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Preserved intellectual functioning in Korsakoff's syndrome? Actual and premorbid intelligence in patients with major or mild alcohol-related cognitive disorder

Rhody Haalboom, Loes van Aken, Serge J. W. Walvoort, Jos I. M. Egger & Roy P. C. Kessels


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Preserved intellectual functioning in patients with major or mild alcohol-related cognitive disorder

Rhody Haalboom, Loes van Aken, Serge J. W. Walvoord, Jos I. M. Egger, and Roy P. C. Kessels

ABSTRACT
Objective: Although alcoholic Korsakoff patients show profound cognitive impairments (including amnesia), intellectual function has typically been assumed to be preserved. Based on more recent models on intelligence, however, it can be hypothesized that although preserved verbal or crystallized abilities may be expected in Korsakoff patients, fluid reasoning may be significantly reduced. Aim of this study was to gain insight in intelligence profiles of patients with alcohol-related cognitive disorders with and without Korsakoff’s syndrome (KS).
Method: Test performance on the Wechsler Adult Intelligence Scale – Fourth Edition (WAIS-IV) and the National Adult Reading Test (NART) was assessed in 34 patients diagnosed with KS, 40 patients with chronic alcoholic-related cognitive disorder without Korsakoff’s syndrome (ALC), and 47 non-alcoholic psychiatric controls (non-ALC).
Results: Analysis revealed significant lower WAIS-IV Full-Scale IQ scores compared to the estimated premorbid NART-IQ in both groups with alcohol-related cognitive disorders (KS and ALC). With respect to the index scores, KS patients performed worse than non-ALC patients on the Perceptual Reasoning and Processing Speed Indices. Performance on the Verbal Comprehension and Working Memory Indices did not differ between groups.
Conclusion: Not all aspects of intelligence are preserved in Korsakoff’s syndrome and implications of assessment of intellectual function in patients with alcohol-use disorder are discussed.

Introduction
Alcoholic Wernicke-Korsakoff syndrome is a chronic psychiatric disorder which is caused by excessive alcohol use in combination with malnutrition, resulting in a deficiency of thiamine (vitamin B1). This deficiency may result in Wernicke’s encephalopathy; an acute physical condition characterized by a clinical triad of confusion, ataxia, and oculomotor abnormalities (Wernicke, 1881). The chronic syndrome of persisting deficits that may occur after Wernicke’s encephalopathy is referred to as Korsakoff’s syndrome (KS), or Alcohol-Induced Major Neurocognitive Disorder, Amnestic/Confabulatory Type, in the nomenclature of DSM-5 (American Psychiatric Association [APA], 2013). Lesions (although not always present or observable using current neuroimaging techniques) have been found in the diencephalon in KS patients, including the mammillary bodies and thalamus, which cause disproportionate anterograde amnesia as well as retrograde amnesia with a temporal gradient (Arts, 2017; Kopelman, 2002). Other characteristics of the syndrome are an almost complete lack of insight, disorientation in time, place and person, achronogenesis (difficulties placing memories in time; Kopelman, 2002), confabulations in the first period after Wernicke encephalopathy (Kessels & Kopelman, 2012), visuoperceptual impairments (Oscar-Berman et al., 2014) and severe executive dysfunction (Maharasingam, Macniven, & Mason, 2013; Moerman-Van den Brink et al., 2019; Van Oort & Kessels, 2009).

In addition to KS, a subgroup of patients with Alcohol Use Disorder (AUD) presents with cognitive impairment in a milder form, not fulfilling the criteria for KS (Green et al., 2010; Oscar-Berman, Kirkley, Gansler, & Couture, 2004). These patients can be classified as having alcohol-related cognitive impairment with an etiology that is qualitatively distinct from the thiamine depletion that causes (Wernicke-)Korsakoff Syndrome (Arts et al., 2017), but that is related to their chronic alcohol use (Hayes, Demirkol, Ridley, Withall, & Draper, 2016). These AUD patients meet the DSM-5 criteria for Alcohol-Induced Mild Neurocognitive Disorder (APA, 2013), with minimal functional decline in daily life due to the cognitive deficits (i.e., not fulfilling the criteria for Alcohol-Related Dementia), without a disproportionate amnesia or confabulations.

