



Intact memory for implicit contextual information in Korsakoff's amnesia

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ABSTRACT

Implicit contextual learning is the ability to acquire contextual information from our surroundings without conscious awareness. Such contextual information facilitates the localization of objects in space. In a typical implicit contextual learning paradigm, subjects need to find a target among a number of distractors during visual search. Some of the configurations of stimuli are repeated during the experiment resulting in faster responses than for novel configurations, without subjects being aware of their repetition. Patients with Korsakoff's syndrome (KS) have been found to show devastating explicit spatial memory. Less is known about their implicit spatial memory abilities. The aim of the present research was to examine whether implicit contextual learning is intact in KS. Therefore, eighteen KS patients and twenty-two age-IQ- and education-matched controls performed the Implicit Contextual Learning task and a paradigm intended to assess explicit, spatial working memory, i.e. the Box task. Intact implicit contextual learning was observed in both the control group and the KS patients. In turn KS patients did have markedly lower explicit spatial working memory scores. The implicit learning effect was not related to the spatial working memory scores. Together these results clearly suggest that implicit and explicit spatial memory have a different neurocognitive basis.

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1. Introduction

Korsakoff's syndrome (KS) is a chronic disorder often caused by severe alcoholism in combination with thiamine (vitamin B₁) deficiency leading to diencephalic, frontal and hippocampal brain damage. The disorder is characterized by severe anterograde and to a lesser extent retrograde amnesia for declarative knowledge (Fujiwara, Brand, Borsutzky, Steingass, & Markowitsch, 2008; Kopelman, 1995, 2002; Paller et al., 1997; Squire, 1982). Although the amnesia in KS patients affects all subdomains of explicit memory, there is evidence that these patients have even more pronounced problems in remembering contextual information, such as spatial memory for coordinate (exact locations of objects in space) as well as categorical (relative) object to location binding (Chalfonte, Verfaellie, Johnson, & Reiss, 1996; Kessels, Postma, Wester, & de Haan, 2000), allocentric (object-to-object relation) and egocentric (self-to-object relation) spatial memory (Holdstock, Mayes, Cezayirli, Aggleton, & Robbins, 1999) and form-

ing associations between temporal order (moment) information and spatial information (Postma, Van Asselen, Keuper, Wester, & Kessels, 2006).

Most of the foregoing studies assessed explicit or conscious memory. However, it is currently unclear whether implicit memory is intact in KS. On the one hand, there is ample evidence for spared implicit memory in verbal repetition priming (Cermak, Verfaellie, Milberg, Letourneau, & Blackford, 1991; Graf, Shimamura, & Squire, 1985), perceptual priming (d'Ydewalle & Van Damme, 2007), motor sequence learning (Nissen, Willingham, & Hartman, 1989) or procedural learning (Fama, Pfefferbaum, & Sullivan, 2006) in KS. On the other hand, some studies did find that conceptually-driven implicit memory was hampered (Brunfaut & d'Ydewalle, 1996), perceptual priming for picture-fragment completion was impaired (Verfaellie, Gabrieli, Vaidya, Croce, & Reminger, 1996), sequence learning is compromised when there is a strong spatial component (Van Tilborg, Kessels, Kruijt, Wester, & Hulstijn, in press), or suggested that intact procedural memory is the result of enhanced instructions rather than intact implicit memory processes (Swinen, Puttemans, & Lamote, 2004). In the latter study procedural learning did not occur in KS without augmented feedback information being present during the learning process.

The present study investigated whether one aspect of implicit memory, namely implicit *spatial* memory, is intact in KS. In daily

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lives, people often make use of implicit spatial memory. We may automatically take the right turn even without having a clear sense where to go. Moreover, we may start searching in the right direction for a hidden object without a conscious place memory. Following the context-memory deficit hypothesis, all facets of the memory for the moment and place an event occurs are thought to be disproportionately disturbed in KS compared to the memory itself (Mayes, Meudell, & MacDonald, 1991), which suggests that implicit spatial memory is hampered in KS. Supportive for this hypothesis was a study by Verfaellie, Milberg, Cermak, and Letourneau (1992) suggesting that KS patients are less able to make use of implicit spatial memory than healthy controls if the test material could not be verbalized.

Conversely, a study by Postma, Antonides, Wester, and Kessels (2008) showed that during an object-location memory task, KS patients demonstrated stronger unconscious influence of previously shown spatial configurations on subsequent trials compared to healthy controls, whereas KS patients performed substantially worse on conscious object-location memory.

