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Subtle object location perception deficits in Korsakoff's syndrome

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ABSTRACT

(Wernicke-)Korsakoff's syndrome (KS) is a neuropsychiatric syndrome, caused by vitamin B1 (thiamine) deficiency often resulting from chronic alcohol consumption. KS is characterized by severe cognitive problems, such as impaired explicit memory and executive functions. Visuospatial perception (VSP) refers to the identification of objects (object perception), and the localization of objects (space perception). Object perception can be described as the cooperation between visual representation and semantic information on the objects' functional properties. Space perception is the mental representation of visual space and objects within it from a more or less fixed view point. Although VSP is fundamental to everyday functioning and higher order cognitive functions, little knowledge is available on VSP in KS. The aim of the present study was therefore to investigate VSP in KS. Fifteen KS patients and 15 healthy controls performed the Visual Object and Space Perception battery (VOSP) for visuospatial functioning. Results show a selectively reduced performance of KS patients on object perception, but not on space perception tasks. Specifically, subclinical problems in the identification of degraded and atypical positioned objects were present in KS, and not related to general cognitive functioning. These results suggest that the thalamic nucleus, a brain circuit most typically damaged in KS, is critically involved in object integration. Moreover, this relative new perspective on VSP related to KS warrants further research on the neuropsychological evaluation of KS to index possible mild deficits in this domain, possibly negatively affecting everyday functioning in KS.

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Korsakoff; visuospatial perception; VOSP; object; space

Introduction

Korsakoff's syndrome (KS) is a neuropsychiatric syndrome, caused by vitamin B1 (thiamine) deficiency (Butterworth, Kril, & Harper, 1993; Kopelman, 1995; Reuler, Girard, & Cooney, 1985). In modern society, KS is often caused by severe alcoholism and self-neglect leading to thiamine depletion (Kopelman, Thomson, Guerrini, & Marshall, 2009). Other causes of thiamine deficiency can lead to KS, such as extreme vomiting after obesity surgery, anorexia nervosa, and multiple forms of cancer (Isenberg-Grzeda, Rahane, DeRossa, Ellis, & Nicolson, 2016; Oudman, Wijnia, Oey, van Dam, & Postma, 2018b; Oudman, Wijnia, van Dam, Biter, & Postma, 2018a). KS is characterized by severe cognitive problems, such as explicit memory deficiencies. The characteristic neuropathology includes neuronal loss, micro-haemorrhages and gliosis in the paraventricular and peri-aqueductal grey matter. Especially, anterograde declarative memory is impaired in KS (Fama, Pfefferbaum, & Sullivan, 2006; Kopelman, 1995). Also, executive dysfunctions are frequently present in KS, such as problems in decision making, mental flexibility, and planning (Brand et al., 2005; Oscar-Berman, Kirkley, Gansler, & Couture, 2004).

The well documented symptomology of KS as noted above centrally emphasizes higher order cognitive (dys) functioning. More elementary, perception based functions have only sparsely been researched thus far. For instance, it is still unclear whether VSP problems might underlie amnesia in KS, or form a discrepant feature of KS. Based on the underlying thalamic-cerebellar pathology critical to KS, it could be assumed that VSP problems do exist and form a discrepant cognitive problem central to KS. Visuospatial perception (VSP) refers to the identification of objects (object perception), and the localization of objects (space perception) (Herrera-Guzmán, Pena-Casanova, Lara, Gudayol-Ferre, & Böhm, 2004). Object perception can be described as the cooperation between visual representation and semantic information on the objects' functional properties (Farah, 2003). Space perception is the mental representation of visual space and objects within it from a more or less fixed view point. This point could entail an egocentric frame of reference, that is spatial information is encoded with respect to the observer's body, or an allocentric frame of reference, encoding position

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with respect to environmental cues independent of the observer's position (Loomis, Da Silva, Fujita, & Fukusima, 1992; Ruotolo, van Der Ham, Iachini, & Postma, 2011).

