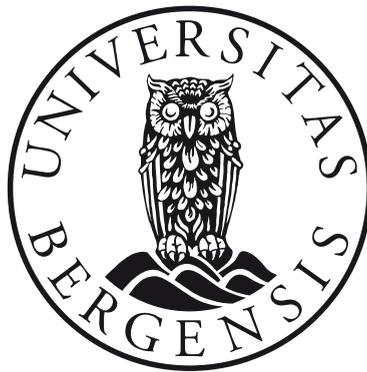


# **Cognitive and psychological functioning in patients with substance use disorder; from initial assessment to one-year recovery**

Egon Hagen



Thesis for the Degree of Philosophiae Doctor (PhD)  
at the University of Bergen

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## **Scientific environment**

This thesis was completed within the institutional framework of the PhD program at the Faculty of Psychology, Department of Biological and Medical Psychology, University of Bergen. I was also affiliated with the Centre for Alcohol and Drug Research, Stavanger University Hospital.

The work was funded by Helse-Vest, Strategic Initiative for Substance Use Research.

## Preface

I have worked with a broad array of clinical neuropsychological issues, both at Rogaland A-Centre in Stavanger and at the Department of Physical Medicine and Rehabilitation at Stavanger University Hospital. This work has revolved mainly around diagnosing patients with different neurocognitive impairments, either as sequelae to chronic substance use disorder (SUD) or due to head trauma, solvent exposure, or other risk factors. On several occasions, I reconnected with patients I had previously diagnosed, who had managed to control their SUD and achieve sobriety. I could not help noticing that some of these patients had made significant improvements in neuropsychological functioning, most likely due to a change in drug use and its associated lifestyle. Hence, I started to question the long-term validity of a single neuropsychological assessment, its corresponding diagnosis, and its ramifications.

I had the privilege of getting to know my current Research Director Dr. Sverre Nesvåg when he was Director at Rogaland A-Center. After Dr. Nesvåg had established the Regional Competence Center for Alcohol and Drug Research (KORFOR) in Stavanger, I had the opportunity to embark on the current PhD project. Dr. Nesvåg and I agreed that we wanted to investigate neurocognitive recovery processes, rather than the commonly investigated neurotoxic effects of different drugs. While his support, enthusiasm and knowledge extend beyond the project, they have been very valuable for both the initiation and completion of it.

Research within this field involves several methodological challenges, which we will detail later in this chapter. One of the main challenges was to motivate the involved clinical institutions to give us access to patients, and on our behalf, to do what was possible to reduce dropout from the research project. We also wanted to retain patients in the project while they were *in* treatment, *out* of treatment, *in* jail, *out* of jail, and for an *extended* period. This work was possible because of the effort and talent of our research assistant Thomas Solgård

Svendsen, who was the first to be recruited in this role. Later, Anne-Lill Mjølhus Njaa was also employed in an equivalent role. Along with Janne Årstad, they played a crucial role in the running of the project and managed to keep attrition low.

The project was built completely from scratch, and few of my colleagues had training and work experience within the field of neuropsychology. I, therefore, knew that it was vital to connect with skilled professionals within this field. The initial process led me to Dr. Espen Walderhaug at Oslo University Hospital who became my main supervisor. He has supported and inspired me during these many years. I was also fortunate to have Professor Astri J. Lundervold at the University of Bergen as my cosupervisor. They have both been vital for the completion of my thesis. Furthermore, Professor James R. McKay, who heads the Centre on the Continuum of Care in the Addictions at the University of Pennsylvania, gave me the opportunity to take part in an international collaboration, and to complete a four-week research stay with his group in the USA. His contribution has been very inspiring, and I sincerely hope this will be the beginning of a lasting collaboration.

Research interest, like addiction, runs in families. Some of my co-authors are also family, and without my nephew, PhD candidate and psychologist Aleksander H. Erga, and my daughter, Katrin P. Hagen, who is soon to be a specialist in clinical neuropsychology, this would have been an even more challenging road to travel.

I am also deeply grateful for the support and inspiration from all my colleagues in the Centre for Alcohol and Drug Research, Stavanger University Hospital. I would like to thank Espen A. Enoksen for handling all the organizational and financial issues around setting up the project. My thanks go to Randi Mobæk, Director of the Department of Young Adults, where I held a parallel advisory role throughout the entire PhD period; her genuine interest in new clinical knowledge and her continuous support have been vital for the completion of the thesis. I am very grateful to all the patients for their participation in the project; they have

contributed to research in a central clinical field, and it is hoped that this will help bring treatment for SUD a small step forward.

Finally, I express my gratitude to my wife Bjørg, for her love, support, and continued trust in the relevance of the project.

# 1. Abstract

Neurocognitive impairment affects quality of life, occupational functioning, and the ability to benefit from therapy. Neurocognitive assessment is thus of importance, but it is expensive and not widely accessible. Therefore, in a hectic clinical setting, a procedure that includes measures that target core cognitive deficits would be beneficial. Paper I investigate the utility of psychometric tests, and a questionnaire-based inventory to assess “hot” and “cold” neurocognitive measures of executive functioning (EF) in adults with substance use disorder (SUD) (Hagen et al., 2016)

Patients with polysubstance use disorder (PSUD) and healthy controls were compared on hot (Iowa Gambling Task) and cold (Stroop and the Trail Making Test) measures of EF, and participants completed a questionnaire assessing everyday EF-related problems (the Behavior Rating Inventory of Executive Function–Adult self-report version (BRIEF-A)). To our surprise, the psychometric measure of hot EF (the Iowa Gambling Task) did not differentiate the patients with PSUD from controls and was not associated with any of the social adjustment indicators. The psychometric measures of cold EF differentiated somewhat between the groups and were associated with one indicator of social adjustment. However, the BRIEF-A differentiated between groups on all the clinical scales and was associated with three out of five social adjustment indicators. We concluded that the BRIEF-A was the most sensitive measure of EF in patients with SUD and should, therefore, be considered as a fundamental part of the clinical routine when assessing patients with SUD.

PSUD is the most common diagnosis among patients seeking treatment for substance use. Compared with single-drug users, polydrug users have an earlier debut of drug use, a higher rate of dropout from treatment, and they report higher levels of general psychological distress; this psychiatric comorbidity increases the risk of relapse. Studies have shown that impaired

psychiatric and cognitive functioning also greatly diminishes patients' subjective perception of satisfaction with life. Even though satisfaction with life is reduced among SUD patients, it has not been thoroughly investigated in patients with PSUD. As satisfaction with life is described as an essential motivator for and predictor of successful treatment, it should be included as a key outcome indicator when evaluating the success of SUD treatment. Thus, paper II investigates whether individuals with PSUD who achieve at least one year of abstinence show greater improvement in satisfaction with life, executive functioning, and psychological distress compared with those who relapse and controls. Results indicated that participants who successfully abstained from substance use for one year showed improved satisfaction with life, executive functioning, and psychological distress compared with participants who relapsed and controls. Our findings suggest that a gradual and careful increase of learning requirements should be implemented, and SUD treatment should initially concentrate on stabilizing the patient and achieving abstinence, while interventions for comorbid problems and more cognitively challenging treatment components are more likely to succeed later in the treatment sequence (Hagen et al., 2017).

Attention-deficit/hyperactivity disorder (ADHD) is a common comorbid disorder among patients suffering from SUD. Compared with SUD patients without ADHD, SUD patients with ADHD are more likely to have developed SUD at a younger age, become polysubstance users, and need inpatient treatment more often. It is well established that the prefrontal cortex is involved in reward mechanisms, emotional processing, and behavioral inhibition, as well as drug use susceptibility. These functional areas have also been associated with the development of ADHD, and thus these two disorders could share a preexisting neurobiological vulnerability. Hence, the possible overlap and interconnections between these disorders are relevant to both research and clinical practice. Paper III investigates whether individuals with PSUD with one year of abstinence show a reduction in ADHD symptoms compared with those

who relapse and controls. ADHD symptoms were measured using the adult ADHD Self-Report Scale (ASRS). Substance use was evaluated by self-reports on the Alcohol Use Disorders Identification Test (AUDIT) and the Drug Use Disorders Identification Test (DUDIT). Results indicate that patients who remained abstinent for one year reported a substantial reduction in ADHD symptoms compared with patients who relapsed and controls. We concluded that confirmation of an ADHD diagnosis should follow a period of abstinence to avoid identification of false-positive cases (Hagen et al., 2017)

# List of publications

## Paper I

Hagen E, Erga AH, Hagen KP, Nesvåg SM, McKay JR, Lundervold AJ, Walderhaug E (2016). Assessment of executive function in patients with substance use disorder: a comparison of inventory- and performance-based assessment. *Journal of Substance Abuse Treatment*, 66:1-8.

## Paper II

Hagen, E., Erga, A. H., Hagen, K. P., Nesvåg, S. M., McKay, J. R., Lundervold, A. J., & Walderhaug, E. (2017). One-year sobriety improves satisfaction with life, executive functions and psychological distress among patients with polysubstance use disorder. *Journal of substance abuse treatment*, 76, 81-87.