Given these inconsistent findings with respect to implicit spatial memory in KS, we aimed to investigate whether patients with from KS are able to implicitly learn spatial regularities despite their diffuse memory impairments. The present study adopted the implicit contextual learning paradigm (Chun, 2000; Chun & Jiang, 1998). In this visual search task a target (T) has to be located among a number of distractors (L). Subjects have to indicate whether the target is rotated to the left or the right. In each session, a set of arbitrary visual contexts are generated by manipulating the spatial configuration of the target and distractors. After training, the target is found faster when configurations are repeated than novel configurations, referred to as implicit contextual learning (Chun, 2000; Chun & Jiang, 1998). This implicit aspect of this learning is supported by an awareness check, that is, when explicit recognition is tested after contextual learning, participants perform at chance level. Furthermore, when subjects were asked whether or not they observed that some contexts were repeated throughout the task, they were unaware of this (Chun & Jiang, 1998). The explanation for the learning effect is that contextual information, such as the positions of objects with respect to each other, can be used to guide our attention to a specific location after repeated rehearsal even without reaching conscious awareness. Implicit contextual learning can already be obtained after 5 or 6 repetitions, indicating that it is a fast effect (Chun & Jiang, 2003). Moreover, the effect can be also observed 1 week after the initial learning phase, indicating it remains in memory for a long period of time (Jiang, Song, & Rigas, 2005).

In order to further examine the interrelations between the implicit context learning task to a more explicit spatial memory we included a spatial working memory test which also has a search component: the Box task. The Box task requires participants to search for objects that are hidden in different boxes that are shown on a screen (Feigenbaum, Polkey, & Morris, 1996; Morris, Evenden, Sahakian, & Robbins, 1987; Van Asselen, Kessels, Wester, & Postma, 2005). It requires participants to keep spatial information in memory both over a very short time period (i.e., keeping it 'on-line') and a more extended time range (possibly marking the transfer from working memory into long term memory). By combining evidence on both an implicit and an explicit spatial tasks we wanted to elucidate possible communalities in neurocognitive basis.

2. Methods for the implicit contextual learning task

2.1. Participants

Twenty-six patients diagnosed with Korsakoff's syndrome participated in this study (18 males). They were all inpatients of the

Korsakoff clinic of the Psychiatric Hospital 'Vincent van Gogh', Venray, The Netherlands. Two male patients were excluded from analysis after dropping out during testing because of motivational problems. For all patients, the current intelligence level of each participant had to be in concordance with the estimation of premorbid functioning based on occupational and educational history to exclude cases of dementia (Oslin, Atkinson, Smith, & Hendrie, 1998). Two patients (1 male) with estimated IQ scores below 80 were excluded because of low intellectual functioning interfering with the testing procedure, possibly caused by alcohol dementia. Also, two patients (1 male) with disproportionate hippocampal atrophy and two patients (2 male) with additional brain infarctions were excluded.

The remaining eighteen patients (12 male) and twenty-two (13 male) age-, premorbid IQ and education matched controls were included in the analysis. All patients fulfilled the DSM-IV criteria for alcohol-induced persisting amnesic disorder (American Psychiatric Association, 2000) and the criteria for Korsakoff's syndrome described by Kopelman (2002). The amnesic syndrome was confirmed by extensive neuropsychological testing. All patients were in the chronic, amnesic stage of the syndrome, none of the patients was in the confusional Wernicke psychosis at the moment of testing. Neuroradiological examination (Magnetic Resonance Imaging for 13 participants and Computed Tomography for 4 participant) showed signs of brain atrophy and nonspecific white-matter lesions in most patients, which are often found in KS but not a necessary criterion for the diagnosis (Kopelman, 2002). No brain abnormalities were found that are at odds with the diagnosis KS (i.e., stroke, tumor). Patients had an extensive history of alcoholism and nutritional depletion, notably thiamine deficiency, verified through medical charts or family reports (see Table 1).

All participants were administered the Dutch version of the California Verbal Learning Test (a task measuring verbal immediate and long-term memory) and scored within the first to the fifteenth percentile on the total number of List A words recalled in Trials 1–5 (standardized for age and gender). For all eighteen patients assessed with the Rivermead Behavioural Memory Task, a moderate to serious disturbance on daily memory was found (Wilson, Cockburn, & Baddeley, 1985). All participants had severe explicit memory deficits (see Table 2) as measured with the California Verbal Learning Test (CVLT) and the Rivermead Behavioural Memory Test (RBMT). Additionally, patients had intact visuospatial short-term memory span, as measured with the Corsi Block-Tapping Test (forward). The Corsi Block-Tapping Task is a standardized span task and a visuospatial analogue to the digit span as an index of verbal short-term memory (Kessels et al., 2000; Kopelman, 1991).

For both the patients and the control group education level was assessed using seven categories, 1 being the lowest (less than primary school) and 7 being the highest (academic degree) (Verhage, 1964). These categories were converted to the internationally applied classification using years of education (Hochstenbach, Mulder, Van Limbeck, Donders, & Schoonderwaldt, 1998). Premorbid IQ was estimated with the Dutch Adult Reading Test (Schmand, Lindeboom, & van Jarskamp, 1992). For all participants, handedness was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971). The study was approved by the Institutional Review Board and written informed consent was obtained in all patients. Table 2 shows a summary of demographic variables, neuropsychological test results and radiological findings for all patients.

