial navigation. This study, therefore, adopted six tasks targeting typical aspects of spatial navigation that have previously been applied in studies in healthy subjects (Van Asselen *et al.*, 2006) and stroke patients (van der Ham *et al.*, 2010). The tasks intended to assess time and distance estimation, landmark recognition and ordering, map drawing, and actual route memory in KS patients and healthy controls after they have navigated through a residential area. In order to further examine whether KS patients had some potential to acquire spatial information during spatial navigation chance, performance was calculated for all six tests by asking a group of healthy controls to perform the tasks without having experienced the original route. Additionally, we also wanted to elucidate whether any residual acquisition in KS was explained by either automatic or effortful processes. As KS is characterized by severe impairments in effortful contextual memory (Kessels *et al.*, 2000), it could be expected that acquisition of spatial information in KS is based on automatic processes. Therefore, the participants were included in an incidental (automatic processes) or intentional condition (automatic and effortful processes). When effortful processes are required for acquisition during spatial navigation, performance would improve under intentional learning conditions. In contrast, if automatic processes would suffice, no difference between the two conditions would be found. On the basis of the severity of the amnesia in KS, we expected residual acquisition in KS to be based on automatic, rather than effortful processes.

Methods

Participants

Twenty-three patients with severe anterograde amnesia, diagnosed with KS participated in this study. The patients were inpatients of a Korsakoff Center in The Netherlands. All patients fulfilled the DSM-IV criteria for alcohol-induced persisting amnestic disorder (American Psychiatric Association, 2000) and the criteria for KS described by Kopelman (2002). The amnestic syndrome was confirmed by neuropsychological testing. All patients were in the chronic, amnestic stage of the syndrome, and none were in the confusional Wernicke psychosis at time of testing. Premorbid IQ was estimated with the Dutch Adult Reading Test (Schmand, Lindeboom, & van Harskamp, 1992), which is the Dutch version of the National Adult Reading Test (Christensen, Hazdi-Pavlovic, & Jacomb, 1991). All included patients had an estimated IQ score above 80, to exclude patients with low intellectual or cognitive functioning interfering with the testing procedure, possibly caused by alcohol dementia (Oslin, Atkinson, Smith, & Hendrie, 1998). All patients had an extensive history of alcoholism and nutritional depletion, notably thiamine deficiency, verified through medical charts. Selected patients did not show neurological disorders (head injury, epilepsy, etc.) or acute psychiatric conditions (psychosis, major depression, etc.) interfering with the testing procedure. All patients were administered a Dutch version of the Rey Verbal Learning Test (Van Der Elst, Van Boxtel, Van Breukelen, & Jolles, 2005), a task measuring verbal immediate and long-term memory and scored within the first to the fifth percentile on the total number of words recalled in Trials 1–5. Table 2 shows a summary of demographic variables and neuropsychological test results for all patients. Additionally, twenty age- and premorbid IQ matched controls were included and performed the exact same tasks as the patients with KS. Last, fifteen healthy participants were included in a control experiment (see below). The study was conducted in accordance to the standards of the declaration of Helsinki. All participants gave informed consent prior to their inclusion in the study.

