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The neuropsychology of alcohol use disorder
A multimethod evaluation of cognition and illness insight

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The neuropsychology of alcohol use disorder:

A multimethod evaluation of cognition and illness insight

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The neuropsychology of alcohol use disorder:
A multimethod evaluation of cognition and illness insight

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Chapter 1

General Introduction
For several decades, there has been consensus in scientific literature that chronic alcohol use has a neurotoxic effect: it negatively affects brain functioning and adaptive behaviour in general (Crews et al., 2005; Harper, 2009; Kalivas & Volkow, 2005; McCrady & Smith, 1986; Oscar-Berman & Marinkovic, 2007). Neuropsychological studies in patients with alcohol use disorders (AUD) demonstrate deficits in attention, memory, and visuospatial functions as well as in executive functions such as problem solving, mental flexibility, planning, and judgement (Bates et al., 2002; Goldstein et al., 2001; Scheurich, 2005). Consequently, treatment components that require these cognitive skills are impeded which easily lead to increased drop-out rates (Allen et al., 1997; Manning et al., 2008; Scheurich, 2005).

During abstinence, these alcohol-related cognitive deficits may partly recover with a combination of thiamine use and a normal diet (Martin et al., 2003) and can thus be considered as a dynamic phenomenon during sustained abstinence. Indeed, several authors demonstrate that these cognitive deficits are (a) to some extent reversible during abstinence (Bates et al., 2002; Fals-Stewart et al., 1994; Loeber et al., 2009; Mann et al., 1999), (b) may remain stable over one year (Horton et al., 2015; Stavro et al., 2013), and (c) in particular with regard to executive functions, may still improve after six years of abstinence (Fein et al., 2006a; McCrady & Smith, 1986). The speed and extent of recovery differs individually depending on age (Goldman, 1983) and time of abstinence (McCrady & Smith, 1986).

Indeed, the alcohol-related cognitive dysfunction must be viewed in the context of pre-existing neuropsychological deficits, education level, and pre-existing personality traits (Yücel et al., 2007) underscoring the fact that pathways leading towards alcohol addiction are complex and difficult to unravel. Moreover, it is known that alcohol is a causal factor in the etiology of anxiety and depression and that, in turn, the presence of psychopathology and personality traits increases the likelihood of alcohol addiction (Verheul et al., 1999). However, often, the symptoms of psychopathology are related to alcohol intoxication and will resolve during abstinence (Becker, 2008; CBO, 2009; Crews et al., 2005).

For Korsakoff’s syndrome (KS) patients, with severe and persistent alcohol related cognitive dysfunction, studies have demonstrated structural changes in the brain (Martin et al., 2003; Pitel et al., 2014) suggesting that there is a marked distinction between KS patients and AUD patients, who typically show less severe cognitive deficits or are cognitively unimpaired. In addition, impaired social cognition, including social perspective taking and judgement, self-awareness, and illness insight, has been suggested to play a pivotal role in severe alcohol addiction (Uekermann & Daum, 2008; Moeller & Goldstein, 2014).
While impaired social cognition is essential for treatment planning and clinical management, there it is still little research on this topic. Moreover, the terms illness insight, self-awareness, anosognosia, and alcoholic denial are often used interchangeably making it difficult to disentangle.

Conceptualisations: Self-awareness, anosognosia, illness insight, and denial

Impaired illness insight has historically been termed anosognosia or being without knowledge of the disease (Babinski, 1914). Later, this term was used to describe the lack of self-awareness for more subtle cognitive impairments (McGlynn & Schacter, 1989), the failure of the patient to acknowledge a symptom even when confronted by it (Amador et al., 1993), and the inability to accurately estimate one’s functional capacity (Prigatano, 2009). Crosson and colleagues (1989) were the first to develop a model of insight including three levels of awareness: (1) intellectual awareness indicating that patients understand their own limitations; (2) emergent awareness indicating that a patient can both recognize his own limitations and is able to solve them or compensate for them; and (3) anticipatory awareness, the highest level where a patient knows his limitation and makes and carries out a plan requiring metacognition and executive functioning skills. Van Schouwen-van Kranen (2014) integrated the theoretical model of Crosson (1989) with the cognitive disabilities model of Allen et al. (1992) into a clinical reasoning framework in traumatic brain injury patients for improving the ability to perform daily tasks. In this hierarchy-based model, the level of insight corresponds with the level of cognitive functioning, that is from attention (the lowest level), to memory, and finally, executive processes (the highest level).

David (1990) used also as a three level hierarchy-based model distinguishing (1) awareness of the illness; (2) the capacity to view symptoms of the disease as abnormal; and, ultimately, (3) treatment adherence. In this model, no neuropsychological domains of functioning were described. Phillipi and co-workers (2012) in turn described a model of self-awareness which is similar to the model of Crosson et al (1989) including: (1) Core self-awareness, a sense of basic ownership over actions and sensory representation; (2) Extended self-awareness, that is core self-awareness plus the autobiographical self; (3) Introspective self-awareness, relying on higher order executive, attentional and metacognitive functions enabling introspection and ability to reflect on one’s actions. The latter is in line with findings of David and colleagues (2012) that introspective self-awareness (or illness insight) might range from total denial of the disease to more subtle metacognitive awareness deficits.
In everyday functioning and treatment rehabilitation, impairments in illness insight are often seen in patients with neurodegenerative diseases (Shany-Ur et al., 2014), traumatic brain injury (Ham et al., 2014), schizophrenia (Kruck et al., 2009), and in addiction (Moeller & Goldstein, 2014). In addiction, Moeller and Goldstein (2014) define self-awareness as “the failure to ascribe personal relevance or significance to internal stimuli or events that have implications for the self—be they environmental cues/feedback, interoceptive sensations, or on-going behaviour” (p. 1). With this definition, the authors aimed to distinguish self-awareness from more specific terms like alexithymia and self-consciousness. This means that a patient may have awareness that there is a problem, but lacks the (cognitive) skills to seek treatment.

Lack of initiative and apathy, often accompanying impaired executive functioning, are often found in patients with alcohol-related deficits (Marinkovic et al., 2009) and must not be mistaken by a lack of motivation or alcoholic denial (Miller & Barasch, 1985; Rinn et al., 2002). Studies demonstrated that alcoholic patients underestimate the amount of alcohol they have used (Lincoln et al., 2011), underestimate the length of their alcohol addiction, and underestimate the severe and adverse consequences of alcohol addiction on daily life and health functioning (Volkow & Li, 2005). Moreover, studies in patients with schizophrenia demonstrate that impaired illness insight is a consequence of cognitive dysfunctions (David et al., 2012; Goldstein et al., 2009) and associated with impaired verbal memory (Keshavan et al., 2004), lower intelligence (Lysaker and Bell, 1994), and executive dysfunction (Drake & Lewis, 2003; Donohoe et al., 2005). The alcohol-related cognitive disorders complicate treatment utility (Bates et al., 2013b) and increase the risk of alcohol relapse (Noël et al., 2002). Cognitive deficits reported in chronic alcoholic patients are often subtle in nature and may be overshadowed by problems in living and working conditions, parenting and/or social problems, and alcohol-related health issues such as head injury, hypertension, blackouts, diabetes, alcohol withdrawal seizures, liver dysfunctions, meningitis, hypoglycemia, hepatic encephalopathy and chronic obstructive pulmonitis (Brust, 2010; Wekking et al., 2004).

The aforementioned theories on illness insight and cognitive functioning can be integrated into a composite model based on several prior authors (see Figure 1). The hierarchy-based model stresses that, although the level of illness insight interacts strongly with the level of cognitive functioning, there is a gradual transition between the levels of cognitive functions and between the levels of illness insight. The highest level of illness insight (e.g., introspective self-awareness, anticipatory awareness) in patients with alcohol-related cognitive dysfunctions places higher demands on cognitive functioning (e.g., intelligence, metacognitive functioning, memory, executive functioning, and
attention) leading to treatment adherence. Based on this thought, a broad subdivision in severe, moderate, and mild cognitive impairment seems more appropriate.

Figure 1  An integrated hierarchy-based model of illness insight combined with the level of cognitive dysfunction for Alcohol Use Disorders (AUD) based on Crosson et al. (1986), David (1990), Moeller & Goldstein (2014), Philippi et al. (2012), and Van Schouwen-van Kranen (2014).

Towards a multimethod evaluation of alcohol related cognition

The DSM-IV TR (APA, 2000) uses criteria for describing two distinct Alcohol Use Disorders (AUD): alcohol abuse and alcohol dependence. However, these labels seem to be insufficient to classify the cognitive deficits, which are often found in chronic alcoholic patients, possibly resulting in the underestimation of these deficits by the clinician. The latter is exactly the issue I want to address in this thesis. During neuropsychological assessment of AUD patients, as a crucial starting point of treatment planning, a clinician may encounter several issues disturbing the clinical picture such as the presence of alcohol-related cognitive dysfunctions, the influence of abstinence on the recovery of cognitive functions, and the level of illness insight on self-report questionnaires. In this thesis, I aim to address the following research questions by means of a multimethod evaluation: (1) are alcohol-related cognitive dysfunctions better defined by using
the DSM-5 (APA, 2013) compared to the DSM-IV (APA, 2000); (2) what is the best timing for conducting a reliable assessment in patients with alcohol-related deficits during abstinence; and (3) what is the utility of self-report questionnaires and performance tests during abstinence, taking into account that cognitive dysfunction and impaired self-awareness might be present.

Objectives and Thesis Outline

In the present thesis, a multimethod evaluation of cognition and illness insight is employed in AUD patients by means of the following methods: classification, self-report and correction methods, performance tasks and rating scales (self and others), as well as a systematic clinician based evaluation. A central theme of this thesis is the role of impaired self-awareness in the behavioral and cognitive assessment of AUD patients in order to achieve a better treatment planning.

Chapter 2 starts with the investigation how alcohol related cognitive deficits are classified according to the DSM-5 (APA, 2013). The conceptualization and classification of AUD are discussed in DSM-5 terms, as compared to the DSM-IV TR (APA, 2000) and identify the need of a different view on alcohol-related cognitive dysfunction in clinical practice. In Chapter 3 reviews the empirical evidence on the length of the abstinence time required before a reliable neuropsychological assessment of cognitive and emotional functioning of AUD patients can be carried out. In Chapter 4 the literature is reviewed with respect to the application of correction methods on the MMPI-2 (Minnesota Multiphasic Personality Inventory-2; Butcher et al., 1989), a self-report questionnaire that is often used for psychological treatment design in AUD patients. This is important for detecting under-reporting tendencies due to impaired self-awareness as well as over-reporting tendencies due to alcohol withdrawal during the acute phase of abstinence. In Chapter 5, the clinical utility of a specific MMPI-2 correction method (Van Balen et al., 1997) is investigated in order to avoid temporarily elevations on multiple clinical scales of the MMPI-2 during the acute phase of abstinence. To this end, the data of a large group of AUD patients, who were assessed after two weeks of abstinence, was used. Chapter 6 reports a study comparing the magnitude of self-reported cognitive complaints with performance on neuropsychological tasks in two distinct AUD patient groups with alcohol-related cognitive dysfunction (including patients fulfilling the criteria for Korsakoff’s syndrome and patients with less pronounced cognitive deficits) in order to examine the concordance between self-reported cognitive complaints and performance on intelligence and memory tasks. In Chapter 7 the
reliability, validity and clinical utility of a rating scale is examined compared with self-report (i.e., the Q8; Bourgeois et al., 2002a; Bourgeois et al., 2002b) in the assessment of impaired self-awareness in AUD. Finally, Chapter 8 provides a summary of the study results described in this thesis along with a discussion of the limitations. Clinical implications are discussed, in particular with regard to the contribution to the advancement of individual treatment planning in AUD patients. The chapter ends with perspectives for future research on the intersection of diagnostic assessment and clinical management of alcohol related cognitive disorders.
General introduction
Chapter 2

Alcohol-related cognitive impairment and the DSM-5

A step towards a better classification of alcohol-related cognitive impairment?

Translated and adapted from:
Abstract

Classification of alcohol-related cognitive impairments in the DMS-IV-TR terms is difficult and, as a result, cognitive deficits may be easily overlooked. The DSM-5 incorporates the category “neurocognitive disorders”, which may be an important improvement in clinical practice. Aim was to compare the DSM-IV-TR and DSM-5 with respect to alcohol-related cognitive dysfunction. The clinical utility of the DSM-5 is discussed, we systematically compared the chapters of the DSM-IV-TR for alcohol-related cognitive impairments and describing the changes that have been incorporated in the DSM-5. Results show that DSM-5 puts a greater focus on alcohol-related cognitive impairment. In addition to a distinction in severity (major or minor neurocognitive disorder), a distinction is made between a non-amnestic and an amnestic-confabulatory type, while symptom duration can be specified (behavioral disorders and/or persisting). In all, alcohol-related neurocognitive dysfunction is described more extensively in the DSM-5 than it was in the DSM-IV-TR, with an essential role for neuropsychological assessment for the classification, diagnosis, and treatment of neurocognitive deficits.
Introduction

For several decades it has been convincingly shown that chronic alcohol use may lead to cognitive disorders (Bates et al., 2002). Specifically, an alcohol intake of more than 21 units a week already constitutes a risk factor for the development of cognitive dysfunction (Jue & Schilt, 2009). In patients with Korsakoff’s syndrome the impairment is evident and memory deficits, executive problems, and the associated changes in personality (such as apathy and behavioral problems) are easily recognized. However, the cognitive impairments often reported in patients with persistent AUD, are more subtle in nature and may go unnoticed, as they can be overshadowed by problems in living, work, or relationship. Alcohol-related cognitive dysfunction varies from mild to severe problems in attention, memory, visuospatial, and executive functions (including planning and organization abilities, cognitive flexibility, decision-making, and working memory) and social-cognitive functions (CBO, 2009; Wester & Kessels, 2012). Alcohol-related dysfunction complicates treatment (Bates et al., 2013b; Bruijnen et al., 2013), increases the risk of alcohol relapse (Noël et al., 2002), and is difficult to classify with the DSM-IV-TR (APA, 2007). The question is whether the DSM-5 (APA, 2014) puts a greater focus on these alcohol-related cognitive dysfunction and how they can best be classified. In the present article we describe how alcohol-related cognitive deficits are classified in the DSM-IV-TR and compare this to the perspectives the DSM-5 offers.

Alcohol-related cognitive disorders as classified in the DSM-IV-TR

In the DSM-IV-TR a distinction is made between alcohol use disorders (AUD) and disorders resulting from alcohol use (alcohol-induced disorders). The first group comprises alcohol misuse/abuse and alcohol dependence, while the second group includes intoxication, withdrawal, delirium, persisting dementia, persisting amnestic disorder, psychotic disorder, mood disorder, anxiety disorder, sexual dysfunction, and sleeping disorders. Cognitive disorders are preferentially diagnosed by means of neuropsychological examination after an abstinence period of at least six weeks (Walvoort et al., 2013).

According to the DSM-IV-TR, severe, persisting alcohol-associated cognitive disorders (Korsakoff’s syndrome) are classified as “alcohol-induced persisting amnestic disorder” (code 291.1). This classification has the drawback that it stresses the amnestic component even though also substantial executive dysfunctions have been demonstrated in patients with Korsakoff’s syndrome (e.g., Van Oort & Kessels, 2009). The DSM-IV-TR additionally offers the classification “alcohol-induced persisting dementia” (code 291.2) when multiple cognitive deficits and severe limitations in daily functioning are present. The criteria for alcohol-
related dementia (Oslin et al., 1998) state that none of the cognitive deficiencies may be attributable to delirium, substance-induced intoxication, or withdrawal. Moreover, the term dementia may be confusing because it is often associated with an underlying neurodegenerative process whereas, following sustained abstinence from alcohol, the cognitive dysfunctions tends to stabilize or may even improve to some extent (Stavro et al., 2013). In the Dutch guidelines on alcohol-related disorders (CBO, 2009) it is even proposed to refrain from using the term “alcoholic dementia” to describe the syndrome because of the lack of scientific evidence of a direct causal relationship between alcohol abuse and dementia.

The diagnosis of “alcohol dependence” (code 303.90) is relevant in the case of chronic alcohol use in the absence of Korsakoff’s syndrome. If neuropsychological assessment reveals neurocognitive impairment, the classification “cognitive disorder-NOS” (code 249.9) is to be added. Although the combination of both classifications do capture the severity of the addiction and cognitive dysfunction, the nature and the extent of the latter symptoms, which neuropsychological domains of functioning are affected, or the implications for treatment remain unclear.

**Alcohol-related cognitive disorders and their classification according to the DSM-5**

In the DSM-5 alcohol addiction (alcohol use disorder) is part of the major group of “substance-related and addictive disorders” (e.g., Van den Brink, 2014). Although alcohol-associated cognitive disorders are briefly mentioned here, one is primarily referred to the separate subcategories “substance/medication-induced major or mild neurocognitive disorder,” of the main category of “neurocognitive disorders.” Apart from alcohol-induced cognitive disorders, this broader category also includes the “old” DSM IV-TR classifications delirium, dementia, and cognitive disorders-not otherwise specified. The DSM-5 states that these neurocognitive disorders need to be acquired, resulting in a decline in cognitive functioning. A severity distinction is made in terms of “major” and “minor” neurocognitive disorders, where this subdivision indicates that the DSM-5 views neurocognitive deficits and the resulting impairments in daily functioning as a continuum (Simpson, 2014).

Major neurocognitive disorders needs to be associated with a significant decline (>2 SDs below the age- and education-corrected mean) in one or more cognitive domains relative to a previous level of functioning, which is preferably determined by neuropsychological testing. It manifestly affects daily functioning in the absence of a delirium or another mental disorder such as depressive disorder or schizophrenia. It can further be verified whether the symptoms are
associated with behavioral disorders, whose current severity can be quantified (mild, moderate, or severe).

Mild neurocognitive disorders are characterized by a mild decline (between 1-2 SDs below the mean) in one or more cognitive domains relative to a previous level of functioning that causes minimal to no limitations in daily life. It is appended that, although the independent performance of activities of daily living as such is not affected, it may require more effort, compensating strategies or adjustments. Also with mild neurocognitive impairments one can specify whether they involve behavioral disorders and whether the cognitive deficits are persisting following continued sobriety.

Korsakoff’s syndrome, then, is to be classified as “major neurocognitive disorder, amnestic-confabulatory type” (code 291.1). Depending on the severity of the observed cognitive deficits in non-Korsakoff patients, a subdivision is made into “major neurocognitive disorder, non-amnestic-confabulatory type” (code 291.2) and “minor neurocognitive disorder” (code 291.89), where, in addition to the classification “neurocognitive disorder”, the classification “severe alcohol use disorder” applies (code 303.90).

To elucidate neurocognitive problems, the DSM-5 offers an extensive description of the neurocognitive domains of functioning, including attention, executive functions, learning and memory, language, perceptual-motor and social-cognitive functions. Per domain, a distinction is made between major and mild neurocognitive impairments with examples of symptoms or observations being given. Although no concrete references are made to specific neuropsychological tests, the examples provide clear clues to neuropsychological diagnostic procedures with which abovementioned neurocognitive dimensions can be assessed.

Discussion and conclusion

With the introduction of the DSM-5, neurocognitive dysfunction resulting from chronic alcohol use can be better classified than was the case with the previous version, the DSM-IV-TR. The DSM-5 distinguishes “major” from “minor” neurocognitive disorders, thus regarding neurocognitive deficits and their severity as a continuum (Simpson, 2014). This perspective emphasizes the relevance of neuropsychological assessments in the diagnosis and classification of alcohol-induced neurocognitive dysfunction. Despite the consideration the DSM-5 gives to neurocognitive disorders, it remains, above all, a classification system. While its classifications facilitate the identification of cognitive deficits, it is neuropsychological testing that will provide invaluable information about
the suspected neuropsychological domains of functioning. Based on these test results, an analysis of strengths and weaknesses can be made from which the following treatment phase can be directed and tailored, guiding the choice of interventions (e.g., behavioral approach, skills training, or a directive approach). This will prevent patients from being overestimated by the therapist during treatment, which will reduce the risk of dropout (Crews et al., 2005; Fals-Stewart & Shafer, 1992).

