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Unraveling Apathy in Korsakoff Syndrome Patients Receiving Long-Term Care With and Without Cerebrovascular Comorbidity

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Background: Korsakoff syndrome (KS) is a severe neuropsychiatric disorder caused by acute deficiency of vitamin B1 and concomitant alcoholism. Patients with KS are particularly vulnerable for cerebrovascular comorbidity. KS is characterized by cognitive and neuropsychiatric symptoms, one of which is apathy. Apathy is a pathological lack of goal-directed behaviors, goal-directed cognitions, and goal-directed emotions. Cerebrovascular accidents are known to carry a risk for developing apathy. Apathy has a dramatic effect on the autonomy and daily lives of patients suffering from this condition.

Methods: We assessed general apathy and related subconstructs in fifteen patients with KS, fifteen patients with KS and cerebrovascular comorbidity who reside in a 24-hour care facility, and fifteen healthy controls.

Results: Compared with healthy controls, both KS patient groups showed higher levels of apathy as rated by a close informant. We found no difference between both KS patient groups and the healthy control group on the self-report section of the Pleasant Activities List, suggesting that motivation is still intact in KS patients. It is important to note a discrepancy was found between self-reporting and proxy reporting on this list. KS patients with cerebrovascular comorbidity showed more severe emotional blunting compared to both KS patients without cerebrovascular comorbidity and healthy controls. The competency to consent was lower in patients compared with healthy controls, but no difference was found between KS patients with cerebrovascular comorbidity and those without.

Conclusions: Our results suggest that KS patients show increased levels of general apathy compared with healthy controls. Patients show a diminished competency to consent and increased emotional blunting, while motivation is not compromised. Cerebrovascular comorbidity in KS forms a high risk for emotional blunting. The results of this study suggest that apathy is a severe problem in KS. More attention in both the literature and clinical practice would benefit this complex patient population.

Key Words: Apathy, Korsakoff Syndrome, Neuropsychiatric Symptoms, Cerebrovascular Comorbidity.

ONE OF THE most profound consequences of persistent alcoholism is Korsakoff syndrome (KS). KS is a severe disorder characterized by neurocognitive and neuropsychiatric symptoms caused by an acute deficiency of vitamin B1 and concomitant alcoholism (Arts et al., 2017). The prevalence of KS varies from 0 to 2% in the general population and sits around 12.5% in individuals with alcohol use disorder (Gerridzen et al., 2017). KS is characterized by atrophy of the diencephalon and cerebellar brain, leading to deficits in episodic memory, executive functioning, and social cognition, such as a lack of empathy, the inability to recognize emotional states correctly, and the inability to adopt another person's perspective (Arts et al., 2017; Drost et al., 2018; Kessels et al., 2014; Kopelman et al., 2009; Oosterman et al., 2011; Oudman et al., 2019; Van Oort and Kessels, 2009). Central neuropsychiatric symptoms in KS are disorders of affect, confabulations, anosognosia, and apathy (Gerridzen et al., 2017; Kessels et al., 2014). Apathy is a complex construct, consisting of multiple subdomains originating from the field of (neuro) psychiatry (Robert et al., 2009). It is commonly found in various cognitive disorders such as dementia (Bandyopadhyay et al., 2014; Gonçalves et al., 2017; Lanctôt et al., 2017; Zhao et al., 2016). Apathy is often described as a pathological loss of, or diminished, goal-directed behavior (a lack of effort and dependency on others to structure activity), goal-directed

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cognition (a lack of interest in learning new things or in new experiences and a lack of concern about one's personal problems), and goal-directed emotions (unchanging affect and lack of emotional responsivity to positive or negative events; Marin, 1990; Marin et al., 1991; Robert et al., 2009). Emotional apathy is related, but functionally different from reduced affect. In emotional blunting, it is possible that patients still experience emotions but are unable to display them, while emotional apathy is the lack of emotions (Gur et al., 2006). Cognitive apathy is defined by difficulty in elaborating the plan of actions necessary for the ongoing or forthcoming behavior. It follows from the dysfunction of several executive functions. Executive functioning consists, among other things, of planning, setting, or maintaining (sub)goals, the competency to consent, and applying strategies to retrieve information from episodic or semantic memory (Gavett et al., 2012; Levy and Dubois, 2006). This particular cognitive domain is necessary to make sound and reasonable judgments to lead a healthy, safe, and independent life. The clinical setting shows KS patients frequently fail at adequately responding to basic home safety predicaments such as extinguishing a cigarette before falling asleep, safely using a stove, or properly taking prescription medication. Apathy can lead to dangerous situations which occur when failing to respond adequately to urgent situations, as well as in everyday life (Hildebrand et al., 2014). In addition to serious consequences for the patients themselves, apathy is known to increase healthcare costs and correlate highly with caregiver distress (Dauphinot et al., 2015; Merrilees et al., 2013; Papastavrou et al, 2007). In the clinical setting, those working closely with KS patients describe apathy as having a profoundly negative influence on a patient's ability to lead an autonomous and structured lifestyle. Despite this clinically reported nexus, there is a lack of empirical research on the prevalence of apathy in KS patients.