One of the few studies looking into VSP in KS was performed by Oscar-Berman et al. (2004). KS patients performed worse on the visuospatial Digit Symbol test than healthy controls, possibly suggesting diminished VSP functioning in KS. Because the speed of processing was also a critical aspect of this paradigm, also information processing limitation could lead to the compromised results of this study. Later, also Fama et al. (2006) showed that KS patients are likely to be impaired in their VSP abilities to some extent. In their experiment, KS patients, individuals with AUDs, and healthy controls identified incomplete or abstract drawing of objects and animals and learn them for delayed recall after one hour. Importantly, both KS patients and individuals with AUDs were impaired in visuoperceptual abilities on the Gollin Incomplete Pictures Test, with the KS group making more errors in identifying line drawings. As the results of this study suggests, also chronic alcoholism can lead to visuospatial difficulties.

Based on the limited available evidence, it is still unclear whether object and space perception is compromised in KS, and what the extent of possible visuospatial problems could be. In contrast, there is some indirect evidence for visuoperceptual disorders in individuals with AUDs. In a study by Beatty, Hames, Blanco, Nixon, and Tivis (1996), findings indicated that individuals with AUDs exhibit mild impairments in general visuospatial functioning. These findings are an acute result of alcohol abuse in individuals with AUDs. Assuming that in individuals with AUDs some visuospatial problems occur, the conclusion can be drawn that KS patients are likely to show these deficits as well. However, based on a discontinuum between functioning in individuals with AUDs and KS patients in other domains such as emotion recognition (Brion et al., 2017) and executive functioning (Brokate et al., 2003), a stronger impairment in KS is not necessarily the case.

In light of the foregoing, the aim of present study was to further investigate visuospatial functions in KS patients. We chose to use the Visual Object and Space Perception Battery (VOSP) (Warrington & James, 1991). This instrument is specifically sensitive to differentiate visual and spatial aspects of VSP in eight subtests. Earlier research in Alzheimer's disease on the VOSP suggested that general VSP is compromised in those patients (Binetti et al., 1998; Quental, Brucki, & Bueno, 2013). In early Alzheimer's disease, patients already showed impairments in the object recognition subtest called "Silhouettes". These selective deficits indicated problems in identification of common objects from atypical perspectives (Binetti et al., 1998). In more advanced Alzheimer's disease, global problems in space and object perception are common (Quental et al., 2013). Also, patients diagnosed with Huntington's disease are known for profound global difficulties in visual perception (Lawrence, Watkins, Sahakian, Hodges, & Robbins, 2000). The central aim of this project is to investigate whether object percetion or visuospatial perception in KS are impaired. Based on previous research in individuals with AUDs, we hypothesized a mild but global visuospatial deficiency, caused by atrophy of the cortex in KS.

Methods

Participants

15 KS patients (3 woman) and 15 (5 woman) healthy controls participated in this project. General characteristics of both groups are represented in Table 1 of the results section. All KS patients were inpatients of "Slingedael" Korsakoff center, Lelie Care Group, in Rotterdam, The Netherlands. All had been diagnosed with KS after extensive neuropsychological assessment, fulfilled the criteria of KS by Kopelman (Kopelman, 2002), and met the DSM-5 criteria for Alcohol-induced Major Neurocognitive Disorder, amnesic-confabulatory type (291.1; American Psychiatric Association, 2013). All patients were in the chronic amnestic stage of the syndrome, and not in the confusional state of Wernicke's Encephalopathy. All patients had been abstinent for at least six months prior to their diagnosis. Patients lived in the clinic, where they were monitored to stay abstinent. Demographic data, such as age, gender and education level, was gathered for both groups of participants (see Table 1).

Participants with known visual problems based on medical history, or self-report, were not included in the project. Information on prior consumption of alcohol was estimated based on the most recent information from medical charts for patients, and based on actual consumption of controls. Control participants were collected via a participant website and family contacts. The data included in this manuscript were obtained in compliance with the Helsinki Declaration. This study was approved by the Utrecht University ethics committee, Faculty of Social Sciences. Participants had to read and sign informed consents prior to testing.

Tasks and stimuli

MoCA: Cognitive assessment

All participants performed a neuropsychological screening task to index their current cognitive

Table 1. Demographic characteristics and neuropsychological test results for the Korsakoff's patients (n = 15) and healthy controls (n = 15).