## Paper III

Hagen, E., Erga, A. H., Nesvåg, S. M., McKay, J. R., Lundervold, A. J., & Walderhaug, E. (2017). One-year abstinence improves ADHD symptoms among patients with polysubstance use disorder. *Addictive Behaviors Reports*, 6 (Supplement C), 96-101. doi:<https://doi.org/10.1016/j.abrep.2017.08.005>

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# 1. Introduction- Background

Providing effective treatment for vulnerable groups with extensive disease burden, such as patients with SUD, represents a major societal challenge. This PhD project aims to shed light on the initial assessment of cognitive impairment among SUD patients, as well as the recovery process in the year after initiation of a new treatment sequence. To ensure a diverse and clinically relevant picture of the dimensions underlying recovery, we have broadened the scope of interest to include measures of satisfaction with life, psychological distress, and ADHD symptomatology, as well as neurocognitive functioning. Our hope is that this project will contribute to more effective substance use treatment programs, both for the patients and for society in general.

## 1.1 The neurocognitive substrate of addiction

Alcohol and drug abuse impacts neurocognitive functioning directly by producing changes in neurochemistry, and indirectly by affecting other organ systems, particularly the liver. The primary mechanism is associated with neurobiological changes that develop from initial positive reinforcement mechanisms to loss of control, the emergence of negative emotional states when access to intake is obstructed, and sensitized (hypersensitive) responses involving compulsive drug intake (Koob, 2008; Leshner, 1997; Robinson & Berridge, 2008).

Chronic substance use can induce changes in synaptic functioning, either by modifying receptor sensitivity, or by changing the synaptic reuptake process, and these require time to stabilize after psychoactive substance intake has finished. Studies have focused on the specific neural pathways involved in mediating and modulating the positive reinforcing effects of drugs, and how these connect to the regulation of reward processes. It is proposed that there are strong conditioning patterns within subcortical circuitry involving a dopaminergic tract

that connects the nucleus accumbens to the ventral tegmental area (VTA), and then back to the nucleus accumbens, prefrontal cortex, and amygdala. This process drives the initial hedonic mechanism (liking) toward obsessive drug-seeking behavior (wanting), and this nonreflective compulsion could represent a causal mechanism initiating relapse even after extended periods of abstinence (Everitt, Dickinson, & Robbins, 2001; Robinson & Berridge, 2008; Tomkins & Sellers, 2001). Repeated use modifies dopamine production, resulting in the dysregulation of brain reward circuitry, and subsequently creating the subcortical biological basis for the addiction (Koob, 2009).

Reward mechanisms have progressively been linked to other neurotransmitter pathways connecting the mesolimbic structures to cortical areas of the brain, and to the prefrontal cortex (PFC). Addictive behavioral patterns are reinforced by sensitized and overactive mesolimbic circuitry, in combination with a weakened executive control of prefrontal cortex (Bechara et al., 2001; Rogers & Robbins, 2001; Schoenbaum & Shaham, 2008; Stalnaker, Takahashi, Roesch, & Schoenbaum, 2009).

PFC impairments have been linked to dysfunctional impulse control, response inhibition, decision-making, and poor goal-driven behavior. Central components are reduced ability to suppress responses, poor attention, poor evaluation of consequences, and a predisposition to short instantaneous rewards over greater and delayed rewards (Cardinal, Winstanley, Robbins, & Everitt, 2004). These impairments have all been associated with addiction (Bechara, Dolan, & Hinds, 2002).

Historically, decision-making and higher-order executive functions (EF) have been understood and investigated as rational and “cool” cognitive processes, predominantly involving the dorsolateral prefrontal cortex (E. K. Miller & Cohen, 2001; Zelazo, Craik, & Booth, 2004). “Cold” EF involves abstract, context-independent tasks without strong emotional or motivational features (e.g., updating, flexibility). “Hot” executive functions

involve, to a larger degree, stimuli and decisions with a more distinct emotional or motivational salience, such as inhibition, emotional control and self-regulation (Kerr & Zelazo, 2004)

“Hot” EF has increasingly been linked to the orbitofrontal cortex (OFC) (Anderson, Barrash, Bechara, & Tranel, 2006; Kerr & Zelazo, 2004). This region is a part of the prefrontal cortex, and shares distinctive circuitry with specific subcortical limbic learning areas involving the basolateral amygdala and nucleus accumbens, consequently giving this region a vital role in enabling associative information regarding outcomes and likely consequences to access working memory. The OFC has circuitry with essential sensory modalities, including gustatory, olfactory, somatosensory, auditory, and visual modalities (Carmichael & Price, 1995). Because it integrates sensory and visceral motor information, in collaboration with its connections with the basolateral amygdala, the OFC has an important role in emotional processing (Nauta, 1971) and goal-directed behavior. Deficiencies in these OFC functions will disrupt the ability to make adaptive decisions and to learn from the negative consequences of decisions. Research indicates similarities between patients with OFC lesions and patients with SUD; both groups exhibit reduced sensitivity to future consequences, and impaired decision-making in real-life situations (Bechara et al., 2001). These impairments are present even after six months of abstinence for patients with PSUD (Fernandez-Serrano, Perez-Garcia, & Verdejo-Garcia, 2011).

## 1.2 SUD, neurocognitive impairments and implications for treatment

Estimates of the prevalence of cognitive deficits among alcohol and drug abusers who seek treatment vary significantly from 30% to 80% (Bates, Bowden, & Barry, 2002; Copersino et al., 2009). Cognitive impairment has an impact on the quality of life, occupational functioning, and the ability to profit from therapy, and thus affects the course of rehabilitation and level of community integration among patients with SUD (Fernandez-Serrano et al., 2011).

Even though the results are not conclusive, findings indicate that neuropsychological status serves as a moderator or mediator of treatment outcome, rather than representing a direct causal relationship (Aharonovich et al., 2006; Aharonovich, Nunes, & Hasin, 2003; W. Fals-Stewart & Schafer, 1992). More specifically, cognitive impairments have been shown to have a negative effect on treatment adherence (Bates, Pawlak, Tonigan, & Buckman, 2006) and attendance at outpatient therapy sessions (Guthrie & Elliott, 1980), to reduce change willingness (Blume & Marlatt, 2009), reduced self-insight (Horner, Harvey, & Denier, 1999), increased denial of substance abuse (Rinn, Desai, Rosenblatt, & Gastfriend, 2002) and increased impulsivity (Clark, Robbins, Ersche, & Sahakian, 2006; Crews & Boettiger, 2009)

Several studies have found that cognitive impairment is associated with poorer treatment outcome, including decreased treatment retention (Aharonovich et al., 2006; William Fals-Stewart, 1993), and less abstinence from the abused substance after treatment termination (Aharonovich et al., 2006). This raises the possibility that negative psychological features previously accredited to clients, such as denial of problem severity and the dearth of motivation and impulsivity, may derive from specific neuropsychological insufficiencies, rather than other psychological and psychosocial factors (William Fals-Stewart, 1997).

Historically, the conceptual model of the treatment for SUD has been similar to that for the treatment of acute medical conditions, assuming that patients entering addiction treatment

should maintain abstinence following a preferably single episode of treatment (McLellan, Lewis, O'Brien, & Kleber, 2000). Unfortunately, this perspective has not yielded promising treatment outcomes. Evidence shows that most alcohol- and drug-dependent patients relapse following cessation of treatment (N. S. Miller, Ninonuevo, Klamen, Hoffmann, & Smith, 1997). Findings indicate that up to 50–60% of patients relapse within six months of treatment cessation, regardless of patient characteristics, type of discharge, or type of addictive drug (Hunt, Barnett, & Branch, 1971; McKay et al., 1997; McKay et al., 2004). Chronic users who continue to abuse alcohol or other drugs despite increasing negative consequences represent the most rigid and impaired subgroup facing treatment (Shaffer & Zinberg, 1985). For this subgroup, addiction progresses into a recurring illness requiring repeated treatment initiatives before patients reach long-term abstinence (McLellan et al., 2000). Consequently, diagnosing and treating patients with SUD involve a complexity of clinical challenges and considerations that are becoming increasingly more problematic, and efforts should be made to identify predictors to enhance recovery and treatment outcomes.

Evidence indicates that patients' self-reports of cognitive functioning do not give an accurate picture of neurocognitive status, and seem to be more closely associated with emotional distress than reflecting the level of cognitive functioning (Shelton & Parsons, 1987). The onset of cognitive deficits is slow and gradual, which could help mask patients' deteriorating functioning (Horner et al., 1999). Studies have also shown that therapists cannot subjectively identify and assess SUD patients' cognitive status (William Fals-Stewart, 1997). Even though there is evidence indicating that this impairment will gradually improve spontaneously during the first six months of sobriety, patients may not be in treatment long enough to achieve significant cognitive improvement. This creates a situation where spontaneous recovery may be too late to be of any real consequence concerning treatment

outcome. Thus, therapy may occur at a time when a person has the most pronounced cognitive impairments and has the least ability to benefit from it (Vocci, 2008).

The relevance of these findings is amplified by treatment procedures based on the assumption that the patient has the cognitive capacity to pay attention, assimilate additional information, integrate this with preexisting cognitive structures, and can use this for behavioral change (Goldman, 1990; Grohman & Fals-Stewart, 2003). Regardless of theoretical foundation, most therapeutic interventions for SUD (i.e., cognitive behavioral therapy, motivational interviewing, and 12-step programs) are verbally based interventions requiring extensive cognitive processing to facilitate cognitive, motivational, and behavioral change (Roehrich & Goldman, 1993). For instance, a common feature of most treatment initiatives involves learning the harmful effects of various drugs, as well as program rules and the overarching treatment philosophy (Grohman & Fals-Stewart, 2003).