Preceding admission to long-term care facilities, patients with KS often experience severe self-neglect frequently resulting in Wernicke's encephalopathy due to nutritional depletion. This carries a heightened risk for developing medical conditions such as stroke (Rehm, 2011; Sechi and Serra, 2007; Wijnia et al., 2012). In addition to heightened risk for cerebrovascular accidents following Wernicke's encephalopathy, lifestyle choices such as frequent smoking and preexisting excessive alcohol consumption further increase the risk for cerebrovascular comorbidities. Stroke itself carries a risk for developing apathy as Caeiro and colleagues (2013) showed with 1 in 3 stroke patients being affected by apathy in the postacute stage. A longitudinal study by Withall and colleagues (2011) showed that 55% of stroke patients were apathetic 15 months after stroke. One of the characteristic traits of Wernicke's encephalopathy is abnormal gait. It is not uncommon for KS patients to frequently fall due to Wernicke's encephalopathy and/or direct intoxication. Frequent falling often leaves patients with an extensive medical history of contusio cerebri, which carries a known risk for developing cerebrovascular dysfunction. KS patients are therefore at risk for direct brain injury due to both Wernicke's encephalopathy as well as cerebrovascular dysfunction, which is known to result from frequent falling (Jullienne et al., 2016).

Various assessment tools can be used to assess apathy such as a patient's self-report, informant-based assessment, and clinical scales. In other diseases where apathy is a prevalent neuropsychiatric symptom such as Alzheimer's, Parkinson's, frontotemporal dementia, and stroke, frequently applied indices include Neuropsychiatric Inventory (NPI; Cummings et al., 1994), Structured Interview for Apathy (SCIA; Starkstein, 2005), Apathy Evaluation Scale (AES; Marin et al., 1991), Dementia Apathy and Interview Rating Scale (Strauss and Sperry, 2002), Lille Apathy Rating Scale (LARS; Sockeel et al., 2006), The Scale for Emotional Blunting (SEB; Abrams and Taylor, 1978), and Dimensional Apathy Scale (Radakovic & Abrahams, 2014). The rating tools vary in how they rate apathy; some make a distinction between subtypes, whereas others rate apathy on a more general level. For example, the SCIA and AES touch on three subtypes of apathy, as the NPI has one question regarding apathy as a single construct, rating its presence, severity, and burden on caregiver. The SEB rates apathy in three domains: behavior, affect, and thought and the LARS rates apathy on nine domains ranging from Everyday Productivity and Taking Initiative to Emotional Responses. There is no specific questionnaire or test developed to measure cognitive apathy as a standalone construct. However, as mentioned previously, cognitive apathy derives from the dysfunction of executive functioning. One of the modules of the Neuropsychological Battery measures executive functioning as well as includes a subtest (Judgment) assessing the function of problem solving and decisional capacity pertaining to home safety.

Following the abovementioned risks that KS, both with and without additional cerebrovascular burden, can have on the cognitive, behavioral and emotional functioning, the aim of this study was to research the effects of KS with and without cerebrovascular comorbidity on general apathy, the ability to have intentions to perform pleasurable activities, the competency to consent, and emotional blunting. It was expected that the KS group with additional cerebrovascular comorbidity (KS + CC) would show higher scores on measures of apathy and their related subconstructs compared with the KS group (KS) and the control group (CG). More specifically, more apathy was expected to be found by higher levels of dependency, a more impaired performance on experiencing emotions, and lowered effort to engage in new activities.