General procedure

The 23 patients and 20 control participants were randomly assigned to the intentional and incidental group. Participants in the intentional group were told that the aim of the experiment was to study route-learning behaviour during a fresh walk outside. They were asked to pay attention to the route they were going to walk, as they would be tested on their knowledge of this route. Participants in the incidental group were told that they needed to accompany the experimenter during a walk outside, to test the effects of fresh air on attention. Both groups walked the same route outside the Korsakoff Center in a neighbouring residential area. At the end of the experiment, participants were asked to indicate whether they had been in the specific residential area before. None of the participants indicated that they had been in this specific residential area before. The route was 400 m. In both groups, conversation was limited to responding shortly but politely to any questions that were asked or comments that were made by the participants. To secure that the walking speed was comparable for all participants, the experimenter explicitly tried to maintain a standard walking gait. This standard walking gait was practiced by the experimenter before the experiment. As we did not want to give any cue to the participants in the incidental condition about the true aim of the study, we chose not to measure time or walking speed. When participants arrived in the test room, they were engaged in distraction tasks for about 25 min. These tasks involved the Location Learning Test (Bucks & Willison, 1997; Kessels, Nys, Brands, van den Berg, & Van Zandvoort, 2006), the Corsi Block-Tapping Test (Kessels, Van Den Berg, Ruis, & Brands, 2008), and the Dutch Adult Reading Test (Schmand *et al.*, 1992). The tests were intended to avoid active rehearsal of the spatial information by the participants (see Table 1 for test results). Next, participants in the incidental group were informed about the true aim of the study. Subsequently, all participants performed six tasks that tested selective aspects of their spatial knowledge. After the final task was performed (Route Walking Task), participants were asked whether they were familiar with the route. None of the patients or control participants mentioned familiarity with the residential area. In the control experiment, healthy participants in the chance condition were instructed to perform the aforementioned six tasks that tested selective aspects of their spatial knowledge by guessing that is, without having seen the original route.

Tasks

Six tasks were included in the current experiment:

(1) Landmark Recognition Task: Sixteen photographs were presented, all of them including a landmark that characterizes either a path (e.g., a red garbage can) or a decision point (e.g., a bicycle rack). Nine photographs were taken along the route (targets) and seven photos were taken in the same area, but not along the route (distractors). Participants had to indicate whether they recognized the landmarks

Table 1. Demographic variables and neuropsychological test results for the Korsakoff's patients ($n = 20$) and healthy controls ($n = 20$) for the incidental and intentional condition ($n = 10$ per condition). A GLM univariate analysis was used for the individual subtests with the between-subject variable Group (Korsakoff's syndrome patients and Controls) and Condition (intentional and incidental condition)

	Korsakoff's patients		Healthy Controls				
	Intentional condition	Incidental condition	Intentional condition	Incidental condition	Group effect (*F*-value)	Condition-effect (*F*-value)	Group × Condition-effect (*F*-value)
Number of participants (m, f)	10 (7:3)	10 (8:2)	10 (3:7)	10 (5:5)			
Age *M* (*SD*)	59.6 (9.2)	59.4 (6.3)	58.3 (8.6)	52.7 (9.3)	2.2	1.1	1.0
IQ *M* (*SD*)[a]	97 (12.3)	101 (13.4)	101.4 (12.1)	100.7 (7.0)	0.3	0.2	0.4
Corsi Span Forward *M* (*SD*)[b]	5 (0.5)	5.1 (0.9)	5.5 (0.9)	4.9 (0.9)	0.4	1.0	1.9
Corsi Span Backward *M* (*SD*)[b]	4.7 (1.2)	5.3 (0.8)	5.6 (0.7)	5.3 (0.9)	2.4	0.3	2.4
Location Learning Test – Learning Index *M* (*SD*)[c]	14.9 (9.4)	24 (17.7)	64.9 (30.1)	46.8 (31.8)	22.8*	0.3	3.2

Note. m, male; f, female; *M*, mean; *SD*, standard deviation; [a]IQ was estimated with the Dutch Adult Reading Test (Schmand *et al.*, 1992). [b]Corsi Block-Tapping Test, reflecting visuospatial memory (Kessels *et al.*, 2008). [c]Learning error (displacement score) was calculated for the Location Learning Test (Bucks & Willison, 1997; Kessels *et al.*, 2006). Learning error in the reference group was $M = 8.1$, $SD = 6.6$. $*p < .001$.

from the route or not and they had to guess if they did not know the answer. The target landmarks are represented in Figure 1. The proportion of correct responses was calculated (Range: 0–100%).

(2) Landmark Ordering Task: Participants were shown six photographs of landmarks taken along the route and were asked to place the photos in the right order, from first-seen landmark to last-seen landmark. If the participants did not know the right order, they had to guess. Participants received two points for a picture on its correct location, one for a picture in a position adjacent to its correct position and zero points for all others (Range: 0–12 points).