It has long been assumed that in KS, intelligence is preserved (Krabbendam et al., 2000). Butters and Cermak (1980), for instance, state that "Despite the severity of Korsakoff patients’ memory impairments, their intellectual functions,
as measured by standardized IQ tests, often remain relatively intact.” (p. 7). There is, however, some evidence that in KS patients only verbal intellectual abilities are preserved (Maharasingam et al., 2013). For instance, studies have demonstrated deficits in measures of the performance IQ even in non-KS alcoholics (Lin, Huang, Lin, & Pan, 2010), and discrepancies between estimates of premorbid intellectual functioning and current novel problem-solving in AUD patients (Ihara, Berriros, & London, 2000). Similar deficits in fluid reasoning can also be argued to be present in alcoholic KS patients.

The subdivision of intellectual functioning into two factors, that is, crystallized intelligence (Gc) and fluid intelligence (Gf), was already proposed by Horn and Cattell (1966) who argued that intelligence is not a unitary construct or a general factor (g) as claimed by Spearman (1927). Gc concerns over-learned and familiar skills, abilities and knowledge that reflect the extent to which someone has gathered (cultural) knowledge and is capable of using this information (Horn & Cattell, 1966). In healthy individuals, Gc is known to remain stable with aging, and to be less susceptible for the consequences of brain injury or brain disease (Rusell, 1980). Gf concerns abilities that contribute to novel problem solving, for instance, concept formation and attainment, reasoning, abstracting, flexibility, adaptation, and decision-making (Horn & Cattell, 1966). Gf is sensitive to the process of aging and to influences of brain injury. The Cattell-Horn- Carroll (CHC) theory of cognitive abilities (Carroll, 1993) describes Gf and Gc as broad abilities in a hierarchy of intellectual functioning. With g on top of this hierarchy, a total of 10–16 broad abilities are defined, which in turn are made up of multiple narrow abilities (Schneider & McGrew, 2018).

The CHC theory guided the development of the Wechsler Adult Intelligence Scale – Fourth Edition (WAIS-IV), the most frequently used intelligence test worldwide (Lichtenberger & Kaufman, 2009). The test contains a core battery of 10 subtests (Block Design, Similarities, Digit Span, Matrix Reasoning, Vocabulary, Arithmetic, Symbol Search, Visual Puzzles, Information, and Coding). The scores of the 10 core WAIS-IV subtests are grouped into four index scores, measuring distinct aspects of intellectual functioning: (1) the Verbal Comprehension Index (VCI), which measures Gc, (2) the Perceptual Reasoning Index (PRI), a measure of Gf and visual processing (Gv), (3) the Working Memory Index (WMI), a measure of Gwm, and (4) the Processing Speed Index (PSI) of the WAIS-IV are measured on top of this hierarchy. The diagnosis of Gc is important because it is sensitive to the processes of aging and to influences of brain injury. The Cattell-Horn-Carroll (CHC) theory of cognitive abilities (Carroll, 1993) describes Gf and Gc as broad abilities in a hierarchy of intellectual functioning. With g on top of this hierarchy, a total of 10–16 broad abilities are defined, which in turn are made up of multiple narrow abilities (Schneider & McGrew, 2018).