MATERIALS AND METHODS

Participants

Fifteen patients diagnosed with KS, and fifteen KS patients with cerebrovascular comorbidity receiving long-term care in Korsakoff Centre Slingedael in Rotterdam, The Netherlands participated in this study. All patients met the DSM-5 criteria for "alcohol-induced major neurocognitive disorder" following extensive neuropsychological evaluation at the time of admission. The presence of anterograde amnesia was measured with the Dutch versions of the Visual Association Test (Lindeboom, 2002) and the Auditory Verbal

Learning Test (Saan & Deelman, 1986). All patients had been abstinent for at least 6 months prior to their KS diagnosis. Patients' medical documentation was often incomplete regarding clear periods of AUD to report on precise periods of alcohol consumption. All patients had preserved intellectual abilities and did not meet the criteria for alcohol dementia. Recent MRI or CT scans were not available for all KS + CC patients. For four patients, a diagnosis of stroke was confirmed by MRI scans, which were obtained from a medical diagnosis list based on letters of discharge from antecedent hospital admissions: one patient had a left hemisphere stroke without specific mention of date or year, one patient had a right hemisphere stroke without specific mention of date or year, one patient was reported to have a lacunar stroke, periventricular and in the pons in 2014, and one patient had a lacunar stroke in the brainstem in 2003. For six patients, cerebrovascular damage and location were not specified further but were reported in medical and/or neuro(psycho)logical reports. Because severe alcohol use disorder often leads to frequent falling, four patients were reported to have cerebrovascular damage as part of a skull base fracture with cerebral contusion. In one patient, cerebrovascular damage was not confirmed in medical or neuro(psycho)logical reports, and this case was excluded from further analysis. All patients were in the chronic amnestic phase of the syndrome and not in the confusional state of Wernicke's encephalopathy. They all had an extensive history of alcoholism and nutritional depletion, notably thiamine deficiency, verified through medical records and none experienced other brain disorders (dementia, epilepsy) or acute psychiatric conditions (psychosis, major depression disorder, anxiety disorder etc.). None of the patients were prescribed psychotropic medication. Additionally, fifteen healthy participants (without physical or mental conditions) were included and performed the same tasks as the patient population. Due to missing or incomplete documentation, slightly different patient and control person numbers could be included in the final data set: 14 KS, KS + CC, and 14 CP were included in the AES-Informant (AES-I) data. 13 KS, 13 KS + CC patients, and 14 CG for the Pleasant Activities List. 15KS, 13 KS + CC, and 15 CG patients were included in the SEB. The patients' regular medication regimes were maintained. All participants signed a written informed consent waiver and were guaranteed that their data would be treated confidentially and according to the ethical standards of the declaration of Helsinki. The research project was approved according to the ethical guidelines of the Social Science Faculty of the Utrecht University.

Procedure

For our study, both self-report, informant-based, and clinical scales were employed to assess general apathy, the ability to have intentions to perform pleasurable activities, competency to consent, and emotional blunting. To assess the extent to which KS and KS + CC patients engaged in activities and if they experienced emotional blunting, patients themselves as well as professionally trained, first responsible caregivers filled in various activity questionnaires and emotional blunting scales. To gain an understanding of the competency to consent in KS and KS + CC, an interview-based assessment was performed regarding judgment skills. For the healthy control group, the participants themselves and their respective partners filled in the same questionnaires as the KS and KS + CC patients and underwent the same interview-based assessment.

Patient Characteristics and Scores of Cognitive Functioning

Data were obtained for age, sex, and educational-level distribution. Oudman et al. (2014) reported that the MMSE has adequate psychometric properties as a screening instrument for the detection of KS and memory failure. Therefore, participants' memory functioning was measured with the Mini Mental State Examination (Folstein et al., 1975). The DEX Self-report and DEX-Independent Report were used as tools to reflect motivational difficulties, behavioral, and cognitive changes, and the Zoo Map test was used as a measure for planning and organizational abilities (Wilson et al., 1997). See Table 1.

Apathy and Related Construct Scores

General Apathy - AES-I. The Dutch version of the AES-I was used to measure the presence and overall severity of apathy in participants. This scale rates a person's thoughts, actions, and emotions over the previous 4 weeks based on reports by a known informant (Marin et al., 1991; Resnick et al., 1998). The AES-I consists of 18 items which are scored on a 4-point Likert scale. The total score ranges from 18 to 72 with a cutoff score of 35. An example of AES-I question: He or she is interested in things (i) Very characteristic, (ii) Somewhat characteristic, (iii) Slightly characteristic, and (iv) Not at all characteristic.

