The Relation between Behavioral, Emotional and Cognitive Apathy and Everyday Executive Dysfunction in Alcoholic Korsakoff's Syndrome

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Received: 15/09/2020 – **Accepted:** 26/04/2021

DOI: 10.15761/0101-60830000000301

ABSTRACT

Background: Apathy is an important neuropsychiatric symptom in alcohol-related cognitive impairment in general, and Korsakoff's syndrome in specific. However, research in patients with Korsakoff's syndrome on the multifaceted nature of apathy is lacking. **Objective:** Aim of the current study was to examine behavioral, cognitive and emotional apathy in alcoholic Korsakoff patients, also investigating the association with overall cognitive and executive dysfunction. **Methods:** We studied 43 patients with Korsakoff's syndrome (mean age 60.9, *SD*=6.5, range 38-70) using the Apathy Evaluation Scale – Informant Version (AES-I) and also administered the Montreal Cognitive Assessment and the Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) as a measure of daily executive problems. **Results:** In our sample, 76% of the Korsakoff patients were classified as being apathetic. AES-I scores correlated with overall cognitive function and were related to observer-rated daily executive problems. **Discussion:** Apathy is highly prevalent in Korsakoff patients and related to overall cognitive dysfunction and everyday executive problems. Our results stress the need to further examine underlying mechanisms of apathy in Korsakoff patients and the need for interventions aimed at reducing apathy.

Kessels RPC / Arch Clin Psychiatry. 2021;48(3): 178-181

Keywords: alcohol use disorder; neuropsychology; neuropsychiatric symptoms; major neurocognitive disorder; apathy syndrome

Introduction

Korsakoff's syndrome (KS) results from thiamine deficiency, mainly occurring following years of chronic alcohol use and malnutrition [1,2]. KS is characterized by chronic cognitive impairment, notably severe anterograde and retrograde amnesia, as well as executive dysfunction. Other symptoms include neuropsychiatric symptoms, such as apathy, confabulations, agitation/aggression, and disinhibition [1,3], which are associated with higher caregiver burden and more frequent psychotropic drug use [4].

Apathy as a neuropsychiatric symptom in KS was already discussed in early literature as *avolition* [1]. It can be considered a disorder of motivation manifesting in the loss of goal-directed activity [5]. Unfortunately, apathy has been poorly studied in patients with KS. An epidemiological study in 281 KS patients used the Neuropsychiatric Inventory – Questionnaire (NPI-Q), only containing one item about apathy ("Does the patient seem less interested in his/her usual activities or in the activities and plans of others"), rated by a professional caregiver showed a prevalence of 49.5% [3]. The Behavioral Rating Scale for Psychogeriatric Inpatients (GIP-28), also containing one item about apathy, was used as one of the outcome measure in a study in which KS patients were taught everyday activities, not showing a beneficial effect of that intervention on apathy symptom severity [6]. A recent KS study in 15 patients with and 15 without cerebrovascular disease investigated apathy using the Apathy Evaluation Scale (AES) and related apathy severity to related constructs (everyday activities, emotional bluntness, competency to consent, and executive dysfunction). However, that study did not find any correlations between apathy and these other constructs, possibly due to the small sample size [7].

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There is increasing evidence that apathy is not a unitary construct, but consists of three core components: a cognitive, affective/emotional, and behavioral component [5,8], but the multidimensional nature of apathy has not been studied in KS using a validated apathy rating scale. Furthermore, with respect to the underlying mechanisms, apathy has been argued to be associated with executive dysfunction [9,10], which is also highly prevalent in KS [1]. However, such an association has not been demonstrated in KS [7]. It could be hypothesized that especially the cognitive and behavioral components of apathy correlate with everyday executive function in KS, but this relation has not yet been studied. The current study aims to 1) investigate the three core components of the apathy syndrome in KS patients, and 2) relate them to overall cognitive dysfunction and everyday life executive dysfunction.