Neurocognitive dysfunction may already be detected during the first contact by using brief screening tools, of which the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) is a good example. The MoCA has already been applied in alcohol-dependent patients (Alarcon et al., 2015), addicted patients (Bruijnen et al., 2013; Copersino et al., 2009), and patients with Korsakoff’s syndrome (Oudman et al., 2014). This brief cognitive screener helps to detect signs of cognitive problems, and provides indications for further examination. As the MoCA comes in three parallel versions, the course of the cognitive functions can be monitored during treatment. By screening patients in an early stage, interventions can be modified to take these cognitive deficits into account, which might otherwise hamper successful treatment.
Alcohol-related cognitive impairment and the DSM-5
Chapter 3

Neuropsychological assessment and alcohol abstinence

Translated and adapted from:
Abstract

There is a vast amount of scientific evidence for the negative effects of alcohol on the functioning of the whole human body and particularly of the brain. The literature, however, is unclear about whether these functions can fully recover and about how long the abstinence period must be before patients with alcohol use disorder (AUD) can be reliably assessed with respect to cognitive and emotional functioning. Aim of the present chapter was to review current findings on the length of the abstinence period required before a reliable neuropsychological assessment can be carried out in AUD patients. Using PubMed, Psycinfo and Medline, we consulted the literature for the period from 1975 to October 2011 relating to the effects of alcohol abstinence on the brain. Results show that the longer the period of abstinence, the greater the improvement in a patient’s neuropsychological functioning. In the case of AUD patients, it takes at least six weeks for neuropsychological functioning to return to a fairly stable level. In conclusion, an abstinence period of at least six weeks is required before a reliable neuropsychological assessment can be carried out. This time period minimizes the disturbance caused by earlier alcohol abuse. The six-week period of abstinence is recommended as a guideline for AUD patients if they are to undergo appropriate and individualized neuropsychological assessment.
Introduction

Alcohol addiction is the most prevalent of all addictions among the general population of substance users (CBO, 2009). There is broad consensus in today’s scientific literature that alcohol affects brain functioning. Neuroimaging research on alcohol-dependent patients shows (a) loss of cerebral volume associated with cognitive decline and behavioral change (Crews, 1999; Oscar-Berman & Marinkovic, 2003); (b) dysfunction of the hippocampus, frontal cortex, basal ganglia, cingulate gyrus, cerebellum, and their interconnections (Bühler & Mann, 2011; Demirakca et al., 2011; Moselhy et al., 2001; Oscar-Berman & Marinkovic, 2003; Scheurich, 2005); and (c) lesions in the anterior thalamic nuclei (e.g., in Korsakoff’s syndrome; Bodani et al., 2009). After several months of abstinence the loss in cerebral volume may partially or even fully be restored due to white matter remyelination (Oscar-Berman et al., 1997). Both animal and human experimental studies found evidence of cell proliferation in the hippocampus during abstinence (Nixon & Crews, 2004; Nixon, 2006; Gazdzinski et al., 2008). From the sixth week of abstinence, apart from improved liver functions (CBO, 2009), significant reductions in the volume of cerebrospinal fluid and the size of ventricular cavities are described (Bartsch et al., 2007; Wobrock et al., 2009), which may develop from improved protein synthesis, dendrite growth (Geller, 1991), or blood flow and rehydration (Wobrock et al., 2009).

An alcohol intake of more than 21 units a week already constitutes a risk factor for the development of cognitive impairment (Jue & Schilt, 2009), with symptoms manifesting in mild to severe attention deficits (reduced alertness and attention span, heightened distractibility, and impaired sustained and divided attention), episodic memory dysfunction (reduced learning, storage and retrieval), visuospatial impairment (diminished visuospatial information processing), and motor deficits. Also executive dysfunction can be present, which may include impaired planning, organization, and control, reduced flexibility in thinking, impaired decision making, reduced working memory (affecting the temporary maintenance of information) and disinhibition. Verbal intelligence and semantic memory remain relatively intact (Bates et al., 2002; Goldstein et al., 2001). Additionally, chronic alcohol use may also result in deficits in social cognition (cognitive processes involved in emotion processing and social interactions) affecting judgement and illness insight (Uekermann & Daum, 2008).

It is known that cognitive deficits and personality changes will to some extent “disappear” after an abstinence period of several weeks to months provided there is no serious secondary or comorbid pathology as optimal recovery would then require more than 12 months (Bates et al., 2002; Bühler &
This implies that test results obtained in too early a stage of abstinence might be obscured by the effects of alcohol on brain functioning, withdrawal symptoms, and the on-going recovery of cognitive functions (Banken & Greene, 2009; Chanraud et al., 2007; Loeber et al., 2009; Mann et al., 1999; Rosenbloom & Pfefferbaum, 2008). These factors need to be taken into account to prevent mere temporary effects of alcohol withdrawal from being measured. Neuropsychological assessment can detect cognitive impairments to help optimize the following treatment phase (Schrimser & Parker, 2008).

Notwithstanding the scientific consensus on the associations between alcohol and negative brain effects, findings are mixed when it comes to the period of abstinence required to allow reliable conclusions about a patient’s current level of cognitive and emotional functioning. In clinical practice the decision when to test, that is, either at an early or a later stage of abstinence, can be a source of tension given that delaying assessments will increase the clinic’s waiting-list period. Also, as tests administered in the acute phase of abstinence will show the effects of alcohol withdrawal rather than the level of cognitive functioning, a too early assessment may lead to clinical misinterpretation.

To investigate these issues, the present paper reviews all systematic studies on the relevance of neuropsychological assessment in abstinent AUD patients, the duration of abstinence at the time of testing, the effects of abstinence on cognitive functioning, and factors complicating neuropsychological assessment.

Method

Our review of the literature started with a search of the Dutch guidelines on disorders in alcohol use (CBO, 2009) and textbooks on psychiatry and (neuro) psychology (e.g., Lishman, 2009; Deelman et al., 2006; Lezak et al., 2012; Butcher, 2009). As none made mention of abstinence durations, we subsequently extended our search to include the PubMed, PsychINFO, and Medline search engines covering the period between 1975 up to October 2011 using the search terms alcohol AND abstinence in combination with the terms cognitive, recovery, neuropsychological, and assessment. Having also examined the reference lists of relevant articles, we next made a selection of the resulting literature on the basis of the following inclusion criteria:

1. Studies needed to describe the recovery mechanisms of the brains of adult (≥ 18 years) alcohol-abstinent patients (N > 10) from a neurological and a neuropsychological perspective;
2. Studies needed to report multiple assessments conducted during the acute stages of alcohol withdrawal or have performed neuropsychological assessment after six weeks of abstinence. Studies investigating other substance use disorders in combination with alcohol dependence and case studies were not included in this review.

Results

Our literature search yielded 28 references for Alcohol AND Abstinence AND recovery AND cognitive, 37 references for Neuropsychological AND Abstinence AND recovery, and 4 references for Assessment AND Abstinence AND recovery. Overlapping studies were excluded, leaving 19 studies for this review.

Relevance of neuropsychological assessment

Various studies convincingly demonstrated the value of neuropsychological assessment in recovering AUD patients to determine individualized treatment interventions and most distinctly so for seemingly symptom-free patients who only showed subtle executive dysfunctions when having to learn new skills. Allowing for these latent, individual deficits will increase the chance of treatment success (Davies et al., 2005; Schrimsher & Parker, 2008). With their study, Crews et al. (2005) underscored that recovery of executive functions is the key to successful treatment outcome. Arguably, these findings suggest that, from a didactical viewpoint it is insufficient to offer interventions comprising psycho-education, verbal group therapy, relapse prevention, social skill training, motivational interviewing, system therapies, or complex weekend planning schemes in the early stages of alcohol abstinence (Allen et al., 1997; Schrimsher & Parker 2008). Many of these psychosocial programs rely on intact cognitive abilities to understand, process, and retain the (verbal) information provided, where it has been shown that cognitive deficits correlate positively with treatment dropout (Fals-Stewart & Schafer, 1992). Bates and colleagues (2005) accordingly propose to save such more complex elements of the intervention that require abstraction reasoning and information processing capacities for a later stage, that is, after one to two months of abstinence. It is therefore essential that neuropsychological assessment is conducted prior to any treatment as, apart from delineating cognitive impairment, it will also uncover the patient’s strengths, allowing interventions to be tailored to the individual.
The duration of abstinence before assessment
Although the relevance of neuropsychological assessment in abstinent AUD patients is widely supported, until now, there is no academic consensus as to their optimal timing. Sherer et al. (1984) posit that a ten-day abstinence should be sufficient to rule out any withdrawal effects. Other researchers suggest an abstinence of three to four weeks before psychiatric diagnoses can be performed (Bradizza et al., 2006). Essentially in line with this, the Dutch multidisciplinary guidelines on disorders of alcohol use (CBO, 2009) cautiously suggest an interval of two to three weeks before depressive or anxiety disorders can be reliably assessed, while adding that in the majority of AUD patients symptoms of depression and anxiety largely disappear spontaneously after one to four weeks. Lezak and colleagues (2012) note that during the first two weeks of abstinence most AUD patients display neuropsychological symptoms, with recovery of cognitive functions being most pronounced after the first week and the optimum recovery becoming manifest in weeks three to six. However, the effects of alcohol on the executive functions appear not to have improved sufficiently after three weeks of abstinence (Cordovil De Sousa et al., 2010; Van Holst & Schilt, 2011), while having had multiple withdrawals may result in more severe executive deficits (Scheurich, 2005).

In conclusion, the recommended abstinence before neuropsychological assessment varies between 10 and 42 days in the literature, with recovery mechanisms playing a major role in this wide time range. In the next section we will expand on the influence of abstinence on cognitive functioning.

Effects of abstinence on the cognitive abilities of AUD patients
Various studies show that cognitive and emotional symptoms improve as a consequence of abstinence, with some reporting full recovery within several weeks (Leber et al., 1981; Mann et al., 1999) and others not until several months (Fein et al., 1990; Sullivan et al., 2000b; Sullivan et al., 2000c). Others argued that cognitive functions do not fully recover even after years of abstinence (Brandt et al., 1983; Fein et al., 2006a). Bartels and colleagues (2007) propose that, when studying functional recovery in abstinent AUD patients, a distinction needs to be made between the acute phase, in which withdrawal symptoms coincide with the recovery of functions following abstinence, and a much more prolonged phase of functional/morphological regeneration during which relapses may delay the cognitive recovery process. If abstinence is maintained, recovery of cognitive functions may even continue for up to two years.

During alcohol intake the ‘alcoholic brain’ undergoes compensation-oriented changes whereby more and other areas need to be activated than is the case in healthy controls, which goes at the cost of accuracy and speed of information...
Neuropsychological assessment and alcohol abstinence

processing (Rosenbloom & Pfefferbaum 2008). Functions that are affected in the acute stages of abstinence are processing speed, verbal episodic memory, working memory, nonverbal reasoning, visuospatial perception, and executive functioning (see Table 1). Davies and co-workers (2005) suggest that the observed memory problems may be (at least partially) explained by underlying deficits in attention and concentration. In their respective studies, Zinn et al. (2004) and Manning et al. (2008) observed signs of executive dysfunction in abstinent AUD patients up until six weeks after alcohol withdrawal. Both research teams, however, remark that the instruments they used to evaluate executive functions may lack ecological validity (2008).

Besides cognitive improvement, research has found evidence of positive changes in emotional functioning during abstinence. Comparing the profiles of AUD patients on the clinical scales of the Minnesota Multiphasic Personality Inventory (MMPI) obtained shortly after admittance to the clinic and after 30 days of abstinence, Dush and Keen (1995) recorded significant MMPI scale reductions. Allen (1996) accordingly recommended postponing MMPI assessment until after the patient’s condition has stabilized. In the acute phase of abstinence amelioration of emotional symptoms coincides with a lessening of withdrawal symptoms such as irritation, agitation, anxiety, sleep disturbance, anhedonia, and pain (Becker, 2008; Schuckit, 2009). Lincoln and colleagues (2011) recently demonstrated how cognitive dysfunction influences the outcomes of self-report questionnaires. They found that AUD patients found it difficult to make an accurate estimation in the first six weeks of abstinence of the quantity of alcohol they had consumed before admission to a clinic, which is attributable to deficits in memory functioning caused by chronic alcohol use.

Factors complicating neuropsychological assessment

Several potentially confounding factors need to be considered when interpreting neuropsychological assessment results during abstinence following chronic alcohol use. The risk of health problems such as head trauma, hypertension, black-outs, diabetes, alcohol withdrawal seizures, liver dysfunction, meningitis, hypoglycemia, hepatic encephalopathy, and chronic obstructive pulmonary disease (COPD; in combination with tobacco use) increases with the number of years of chronic drinking (Brust, 2010; Wekking et al., 2004), while all conditions can affect outcomes, as will persistent symptoms associated with depressive, mood and anxiety disorders. Other factors of influence are the age of the patient (Munro et al., 2000), the use of other substances (polydrug use, medication), and comorbid personality disorders.
Table 1  Studies examining the effect of abstinence on the recovery of cognitive functions in AUD patients

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Sample</th>
<th>Abstinence period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bartels et al., 2007</td>
<td>N=50 (30 with amnesia, 11 non-amnesic; 9 multi-domain)</td>
<td>T1: 2 to 3 weeks; T2: 3, 6, 12, and 24 months; N=32</td>
</tr>
<tr>
<td>Bartsch et al., 2007</td>
<td>N=15</td>
<td>T1: at admission; T2: &gt; 6-7 weeks</td>
</tr>
<tr>
<td>Bates et al., 2005</td>
<td>N=169 (alcohol and drugs)</td>
<td>T1: at admission; T2: &gt; 6 weeks</td>
</tr>
<tr>
<td>Bendszus et al., 2001</td>
<td>N=17</td>
<td>MRI</td>
</tr>
<tr>
<td></td>
<td>N=12 controls</td>
<td>T1: 1-3 days; T2: 36-39 days</td>
</tr>
<tr>
<td>Brandt et al., 1983</td>
<td>N=134</td>
<td>3 groups: 1-3 month; 1-3 year; &gt;5 year</td>
</tr>
<tr>
<td></td>
<td>N=76 controls</td>
<td></td>
</tr>
<tr>
<td>Cordovil De Sousa Uva</td>
<td>N=35</td>
<td>T1: 1-2 days; T2: 14-18 days</td>
</tr>
<tr>
<td>et al., 2010</td>
<td>N=22 controls</td>
<td></td>
</tr>
<tr>
<td>Davies et al., 2005</td>
<td>N=43</td>
<td>T1 &gt; 6 weeks</td>
</tr>
<tr>
<td></td>
<td>N=58 controls</td>
<td></td>
</tr>
<tr>
<td>Dush &amp; Keen 1995</td>
<td>N=525</td>
<td>T1: 1-2 days; T2: 30 days</td>
</tr>
<tr>
<td>Fein et al., 2006</td>
<td>N=48</td>
<td>T1: &gt; 6 year</td>
</tr>
<tr>
<td>Gazdzinski et al., 2008</td>
<td>N=13 + smoking and N=11 – smoking</td>
<td>T1: 1 week; T2: &gt; 1 month</td>
</tr>
<tr>
<td>Leber et al., 1981</td>
<td>N=32</td>
<td>T1: 3 weeks; T2: 11 weeks</td>
</tr>
<tr>
<td></td>
<td>N=16 controls</td>
<td></td>
</tr>
<tr>
<td>Mann et al., 1999</td>
<td>N=49</td>
<td>T1: at admission; T2: &gt; 5 weeks</td>
</tr>
<tr>
<td></td>
<td>N=49 controls</td>
<td></td>
</tr>
</tbody>
</table>
## Studies examining the effect of abstinence on the recovery of cognitive functions in AUD patients

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Sample</th>
<th>Abstinence period</th>
<th>Cognitive domain/ MRI</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bartels et al., 2007</td>
<td>N=50 (30 with amnesia, 11 non-amnesic; 9 multi-domain)</td>
<td>T1: 2 a 3 weeks, T2: 3, 6, 12, and 24 months; N=32</td>
<td>Visuo-spatial, verbal comprehension, attention, verbal and non verbal memory, Attention, MRI.</td>
<td>Amnesia: ↑ Non-amnesic and multidomain: ≠</td>
</tr>
<tr>
<td>Bartsch et al., 2007</td>
<td>N=15</td>
<td>T1: at admission, T2: &gt; 6-7 weeks</td>
<td>Verbal comprehension, attention, executive functions, processing speed, and verbal memory, MRI and MR spectroscopy</td>
<td>Attention: ↑</td>
</tr>
<tr>
<td>Bates et al., 2005</td>
<td>N=169</td>
<td>T1: at admission, T2: &gt; 6 weeks</td>
<td>Verbal comprehension, attention, executive functions, processing speed, and verbal memory</td>
<td>Memory: ↑ Other functions: ≠</td>
</tr>
<tr>
<td>Bendszus et al., 2001</td>
<td>N=17, N=12 controls</td>
<td>MRI</td>
<td></td>
<td>Correlation between brain volume and cognitive performance</td>
</tr>
<tr>
<td>Brandt et al., 1983</td>
<td>N=134, N=76 controls</td>
<td>3 groups: 1-3 month, 1-3 year, &gt;5 year</td>
<td>Memory, visuospatial, intelligence, attention, verbal memory</td>
<td>Improvement after 1 year. Long term memory: ≠</td>
</tr>
<tr>
<td>Cordovil De Sousa Uva et al., 2010</td>
<td>N=35, N=22 controls</td>
<td>T1: 1-2 days, T2: 14-18 days</td>
<td>Attention, executive functions EF</td>
<td>EF: ≠</td>
</tr>
<tr>
<td>Davies et al., 2005</td>
<td>N=43, N=58 controls</td>
<td>T1 &gt; 6 weeks</td>
<td>Processing speed, verbal comprehension, visuospatial, verbal memory, and attention</td>
<td>Prefrontal functioning, attention, and processing speed: ≠</td>
</tr>
<tr>
<td>Dush &amp; Keen 1995</td>
<td>N=525</td>
<td>T1: 1-2 days, T2: 30 days</td>
<td>Emotional functioning</td>
<td>All Clinical scales: ↓, clinical Scale 4: ≠</td>
</tr>
<tr>
<td>Fein et al., 2006</td>
<td>N=48</td>
<td>T1: &gt; 6 year</td>
<td>Premorbid intelligence, visuospatial, attention, processing speed, and executive functions, MRI</td>
<td>Visual organisation: ≠, other functions: ↑</td>
</tr>
<tr>
<td>Gazdzinski et al., 2008</td>
<td>N=13 + smoking and N=11 – smoking</td>
<td>T1: 1 week, T2: &gt; 1 month</td>
<td>Non-verbal memory</td>
<td>Smoking has adverse effects on medial temporal lobe functioning, metabolic: ↑</td>
</tr>
<tr>
<td>Leber et al., 1981</td>
<td>N=32, N=16 controls</td>
<td>T1: 3 weeks, T2: 11 weeks</td>
<td>Non-verbal memory</td>
<td>At T2: some recovery of cognitive functioning. Possibly right hemisphere deficits.</td>
</tr>
<tr>
<td>Mann et al., 1999</td>
<td>N=49, N=49 controls</td>
<td>T1: at admission, T2: &gt; 5 weeks</td>
<td>Attention, verbal memory, and premorbid intelligence, MRI</td>
<td>Visual organisation: ≠, other functions: ↑</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T1: 5 of 12 tasks: ↓, T2: in 4 of these 5 tasks: ↑, Verbal short term memory: ≠</td>
</tr>
</tbody>
</table>
The question remains whether persistent cognitive dysfunction points to a condition resulting from the patient’s chronic alcohol use or to a pre-existing susceptibility to alcoholism (van Holst & Schilt, 2011). A premorbid vulnerability due to genetic or environmental factors, education, gender (Hopenbrouwers et al., 2010), and a vulnerability of the brain to alcohol in combination with the toxic effect of alcohol, will contribute to the severity of the cognitive dysfunction. Moreover, indirect effects of alcohol play a role, such as other organ failure and traumatic brain injury. Indisputably, complex interactions of (potentially) mutually reinforcing factors are present. Aside from these factors and associations, it has been shown that repeated episodes of binge drinking (periods during which large volumes of alcohol are consumed within a short space of time) and having undergone more than two detoxifications will cause permanent neurological damage to the brain resulting in persistend neurological impairment, or contributing to dementia (Becker 2008; Brust, 2010; Duka et al., 2003).

Even though the nature and severity of pathology may differ widely between patients, routine neuropsychological evaluation after a fixed term of abstinence is highly recommended. Complementing diagnostic examinations, auto-anamnesis, hetero-anamnesis, careful history taking, and scrutiny of

Table 1 Continued

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Sample</th>
<th>Abstinence period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manning et al., 2008</td>
<td>N=30</td>
<td>T1: 4 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2: 26 days</td>
</tr>
<tr>
<td>Munro et al., 2000</td>
<td>N=36 (55-83 year)</td>
<td>N=18: 1 month-6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N=18 &gt; 6 months</td>
</tr>
<tr>
<td>Rourke &amp; Grant 1999</td>
<td>N=35</td>
<td>T1: 7-21 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2: 125-133 days</td>
</tr>
<tr>
<td>Schrimsher &amp; Parker 2008</td>
<td>N=58</td>
<td>T1: at admission</td>
</tr>
<tr>
<td></td>
<td>(N=15 alcohol; N=43 poly)</td>
<td>T2: &gt; 24 days</td>
</tr>
<tr>
<td>Sullivan et al., 2000</td>
<td>N=42</td>
<td>T1: 1 month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2: 2 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3: 12 months</td>
</tr>
<tr>
<td>Wobrock et al., 2009</td>
<td>N=56</td>
<td>T1: at admission</td>
</tr>
<tr>
<td></td>
<td>N=45 controls</td>
<td>T2: 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3: 9 months</td>
</tr>
<tr>
<td>Zinn et al., 2004</td>
<td>N=27</td>
<td>T1:1-58 days</td>
</tr>
<tr>
<td></td>
<td>N=18 controls</td>
<td></td>
</tr>
</tbody>
</table>

Note. ↑ = improvement; ↓ = deterioration; ≠ = no improvement/ no deterioration.
Neuropsychological assessment and alcohol abstinence

self-reported and previous clinician-recorded medical histories that allow a good overview of the patients’ problems and social environment, neuropsychological assessment affords a reliable comparison of data serving both research and clinical purposes.

**Discussion and conclusion**

In the majority of recovering people with alcohol use disorder, cognitive performance improves in proportion to the length of alcohol abstinence, with empirical findings indicating that recovery to a relatively stable condition tends to take three to five weeks. This applies in particular to verbal skills and visuospatial abilities while executive functions (problem-solving abilities and learning) take longer to recover.