It is well known that neurocognitive assessment services are scarce, costly, and generally unavailable to SUD patients. Hence, it is critical to develop, evaluate, and apply testing procedures that could be made more readily available in a busy clinical setting. This was the motivation for the current project, particularly in paper I where we focused on comparing the utility of psychometric tests and a questionnaire-based inventory to assess “hot” and “cold” neurocognitive measures of EF in adults with SUD. Paper II and III had a longitudinal design and aimed to explore the recovery process, particularly among patients who manage to stay sober for a period of one year, as measured by a broad array of output indicators.

## 2. Aim and research questions

1. The need for clinic-friendly neurocognitive measures was the motivation for Paper I. We investigated two theoretical EF components, referred to as “cold” and “hot” EF, in a group of patients with SUD. This included psychometric performance tests and a questionnaire-based inventory. *With an aim to document EF impairment in patients with SUD of importance to real-life social adjustment, paper I compared performance-based measures and a questionnaire-based inventory. We investigated their efficiency in characterizing the SUD patients when compared to a control group.*
2. Several studies have found a co-occurrence between mental distress and dose-related polydrug use and a reduction of mental distress among abstinent patients. However, focus on a broader spectrum of output indicators was needed to shed light on the recovery process for this important and highly vulnerable subgroup of SUD patients. Paper II featured a prospective design and a control group, and was used to address the following question. *Will individuals with polysubstance use disorder who achieve at least one year of abstinence show greater improvement in satisfaction with life, executive functioning, and psychological distress than those who relapse and controls?*
3. ADHD is a common comorbid disorder in patients suffering from SUD. ADHD has an adverse consequence on the course of SUD, and SUD patients with comorbid ADHD have an increased risk of developing SUD at a younger age, and become polysubstance users, and need inpatient treatment more often than SUD patients without ADHD. Paper III investigated changes in self-reported ADHD symptoms in people with polysubstance use disorder during the year following the initiation of treatment. Using

a prospective design and a control group, we addressed the following question. *Will individuals with polysubstance use disorder who remain abstinent for one year show a greater improvement in ADHD symptoms than those who relapse and controls?*

### 3. Design, material, and methods

#### 3.1 Research challenges

Research within this field is faced with several interpretive challenges as to the origins of cognitive deficits associated with SUD. Psychiatric comorbidity, medical risk factors (head trauma, HIV – malnutrition, overdoses), genetic predispositions, premorbid vulnerability (genetic, psychosocial and environmental), co-occurring use of multiple drugs, could all play a significant part in the causal factors leading to the current neuropsychological impairment profile. Many of the extensive RCT studies within this field have excluded clients with comorbid conditions, polydrug use, etc. Consequently, findings could be based on a client sample that does not portray the heterogeneity in the patient population. We wish to avoid this by including patients with comorbid conditions as well as polydrug use and also to establish the necessary logistics to follow patients in the study even if they drop out of treatment.

As mentioned previously there is generous evidence of an association between various aspects of SUD and cognitive impairment, but the direct versus the indirect role of the different substances are not clear. Theoretically, several cognitive deficits could be viewed as antecedents to the onset of SUD, especially involving executive functions connected to long-term decision making and impulsivity (Nigg, Blaskey, Huang-Pollock, & Rappley, 2002; Nigg et al., 2006). However, the aim of paper I is not to address the *source* of executive impairments, but to assess different assessment methods at an early clinical evaluation, and to investigate their efficiency in characterizing the SUD group, and several social adjustment indicators, when compared with a control group. Likewise, the *two next* papers are dealing with recovery of executive and psychological functioning throughout one-year and do not focus on the origin of cognitive symptoms.

Previous treatment studies of impaired cognitive functions in SUD patients have several limitations. They have primarily dealt with the acute and subacute effects of chronic alcohol and drug use (Fernandez-Serrano et al., 2011; Vik, Cellucci, Jarchow, & Hedt, 2004; Yucel, Lubman, Solowij, & Brewer, 2007), and studies of long-term recovery do not always require a 14-day drug-free period prior to baseline testing (Fernandez-Serrano et al., 2011). Other studies have small sample sizes, often with a focus on patients with one primary addiction (Badiani, Belin, Epstein, Calu, & Shaham, 2011; Buelow & Suhr, 2009; Stavro, Pelletier, & Potvin, 2013). Also, many studies have used cross-sectional designs and are therefore unable to track changes in individual patients over time (van Holst & Schilt, 2011). There is also considerable variability in the follow-up rates, ranging from 40% to 98% (Cottler, Compton, Ben-Abdallah, Horne, & Claverie, 1996; Desmond, Maddux, Johnson, & Confer, 1995; Stinchfield, Niforopoulos, & Feder, 1994), and some studies have not included a follow-up procedure for a control group (Schulte et al., 2014).

A key challenge in this study has been to retain patients over a period of one-year. Previously considerable variability has been reported on the follow-up rates from patients with SUD, ranging from 40 to 98 % (Cottler et al., 1996; Desmond et al., 1995; Stinchfield et al., 1994). This significant disparity in retention complicates not only our ability to make accurate statistical power estimates of the number of participants needed but could, if not dealt with – impact our ability to draw conclusions and generalizations from our investigation. We have applied a diversified strategy to retain participants, ranging from contact and scheduling measures, SMS reminders, financial incentives, and flexibility in procedures and visit characteristics. For a detailed description of the follow-up procedures in the project see Svendsen et al. (Svendsen et al., 2017).

## 3.2 Design, recruitment and data collection

The studies were all part of a prospective, longitudinal cohort study of a SUD patient sample who started a new treatment sequence in the Stavanger University Hospital catchment area. The three papers present data collected from SUD patients admitted to both outpatient and residential treatment facilities. To minimize contamination from drug withdrawal and acute neurotoxic effects from psychoactive substance, participants were tested after two weeks of abstinence (L. Miller, 1985). The project was approved by the Regional Ethical Committee (REK 2011/1877).

## 3.3 Paper I: Participants and procedures

One hundred and fifty participants were recruited from outpatient and residential treatment facilities within the region, across ten enrollment sites. Patients were recruited between March 2012 and May 2013. Consecutive enrollment continued until the required number of participants were recruited. The SUD group included patients reporting use of more than one drug at a single occasion or a history of having injected or abused multiple drugs, based on responses to the Alcohol Use Disorders Identification Test (AUDIT) (Bohn, Babor, & Kranzler, 1995) and the Drug Use Disorders Identification Test (DUDIT) (A. C. Voluse et al., 2012). Five patients were excluded due to not having a substance-related addiction. One patient was excluded due to only using cannabis, one due to only using opioids, and 14 due to only using alcohol. The control group ( $n = 38$ ) was a convenience sample recruited using posters at social welfare and primary care offices. Controls and patients were offered compensation of NOK 400 for baseline testing. Nine patients (seven 17-years of age, two 16-years of age) were excluded due to age. The final group consisted of  $n = 126$  SUD patients and  $n = 32$  controls.

### **3.3.1 Inclusion procedure**

To be eligible for admission to the study, patients needed to: a) sign a written informed consent to participate; b) embark on a new treatment sequence within the substance abuse treatment service, and c) be at least 18 years of age. Patients also had to have been enrolled in the program to which they were admitted for at least two weeks, and abstinence was verified through self-report, for both inpatients and outpatients. In one of the first treatment sessions (1–3), patients were given an information sheet with a short project description.

### **3.3.2 Measures**

Cold EF were measured with the computerized Stroop test (Stroop CW) (Golden & Freshwater, 1978). Stroop is an assessment of attention, interference, and inhibition of dominant responses (MacLeod, 1991). Another measure of cold EF is the Trail Making Test (TMT) (Kortte, Horner, & Windham, 2002; Strauss, Allen, Jorgensen, & Cramer, 2005). TMT provides data on visual-conceptual and visual-motor tracking and set shifting. Longer time to finish indicates impairment.

Hot EF was examined using the Iowa Gambling Task (IGT) (Bechara, Damasio, Damasio, & Anderson, 1994). The key task in the IGT is to make advantageous long-term decisions in conditions of uncertainty. For this test, subjects are given \$2,000 to start, and their task is to maximize profit across 100 trials by choosing cards from one of four decks. After ten selections from decks A and B, the subject will have earned a net loss of \$250, whereas decks C and D result in a net gain of \$250. Consequently, decks A and B are the “risky” decks. It is assumed that the perception of risk within the IGT increases across trials, as subjects gain experience with the win/loss contingencies in the various decks (i.e., later trials have stronger emotional, or risky, associations) (Brand, Recknor, Grabenhorst, & Bechara, 2007).

The BRIEF-A is a self-report questionnaire composed of nine subscales and three composite scores. The Behavioral Regulations Index (BR-index) consists of the subscales Inhibit, Shift, Self-Monitor, and Emotional-Control. The subscales Initiate, Plan/Organize, Working Memory, Organization of Materials, and Task-Monitor comprise the Metacognition Index (MI). The BRI and MI can be combined to produce the overall Global Executive Composite (GEC). Validity scales were examined, and two controls- and ten SUD participants profiles were excluded due to invalid response styles.