The aim of the current study is to gain more insight into the profile of intellectual functioning in KS and non-KS AUD patients, as this is relevant for interpreting neuropsychological assessments in patients with AUD. Furthermore, no recent studies have examined intellectual functioning in both KS and AUD patients using the WAIS-IV, which relies more strongly on fluid reasoning compared to previous versions of Wechsler’s intelligence test. The intelligence test scores of KS patients in this study are compared to the performance of two other groups of patients: 1) patients with alcohol-related cognitive disorders not fulfilling the criteria for Korsakoff’s syndrome (ALC) who are expected to show milder cognitive deficits than the KS group, and 2) patients with other psychiatric disorders unrelated to alcohol-use disorder (non-ALC). Patients in this latter group are included to control for comorbid psychiatric disorders and socioeconomic status (Rosenbloom, O’Reilly, Sassoon, Sullivan, & Pfefferbaum, 2005), which may affect their performance on intelligence tests and even result in subtle executive deficits (Egger, De Mey, & Janssen, 2007). These three groups make it possible to identify the contribution of the KS etiology (as opposed to non-KS AUD) and chronic AUD (by including psychiatric controls without a history of AUD) to the performance on the intelligence test. We expected unimpaired scores on the Verbal Comprehension Index (VCI) and no significant differences between this measure of crystallized intelligence and estimated premorbid intelligence both in AUD patients with and without KS (cf. O’Mahony & Doherty, 1996; Schottenbauer, Momenan, Kerick, & Hommer, 2007; Van Aken et al., 2014). Lowered scores on the Perceptual Reasoning Index (PRI), which relies on Gf, and the Processing Speed Index (PSI) of the WAIS-IV are expected especially in KS patients and to a lesser extent in non-KS AUD patients, compared to a non-alcoholic psychiatric control group. Furthermore, we expect lowered scores on the revised Working Memory Index (WMI) of the WAIS-IV, because of previously reported working memory deficits in KS at higher executive demands (Pitel et al., 2008).

**Method**

**Participants**

A total of 121 participants were included (mean age = 50.25, SD = 12.63, 63.6% men), all recruited from the Centres of Excellence for Neuropsychiatry and for Korsakoff and Alcohol-Related Disorders of Vincent van Gogh Institute for Psychiatry in Venray, the Netherlands.
The first group consisted of 34 inpatients diagnosed with KS (mean age = 57.82 SD = 7.38, 79.4% men). All KS patients fulfilled the DSM-5 (APA, 2013) criteria for Major Neurocognitive Disorder due to Alcohol, Amnesic/Confabulatory subtype (code 291.1), which requires the presence of cognitive deficits that results in severe deficits in social functioning, in the absence of delirium or dementia, with a history of alcohol-abuse disorder. In addition to the DSM-5 classification, the KS patients had to fulfill the criteria for alcoholic Korsakoff’s syndrome (Kopelman, 2002), which includes evidence for a history of Wernicke encephalopathy, confabulation behavior and history of malnutrition or thiamine deficit.

The second patient group consisted of 40 inpatients diagnosed with alcohol-use disorder and cognitive deficits (ALC; mean age = 53.15, SD = 9.56, 80.0% men). All fulfilled the DSM-5 criteria for Minor Neurocognitive Disorder due to Alcohol (code 291.89).

The third non-ALC group consisted of 47 patients (Mage = 42.3, SD = 13.62, 38.3% male) classified with other DSM-5 psychiatric disorders, mainly anxiety and depression. These patients were referred to the Centre of Excellence for Neuropsychiatry for neuropsychological examination.

Inclusion criteria for all patient groups were age above 18 and under 70 years, no other somatic conditions that could interfere with the test results (e.g., stroke), able to complete the test sessions, and able to speak and understand the Dutch language. Patients were excluded when they met DSM-5 criteria for schizophrenia or other psychotic disorders, mainly anxiety and depression. These patients were referred to the Centre of Excellence for Neuropsychiatry for neuropsychological examination.

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### Materials
The core battery of 10 subtests of the Dutch version of the WAIS-IV was used in this study (Block Design, Similarities, Digit Span, Matrix Reasoning, Vocabulary, Arithmetic, Symbol Search, Visual Puzzles, Information, and Coding). Split-half reliability for the subtests varied between .75 and .93 in the complete sample according to the Dutch WAIS-IV technical manual (Wechsler, 2012b). Split-half reliabilities of the index scores VCI, PRI, WMI, PSI, and the Full-Scale IQ score (FSIQ) respectively, were .96, .93, .92, .88 and .97 (Wechsler, 2012b).

The Dutch version of the NART (Schmand, Bakker, Saan, & Louman, 1991) was administered as a measure of premorbid verbal intelligence by asking participants to read aloud 50 irregular words. Interrater reliability of the Dutch version of the NART is .96. The internal consistency of the tests varies between .91 and .95 (Schmand et al., 1991). The Behavioural Assessment of the Dysexecutive Syndrome (BADS; Wilson, Alderman, Burgess, Emslie, & Evans, 1996) was included for descriptive purposes as a measure of executive dysfunction.