It is noteworthy that in the current literature the main focus is on psychiatric and psychotherapeutic approaches. This carries the risk that treatments will predominantly be symptomatic, given that withdrawal phenomena and complicating factors will stand out. If (residual) cognitive deficits that will be
different for each recovering patient are not detected, there is the additional risk of overestimating the patient by the therapist (Crews et al., 2005).

As early as in 1981, Leber et al. concluded that the duration of abstinence is a crucial variable where neuropsychological outcomes are concerned. The current literature is still at odds as to the timing of neuropsychological assessment in abstinent AUD patients. While some studies report full or clinically significant recovery of cognitive functions within a few weeks, others do not observe any actual functional improvement until years later or note no improvement at all. There is consensus in regard to the positive effects of adequate nutrition and thiamine replacement on the recovery of cognitive and emotional symptoms and the presence of alcohol-induced cognitive deficits influencing treatment success.

Detailed neuropsychological assessment of patients with AUD is a prerequisite for effective, personalized treatment. Given the state of the art in the field, an abstinence period of at least six weeks is recommend to guarantee reliable neuropsychological assessment outcomes, where recovery of liver and other organ functions is crucial (Gazdzinski et al., 2008; Geller, 1991; CBO, 2009; Wobrock et al., 2009). During this six-week interval, the brain is allowed to regenerate, preventing unnecessary disturbance of the clinical picture and the associated risk of inadequate treatment interventions. Concerning the present findings future research should aim at relationship between somatic and neuropsychological markers.
Chapter 4

Assessment of psychopathology and personality with the MMPI-2 in patients with alcohol use disorder (AUD): Should we not correct for associated cognitive dysfunctions?

Published as:
Abstract

Treatment planning of Alcohol Use Disorders (AUD) patients is often preceded by the assessment of psychopathology and personality with the Minnesota Multiphasic Personality Inventory (MMPI-2). However, in the acute phase of abstinence, both physical and cognitive problems can cause temporary elevations on multiple clinical scales of the MMPI-2 resulting in inadequate interpretation and treatment planning. Over the past years, several correction procedures were developed to correct for these problems in different neurological disorders, but until this date, there are no published data available on correction procedures for AUD patients. An extensive literature search is performed in Pubmed, Medline, and Psychinfo for the period from 1975 through 2011 resulted in thirty-five studies on MMPI (-2) correction procedures typically developed for neurological patient groups. Review of the literature demonstrates that, given the similarity of cognitive deficits in patients with AUD and in those with Traumatic Brain Injury (TBI), the use of an MMPI-2 neurocorrective procedure may be helpful to avoid over-interpretation of psychopathology and personality profiles during the acute phase of abstinence and to formulate more adequate treatment planning. Further empirical research should focus on the development and validation of such a neurocorrective procedure, that specifically addresses the alcohol-induced cognitive symptoms during the acute phase of withdrawal.
Introduction

It is common practice to assess emotional functioning in patients with Alcohol Use Disorders (AUD) and to use this information in the process of treatment design and planning. To this end, often, the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) is applied. The MMPI-2 is internationally the most widely used self-report questionnaire for the assessment of personality and psychopathology (Butcher, 2006). It is well known that individuals who enter substance abuse treatment centres, often experience emotional discomfort and distress as part of their multi-problem crisis. Such a crisis nearly always precedes admission to an addiction clinic (Becker, 2003; Bartels et al., 2007; Schuckit, 2009) and is associated with elevations on multiple clinical scales of the MMPI-2 (Forbey & Ben-Porath, 2007).

During the process of abstinence, withdrawal of alcohol can lead to a variety of physical, emotional, and cognitive complaints. The physical symptoms disappear within days whereas the cognitive, emotional, and motivational deficits, caused by the neurotoxic effect of alcohol, tend to persist during several weeks after admission (e.g., Becker, 2008).

Several reports of cognitive dysfunctions are found in patients with AUD, including deficits in memory, executive attention, planning, the processing of environmental feedback, working memory, and response inhibition (Goldstein et al., 2001; Scheurich, 2005; Loeber et al., 2009). Also, a gradual decline of social and emotional functioning is described, for example in the studies on personality change by Bates, Barry, and Bowden (2002), and Scheurich (2005). This is in line with studies demonstrating the toxic effect of alcohol on brain functioning and adaptive behaviour in general (Allen et al., 1997, Moselhy et al., 2001; Crews et al., 2005; Davies et al., 2005; Kalivas & Volkow, 2005; Oscar-Berman & Marinkovic, 2007; Schuckit, 2009).

To some extent, cognitive functions recover during abstinence (Mann et al., 1999; Martin et al., 2003; Sullivan & Pfefferbaum, 2005; Manning et al., 2008). This recovery process can last up to several years (Bates et al., 2002; Fein et al., 2006a). Withdrawal symptoms can influence the response pattern on self-report questionnaires in such a way that the level and pattern of scale-scores leads to clinical misinterpretation (Johnson-Greene et al., 2002). Dush and Keen (1995) found that over 30 days of abstinence, the overall elevation of MMPI clinical scales in AUD patients tended to decline and the profiles became less distinctive. This is in accordance with MMPI and MMPI-2 studies on patient groups with neurological deficits, where the influence of psychological disturbance leads to unreliable scores and wrong treatment indication (Alfano et al., 1993; Van Balen et al., 1997; Van Balen et al., 1999).
In order to deal with the influence of cognitive deficits on the MMPI, and later on the MMPI-2, several correction procedures were developed for different neurological disorders over the past years. These correction procedures are based on the identification of neurologically relevant items (NRI’s), which refer to neurological symptoms, like attention problems, headache, nausea, physical discomfort, and loss of energy. These symptoms are also observed in AUD patients during abstinence (Becker, 2008). Although there is a remarkable similarity between the neuropsychological profile of patients with chronic substance abuse and that of patients with mild traumatic brain injury (MTBI; Lange et al., 2008), until this date, no studies on correction procedures in AUD patients were found, and no systematic research has been conducted to the use of MMPI-2 correction procedures in AUD patients during abstinence.

Therefore, the aim of this study is to review the clinical relevance of using correction procedures in AUD patients during the acute phase of abstinence. Given the long tradition of MMPI and MMPI-2 research in AUD patients, the most relevant findings on alcohol related profiles will be summarized first.

The MMPI-2 in the assessment of AUD patients
The MMPI-2 is a self-report questionnaire with 567 statements to be answered with True or False. The MMPI-2 can be administrated with individuals who are at least 18 years old and have at least a sixth grade level of reading ability. After scoring by hand or computer, the individual’s profile can be compared with profiles from the normative sample (Butcher, 2006). In the development of the MMPI-2, apart from the MacAndrew Alcoholism Scale Revised (MAC-R; MacAndrew, 1965) that was already part of the original MMPI, two novel substance abuse scales were added: the Addiction Potential Scale and the Addiction Admission Scale (APS; AAS; Weed et al., 1992). However, since our main focus is the correct assessment of psychopathology in AUD patients, the specific investigation of these alcoholism scales is beyond the scope of this article. For further reading, see Banken and Greene (2009).

Most of the MMPI and MMPI-2 studies investigate the clinical scales by their elevations and code types, as described by Graham (2006). Although it is clear that there is no unique alcohol personality in AUD patients (Banken & Greene, 2009), code types are used to identify, in a quick way, AUD patients with similar treatment needs in improving treatment outcome (Allen, 1996). Graham and Strencher (1988) found, in their review of the use of the MMPI in AUD patients, that the most consistent finding between alcoholic and non-alcoholic patients was a high score on clinical scale 4, which is quite stable over time, but not unique to AUD patients only. Egger and co-workers (2007) distinguished three types of alcohol dependence: (a) the antisocial, immature, risk-taking type;
(b) the negativistic, alienated, schizoid type, and (c) the anxious, passive, introverted type. In this study it was pointed out, however, that such a distinction is not independent of other psychological and cognitive deficits during abstinence, for example inhibitory dysfunctions. On the other hand, a study with Korsakoff Syndrome patients demonstrated low psychopathology and undisturbed personality patterns on their “flat” MMPI-2 profile, indicating the illusion of a problem free and well-adjusted patient group. The authors emphasized the need for further investigation into the lack of (illness) insight that accompanies several neuropsychiatric and neuropsychological phenomena (Egger et al., 2002).

Other studies identified the code type 2-4/4-2 (Schroeder & Piercy, 1979; Graham & Strenger, 1988; Johnson et al., 1992; Lesswing & Dougherty, 1993; Donovan et al., 1988) indicating psychopathic deviation, acting out behaviour, and a negative treatment attitude. However, the MMPI was administered in the first two weeks after admission, where the influence of detoxification can affect its outcome. The latter is convincingly demonstrated in the study by Dush and Keen (1995) where the typologies of AUD patients directly after admission and after 30 days of treatment were investigated. The authors found a dramatic overall reduction in pathology on all clinical scales, with the exception of clinical scale 4. They concluded that the MMPI typology itself does not remain stable due to influence of treatment, detoxification over 30 days, the passage of time (from the crisis environment), and regression to the mean.

In short, during the acute phase of abstinence, the AUD patient is hampered by cognitive disturbances due to influence of withdrawal of alcohol, which in turn might be reflected on the MMPI-2 scales. It will take at least six weeks before there is a recovery of functioning to a somewhat stable level in AUD patients. Bates and co-workers (2002) found that the level of neuropsychological functioning will increase with the length of the abstinence period, because during such a period, the brain will have time to regenerate (Geller, 1991; Gazdzinski et al., 2008; Wobrock et al., 2009).
Method

An extensive literature search was performed in Pubmed, Medline, and Psychinfo for the period from 1975 through October 2011. On each of the combined search terms Alcohol AND Neurocorrection, Abstinence AND Neurocorrection, Alcohol AND Neurologically Relevant Items, Abstinence AND Neurologically Relevant Items, no articles were found. In the absence of such studies, the usefulness of existing MMPI-2 correction procedures, originally developed for neurological patient groups, is examined. Therefore, each of the combined search terms MMPI* AND Neurocorrection, MMPI* AND correction, MMPI* AND neurologically relevant items, MMPI* AND correction procedure, and MMPI* AND neurologic were used to search the Psychinfo, Pubmed, and Medline database (Table 1).

Only studies on MMPI and MMPI-2 correction procedures, their clinical relevance, and studies that commented these procedures, were included. Studies on K-correction were excluded. Twenty-seven articles matched the criteria and eight studies were added by reference and citation analysis. A total of thirty-five articles were studied.

Table 1  Search terms and hits in Pubmed, Psychinfo and Medline

<table>
<thead>
<tr>
<th>Search term</th>
<th>Pubmed</th>
<th>Psychinfo</th>
<th>Medline</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMPI* AND neurocorrection</td>
<td>2 (2)</td>
<td>0 (2)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>MMPI* AND correction</td>
<td>13 (74)</td>
<td>17 (67)</td>
<td>11 (161)</td>
</tr>
<tr>
<td>MMPI* AND Neurologically relevant items</td>
<td>2 (3)</td>
<td>2 (2)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>MMPI* AND correction procedure</td>
<td>7 (27)</td>
<td>3 (15)</td>
<td>3 (15)</td>
</tr>
<tr>
<td>MMPI* AND neurologic</td>
<td>9 (74)</td>
<td>5 (71)</td>
<td>7 (171)</td>
</tr>
</tbody>
</table>

Remaining articles without overlap                | 27     |
Additional articles by reference and citation analysis | 8     |
Total studied articles                             | 35     |

Note. MMPI= Minnesota Multiphasic Personality Inventory. In parentheses the amount of articles, in bold the amount of articles who met the criteria of the current study.
Results

MMPI-2 and correction procedures

Baldwin (1952) was one of the first to apply a correction procedure in patients with Multiple Sclerosis (MS). MMPI items, which refer to neurological symptoms, were removed before scoring. In the development of correction procedures, different names were used for items, which refer to a neurological content. For convenience, the current study uses the term neurologically relevant items (NRI’s). Besides the development of correction procedures in patients with MS (Meyerink et al., 1988; Nelson et al., 2003), procedures were developed in different patient groups, including epilepsy (Derry et al., 1997; Nelson et al., 2004), cerebrovascular disease (Gass, 1992), stroke (Gass & Lawhorn, 1991; Gass, 1996), spinal cord injury (SCI; Kendall et al., 1978; Rodevich & Wanlass, 1995; Barncord & Wanlass, 2000), obstructive sleep apnea (Gale et al., 1999), and traumatic brain injury (TBI; Alfano et al., 1990; Alfano et al., 1993; Cripe et al., 1995; Gass & Wald, 1997; Van Balen et al., 1997). A correction procedure involves constructing a set of neurologically relevant items contained within existing personality or emotional scales that measures neurologic dysfunction. The effects of these NRI’s are thus separated out and examined independently of emotional functioning. In this way, purer estimates of cognitive and emotional functioning can be obtained in groups of brain-damaged individuals (Nelson & Cicchetti, 1995).

Correction procedures are available for the MMPI, the MMPI-2, and the MMPI-2 short form. The procedures differ in the amount of a) NRI’s that are endorsed; b) in the way these NRI’s are selected, and c) how they are implemented in the scoring procedure. Although several procedures have been developed for comparable patient groups, there are differences in the amount of NRI’s that were identified (see table 2). For instance, in TBI patients, Alfano et al (1990) identified 44 NRI’s. In a follow up study, 13 NRI’s were derived from these 44 NRI’s (Alfano et al., 1993). Gass (1991) identified 14 and 15 NRI’s for the MMPI-2 short form. Gass and Russell (1991) identified 42 NRI’s, Artzy (in Brulot et al., 1997) identified 18 NRI’s, and Van Balen et al (1997) identified 24 NRI’s. In using a correction procedure both the MMPI and the MMPI short form are used, explaining some of the differences in the amount of the NRI sets. However, the main difference is explained by the methodology used to identify items in both patients with TBI and patients with epilepsy, multiple sclerosis, stroke, and spinal cord injury. Most of the correction procedures are based on the clinical experience of medical specialists, familiar with neurological patient groups. These specialists were asked to identify items in the MMPI booklet, which reflect neurologic symptoms
Table 2  Summary of MMPI-2 correction procedures and associated clinical scales

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Authors</th>
<th>Number of NRI's</th>
<th>Method</th>
<th>Deleted/prorated</th>
<th>Form</th>
<th>Affected clinical scales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td>Derry et al., 1997</td>
<td>19</td>
<td>Empirical</td>
<td>Deleted</td>
<td>MMPI-2</td>
<td>1, 2, 3, 7, 8</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>Nelson et al., 2004</td>
<td>25</td>
<td>Combined: statistical and empirical</td>
<td>Deleted</td>
<td>MMPI-2</td>
<td>1, 2, 3, 8</td>
</tr>
<tr>
<td>MS</td>
<td>Baldwin, 1952</td>
<td>12</td>
<td>Empirical</td>
<td>Deleted</td>
<td>MMPI</td>
<td>1, 2, 3, 8</td>
</tr>
<tr>
<td>MS</td>
<td>Meyerink et al., 1988</td>
<td>30</td>
<td>Empirical</td>
<td>Deleted</td>
<td>MMPI</td>
<td>1, 2, 3, 8</td>
</tr>
<tr>
<td>MS</td>
<td>Nelson et al., 2003</td>
<td>19</td>
<td>Statistical</td>
<td>Deleted</td>
<td>MMPI-2</td>
<td>1, 2, 3, 8</td>
</tr>
<tr>
<td>SCI</td>
<td>Barncord and Wanlass, 2000</td>
<td>49</td>
<td>Empirical</td>
<td>Deleted</td>
<td>MMPI-2</td>
<td>1, 2, 3, 7, 8</td>
</tr>
<tr>
<td>SCI</td>
<td>Kendall et al., 1978</td>
<td>10</td>
<td>Statistical</td>
<td>Deleted</td>
<td>MMPI</td>
<td>1, 2, 3, 4, 8</td>
</tr>
<tr>
<td>SCI</td>
<td>Rodevich and Wanlass, 1995</td>
<td>28</td>
<td>Empirical</td>
<td>Deleted</td>
<td>MMPI-2</td>
<td>1, 2, 3, 7, 8</td>
</tr>
<tr>
<td>Stroke</td>
<td>Gass, 1992</td>
<td>21</td>
<td>Statistical</td>
<td>Prorated</td>
<td>MMPI-2 short form</td>
<td>1, 2, 3, 7, 8</td>
</tr>
<tr>
<td>TBI</td>
<td>Alfano et al., 1990</td>
<td>44</td>
<td>Empirical</td>
<td>Deleted</td>
<td>MMPI</td>
<td>1, 2, 8</td>
</tr>
<tr>
<td>TBI</td>
<td>Alfano et al., 1993</td>
<td>13</td>
<td>Empirical</td>
<td>Deleted</td>
<td>MMPI</td>
<td>1, 2, 8</td>
</tr>
<tr>
<td>TBI</td>
<td>Artzy, 1994</td>
<td>18</td>
<td>Statistical</td>
<td>Deleted</td>
<td>MMPI-2</td>
<td>1, 2, 3, 7, 8</td>
</tr>
<tr>
<td>TBI</td>
<td>Gass and Russell, 1991</td>
<td>42</td>
<td>Empirical</td>
<td>Prorated</td>
<td>MMPI-2 short form</td>
<td>1, 2, 3, 7, 8</td>
</tr>
<tr>
<td>TBI</td>
<td>Gass, 1991</td>
<td>14</td>
<td>Empirical</td>
<td>Prorated</td>
<td>MMPI-2 short form</td>
<td>1, 2, 3, 7, 8</td>
</tr>
<tr>
<td>TBI</td>
<td>Gass and Wald, 1997</td>
<td>15</td>
<td>Statistical</td>
<td>Prorated</td>
<td>MMPI-2 short form</td>
<td>1, 2, 3, 7, 8</td>
</tr>
<tr>
<td>TBI</td>
<td>Van Balen et al., 1997</td>
<td>24</td>
<td>Empirical</td>
<td>Prorated</td>
<td>MMPI-2</td>
<td>1, 2, 3, 7, 8</td>
</tr>
</tbody>
</table>

Note. MMPI = Minnesota Multiphasic Personality Inventory, MS = Multiple Sclerosis, NRI = Neurologically Relevant Items, SCI = Spinal Cord Injury, TBI = Traumatic Brain Injury.

that can be viewed as part of the illness. Based on the degree of agreement between the specialists, items were included in the correction procedure (Meyerink et al., 1988; Alfano et al., 1990; Gass & Russell, 1991; Alfano et al., 1993; Rodevich & Wanlass, 1995; Van Balen et al., 1997; Barncord & Wanlass, 2000;
There is a difference in the amount of specialists who were questioned, ranging from two (Meyerink et al., 1988; Derry et al., 1997; Barncord & Wanlass, 2000; Derry et al., 2002) through 40 (Van Balen et al., 1997).

Other authors used a statistical procedure to select NRI’s by comparing the scores of neurological patients with the scores of a normative group. Items were only included in the procedure if they were statistically different. For instance, Kendall and colleagues (1978) used factor analysis to differentiate between SCI patients and a matched non-hospitalised control group. Nelson and colleagues (2004) used a combined statistical and empirical procedure in order to enhance the validity of MMPI-2 in patients with epilepsy. In their study, a board-certified epileptologist analysed each MMPI-2 item and selected 15 items, which reflect the symptoms of epileptic seizures. The statistical procedure distinguished 13 items from epilepsy patients with normal controls. The combined statistical and empirical procedure identified 25 NRI’s. In another study, in patients with MS, Nelson and colleagues (2003) used a procedure consistent with that used by Gass (1992) and Gass and Lawhorn (1991) in their MMPI-2 correction studies. This correction procedure involves the following steps: 1) identification of items endorsed by more than 25% of patients with MS; 2) statistical analysis to determine which items significantly differentiated patients with MS from controls, and 3) to determine item inter relatedness.

The correction depends on the responses of the patient to the 14 items. As a result, the amount of items can vary, ranging from none to substantial. On the other hand, Artzy (in Brulot et al., 1997) compared item endorsement frequency of persons with closed head injuries with persons of the normative sample. Item responses frequencies were contrasted between normals and patients. Items that statistically discriminated between normals and patients were included in the correction procedure. Sixty items were found, that differentiated between head injured patients and the normative group; Eighteen items differentiated between the head injured group and patients with chronic pain. In the development of this procedure, Artzy followed the “empirical keying” method of the MMPI to select the NRI’s. However, in the application of such a procedure there is a chance that items are included in a correction procedure that statistically differentiate between groups, but have no relation to the theoretical construct being studied, as demonstrated by LaChapelle and Alfano (2005). This underscores the importance of a sound theoretical basis in obtaining the proper neurological items.

Another important finding is the way the correction procedures are implemented in the scoring procedure. In some studies on correction procedures, the NRI’s must be deleted before scoring (Kendall et al., 1978; Alfano et al., 1990; Alfano et al., 1993; Artzy (in Brulot et al., 1997); Derry et al., 1997; Nelson et al.,
Some authors recommend to score the MMPI twice, corrected and uncorrected, to specify the minimum and maximum limits for the patient on each of the affected scales (Kendall et al., 1978; Alfano et al., 1993). Van Balen et al., (1999) identified 24 NRI’s, in TBI patients, by comparing the normative sample with the correction procedures rescored (NRI’s scored in a pathological direction were rescored in the non pathological direction) and prorated (a statistical correction adopted from Gass and Russell (1991) to avoid overcorrection). In the NRI-prorated procedure, within each scale, the prorated raw score is estimated by

\[ NNe + (PNe \times NNe / NN) \]

where NNe is the number of Non-NRI endorsements, PNe the patient’s NRI endorsement, and NN the total number Non-NRI endorsements.