Intentions to Perform Pleasurable Activities - Pleasant Activities List (PAL). To assess the intention to perform pleasurable activities, the Dutch scale of the Pleasant Activities List (PAL) was used (Koks and Roozen, 2005; Roozen et al., 2008). This list intends to measure the level of effort or motivation for undertaking activities. The PAL consists of 139 items, which can be divided into 10 different activity subscales, such as social, domestic, or sensation-seeking activities. The questionnaire is scored on a 5-point Likert scale and rates how frequently (PAL-f) a participant performs a certain activity and how pleasurable (PAL-p) that activity is perceived by the participant. There are no clearly defined cutoff scores. An example of a PAL question: Playing cards. How frequent? (i) not at all, (ii) a little, (iii) considerably, (iv) sufficiently, (v) very. How pleasurable? (i) not at all, (ii) a little, (iii) considerably, (iv) sufficiently, (v) very.

Competency to Consent - The Judgment Scale of the Neuropsychological Assessment Battery (NAB). A Dutch translation of the Judgment scale, a subtest of the Neuropsychological Assessment Battery (NAB) was used to assess the competency to consent (White and Stern, 2003). On the Judgment scale, the capability of making sound and safe decisions is measured to screen for executive functioning. NAB Judgment is an interview-based assessment containing 10 practical questions involving home safety, health concerns, and daily living activities, with participants' answers being rated with a score of a zero, one, or two. The total score ranges from 0 to 20. A score of 12 or lower indicates problems in judgment such as impaired problem-solving capability, poor knowledge of important aspects of home safety and health/medical issues, as well as reduced decisional capacity in these areas (Gavett et al., 2012; MacDougall and Mansbach, 2013). When available, the score from the patient's medical records was used. An example of a NAB judgment scale question: Why is it important to tell your doctor all the medications you are taking?

Emotional Apathy - SEB. To measure emotional blunting, the SEB was used (Abrams and Taylor, 1978). The scale consists of 16 items scored on a 3-point Likert scale by an independent evaluator. The SEB examines pleasure-seeking behavior, affective blunting, and cognitive blunting. The total score ranges from 0 to 26. A score above 21 indicates emotional blunting. An example question from the SEB: Affect. 1. Absent, shallow, incongruous mood. Rating 0 1 2 (0 = absent, 1 = slight or doubtful, 2 = clearly present).

See Table 2 for general apathy, intention to perform pleasurable activities, competency to consent, and emotional blunting scores.

Data Analyses

The statistical analysis was performed using SPSS Statistics 20 (IBM SPSS statisics for Windows, Armonk, NY, USA). An effect

Table 1. Summary of Demographic Variables and Executive Test Scores for All Participants

Measurement	KS patients	KS + CC patients	CG	Significance
Number (number of males)	15 (9)	14 (11)	15 (9)	$\chi^2(2) = 1.46$, $p = 0.48$
Age in years	64.1 (7.1)	64.1 (6.3)	60.5 (6.5)	$F(2, 41) = 1.47$, $p = 0.24$
Educational level *Mo* (*range*)[a]	5 (2 to 7)	4 (2 to 7)	6 (4 to 7)	$\chi^2(2) = 9.45$, $p < 0.01$
MMSE[b]	22.4 (3.1)	24.7 (2.9)	29.1 (0.9)	$F(2, 40) = 27.1$, $p < 0.001$
DEX Self Report[c]	14.3 (12.9)	15.9 (7.9)	11.4 (5.8)	$F(2, 41) = 0.871$, $p = 0.426$
DEX-Independent Report[d]	29.7 (11.9)	40.1 (17.6)	7.7 (5.6)	$F(2, 39) = 24.6$, $p < 0.001$
Zoo Map test[e]	1.3 (1.1)	0.8 (1.0)	3.3 (0.6)	$\chi^2(2) = 25.5$, $p < 0.001$

CG, control group; KS, Korsakoff's syndrome; KS + CC, Korsakoff's syndrome with cerebrovascular comorbdity; MMSE, Mini Mental State Examination.