Methods

Participants

Forty-three patients with KS participated in this study (see Table 1 for demographics). Of these, 34 were inpatients of Atlant Korsakoff centre of expertise in Beekbergen and 9 inpatients of the Centre of Excellence for Korsakoff and Alcohol-Related Cognitive Disorders of Vincent van Gogh Institute for Psychiatry in Venray, the Netherlands. Patients participated in a larger study on cognitive and behavioral dysfunction in KS [11], but the data reported in the present paper have not been published before. Inclusion criteria were: meeting the KS criteria,1 the DSM-5 criteria for Alcohol-induced Major Neurocognitive Disorder, Amnestic-Confabulatory Type, no brain disorders unrelated to alcohol (e.g., stroke), and aged <70. All patients had to be in the chronic stage and abstinent from alcohol (*M* duration 6.6 years, range 5 months-16 years). All patients provided written informed consent; if patients were not legally competent, their legal representative also signed the informed consent form.

Materials

Apathy was measured with the Dutch version of the18-item Apathy Evaluation Scale – Informant version (AES-I).7 Professional caregivers who knew the patient well rated the patients on a 4-point Likert scale (maximum score=72). A score of ≥42 indicates an apathy syndrome. Also, the *cognitive* (max=32), *behavioral* (max=20) and *emotional* (max=8) subscores were computed [7]. General cognitive functioning was measured with the validated Dutch version of the Montreal Cognitive Assessment (MoCA; max=30, higher score reflects better cognitive function, score <25 indicative for substance-induced neurocognitive disorder) [12]. Observer-rated everyday executive functioning was assessed using the validated Dutch informant version of the Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A) [13] which includes the main subscales Metacognition and Behavioral Regulation, and 9 subscales (see Table 1), with higher scores reflecting more executive problems. Observer ratings were used rather than self-reports of daily executive problems, as impaired awareness of deficits is common in patients with alcohol-induced cognitive disorders.

Analyses

All analyses were performed in IBM SPSS 27.0. First, the normality of all variables was checked using Q-Q plots. Next, for descriptive purposes, we computed the number of patients who were rated at or above the established AES-I cut-off score indicative for an apathy syndrome, scored below the cut-off score on the MoCA and scored in the clinically impaired range on the BRIEF-A (i.e., >2 SD above the normative mean). Paired sample *t*-tests comparing the mean item scores per subscale were performed to enable direct comparisons between subscales with different ranges (α=0.05). Also we computed Pearson correlation coefficients (*r*) between the AES-I subscales, the BRIEF-A subscales and the MoCA (α=0.01).

Results

The normality assumption was met for all variables. All patients performed below the cut-off score of 25 on the MoCA indicative for a substance-induced neurocognitive disorder. Thirty-one (72.1%) patients performed at or above the established AES-I cut-off score indicative for an apathy syndrome. On the BRIEF-A 18 patients (41.9%) performed in the clinically impaired range. More severe cognitive (M=2.69, SD=0.74) than emotional (M=2.51, SD=0.83) apathy ratings were found ($t(42)$=2.08, P=0.044) and a trend towards more behavioral (M=2.69, SD=0.76) than emotional apathy ($t(42)$=1.8, P=0.081), but there were no differences between the cognitive and behavioral ratings ($t(42)$=0.1, P=0.907) (Table 1).

Table 2 shows the correlations of the AES-I with the MoCA and the BRIEF-A. Significant correlations between the MoCA and AES-I Total score and AES-I Behavioral subscores ($r \geq |-.41|$) were found, but no significant correlations between the MoCA and AES-I Cognitive and AES-I Emotional ($r \leq |-0.36|$) subscores. None of the AES-I measures correlated significantly with the BRIEF-A Behavioral Regulation main scale or any of its subscales ($r \leq .38$). All AES-I subscales significantly correlated with the BRIEF-A Metacognition main scale and four of its subscales: Initiate, Working memory, Plan/Organize, and Task monitoring ($r \geq .43$), but not the subscale Organization of materials ($r \leq .36$) (Table 2).

Table 1. Demographic variables and results for the MoCA, AES-I and BRIEF-A main and sub-scales of the Korsakoff patients (N=43).