2.2. Procedure

2.2.1. Equipment and stimuli for the implicit contextual learning task

For the implicit contextual learning paradigm the software package Presentation (Neurobehavioral Systems) was used to

Table 1
Summary of demographic variables for all participants.

Measurement	Patients	Controls	Significance
Number (number of males)	18 (12)	22 (13)	$\chi^2(1) = 0.57, p = 0.45$
Handedness (R:L:R&L) ^a	14:3:1	19:2:1	$\chi^2(2) = 1.01, p = 0.60$
Educational level μ (SD) ^b	4.5 (0.8)	4.6 (0.9)	$U(38) = 0.85, p = 0.44$
Years of education μ (SD) ^c	10.1 (2.0)	10.2 (1.9)	$t(38) = 0.20, p = 0.84$
IQ estimation mean (SD) ^d	98.1 (8.5)	102.1 (8.3)	$t(38) = 1.51, p = 0.14$

^a Handedness was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971).

^b Educational level was assessed in 7 categories: 1, primary school; 7, academic degree (Verhage, 1964).

^c Years of education were calculated based on the years of education corresponding to the Dutch educational level (Hochstenbach et al., 1998).

^d IQ was estimated with the Dutch Adult Reading Test (Schmand et al., 1992).

present the visual search task. Eleven distractor stimuli (L) and one target stimulus (T) were presented each trial. The color of all stimuli was white on a grey background. The distractor stimuli were created to make them look similar to the target stimulus (see Fig. 1). The stimulus size was $0.92^\circ \times 0.92^\circ$. Target location was balanced for distance from the screen's center and screen half (left/right). Distractor stimuli could be rotated 0° , 90° , 180° , 270° and the target stimulus could be rotated 90° or 270° . The direction of rotation of the target stimulus was randomly defined, in order to prevent subjects from learning fixed stimulus–response associations. Target position were generated by randomly placing 11 distractors and 1 target in an invisible grid of 12 rows \times 12 columns (144 possible positions), with individual points separated by 2.3° .

2.2.2. Procedure for the implicit contextual learning task

Participants were seated in a comfortable chair in front of the computer screen in a semi-darkened room. The computer screen was positioned 50 cm in front of the participant.

The instructions were visually presented on the screen. Participants were instructed to locate a target stimulus as quickly as possible and indicate its orientation by pressing one out of two identical orientations on a button box, developed for experimental testing (see Fig. 1). In the center of the screen, a short instruction was presented before each trial during 1250 ms. Each block consisted of 24 trials, including 12 trials with a new configuration and 12 trials with a configuration that was repeated throughout the experiment (once in every block). Target position in both repeated and new trials were randomly defined from the same set of positions. Only the positions of the items in the repeated configuration were constant. The participant had to press a button to start the practice phase. During practice, 24 trials were given, including only new spatial configurations. If participant did not understand the task after the practice session, or was still making many errors, the practice trials were repeated until a full understanding of the procedure was established. After practice the experiment started with instructions on the computer screen. 16 Blocks were presented on

Table 2
Demographic variables, neuropsychological test results, and radiological finding of the Korsakoff's patients.

Patient	Gender	Age	Handedness ^a	Education ^b	IQ ^c	Verbal learning ^d	RBMT ^e	Spatial Span ^f	Radiological findings ^g
1	M	62	Right	3	94	<1	8	5	Diffuse WML and mild degeneration MB*
2	F	47	Right	4	95	1–5	7	5	Mild WML*
3	F	44	Right	5	92	<1	7	5	Mild degeneration MB*
4	M	48	Right	5	101	<1	4	5	Mild diffuse cortical atrophy*
5	M	46	Bidextral	5	103	5–15	17	4	Cortical atrophy; degeneration diencephalon including MB*
6	F	42	Left	4	81	<1	8	5	Mild cortical and cerebellar atrophy, degeneration of MB*
7	M	47	Left	6	107	5–15	8	7	Degeneration of MB*
8	M	57	Right	6	115	1–5	8	7	No abnormalities*
9	M	53	Right	4	105	<1	5	6	Cortical atrophy and mild degeneration of MB*
10	M	61	Right	4	104	<1	2	6	Cortical and cerebellar atrophy**
11	F	61	Right	3	94	<1	3	5	Mild frontal WML; mild degeneration of MB*
12	M	57	Right	5	97	<1	1	5	Diffuse cortical atrophy**
13	M	59	Right	4	87	<1	12	4	No abnormalities**
14	F	50	Right	4	88	<1	4	N.A.	No abnormalities**
15	M	62	Right	4	97	<1	6	5	WML; degeneration of MB*
16	F	51	Left	5	109	<1	4	5	Mild cerebellar atrophy, mild degeneration of MB*
17	M	49	Right	4	102	5–15	2	5	N.A.
18	M	64	Right	5	95	5–15	2	N.A.	Mild cortical atrophy*
		$M = 53.3$ $SD = 7.1$		$M = 4.4$ $SD = 0.9$	$M = 98.1$ $SD = 8.5$				

N.A., not available; Education, education level; RBMT, Rivermead Behavioural Memory Test; WML, white-matter lesions; MB, mammillary bodies.