[a]Educational level was assessed in 7 categories: 1: < primary school; 7 = academic degree (Verhage, 1964)

[b]Mini Mental State Examination, reflecting general cognitive functioning (Folstein et al., 1975)

[c]Self-rating dysexecutive questionnaire, reflecting behavioral difficulties associated with executive functioning (Wilson et al., 1997)

[d]Independent, rating dysexecutive questionnaire, reflecting behavioral difficulties associated with executive functioning (Wilson et al., 1997)

[e]Zoo Map test, reflecting planning and organizational abilities (Wilson et al., 1997)—There was an overall statistical effect (Chi-square = 25.5, $p < 0.001$), suggesting a difference between the patient groups and controls. In post hoc Mann–Whitney *U*-tests, the control group scored statistically higher than the KS patients ($U(30) = 12.5$, $p < 0.001$) and KS + CC patients ($U(28) = 6.0$, $p < 0.001$). The patient groups did not statistically differ ($U(28) = 76.0$, $p = 0.339$).

for education was found. Therefore, for all analyses, education was added as a covariate. The normality assumption was met for all included variables (Kolmogorov–Smirnov test ranging between 0.55 and 1.26, ps < 0.086). Levene's test for homogeneity was met for all variables except the SEB. A MANOVA was performed with the AES-I, PAL, NAB-jdg, and SEB as dependent variables and the groups as between-subject independent variables, to study the influence of KS and KS + CC on general levels of apathy and additional subconstructs of apathy.

RESULTS

Table 1 shows a summary of the demographic variables and test results of the three groups. Patients did not differ significantly regarding age and sex, but they did have a lower level of education.

Table 2 shows the scores for general apathy, intention to perform pleasurable activities, competency to consent, and emotional blunting scores in KS and KS + CC and control group. The reported scores are the mean + standard deviation, the significance level corrected for educational level and, where applicable, a Bonferroni correction.

There is an overall effect of group on the general apathy scales: $F(10, 58) = 6.187$, $p < 0.000001$, Eta-squared = 0.516, suggesting more apathy in the patient groups than in the healthy controls. The between subjects effect is statistically significant for the AES, $F(2, 32) = 24.548$, $p < 0.000001$, eta-squared = 0.605, the SEB, $F(2, 32) = 16.976$, $p < 0.00001$, eta-squared = 0.515, and the NAB, $F(2, 32) = 12.910$, $p < 0.0001$, eta-squared = 0.447. For both the PAL-f, $F(2, 32) = 0.383$, $p = 0.685$, and the PAL-p, $F(2, 32) = 0.345$, $p = 0.711$, there was no significant group effect. In post hoc Bonferroni corrected pairwise comparisons, KS patients scored significantly lower than healthy controls (mean difference = −21.042) on the AES ($p < 0.00001$). Also, KS + CC patients scored significantly lower on the AES (mean difference = −24.909), ($p < 0.00001$). The difference between both patient groups was not significantly different (mean difference −3.867, $p = 0.913$). On the emotional blunting scale (SEB), KS patients scored significantly higher than healthy controls (mean difference = −5.979, $p < 0.05$), and KS + CC patients also scored higher than controls (mean difference = −13.273, $p < 0.00001$). Also, KS + CC patients scored higher than KS patients (mean difference: −7.294, $p < 0.01$). On the NAB-jdg scale, KS patients scored significantly worse than healthy controls (mean difference = 6.266, $p < 0.001$), and KS + CC patients scored lower than controls (mean difference = 5.909, $p < 0.005$). Scores of KS patients and KS + CC patients were comparable (mean difference = −.354, p = 1).

Correlations

We correlated the AES, PAL-frequent, PAL-pleasurable, SEB, NAB, DEX-informant, DEX Self-report, and Zoo Map test in CG, KS, and KS + CC. The AES did not correlate with any of the other characteristics in the three groups (ps > 0.159), suggesting no relationship between apathy, executive functioning, emotional blunting, and intentions to perform pleasurable activities. PAL-frequent was correlated with PAL-pleasurable in CG ($R = 0.641$, $p < 0.05$), KS ($R = 0.635$, $p < 0.05$), and KS + CC ($R = 0.836$), suggesting that activities that were rated as pleasurable were often also performed frequently in patients and controls. None of the other characteristics correlated with PAL-frequent (ps > 0.103). PAL-pleasurable was negatively correlated with emotional blunting in KS + CC patients ($R = -0.608$, $p < 0.05$), suggesting that KS + CC patients who rated more activities as pleasurable often showed less emotional blunting. PAL-pleasurable was not related to any of the other characteristics (ps > 0.065). In the CG, emotional blunting

Table 2. General Apathy, Emotional Apathy, Motivational Apathy, and Behavioral Apathy in Korsakoff's Syndrome, Korsakoff's Syndrome With Cerebrovascular Comorbdity, and the Control Group