(3) Map Drawing Task: Participants were shown a map of the area in which they had walked a route and were given the instruction to draw the route on the map (see Figure 1). The starting point was given by the researcher. One point was given for each correct decision point that was included and another one when the right direction was chosen at a decision point. Moreover, one point was subtracted for each passed decision point that was not along the route. (Range: 0–29 points).

(4) Time Estimation Task: Participants were asked to estimate the time it took to walk the route (~circa 6 min). The correct answer was subtracted from the estimated answer to calculate the size of the error. There were no minimum or maximum scores on this task.

(5) Route Length Estimation Task: Participants were asked to estimate the distance of the route (400 m). The correct answer was subtracted from the estimated answer in order to calculate the size of the error. There were no minimum or maximum scores on this task.

Figure 1. A map of the residential area showing the route that participants walked during the learning phase, and the positions of landmarks along the route.

(6) Route Walking Task: Participants had to navigate the route from beginning to the end. The researcher walked along with the participants and corrected them if they made a wrong turn. The number of correct turns was counted (Range: 0–15 correct turns).

Analysis

In line with a previous report on route acquisition (Van Asselen *et al.*, 2006) a MANOVA was used with a within-subject variable Task (landmark recognition, landmark ordering, route time estimation, route distance estimation, map drawing task, route walking task) and the between-subject variables Group (patient and controls) and Condition (intentional and incidental). Both results of the MANOVA and subsequent ANOVAs are presented. In the control experiment, the performance of KS patients per subtest was compared to performance of the healthy control chance group by means ANOVAs (chance group and KS patients). A p-value of less than .05 was considered statistically significant.

Results

Demographic variables and neuropsychological results

Three patients were excluded from analysis, because they were unable to complete the experiment without physical assistance of a transport wheelchair pushed by a member of the nursing staff. The remaining 20 patients and 20 healthy controls were included in the analysis. In the control experiment, 15 additional healthy participants were enrolled. They were mainly adult visitors of an open day of the institute and were about evenly divided between men and woman. Table 1 gives a summary of demographic variables and neuropsychological test results for the patient groups and the healthy control groups, split on condition (intentional vs. incidental). Table 2 shows a summary of demographic variables and neuropsychological test results for all patients.

Results for the route learning tasks

Multivariate GLM showed a significant overall group effect, $F(6, 31) = 5.0$, $p < .01$, $\eta_p^2 = .490$, suggesting that healthy controls performed better than KS patients. Scores per task are displayed in Table 3.

Between-subject effects for the different tasks separately showed that the healthy controls performed better than the KS patients on the landmark recognition task, $F(1, 36) = 4.9$, $p = .033$, $\eta_p^2 = .120$, the route time estimation task, $F(1, 36) = 8.6$, $p = .006$, $\eta_p^2 = .193$, the map drawing task, $F(1, 36) = 5.9$, $p = .021$, $\eta_p^2 = .140$, and the route waking task, $F(1, 36) = 22.9$, $p < .001$, $\eta_p^2 = .389$, suggesting that performance of KS patients was hampered on a majority of route learning tasks. Both groups performed comparably on the route distance estimation task, $F(1, 36) = 3.1$, $p = .089$, $\eta_p^2 = .078$, suggesting that specific aspects of route learning are relatively preserved in KS. Performance on the landmark ordering task was comparable in both groups, $F(1, 36) = 0.1$, $p = .787$, $\eta_p^2 = .002$, but performance was very low in both groups. Performance was equal for both learning conditions on all subtasks ($ps > .14$; $\eta_p^2 < .06$). Moreover, the intention to learn did not modulate the performance on the landmark recognition task, $F(1, 36) = 0.95$, $p = .336$, $\eta_p^2 = .026$, the landmark ordering task,