Specific information on substance abuse was based on self-reported responses on the AUDIT (Bohn et al., 1995) and the DUDIT (A. C. Voluse et al., 2012). The Wechsler Abbreviated Scale of Intelligence (WASI) was included as a control variable because there was a significant difference between controls and SUD patients in the univariate analysis, and to ensure that EF deficits could not be attributed to general abilities. An interview based on items from the preliminary version of the National Quality Register for Substance Abuse Treatment was used to collect demographics, type of addiction, initial age at use, treatment and work history, educational, and vocational data. Social adjustment scores were obtained based on a yes/no responses and included the following categories: permanent housing, criminal lifestyle, conflict with caregivers, friends outside the drug environment, and stable income.

### **3.3.3 Analysis**

Binary logistic regression analyses (enter method) were applied to assess independent correlates of SUD status and categorical variables indicating social adjustment. In these analyses, control variables (age, sex, years of education, and WASI Total IQ), and raw scores from the cold EF, hot EF, and BRIEF-A BRI and MI were sequentially entered into the analyses. A multiple linear regression was performed to predict the number of previous

treatment attempts. As a quantified measure of goodness-of-fit, Nagelkerke's  $R^2$  was estimated and reported. Due to the significant difference in WASI total IQ between controls and patients, WASI total IQ was included in a control variable in these analyses.

## 3.4 Paper II

This study used the same cohort and the same inclusion procedure as the first study and compared development from baseline to 12-months follow-up. At the one-year follow-up, patients were defined as relapsing to a significant level of use if they had an AUDIT score  $\geq 8$  or DUDIT score  $\geq 2$  for women and  $\geq 6$  for men (Bohn et al., 1995; Andrew C Voluse et al., 2012).

### 3.4.1 Measures

#### 3.4.2 Satisfaction with Life

Satisfaction with life was assessed baseline and one year later with the Satisfaction With Life Scale (SWLS) (Diener, Emmons, Larsen, & Griffin, 1985). This is a self-report questionnaire including five items measuring the global life satisfaction experienced by the respondent. The SWLS has demonstrated good psychometric characteristics (Pavot & Diener, 2008).

#### 3.4.3 Executive Functions

This study assessed executive functions by asking the participants to complete the Behavior Rating Inventory of Executive Function-Adult version (BRIEF-A) (Gioia, Isquith, Guy, Kenworthy, & Baron, 2000; Roth, Isquith, & Gioia, 2005) at baseline and one year later. The BRIEF-A has been shown to have high ecological validity (Gioia et al., 2000; Roth et al., 2005), and to be associated with substance use status as well as several social adjustment

indicators in patients with a history of PSUD. The BRIEF-A includes three composite scores including sets of subscales. A Behavioural Regulation Index (BRI-index) is calculated from the Inhibit, Shift, Self-Monitor and Emotional Control subscales. The BRIEF-A Metacognition Index (MI) is calculated from the Initiate, Plan/Organize, Working Memory, Organization of Materials, and Task Monitor subscales. Validity scales of the BRIEF-A were examined, using the cut-off scores proposed by the original authors (Gioia et al., 2000). Invalid response style led to the exclusion of one control and nine SUD participants at baseline, and three controls and five SUD participants at the one-year follow-up. The final sample included the 30 controls and 101 SUD patients with valid BRIEF-A protocols.

#### **3.4.4 Intellectual functions**

The Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) was used to estimate intellectual function (IQ) by including two tests of verbal crystallized abilities (Vocabulary and Similarities) and two tests of nonverbal fluid-visual abilities (Block Design and Matrices) (Canivez, Konold, Collins, & Wilson, 2009).

#### **3.4.5 Psychological distress**

Psychological distress was measured at baseline and one year later using the Symptom Checklist-90-R (SCL-90-R) (Derogatis, 1994). This is a 90-item self-report symptom inventory that yields measures of nine symptom domains of psychological distress. This study includes the nine subscales and the summary score; Global Severity Index (GSI) (Derogatis, 1994).

### 3.4.6 Statistical Analyses

Group differences were analyzed using *t*-tests, Mann–Whitney *U* tests, and Pearson’s chi square-tests when appropriate. Levene’s test was used to select the appropriate *p*-values based on whether the assumption of equal variances within groups was met. Histograms, Q–Q plots, Kolmogorov–Smirnov tests, and Shapiro–Wilk tests were used to investigate normality.

The research question was analyzed using mixed between-within subjects’ ANOVA to compare changes in abstainers, relapsers, and controls from the baseline to the one-year follow-up. Variables, where the three groups have similar patterns of change from baseline to one year, will not have a statistically significant interaction effect (the null hypothesis). Variables, where one group has a different pattern of change from the other two groups, are expected to show an interaction. To determine the cause of interaction effects, Wilcoxon signed rank tests were used to evaluate median change from baseline to one year within each group. Effect sizes were calculated as Cohen’s *r* for nonparametric data, where 0.3 is considered a medium and 0.5 is considered a large effect (Cohen, 1988). Main effects were not interpreted in the presence of a statistically significant interaction (Bordens & Abbott, 2002).

## 3.5 Paper III

### 3.5.1 Participants and procedures

Same as article two

### 3.5.2 Measures

#### 3.5.3 Adult ADHD Self-Report Scale (ASRS)

The ASRS is a frequently used screening instrument for ADHD (Kessler et al., 2005). It is composed of 18 items that reflect the symptoms used to define ADHD according to the fifth edition of the Diagnostic and statistical manual of mental disorders (DSM-V) (Association, 2013). The results from this scale assess the presence of ADHD symptoms, but on its own, it is not an adequate diagnostic tool.

Symptoms are rated on a 5-point Likert-type scale (0–4 = never, rarely, sometimes, often, and very often), with a range of 0 to 72 for the 18-item instrument. This instrument has previously been validated in SUD populations (Dakwar et al., 2012; Van de Glind et al., 2013).

In this study, we included a sum score across all the 18 ASRS items, a sum score for the ASRS items that assess inattention (items 1–4 and 7–11), and a sum score for the items that assess hyperactivity/impulsivity (items 5, 6, and 12–18).

To highlight the severity of individual items in the ASRS, we dichotomized responses to the ASRS items into “severe/not severe” according to recommendations by Kessler et al. (Kessler et al., 2005). Lastly, we used the "severe/not severe" dichotomized items to identify clinically significant ASRS profiles. The ASRS profile was dichotomized as "clinically significant" if  $\geq 9$  items were dichotomized as “severe”, and "not clinically significant if  $< 9$  items were dichotomized as severe". This method is commonly used in clinical practice, and in line with the original recommendations by Kessler et al. (Kessler et al., 2005).

### 3.5.4 Statistical analyses

Data were assessed for normality with histograms, Q-Q plots, Kolmogorov–Smirnov tests, and Shapiro–Wilk tests. Visual inspection of histograms and Q-Q-plots revealed that ASRS-scores at baseline and one-year follow-up did not deviate from normality. This was also evident from the Kolmogorov-Smirnov test ( $D_{(149)} = 0.05$ ,  $p = 0.200$ ; and 1 year  $D_{(149)} = 0.06$ ,  $p=0.200$ , respectively) and Shapiro-Wilk test (baseline  $w_{(149)} = 0.99$ ,  $p=0.651$ ; and 1 year  $w_{(149)} = 0.99$ ,  $p=0.327$ ). Sub-analysis of normality for each participant group yielded similar results. As the data were normally distributed, parametric statistics were used throughout. Mixed ANOVA was used to compare changes in abstainers, relapsers, and controls from baseline to the one-year follow-up. Variables for which one group’s responses differed from those of the other two groups were expected to show a significant interaction. To determine the cause of interaction effects, a paired samples t-test was used to evaluate mean change from baseline to one-year within each group. Effect sizes were calculated as Cohen’s  $d$  for paired samples and parametric data, where 0.5 was considered a medium effect and 0.8 was considered a large effect (Cohen, 1988). Main effects were not interpreted in the presence of a statistically significant interaction (Bordens & Abbott, 2002).

Lastly, the frequency of individual items dichotomized as severe was estimated for each group (i.e., abstinent, relapsed, and control), and changes in frequency during the one-year follow-up were investigated for each item using a repeated measures ANOVA. As multiple comparisons were made, Bonferroni adjusted P-values ( $0.05/18 = 0.003$ ) were used to establish statistical significance.

## 4. Results

### 4.1 Paper I

The psychometric test of hot EF (the Iowa Gambling Task) did not discriminate patients with PSUD from controls and was not related to social adjustment. The psychometric tests of cold EF distinguished to some extent between the groups and were associated with one indicator of social adjustment. The BRIEF-A differentiated between groups on all the clinical scales and was associated with three out of five social adjustment indicators (“criminal lifestyle,” “conflict with a caregiver,” and “stable housing.”).

### 4.2 Paper II

Executive functions (EF) measured by the self-report instrument BRIEF-A improved in the group of abstinent patients between baseline and one-year, but this was not the case with the patients that relapsed. Improvement of EF is very promising, considering that maladaptive, impulse-driven behavior is strongly associated with a substance using lifestyle (Crews & Boettiger, 2009). Notably, in spite of the improvement in EF in the abstainers, they still reported somewhat reduced function compared with controls, which indicates that they still had some degree of susceptibility related to impaired EF, even after a year of abstinence. Psychological distress also decreased in the abstinent group. At the one-year follow-up, the discrepancy between the abstinent group and the controls almost vanished, suggesting a normalization of psychological distress following one year of abstinence. This finding is in line with previous research that has found a reduction of psychological distress among patients who stopped using multiple drugs (Andreas, Lauritzen, & Nordfjærn, 2015).