Although there is a broad variety of correction procedures in different patient groups, they correspond strongly to the way they act on the clinical scales. All correction procedures reduce the level of pathology on clinical scales 1, 2, and 8 to distinguish physical from psychological complaints, in order to make a more reliable diagnose regarding emotional disorders (Table 2). Most of the correction procedures reduce the level of pathology on clinical scales 1, 2, 3, 7, and 8, because these clinical scales contain the most neurological relevant items (Cripe, 1989; Gass, 1991).

Validity and clinical utility of the correction procedures

Since the development of MMPI correction procedures, several validity studies were published in order to evaluate its use in clinical practice. Several critiques pointed at the fact that these procedures assume the profiles of neurologic patients to be relative homogeneous, that correction procedures lack specificity for neurological impairment, and that they compromise the integrity of the MMPI as such (Cripe et al., 1995; Arbisi & Ben-Porath, 1999; Edwards et al., 2003). Also, Greene et al (1997) criticized the correction procedures for their poor empirical validity and advised clinicians to be cautious in using these sets of correction items until they have been validated empirically across several settings. Moreover, Cripe et al (1995) suggest that any given item of the MMPI may be endorsed for a variety of reasons and that resulting scale elevations for two individuals can be the same for different reasons.

Replication studies, such as Dunn and Lees-Haley (1995) found that only 5 of the 14 NRI’s, identified by Gass (1991), discriminated significantly between head-injured and non head-injured patients in a forensic setting. However, the correction effect is not clinical significant. Smith and Heilbronner (2000) used
these NRI’s in a sample of mild TBI patients in litigation and concluded that patients are more likely to endorse anxiety and cognitive disturbances early on after the injury. With time, they report fewer of these symptoms. This is in line with the findings that NRI’s reflect acute neurologic symptoms that are likely to resolve following mild head injury (Rayls et al., 1997; Rayls et al., 2000).

Glassmire et al (2003) investigated three correction procedures (Alfano et al., 1993; Gass, 1991; Gass & Wald 1997) on sensitivity and specificity. They found a strong sensitivity in discriminating Closed Head Injury (CHI) patients from normal individuals, but a poor specificity when discriminating CHI from psychiatric patients. These findings are not surprisingly, since in most psychiatric patients severe cognitive deficits are found. Brulot, Strauss, and Spellacy (1997) compared the correction procedures developed by Alfano (Alfano et al., 1993), Artzy (in Brulot et al., 1997), and Gass (1991) in patients with suspected head injury. The authors found that the NRI’s lack discriminant validity. Edwards and colleagues (2003) compared three correction procedures (Meyerink et al., 1988; Alfano et al., 1990; Gass, 1991) and concluded that these three correction procedures are not specific in distinguishing patients with closed head injury and psychiatric patients, it undermines the statistical integrity of the MMPI, and the meaning of scale elevations are less clear after correction. However, in 66% of their sample, no information is present regarding premorbid psychiatric functioning, or drug and alcohol abuse. Patients were administrated ranging from 1 month to 7 years following suspected head injury, while it is well known that the symptoms of acute neurologic consequences of mild head injury are likely to resolve after 3-6 months post injury (Rayls et al., 2000). In a replication study of the 44 NRI’s identified by Alfano et al (1990), Hamilton et al (1995) found evidence that these NRI’s discriminate between neurological and non-neurological groups. In addition, the authors suggest that in head-injured patients, emotional manifestations are more likely to be expressed in terms of cognitive, somatic, or behavioural dysfunction, caused by a lack of insight or other cognitive impairments resulting from brain damage, trouble expressing appropriate affect, decreased levels of arousal, or location of maximal damage. The latter implies that the danger of over scoring psychopathology in neurological patient groups remains when using the MMPI-2. This is in line with the recommendations of Hayes and Granello (2009), in their study with patients with MS, to score the MMPI-2 twice (with and without neurocorrections) to note differences that may be based on physical symptoms. Also, they recommend the use of a clinical interview that highlights MS symptoms to increase the effectiveness of MMPI-2 assessment in treatment planning.

Arbisi and Ben-Porath (1999) stated that, in order to obtain an accurate measure of psychopathology, the NRI’s must be scored in a different direction (prorated).
Also a cautious clinical application of the correction procedure is recommended, especially when using the MMPI-2 to assess the presence of affective disturbance following head injury. Therefore, the authors emphasize the importance of investigating the predictive validity of corrected and uncorrected profiles for the improvement of reliable and valid MMPI-2 assessment in neurological patient groups in the future.

**Discussion and conclusion**

In clinical practice, the MMPI-2 can be a helpful instrument in the assessment of emotional functioning in patients with cognitive, emotional and motivational deficits and pre-existent personality factors (Arbisi & Ben-Porath, 1999). However, during early abstinence, uncorrected MMPI-2 scales tend to reflect symptoms of withdrawal and cognitive recovery thus leading to overestimation of levels of psychopathology. Given the close similarity between TBI patients, in the early phase of recovery, and AUD patients, in the acute phase of abstinence, it is remarkable that, until now, no research has been conducted in which MMPI-2 typologies of AUD patients have been examined as to the validity of their interpretation when a neurobehavioural correction procedure would have been applied. This undocumented aspect of assessment in patients with AUD should be addressed in clinical research, particularly because both cognitive and emotional factors play an important role in the understanding of the patient’s self-reported condition and of its course during abstinence.

The effects of abstinence and cognitive recovery on multiple scales of the MMPI-2, can easily lead to inadequate treatment planning, resulting in a more symptomatic approach. Such an approach (e.g. verbal group therapy for depression or anxiety, and long psychotherapeutic sessions) is inadequate because it ignores the underlying cognitive deficits during the acute phase of abstinence and increases the risk of drop-out (Crews et al., 2005) even in apparently “clinically healthy” abstinent AUD patients (Davies et al., 2005). Allen (1996) concluded in his study, that repeating the MMPI during treatment, could assist in planning later treatment stages. He also recommends the delay of testing until the patients’ condition has been stabilized after detoxification. This is in line with the findings of Dush and Keen (1995) where all clinical scales declined, except for clinical scale 4, over a period of 30 days of abstinence. Although one could argue that MMPI-2 assessment should be postponed until most symptoms are in remission, clinically, the early availability of information on psychological and socio-emotional functioning is of great importance to effective treatment design.
Everything leads to the conclusion that detection of cognitive deficits is of major importance to the design of proper treatment strategies and to the maximisation of its outcome and not to rely on one measure only (Allen et al., 1997; Davies et al., 2005; Scheurich, 2005). Currently, a forthcoming study on the effect of neurobehavioral correction on MMPI-2 profile configuration of AUD patients, shows that uncorrected profiles in AUD patients tend to overestimate the levels of psychopathology; and underrate levels of disinhibitory behaviours and impulsive traits, leading to diagnostic drift and inadequate treatment planning (Walvoort et al., 2012). In this study, only the correction effects on the clinical scales were investigated. It is well known that the clinical scales have an item overlap and consist of demoralisation items. For instance, clinical scales 2 and 7 contain items to be related to anxiety, depression, and other emotional distress, assessing more demoralization than personality, psychopathology (Graham, 2012). In order to avoid item overlap and to reduce demoralization, the MMPI-2 Restructured Clinical (RC) scales were developed (Tellegen et al., 2003). Recent studies of Van der Heijden and co-workers (Van der Heijden et al., 2008; Van der Heijden et al., 2010) indicate that the RC scales have a better internal consistency and a lower scale level intercorrelation than the clinical scales and as a result provide a higher density of information.

Another promising development in the assessment of AUD patients and neurological patients is the MMPI-RF. The MMPI-RF is shorter, is based on the RC-scales and has new scales for both somatic and neurological complaints. Recent research demonstrates also meaningful relations between the MMPI-RF and the Temperament and Character Inventory (TCI; Van der Heijden et al., 2013a), the Millon Clinical Multiaxial Inventory- III (Van der Heijden et al., 2012a), and in relation to DSM IV (Van der Heijden et al., 2013b). Until now, there are no studies on correction procedures and its impact on RC-scales or the MMPI-RF scales. Validation studies are needed in order to justify this non-standard scoring procedure. Especially in forensic and litigation procedures, where clinicians are bound by standard assessment protocols. Future research on the interplay between personality and cognition and validation studies of MMPI-2 correction procedures are needed to address this issue.

The current review stipulates that in the acute phase of abstinence, a correction procedure is necessary to avoid misinterpretation of complaints leading to inadequate treatment planning. Along with the withdrawal effects of alcohol, AUD patients also have problems in social cognition (self-awareness and illness insight) caused by the toxic effect of chronic alcohol use (Oscar-Berman & Marinkovic, 2007). Recent evidence suggests that alcohol related impairments in emotional functions, may be observed when the cortico-limbic circuitry is unable to compensate for the hypo-activity of the amygdala, resulting in
continued alcohol abuse and a wide array of behavioural problems including disinhibition, impulsivity, and interpersonal difficulties (Marinkovic et al., 2009). In addition, other aspects of neuropsychological functioning will affect the clinical scales during MMPI-2 administration, including understanding the MMPI-2 statements, the level of difficulty of the statements (e.g. double negatives), and reduced mental effort (e.g. sustained attention, working memory capacity, information processing speed, and decision making). Moreover, a study with a homogeneous group of Korsakoff patients, found deficits in a story comprehension task specifically caused by executive dysfunction (Oosterman et al., 2011). That cognitive dysfunction can influence self-report is also shown in a recent study with alcohol dependent patients by Lincoln and colleagues (2011). They found impairments in the estimation and self-evaluation of past alcohol intake that could be attributed to verbal memory dysfunctions contingent upon chronic alcohol abuse. These studies suggest that AUD patients are both hampered by the somatic complaints and cognitive deficits during abstinence. Although it is clear that the somatic complaints “disappear” during abstinence (Becker, 2008), the influence of the alcohol related cognitive deficits (e.g. executive functioning, social cognition and memory) on the MMPI-2 may be greater than expected.

This review supports the thought that, in order to acquire a sound diagnostic MMPI-2 profile in AUD patients, an MMPI-2 correction procedure is necessary. In developing such a correction procedure, the following steps will be required: First, a theoretical framework must be given, in which the correction items reflect the alcohol-induced cognitive deficits during abstinence. Second, the use of a pro-rated procedure is necessary in maintaining the statistical procedure of the test. Third, validation studies are needed to investigate the utility in clinical practice.

In conclusion, when AUD patients are assessed in the acute phase of abstinence, the application of an MMPI-2 correction procedure may be of critical relevance for the correct interpretation of the psychopathology and personality profile. From there on, adequate and individualized treatment planning requires repeated evaluation of a patients’ emotional and cognitive functioning. Further investigations should focus on the development and validation of the aforementioned correction procedure and on its relation with cognitive recovery.
MMPI-2 assessment in AUD patients
Chapter 5

Neurocognitive parameters should be incorporated in the MMPI-2 assessment of patients with alcohol use disorders

Published as:
Abstract

Treatment planning for Alcohol Use Disorder (AUD) patients is often preceded by the assessment of psychopathology and personality with the Minnesota Multiphasic Personality Inventory (MMPI-2). However, during periods of abstinence, cognitive impairments (e.g., attention, memory, and executive dysfunctions) related to neurological and somatic pathology may affect level and pattern of MMPI-2 scale-scores, resulting in clinical misinterpretation. A re-analysis of the data of the Egger et al study (2007) is conducted in order to examine the clinical significance of the MMPI-2 profiles of 222 AUD patients (mean age 42.2 ± 9.6 years; 76.6% men) by using Neurological Relevant Item (NRI) correction procedures. Hierarchical cluster analyses of NRI-corrected solutions were compared to the original MMPI-2 profile.

Results show that impulsiveness and psychopathic deviation were identified as a common denominator and that uncorrected MMPI-2 assessment in AUD tends to overstress psychopathology and to overlook disinhibitory traits in early abstinence, caused by chronic alcoholism.
Introduction

For decades, it is reported that personality traits are important predictors both of treatment success and treatment drop-out in patients with Alcohol Use Disorders (AUD) (Crews et al., 2005; Müller et al., 2008). As a consequence, it is common practice to assess personality traits in AUD patients and to use this information in the process of treatment design and planning. For such an assessment of personality traits, often, the Minnesota Multiphasic Personality Inventory-2 (MMPI-2) is used. The MMPI-2 is the most widely used self-report questionnaire for the assessment of emotional functioning (Butcher, 2006).

With respect to patients with AUD, several studies with the original MMPI tried to define typologies or ‘code types’ of AUD patients (Graham & Strenger, 1988; Donavan et al., 1989; Johnson et al., 1992; Lesswing & Dougherty, 1993). These code types are still reported to be valid, despite the thorough revision that the MMPI has undergone for the construction of the MMPI-2 (Graham, 2006). In their MMPI-2 typology study of AUD patients, Egger et al. (2007) differentiated three types of alcohol dependence: (a) the antisocial, immature, risk-taking type, (b) the negativistic, alienated, schizoid type, and (c) the anxious, passive, introverted type. Although they found evidence for convergent validity with measures of temperament and character, they nevertheless concluded that cluster differences may have been influenced by cognitive deficits during abstinence (e.g., inhibitory dysfunctions). While MMPI-2 assessment is still standard procedure in many clinical settings, there is scarce evidence for the treatment utility of this diagnostic approach, that is, for the degree to which this form of diagnostic assessment enhances treatment outcome (Sher et al., 2005; Nelson-Gray, 2003). One possible explanation for poor outcome is that underlying cognitive features can affect the endorsement of items from a self-report questionnaire in such a way that the level and pattern of scale-scores leads to clinical misinterpretation (Johnson-Greene et al., 2002). This is in accordance with the fact that there is a growing body of evidence that the chronic use of alcohol influences brain functioning and adaptive behaviour in general (Crews et al., 2005; Allen et al., 1997; Davies et al, 2005; Kalivas & Volkow, 2005; Moselhy et al., 2001; Oscar-Berman & Marinkovic, 2003; Oscar-Berman & Marinkovic, 2007; Schuckit, 2009).

Indeed, several reports of cognitive dysfunctions are found in patients with AUD, including deficits in memory, executive attention, planning, the processing of environmental feedback, working memory, response inhibition (Goldstein et al., 2001; Loeber et al., 2009; Scheurich, 2005), and a gradual decline of social and emotional functioning (Scheurich, 2005; Bates et al., 2002). All lead to the conclusion that detection of cognitive deficits is of major importance to the
design of proper treatment strategies and to the maximisation of its outcome (Scheurich, 2005; Allen, 1996).

**Recovery during abstinence**

Although some cognitive functions will be permanently affected by chronic alcohol abuse, not all of them are irreversible. Manning and colleagues (2008) describe AUD patients who after a longer period of abstinence show a gradual improvement of executive functioning. They conclude that, shortly after admission, a treatment program will easily outweigh the patient’s cognitive capacities, whereas later on, when executive functioning, attention, memory and planning have gradually improved, patients may be more responsive to such a treatment program.

This is in line with studies who found a significant recovery of functions after detoxification Mann et al., 1999; Martin et al., 2003). Bates et al. (2002) point out that some functions return after several weeks, but others can take years to recover. A study on cognitive performance on long-term abstinent AUD patients (average period of abstinence = 6.7 years) reveals the recovery of most of the cognitive functions, except the spatial information processing ability (Fein et al., 2006a). Recovery of executive functioning is seen as the key towards a successful treatment (Crews et al., 2005). Moreover, in AUD patients assessed with the MMPI and the Halstead-Reitan Neuropsychological Test Battery, a strong relationship was demonstrated between emotional distress (anxiety and depression) and executive functioning due to frontal lobe dysfunction common to cognitive and affective domains (Johnson-Green et al., 2002).

Apart from cognitive functioning, several studies also point at the partial recovery of emotional and somatic functioning. Dush and Keen (1995), for instance, found that AUD patients, who were retested 30 days after inpatient treatment, showed a dramatic overall reduction in pathology and presume this to be due to the influence of toxicity and exaggerated symptomatology in the first month of abstinence. Other authors have suggested to view the consequences of AUD as a special form of traumatic brain injury (TBI) (Lange et al., 2008; Lee et al., 2008). Reitan and Wolfson (1997), in their review on emotional disturbances and interaction with neuropsychological deficits, indeed found that head injured patients who recovered on neuropsychological functions, also demonstrated MMPI-“recovery,” i.e., decrease in profile level. In contrast, patients with serious cognitive deficits continued to demonstrate deviant profiles. This corroborates the findings of Johnson-Greene et al (2002) who noted that in some of these patients, the MMPI may be measuring the severity of brain dysfunction rather than their emotional distress, and suggests a replication with the MMPI-2.
The above studies underscore the scientific prudence that is needed in the interpretation of self-reports made by AUD patients. Nevertheless, it would be highly beneficial when a clinician, in the early phases of treatment, could have measures of both cognitive and emotional functioning at his disposal.

**Neurobehavioural correction**

In order to cope with the emotional and cognitive disturbances that may hamper adequate assessment, and to increase the validity of the MMPI-2 interpretation, several correction procedures were developed over the years and used in different patient groups on the MMPI (Hamilton et al., 1995; Gass, 1992) and, later, on the MMPI-2 (Gass, 1992; Gass & Wald, 1997; Barnard & Wanlass, 2000; Van Balen et al., 1997). The Dutch adaptation of the MMPI-2 (Derksen et al., 2006) provides a so-called neurological filter (Neurologically Relevant Items; NRI’s) for patients with damage to the central nervous system. The authors describe the NRI’s as items “related to symptoms associated with the direct sequelae of neurological pathology, such as lack of energy, muscle paralysis, slowness of information processing, trouble in concentrating or memory disorders” (Van Balen et al., 1997). The NRI’s contain items about symptoms related to attention, concentration, headaches, dizziness, visual difficulties, pain, mobility, nausea and loss of energy, the typical symptoms that AUD patients experience during withdrawal of alcohol. The physical symptoms tend to disappear within days, while the psychological distress symptoms take more time (Becker, 2008).

Van Balen and colleagues (1997) identified their NRI’s by asking a group of 40 experts (10 neuropsychologists, 10 neurologists, 10 psychiatrists and 10 physiatrists), who were familiar with brain damaged patients, for their opinion on MMPI-2 statements in three patients groups, i.e., patients with TBI, stroke, and whiplash. For the whole group, 48 NRI’s were found of which 26 were specific for the whiplash group, 25 for the stroke group and 24 for the TBI group. The latter group was studied in more detail by comparing the item endorsements of the TBI patients with those in the normative sample. The TBI protocols were then scored using both the *rescored* correction procedure (NRI’s scored in a pathological direction were rescored in the non-pathological direction) and the *prorated* correction procedure (a statistical correction adopted from Gass & Russell (1991) to avoid overcorrection). It was concluded that in the acute phase of TBI, a prorated correction procedure is the preferred choice. The 24 NRI’s load on clinical scales 1, 2, 3, 7 and 8, content scales HEA and WRK. This is in line with findings where the clinical scales 1, 2, 3, 7 and 8 have been identified as containing the most neurological relevant items (Gass & Russel, 1991). The 24 NRI correction has proven to be a reliable and valid tool in studies with brain-damaged patients (Van Balen et al., 1999).
In spite of its relevance for assessment practice, until now, no research has been conducted in which MMPI-2 typologies of AUD patients have been examined as to the validity of their interpretation when a neurobehavioural correction procedure would have been applied. This is a remarkable lack in clinical knowledge, particularly because both cognitive and emotional factors play an important role in the understanding of the patient’s self-reported condition and of its course during abstinence. Unfortunately, while the NRI correction procedure was not available at the time, the original study of Egger et al (2007) does not address the difference in uncorrected and corrected profiles. However, re-analysis of its data would enable the study of the clinical significance of the MMPI-2 neurobehavioural (NRI) correction procedure in patients with AUD. The present study aims exactly at this.

Methods

Participants and procedure
We used the patient group of the study in 2007 including 222 alcohol dependent inpatients admitted to the St Paschalis addiction treatment centre of the Dutch Vincent van Gogh Institute for Psychiatry. All patients were classified as alcohol dependent according to DSM-IV criteria and 76.6% of them were men. Mean age of the total group was 42.2 years (SD = 9.6). The DSM IV classifications were obtained based on extensive neuropsychiatric assessment including a clinical interview comprising the elements of the CPRS (Åsberg et al., 1978) conducted by an experienced neuropsychiatrist committed to the clinic. Patients performing below average intellectual abilities were excluded from participation in this research. Patients participated only after obtaining informed consent. They completed the Dutch version of the MMPI-2 after 14 days of abstinence as a part of the regular diagnostic process (2007). In order to systematically compare corrected with uncorrected MMPI-2 profiles, uncorrected scores, NRI-deleted scores, and NRI-prorated scores were computed. In the NRI-deleted procedure, the 24 NRI’s are discarded before scoring. In the NRI-prorated procedure, scoring was performed according to the description of Van Balen et al. (1999). Here, within each scale, the prorated raw score is estimated by

\[(1) \quad NNe + ( PNe \times NNe / NN )\]

where NNe is the number of Non-NRI endorsements, PNe the patient’s NRI endorsement, and NN the total number Non-NRI endorsements. Because Alfano et al. (1990; Alfano et al., 1993) have successfully employed the deletion procedure
in patients with closed head injury and patients with neurologic dysfunction and since there are no prior studies about correction procedures in AUD patients, we decided to include both procedures in order to be able to compare them in the current study.