### Procedure and analysis
Intelligence testing took place after a period of at least six weeks of abstinence of alcohol to avoid the (sub)acute effects of alcohol on the brain, the effects from withdrawal symptoms on cognition and the ongoing recovery of cognitive functions (Mann, Günter, Stetter, & Ackermann, 1999; Rosenbloom & Pfefferbaum, 2008). Data collection was part of a more extensive neuropsychological assessment, performed by a qualified neuropsychologist. The WAIS-IV was administered and scored according to the guidelines described in the test’s manual (Wechsler, 2012a). The standardized age-adjusted scaled subtest scores were used for all analyses. The Dutch version of the NART was scored according to the Dutch guidelines described in the manual (Schmand et al., 1991), with age correction according to Mulder, Dekker, and Dekker (1996), converted to an IQ estimate.

Data were analyzed using IBM SPSS Statistics 25. Paired-sample t-tests were performed to compare the NART-IQ to the WAIS-IV FSIQ and the four Index Scores for each group. Next, analysis of variance (ANOVA) was performed comparing the NART as well as the WAIS-IV FSIQ. Index Scores and subtest scores across the groups. Post-hoc Dunnett comparisons were performed comparing the KS group with the ALC and non-ALC groups, respectively. There were incidental missing values for some of the variables, for which the degrees of freedom were adjusted.

### Results
Mean scaled scores and standard deviations of all groups on Full-Scale IQ score (FSIQ), indices (VCI, PRI, WMI, and PSI) and the 10 core subtests are presented in Table 2. The three different patient groups did not differ with respect to level of education (KS: Mean Rank = 48.5; ALC: Mean Rank = 54.04; non-ALC: Mean Rank = 64.93; H (corrected for ties) = 5.153, df = 2, N = 111, p = .077) or on the NART-IQ (F(2,107) = .749, p = .475). Groups differed in age (non-ALC patients were significantly younger; F(2) = 22.33, p < .0005), but this was obviated by using age-adjusted scaled intelligence scores.

### Table 1. Demographic information of the patients with Korsakoff’s syndrome (KS), the patients with alcohol-use cognitive impairment (ALC) and the non-alcoholic psychiatric controls (non-ALC).

<table>
<thead>
<tr>
<th></th>
<th>KS</th>
<th>ALC</th>
<th>non-ALC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD)</td>
<td>57.82 (7.38)</td>
<td>53.15 (9.56)</td>
<td>42.30 (13.62)</td>
</tr>
<tr>
<td>Range</td>
<td>44–69</td>
<td>30–69</td>
<td>19–67</td>
</tr>
<tr>
<td>Sex %</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Education level*</td>
<td>Mean</td>
<td>4.06</td>
<td>4.35</td>
</tr>
<tr>
<td>Range</td>
<td>1–7</td>
<td>2–6</td>
<td>2–7</td>
</tr>
<tr>
<td>BADS</td>
<td>Mean standard score (SD)</td>
<td>82.6 (15.1)</td>
<td>85.7 (19.1)</td>
</tr>
</tbody>
</table>

### Classification
- Impaired
- Borderline
- Low-average
- Average
- High-average
- Superior
- Very superior
- Not available

- 91 (Eichinger et al., 1991) was used as a measure of premorbid verbal intelligence by asking participants to read aloud 50 irregular words. Interrater reliability of the Dutch version of the NART is .96. The internal consistency of the tests varies between .91 and .95 (Schmand et al., 1991). The Behavioural Assessment of the Dysexecutive Syndrome (BADS; Wilson, Alderman, Burgess, Emslie, & Evans, 1996) was included for descriptive purposes as a measure of executive dysfunction.