However, it should be emphasized that the second study focuses on a broader spectrum of output indicators than previously reported.

There was also a significant difference in perceived satisfaction with life as measured by SWLS between the abstinent and relapse groups after one year. The importance of this finding is substantiated by previous studies showing an association between satisfaction with life and subsequent symptoms in recovery, where satisfaction with life increases through early recovery to stable abstinence (Laudet, Morgen, & White, 2006).

### 4.3 Paper III

The third paper compared patients with PSUD who remained abstinent, patients who relapsed, and healthy controls on changes in self-reported ADHD symptoms from baseline to follow-up assessment one-year later. The abstinent group showed a substantial reduction of ADHD symptoms compared with the relapse and control groups. In fact, the scores of the abstinent group at follow-up were only slightly higher than those of the healthy controls, who were in the normal range for ADHD symptoms at both baseline and follow-up. The improvements in the abstinence group were particularly prominent on the ASRS items that reflect problems related to sustained attention, concentration, and restlessness.

## 5. Discussion

### 5.1 Discussion and conclusions

### 5.2 Paper I

Several studies have supported the validity of the BRIEF scales and other rating scales in assessing every-day executive functioning (Isquith, Roth, & Gioia, 2013). Responses on BRIEF-A was significantly raised on all the nine scales for SUD patients compared to the controls. Previous studies have found similar outcomes, where patients with PSUD report significantly more executive dysfunctions on BRIEF-A, compared to non-users (Hadjiefthyvoulou, Fisk, Montgomery, & Bridges, 2012).

The PSUD group performed slightly (but not significantly) better on the hot EF, measured by the IGT total score. Functional impairments based on IGT have been found in individuals with alcohol, cocaine, and opioid use disorders, relative to healthy controls (Bartzokis et al., 2000; Bechara & Damasio, 2002; Bechara et al., 2001). However, findings are not conclusive, and some studies have shown that groups of healthy controls do not learn to successfully select cards from the advantageous decks, and also showing high variance in anticipatory electro-dermal responses (Dunn, Dalgleish, & Lawrence, 2006). The opposing findings from some studies, where controls perform poorly on IGT while not showing any deficiencies in real-life decision-making, makes it uncertain whether IGT performance have predictive value on real-life functioning.

Similar to our findings, it has proven difficult to establish associations between neuropsychological performance tests and rating scales of EF, and this has raised questions whether the two assessment approaches address different cognitive functions or different applications of cognitive skills (Isquith et al., 2013; McAuley, Chen, Goos, Schachar, &

Crosbie, 2010). Isquith, Roth, and Gioia (2013) offer a possible frame of clarification where neuropsychological performance tests are hypothesized to assess cold aspects of EF, and rating scales address a hot emotional aspect of EF. With regards to the BRIEF-A, this hypothesis draws support from research that has applied confirmatory factor analysis of the BRIEF-A scales and detected a distinct emotional regulatory factor, involving of the Emotional Control and Shift scales (Gioia, Isquith, Retzlaff, & Espy, 2002). Studies have questioned if the BRI index is, in fact, a measure of hot EF, in contrast to the less emotive items constituting the remaining scales (Egeland & Fallmyr, 2010). This distinct hot factor, in BRIEF, has been replicated in several studies (McCandless & O' Laughlin, 2007; Peters, Algina, Smith, & Daunic, 2012). On the other hand, a recent study, (Skogli, Egeland, Andersen, Hovik, & Øie, 2014) on hot and cold EF in ADHD found no correlation between any of the BRIEF scales and performance-based measures of hot performance EF. The correlation matrix displayed a marginally higher correlation between cold EF tests and cold BRIEF scales than with the hot BRIEF scales. Overall cold BRIEF scales reached moderate correlation with cold EF tests. To our knowledge, the majority of these findings have been based on studies of with Attention Deficit Hyperactivity Disorder, and we have not succeeded in finding previous studies investigating associations between neuropsychological performance tests and rating scales of EF in adult SUD samples.

#### *4.2 Social adjustment*

BRIEF-A was associated with SUD as well as some indicators of social adjustment in SUD patients. Even when controlling for significant demographic variables, the BRI in BRIEF-A was associated with several domains of social adjustment, where increased scores on the BRI of the BRIEF-A were related to both substance abuse and lower social functioning. The BRI consists of four subscales crucial for real-life adaptive social behavior, which offers a plausible explanation for our findings. The Inhibit scale assesses the ability to assert impulse control

(go/no-go), and to what extent one can inhibit, stop or adjust one's behavior when called for by the circumstances. The Shift scale assesses one's ability to flexibly adjust to alternating situations, tasks or aspects of challenges. The Emotional control scale assesses one's ability to regulate the expression of emotional responses, while the Self-Monitor scale assesses interpersonal awareness and to which extent one understands how one's behavior affects others (Roth et al., 2005). The BRIEF-A questionnaire measure participant's subjective evaluation of their function in real-life situations and our findings suggest that the BRIEF-A have a higher ecological validity than results obtained on performance-based tests.

We did not find any association between performance-based assessment of hot or cold EF and SUD, or social adjustment in the SUD group. There is a lack of studies detailing the link between performance-based measures of hot and cold EF in SUD and their relationship with social adjustment. However, regarding neurocognitive predictors of social adjustment, studies of patients with closed brain injury indicates that impairments in overall social adjustment (occupational status, leisure activities, social contacts and family life), are closely linked to the severity of the damage and subsequent cognitive sequela, (Oddy, Coughlan, Tyerman, & Jenkins, 1985).

Our findings suggest that representative and frequently used neurocognitive performance-based assessments might render a false negative conclusion in an initial evaluation, while a questionnaire-based self-evaluation is associated with impaired social adjustment and substance abuse. The lack of relationships between self-rating measures and performance-based measures of EF could imply that they measure different aspects of executive functions, and some suggest that performance measures are particularly sensitive to components of executive functions in isolation, while rating scales assess the application of those skills, (Isquith et al., 2013). It has been argued that traditional neuropsychological tests artificially fractionate an integrated functional network (Burgess, 1997) and that the

operationalization and types of methods used to measure EF impact the conclusions and interpretations we can make.

Our results indicate that IGT and BRIEF-A BRI assess two different cognitive constructs. IGT is presumably sensitive to subtle, unconscious perceptions of somatosensory feedback or “hunches” to guide decision-making, whereas the BR index from BRIEF-A captures the responder's own view of his or her ability to maintain appropriate control of their behavior and emotional responses (Roth, Isquith, & Gioia, 2005). This is supported by recent findings showing only minimal correlations between the two types of measures (Toplak, West, & Stanovich, 2013), providing further support for the hypothesis that there are separate EF pathways measured by IGT versus BRIEF-A (Sonuga-Barke, 2003).

### **5.2.1 Conclusion**

The BRIEF-A inventory was the most sensitive measure to identify group affiliation and social adjustment among patients with PSUD, followed by measures of cold EF. It is well known that neurocognitive assessment services are scarce, expensive, and unavailable to SUD patients. Hence, it is crucial to develop, evaluate, and apply testing procedures that could be made more readily available in busy clinical settings and that could also be administered by a broader array of professions. Our data indicate a promising potential for inventory-based EF assessment in SUD patients as measured by BRIEF-A. Self-report measures of EF can be valuable, cost-effective, and accurate at an initial clinical evaluation, providing important complementary measures to performance-based tests.

## **5.3 Paper II**

The multimodal improvement of satisfaction with life and self-reported executive functions and the decrease of psychological distress following one year of abstinence is

compelling. Most therapeutic interventions for SUD, including, cognitive behavioral therapy, motivational interviewing, and 12-step programs, are orally based treatment requiring widespread cognitive processing to facilitate cognitive, motivational, and behavioral change (Roehrich & Goldman, 1993). For instance, a common characteristic of most treatment initiatives includes learning the detrimental effects of several drugs, as well as the teaching of program rules and principal treatment philosophy (Grohman & Fals-Stewart, 2003), thus constituting a distinct learning prerequisite at the start of therapy. Our findings suggest that a gradual and careful step-up of learning requirements should be adopted, and emphasize that SUD treatment should primarily focus on stabilizing the patient and reaching abstinence, while interventions for co-morbid problems and more cognitively challenging treatment components be more likely to succeed later in the treatment sequence, as cognitive functioning improves. Moreover, these results raise the possibility that interventions specifically designed to improve cognitive function, such as memory training (Bickel, Yi, Landes, Hill, & Baxter, 2011), might facilitate somewhat more rapid recovery of cognitive function in this population.

### **5.3.1 Conclusion**

To date, few studies have investigated the natural progression of recovery regarding this combination of outcome indicators in patients with PSUD. Our study provides support for the view that there is a clinically significant recovery in satisfaction with life, executive functions and psychological distress for patients with PSUD following one-year of abstinence. This improvement from admission to one-year, suggests that a gradual progression of treatment should be adopted to ensure that the patients have the prerequisites for receiving treatment in a broad array of dimensions. By this, our findings could shed light on the recovery process for this group of patients. It highlights the necessity of an ongoing diagnostic approach as the clinical picture at the admission of treatment could be dramatically improved for patients

suffering from PSUD. This knowledge could provide hope for patients, as well as a therapist, simply by highlighting the importance of time and continued abstinence. This might subsequently reduce dropout numbers and improve the recovery process for these patients. Future research should consider the timing and sequence of interventions in SUD treatment.