^a Handedness was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971).

^b Education level, was scored using 7 categories: 1, lowest (less than primary school); 7, highest (university degree) (Verhage, 1964).

^c IQ was estimated with the Dutch Adult Reading Test (Schmand et al., 1992).

^d Percentile scores for the total performance on the first five learning trials, measured with the Dutch version of the California Verbal Learning Test, for measurement of long-term memory (Mulder, Dekker, & Dekker, 1996).

^e Raw scores. Memory test for everyday memory. <10, severely impaired, 10–15, moderately impaired, 16–21, mildly impaired (Van Balen & Wimmers, 1992).

^f Corsi Block-Tapping Test forward span, reflecting visuospatial memory (Kessels et al., 2000).

^g Neuroradiological examination by magnetic resonance imaging (MRI) scan* or CT scan**.

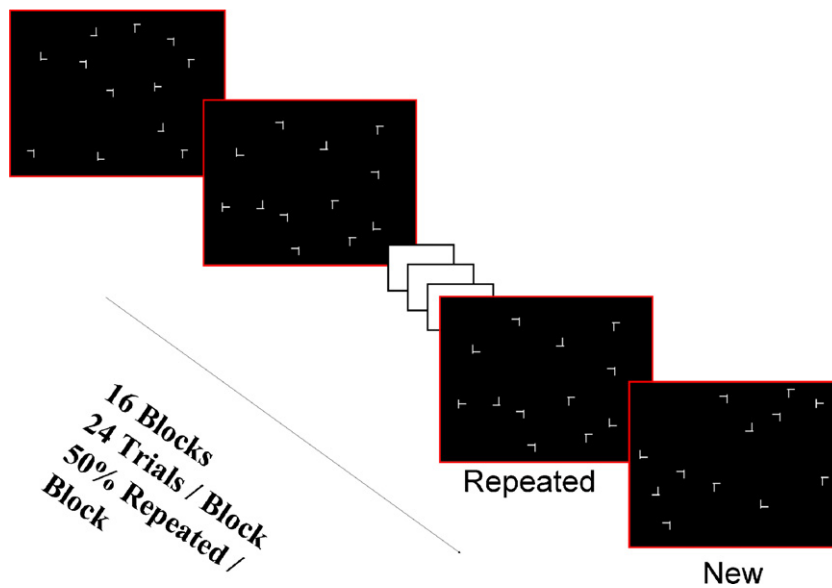


Fig. 1. Example of a display in the implicit contextual learning task. 50% of the configurations were repeated throughout the experiment and 50% were randomly generated.

the screen. After each block a 10 s interval was given to assure a short rest after each block. Moreover, instructions were repeated after the interval to assure the goal of the task to be known. Subjects could manually continue the experiment by pressing the button with the left orientation.

Immediately after finishing the task, an awareness check was performed by asking all participants the following three questions: (1) 'Did you notice anything during the experiment?' (2) 'Did you notice that some of the configurations were repeated?' (3) 'Did you try to remember the repeated configurations?' Finally, in order to verify whether context information was memorized implicitly, a Recognition memory control task was applied. This task consisted of 24 trials, including the 12 configurations that were repeated during the contextual cueing task and 12 new configurations. Repeated and new configurations were presented in a random order and participants were instructed to indicate whether the configuration was repeated during the experiment by pressing "yes" or "no" on the button box.

2.2.3. Procedure for the Box task

For the Box task, pictures of closed boxes were displayed on different locations within a square of $28.5^\circ \times 29.7^\circ$ on a 15 in. touch-sensitive LCD computer monitor (ELO AccuTouch, 2001). Each trial (see Fig. 2), a colored target object (e.g. apple, clock) was presented in icon-format ($\pm 1.6^\circ$ by 1.6°). Participants were instructed to find the target object, which was hidden in one of the white boxes ($\pm 1.6^\circ$ by 1.6° cm). By touching them, the boxes could be opened, after which an empty box or the target object was shown. Empty boxes remained open for two seconds, while the target was shown until the participant initiated a new search for a new target object. This new object was shown after the participants pressed a 'Start' button on the screen. Importantly, a target object that was found remained in the box and was the only object that could be located in that box. In the search for a new target object participants had to remember which object was previously filled with an object, because this object remained in this box. After locating objects in all boxes shown on the screen a new set of boxes was presented. The task began with two practice trials of three boxes, after which two trials of four, six, eight and ten boxes were used (see Kessels, Meulenbroek, Fernandez, & Olde Rikkert, 2010; Van Asselen et al., 2005, for a more detailed description of the task). No time limit was set.