	Mean	SD	Range
Age	60.9	6.5	38–70
Sex (m:f) N	33:10		
MoCA	17.2	3.1	9–24
Education level N			
Low	24		
Average	12		
High	7		
AES-I			
Total score	48.4	12.7	25–70
Cognitive scale	21.5	5.9	10–32
Behavioural	31.5	3.8	5–20
Emotional	5.0	1.7	2–7
BRIEF-A			
Total Score	145.3	27.1	83–190
Behavioral Regulation Index	55.6	13.4	31–84
Inhibit	14.0	3.7	9–22
Shift	13.3	2.9	6–17
Emotional control	17.4	5.9	10–29
Self-monitoring	10.9	3.5	6-18
Metacognition Index	89.7	17.9	51–116
Initiate	18.1	3.7	10-24
Working memory	17.5	3.9	8–24
Plan/Organize	23.2	4.6	12–30
Task monitoring	13.0	3.5	6–18
Organization of materials	17.9	4.7	8–24

MoCA = Montreal Cognitive Assesment; AES-I = Apathy Evaluation Scale – Informant Version; BRIEF-A = Behavior Rating Inventory of Executive Function – Adult Version

Table 2. Pearson correlation coefficients of the AES-I subscales with the BRIEF-A subscales and the Montreal Cognitive Assessment (MoCA).

	AES-I Scale			
BRIEF-A Scale	Total	Cognitive	Behavioral	Emotional
Behavioral Regulation Index	.27	.22	.25	.21
Inhibit	.38	.35	.34	.26
Shift	.27	.21	.28	.37
Emotional control	.10	.06	.10	.03
Self-monitoring	.23	.21	.20	.16
Metacognition Index	.60*	.56*	.57*	.50*
Initiate	.67*	.62*	.66*	.53*
Working memory	.52*	.48*	.50*	.46*
Plan/Organize	.51*	.46*	.50*	.43*
Task monitoring	.62*	.57*	.61*	.48*
Organization of materials	.36	.35	.28	.30
MoCA	-.41*	-.36	-.44*	-.20

* P<.01; AES-I = Apathy Evaluation Scale – Informant Version; BRIEF-A = Behavior Rating Inventory of Executive Function – Adult Version

Discussion

This study is the first to examine the multifaceted nature of apathy in KS. 72.1% of the KS patients could be classified as having an apathy syndrome, with highest ratings given on the cognitive and behavioral apathy subscales, compared to emotional apathy. With respect to executive problems in daily life as measured with the BRIEF-A, apathy was related to observed problems in metacognitive behavior, specifically with initiation, working memory, planning and organization. However, no correlations were found between any of the apathy subscales and the observed problems in behavioral regulations (shifting, inhibition, emotional control and monitoring). Our finding illustrates the need to further examine the relation between apathy and of observational and performance measures of executive function in KS.

Our study also has several limitations. First, although the prevalence of apathy in our sample was high, the range of some of the AES subscales is limited compared to the total score (with the emotional subscale only consisting of two items). Recently, the Apathy Motivation Index (AMI) [5] was developed to overcome shortcoming of existing apathy scales that may not capture the full range of apathetic symptoms, but this instrument has not been applied in KS yet. Another limitation is the modest sample size of 43 patients. Larger samples are needed to replicate and extend the current study (e.g., by performing factor analysis). Furthermore, apathy as a syndrome may overlap with depression [5], which we did not measure directly in the current study. Moreover, our measure of executive dysfunction was limited to an extensive behavioral assessment, but did not include performance-based measures of executive function. While it has been argued that behavioral assessment of executive function may be more ecological valid than the use of performance-based neuropsychological executive tests, performance-based tests may capture other aspects of executive function than behavioral ratings [14]. Studies in other disorders, for instance, have demonstrated correlations between apathy ratings and the performance on neuropsychological executive tests. That is, apathy was found to be related to tests of concept shifting, inhibition and working memory in Alzheimer's dementia [9], and to response initiation, but not shifting or inhibition, in Parkinson's disease [10]. However, a study in frontotemporal dementia did not show any correlations between apathy and response initiation as a measure of executive function [15]. These mixed findings and the lack of studies on apathy in KS illustrate the need for more research on the cognitive correlates of apathy.

In all, we report a high prevalence of apathy in KS patients that involves the behavioral, cognitive and emotional apathy domains. Apathy severity was related to overall cognitive dysfunction. An association between apathy and metacognitive, but not behavioral, everyday executive problems was found. As apathy is associated with high caregiver burden and worse every-day functioning, interventions targeting apathy are clearly needed. Future studies using apathy measures with a more extensive scoring range and performance-based executive function measures in larger samples are required to further examine the underlying neurocognitive mechanisms of apathy in KS patients, which may result in a larger proportion of explained variance.