## 5.4 Paper III

SUD complicates the diagnostic procedures for patients with comorbid ADHD symptoms of hyperactivity, impulsivity, and inattention. These symptoms are, however, not limited to individuals with an ADHD diagnosis. Patients with SUD can develop impulsivity and hyperactivity, and have difficulty with attention as a result of the neurotoxic effects of the drugs that they use and the lifestyle associated with SUD (Yuan et al., 2009). Impulsivity and executive dysfunctions have been associated with almost all phases of SUD (Stevens et al., 2014), as individuals with these characteristics have an increased probability of starting to use drugs, more destructive intensification of use, and more relapses after treatment (Jentsch, 2009; Robbins, Gillan, Smith, de Wit, & Ersche, 2012; Winstanley, Olausson, Taylor, & Jentsch, 2010).

Systematic use of screening tools to identify ADHD in childhood is infrequent, which creates a risk of leaving cases undetected (Wilens et al., 2011). If these individuals later develop SUD, their attentional and impulsivity problems may be addressed for the first time as part of their SUD treatment. Our findings suggest that active SUD and the associated lifestyle could account for some of the problems related to sustained attention, concentration, and restlessness, as these ADHD symptoms were substantially reduced in our clinical sample after one year of abstinence. The clinical importance of this result is strengthened by previous studies with the same cohort that have demonstrated improved executive functions, increased

satisfaction with life, and reduced psychological distress (E Hagen et al., 2017). Thus, our findings support the recommendation from previous research that there should be a “treatment hierarchy” that begins with a treatment of the most prominent SUD symptoms and stabilization of the drug addiction (Wilens, 2004).

The reduction in ADHD symptoms in the two PSUD groups in this study was compelling. The abstinence group showed a more profound reduction in severe ADHD symptoms, but the relapse group also showed some improvements. It is possible that, on average, SUD treatment improves ADHD symptomatology because it introduces a phase of stability and reduced substance use. Several interventions are recommended for SUD, including motivational interviewing, cognitive-behavioral therapy, contingency management, and social skills training (Horsfall, Cleary, Hunt, & Walter, 2009). These treatments all require cognitive processing (Roehrich & Goldman, 1993). This could include learning about program rules, treatment viewpoint, and the adverse consequences of various drugs (Grohman & Fals-Stewart, 2003), all of which represent a considerable learning prerequisite at the start of therapy. However, the present results suggest that a careful and stepwise approach to learning requirements should be adopted in treatment. This could be achieved through focus on stabilizing the patient, providing structure, and supporting abstinence from substance use.

Diagnosing ADHD with active SUD is challenging. The risk of false-positive ADHD diagnoses in patients assessed by ASRS has been reported (Lugoboni et al., 2017; Roncero et al., 2015). Thus, our finding is a reminder that a period of abstinence, preferably evident by urine tests or other means of substance monitoring, should be in place before providing conclusions regarding an ADHD diagnosis.

### **5.4.1 Conclusion**

To our knowledge, this is the first study to report improvement of ADHD symptoms for people with PSUD during a 12-month treatment sequence. Our data suggest that there is a clinically (as well as a statistically) significant reduction in self-reported ADHD symptoms for SUD patients following one year of abstinence. This is useful knowledge for patients suffering from comorbid SUD and ADHD, as well as for clinicians. Our finding is a reminder that the assessment of ADHD should follow a period of abstinence to avoid false-positive ADHD diagnoses. Instead of focusing on ADHD as a persistent disorder, treatment should focus on how to support stable abstinence and how this may reduce ADHD-like symptoms.

## **5.5 Strengths and limitations**

The study applied broad inclusion criteria, and patients were not excluded due to polydrug use, comorbid conditions or dropout from treatment. Hence it is likely that the participants reflect some of the heterogeneity characterizing clinical SUD populations. Considerable efforts and resources were applied to ensure that we managed to keep attrition low (Svendsen et al., 2017), and we applied a dynamic assessment procedure that allowed for flexible assessment adjusted to the individual characteristics of the participants. We also applied a control group and also included a follow-up procedure for the control group. Practical implications of our findings in the PhD project have been and will continue to be presented to all the participating institutions in the project. We have so far held 4 town-hall meetings at “Folkets hus” in Stavanger where results and implications for treatment have been presented.

Participants were recruited from different treatment facilities within the Stavanger University Hospital region. The patients were asked by their counselor whether they wished to participate. We have no data describing the patients that declined to participate. However,

a Norwegian study found a threefold increase in the rate of disability pensions among patients who chose not to participate in the Hordaland Health Study (Knudsen, Hotopf, Skogen, Øverland, & Mykletun, 2010). Furthermore, nonparticipants were characterized by poorer lifestyle habits including smoking, drug, and alcohol abuse (Korkeila et al., 2001; Shahar, Folsom, Jackson, & The Atherosclerosis Risk in Communities Study, 1996) and had lower scores on indicators of somatic and mental health (Drivsholm et al., 2006). It is, therefore, possible that the patients that declined research participation would have increased, rather than decreased, the group differences reported here.

The SUD and control groups were different on several demographic variables. Age, sex, education, and IQ were included as covariates in the statistical analyses to adjust for this limitation somewhat. The significant difference in education between the SUD and control group was challenging to avoid. It was almost impossible to find control participants with fewer than ten years of education that did not have a substance-abuse problem. There was no significant age difference between patients and controls, which was a strength of the study as age is known to significantly impact neurocognitive functions.

## 6. Concluding remark and clinical implications

Clinicians routinely focus on connecting with and treating patients based on their current psychiatric and emotional state and base their diagnosis and treatment efforts on those evaluations. However, neuropsychological assessment services are rare, expensive, and often involve a long waiting list for a thorough assessment. In paper I, we examined the use of a questionnaire-based inventory and several other performance-based measures of executive functions to assess their sensitivity to discriminate between patients with SUD and controls and to assess how these measures are associated with indicators of social adjustment. Our data indicate a promising potential for inventory-based EF assessment in SUD patients as measured by BRIEF-A. Self-report measures of EF can be valuable, cost-effective, and precise at an initial clinical evaluation, providing central complementary measures to performance-based tests. Application of questionnaire-based inventories like Brief- A in the clinical units may also contribute to more focus on neurocognitive issues as well as providing a better basis for ward personell in communicating with the specialized neuropsychological treatment services. Paper II and III provide an argument for adopting a longitudinal diagnostic approach, as the diagnostic picture at the initial stage of treatment could be significantly altered if the patients manage to stay sober for one year. Premature diagnostic conclusions could inflict false-positive diagnoses on patients regarding psychological status, EF, life dissatisfaction, and ADHD symptomatology. Finally, our findings particularly in paper II and III support and substantiate my initial curiosity mentioned in the preface, where I frequently observed a dramatic improvement among patients I had previously diagnosed and who managed to abstain from further substance use.

## 7. Future research

Future research could focus on long-term cognitive restitution, beyond the scope of one-year, focusing on the associations between changes in neurocognitive and psychological functioning and its effect on a broad array of outcome indicators, such as treatment efficacy, quality of life, mortality and occupational status.

This could be done by combining cohorts like the Stayer cohort with other relevant national cohorts and compare these data with a selection of Norwegian national registries. Notification to the national registries is compulsory and the problem of loss to follow up is therefore negligible, and information bias is avoided. Linkage to registries is possible to repeat, and the clinical cohort may, therefore, be followed over several years without any inconvenience for the patient. Linkage of clinical data (testing and questionnaire data) and registry data could result in an enriched dataset with a wide variety of information that complete each other. This long-term perspective with numerous output indicators could prove vital in detailing the recovery process for this group of highly vulnerable patients. This could contribute to a better scientific and clinical understanding of the dynamic relationship between cognitive restitution, behavioral aspects of SUD, and treatment response, and could prove vital in tailoring SUD treatment programs.

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## Paper I



## Regular articles

## Assessment of Executive Function in Patients With Substance Use Disorder: A Comparison of Inventory- and Performance-Based Assessment



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## ABSTRACT

**Introduction:** Chronic polysubstance abuse (SUD) is associated with neurophysiological and neuroanatomical changes. Neurocognitive impairment tends to affect quality of life, occupational functioning, and the ability to benefit from therapy. Neurocognitive assessment is thus of importance, but costly and not widely available. Therefore, in a busy clinical setting, procedures that include readily available measures targeting core cognitive deficits would be beneficial. This paper investigates the utility of psychometric tests and a questionnaire-based inventory to assess “hot” and “cold” neurocognitive measures of executive functions (EF) in adults with a substance use disorder. Hot decision-making processes are associated with emotional, affective, and visceral responses, while cold executive functions are associated with rational decision-making.

**Material and Methods:** Subjects with polysubstance abuse ( $n = 126$ ) and healthy controls ( $n = 32$ ) were compared on hot (Iowa Gambling Task) and cold (Stroop and the Trail Making Test) measures of EF, in addition to a questionnaire assessing everyday EF related problems (BRIEF-A; Behavior Rating Inventory of Executive Function – Adult, self-report version). Information about the substance abuse and social adjustment were assessed by self-report. Logistic regression analyses were applied to assess independent correlates of SUD status and social adjustment. A multiple linear regression was performed to predict the number of previous treatment attempts.