Table 2. Demographic variables and neuropsychological test results of the Korsakoff's patients ($n = 20$)

Patient	Gender	Age	IQ[a]	Verbal learning[b]	Spatial span forward[c]	Spatial span backward[c]	Learning error (displacement score)[d]
1	M	56	114	<5	6	6	45
2	M	57	118	<5	5	3	28
3	M	50	91	<5	6	6	82
4	M	67	103	<5	6	6	57
5	M	45	105	<5	5	6	136
6	F	50	98	<5	5	5	102
7	F	60	111	<5	5	5	41
8	F	64	104	<5	4	5	58
9	M	65	127	<5	6	6	26
10	M	64	89	<5	5	4	74
11	M	57	84	<5	5	4	85
12	M	64	99	<5	5	5	47
13	M	60	103	<5	5	6	57
14	M	68	93	<5	4	4	84
15	M	58	94	<5	6	5	36
16	M	49	84	<5	4	6	21
17	F	55	108	<5	5	6	23
18	M	56	81	<5	5	5	90
19	F	71	93	<5	5	4	101
20	M	74	81	<5	4	3	99
		$M = 59.5$	$M = 99.0$		$M = 5.1$	$M = 5$	$M = 64.6$
		$SD = 7.7$	$SD = 12.7$		$SD = 0.7$	$SD = 1$	$SD = 32.1$

Note. M, Male; F, Female; IQ, Intelligence Quotient; *M*, Mean; *SD*, Standard deviation. [a]IQ was estimated with the Dutch Adult Reading Test (Schmand *et al.*, 1992). [b]Percentile scores for the total performance on the first five learning trials, measured with the Dutch version of the Rey Verbal Learning Test, for measurement of long-term memory (Van Der Elst *et al.*, 2005). [c]Corsi Block-Tapping Test, reflecting visuospatial memory (Kessels *et al.*, 2008). [d]Learning error (displacement score) was calculated for the Location Learning Test (Bucks & Willison, 1997; Kessels *et al.*, 2006). Learning error in the reference group was $M = 8.1$, $SD = 6.6$.

$F(1, 36) = 0.30$, $p = .589$, $\eta_p^2 = .008$, the route time estimation task, $F(1, 36) = 1.1$, $p = .299$, $\eta_p^2 = .030$, or distance estimation task, $F(1, 36) = 0.74$, $p = .396$, $\eta_p^2 = .020$. Importantly, however, there was a significant Group × Condition interaction on the map drawing task, $F(1, 36) = 5.5$, $p = .025$, $\eta_p^2 = .133$, and the route walking task, $F(1, 36) = 6.1$, $p = .018$, $\eta_p^2 = .145$, showing that the intention to learn modulated the performance on both tasks discrepantly in the patient and control group. *Post-hoc* ANOVAs did not reveal an effect of gender ($ps > .37$; $\eta_p^2 < .03$). Moreover, *post-hoc* ANOVAs were performed for the map drawing task and the route walking task for both groups separately, to scrutinize the significant Group × Condition interactions. In the control group, the intention to learn was beneficial for both the map drawing task, $F(1, 19) = 17.6$, $p = .001$, $\eta_p^2 = .495$, and the route walking task, $F(1, 19) = 29.2$, $p = .041$, $\eta_p^2 = .212$. For the patient group, the intention to learn was not beneficial for the map drawing task, $F(1,19) = .23$, $p = .637$, $\eta_p^2 = .013$, or the route walking task, $F(1, 19) = 1.6$, $p = .221$, $\eta_p^2 = .082$.