	Korsakoff's patients	Healthy controls	
Number of patients (m)	15 (12)	15 (10)	$\chi^2(1) = .682$, $p = .409$
Age M (SD)	61.80 (7.46)	56.20 (10.74)	$t(30) = 1.659$, $p = .108$
Educational level M (SD)[a]	4.67 (.82)	4.67 (.72)	$U = 109.50$, $z = -.138$, $p = .891$
MOCA total score M (SD)[b]	19.20 (2.76)	25.93 (1.16)	$t(30) = -8.716$, $p = .000$
Alcohol use in grams per day M (SD)[c]	259.0 (108.93)	5.65 (5.81)	$t(30) = 8.995$, $p = .000$

m = male, M = Mean, SD = Standard Deviation.
[a]Educational level was assessed in 7 categories: 1, primary school; 7, academic degree (Verhage, 1964).
[b]Montreal Cognitive Assessment Score, reflecting general cognitive functioning (Nasreddine et al., 2005).
[c]The amount of alcohol use was determined by medical files and hetero-anamnestic data for patients and self-report for controls. Patients stopped drinking alcohol for more than six months prior to testing.

functioning. The MoCA test was used (Nasreddine et al., 2005). This is a one-page, 30 points test, which can be administered in 10 minutes. It consists of small subtasks, indexing several aspects of cognitive functioning. There is a short-term memory task (5 points), which involves two learning trials of five words and delayed recall after approximately 5 minutes. A visuospatial task is the clock-drawing task (3 points) and a three-dimensional cube copy (1 point). Executive functions are measured by an alternation task, adapted from the Trail Making B task (1 point), a phonemic fluency task (1 point) and a two-item verbal abstraction task (2 points). Attention, concentration and working memory are assessed by a sustained attention task (tapping task, 1 point), a number subtraction task (3 points) and digits forward and backward (1 point each). Language is measured by an animal naming task (3 points), repeating of complex sentences (2 points) and the earlier mentioned fluency task. Orientation in time and place is evaluated using questions (6 points).

VOSP battery

All participants completed the VOSP battery. The VOSP consists of a screening test and eight clinical tests. Object perception is measured by the Incomplete Letters, Silhouettes, Object Decision, and Progressive Silhouettes tests, and space perception is measured by the Dot Counting, Position Discrimination, Number Location, and Cube Analysis tests (Warrington & James, 1991).

Screening test

A screening test is included to exclude patients for whom the VOSP is invalid; a short test measuring normal visual abilities. In this task, stimuli are random patterns, of which half or more of the figure X is presented. Participants have to indicate whether the X is present in the stimuli or not.

VOSP 1-4: Tests of object perception

Incomplete letters

The incomplete letters test (VOSP 1) measures the ability to identify shapes with degraded perceptual clarity. The test includes 20 stimulus cards, each picturing a letter degraded by 70%, and examinees are asked to identify the letters. The maximum score on this subtest is 20 points. In a general population, the 5% cut-off value of this test is 16 points (Warrington & James, 1991).

Silhouettes

The Silhouettes Test (VOSP 2) measures the ability to identify common objects (animals and objects) pictured from atypical perspectives. The test consists of 30 silhouette drawings created by rotating the objects. The maximum score on this subtest is 30 points. In a general population, the cut-off value of this test is 15 points (Warrington & James, 1991).

Object decision

The Object Decision Test (VOSP 3) test requires examinees to select the silhouette drawing of a real object between three distractor images (20 trials). The maximum score on this subtest is 20 points. In a general population, the 5% cut-off value of this test is 14 points (Warrington & James, 1991).

Progressive Silhouettes

The Progressive Silhouettes Test (VOSP 4) requires the identification of objects rotated so that the defining features of the object are faded. The task consists of two series of stimulus cards, each consisting of 10 silhouette drawings, with each drawing revealing progressively more details of the object (a gun and a trumpet). The maximum score on this subtest is 20 points, with higher scores reflecting lower task performance. In a general population, the 5% cut-off value of this test is 15 points (Warrington & James, 1991).

VOSP 5-8: Tests of spatial perception

Dot counting

The Dot Counting Test (VOSP 5) requires examinees to identify the number of stimuli (dots) presented randomly (10 trials). The maximum score on this subtest is 10 points. In a general population, the 5% cut-off value of this test is 8 points (Warrington & James, 1991).