**Results:** The psychometric test of hot EF (the Iowa Gambling Task) did not differentiate the patients with polysubstance abuse from controls, and was not associated with social adjustment. The psychometric tests of cold EF distinguished somewhat between the groups and were associated with one indicator of social adjustment. The BRIEF-A differentiated between groups on all the clinical scales and was associated with three out of five social adjustment indicators (“criminal lifestyle,” “conflict with caregiver,” and “stable housing.”).

**Conclusions:** The BRIEF-A inventory was the most sensitive measure of executive function in patients with substance use disorder, followed by measures of cold executive function. BRIEF-A should therefore be considered as an integral part of the clinical routine when assessing patients with SUD.

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**Abbreviations:** SUD, Substance Use Disorder; EF, executive function; IGT, Iowa Gambling Task; BRIEF-A, Behavior Rating Inventory of Executive Function – Adult version; TMT A + B, Trail Making Test parts A and B; Stroop CW, The computerized Stroop Color Word test; AUDIT, The Alcohol Use Disorders Identification Test; DUDIT, The Drug Use Disorders Identification Test; WASI, Wechsler Abbreviated Scale of Intelligence; MI, Metacognition Index; BRI, Behavioral Regulation Index; GEC, Global Executive Composite.

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### 1. Introduction

Chronic substance use disorder (SUD) is associated with cognitive impairment (Rogers & Robbins, 2001; Vik, Cellucci, Jarchow, & Hedt, 2004; Yucef, Lubman, Solowij, & Brewer, 2007), with prevalence estimates varying between 20% and 80% among treatment-seeking abusers of alcohol and drugs (Bates, Bowden, & Barry, 2002; Copersino et al., 2009).

Although the majority of studies have focused on disorders related to alcohol use, there is growing evidence indicating similar cognitive

deficits associated with polysubstance use (Fernandez-Serrano, Perez-Garcia, & Verdejo-Garcia, 2011; Grant & Judd, 1976; Vik et al., 2004). More specifically, abusers of alcohol, opiates, and stimulants show impairment on tasks assessing different aspects of executive function (EF), including decision-making and emotional control (Barry & Petry, 2008; Bechara, 2005; Dolan, Bechara, & Nathan, 2008; Verdejo-Garcia & Bechara, 2010; Verdejo-Garcia, Bechara, Recknor, & Perez-Garcia, 2006). Central symptoms of EF deficits include reduced sensitivity to future consequences and impaired decision-making in real-life situations (Bechara et al., 2001; Grant, Contoreggi, & London, 2000; Schoenbaum & Shaham, 2008), reduced ability to suppress responses and evaluate consequences, as well as a preference for smaller, instantaneous rewards over larger, delayed rewards (Cardinal, Winstanley, Robbins, & Everitt, 2004). These deficits commonly present even after 6 months of abstinence among polysubstance abusers (Fernandez-Serrano et al., 2011).

EF dysfunction has an impact on quality of life and occupational functioning, which subsequently affects the course of rehabilitation therapy and level of community integration among patients with SUD (Fernandez-Serrano et al., 2011). In a clinical context, patients with polysubstance abuse may demonstrate intelligence, learning and memory, language, and attention within the normal range, but may still show considerable impairment in emotional function, decision-making, and social behavior (Bechara, 2005). More specifically, an association has been reported between cognitive deficits and low treatment adherence (Bates, Pawlak, Tonigan, & Buckman, 2006), poor attendance at outpatient therapy sessions (Guthrie & Elliott, 1980), low willingness to change (Blume & Marlatt, 2009), reduced self-insight (Horner, Harvey, & Denier, 1999), denial of substance abuse (Rinn, Desai, Rosenblatt, & Gastfriend, 2002), increased impulsivity, and less abstinence from the substance of abuse following treatment termination (Aharonovich et al., 2006). Impaired EF has also been linked to medical and legal problems among this patient group (Bechara et al., 2001; Paulus, Tapert, & Schuckit, 2005).

With neurocognitive deficits recognized as an adverse variable affecting recovery and treatment adherence in SUD patients, a thorough examination of cognitive functioning, including assessment of EF, is of paramount importance with regard to formulation of an effective and clear individual treatment plan, and by this to facilitate improved everyday coping and functioning in this patient population.

However, neurocognitive assessment services are both expensive and time consuming. Furthermore, specialized neuropsychological expertise is usually rare in outpatient settings of SUD treatment. The infrequent inclusion of cognitive assessment in clinical practice was illustrated in a recent study from Norway (Vaskinn & Egeland, 2012), in spite of being recognized as important in the Norwegian national guidelines for diagnosing and treating patients with SUD.

To sum up, it is important to develop and apply assessment protocols that both are brief and simple enough to be included in a busy clinical setting, and of importance to real-life situations and treatment.

The need for clinic-friendly neurocognitive measures motivated the present study to investigate two theoretical EF components, referred to as “cold” and “hot” EF, in a group of patients with SUD. Both hot and cold neurocognitive processes are involved in decision-making (Seguin & Zelazo, 2005). Hot and cold decision-making processes are rarely investigated simultaneously. Often studies tend to emphasize the cold pathway at the expense of the hot pathway (Seguin, Arseneault, & Tremblay, 2007). Previous studies have found, that when compared with controls, SUD patients exhibit lower scores on performance based measures on EF and emotion processing measures, and PET studies have established an association between specific neural correlates related to cold and hot executive functions, respectively (Moreno-López et al., 2012).

Related to decision-making, cold EF refers to abilities of importance when contrasting various alternatives and comparing risk/benefit ratios (Seguin et al., 2007). Cold cognitive processes are thus involved in a wide range of abilities, including the ability to keep attention sustained and focused, to be cognitively flexible, and to be able to plan and organize

goal-directed behavior (Burgess, 2000; Stuss, Shallice, Alexander, & Picton, 1995). These abilities are commonly measured by psychometric tests such as the Stroop test (MacLeod, 1991) and the Trail Making Test (Kortte, Horner, & Windham, 2002; Strauss, Allen, Jorgensen, & Cramer, 2005). Neurobiologically, these cognitive processes are shown to be particularly associated with activation in dorsolateral prefrontal cortex (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006).

Hot EF involves processes with a more distinct emotional or motivational salience (Kerr & Zelazo, 2004; Zelazo & Müller, 2002), and have increasingly been linked to the orbitofrontal cortex (Anderson, Barrash, Bechara, & Tranel, 2006; Kerr & Zelazo, 2004). Impaired hot EF have a strong impact on behavioral choices in everyday situations, especially when stimuli with distinct emotional salience interact with logical or cold EF (Sonuga-Barke, 2003). The conventional method for assessing hot EF has been performance-based decision-making tasks with emotional-laden contingencies (Chan, Shum, Touloupoulou, & Chen, 2008). A key challenge for participants in these tasks is to make long-term advantageous decisions in uncertain and ambiguous test settings. The Iowa Gambling Task (IGT) is one such test (Bechara & Damasio, 2002), where impairments has been shown in individuals with alcohol, cocaine, and opioid use disorders (Bartzokis et al., 2000; Bechara & Damasio, 2002; Bechara et al., 2001). It has even been argued that the high proportion of relapse after treatment discharge may be attributed to impaired hot EF, particularly when exposed to emotional-laden situations previously associated with substance abuse (Hunt, Barnett, & Branch, 1971; McKay et al., 1997, 2004).

In addition to performance-based tests, EF can also be investigated using self-report scales or questionnaires in which participants are asked about their function in real-life situations. These scales, for example the 75-item Behavior Rating Inventory of Executive Functions – Adult Version (BRIEF-A) (Roth, Isquith, & Gioia, 2005; Roth, Lance, Isquith, Fischer, & Giancola, 2013), have been shown to have a higher ecological validity than results obtained in a structured test environment (Isquith, Roth, & Gioia, 2013; Roth et al., 2005). Furthermore, they clearly have time and cost advantages over laboratory-based performance measures.

With an aim to document EF impairment in patients with SUD of importance to real-life social adjustment and treatment, the present study included a set of tests of the theoretical cold and hot components of EF, including both psychometric tests and a questionnaire-based inventory (BRIEF-A). We investigated their efficiency in characterizing the SUD patients when compared to a control group.

## 2. Material and methods

### 2.1. Design

The study was part of a prospective, longitudinal cohort study of an SUD patient sample who started a new treatment sequence in the Stavanger University Hospital catchment area. This paper presents data collected from SUD patients admitted to both outpatient and residential treatment facilities. To minimize contamination from drug withdrawal and acute neurotoxic effects from psychoactive substance, participants were tested after 2 weeks of abstinence (Miller, 1985). The project was approved by the Regional Ethical Committee (REK 2011/1877).

### 2.2. Participants and procedures

One hundred and fifty participants were recruited from outpatient and residential treatment facilities within the region, across 10 enrollment sites. Patients were recruited between March 2012 and May 2013. Consecutive enrollment was continued until the required number of participants was recruited. The SUD group included patients reporting use of more than one drug at a single occasion or a history of having injected or abused multiple drugs, based on responses to the Alcohol Use Disorders Identification Test (AUDIT) (Bohn, Babor, &

**Table 1**  
Substance use and treatment history.

	SUD patients (n = 126)
Age at initial use	13.1 (2.0)
Years of drug abuse	15.2 (8.0)
AUDIT total score	14.8 (10.5)
DUDIT total score	35.9 (8.5)
Have injected? n	82 (65.1%)
Treatment attempts, n	
0	44 (34.9%)
1	36 (28.6%)
2	19 (15.1%)
3	9 (7.1%)
4	7 (5.6%)
≥5	11 (6.5%)

All data are mean (SD) unless otherwise indicated.