Results for the control experiment

Table 3. Mean scores (*SD*) of the intentional and incidental group on the six spatial navigation tasks for the Korsakoff's syndrome patients ($n = 20$), control subjects ($n = 20$) and chance condition ($n = 15$). Chance performance was calculated by asking a group of healthy controls to perform the tasks without having experienced the original route

	Korsakoff's patients		Healthy controls		
	Intentional condition	Incidental condition	Intentional condition	Incidental condition	Chance condition
Landmark recognition task (percentage correct *M*, *SD*)	53.1% (11.9%)	53.1% (14.5%)	64.4% (8.4%)	57.5% (8.7%)	45.8% (0.1%)
Landmark ordering task (*M*, *SD*)	4.2 (2.7)	4.3 (1.3)	4.4 (2.3)	3.7 (2.8)	3.1 (2.6)
Route time estimation task (absolute difference in minutes; *M*, *SD*)	5 (3.8)	7.3 (6.4)	2.6 (2.2)	2.2 (2.2)	13.9 (8.4)
Route distance estimation task (absolute difference in metres; *M*, *SD*)	547.5 (577.2)	465 (508.8)	210 (166.3)	350 (253.6)	1246 (1133.3)
Map Drawing Task (*M*, *SD*)	12.6 (9.4)	14.8 (11.1)	24.9 (5.7)	15.0 (4.8)	5.1 (5.1)
Route Walking Task (*M*, *SD*)	11.7 (.8)	12.3 (1.3)	14.2 (.6)	13.1 (1.4)	10.1 (1.4)

Note. *M*, mean; *SD*, standard deviation.

Korsakoff's syndrome patients performed significantly better than the chance group on the route time estimation, $F(1, 33) = 11.1$, $p = .002$, $\eta_p^2 = .251$, route distance estimation, $F(1, 33) = 6.6$, $p = .015$, $\eta_p^2 = .168$, map drawing task, $F(1, 33) = 9.2$, $p = .005$, $\eta_p^2 = .219$, and the route walking task, $F(1, 33) = 19.8$, $p < .001$, $\eta_p^2 = .375$, but not the landmark recognition, $F(1, 33) = 3.8$, $p = .061$, $\eta_p^2 = .102$, and ordering task, $F(1, 33) = 2.0$, $p = .163$, $\eta_p^2 = .058$. The results indicate that although KS patients are impaired on a majority of route learning tasks, performance is still better than chance level on four of the six tasks on route learning. Implications of this finding are elaborated below in the discussion. Healthy controls performed significantly better than the chance group on the route walking task, $F(1, 33) = 62.2$, $p < .001$, $\eta_p^2 = .653$, map drawing task, $F(1, 33) = 46.3$, $p < .001$, $\eta_p^2 = .584$, route time estimation, $F(1, 33) = 34.4$, $p < .001$, $\eta_p^2 = .510$, landmark recognition, $F(1, 33) = 27.0$, $p < .001$, $\eta_p^2 = .450$, and the route distance estimation, $F(1, 33) = 14.1$, $p = .001$, $\eta_p^2 = .299$, but not the ordering task, $F(1, 33) = 1.1$, $p = .300$, $\eta_p^2 = .032$. The results indicate that specifically the ordering task was too complicated for all participants.

Discussion

The aim of this study was to assess to what extent KS patients can acquire spatial information during spatial navigation despite the presence of amnesia. Furthermore, we examined whether any residual acquisition in KS was based on automatic or effortful coding processes. Compared to the results of a matched control group KS patients showed hampered performance on the landmark recognition task, the route time estimation task, the map drawing task and the route walking task after walking a route through a residential area. Importantly, performance was relatively spared on the route distance estimation task. Moreover, in KS performance was superior on the route time and distance estimation tasks, the map drawing task and the route walking task compared to a chance group consisting of healthy individuals who performed the spatial tasks without actually ever having walked the route. The results of this study clearly show that KS patients still acquire spatial information during navigation, although they are hampered on a majority of route learning tasks compared to healthy controls. With respect to the underpinning of residual acquisition in KS, the present results suggest that acquisition in KS is automatic rather than effortful, since no significant differences were obtained between the incidental (automatic) and intentional (effortful and automatic) condition for any of the route-learning components, whereas for the healthy controls the intention to learn was beneficial for the map drawing task and the route walking task.