Measures
The MMPI-2 has been translated and standardized for Belgium and The Netherlands in 1993 (Derksen et al., 1993). Translation occurred according to international standards (Butcher, 1996). Internal consistency coefficients of the Clinical Scales are slightly lower in the Dutch normative sample than in the American normative sample. Cronbach’s alpha ranges from .31 (Scale 5 for women) to .85 (Scale 7 for men) with an average of .64. Test-retest reliability coefficients of the Clinical Scales range from .43 to .86, with an average of .69. The Dutch norms highly correspond with those of the American MMPI-2 (Butcher et al., 1989; Sloore et al., 1996). Detailed information about the psychometric properties of the Dutch-language version of the MMPI-2 and the translation process is presented in the new edition of the MMPI-2 manual (Derksen et al., 2006). The validity of the Clinical Scales, Content Scales and PSY-5 Scales has been reported in relation to diverse Dutch clinical samples (Van der Heijden et al., 2010; Van der Heijden et al., 2008; Egger et al., 2003a; Egger et al., 2003b; Egger et al., 2003c; Derksen & de Mey, 1992; Vendrig, 1992).

Analysis
In line with the original study of Egger et al (2007), the NRI-corrected clinical scales are cluster analyzed in order to revisit the earlier described typology. Hierarchical cluster analysis of the Ward’s method of the mean centered profiles was performed according to the procedure as described by Morey (1991). In addition, frequency of code types will be recorded per cluster to analyse the changes caused by the correction procedure.
Results

Both NRI deleted and NRI prorated corrected mean MMPI-2 profiles are lower than the original mean profiles. After *NRI deleted* correction, significant differences with the original clinical scales 2, 3, 7, and 8, indicate less dysphoric, somatic and apathetic symptoms (medium effect sizes). A similar pattern is found after *NRI prorated* correction, where differences are significant on 3 indicating lower levels of stress reactivity. Table 1 shows that the deleted correction procedure not only affects scales 1, 2, 3, 7, and 8, but also the other clinical scales. The results are summarized in Table 1.

**Table 1** Mean scale scores of the original, deleted and prorated scales in 222 AUD patients

<table>
<thead>
<tr>
<th>MMPI-2 Scale</th>
<th>Original Mean</th>
<th>Original SD</th>
<th>Deleted Mean</th>
<th>Deleted SD</th>
<th>Cohen's $d$</th>
<th>Prorated Mean</th>
<th>Prorated SD</th>
<th>Cohen's $d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>L</td>
<td>46.53</td>
<td>9.61</td>
<td>46.53</td>
<td>9.61</td>
<td>-</td>
<td>46.53</td>
<td>9.61</td>
<td>a</td>
</tr>
<tr>
<td>F</td>
<td>73.69</td>
<td>21.54</td>
<td>70.82</td>
<td>20.82</td>
<td>.14</td>
<td>73.69</td>
<td>21.54</td>
<td>b</td>
</tr>
<tr>
<td>K</td>
<td>41.22</td>
<td>10.97</td>
<td>39.99</td>
<td>10.63</td>
<td>.11</td>
<td>41.22</td>
<td>10.97</td>
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<tr>
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<td>12.42</td>
<td>.10</td>
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<td>13.53</td>
<td>.53</td>
</tr>
<tr>
<td>2</td>
<td>68.72</td>
<td>15.05</td>
<td>61.65</td>
<td>12.59</td>
<td>.51</td>
<td>63.28</td>
<td>14.08</td>
<td>.37</td>
</tr>
<tr>
<td>3</td>
<td>63.00</td>
<td>15.61</td>
<td>56.87</td>
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<td>.73</td>
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<td>74.62</td>
<td>13.69</td>
<td>74.94</td>
<td>12.46</td>
<td>-.02</td>
<td>74.62</td>
<td>13.69</td>
<td>b</td>
</tr>
<tr>
<td>5</td>
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<td>11.30</td>
<td>54.98</td>
<td>10.38</td>
<td>-.02</td>
<td>54.80</td>
<td>11.30</td>
<td>b</td>
</tr>
<tr>
<td>6</td>
<td>70.04</td>
<td>14.82</td>
<td>70.37</td>
<td>15.23</td>
<td>-.02</td>
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<td>15.26</td>
<td>65.96</td>
<td>12.20</td>
<td>.33</td>
<td>67.76</td>
<td>14.25</td>
<td>.19</td>
</tr>
<tr>
<td>8</td>
<td>70.29</td>
<td>15.85</td>
<td>64.25</td>
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<td>.31</td>
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<td>.30</td>
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<td>9</td>
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<td>60.15</td>
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<td>.16</td>
<td>62.37</td>
<td>13.95</td>
<td>b</td>
</tr>
<tr>
<td>0</td>
<td>58.17</td>
<td>12.38</td>
<td>56.88</td>
<td>11.91</td>
<td>.11</td>
<td>58.17</td>
<td>12.38</td>
<td>b</td>
</tr>
</tbody>
</table>

*Note.* L= Lie, F= Infrequency, K= Correction, 1= Hypochondriasis, 2= Depression, 3= Hysteric, 4= Psychopathic deviate, 5= Masculinity/femininity, 6= Paranoia, 7= Hymenia, 8= Schizophrenia, 9= Hypomania, 0= Social Introversion. a The prorated correction procedure only affects clinical scales 1, 2, 3, 7, and 8. b Medium effect size. c Large effect size.
Cluster analysis of both NRI prorated and NRI deleted corrected profiles, reveals three clusters that show several significant differences, representing contrasting typologies of AUD patients compared to the original profiles (Table 2). While this is true for the clustering of both NRI prorated and NRI deleted data, the cluster profiles, however, share a prominent elevation of scale 4, indicating that impulsivity/disinhibition and lack of insight is at the core of all typologies.

**Table 2** Code types of the original, NRI-deleted, and NRI-prorated MMPI-2 profiles of 222 AUD patients, according to Graham (2006)

<table>
<thead>
<tr>
<th>Correction method</th>
<th>Cluster 1</th>
<th>Cluster 2</th>
<th>Cluster 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>P</td>
<td>Code type</td>
</tr>
<tr>
<td>Original</td>
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<td>55</td>
<td>4</td>
</tr>
<tr>
<td>Deleted</td>
<td>92</td>
<td>42</td>
<td>4</td>
</tr>
<tr>
<td>Prorated</td>
<td>81</td>
<td>36</td>
<td>4-2</td>
</tr>
</tbody>
</table>

Note. P = percentage. * A well defined code type of the prorated MMPI-2 profile in cluster 2 is not present. Clinical scales 4,6,7, and 8 are all elevated.

Discussion and conclusion

This first study on the effect of neurobehavioural correction on MMPI-2 profile configuration of patients with AUD results in two important findings that, when not recognized, can easily lead to diagnostic drift and inadequate treatment planning. First, the decrease in scores of the corrected profiles as compared to the original ones, reflects the overrepresentation of somatic complaints and demoralizational beliefs during the “acute phase,” usually the first month of abstinence. This is in accordance with clinical observations in AUD patients during abstinence and earlier findings that these somatic complaints are merely a reflection of the patient’s multi-problem crisis that nearly always precedes admission to an addiction clinic (Schuckit, 2009; Becker, 2008; Bartels et al., 2007) producing elevations on MMPI-2 profiles (Allen, 1996; Dush & Keen, 1995; Forbey & Ben-Porath, 2007).

Second, although several “typologies” can be discerned in these patients, both impulsiveness/disinhibition and problems in self-reflective capacities, tend to dominate the clinical picture, which suggests that in all AUD patients, a fundamental process can be identified that is associated with the documented effects on brain functioning of (excessive) alcohol exposure (Crews, 2005; Kalivas & Volkow, 2005; Oscar-Berman & Marinkovic, 2007; Harper, 2009).
There is a remarkable similarity between the here presented MMPI-2 profiles and those described by Dush and Keen (1995). Our current profiles show a prominent elevation of MMPI-2 clinical scale 4 representing impulsivity/disinhibition, lack of insight, immaturity, irresponsibility, low motivation to change, and less environmental adaptivity (Graham, 2006). Impulsiveness is a common trait in AUD patients. It increases due to the toxic effect of alcohol on the prefrontal brain regions and causes, for instance, impaired decision making which, in turn, might affect treatment outcome (Bowden-Jones et al., 2005; Feil et al., 2010). As such, it is a major risk factor, a vulnerability, for the development of alcohol addiction (Fein et al., 2006b; Verheul et al., 1999). Earlier clinical, neuropathological and neuroradiological studies found, along with the above mentioned effects of alcohol on the cortex, alcoholic cerebellar degeneration in more than 25% of AUD patients (Atunez et al., 1998; Deshmukh et al., 2002; Linboe & Loberg, 1988; Torvik et al., 1982). The symptoms of alcoholic cerebellar degeneration resemble the symptom-complex known as the Cerebellar Cognitive Affective Syndrome (CCAS; Schmahmann & Sherman, 1998) and may be indicative for the contribution of the cerebellum in the process of modulating higher-order cognitive and emotional functions (Schmahmann, 2004; Fitzpatrick et al., 2008).

The impairments in social cognition in AUD patients, such as facial affect perception, emotional prosody, theory of mind, empathy, humor processing, self-awareness, interoception, and illness insight, are well documented (Uekermann & Daum, 2008; Goldstein et al., 2009; Volkow et al., 2011). That cognitive dysfunctions can influence self-report is also shown in a recent study with alcohol dependent patients by Lincoln et al (2011). They found impairments in the estimation and self-evaluation of past alcohol intake that could be attributed to verbal memory dysfunctions contingent upon chronic alcohol abuse. Moreover, a study with a homogeneous group of Korsakoff Syndrome patients, found deficits in a story comprehension task specifically caused by executive dysfunction (Oosterman et al., 2011). This implies that AUD patients, when filling out the 567 items of the MMPI-2, might as well be hampered by both the somatic complaints and reduced executive functioning during the acute phase of abstinence.

In early abstinence, uncorrected MMPI-2 scales tend to reflect symptoms of withdrawal and cognitive recovery, overestimating levels of psychopathology, and tend to underrate disinhibitory behaviours and impulsive traits. The acute effects of alcohol withdrawal and the partial recovery of cognitive functioning over time, appears to be associated with the decrease of MMPI-2 scales, which can therefore not be merely attributed to the effects of treatment only. The latter is suggested by Polimeni, Moore and Gruenert (2010) but the absence of cognitive
Our findings suggest that in the acute phase of abstinence the withdrawal effects can easily lead to inadequate treatment planning, resulting in a more symptomatological approach. Such an approach (e.g., verbal group therapy for depression or anxiety and long psychotherapeutic sessions) is inadequate because it ignores the underlying cognitive deficits during the acute phase of abstinence and increases the risk of treatment drop out (Crews et al., 2005).

Despite the fact that the NRI-correction procedure is originally developed for the assessment of patients with TBI (Van Balen et al., 1997), it appears to be a useful tool to disentangle “demoralisation” and cognitive deficits in AUD patients during abstinence. Deleting NRI’s from the item pool, however, compromises the integrity of the MMPI-2 (Edwards et al., 2003; Arbisi & Ben-Porath, 1999). Hence, Arbisi & Ben-Porath (1999) in their review on correction procedures, suggest that NRI’s must be scored in a different direction in order to obtain an accurate measure of psychopathology (prorated scoring). They also recommend caution in the clinical application of the correction procedure, especially when using the MMPI-2 to assess the presence of affective disturbances following head injury. The present study on the assessment of AUD patients during the acute phase of abstinence, underscores their warning and calls for the inclusion of more than one diagnostic measure when conducting treatment planning.

The use of an MMPI-2 prorated correction procedure in AUD patients is warranted in the acute phase of early abstinence to avoid diagnostic misinterpretations that may affect treatment. Relevant variables for better treatment planning can specifically be found within the neurocognitive domain (e.g., cognitive and emotional functioning) with the adoption of neuropsychological measures in the assessment of AUD patients.

Conclusions
This study supports the use of a neurocorrective approach on the MMPI-2 to enhance validity and reliability in AUD patients during the acute phase of abstinence. In using a well-documented correction procedure, we found that impulsivity and psychopathic deviation can be identified as a common denominator in this group of AUD patients. “Corrected” MMPI-2 assessment can, therefore, be helpful in the accurate identification of the above aspects and does justice to the effects of alcohol related cognitive deficits on the diagnostic process.
Given the adverse effects of alcohol on the entire brain resulting in a wide array of cognitive deficits associated with AUD, it is expected that the application of such a correction procedure would provide patient descriptives (profiles, code types) in greater detail, thus enabling more adequate treatment selection. In alcohol abuse treatment settings, validation studies are warranted to substantiate the relation between the NRI-correction procedure and relevant neuropsychological measures. Future studies must focus on investigating the validity of a correction procedure in AUD, its utility in treatment planning, and the role of underlying alcohol related cognitive deficits, such as problems in executive functioning, illness insight and personality traits in AUD patients during abstinence.
MMPI-2 neurobehavioural correction in AUD patients
Chapter 6

Self-awareness of cognitive dysfunction: self-reported complaints and cognitive performance in patients with Alcohol-Induced Mild or Major Neurocognitive Disorder

Published as:
Abstract

Patients with Korsakoff’s syndrome (KS) typically have difficulties in recognizing the impact of their alcohol-related cognitive deficits on daily-life functioning. In this study, mean scores on self-reported complaints (measured with Minnesota Multiphasic Personality Inventory-2-Restructured Form; MMPI-2RF) and cognitive performance (measured with the Wechsler Adult Intelligence Scale-Third edition; WAIS-III; and the California Verbal Learning Test; CVLT) are compared between two matched patient groups with severe (KS) and mild alcohol-related cognitive disorders or non KS (NKS). KS patients demonstrate significantly lower scores on the WAIS-III indices and on the CVLT than the matched NKS group, and significantly higher scores on MMPI-2-RF validity scales that indicate denial of psychological complaints. Both groups are in the normal range on MMPI-2-RF Cognitive Complaints (COG) and Neurological Complaints (NUC) scales compared with the normative sample. Finally, self-reported complaints and cognitive performance are not correlated significantly in both groups. Despite their alcohol-related cognitive impairments, both groups report no cognitive complaints at all indicating self-awareness impairment. In addition to KS patients, also NKS patients are at risk that their apparently “without cognitive complaints” appearance on self-report questionnaires can be easily overlooked. These findings may have important clinical implications for diagnostic and treatment purposes.
Introduction

Alcohol use inhibits higher-order cognitive processes (executive functions), reducing the level of self-awareness leading towards increasing alcohol use (Goldstein et al., 2009). Eventually, in patients with Korsakoff’s syndrome (KS), the toxic effects of chronic alcohol misuse and thiamine deficiency on whole brain functioning are expressed in clinical, neurological, cognitive and pathological features of KS and Wernicke’s KS (Kopelman, 2002; Van Oort & Kessels, 2009). Impairments in memory and executive function (EF) are core symptoms of KS (Van Oort & Kessels, 2009), but are also present in patients without Korsakoff’s syndrome (NKS; Ihara et al., 2000; Oscar-Berman et al., 2004; Loeber et al., 2009). Besides the cognitive dysfunction, specific behavior (e.g., apathy and impaired self-awareness) is found in KS patients, describing themselves on self-report questionnaires as having no problems at all, leading towards a “without complaints” appearance (Egger et al., 2002; Thomson et al., 2012).

Cognitive dysfunction is already present in apparently healthy alcoholic patients (Bruijnen et al., 2013). In these patients lower cognitive performances on tests of memory and executive functioning are related to impaired self-awareness, apathy, and unrealistic expectations in daily life affecting treatment compliance and increasing treatment drop-out rates (Bowden-Jones et al., 2005; Goldstein et al., 2009; Kornreich et al., 2001; Marinkovic et al., 2009; Noël et al., 2002; Rinn, et al., 2002; Verdejo-Garcia & Pérez-Garcia, 2008). A better cognitive ability (e.g., IQ, executive function, and memory) is associated with metacognition (or knowing about knowing) leading towards a better self-awareness. Especially the ventral and dorsomedial prefrontal cortices are involved in reflective processing (David et al., 2012; Van der Meer et al., 2010) as well as the rostral anterior cingulate cortex (Moeller & Goldstein, 2014). These brain areas are also affected by the negative consequences of chronic alcohol use (Ratti et al., 2002; Moeller & Goldstein, 2014), resulting in impairments in facial affect perception, emotional prosody, theory of mind, and cognitive control over thoughts and behavior (Uekermann & Daum, 2008; Goldstein et al., 2009; Oscar-Berman et al., 1990; Montagne et al., 2006; Wilcox et al., 2014). In addition, Shimamura and Squire (1986) found that metamemory (the knowledge that people have of their memory function) is impaired in KS patients, but not in patients with amnesia. Metamemory can be viewed as part of metacognition, suggesting a link with executive functioning impaired in KS patients (Van Oort & Kessels, 2009). Moreover, metamemory impairment is also present NKS patients who evaluate their memory capacity just as good as healthy controls do (Le Berre et al., 2010). This finding is in line with self-report studies demonstrating that alcoholic
patients are inaccurate in estimating their own drinking behavior (Lincoln et al., 2011). Consequently, NKS patients may underestimate their cognitive dysfunctions and, as a result, overestimate their cognitive capacities, which may lead to inadequate treatment.

Impaired self-awareness in alcoholic patients has never been investigated by means of comparing the outcome of self-reported cognitive complaints and cognitive performance tasks. This comparison is of interest for both the concept of illness insight and treatment utility in patients with Korsakoff’s syndrome (KS) and in non Korsakoff’s syndrome (NKS) patients with alcohol-related cognitive dysfunction (ARCD). From a theoretical perspective, investigating the relationship between self-reported cognitive complaints and cognitive performance may provide more clarity on the concept of self-awareness. So far, no studies have been reported investigating this relationship empirically. Therefore, the aim of the present study is to investigate the relationship between self-reported cognitive complaints and cognitive performance in patients with Korsakoff’s syndrome (KS) and a matched group of non-Korsakoff patients (NKS) with ARCD.

Based on Horton et al. (2014), Stavro et al. (2013), Segobin et al. (2015), and Egger et al. (2002), the following hypotheses were formulated in the current study: Because of the persistent nature of the cognitive dysfunctions found in several studies on alcohol-related cognitive dysfunctions, both patient groups (e.g., KS and NKS patients) are expected to report fewer cognitive complaints than the normative group, indicating impaired self-awareness. In comparing both groups a) H1 : KS patients report less cognitive complaints than NKS patients versus H0: both groups do not differ on reporting cognitive complaints. b) H1 : KS patients perform worse on cognitive performance tasks than NKS patients versus H0: both groups do not differ on cognitive performance tasks. c) Finally, we expect to find a correlation between cognitive performance (WAIS III scores and CVLT) and self-reported complaints (MMPI-2-RF). We expect that worse cognitive performance correlates with a lower illness insight resulting in less self-reported cognitive complaints on the MMPI-2-RF scales. H1 : There is a negative correlation between self-performance and self-reported complaints, and this negative correlation will be stronger in the KS group. H0: The negative correlation between self-performance and self-reported complaints do not differ between both groups.
Method

Participants
At the Centre of Excellence for Korsakoff and Alcohol-Related Cognitive Disorders, the main goal is to assess all admitted patients for alcohol-related cognitive dysfunction, ranging from Mild Neurocognitive Disorder to Major Neurocognitive Disorder (e.g., Korsakoff’s syndrome). Thirty-four KS patients were selected from an existing dataset (Wester et al., 2014) fulfilling the selection criteria described in Figure 1. Another 22 NKS patients with alcohol-related cognitive dysfunction were matched for age, sex, and level of education from the same dataset. The additional 12 patients were selected blind from an MMPI-2 database. Selection was only based on the criterion that the NKS patients were matched with the KS patients on demographic variables (at group level), without any knowledge of test results, meeting the criteria described in Figure 1. All patients participated as part of a regular assessment procedure residing at the Centre of Excellence for Korsakoff and alcohol-related cognitive disorders of the Vincent van Gogh Institute for Psychiatry in Venray, the Netherlands.

In order to clarify the difference between both groups, the DSM 5 criteria were used in a retrospective way. The KS patients fulfill the DSM-5 criteria for Alcohol-Induced Major Neurocognitive Disorder (APA, 2013) including the presence of a persistent memory impairment resulting in severe deficits in social functioning, the absence of delirium or dementia due to a neurodegenerative disease, a history of alcohol-abuse disorder, evidence for a history of Wernicke encephalopathy, confabulation behavior ans history of malnutrition or thiamine deficit, as established by neurologival, psychiatric, neuroradiological, and neuropsychological examinations. None of the patients had any evidence for brain abnormalities that could account for their condition apart from atrophy or white-matter lesions associated with the chronic alcohol abuse and none fulfilled the proposed criteria for alcohol-related dementia (Oslin et al., 1998). None of the participants had hearing problems, language or communication deficits, or visual agnosia that could confound the performance on memory tests. The matched NKS patients had a history of chronic alcohol abuse with mild neurocognitive impairments and all met the DSM-5 criteria for alcohol-Induced Mild Neurocognitive Disorder (APA, 2013). The neurocognitive impairments were not due to another medical condition or use of other substances. In both groups, the cognitive deficits were substantiated by neuropsychological assessment.