2.3. Analysis

2.3.1. Analysis for the implicit contextual learning task

The total implicit contextual learning task consisted of 16 blocks. Before analysis, all response times longer than 20 s were removed as outliers. Furthermore, trials in which an error was made were excluded from the analyses on implicit contextual learning as well as trials with a response time longer than 2 SD above the individual mean (Barnett & Lewis, 1994). For statistical analysis, the blocks were collapsed into 4 epochs of 4 blocks each. In line with previous patient studies and the original report of implicit contextual learning, we only used the second half of the experiment for statistical analysis (Chun & Jiang, 1998; Chun & Phelps, 1999; Manns & Squire, 2001; Van Asselen et al., 2009). For the implicit contextual learning task a $2 \times 2 \times 2$ repeated measures ANOVA with 'epoch' (epoch 3 and 4) and 'type' (repeated and novel configurations) as within-factors and 'group' (patients and control participants) as between-factor was performed. The main variable of interest was the interaction between the contextual learning effect (factor 'type') and both groups (patients and controls). To quantify the results of the statistical analysis, contextual learning was measured as the difference in reaction times between repeated and novel items.

2.3.2. Analysis for the Box task

Set size is defined as the total number of boxes. For a set size of 4, 4 objects need to be located in separate boxes. One search is defined as the boxes that a participant needs to open to locate one object in the presented boxes. A trial is defined as all searches for one set size.

Three types of measures were defined (Van Asselen et al., 2005):

- (1) Within-search errors were made when a participant returned to an already opened box within one search. The number of within-search errors was calculated by accumulating the total number of within-search errors per set size.
- (2) Between-search errors were made when a participant returned to a box where a target object was found in one of the previous searches. The total number of between-search errors was calculated by accumulating the total number of between-search errors per set size.

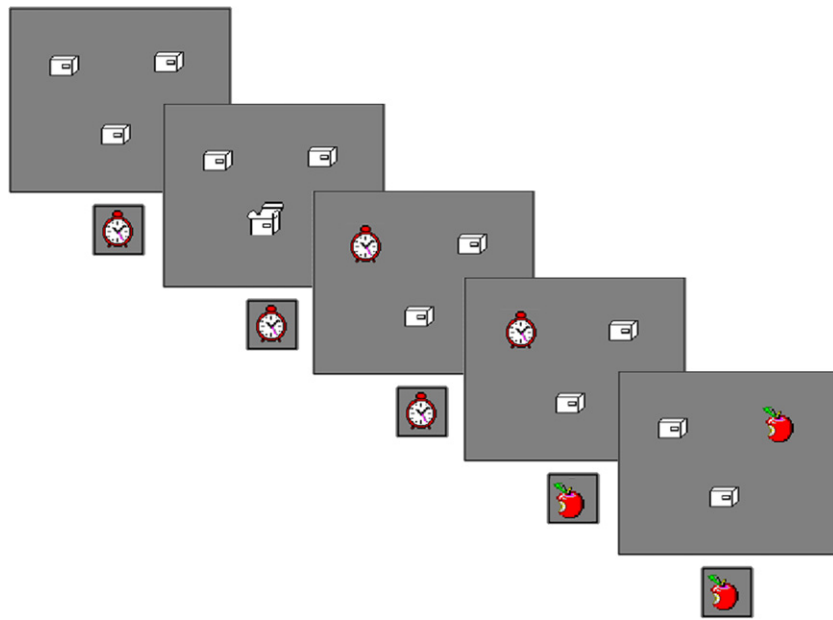


Fig. 2. Example of a search display in the Box task for a search through three boxes. Two target objects (clock, apple) are presented. In the fourth picture, an error trial is illustrated.

Both measures were analyzed separately by means of a 2×4 repeated measures ANOVA including the between-subject factor 'group' (patients and control participants) and the within-subject factor 'set size' (4, 6, 8, 10 boxes). Three 2×2 repeated measures ANOVA were performed to calculate differences for the transitions between the within-subjects factor 'set size' (4 and 6; 6 and 8; 8 and 10) and the between-subject factor 'group' (patients and control participants).

2.3.3. Correlational analysis

Pearson's correlation coefficients (r , two-tailed) were calculated for the average search times on novel items in the implicit contextual learning task and the total numbers of between-errors and within-errors in the Box task to investigate the relationship between spatial working memory and contextual learning. Pearson's r was also computed for the contextual learning effect, calculated as the total difference between the reaction times on repeated and novel items in the implicit contextual learning task, and the between-errors and within-errors in the Box task to elucidate a possible relationship between search efficiency and spatial working memory.

3. Results

3.1. Results for the implicit contextual learning task

3.1.1. Implicit contextual learning

Fig. 3 depicts the average reaction times per epoch for new and repeated items in the implicit contextual learning task in patients and controls. Although both KS patients and controls made a small number of errors, patients made significantly more errors than controls (patients: 3.2% (SD=2.7%), controls: 0.6% (SD=0.6%), $t(38)=4.2$, $p<0.001$). Furthermore, few trials were excluded because of delayed response (patients: 4.0% (SD=0.9%), controls: 4.0% (SD=0.7%)).