Position discrimination

The Position Discrimination Test (VOSP 6) consists of two squares, each containing a black dot, and examinees have to choose which of the squares contains the dot in the center of the square (20 trials). The maximum score on this subtest is 20 points. In a general population, the 5% cut-off value of this test is 18 points (Warrington & James, 1991).

Number location

The Number Location Test (VOSP 7) consists of ten trials with two squares: one square presents a random array of numbers and the other contains a black dot. Examinees determine the number in the upper square that corresponds best with the position of the location of the dot in the bottom square (10 trials). The maximum score on this subtest is 10 points. In a general population, the 5% cut-off value of this test is 7 points (Warrington & James, 1991).

Cube analysis

The Cube Analysis test assesses the ability to interpret three-dimensional space represented in two dimensions. Participants are asked to determine the number of blocks represented in the drawings, also blocks that may not be visible (10 trials).

The maximum score on this subtest is 10 points. In a general population, the 5% cut-off value of this test is 6 points (Warrington & James, 1991).

Procedure

All participants were tested individually in the experiment. At first, they answered questions on the general demographic characteristics. All participants were tested with respectively the MoCA test, followed by the screening test and eight subtests of the VOSP. This study is approved by the FETC.

Analyzes

Demographic characteristics were reported. Eight non-parametric Mann-Whitney U tests were performed to examine the effect of KS on visuospatial functioning for subtest 1–8 of the VOSP. Non-parametric statistics were introduced because of the large majority of participants obtaining a perfect score, thus violating the normality assumption of parametric statistical tests. A p-value of less than .05 was considered statistically significant.

Results

Demographic characteristics

Demographic details are represented in Table 1. Both MoCA scores for general cognitive functioning, and estimated prior alcohol use in grams per day were significantly different between both groups, with lower cognitive scores, and higher alcohol use consumption in KS patients (see Table 1). As expected, these results suggest that patients with KS had more cognitive problems, and had higher previous alcohol consumption than healthy controls.

Object and space perception in KS

Table 2 represents the total scores per subtests, standard deviations, and non-parametric comparisons. Only subtest 1 and 2 showed statistical significance, indicating that the ability to identify shapes with degraded perceptual clarity and the ability to identify common objects (animals and objects) pictured from

Table 2. Visual object and space perception battery task performance in Korsakoff's syndrome patients (n = 15), and healthy controls (n = 15), Means and (Standard Errors).

	Korsakoff's patients	Healthy controls	Average Skewness/ Average Kurtosis	Statistics
Object perception				
VOSP subtest 1	19.07 (.15)	19.60 (.13)	−.29/-.55	$U = 61.5$, $z = 2.39$, $p = .017$
VOSP subtest 2	17.53 (1.16)	21.47 (1.13)	−.76/1.55	$U = 59.0$, $z = 2.23$, $p = .026$
VOSP subtest 3	17.53 (1.64)	17.33 (2.23)	−1.0/.24	$U = 112.5$, $z = 0$, $p = 1.0$
VOSP subtest 4	11.00 (.42)	9.53 (.58)	−.03/-.87	$U = 77.0$, $z = 1.48$, $p = .139$
Space perception				
VOSP subtest 5	9.87 (.09)	9.60 (.24)	−2.94/8.88	$U = 103.0$, $z = .61$, $p = .544$
VOSP subtest 6	19.53 (.21)	19.53 (.17)	−1.83/3.87	$U = 106.0$, $z = .32$, $p = .751$
VOSP subtest 7	8.87 (.50)	8.93 (.43)	−2.12/4.65	$U = 110.0$, $z = .12$, $p = .908$
VOSP subtest 8	9.27 (.28)	9.27 (.35)	−1.96/4.32	$U = 112.0$, $z = 0.24$, $p = 1.0$

atypical perspectives, show subtle problems in KS, while other visuospatial functions are intact.

Discussion

The aim of present study was to assess object and space perception in KS. Results show a significant difference in task performances on object perception tasks between KS patients and healthy controls. Notably, the ability to identify degraded shapes, and objects from atypical perspectives is compromised in KS. Subtle difficulties were present in KS, reflecting basal problems in object integration underlying KS.