Measurement	KS patients	KS + CC patients	CG	Ancova, corrected for educational level	KS versus KS + CC Bonferroni corrected	Post hoc comparisons
General apathy						
AES—I[a]	43.5 (9.9)	47.4 (10.1)	22.9 (6.1)	$F(2, 36) = 25.58$, $p < 0.001$	−3.8, $p = 0.873$	CG < (KS = KS + CC)
Behavioral apathy						
PAL—Often[b]	2.0 (.07)	1.8 (0.8)	1.9 (0.3)	$F(2, 34) = 0.75$, $p = 0.481$		
PAL—Pleasurable[c]	2.4 (0.4)	2.5 (0.8)	2.6 (0.5)	$F(2, 33) = 0.07$, $p = 0.931$		
Emotional apathy						
SEB[d]	7.3 (6.8)	14.6 (8.2)	0.5 (1.3)	$F(2, 38) = 17.8$, $p < 0.001$	−7.1, $p < 0.01$	CG < (KS < KS + CC)
Cognitive apathy						
NAB[e]	12.3 (4.3)	11.8 (2.9)	17.0 (2.6)	$F(2, 39) = 6.8$, $p < 0.005$	1.3, $p = 0.646$	CG < (KS = KS + CC)

CG, control group; KS, Korsakoff's syndrome; KS + CC, Korsakoff's syndrome with cerebrovascular comorbidity.
[a]Apathy Evaluation Scale—Informant, as a global measure of apathy as indexed by an informant (Marin et al., 1991).
[b]Pleasurable Activities List—How frequently the participant performs a pleasurable activity. Average score (GA; Koks and Roozen, 2005).
[c]Pleasurable Activities List—How pleasurable the participant rates a pleasurable activity. Average score (GA; Koks and Roozen, 2005).
[d]Scale for Emotional Blunting, indexing emotional apathy (Abrams and Taylor, 1978).
[e]Neuropsychological Assessment Battery—Judgment, indexing the cognitive ability to perform activities (MacDougall and Mansbach, 2013).

was negatively related with the Zoo Map test ($R = -0.652$, $p < 0.01$), suggesting more emotional blunting in controls who did not obtain the maximum score on planning performance. Blunting was not related to any other characteristics ($ps > 0.124$). The DEX-informant ($ps > .131$), DEX Self-report ($ps > 0.060$), and NAB ($ps > 0.064$) did not correlate with any other test result. Despite the correlation in CG, the Zoo Map test also did not correlate with any characteristics ($ps > 0.106$).

DISCUSSION

The aim of this study was to research the effects of KS with and without cerebrovascular comorbidity on general apathy and related subconstructs in three domains: behavioral, cognitive, and emotional. Throughout the years there have been a myriad of definitions for apathy. Our current study rated the presence of apathy in KS and KS + CC according to the widely used AES as well as through related subconstructs measured with the Pleasant Activities List, NAB Judgment Scale, and the SEB. Apathy has been known to be one of the key characteristics in KS in earlier studies by Arts and colleagues (2017). Despite the major effect of apathy in KS, this phenomenon remains mostly untouched in the literature. In one of the few existing KS studies, Gerridzen and colleagues (2018) reported that estimates of the severity of apathy vary widely. The authors pointed out that low severity scores conflict with experiences from clinical practice as reported in previous studies such as Egger and colleagues (2002). It is currently unknown whether patients with KS and cerebrovascular comorbidity experience more apathy compared with KS patients without neurovascular complications. With clinical observations reporting a high prevalence of apathy in KS and there existing a known correlation between apathy and stroke (Brodaty et al., 2005; Withall et al., 2011), it is of interest to study apathy in KS with and without cerebrovascular accidents, as this subcategory of KS patients appear to be at heightened risk for experiencing apathy. This is one of the first studies to systematically investigate apathy in these patient groups.

The results of this present study indicate that KS patients with and without cerebrovascular comorbidity show severe general apathy as rated by a close informant. Upon further inspection, it was found that KS and KS + CC patients are severely impaired regarding competency to consent. Additionally, increased emotional blunting was found in KS and KS + CC patients compared with the healthy controls, with cerebrovascular comorbidity patients showing even stronger pathological emotional expression compared with KS patients. Against expectation, both the KS and the KS + CC group expressed the same levels of engagement and enjoyment in pleasant activities, meaning KS and KS + CC patients did not subjectively report any pathological levels of motivation compared with the control. In sum, the results of this study suggest that apathy should indeed be considered as one of the hallmark syndromes of KS.