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First, we compared the premorbid IQ estimate (NART) with the WAIS-FSIQ and the four Index Scores. In KS patients the FSIQ was significantly lower than the premorbid estimate (t(32) = 7.09, p < .0005). Significant differences were also found for ALC patients in which the FSIQ was significantly lower than the NART-IQ (t(32) = 4.93, p < .0005), but not for non-ALC patients (t(33) = 1.85). For KS patients, VCI scores also differed significantly (with lower scores) from the NART-IQ; (t(32) = 3.05, p = .005). For ALC patients and non-ALC patients, VCI scores did not differ from the NART-IQ (ALC: t(39) = 0.01; non-ALC: t(33) = 0.08). PRI scores were significantly lower than the NART-IQ in KS patients and ALC patients, respectively (KS: t(32) = 4.93, p < .0005; ALC: t(39) = 3.20, p < .005), but not for non-ALC patients (t(33) = 0.69). WMI scores also differed significantly from the NART-IQ in KS patients and ALC patients, respectively, with lowered WMI scores (KS: t(32) = 2.17, p < .05; ALC: t(39) = 2.84, p < .01), but not for non-ALC patients (t(35) = 1.65). PSI scores differed also significantly from the NART-IQ in KS patients and ALC patients, respectively, with lower PSI scores (KS: t(32) = 6.41, p < .0005; ALC: t(39) = 3.50, p < .001), but not for non-ALC patients (t(36) = 1.40).

Next, we compared the WAIS-IV FSIQ and Index Scores across the three groups (overall ANOVA), followed by Dunnett post-hoc tests comparing the KS group with the ALC and non-ALC group, respectively. Here, we found significant differences between groups on the FSIQ (F(2,114) = 4.95, p < .01), PRI (F(2,114) = 8.58, p < .0005) and PSI (F(2,118) = 8.29, p < .0005), but not on the VCI (F(2,114) = 0.64) or WMI (F(2,117) = 1.11).

Post-hoc Dunnett comparisons revealed significant FSIQ differences between KS patients and non-ALC patients (p < .01), but not between the KS group and the ALC group (p = .83). Significantly lower PRI and PSI performances were only found in the KS patients compared to the non-ALC patients (p < .0005). ALC patients did not significantly differ from KS patients (PRI: p = .64; PSI: p = .25).

Performances of the three patient groups on the individual subtests are presented in Table 2. As expected, KS patients performed significantly worse than non-ALC patients on Block Design (p < .0005), Matrix Reasoning (p ≤ .01), Visual Puzzles (p ≤ .002), Symbol Search (p < .0005) and Coding (p ≤ .001). No differences were found between the KS and ALC groups at the level of the subtests.

### Discussion

Aim of the current study was to gain insight into the spared and impaired aspects of intelligence in KS patients using the WAIS-IV. Results show that FSIQ scores are not preserved in patients with KS or non-KS alcohol-related cognitive disorders. More specifically, both PRI and PSI scores were significantly lower in the KS group compared to the psychiatric control group, indicating that fluid reasoning, visual processing skills and processing speed (or Gf, Gv, and Gs) are all impaired in KS patients. At the subtest level, lower performances were found on Block Design, Matrix Reasoning, Visual Puzzles, Symbol Search and Coding, in KS patients compared to the performance of psychiatric controls. No group differences were found in VCI and WMI performance, indicating preserved crystallized ability and working memory.

In accordance with our hypotheses, the lower performance on PRI and PSI in the KS patients implicates a decline of fluid intelligence (Gf), visual processing, and processing speed in KS patients, in line with evidence on executive dysfunction in KS (Maharasingam et al., 2013; Van Oort & Kessels, 2009) and previous research on information processing speed in patients with chronic alcohol-related cognitive disorders (Oscar-Berman et al., 2014). Contrary to the hypothesis, no differences were found on the WMI between the three groups. Although performance on Wechsler’s Digit Span has been shown to be preserved in earlier studies (Pollux et al., 1995), the WMI has been fully revised in the WAIS-IV, making this index more cognitively demanding. Still, the currently available WAIS-IV WMI subtests do not cover the full concept of working memory, as already acknowledged by Engeland (2015). Since working memory is a key element of executive function (Engelhardt et al., 2016), deficits in working-memory functions with high executive demands are expected in KS. Conway et al. (2005) make a distinction between the traditional concept of short-term memory capacity (STM), measured by span tasks, and working memory capacity (WMC). WMC is thought to reflect primarily domain-general executive...
attention, “a capability whereby memory representations are maintained in a highly active state in the face of interference, and these representations may reflect action plans, goal states, or task-relevant stimuli in the environment” (Conway et al., 2005, p. 771). Since working memory impairments have been found in both KS patients and ALC patients (Pitel et al., 2008), tests that recruit a higher working-memory load may be able to capture the working-memory deficits of KS patients (cf. Van Geldorp, Bergmann, Robertson, Wester, & Kessels, 2012).