Education level was assessed using 7 categories in accordance with the Dutch educational system (1 = less than primary school; 7 = university degree; Verhage, 1964). The modus of the education level was 4 (range 2-7 for both groups). Both samples consisted of 26 men and 8 women. Mean age was 55.5 years.
Both groups did not differ on their estimated verbal IQ ($t(1) = .05, p = .82$) assessed using the Dutch version of the National Adult Reading Test (NART; Nelson & Willison, 1991), and are comparable on their level of education ($U = 577, p = .99$). Mean lifetime of chronic alcohol consumption was 13.38 years (SD = 9.4) in the KS group and 13.94 years (SD = 8.5) in the NKS group. Although, all participants had no history of comorbid drug abuse or psychiatric disorders, all fulfilled the DSM-5 criteria for Tobacco Use Disorder. During the assessment process, apart from gait and balance abnormalities in patients with KS, no other relevant medical conditions were manifest.

**Measures**

All participants completed a neuropsychological assessment and the Dutch language version of the MMPI-2 (Derksen, 2006) as part of the regular diagnostic process. The Minnesota Multiphasic Personality Inventory-2-Restructured Form (MMPI-2-RF; Ben-Porath & Tellegen, 2008; Ben-Porath, 2012; Tellegen & Ben Porath, 2008) scale scores were derived from the original MMPI-2 booklet administration (Van der Heijden et al., 2010). Detailed information about the
Psychometric properties of the Dutch-language version of the MMPI-2-RF and the translation process is presented in the MMPI-2-RF manual (Van der Heijden et al., 2013). In the analysis three MMPI-2-RF validity scales (L-r, F-r, and K-r) and two MMPI-2-RF cognitive complaints scales were used. The L-r scale consists of 14 items measuring uncommon virtues (e.g., item 182: “I am entirely self-confident”), the F-r scale consists of 32 items measuring infrequent symptoms (e.g., item 46: “when I am with people I am bothered by hearing very strange things”), and the K-r scale consists of 14 items measuring adjustment validity (e.g., item 80: “I have a few quarrels with members of my family”). Both COG and NUC scales consist of 10 items each describing cognitive (COG; e.g., item 59: “my memory seems to be all right”) or neurological (NUC; e.g., item 162: “I seldom or never have dizzy spells”) complaints. Cronbach’s alphas for the NUC and COG scales are comparable with the normative data (i.e., .68 < Cronbach’s alpha < .78 which is considered acceptable; Ben-Porath & Tellegen, 2008; Nunnally, 1978).

Cognitive performance was measured with the Dutch-language version of the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III; Wechsler, 2005). The standardized index scores (M=100; SD= 15) were computed according to the Dutch test manual and used in the analysis. The Verbal Comprehension Index (VCI) consists of the subtests Vocabulary, Similarities, and Information. The Perceptual Organization Index (POI) consists of the subtests Block Design, Matrix Reasoning, and Picture Completion. The Working Memory Index (WMI) consists of Letter Number Sequencing, Digit Span, and Arithmetic. The Processing Speed Index (PSI) consists of the subtests Digit Symbol Coding and Symbol Search. The WAIS-III indexes are valuable in assessing cognitive impairment (Van der Heijden et al., 2012). Especially the PSI has proven to be sensitive in detecting acquired brain damage (Martin et al., 2000).

To assess episodic memory, the Dutch-language version of the CVLT (Delis et al., 1987; Mulder et al., 1996) was used. The CVLT is a word-list learning test that has proven to be sensitive in detecting memory impairment in ARCD patients (Wester et al., 2014). The total CVLT raw score after five trials of 16 words (CVLT Total immediate recall) and the delayed free recall raw score after 20 minutes (CVLT recall) were computed and are used in the analysis.

Procedure and analysis
All participants were recruited through Vincent van Gogh Institute for Psychiatry, and all data were collected as part of routine clinical assessment. The study was carried out in accordance with the Declaration of Helsinki and the Guidelines for Good Clinical Practice established by the International Conference on Harmonisation (CPMP=ICH=135=95) and approved by the Vincent van Gogh
Institutional Review Board (decision #66). The confidentiality of participants’ identities was maintained throughout the study process. Informed consent was obtained from all participants. To rule out withdrawal effects, both the neuropsychological assessment and the MMPI-2 were administered after patients had been abstinent from alcohol or other non-medical drugs for at least six weeks (Walvoort et al., 2013). Minimal length of abstinence was at least 42 days in both groups (range KS = 42 – 600 days; range NKS = 42- 180 days). In order to rule out reading problems, all participants were evaluated on their education level (at least fifth grade), in combination with the MMPI-2-RF VRIN-r <60 and TRIN-r < 60, as specified in the Manual for Administration, Scoring, and Interpretation (Ben-Porath & Tellegen, 2008). In this study, MMPI-2-RF profiles were considered valid if they had a CNS-r raw score of less than 18, VRIN-r and TRIN-r T-scores of less than 80, and FP-r T-score of less than 100, and a F-r T-score of less than 120 (Ben-Porath & Tellegen, 2008).

SPSS version 22.0 was used for all of the statistical analyses. Table 1 presents descriptive statistics for both groups. A one-way ANOVA between both groups was conducted to compare the differences in mean scores on WAIS-III index scales (VCI, PRI, WMI, and PSI), CVLT total immediate and delayed recall scores, and MMPI-2-RF (K, L, F, COG, and NUC) scales. Bivariate correlations were computed between the aforementioned MMPI-2-RF scales, the WAIS-III Index scales, and the CVLT total immediate and delayed recall scores for both groups. In addition, to investigate if the obtained correlations between both groups were significant, Fisher’s Z-scores were computed. In computing the bivariate correlations, the uncorrected MMPI-2-RF raw scores are used in the statistical analysis (Tellegen & Ben-Porath, 2008; Butcher et al., 1995). The MMPI-2-RF raw scores were used because these are not affected by characteristics of the normative sample and thus comparable for different cultures (e.g., US and The Netherlands).

Results

As Table 1 indicates, the KS group demonstrates significantly lower scores on the WAIS-III indices (Perceptual Organization and Processing Speed) and the CVLT (immediate total score and delayed recall) than the matched NKS group. As to behavioral characterization and test taking attitude of both groups, notably, disorientation in space, time and person, and a more flattened curve on the five trials of the CVLT were found in KS patients.

KS patients demonstrate lower scores than NKS patients on the F-r scale and higher on the L-r and K-r scale, indicating an under-reporting bias. Both scores on the NUC and COG scales are within the normal range, suggesting that both
patient groups do not report more cognitive complaints compared to the normative data ($M = 50, SD = 10$, $N = 2150$; Van der Heijden et al., 2013).

Overall, self-reported cognitive complaints did not correlate with the cognitive performance tasks (see Table 2). However, the COG scale correlated

| Table 1 Descriptives (mean scores, standard deviations,) of both groups on age, WAIS III indexes, CLVT raw scores, and MMPI-2-RF T-scores |

<table>
<thead>
<tr>
<th></th>
<th>NKS patients</th>
<th>KS patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 34</td>
<td>N = 34</td>
</tr>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
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<tr>
<td><strong>WAIS III</strong></td>
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<tr>
<td>VCI</td>
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</tr>
<tr>
<td>POI</td>
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</tr>
<tr>
<td>WMI</td>
<td>90.12</td>
<td>13.33</td>
</tr>
<tr>
<td>PSI</td>
<td>89.50</td>
<td>14.48</td>
</tr>
<tr>
<td><strong>CVLT</strong></td>
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<td></td>
</tr>
<tr>
<td>Total score</td>
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</tr>
<tr>
<td>Recall score</td>
<td>7.47</td>
<td>4.81</td>
</tr>
<tr>
<td><strong>MMPI-2-RF</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F-r</td>
<td>70.88</td>
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</tr>
<tr>
<td>L-r</td>
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<td>K-r</td>
<td>43.91</td>
<td>8.18</td>
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<tr>
<td>NUC</td>
<td>63.59</td>
<td>13.42</td>
</tr>
<tr>
<td>COG</td>
<td>60.53</td>
<td>14.88</td>
</tr>
<tr>
<td><strong>F value</strong></td>
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<td>F(1,66) = .18</td>
</tr>
<tr>
<td><strong>p value</strong></td>
<td>.56</td>
<td>.19</td>
</tr>
<tr>
<td><strong>η²</strong></td>
<td>.00</td>
<td>.19</td>
</tr>
</tbody>
</table>

Note. Mean scores and standard deviations of the MMPI-2-RF are T-scores; in parentheses are the raw scores; NKS = Alcohol-related cognitive dysfunction Non-Korsakoff; KS = Korsakoff’s syndrome; VCI = Verbal Comprehension Index; POI = Perceptual Organization Index; WMI = Working Memory Index (WMI); PSI = Processing Speed Index; F-r = Infrequent responses; L-r = Uncommon Virtues; K-r = Adjustment Validity; NUC = Neurological Complaints; COG = Cognitive Complaints; $η²$ = partial eta squared; According to Miles & Shevlin (2001) $η²$ of .02 is regarded to be small; .13 = medium; .26 = large.
significantly with PSI in the KS group, indicating that more self-reported cognitive complaints are accompanied by a lower level of processing speed. The COG scale and PSI are not correlated in the NKS group and the correlations between COG and PSI significantly differ for both groups (i.e., $Z = 1.78$, $p = .04$). This specific correlation may be explained by a small number of outliers in the Korsakoff group (four cases). We found four patients who scored 2 SD above the mean (1 patient scored 2 SD above the mean PSI score, and 3 patients scored 2 SD above the mean COG score). When those four cases are excluded from the analysis, the correlation between PSI and COG is no longer statistically significant.

**Discussion and conclusion**

This study is the first to investigate the relationship between self reported cognitive complaints and cognitive performance in two matched groups of KS and NKS patients. The MMPI-2-RF validity scales confirm the hypothesis that KS patients show denial and social desirability in self-reporting symptoms. In addition, no cognitive complaints on the MMPI-2-RF NUC and COG scales are being reported despite the cognitive dysfunctions in KS patients present on cognitive tests.

Regarding cognitive complaints, both groups do not differ from those reported by a Dutch normative healthy sample.
Compared to the NKS patients, KS patients perform significantly lower on PSI on the WAIS-III, but not on the COG scales in the MMPI-2-RF. This means that KS patients report the same amount of cognitive complaints than NKS patients, yet their speed processing capacity is lower. It was hypothesized that the severity of cognitive impairment would come with increased under-reporting of self-reported complaints. However, we did not find significant correlations between self-reported cognitive complaints and cognitive performance in both groups, except for the correlation between COG and PSI in the KS group. This particular correlation may be explained by a small number of outliers in the Korsakoff group (four cases).

In our study, the differences in the L-r/F-r/K-r score profile demonstrates a denial of psychological complaints and lower scores on infrequent complaints in the KS group. This under-reporting response style (i.e., L-r > F-r > K-r; trying to present themselves in a favorable way, Ben-Porath & Tellegen, 2008) is typical for KS patients (Egger et al., 2002). The combination of the L-r > F-r > K-r configuration and average scores on NUC and COG scales seems to be able to accurately detect the under-reporting tendency of KS patients underscoring the inclusion of validity scales in self-report questionnaires to ensure reliable responding.

KS patients perform significantly worse on processing speed, perceptual reasoning and memory performance than NKS patients. These findings support the notion that, in addition to the cognitive dysfunctions, a gradual process of impaired self-awareness would evolve in chronic alcoholic patients. This is in line with recent brain neuroimaging findings that showed a graded pattern of
cerebrospinal fluid enlargement, especially in the lateral ventricles and Sylvian fissures ranging from NKS to KS (Le Berre et al., 2015) where only the medial thalami, mammillary bodies, and corpus callosum are more severely damaged in KS patients (Pitel et al., 2012). This means that in addition to KS patients, also NKS patients are at risk that their apparently “without cognitive complaints” appearance on self-report questionnaires can be easily overlooked or misinterpreted as a lack of motivation by the therapist (Rinn et al., 2002) leading towards under diagnosis or inadequate treatment (Horton et al., 2014; Thomson et al., 2012). Studies in different patient groups show that self-report is moderately correlated with performance tasks (Carone & Ben-Porath, 2014; Gervais et al., 2009), indicating that it is difficult to measure self-awareness impairment with self-report questionnaires only. Therefore, in addition to a heteroanamnesis, information on cognitive functioning is essential in the treatment of patient with chronic alcohol use. Cognitive functions can be measured accurately with relatively short cognitive screening tools, like the Montreal Cognitive Assessment test (MOCA; Nasreddine et al., 2005) in alcohol-dependent patients (Alarcon et al., 2015) and in addicted patients (Bruijnen, et al., 2013; Copersino et al., 2009).

A limitation of the present study is that information of a healthy control group and information regarding their cognitive performance on the neuropsychological tests used in the present study is lacking. Another limitation is that we did not measure the impairment in executive functions that affects self-awareness (Goldstein et al., 2009).

In sum, the current study adds to the limited research on self-awareness in KS patients. For a better understanding of the concept of self-awareness and treatment of ARCD patients, more research is needed that focuses on measuring self-awareness and cognitive control in KS and NKS patients and investigates the effectiveness of cognitive rehabilitation programs, especially in NKS patients. In this perspective, cognitive rehabilitation studies of training cognitive control and working memory are promising (Bates et al., 2013; Kiluk & Carroll, 2013).
Chapter 7

Measuring illness insight in patients with alcohol-related cognitive dysfunction using the Q8 questionnaire: A validation study

Published as:
Abstract

Impaired illness insight may hamper treatment outcome in patients with alcohol-related cognitive deficits. In this study, a short questionnaire for the assessment of illness insight (e.g., the Q8) is investigated in patients with Korsakoff’s syndrome (KS) and Alcohol Use Disorder (AUD) patients with mild neurocognitive deficits. First, reliability coefficients are computed and internal structure is investigated. Then, comparisons are made between patients with KS and patients with AUD. Furthermore, correlations with the DEX questionnaire are investigated. Finally, Q8 total scores are correlated with neuropsychological tests for processing speed, memory, and executive function. Results show that the internal consistency of the Q8 was acceptable (i.e., Cronbach’s alpha = .73) The Q8 items represent one factor and scores differ significantly between AUD and KS patients. The Q8 total score, related to the Dysexecutive Questionnaire (DEX) discrepancy score and scores on neuropsychological tests as was hypothesized, indicates that a higher degree of illness insight is associated with a higher level of cognitive functioning.

In sum, the Q8 is a short, valid and easy to administer questionnaire for assessing illness insight in patients with moderate and severe alcohol-related cognitive dysfunction.
Introduction

Impairments in memory and executive function (EF) are core symptoms of Korsakoff’s syndrome (Van Oort & Kessels, 2009), but are also present in patients with alcohol use disorder (AUD) (Goudriaan et al., 2006; Ihara et al., 2000; Oscar-Berman et al., 2004; Loeber et al., 2009; McCrady & Smith, 1986). Both memory and EF are key features for a successful behavioral change to remain abstinent and to restore societal functioning (Blume & Marlatt, 2009; Crews et al., 2005; Le Berre et al., 2012; Tate et al., 2014). One consequence of these cognitive dysfunctions in patients with AUD is impaired illness insight (David et al., 2012; Goldstein et al., 2009). That is, patients typically underestimate the amount of alcohol they have used (Lincoln et al., 2011; Le Berre et al., 2010), and the duration of their alcohol addiction, but also misjudge the severe and adverse consequences of alcohol addiction on daily life and health functioning (Volkow & Li, 2005). Impaired illness insight can be regarded as a continuum ranging from total denial of the disease to more subtle metacognitive awareness deficits (David et al, 2012). Illness insight comprises awareness of illness, the capacity to view symptoms of the disease as pathological, and treatment adherence (David, 1990).

In patients with Korsakoff’s syndrome (KS), overestimation of their memory abilities or a failure to recognize their severity is common due to impaired metamemory (Le Berre et al., 2010; Shimamura & Squire, 1986). Compared to the information given by the patients themselves, information given by relatives, therapists, and other professional caregivers report that these patients show poorer insight into and less awareness of their cognitive deficits (Verdejo-García & Perez-García, 2008). Impaired illness insight in alcohol-dependent patients might be related to their severe retrograde amnesia, including deficits in autobiographical memory (Poncin et al., 2015).

A wide network of brain structures has been identified as being crucial for self-awareness, and includes the prefrontal and posterior parietal cortex (Moeller & Goldstein, 2014; Prigatano & Johnson, 2003), the rostral part of the anterior cingulate cortex, the insula (Goldstein et al., 2009; Moeller & Goldstein, 2014), and the precuneus (Cavanna & Trimble, 2006). Typically, these brain areas are susceptible to the negative effects of alcohol use (Bates et al., 2002; Goldstein et al., 2009; Rosenbloom & Pfefferbaum, 2008; Sullivan & Pfefferbaum, 2005). While this would indicate that functional and structural changes in brain functioning underlie impaired illness insight, clinically, lack of illness insight is often misinterpreted as a motivational problem (Dean et al., 2015; Moeller et al., 2014) or alcoholic denial (Duffy, 1995; Rinn et al., 2002). Moreover, these alcohol-related cognitive deficits can affect the results of self-report questionnaires in such a way that it can lead to clinical misinterpretation (Egger et al., 2002; Johnson-Greene
et al., 2002; Lincoln et al., 2011; Walvoort et al., 2012). In order to avoid this misinterpretation of alcohol-related cognitive deficits, the combined use of self-report information and information reported by informants who know the patient very well, is essential for adequate diagnosis and in particular for the assessment impaired self-awareness.

Bourgeois and colleagues (2002a; 2002b) developed and validated a short questionnaire for measuring illness insight, the Q8 questionnaire, available in the French language. The Q8 is a short and easy to administer questionnaire for measuring illness insight by means of answering eight questions by the patient (see Appendix 1 for an English translation of the original French questions). After the patient has completed the Q8, a clinician who knows the patient very well rates each response with respect to its adequacy. The total score is the sum of the item scores (maximum = 8). A score of ≤ 2 indicates no illness insight; a score of 3 – 5 indicates poor illness insight and a score ≥ 6 indicates good illness insight. Bourgeois and colleagues examined the Q8 in a mixed-etiologic psychiatric sample with severe psychopathology (e.g., patients with schizophrenia, bipolar depression, and addiction. However, despite of the fact that the Q8 was specifically designed for measuring levels of illness insight, until now, no research has yet been published about the use in patients with alcohol-related cognitive deficits.

Therefore, in the present study we aim to investigate the psychometric properties of the Dutch language version of the Q8 in patients with severe and mild alcohol-related cognitive deficits. First, the internal consistency is investigated. Second, the internal structure is investigated. We expect all 8 items to represent one factor. Third, the difference in Q8 total scores between KS patients and AUD patients with moderate cognitive deficits is considered. We expect that KS patients have a lower Q8 total score than other AUD patients. Fourth, the Q8 scores are correlated with the Dysexecutive Questionnaire (DEX) discrepancy score, a widely used measure to assess daily executive problems in daily life as reported by the patient and an informant (Wilson et al., 1996). We expect that a lower DEX discrepancy score correlates with a lower Q8 total score indicating impaired illness insight. Finally, correlations of the Q8 with neuropsychological tests for executive functioning, memory, and processing speed are calculated. We hypothesize that impaired illness insight (i.e., a lower Q8 total score) correlates higher with severe cognitive dysfunction in KS patients than in AUD patients with moderate cognitive deficits.
Method

Participants
All data were collected as part of routine outcome monitoring of clinical testing and all patients signed a treatment plan. The confidentiality of participants’ identities was maintained throughout the study process. The procedure was approved by the Vincent van Gogh Insitutional Review Board. The study was carried out in accordance with the Declaration of Helsinki and the Guidelines for Good Clinical Practice established by the International Conference on Harmonization (CPMP/ICH = 135/95). Ninety-seven patients completed the Q8 as part of routine clinical assessment (see Table 1.). All were inpatients of the Centre of Excellence for Korsakoff and alcohol-related cognitive disorders of the Vincent van Gogh Institute for Psychiatry in Venray, the Netherlands. Forty-two patients were diagnosed as KS patients fulfilling the DSM-5 criteria for Alcohol-Induced Major Neurocognitive Disorder (APA, 2013) including the presence of a persistent memory impairment resulting in severe deficits in social functioning, the absence of delirium or dementia, a history of alcohol-abuse disorder, evidence for a history of Wernicke encephalopathy, confabulation behaviour, and history of malnutrition or thiamine deficit, as established by neurological, psychiatric, neuroradiological, and neuropsychological examinations.

The AUD group consisted of 55 patients with a history of chronic alcohol abuse with mild neurocognitive impairments. All AUD patients met the DSM-5 criteria for Alcohol-Induced Mild Neurocognitive Disorder (APA, 2013). The neurocognitive impairments were not due to another medical condition or use of other substances. In both groups, the cognitive deficits were substantiated by neuropsychological assessment.

All patients were at least 42 days abstinent from alcohol at the time of testing. Education level was assessed using 7 categories in accordance with the Dutch educational system (1 = less than primary school; 7 = university degree; Verhage, 1964). No significant differences were found between the groups regarding sex distribution ($\chi^2(1)= .000, p = .996$). Descriptives of the total group (N=97) and differences between the Korsakoff (N = 42) and AUD patients (N = 55) are listed in Table 1.