General Apathy

Caregivers for the KS and KS + CC patients reported higher levels of apathy compared with the levels reported by the partners for the healthy control participants. Most patients turned out to be severely apathetic when rated by their caregiver, indicating a seriously compromised quality of life. Patients with heightened levels of apathy require intensive care and guidance regarding the everyday life skills that are imperative to their overall well-being. This may include getting up in the morning, sufficient self-care, attending to wounds or impaired skin health, as well as ensuring sufficient levels of food and drink intake (Kopelman et al., 2009). This could suggest an increased level of burden for those caring for KS patients as they require frequent and

intense daily guidance. If left to their own devices, KS patients are known to show severe levels of self-neglect, often being admitted to a hospital with life-threatening illness. However, our current study did not specifically rate caregiver burden. This, therefore, warrants future research regarding apathy in KS and caregiver burden. Our current study is in line with the reported experience in the clinical practice, indicating that there exists a high prevalence of severe apathy in Korsakoff patients. In other disorders, such as Alzheimer's and vascular dementia, apathy is known to be a prevalent symptom. Earlier research by Mega and colleagues (1996) found that apathy was the most common behavioral symptom in Alzheimer's, exhibited by 72% of patients. Similar findings were reported by more recent research, which reported a high prevalence and persistence rate of apathy in Alzheimer patients (van der Linde et al., 2017). In that study, apathy was defined using participant-based questions regarding slow thinking and talking, decreased decisiveness, loss of energy and interest, as well as informant-based questions regarding loss of energy, interest, and giving up a special skill or hobby. Tiel and colleagues (2019) found significantly higher apathy scores in vascular dementia using the NPI compared with AD, showing that apathy is more prevalent in patients with a higher vascular load.

Intentions to Perform Pleasurable Activities

When assessing self-reporting of activities, it was found that KS and KS + CC patients did not report lower levels of intentions to perform pleasant activities. In other words, they report to engage in just as many activities and experience just as much enjoyment from these activities as the healthy control group. Our results are in contrast with earlier findings by Gerridzen and colleagues (2017) and our own proxy reports on apathy. Additionally, caregivers report severe levels of apathy. This is supported by their clinical experience, which shows severe cases of apathy where it can be a daily struggle to get patients out of bed, into the shower or to a meal. This large discrepancy can be explained by the earlier mentioned anosognosia, or lack of disease insight and awareness which is a key symptom in KS (Gerridzen et al., 2017; Walvoort et al., 2016). This would mean that the patients simply are not aware of their increased levels of apathy and thus perceive themselves to be functioning at normal activity levels. Ideally, apathy assessment should be structured with input from the patient, caregiver, and clinician (Robert et al., 2009). However, a lack of disease awareness in KS might argue against self-evaluation, perhaps making KS patients not an ideal population to self-report on the presence of apathy. However, rating apathy by means of self-reporting can provide useful information regarding certain aspects of intrinsic motivation. Our study provides some insight into what appears to be an intact motivation despite not acting upon that motivation by actually engaging in activities. Preserved motivation deserves further study, specifically with respect to whether it can be employed to alleviate apathy. Another explanation for the normal levels of self-reporting of activities in KS and KS + CC patients could be that living in a 24-hour care facility automatically instills daily structure and routines. This may cause them to report certain levels of activity when in fact these are externally driven by the repeated efforts of caregivers, perhaps causing a false sense of independent, self-driven activities and engagement levels.

Competency to Consent

It was found that KS and KS + CC patients are less capable of making sound decisions regarding home safety and health concerns compared with the control group. The NAB Judgment scale questionnaire has been examined in populations of Alzheimer's disease and Traumatic Brain Injury, but not in KS (Gavett et al., 2012; Zgaljardic et al., 2011). In addition to the earlier mentioned dysexecutive functioning in KS, this study provides evidence for impaired judgment in KS pertaining to home, health, and medical safety—complex cognitive skills within the domain of executive function (Strauss et al., 2006). Within the KS population, this specific assessment of judgment can be of particular importance since it is not rare for KS patients to be required to receive 24-hour care for a limited amount of time despite their preference for wanting to return home. Using a tool which specifically measures home safety functioning could be of added value to standard neuropsychological tests when assessing a patient's ability to return home safely. In future research, we will look at the possibility to retrain certain basic home safety skills in the hope of expanding levels of independence.