A significant main effect for stimulus type was found [$F(1,38)=18.7$, $p<0.001$], indicating that reaction times were faster on repeated items compared to new items. Furthermore, an effect of epoch was determined [$F(1,38)=9.4$, $p<0.01$], indicating that reaction times in the last epoch were faster than reaction times in

the third epoch. Moreover, a group effect [$F(1,38)=13.5$, $p<0.001$] was found, indicating that overall patients were slower than controls. Importantly, the group \times type interaction was not significant [$F(1,38)=0.17$, $p=0.69$], which shows that implicit contextual learning in the KS patient group was not different from implicit contextual learning in the control group. For patients an average contextual learning of 137.1 ms was found (SD=253.6), while for control subjects this was 165.7 ms (SD=188.9). Furthermore, the type \times epoch interaction was not significant [$F(1,38)=0.02$, $p=0.88$], indicating that for epoch 3 the difference in response times between repeated and new were identical for epoch 4. Also, the type \times epoch \times group interaction was not significant [$F(1,38)=0.03$, $p=0.86$], showing that both patients and controls showed no relative difference in reaction times on epoch 3 and 4 for repeated and novel items.

In light of the slower visual search in the KS patient group relative to the control group, we determined whether differences

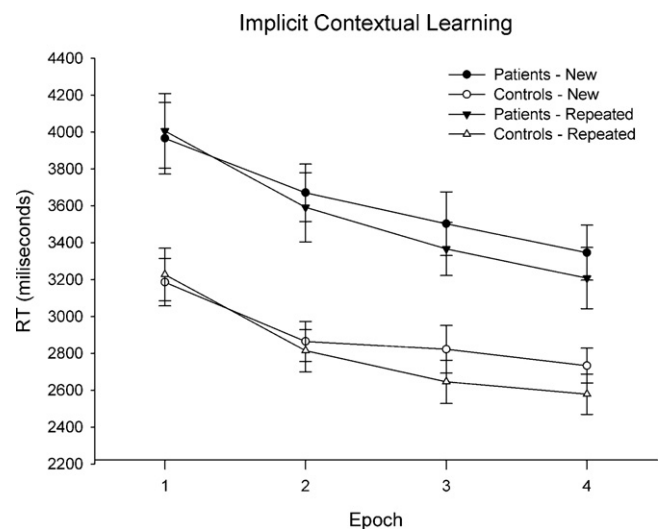


Fig. 3. Mean reaction times (RT) in milliseconds (ms) for the Repeated and New trials as a function of Epoch (1–4) for Korsakoff's syndrome patients ($n=18$) and the control group ($n=22$). Error bars indicate standard error of the mean.

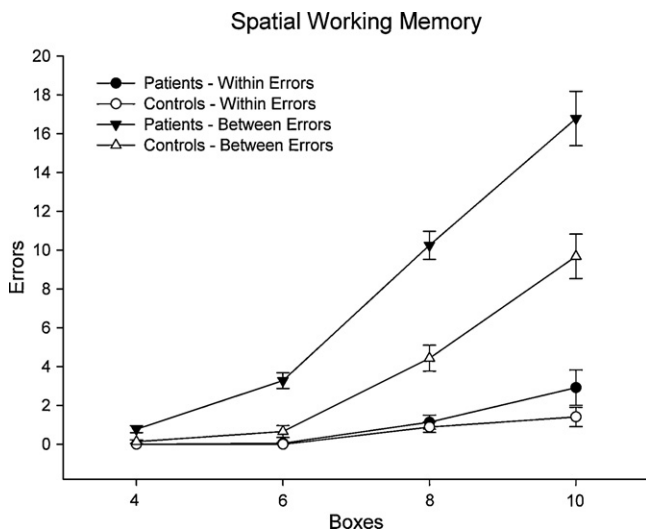


Fig. 4. Average number of within- and between-search errors (set sizes 4, 6, 8, and 10) for Korsakoff's syndrome patients ($n = 22$) and the control participants ($n = 18$). Error bars indicate standard error of the mean.

in the magnitude of learning was apparent on a measure that equated speed by expressing learning as a proportion of one's baseline speed (i.e., novel-repeated/novel, calculated per epoch; see Barnes et al., 2008 for a more detailed description of the procedure). Proportional learning scores computed for each participant were analyzed in a group \times epoch ANOVA. The main effect of group [$F(1,38) = 0.84, p = 0.37$] and the group \times epoch interaction [$F(1,38) = 0.146, p = 0.71$] were not significant, indicating that measures of proportional learning did not differ between the KS patient group and the control group. For patients an average proportional contextual learning of 3.8% (SD = 7.1%) was found, while for control subjects this was 5.7% (SD = 6.5%).