Measures
Questionnaires
The Q8 has been developed and validated in French. For this study, the Q8 (Bourgeois et al., 2002a; 2002b) was translated into Dutch and slightly adapted using the original French questions by a clinical neuropsychologist with expertise in alcohol related cognitive disorders (Dr. Arie Wester). Consensus was reached...
Table 1  Descriptives of the total group (N=97) and differences between Korsakoff (N = 42) and AUD patients (N = 55)

<table>
<thead>
<tr>
<th></th>
<th>Total (n=97)</th>
<th>KS (n=42)</th>
<th>AUD (n=55)</th>
<th>t</th>
<th>U</th>
<th>p</th>
<th>d</th>
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</thead>
<tbody>
<tr>
<td><strong>Education (mode and range)</strong></td>
<td>4 (2-7)</td>
<td>4 (2-6)</td>
<td>4 (2-7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Alcohol use in years (range)</strong></td>
<td>2-55</td>
<td>2-48</td>
<td>2-55</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Abstinence in days (range)</strong></td>
<td>42-693</td>
<td>42-693</td>
<td>42-186</td>
<td>1.14</td>
<td>.26</td>
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**Cognitive measures**

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Sd</th>
<th>Mean</th>
<th>Sd</th>
<th>Mean</th>
<th>Sd</th>
<th>t</th>
<th>p</th>
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<tbody>
<tr>
<td>Age</td>
<td>55.84</td>
<td>8.66</td>
<td>57.36</td>
<td>8.77</td>
<td>54.67</td>
<td>8.47</td>
<td>1.52</td>
<td>.13</td>
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</tr>
<tr>
<td><strong>NART</strong></td>
<td>92.43</td>
<td>15.10</td>
<td>89.67</td>
<td>14.64</td>
<td>94.55</td>
<td>15.55</td>
<td>-1.59</td>
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<td>.12</td>
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<tr>
<td><strong>PSI</strong></td>
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**Questionnaires**

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<tr>
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<tbody>
<tr>
<td>DEX-S</td>
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<td>-3.69</td>
<td>.00</td>
<td>-0.75</td>
</tr>
</tbody>
</table>

Note. Bold = p < 0.05.; NART = National Adult Reading Test (standard score); PSI = WAIS III processing Speed Index (standard score); CVLT = California Verbal Learning Test (raw score); MSET = Modified Six Elements Test (standard score); DEX-S = DEX self (raw score); DEX-I = DEX informant (raw score); DEX-D = Discrepancy score of DEX Self (raw score) minus DEX informant (raw score); Q8 Total score (raw score).
Measuring illness insight in alcohol-related cognitive dysfunction

in the translation by all authors. The resulting research version of the Q8 consists of eight questions (see Appendix 1), for example: “Do you experience limitations in your professional life, your family life, or in your social life?” and was administered five weeks after admission to the clinic. An internal consistency of 0.81 was found in a previous study (Bourgeois et al., 2002a; 2002b).

The DEX, a subtest of the Behavioural Assessment of the Dysexecutive Syndrome (BADS; Wilson et al., 1996) was administered. There are two versions; a patient rating scale (DEX-S) and a rating scale for informants (DEX-I; e.g., relatives, friends, or professional caregivers) who know the patient very well in relation to the daily activities/functioning. Both versions are 20-item scales in which each item is rated 0 = never, 1 = occasionally, 2 = sometimes, 3 = fairly often, or 4 = very often. The DEX incorporates cognitive, affective, and behavioural aspects of the dysexecutive syndrome. An example of such a question is “I find it difficult to keep my mind on something, and am easily distracted”. Both the patient and his/her primary professional caregiver from our department completed the DEX. In order to investigate the dissociation between self-report and behaviour, which is commonly seen in addiction (Goldstein et al., 2009), discrepancy scores for the DEX (DEX-D) were calculated by subtracting the informant scores from the self-ratings (David et al., 2012; Wilson et al., 1996). A negative discrepancy score indicates higher ratings by the patient than by the caregiver, suggestive of illness insight while a positive discrepancy score instead points at a lower rating by the caregiver than by the patient and a lack of illness insight. Validity of DEX-D scores for detecting poor insight has been established previously. David and co-workers (2012) for instance found that DEX-D was highly discrepant in patients with Alzheimer and patients with brain injury and should be regarded as a measure of awareness of dysexecutive symptoms.

Neuropsychological measures

The Modified Six Elements Test (MSET) of the Behavioural Assessment of Dysexecutive Syndrome (BADS; Wilson et al., 1996) was used as a cognitive measure of daily executive functioning (Fernández-Serrano et al., 2010) and discriminates at a clinically significant level between KS and Non Korsakoff’s Syndrome patients (cf., Van Oort & Kessels, 2009; Maharasingam et al., 2013).

The delayed free recall raw score of the Dutch version of the California Verbal Learning Test (CVLT; Delis et al., 1987) was used in the analysis. The CVLT is a word-list learning test that has proven to be sensitive in detecting memory impairment in chronic alcoholic patients (Wester et al., 2014; Walvoort et al., 2016).
Finally, the Processing Speed Index (PSI) of the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III; Wechsler, 2005) was used, which consists of the subtests Digit Symbol Coding and Symbol Search. The PSI has proven to be sensitive in detecting impairment in processing speed (Walvoort et al., submitted).

**Procedure and analysis**

Informed consents were obtained from all participants. The assessment of the DEX-questionnaires and the neuropsychological tests were administered after patients had been abstinent from alcohol or other non-medical drugs for at least six weeks (Walvoort et al., 2013). The neuropsychological tests were assessed by an experienced psychologist. In this study, the Q8 questionnaire was evaluated by an experienced clinical neuropsychologist who knows the patient well, two weeks prior neuropsychological assessment. Reliability of the Q8 was measured by computing Cronbach’s alpha and split half reliability. Internal structure of the Q8 is investigated by principal component analysis with varimax rotation. Parallel analysis was performed to determine the number of components that should be extracted (Glorfeld, 1995; Horn, 1965). Independent T-test’s were performed to measure differences between KS patients and AUD patients (see Table 1.). Pearson correlations coefficients were computed between the Q8, the DEX-S, DEX-I, DEX-D score, and the neuropsychological measures (MSET, CVLT and PSI) for both groups pooled together.

**Results**

Cronbach’s alpha for the Q8 questionnaire is .73, a Spearman-Brown coefficient of .70, which are acceptable (Nunnally, 1978). PCA on the items in the total sample revealed one component accounting for 35% of the variance. PCA was repeated in both subsamples to investigate whether the factor structure was robust in both subsamples. In both subsamples one factor appeared with somewhat higher loadings in the KS subsample (M = .63) than in the AUD subsample (M= .47). The coefficient of congruence, used to compare the factors in both subsamples is .89. As a rule of thumb, Harman (1976) proposed that factors are congruent if the coefficient of congruence is equal to or greater than .94.

As Table 1 indicates, the KS group demonstrated significantly lower scores on the Q8 questionnaire than the AUD controls. On the Q8, 64 % of the KS patients scored < 2 versus 23 % of the AUD controls. Table 2 demonstrates significant correlations between the Q8 and the DEX, CVLT recall, MSE, and PSI. Correlations of .10 are considered to be small, correlations of .30 can be considered
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medium (Cohen, 1992). The positive correlations between Q8 and the DEX-S indicate that a higher level of illness insight is associated with a higher level of self-reported complaints on the DEX-S. Significant negative correlations between the Q8 and DEX-I were found, indicating that lower scores on the Q8 are associated with higher levels of observed dysexecutive symptoms by the informant. Moreover, the DEX-D score showed a positive correlation with the Q8, indicating that lower DEX-D scores (more symptoms observed by the professional caregiver than by the patient) are related with lower scores on the Q8. Positive correlations between the neuropsychological measures (MSET, CVLT, and PSI) and the Q8 were found, revealing that better cognitive performance is associated with a higher level of illness insight.

<table>
<thead>
<tr>
<th></th>
<th>DEX total score</th>
<th>Neuropsychological measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Self</td>
<td>Informant</td>
</tr>
<tr>
<td>Q8</td>
<td>.26*</td>
<td>-.30**</td>
</tr>
</tbody>
</table>

Note. * = P < .05; ** = p < .01; Discrepancy = DEX-Self minus DEX-Informant score; CVLT = California Verbal Learning Test; MSET = Modified Six Elements test; PSI = WAIS-III Processing Speed Index.

Discussion and conclusion

This study is the first in using the Q8 questionnaire in patients with severe and moderate alcohol-related cognitive dysfunction for assessing illness insight. Internal consistency, split-half reliability and factor analysis proved that the Q8 has acceptable psychometric characteristics to assess (lack of) illness insight in patients with moderate to severe AUD. The Q8 scores of KS patients differ from AUD patients with less severe cognitive impairments and the Q8 demonstrates medium correlations with the discrepancy score of the DEX (DEX-D), contributing to the concurrent validity of the Q8. These findings demonstrate the concurrent validity of the Q8 total score. Finally, as expected, better illness insight, as measured with the Q8, correlated with a better performance on measures of executive function (the MSET), memory (CVLT delayed free recall) and processing speed (PSI).

Since the Q8 incorporates self-reported thoughts and beliefs of the patient as well as an evaluation by a caregiver who knows the patient very well, it has
clinical potential as a valid tool for assessing illness insight in patients with severe psychopathology. Since it comprises eight items, it has a shorter administration time than the DEX-D. In addition, the Q8 measures illness insight in a more direct way than the DEX-D. The DEX-D, being a measure of awareness in dysexecutive symptoms, is a more indirect way of measuring illness insight by comparing the “self” and “other” ratings (David et al., 2012). It should be noted that it is not always easy to gather information of relevant others, because the social network of AUD patients is often limited.

Another limitation of the Q8 is that no data on test-retest reliability are available from the Bourgeois studies (2002a; 2002b) nor from the present study. Future research should address this and could also examine the use of the Q8 in addicted patients without cognitive dysfunction, as the addiction itself also affects illness insight and self-awareness (Goldstein & Volkow, 2011; Moeller & Goldstein, 2014; Verdejo-García & Perez-García, 2008; Volkow et al., 2012). Also, it would be interesting to evaluate the course of illness insight by assessing the Q8 on several occasions during abstinence. Kim et al., (2007), for instance, examined 117 male alcoholic patients up to one year of abstinence after treatment using a self-report questionnaire, and found that insight might improve during the course of abstinence. Alternatively, one could argue that this improved insight may be due to improved cognitive function, in line with findings that cognitive function in alcoholic patients recovers to some extent during abstinence (e.g., Stavro et al., 2013; Walvoort et al., 2013).

In conclusion, the results of this study confirm that the Q8 questionnaire is a reliable and valid measure that provides a significant contribution to the assessment of illness insight in patients with moderate and severe alcohol-related cognitive dysfunctions. It should be stressed, that the assessment of illness insight should always be performed by using different sources of information (e.g., neuropsychological measures, self-report questionnaires and information from professional caregivers) to further optimize clinical decision making and treatment selection.
Measuring illness insight in alcohol-related cognitive dysfunction
Chapter 8

Summary and discussion
The main objective of this thesis is the multimethod evaluation of cognition and illness insight in patients with Alcohol Use Disorders (AUD). In this, an overview of the main findings of this thesis will be presented. Additionally, strengths and limitations will be discussed. Finally, clinical implications and directions for future research will be provided.

Main findings

In Chapter 2 the classification of alcohol-related cognitive deficits according to the DSM-5 (APA, 2013) was studied as compared to the DSM-IV TR (APA, 2000). The main conclusion is that the DSM-5 puts a greater focus on alcohol-related cognitive dysfunction, with an essential role for neuropsychological assessment for the classification, diagnosis of neurocognitive deficits, and for setting up treatment design and planning. Thus, neuropsychological testing is essential for evaluating the cognitive domains of functioning and to reveal cognitive strengths and weaknesses that guide treatment planning.

The timing of neuropsychological testing is important: if performed too early during abstinence, the effects of alcohol withdrawal can affect the assessment. Empirical evidence on the required period for abstinence before a reliable neuropsychological assessment of AUD patients can be carried out was reviewed and presented in Chapter 3. The aim was to come up with a suggestion regarding the abstinence time needed to perform a sound neuropsychological assessment. The literature review indicated that recovery to a relatively stable condition tends to take up three to five weeks. To ensure reliable neuropsychological assessment, an abstinence period of at least six weeks is recommended. During this six-week interval, the brain is allowed to regenerate and the patient’s physical state improves, allowing a more reliable assessment of the underlying neurocognitive and behavioural deficits for treatment purposes.

In setting up a proper psychological treatment design in AUD patients, self-report questionnaires are frequently used to obtain information about comorbid psychopathology and personality traits. However, chronic alcohol use and alcohol withdrawal may bias the outcome of self-report questionnaires in two ways. First, withdrawal effects of alcohol during abstinence may cause emotional and somatic discomfort that should be distinguished from other forms of (comorbid) psychopathology. Second, chronic alcohol use may lead to cognitive dysfunction and impaired illness insight affecting self-evaluations with questionnaires. One of the most frequently used psychological tests to evaluate personality and psychopathology in AUD patients, the Minnesota Multiphasic Personality Inventory (MMPI-2; Butcher, 1996), provides different
methods to adjust for these distorting effects of alcohol withdrawal and cognitive impairment on self-report. Chapter 4 systematically reviewed the literature to what extent the available MMPI-2 correction methods, originally developed for use in neurological patients, can be used in AUD patients during the acute phase (< 6 weeks) of abstinence. Results demonstrated that, given the similarity of cognitive deficits in patients with AUD and in those with Traumatic Brain Injury (TBI), the use of a MMPI-2 correction method can be helpful in the interpretation of psychopathology and personality profiles during the acute phase of abstinence.

In Chapter 5 the clinical utility of a particular MMPI-2 correction method (i.e., Van Balen et al., 1997) was empirically evaluated in a group of 222 AUD patients during the acute phase of abstinence (14 days). In this study, corrected and uncorrected profiles were compared. The result demonstrated that the decrease in scores of the corrected profiles, as compared to the original ones, reflected primarily an overrepresentation of somatic complaints and demoralizational beliefs during the acute phase of abstinence. This was in accordance with clinical observations and earlier findings that these somatic complaints were merely a reflection of the patient’s acute problems in multiple somatic, cognitive and behavioural domains. Such a state in itself produces elevations on MMPI-2 profiles and nearly always precedes admission to an addiction clinic. Furthermore, both impulsiveness/disinhibition and problems in self-reflective capacities dominated the differences between the corrected and uncorrected MMPI-2 scores in AUD patients. This suggests that uncorrected MMPI-2 scales tend to overstress psychopathology and to overlook disinhibitory personality traits caused by chronic alcoholism during the six weeks period of abstinence. Based on these findings, it is recommended to either delay the assessment with self-report questionnaires for at least six weeks or use the reported MMPI-2 correction procedure during the acute phase of abstinence.

In Chapter 6 the concordance of self-reported cognitive complaints on the MMPI-2-RF with performance on cognitive tasks was examined to empirically evaluate the consequences of cognitive dysfunction and lack of insight. Two matched patient groups with severe and moderate alcohol-related cognitive dysfunction, i.e., fulfilling the criteria for Korsakoff’s syndrome (KS) and Non-Korsakoff cognitively impaired AUD patients, respectively, were used in this empirical evaluation. All 64 participants were tested after an abstinence period of at least six weeks. Regarding cognitive complaints, both groups did not differ from those reported by a Dutch normative healthy sample. In line with reported clinical features of KS patients (Egger et al., 2002), KS patients demonstrated denial and social desirability in self-reporting symptoms. In addition, KS patients did not report any cognitive and neurological complaints on the self-report questionnaire (i.e., the MMPI-2-RF cognitive and neurological
complaints scales) despite the evident dysfunction on cognitive performance tasks. Moreover, a typical MMPI-2-RF under-reporting response style in the KS group was found. All these findings appeared to be related with impaired illness insight.

In order to assess lack of illness insight in AUD patient with a different method, the psychometric characteristics of an illness insight questionnaire, the Q8, were investigated in Chapter 7. The Q8 is a short questionnaire for the assessment of illness insight by means of answering eight questions by the patient. After completion of the Q8, a clinician who knows the patient very well rates each response with respect to its adequacy. The utility of the Q8 in 97 AUD patients with mild (55 patients) to severe (42 KS patients) cognitive dysfunction was investigated. It was found that the Q8 is a reliable and valid measure for the assessment of illness insight in patients with AUD and severe comorbid psychopathology. Better illness insight, as measured with the Q8, was related to a better performance on measures of executive function, memory and processing speed. Furthermore, the Q8 was able to discriminate between patients with and without Korsakoff’s syndrome contributing to the clinical diagnosis of Korsakoff’s syndrome.

In sum, by using a multimethod evaluation of psychopathology, cognitive complaints, cognitive functioning, and illness insight in patients with AUD, it can be concluded that (1) while DSM-5 classification necessitates the identification of cognitive deficits, additional neuropsychological assessment is obligatory to information about the neuropsychological domains of functioning; (2) it is preferred to apply an abstinence period of at least six weeks before neuropsychological testing and self-report questionnaires can be reliably administered; (3) knowledge of the obscuring effects effects of alcohol withdrawal, alcohol-related cognitive dysfunctions, and lack of illness insight on self-report questionnaires and cognitive functioning, will contribute to better understanding of AUD patients. All of this results in a more reliable and comprehensive profile of an individual’s weaknesses and strengths, in order to achieve a better treatment indication.

**Strengths and limitations**

A major strength of this thesis is that, by means of a multimethod evaluation, cognition and illness insight in AUD patients are examined from multiple perspectives to fill in the gaps in literature regarding the assessment issues. Moreover, specific patient groups with mild to severe cognitive dysfunctions are used, which are usually difficult to find for participation in clinical research.
Another major strength is that the results of the studies in this thesis lead directly to concrete recommendations for assessment and treatment planning in clinical practice. Furthermore, the studies in the present thesis use multiple measures. As a consequence, the conclusion regarding assessment of psychopathology and cognitive functions in AUD patients is more sound as single method variance is avoided.

Some limitations also need to be considered. First of all, the studies in the current thesis did not include non-alcoholic control groups. One could argue that comparisons of the results with either a healthy control group or a group of non-alcoholic psychiatric patients may reveal how specific the pattern of cognitive dysfunction and reported complaints for AUD patients is. On the other hand, a broad variety of AUD patients with mild to severe psychopathology were included in the current thesis, allowing a more dimensional approach to AUD-related problems. Another limitation might be that, even though an abstinence period of at least six weeks is recommended, this thesis provides no data regarding the assessment of AUD patients both at admission to the clinic and during six weeks of abstinence. By doing so, it becomes clearer whether the reported symptoms and complaints are associated with alcohol withdrawal or with alcohol-related cognitive disorders. Although a six-week abstinence period is warranted before a reliable neuropsychological assessment can be carried out, it must be noted that cognitive recovery varies greatly by individual (Oscar-Berman et al., 2014). Conversely, while in clinical practice it is common to assess patients according to a method of classification and categorization, this thesis demonstrates that assessment in a more dimensional way gives a better view of reality, providing more tools for treatment purposes. This corresponds with the way the DSM-5 conceptualizes alcohol-related cognitive deficits.

Conclusions, clinical implications, and directions for future research

In this thesis, a multimethod evaluation of cognitive complaints and illness insight in AUD is investigated. First by controlling for the effects of abstinence by using an abstinence period of at least six weeks and second by using multiple measurements for treatment purposes. Although this thesis focuses primarily on assessment and indication, some thoughts upon treatment utility and future research are presented.

The notion that cognitive deficits and impaired illness insight might be present in AUD patients will lead to more understanding of AUD patients. Neuropsychological assessment should be highly recommended in assessing the
skills that are needed, affected or still intact, for choosing suitable treatment goals for either cognitive rehabilitation training and/or (external) compensating techniques. Before neuropsychological assessment can take place, however, a patient must have been abstinent from alcohol for a period of at least six weeks. The combination of sustained abstinence and the effects of adequate nutrition and thiamine replacement have a positive effect on the recovery of cognitive functions. Moreover, patients with persistent AUD who already show cognitive problems and who do not receive thiamine replacement are at risk for developing chronic cognitive dysfunction, Wernicke’s encephalopathy, or even death (e.g., Thomson et al., 2013). Concerning the present findings it would be interesting to investigate, by means of repeated assessment, the alcohol-related cognitive deficits during the course of abstinence. By using multiple moments of testing a clinician can get a clear picture of the skills that may recover during treatment and can fine tune treatment strategies and set new treatment goals. Moreover, a study of Dennis et al. (2007) concluded that in addicted patients the risk of relapse is problematic during the first three years of abstinence, indicating that the application of an abstinence period and long-term strategies and programs should also be investigated for other types of addictive substances.

Impaired awareness of cognitive deficits is associated with a lesser need to seek treatment, to set treatment goals, and to use learned skills to maintain abstinent of alcohol and other addictive substances (e.g., Rinn et al., 2002; Verdejo-Garcia & Pérez-Garcia, 2008). Although research is limited, this thesis investigated the use of an illness insight questionnaire (the Q8) in AUD patients with severe psychopathology. Since, the Q8 has not been studied in AUD patients without cognitive dysfunction, future studies should investigate if adjustment of the Q8 will detect impairment in illness insight at an early stage of addiction treatment in AUD and addicted patients without cognitive deficits.