According to Warrington and James (1991) and Warrington and Taylor (1978), object perception itself can be divided into perceptual categorization and semantic categorization, which are hierarchical organized in the brain. The first two tasks of the VOSP require basal perceptual organization and categorization of information, but are not so much dependent on semantic categorization. As our results show, specific problems in basal object integration are common in KS. This finding of basic perceptual organization and categorization difficulties has been earlier shown by Fama et al. (2006), although the extent of this problem was not reviewed in detail. In their study on visuospatial memory and learning, subtle deficits in identifying incomplete or abstract drawings were visible in four patients diagnosed with KS. Our results corroborate and extend those findings by showing consistent object integration difficulties in KS.

Object perception is a part of the ventral stream of the cortex (Shen, Hu, Yacoub, & Ugurbil, 1999; Warrington & Taylor, 1978). For basic processes in object recognition, particularly the right posterior regions of the brain are important (Rapport, Millis, & Bonello, 1998). It could therefore be possible that KS patients do have subtle deficiencies in the right posterior area of the cortex, resulting in subtle apperceptive gnostic problems. However, it is even more likely that thalamic nucleus atrophy that is central to KS results in the observed object recognition difficulties. In recent MRI investigations, thalamic nuclei have consistently been reported to activate during object recognition (Saalman, Pinsk, Wang, Li, & Kastner, 2012). Recently, the thalamic nucleus has been put forward as an active regulator of visuospatial information (Saalman et al., 2012). Since the difficulties in object recognition of KS patients are rather subtle, it could be that modulatory effects of the thalamus on visuoperception play a central role underlying this deficiency. Importantly, both sensory discrimination, and deriving of meaning of objects (associative gnosis) are intact in KS, reflecting that object recognition difficulties are rather specific in KS (Warrington & James, 1991).

One could assume that alcohol consumption prior to KS could explain the effects of the present study. Earlier findings indicated that individuals with AUDs exhibit mild impairments in visuospatial skills that require executive demands (Beatty et al., 1996; Fama et al., 2006). In the present study, such effects were not clear, and task performance relying on executive functioning was normal. A discrepancy between the present study and object perception in individuals with AUDs is the long duration of sobriety in our sample minimizing the direct adverse effects on the brain. In future projects it would be relevant to include a group of individuals with AUDs that have had longer periods without alcohol.

There are a number of methodological concerns involving the sensitivity of the various tests and the pattern of performance over the tests within one domain (i.e., object recognition vs spatial perception). For example, it could be argued that the number of patients in current study is relatively small, having negative implications for the statistical power in the experiment. However, the number of patients in current study does not differ from earlier studies in KS (Beatty et al., 1996; Fama et al., 2006; Oscar-Berman et al., 2004). It is of interest to compare the current results to those found for visuospatial functioning in other patients groups. Earlier research in patient groups, such as Alzheimer's Disease patients and Huntington Disease suggests general effects of the neurological diseases on visuospatial functioning (Binetti et al., 1998; Lawrence et al., 2000). In contrast, KS patients experienced only selective effects. As found in the study of Binetti et al. (1998) and Quental et al. (2013), Alzheimer patients showed impairments on visuospatial tasks, mostly object perception tasks but also some deficits in space perception were found, which somewhat surprisingly correlated with concurrent language impairments in AD. Also in contrast to the study on perception in Huntington's disease (Lawrence et al., 2000), in which recognition of patterns and spaces is impaired, our current study only found impaired object perception in KS patients.

In conclusion, results of present study indicate selective impairments of KS in object perception. Mainly, object integration and categorization was subtly impaired in the identification of degraded or slightly abstract objects. In light of the fact that most other VSP tests revealed normal performance, specifically the identification of abstract or degraded objects is impaired in KS. More knowledge about KS and its characteristics will be very useful in improving or changing the diagnostic process and in the development of further treatments or types of therapy. Future research should further establish

whether VSP testing should form a indispensable part of the neuropsychological evaluation of KS to index possible mild deficits in this domain.

Disclosure statement

No potential conflict of interest was reported by the authors.

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