3.1.2. Recognition memory

None of the participants reported to have noticed the repeated configurations spontaneously, and no participant reported this after being explicitly asked. Importantly, explicit recognition of repeated configurations was not above chance level for both the patient and control group (patients: 50.2% (SD = 8.9) pooled hits and correct rejections, [$t(17) = 0.1, p = 0.91$], controls: 51.4% (SD = 9.9) pooled hits and correct rejections [$t(21) = 0.7, p = 0.52$]). This indicates that the observed learning effect is not the result of explicit knowledge of the location of the target. Moreover, the percentage of hits during the recognition task was not significantly different between both groups [patients: 47.2% (SD = 27.8%), controls 42.7% (SD = 28.7%), $t(38) = 0.5, p = 0.62$], neither was the number of false alarms [patients: 46.8% (SD = 23.9%), controls 40.8% (SD = 27.9%), $t(42) = 0.7, p = 0.48$], indicating that both patients and controls do not show explicit recognition to the same extent.

3.2. Results for the Box task

3.2.1. Within-search errors

Relatively few within-search errors were made by the patient and control group in absolute terms (see Fig. 4). Patients did not make more within errors than controls [$F(1,38) = 2.5, p = 0.13$]. A main effect was found for set size [$F(3,114) = 16.3, p < 0.001$]. Post hoc testing indicate that more errors were made in the condition with ten boxes than eight boxes [$F(1,38) = 5.9, p < 0.05$], eight than six boxes [$F(1,38) = 23.1, p < 0.001$], but not six than four boxes [$F(1,38) = 2.6, p = 0.11$]. However, the group \times set size interaction

was not significant [$F(3,114) = 1.9, p = 0.12$] indicating that both groups performed identical for all set sizes.

3.2.2. Between-search errors

KS patients made more between-search errors than control participants [$F(1,38) = 38.2, p < 0.001$]. A main effect was found for set size [$F(3,114) = 123.4, p < 0.001$]. Post hoc tests (see Fig. 4) indicated that more errors were made in the condition with ten boxes than eight boxes [$F(1,38) = 32.1, p < 0.001$], eight than six boxes [$F(1,38) = 129.4, p < 0.001$], and six than four boxes [$F(1,38) = 47.2, p < 0.001$]. The group \times set size interaction was significant [$F(3,114) = 7.9, p < 0.001$]. Post hoc tests indicate that KS patients were more impaired than controls for the transition from four to six boxes [$F(1,38) = 20.2, p < 0.001$] and six to eight boxes [$F(1,38) = 11.5, p < 0.005$], but not for eight to ten boxes [$F(1,38) = 0.4, p = 0.54$].

4. Correlational analysis between the implicit contextual learning paradigm and the Box task

The average search times on new, unrepeated items of the implicit contextual learning paradigm was positively correlated with the total number of between-search errors [$r(39) = 0.47, p < 0.005$], indicating that there is a moderate relationship between speed of processing in the implicit contextual learning task and number of errors on explicit spatial working memory in the Box task. However, the implicit contextual learning effect showed no relation with between-search errors [$r(39) = -0.07, p = 0.67$], suggesting that implicit contextual learning is dissociable from explicit spatial working memory as measured by the Box task. The average search times on new items of the implicit contextual learning paradigm did not significantly correlate with the total number of within-search errors [$r(39) = 0.10, p = 0.55$], neither did implicit contextual learning [$r(39) = -0.22, p = 0.18$]. This suggests that short-span spatial working memory is not related to search efficiency or implicit contextual learning.

5. Discussion

The aim of this study was to investigate whether patients with Korsakoff's syndrome (KS) are able to implicitly learn spatial regularities despite marked problems with regard to conscious memory operations. In order to further examine the interrelations between implicit and explicit spatial memory influences we directly compared performance on an implicit spatial memory task to spatial working memory scores in KS. The results of the present study indicate that individuals with Korsakoff's syndrome (KS) show intact ability to acquire contextual information from our environment after repeated presentation without conscious awareness. This is in contrast with the severely impaired spatial working memory performance in KS as measured by the between-search errors in the Box task. This underscores that implicit spatial learning and conscious spatial memory have a different neurocognitive basis. In line with this we observed no correlation between the Box task performance and the Implicit context learning. Interestingly, average search times on new items in the implicit contextual learning paradigm showed a negative correlation with performance on the Box task. This suggest that general search efficiency is related to working memory, whereas implicit contextual learning is not.

The results of this study are in line with previous observations of intact unconscious influence on spatial memory in KS (Postma et al., 2008) and support several other studies on verbal and procedural implicit memory in KS reporting intact implicit memory (Cermak et al., 1991; d'Ydewalle & Van Damme, 2007; Fama et al.,

2006; Graf et al., 1985; Verfaellie et al., 1996). Conversely, an important difference between previous studies on implicit learning and the current study is the fact that implicit contextual learning is not based on the association between perception and motor responses, or verbal material, but is a pure and direct measure of implicit spatial memory (Chun, 2000; Van Asselen et al., 2009). The results of this study contradict evidence for diminished implicit memory in KS (e.g. Brunfaut & d'Ydewalle, 1996; Verfaellie et al., 1992) or suggestions that implicit memory in KS is merely the result of enhanced instructions (Swinnen et al., 2004) or findings of relatively diminished implicit spatial memory in KS (Van Tilborg et al., in press; Verfaellie et al., 1992). Moreover, the results of our study indicate that not all individuals with amnesia experience impaired implicit spatial learning. Previous research on amnesic patients with medial temporal lobe amnesia showed no implicit spatial memory after rehearsal (Chun & Phelps, 1999). Manns and Squire (2001) suggested that more extensive damage to the temporal lobe is crucial to find diminished implicit spatial learning.