This is the first case-controlled study to investigate whether residual acquisition of information relevant to spatial navigation is present in KS. Earlier studies have already indicated that despite the presence of amnesia, KS patients are still able to benefit from repeated presentation of spatial configurations in faster detection of stimuli (Oudman *et al.*, 2011; Postma *et al.*, 2008). Conversely, an important difference between previous studies on repetitions of spatial information and the current study is that our study focused on the acquisition of spatial information in a real-life navigation experiment, instead of a computer paradigm on retrieval of contextual information. The results of the current study therefore extend findings of preserved contextual acquisition in KS to real-life navigation, but also indicate that acquisition occurred in KS after just one exposure of the route. Both findings are relevant to the study of contextual learning in KS, since there is profound damage to memorizing contextual information (Kessels *et al.*, 2000).

One of the remarkable findings of the current study is that distance estimation was relatively spared in the KS group, whereas time estimation was clearly hampered compared to a control group. A possible explanation for this finding is that distance estimations are more dependent on kinaesthetic and motor learning than time estimation. Support for the view that distance estimations are moderated by kinaesthetic is given by studies that suggest that distance estimations in virtual environments are systematically underestimated when there is no body movement or perceived control of body movement (Von Stülpnagel & Steffens, 2013; Waller & Richardson, 2008). Patients with Parkinson's disease do underestimate distances in their environment, possibly due to a lack of kinaesthetic feedback following damage to the striatum of the brain (Demirci, Grill, McShane, & Hallett, 1997). Recent studies suggest that implicit motor learning is relatively preserved in KS when the task at hand does not require multiple motor operations (Van Tilborg, Kessels, Kruijt, Wester, & Hulstijn, 2011), thus allowing the possibility of spared distance estimations based on motor learning. Nevertheless, the finding of preserved distance estimations should be interpreted with caution because of large variations in both the patient and control group.

Interestingly in this study, it was found that KS patients performed better than a chance group on route time and distance estimation tasks, a map drawing task and during actual route walking. With respect to actual route walking, the results of this study are consistent with a previous study on repeated route walking in KS (Kessels *et al.*, 2007). In this study, ten patients with KS walked two routes five times following two teaching techniques. In a test phase KS patients scored better than chance level (about 3 out of 18 possible errors). Importantly, the current results show that even after passing the route once, KS patients performed better than chance level walking the route, although their results were deteriorated compared to a matched control group. This suggests that despite the presence of amnesia, route learning is still possible to some extent in, KS patients.

Regarding a better than chance level performance on time estimations, the finding of some residual ability to estimate time is consistent with earlier research on estimating time intervals in KS and patients with frontal lesions (Mimura, Kinsbourne, & O'Connor, 2000). In their study, frontal lesion patients were less accurate than KS patients in estimating time intervals, who in turn were outmatched by control participants. The authors suggested that both episodic and working memory play a role in time estimations. An important difference between the current results and the results of Mimura *et al.* (2000) is that KS patients in our study all overestimated the time, while the patients in the earlier study tended to underestimate the time intervals. A possible explanation for this finding is that patients in the current study had to estimate the time they walked a route. In an earlier study patients had to estimate an interval between two stimuli without performing any other action. Earlier research on implicit motor learning suggested that motor sequence learning is relatively preserved when the task at hand does not require multiple motor operations (Van Tilborg *et al.*, 2011). This could possibly contribute to the discrepancy between time estimations in the current study and an earlier study (Mimura *et al.*, 2000).