Although VCI in this study is relatively preserved, as hypothesized, the results are not entirely in line with previous studies concerning crystallized intelligence in KS patients (O’Mahony & Doherty, 1996; Victor, Talland, & Adams, 1959). That is, VCI in KS patients does not seem fully preserved when compared to the NART-IQ. A possible explanation is that performances on VCI subtests also contain elements of fluid intellectual functioning, for example, by using a strategy to retrieve information from the mental lexicon. Another explanation is that the NART measures a more elementary part of Gf that is mainly based on existing knowledge and VCI contains more specialized Gc capacities by asking patients to actively use their Gc knowledge in the different subtasks. Furthermore, the claim that the NART score is unaffected by cognitive deterioration, including KS, has also been debated (O’Carroll, Moffoot, Ebmeier, & Goodwin, 1992).

Moreover, visual inspection of the data also shows that both the mean estimated premorbid IQ and the WAIS-IV VCI as an index of Gc of all three groups are in the low-average range (80–89). It may be expected that psychiatric patients in a specialized hospital on average have a lower expected overall intelligence than the general population, which may be due to having a lower socioeconomic status, lower educational attainment because of their psychiatric history (our study samples overall have a less than average education level), use of medication, or non-specifics effects of the psychiatric disorder during the patients’ lifespan. This illustrates the need to include adequate control groups for any psychiatric sample rather than to rely on normative data.

A strength of the current study is the inclusion of a non-ALC reference group. Differences found in the intellectual functioning of KS and ALC patients cannot be merely attributed to having a psychiatric disorder. The present study also has some limitations. First, due to its cross-sectional nature, it is not possible to detect a decline in cognitive performance over time. Second, although the samples used are relatively large when compared to samples described in earlier studies about Korsakoff’s syndrome, it remains desirable to study larger groups of KS patients, given the wide range of individual differences within the group of KS patients. Furthermore, although the period of six weeks of abstinence used in this study is already longer than the abstinence in earlier investigations on Korsakoff’s syndrome (Cordovil De Sousa Uva et al., 2010; Manning et al., 2008; Schrimsher & Parker, 2008), an even longer period of abstinence or inclusion of follow-up measurements is advised for future research because of the possibility of further recovery of cognitive functions in groups of alcohol-related cognitive-disordered patients. We also do not have reliable information about the duration and extent of the patients’ alcohol use. The question remains whether the differences found are caused by the effects of alcohol (ethanol neurotoxicity), the effects of thiamine deficiency or comorbid effects by somatic (and other) side effects of AUD (Arts et al., 2017; Bodani, Reed & Kopelman, 2009), and the extent to which these effects affect the different groups of chronic alcohol-dependent individuals. Also, the non-ALC control group is younger, which may explain their preserved intellectual profile – albeit that we used age-adjusted standard scores in all our analyses. Finally, apart from the BADS, no standardized neuropsychological data set is available for the three groups in the present study for the non-executive domains. Further research should take these limitations into account.

Concluding, KS patients showed impaired processing speed, fluid abilities, and visual processing in comparison to psychiatric patients without AUD, while crystallized knowledge and working memory capacities were relatively preserved. A lowered Gc is found when compared to estimations of premorbid intelligence. Clearly, our findings show that various aspects of intelligence are affected differently in KS. This is relevant for clinical practice, as our result indicates that in KS the FSIQ as assessed using the WAIS-IV is not preserved, but largely affected by the deficits in fluid reasoning. While a disproportionate amnesia is obviously still a core deficit in KS, the memory deficits should be related to measures of crystallized intelligence during the diagnostic stages rather than to fluid reasoning ability, in addition to measures of other cognitive domains (see Heirene, John, & Roderique-Davies, 2018, for an overview). Furthermore, non-pharmacological interventions aimed at either KS patients or non-KS AUD patients should take the patient’s impairments in mental flexibility, learning, and information processing into consideration.

Disclosure of potential conflicts of interest

The authors report no conflict of interest.

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