Emotional Blunting

Deficits in emotional expression have been reported in various neurocognitive disorders such Alzheimer's disease, Parkinson's disease, and stroke patients as well as in long-term alcoholic men (Bowers et al., 2006; Marinkovic et al., 2009; Robert et al., 2002). To date, no study has looked at the effects of KS on emotional blunting. In line with our expectations, both KS and KS + CC patients show increased blunting compared with the control group. This is not entirely unexpected as Arts and colleagues (2017) state that KS patients are often described as emotionally flat and affectively detached. This creates further implications in social situations for this specific patient group. The burden on social situations is potentially further compromised by recent findings in a study by Drost and colleagues (2018) who researched various aspects of social cognition in KS and found impairment in social behavior. Looking at the aforementioned strains on affective and social functioning, it would not be presumptuous to state that KS + CC patients have a heightened risk for experiencing problems in social situations and interpersonal relationships. This is of particular interest to those working with KS and KS + CC patients in a 24-hour care facility, as patients often live in a group setting where altercations are not uncommon. Emotional

blunting and lack of appropriate social behavior should be studied in this specific population in order to gain a better understanding of potential triggers for altercations and implications on social interactions and interpersonal relationships in KS patients. In our study, emphasis should be placed on KS + CC patients showing increased levels of emotional blunting. However, our study does not directly link cerebrovascular comorbidity as a causal relationship with apathy. Our findings warrant future research to explore this relationship and be able to provide a clear statement.

Limitations

A limitation of this study is that we applied a combination of both proxy-based reports and self-reporting, while instruments such as the AES are also developed as self-assessment tools for apathy. A reason to do so was that anosognosia, which is common in KS, leads to a compromised ability to self-assess apathy (Egger et al., 2002). A limitation worth mentioning is that many of the lists employed are not available in Dutch and have therefore not been properly validated. Another limitation is the possible selection of a subgroup of patients in this study. A large majority of KS patients in the Netherlands reside in long-term care facilities, making it possible that the selected subgroup of patients requires more intensive care than patients residing outside of long-term care facilities. We nevertheless aimed to get a sample of typical KS patients in the present study. Another limitation of this study is that cognitive performance was vastly impaired in KS patients, possibly causing apathy. There was however large variety on the MMSE, despite globally low scores on the AES, suggesting that apathy forms a distinctive syndrome within KS patients. Lastly, another possible limitation is the relatively small sample size. Studies pertaining to KS, however, frequently consist of smaller sample sizes due to the obscure nature of this population (Drost et al., 2018).

Recommendations for Future Research

Our results show a clear presence of general apathy in KS. This makes it of great importance to further study the effects of apathy in KS as well as focusing on treatment to relieve its consequences. Our study shows the presence of intact motivation to engage in activities which could potentially be useful in finding a patient-focused approach that uses this motivation and combines it with externally driven cues to engage in actions. Procedural learning principles in KS patients are known to be relatively intact (Oudman et al., 2015). Examples in the clinical practice are of patients routinely walking to the location where they can collect their weekly allowance to purchase food, drinks, or nicotine. Perhaps it would be of interest to combine these operant conditioning principles to intact procedural learning conditioning in order to treat apathy. It could also be of interest to investigate the evidence-based Community Reinforcement Approach (CRA) to help reduce the consequences of apathy in KS. This approach has been applied in chronic substance abusers with positive results (Meyers et al., 2011). In CRA, operant conditioning principles are applied to substitute addiction related behavior with new, pleasant, and healthier reinforcers. One of the central parts of this approach is to activate people to gain new, valuable experiences to contrast addiction and concomitant apathy. Patients are activated through positive reinforcement, which creates new rewarding behavior. Through reinforcement, patients may initiate more action independently, which in turn could help reduce apathy.

CONCLUSION

In conclusion, this study has provided insight into the presence of the underlying neuropsychiatry in KS. KS patients with and without cerebrovascular comorbidity are observed to experience increased levels of general apathy, lower competency to consent, and more emotional blunting compared with a control population. More specifically, patients with cerebrovascular comorbidity experience even higher levels of emotional blunting in comparison with KS patients without cerebrovascular comorbidity. A discrepancy was found between the self-reporting of the intention to perform pleasurable activities and the proxy-reporting on general levels of apathy and related subconstructs, proving that KS patients might be an unreliable source when it comes to self-reporting on intention to engage in activities. However, the intact motivation expressed by KS patients when incorrectly reporting normal levels of engagement and enjoyment, might be useful in offering support for treating apathy.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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