The combination of self-report questionnaires (and correction methods; Chapter 5), performance tasks (Chapter 6), rating scales (self and others), and a systematic evaluation by clinician (Chapter 8) provides a broad picture of the patient’s cognitive and behavioural abilities leading to a more individualized treatment. By using a multimethod approach a clinician can interpret the reported complaints more accurate, reducing the risk of overburdening the patient during treatment, supporting the thought that self-awareness in AUD patients should not be confused with a lack of motivation.

Assessment of cognitive abilities before selecting a treatment will prevent the start of a treatment without the knowledge whether an AUD patient will actually benefit from it. By using a quick and easy to use cognitive screening instrument, such as the MoCA (Nasreddine et al., 2005), cognitive deficits can be detected in an early stage of treatment in AUD patients as well as in patients
with other substance use (e.g., Bruijnen et al., 2013; Copersino et al., 2009). From thereon, further investigation to assess neuropsychological domains of functioning or to design a proper treatment planning can start. In this view, the recent developed screening tool the BEARNI (Brief Evaluation of Alcohol-Related Neuropsychological Impairments), especially designed for assessing alcohol-related cognitive deficits (Ritz et al., 2015) is promising, supporting the findings in this thesis that alcohol-related cognitive disorders should be taken into account during treatment. Moreover, although research is still limited, the expectation is that emotional functioning in AUD patients will improve if cognitive functioning recovers.

Future studies should focus on cognitive dysfunctions during the course of abstinence in AUD and other addictive substances by using cognitive screening tools, neuropsychological assessment, refining the illness insight scale for the use in AUD patients and in addicted patients, leading towards effective, personalized treatment interventions.
References


E
F


G


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Z

### Q8 Questions

<table>
<thead>
<tr>
<th>Q8 Questions</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Why are you here?</td>
<td></td>
</tr>
<tr>
<td>2. Do you feel that you are ill?</td>
<td>(0/1)</td>
</tr>
<tr>
<td>3. Which disease or disorder do you have?</td>
<td>(0/1)</td>
</tr>
<tr>
<td>4. What is the cause of this?</td>
<td>(0/1)</td>
</tr>
<tr>
<td>5. Do you suffer psychologically or do you experience feelings of guilt?</td>
<td>(0/1)</td>
</tr>
<tr>
<td>6. Do you experience limitations in your professional life,</td>
<td>(0/1)</td>
</tr>
<tr>
<td>your family life, or in your social life?</td>
<td></td>
</tr>
<tr>
<td>7. How can we help you?</td>
<td>(0/1)</td>
</tr>
<tr>
<td>8. Do you think you can be treated?</td>
<td>(0/1)</td>
</tr>
</tbody>
</table>

**Q8 TOTAL SCORE**  
(0/8)
Nederlandse samenvatting
In dit proefschrift worden zes studies beschreven met als doel om met behulp van verschillende methodes cognitie en ziekte-inzicht te evalueren bij de indicatie-stelling van patiënten met alcoholgerelateerde cognitieve stoornissen. De methoden in dit proefschrift omvatten classificatie, zelfrapportage (inclusief correctiemethoden), beoordelingsschalen, en neuropsychologisch testonderzoek waarbij rekening gehouden wordt met de abstinentietermijn die noodzakelijk is om de onthoudingseffecten van alcohol te minimaliseren. Allereerst wordt het begrip ziekte-inzicht nader uitgewerkt.

### Alcohol, cognitie en ziekte-inzicht

Al enkele decennia is duidelijk dat langdurig overmatig alcoholgebruik een toxisch effect heeft op het functioneren van de hersenen en kan leiden tot cognitieve stoornissen (Crews et al., 2005; Harper, 2009; Kalivas & Volkow, 2005; McCrady & Smith, 1986; Oscar-Berman & Marinkovic, 2007). Deze cognitieve stoornissen uiten zich op de domeinen aandacht, geheugen, visueel spatiële functies en problemen in het executief functioneren, waaronder het probleemplossend vermogen, de mentale flexibiliteit, de planning en de oordeels vorming (Bates et al., 2002; Goldstein et al., 2001; Scheurich, 2005). Doordat behandelprogramma-onderdelen veelal een beroep doen op bovengenoemde cognitieve domeinen, is het niet verwonderlijk dat dergelijke behandelingen meestal niet succesvol zijn (Allen et al., 1997; Manning et al., 2008; Scheurich, 2005). Daarnaast is het belangrijk dat er gestreefd wordt naar abstinentie van alcohol. Tijdens abstinentie kunnen de alcoholgerelateerde cognitieve stoornissen (a) deels herstellen (Bates et al., 2002; Fals-Stewart et al., 1994; Loeber et al., 2009; Mann et al., 1999), (b) redelijk stabiel blijven over een periode van een jaar (Horton et al., 2015; Stavro et al., 2013) en (c) zelfs tot zes jaar later nog verbeteren, hetgeen het geval is voor het executief functioneren (Fein et al., 2006a; McCrady & Smith, 1986). De combinatie van het toedienen van thiamine (vitamine B1) en een normaal dieet is hierbij van doorslaggevend belang (Martin et al., 2003), waarbij het herstel samenhangt met leeftijd (Goldman, 1983), de abstinentietijd (McCrady & Smith, 1986) afgezet tegen de context van reeds bestaande cognitieve stoornissen, het opleidingsniveau en de persoonlijkheidskenmerken (Yücel et al., 2007). Daarnaast is bekend dat alcoholgebruik een causaal verband heeft met het ontwikkelen van angst en depressie, en ook dat aanwezige psychopathologie en persoonlijkheidstrekkens de kans op alcoholverslaving vergroten (Verheul et al., 1999). Hoewel de literatuur aantoont dat bij langdurig alcoholgebruik ook de sociaal-cognitieve functies (waaronder perspectiefname, oordeelsvorming, zelf bewustzijn en ziekte-inzicht) zijn aangetast (Uekermann & Daum, 2008; Moeller...
& Goldstein, 2014), wordt hier nog onvoldoende rekening mee gehouden in de diagnostiek en de daaropvolgende behandel fase.

Een tekort aan ziekte-inzicht, ook wel anosognosie genoemd (Babinski, 1914), wordt gezien bij patiënten die geen weet hebben van de eigen ziekte en daarmee ook geen noodzaak zien om in behandeling te gaan. Crosson et al. (1989) waren de eersten die een trapsgewijs model voor ziekte-inzicht hebben ontwikkeld bestaande uit drie niveaus. Het eerste niveau is dat van het intellectueel besef, ofwel het kennen van de eigen beperkingen; het tweede niveau betreft het besef van zowel de eigen beperkingen alsmede het compenseren hiervoor; en het derde niveau wordt gedefinieerd door het besef van de eigen beperkingen, de compensatiemogelijkheden en tevens de vaardigheid om te kunnen anticiperen. Het derde niveau vereist intacte planningsvermogens en metacognitieve vaardigheden. Dit trapsgewijze model is door Van Schouwen-van Kranen (2014) verder uitgewerkt. Hierbij is het model van Crosson et al. (1989) geïntegreerd met een hiërarchisch model van cognitief functioneren, met aandacht als basale vaardigheden, gevolgd door geheugen, en tot slot de executieve functies (planning) als meest complexe cognitieve functie (Allen et al., 1992). In dit hiërarchisch georganiseerde model correspondeert de hoogte van het cognitief functioneren met de mate van ziekte-inzicht, variërend van laag cognitief functioneren en beperkt tot geen ziekte-inzicht tot en met hoog cognitief functioneren en ziekte-inzicht. Deze inzichten werden bevestigd door studies die aantonen dat de mate van ziekte-inzicht varieert van een totale ontkennin gen van de eigen problematiek tot subtielere metacognitieve problemen (David et al., 2012). Problemen met ziekte-inzicht komen onder meer voor bij patiënten met neurodegeneratieve aandoeningen (Shany-Ur et al., 2014), niet-aangeboren hersenletsel (Ham et al., 2014), schizofrenie (Kruck et al., 2009), en verslavingsproblematiek (Moeller & Goldstein, 2014). Bij patiënten met alcoholgerelateerde cognitieve stoornissen wordt vaak een tekort aan initiatiefname, een beperkt ziekte-inzicht, apathie en verstoorde executieve functies gevonden (Marinkovic, et al., 2009), waarbij een beperkt ziekte-inzicht niet verward moet worden met een gebrek aan motivatie (Miller & Barasch, 1985; Rinn et al., 2002).
Naar een meervoudige evaluatie van alcoholgerelateerde cognitieve stoornissen

Alcoholgerelateerde cognitieve stoornissen zijn moeilijk te classificeren middels de DSM-IV TR (APA, 2000) en kunnen bijgevolg leiden tot zowel overschatting als onderschatting van de (onderliggende) cognitieve stoornissen in de klinische praktijk. Het is dus van belang dat voorafgaand aan de behandeling duidelijk moet zijn welke cognitieve vaardigheden intact zijn en welke niet. Bij het opstellen van een dergelijk sterkte- en zwakteprofiel kan een behandelaar een aantal problemen tegen komen die het beeld kunnen vertroebelen, zoals de invloed van abstinentie op het herstel van cognitieve stoornissen en de invloed van het beperkt ziekte-inzicht en cognitieve stoornissen op de uitkomsten van zelfrapportagevragenlijsten.

Om duidelijkheid te kunnen krijgen over de manier waarop alcoholgerelateerde cognitieve stoornissen het best kunnen worden geclasseerd in DSM-terms, werd in hoofdstuk 2 de classificatie van alcoholgerelateerde cognitieve stoornissen volgens de DSM-5 (APA, 2013) vergeleken met die volgens de DSM-IV TR (APA, 2000). De belangrijkste conclusie uit deze studie is dat alcoholgerelateerde cognitieve stoornissen in DSM-5-terms beter geclasseerd kunnen worden, omdat hierin een prominente rol is weggelegd voor neuropsychologisch onderzoek.

De timing van een dergelijk neuropsychologisch onderzoek is belangrijk: als neuropsychologisch onderzoek te vroeg tijdens de abstinentieperiode wordt uitgevoerd, kunnen de alcoholgerelateerde onthoudingseffecten zowel de uitkomsten beïnvloeden van (zelfrapportage)vragenlijsten, van neuropsychologische tests, alsook van de behandeling. In hoofdstuk 3 is gezocht naar wetenschappelijk bewijs aangaande de abstinentietijd die nodig is om betrouwbare neuropsychologisch onderzoek uit te kunnen voeren bij patiënten met stoornissen in alcoholgebruik. Het doel van deze studie was om met een voorstel te komen wanneer neuropsychologische onderzoek het best uitgevoerd zou kunnen worden. De bestudeerde wetenschappelijke literatuur toonde wisselende termijnen van cognitief herstel variërend van drie tot vijf weken abstinentie. Om betrouwbare neuropsychologisch onderzoek uit te kunnen voeren werd een abstinentietermijn van minimaal zes weken voorgesteld. Gedurende deze zes weken ontwikkelt het cognitief functioneren zich tot een relatief stabiel niveau, waardoor betrouwbaarder onderzoek naar cognitieve mogelijkheden en beperkingen uitgevoerd kan worden.

Voor psychologische behandeldoeleinden wordt in de verslavingszorg frequent gebruik gemaakt van zelfrapportagevragenlijsten. Op deze manier kan informatie verzameld worden over aanwezige psychopathologie en persoonlijkheidstrekkens. Echter, chronisch alcoholgebruik en alcoholonttrekking kunnen de uitkomsten
van deze vragenlijsten op twee manieren vertroebelen. In de eerste plaats kunnen alcoholonthoudingseffecten emotionele en somatische klachten veroorzaken die tijdens de acute fase van abstinentie moeilijk te onderscheiden zijn van (comorbide) psychopathologie. In de tweede plaats kan chronisch alcoholgebruik leiden tot cognitieve stoorheden en een verminderd ziekte-inzicht, die de uitkomsten van dergelijke vragenlijsten kunnen beïnvloeden. Een van de meest gebruikte en wetenschappelijk onderzochte zelfrapportagevragenlijsten om persoonlijkheidstrekkers en psychopathologie bij mensen met een alcoholverslaving te meten is de Minnesota Multiphasic Personality Inventory (MMPI-2; Butcher, 1996). Voor de MMPI-2 zijn onder meer voor neurologische patiënten, een aantal methodes beschreven om te corrigeren voor de verstorende effecten van hersenletsel op de MMPI-2. In hoofdstuk 4 is de literatuur systematisch onderzocht met de vraag in hoeverre de voorhanden zijnde MMPI-2 correctiemethodes toepasbaar zijn voor patiënten met stoornissen in alcoholgebruik tijdens de eerste fase van abstinentie (< 6 weken). Uit de resultaten blijkt dat, gezien de overeenkomst tussen cognitieve stoorheden bij patiënten met stoornissen in het gebruik van alcohol en patiënten met traumatisch hersenletsel, het gebruik van een correctiemethode voor de MMPI-2 ondersteunend kan zijn bij het interpreteren van psychopathologie en persoonlijkheidstrekkers tijdens de eerste fase van abstinentie.

In hoofdstuk 5 is het gebruik van een correctiemethode voor de MMPI-2 (ontwikkeld door Van Balen et al., 1997) empirisch geëvalueerd bij een groep van 222 patiënten met stoornissen in het gebruik van alcohol tijdens het begin van abstinentie (de eerste 14 dagen). Uit de vergelijking van gecorrigeerde en ongecorrigeerde MMPI-2-profielen komt naar voren dat correctie de geraappte somatische klachten en demoralisatie, die doorgaans voorkomen tijdens de beginfase van abstinentie, kan verlagen. Dit komt overeen met de klinische observaties en eerdere bevindingen dat de somatische klachten het acute klinische beeld kunnen bepalen en daarmee de cognitieve en gedragsmatige problemen overschaduwen. Daarnaast toont de studie aan dat ongecorrigeerde MMPI-2-schalen sterk de nadruk leggen op ernstige psychopathologie waardoor specifieke trekken als disinhibitie en problemen met zelfreflecterend vermogen gemakkelijk als onderliggende factoren over het hoofd worden gezien. Kortom, gebaseerd op deze bevindingen wordt voorgesteld om het testonderzoek uit te stellen tot minimaal zes weken abstinentie of anderszins een MMPI-2-correctieprocedure toe te passen tijdens de acute fase van abstinentie.

In hoofdstuk 6 is de relatie tussen zelfgerapporteerde cognitieve klachten, gemeten met de herziene versie van de MMPI-2, de MMPI-2-RF, en de prestaties op cognitieve taken onderzocht door twee vergelijkbare patiëntgroepen met ernstige (korsakovsyndroom) en matige neurocognitieve stoornissen door alcohol
met elkaar te vergelijken. De 64 deelnemende patiënten zijn getest na een abstinentietermijn van minimaal zes weken. Zoals verwacht rapporteerden korsovpatiënten geen cognitieve of neurologische klachten op de zelfrapportage vragenlijst (MMPI-2-RF) terwijl er sprake was van evidente cognitieve stoornissen middels neuropsychologische tests. Dit lijkt overeen te komen met de klinische kenmerken van korsovpatiënten, zoals ontkenning van de eigen klachten en sociaal wenselijk gedrag (Egger et al., 2002). Bovendien werd er in de groep korsovpatiënten een MMPI-2-RF-antwoordtendentie gevonden die kenmerkend is voor de onderrapportage van klachten. Daarnaast bleek dat beide groepen niet van elkaar verschillen ten aanzien van de zelfgerapporteerde cognitieve klachten. Beide groepen rapporteerden ongeveer evenveel cognitieve klachten als de gemiddelde Nederlander (de normgroep van de test), terwijl er veel meer cognitieve problemen werden gezien op neuropsychologische tests. Deze bevindingen lijken samen te hangen met een beperkt ziekteinzicht.

Om ziekteinzicht bij patiënten met stoornissen in het gebruik van alcohol vast te kunnen stellen zijn in hoofdstuk 7 de psychometrische aspecten van een vragenlijst gericht op ziekteinzicht (de Q8; Bourgeois et al., 2002a; Bourgeois et al., 2002b) onderzocht. De Q8 is een korte vragenlijst bestaande uit acht vragen die door de patiënt ingevuld moeten worden. Na het invullen van deze lijst worden de Q8-items beoordeeld op hun adequaatheid door een clinicus die de patiënt goed kent. De toepasbaarheid van de Q8 is onderzocht in een groep van in totaal 97 patiënten met matige (55 patiënten) tot ernstige (42 patiënten met het syndroom van Korsakov) alcoholgerelateerde cognitieve stoornissen. De Q8 bleek een betrouwbaar en valide instrument om de mate van ziekteinzicht vast te kunnen stellen bij patiënten met stoornissen in het gebruik van alcohol met comorbid ernstige psychopathologie. Een beter ziekteinzicht (een hogere Q8-totaalscore) lijkt samen te hangen met betere prestaties op taken die executief functioneren, geheugen en verwerkingssnelheid meten. Daarnaast is de Q8 in staat om onderscheid te maken tussen patiënten met ernstige cognitieve stoornissen (Korsakov) en matige cognitieve stoornissen, waarmee het een bijdrage levert aan de klinische diagnose van het syndroom van Korsakov.

Tot besluit

Samenvattend, door gebruik te maken van een meervoudige ("multimethode") evaluatie van psychopathologie, cognitieve klachten, cognitief functioneren en ziekteinzicht bij patiënten met alcoholgerelateerde (cognitieve) stoornissen kunnen de volgende conclusies getrokken worden: (1) waar de DSM-5 classificatie
bijdraagt aan de identificatie van cognitieve stoornissen, is het neuropsychologisch
onderzoek een onmisbaar onderdeel om informatie te vergaren over de neuro-
psychologische cognitieve domeinen voorafgaand aan de behandeling; (2) een
abstinentietermijn van minimaal zes weken moet in acht genomen worden
voordat neuropsychologisch onderzoek en zelfrapportagevragenlijsten betrouwbaar
c kunnen worden afgenomen en geïnterpreteerd; (3) kennis van de vertroebelende
effecten van alcohol onthouding, onderliggende alcoholgerelateerde cognitieve
stoornissen en een beperkt ziekte-inzicht op zelfrapportagevragenlijsten en het
functioneren kan leiden tot een beter begrip van deze doelgroep. Door een
multimethodische evaluatie kan er een betrouwbaar cognitief profiel worden
opgesteld met sterktes en zwaktes van de patiënt, waarmee de behandeling
beter en effectiever kan worden ingericht. Door het opnemen van meerdere
meetmomenten tijdens de behandeling kan er een duidelijk beeld verkregen
worden van de vaardigheden die herstellen tijdens de abstinentie en behandeling.
Op deze wijze kan de behandelaar de behandeling verfijnen en is de verwachting
dat deze (geïndividualiseerde) behandelaanpak de kans op overvraging en het
voortijdig afbreken van de behandeling verkleint.
Dankwoord
Dankwoord

De basis van dit proefschrift is gelegd bij de opleiding tot klinisch neuropsycholoog. Het begon met een praktijkonderzoek naar alcoholabstinentie en werd uiteindelijk een heus promotietraject. Gedurende dit traject had Dr. Arie Wester, oprichter van de Korsakovkliniek in Venray, grote betrokkenheid als supervisor, begeleider en collega. Zijn collegialiteit, deskundigheid, rust, relativeringsvermogen en leiderschap hebben veel voor mij betekent. Vandaar dat ik dit proefschrift aan hem wil opdragen.

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Publications
International papers


Papers in Dutch


Book chapters


Posters


Egger, J.I.M., Verhoeven, W., Feenstra, I., Walvoort, S.J.W., de Leeuw, N. Impaired executive function, weak motor skills, and a rare form of epilepsy in an intellectually disabled girl with a 8q12.3q13.2 microdeletion. International Neuropsychological Society mid-year meeting, 10-13 July 2013, Amsterdam.


Serge Walvoort was born in Aalten, Netherlands, on September 27, 1972. In 1990, he completed the highschool at the Christelijke Scholengemeenschap in Aalten and obtained his teacher’s degree at PABO Iselinge in Doetinchem in 1994. During this study his interest in the remediation of learning disabilities and behaviour at childhood grew and after acquiring his teacher’s degree, he started to study Educational Science at the Radboud University in Nijmegen. His master thesis examined the self-fulfilling phrophecy tendency of teachers towards children of Moluccan immigrants in primary schools. In 1997, he acquired his master’s degree. For five years he worked as an educationalist for the remediation of learning disabilities and behaviour in primary and secondary schools at the Kempen Schoolbegeleidingsdienst in Eersel where he obtained his clinical degree (as healthcare psychologist). From 2003 until 2008, he worked at the Reinier van Arkel Institute for child and adolescent psychiatry in Vught. In 2008, he started at the Vincent van Gogh Institute for Psychiatry, where he enrolled in the specialized clinical neuropsychology postgraduate residency. Part of this education program was to set up a scientific study, which formed the basis of the present thesis. In 2012, he was registered as a certified clinical neuropsychologist. Presently, he works at the Centre of Excellence for Korsakoff and alcohol-related cognitive disorders of Vincent van Gogh Institute for Psychiatry in Venray. His activities include patient care, clinical research, education, and from 2015, as head of department. In addition, since 2014 he is responsible for the clinical neuropsychology residency at Huize Padua, GGZ Oost Brabant in Boekel.

The neuropsychology of alcohol use disorder:
A multimethod evaluation of cognition and illness insight

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