One of the strengths of the current study compared to earlier studies on implicit memory in KS is the relatively large sample size of KS patients ($n=18$) that have been recruited for this study. While recent studies indicative of intact implicit memory in KS recruited groups with comparable size (d'Ydewalle & Van Damme, 2007; Postma et al., 2008), earlier evidence was sometimes based on very small groups with limited power. Since most reports on disturbed implicit memory in KS have sample sizes smaller than ten patients (Brunfaut & d'Ydewalle, 1996; Swinnen et al., 2004; Verfaellie et al., 1992), these studies are more vulnerable to random sample variations affecting the conclusions of the studies. However, divergent observations on implicit memory performance in amnestics in the literature possibly also indicates that the presence or absence of difference with healthy volunteers depends on the type of task that is used and the sub-form of implicit memory that is being studied (Ostergaard, 1999; Postma et al., 2008; Van Tilborg et al., in press). Moreover, previous studies applied various types of implicit contextual learning paradigms that varied greatly with respect to number and type of trials. Systematic and direct comparison of different implicit learning paradigms may shed light onto some of the discrepancies. Therefore, this question warrants investigation in future studies.

The results on the Box task replicate and extend earlier results reported for KS patients (Van Asselen et al., 2005). The profile for within-search errors followed a comparable pattern in the current research and the original report. However, the number of within-search errors did not differ between the KS patients and controls, while in the original study by van Asselen and colleagues (2005) a significant difference was obtained also for the within-search errors, albeit that absolute differences and effect sizes were small. This discrepancy possibly relates to subtle differences between both studies; such as higher educational levels for the current patient group and somewhat more stringent inclusion criteria for the current study (e.g. $IQ > 80$, to exclude possible cases of alcohol dementia). Although it could be expected to find more within-search errors for higher working memory loads in the KS patient group compared to controls, no such relationship became clear. Nevertheless, between-search errors, indicative of elaborated processing in spatial working memory, become progressively more prominent in KS with higher working memory loads. Importantly, in order to avoid between-search errors in the box task, spatial information has to be kept in memory over a longer time period, whereas the Corsi Block Tapping task requires spatial information to be kept in memory over a very short time period (Van Asselen, Kessels, Neggers, Kappelle, Frijns, & Postma, 2006). This possibly explains why all patients had intact visuospatial short-term memory span (Table 2) while more between-search errors

became evident in the box task. The pattern of errors of the current study indicate that spatial working memory is hampered in KS, but specifically the transition of information from short span to middle long span is affected, reflected by the significant problems during between-search.

Previous research has indicated that specifically damage to both the right dorsolateral prefrontal cortex and right posterior parietal cortex was correlated with the number of between-search errors in stroke patients during a comparable Box task as applied in our study (Van Asselen et al., 2006). The results of the current study appear to be in line with this finding, since KS is known to damage the prefrontal cortices (e.g. Kopelman, Thomson, Guerrini, & Marshall, 2009). However, we should be cautious with respect to relating our findings to the specific lesion locations, since the lesions in Korsakoff patients are not limited to the prefrontal cortex or the diencephalon (see also Table 2).

Recent evidence shows that the basal ganglia are of critical importance for implicit contextual learning, since both patients with Parkinson's disease or Huntington's disease show no evidence for intact implicit contextual learning (Van Asselen et al., 2009, 2010). Although the aim of the current study was not to unravel the underlying neural structures in detail, previous neuroimaging studies found evidence for damage to the dorsomedial thalamus and mammillary bodies in KS patients. The results of our study therefore stress the importance of differentiating between subcortical structures underlying memory functions, since KS is profoundly known for its diencephalic disturbance, but not the basal ganglia (Kopelman, 1995; Sullivan & Pfefferbaum, 2009).

6. Conclusion

In conclusion, this study has demonstrated that individuals with Korsakoff's syndrome (KS) show intact ability to acquire contextual information from the environment after repeated presentation without conscious awareness. They do so to the same degree as matched healthy controls. This implicit contextual learning was found to be unrelated to spatial working memory performance, whereas general search times on new items were related to implicit contextual learning. This suggests that intact implicit contextual learning in KS is not directly related to spatial working memory. Together these results suggest that implicit and explicit spatial memory have a different neurocognitive basis. Moreover, this study suggests that a clear distinction can be made between damaged implicit contextual learning in Parkinson's and Huntington's disease after subcortical damage to the basal ganglia, compared to subcortical damage in KS.

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