Acknowledgments

The authors thank Karina Burger, Leonie Mengerink and Melissa van Zeist for their help in data collection. This work was partially supported by funding from the Topcare Foundation [Date: 2015-10-19]

Ethics Approval

The study was approved by the Ethics Committee of the Faculty of Social Sciences of Radboud University (ECSW2015-1210-343) and the institutional review boards of Korsakoff Centre Atlant (mdz/mp/2015-005) and Vincent van Gogh Institute for Psychiatry (CWOP15.04365).

Conflict of Interest Statement

The authors report no financial relationships with commercial interests or other conflicts of interest in relation to this manuscript.

References

1. Arts NJM, Walvoort SJW, Kessels RPC. Korsakoff's syndrome: a critical review. Neuropsychiatr Dis Treat. 2017;13:2875–2890
2. Bowden SC. Is there more than one neuropsychological disorder commonly associated with alcohol dependence? Drug Alcohol Rev. 1992;11:299-304.
3. Gerridzen IJ, Hertogh CMPM, Depla MF, Veenhuizen RB, Verschuur EML, Joling KJ. Neuropsychiatric symptoms in people with Korsakoff syndrome and other alcohol-related cognitive disorders living in specialized long-term care facilities: prevalence, severity, and associated caregiver distress. J Am Med Dir Assoc. 2018;19:240–247
4. Gerridzen IJ, Goossensen MA. Patients with Korsakoff syndrome in nursing homes: characteristics, comorbidity, and use of psychotropic drugs. Int Psychogeriatr. 2014;26:115-121
5. Ang YS, Lockwood P, Apps MA Muhammed K, Husain M. Distinct subtypes of apathy revealed by the Apathy Motivation Index. PLoS One. 2017;12:e0169938
6. Rensen YCM, Egger JIM, Westhoff J, Walvoort SJW, Kessels RPC. The effect of errorless learning on psychotic and affective symptoms, as well as aggression and apathy in patients with Korsakoff's syndrome in long-term care facilities. Int Psychogeriatr. 2019;31:39–47
7. Oey MJ, Brouwer VHEW, Buijs MJ, Wijnia JW, Postma A, Oudman E. Unraveling Apathy in Korsakoff syndrome patients receiving long-term care with and without cerebrovascular comorbidity. Alcohol Clin Exp Res. 2021;45:131-139.
8. Marin RS, Biedrzycki RC, Firinciogullari S. Reliability and validity of the Apathy Evaluation Scale. Psychiatry Res. 1991;38:143–162
9. McPherson S, Fairbanks L, Tiken S, Cummings JL, Back-Madruga C. Apathy and executive function in Alzheimer's disease. J Int Neuropsychol Soc. 2002;8:373–381

10. Meyer A, Zimmermann R, Gschwandtner U, Hatz F, Bousleiman H, Schwarz N, Fuhr P. Apathy in Parkinson's disease is related to executive function, gender and age but not to depression. Front Aging Neurosci. 2015;6:350
11. Moerman-van den Brink WG, van Aken L, Verschuur EML, Walvoort SJW, Egger JIM, Kessels RPC. Executive dysfunction in patients with Korsakoff's syndrome: a theory-driven approach. Alcohol Alcoholism. 2019;54:23–29
12. Bruijnen CJWH, Jansen M, Dijkstra BAG, Walvoort SJW, Lugtmeijer S, Markus W, De Jong CAJ, Kessels RPC. The Montreal Cognitive Assessment as a cognitive screen in addiction health care: a validation study for clinical practice. J Subst Use. 2018;24:47-54
13. Roth RM, Isquith PK, Gioia GA. BRIEF-A: Behavior Rating Inventory of Executive Function - Adult Version. Psychological Assessment Resources: Lutz, FL, 2005.
14. Beerten-Duijkers JCLM, Vissers CTWM, Rinck M, Barkley RA, Egger JIM. Dutch translation and adaptation of the Barkley Deficits in Executive Functioning Scale (BDEFS). Arch Clin Psychiatry. 2019;46(4):89-96
15. Gonçalves SAB, Caramelli P, Mariano LI, Guimarães HC, Gambogi LB, Resende EPF, Teixeira AL, de Souza LC. Apathy in frontotemporal dementia is related to medial prefrontal atrophy and is independent of executive dysfunction. Brain Res. 2020;1737:146799