In the current experiment, KS patients performed better than a chance group on a map drawing task, but were clearly hampered compared to a healthy control group. Moreover, healthy controls performed better on a map drawing task if they intended to remember the route. This is the first study to investigate drawing a route on a map in KS. Earlier evidence on patients with unilateral temporal lobectomy revealed that patients with right hemispheric temporal lobectomy and to a lesser extent left hemispheric temporal lobectomy show problems in drawing a map of a previously learnt route (Spiers *et al.*, 2001). Moreover, a study on the effects of intentionality on spatial navigation also showed that specifically the map drawing task requires intentionality for good performance (Van Asselen *et al.*, 2006). The results of the current controls replicate this finding. On the basis of the studies by Spiers *et al.* (2001) and Van Asselen *et al.* (2006) one could conclude that intentionality, but also intact episodic memory is required for effective map drawing. Nevertheless, the KS patients in the current experiment outperformed a chance group, suggesting that besides an intentional and/or episodic memory system also an automatic memory system contributes to effective map drawing. This finding contradicts the opinion that learning in KS is restricted to mere priming-effects (Hayes *et al.*, 2012).

The current results have practical implications for the diagnosis and rehabilitation of route learning in KS. An earlier study already indicated that patients with KS are able to increase task performance on a route walking task after repeated exposure to the route (Kessels *et al.*, 2007). Our results extend this finding by suggesting that patients with KS are able to reasonably perform a route walking task after single-shot exposure to the route, while the recognition and ordering of landmarks is vastly compromised. In the diagnostic phase of KS, this indicates that instead of focusing on performance on neuropsychological tests for long-term memory to predict route learning, it is relevant to actually test the ability to remember routes in patients with KS. Currently, numerous patients with KS are placed in closed long-term care facilities without the opportunity to leave the clinic, while current evidence indicates that patients with KS might be able to learn new routes despite their global amnesia.

It is likely that the basal ganglia contributed to acquisition of preserved route learning in KS. Recent studies show that the basal ganglia are of critical importance for acquisition of contextual information from our surroundings without conscious awareness, since patients with Parkinson's disease or Huntington's disease show no evidence for implicit contextual learning, while this form of learning is intact in KS (Oudman *et al.*, 2011; Van Asselen *et al.*, 2009; van Asselen *et al.*, 2012). Neurological damage in KS is found in the diencephalic structures of the brain (Kopelman, 2002). It is, therefore, likely that damage to these brain structures contributed significantly to the severely hampered performance on explicit measures of route learning.

In the current experiment, task performance on the landmark recognition task was low in KS patients and healthy controls. We assume that buildings in the environment did not differ much in saliency, contributing to this poor performance on landmark recognition.

There are some methodological considerations that have to be taken into account in the interpretation of the present findings. In the experiment, we did not want to give any cue to the participants in the incidental condition about the true aim of the study, so we chose not to measure time or walking speed. The experimenter tried to keep a standard walking gait for all participants, which was practiced before the experiment took place. We assume that by keeping a standard walking gait there were minimal differences in walking speed between groups that could not explain the large task performance differences between groups.

For practical reasons we chose to perform the route learning task in the neighbourhood of the institute. None of the patients or control participants mentioned familiarity with the residential area after explicitly being asked by the experimenter (admittedly there is a high chance that patients would have forgotten if they had). We can be confident that familiarity with the environment was limited in the patients, since it is the institute's policy to not allow outside exploration without specific authorization to do so.

It could be argued that the number of patients in this study is relatively small, having negative implications for the statistical power in the experiment. We would like to stress that the number of participants in this study does not differ from earlier studies on spatial navigation (e.g., Van Asselen *et al.*, 2006). In a recent review on implicit learning KS only a small minority of studies included more than 10 KS patients (Hayes *et al.*, 2012). We suggest that our results require replication in larger samples of KS patients. Moreover, the results of the current study limit to the specific group of KS patients as a recent study suggests that acquisition during spatial navigation is compromised to a larger extent in dementia (Kessels, van Doormaal, & Janzen, 2011).

In conclusion, the results of the present study indicate that KS patients could acquire spatial information during spatial navigation, although task performance is generally deteriorated compared to healthy controls. Distance estimations of the route are intact and performance on time estimations of the route, map drawing task and route walking task were better than chance levels. Acquisition of spatial material in KS was irrespective of the intention to learn. The current study suggests that despite the presence of amnesia, patients with KS have a residual memory potential to acquire spatial information during spatial navigation.

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