Kranzler, 1995) and the Drug Use Disorders Identification Test (DUDIT) (Voluse et al., 2012). Scores on these tests are summarized in Table 1. Five patients were excluded due to not having a substance-related addiction. One patient was excluded due to only using cannabis, one due to only using opioids, and 14 due to only using alcohol. We did not exclude patients with comorbid psychiatric conditions. The control group (n = 38) was a convenience sample recruited using posters at social welfare and primary care offices. Controls and patients were offered compensation of NOK 400 for baseline testing. Nine patients (seven 17-years of age, two 16-years of age) were excluded due to age. The final group consisted of n = 126 SUD patients and n = 32 controls. Baseline demographic variables for the control vs the SUD groups are summarized in Table 2.

### 2.3. Inclusion procedure

To be eligible for admission to the study, patients needed to: a) sign a written informed consent to participate; b) embark on a new treatment sequence within the substance abuse treatment service; and c) be at least 18 years of age. Patients also had to be enrolled in the program to which they were admitted for at least 2 weeks, and abstinence was verified through self-report, for both inpatients and outpatients. In one of the first treatment sessions (1–3), patients were given an information sheet with a short project description.

### 2.4. Measures

Cold EF is commonly measured with the computerized Stroop test (Stroop CW) (Golden & Freshwater, 1978). Stroop is an assessment of attention, interference, and inhibition of dominant responses (MacLeod, 1991). Longer reaction times and number of errors indicate impaired performance. Another measure of cold EF is the Trail Making Test (TMT) (Kortte et al., 2002; Strauss et al., 2005). TMT provides data on visual–conceptual and visual–motor tracking and set shifting.

**Table 2**  
Demographic variables for the control and SUD groups.

	Controls (n = 32)	SUD patients (n = 126)	P-value
Male, n	13 (40.6)	85 (67.5)	0.005 <sup>a</sup>
Age	33.7 (13.0)	28.5 (8.0)	0.064 <sup>b</sup>
Years of education	14.5 (3.1)	11.7 (1.8)	0.001 <sup>c</sup>
Native Norwegian, n	32 (100)	120 (95.2)	1.000 <sup>d</sup>
Permanent home, n	32 (100)	71 (56.3)	0.001 <sup>a</sup>
Stable income, n	29 (90.6)	87 (69.0)	0.014 <sup>a</sup>
Criminal lifestyle, n	0 (0.0)	32 (25.4)	0.001 <sup>a</sup>
Years of work experience	11.6 (9.4)	5.8 (5.9)	0.001 <sup>b</sup>
WASI Total IQ	106.2 (13.2)	98.6 (11.6)	0.002 <sup>c</sup>

<sup>a</sup> Pearson's  $\chi^2$ .

<sup>b</sup> Mann–Whitney U Test.

<sup>c</sup> Independent samples t-test.

<sup>d</sup> Fisher's exact test. All data are mean (SD), unless otherwise specified.

There are two test subsections: Trail Making-A (TMT-A), in which the targets are all numbers, and Trail Making-B (TMT-B), in which the subject alternates between numbers and letters. TMT-B is sensitive to cognitive flexibility, sequencing, motor speed, and response inhibition. Longer time to finish indicates impairment.

Hot EF has predominantly been examined using the Iowa Gambling Task (IGT) (Bechara, Damasio, Damasio, & Anderson, 1994). The key challenge in the IGT is to make advantageous long-term decisions in conditions of uncertainty. For this test, subjects are given \$2,000 to start and their task is to maximize profit across 100 trials by choosing cards from one of four decks. After 10 selections from decks A and B, the subject will have earned a net loss of \$250, whereas decks C and D result in a net gain of \$250. Consequently, decks A and B are the “risky” decks. The hot element of IGT varies throughout the testing procedure. It is assumed that the perception of risk within the IGT increases across trials, as subjects gain experience with the win/loss contingencies in the various decks (i.e. later trials have stronger emotional, or risky, associations) (Brand, Recknor, Grabenhorst, & Bechara, 2007).

The BRIEF-A is a self-report questionnaire composed of nine subscales and three composite scores. The Behavioral Regulations Index (BR-index) consists of the subscales inhibit, shift, self-monitor and emotional-control. The subscales initiate, plan/organize, working memory, organization of materials, and task-monitor comprise the Metacognition Index (MI). The BRI and MI can be combined to produce the overall global executive composite (GEC). Validity scales were examined, and two control and 10 SUD participants' profiles were excluded due to invalid response styles.

Specific information on substance abuse was based on self-reported responses on the AUDIT (Bohn et al., 1995) and the DUDIT (Voluse et al., 2012). The Wechsler Abbreviated Scale of Intelligence (WASI) was included as a control variable, because there was a significant difference between controls and SUD patients on the univariate analysis, and to ensure that EF deficits could not be attributed to general abilities. After ensuring validity of WASI's index levels, WASI full scale score was used in further analysis. Experienced and trained psychometric staff administered all tests. An interview based on items from the preliminary version of the National Quality Register for Substance Abuse Treatment was used to collect demographics, type of addiction, initial age at use, treatment and work history, educational, and vocational data. Social adjustment scores were obtained based on a yes/no responses from the same quality register, and included the following categories: permanent housing, criminal lifestyle, conflict with caregivers, friends outside the drug environment, and stable income.

### 2.5. Statistical analyses

All statistical analyses were performed using IBM SPSS software (v. 22 for Windows). *P*-values < .05 were considered statistically significant. Group differences were analyzed using Student's *t*-test, Mann–Whitney tests, Pearson's  $\chi^2$  test and Fisher's exact probability test (for 2 × 2 tables) as appropriate. Normality was controlled for using histograms and Kolmogorov–Smirnov test, and Levene's test was used to select the appropriate *p*-values based on whether the assumption of equal variances within groups was met. Effect sizes are reported as Cohen's *d* (standardized mean differences), for which 0.3 is considered a small, 0.5 a medium, and ≥0.8 a large effect (Cohen, 1992).

Binary logistic regression analyses (enter method) were applied to assess independent correlates of SUD status and categorical variables indicating social adjustment. In these analyses, control variables (age, sex, years of education, and WASI Total IQ), and raw scores from the cold EF, hot EF, and BRIEF-A BRI and MI, were sequentially entered to the analyses. A multiple linear regression was performed to predict the number of previous treatment attempts. As a quantified measure of goodness-of-fit, Nagelkerke's  $R^2$  was estimated and reported. Due to the significant difference in WASI total IQ between controls and patients, WASI total IQ was included in a control variable in these analyses.

### 3. Results

#### 3.1. Demographics, substance abuse, and treatment history

A summary of the demographic variables is presented in Table 2. There were significant differences in gender (40.6% vs 67.5% males in control and SUD group) and years of education ( $14.5 \pm 3.1$  vs  $11.7 \pm 1.8$ ) between the controls and SUD groups. The mean years of work experience was  $11.6 (\pm 9.4)$  in controls, compared to  $5.8 (\pm 5.9)$  in the SUD group. There was also a moderate but significant group difference in WASI Total IQ score in favor of the control group ( $d = 0.611, p = 0.002$ ).

A summary of substance use and treatment history for SUD patients is presented in Table 1. The mean debut age of drug use was  $13.1 (\pm 2.0)$ , and the mean years of drug abuse was  $15.2 (\pm 8.0)$  years. The mean AUDIT score was  $14.8 (\pm 10.5)$ , and mean DUDIT score was  $35.9 (\pm 8.5)$ . The majority (65.1%) of the patients had tried injection as a form of drug administration. For a detailed overview of the treatment history of the patients, please refer to Table 1.

#### 3.2. SUD vs control: executive functions

A summary of performance on cognitive tests for controls and SUD patients is presented in Table 3. The control group significantly outperformed the SUD group on the Stroop CW variables word reading, color naming and color/word naming, with moderate effect sizes. There was no group difference on the Stroop Interference task. There was a significant group difference on TMT part A ( $d = 0.452, p = 0.028$ ) but not TMT part B ( $d = 0.086, p = 0.658$ ). The SUD group was slightly better on IGT but this did not reach statistical significance for either the total score or the learning curve IGT variables. There was a significant increase in standard T-scores between SUD patients and controls on all BRIEF-A subtests.

The results of all the regression analyses are summarized in Fig. 1. Overall, SUD status was significantly associated with control variables ( $\chi^2 = 53.53, p < 0.001; R^2 = 0.336$ ), and the BRIEF-A BRI and MI ( $\chi^2 = 15.90, p < 0.001; R^2 = 0.110$ ). SUD status was not associated

with hot ( $\chi^2 = 1.49, p = 0.223; R^2 = .010$ ) or cold EF measures, although the association is close to statistical significant for cold EF ( $\chi^2 = 12.23, p = 0.057; R^2 = 0.088$ ).

#### 3.3. Social adjustment

Overall, social adjustment variables were not linked to control variables; except that higher education was significantly related to “stable income” ( $B = 0.345, p = 0.005$ ) and “friends outside the drug environment” ( $B = 0.464, p = 0.008$ ). Increased age was also significantly related to “stable income” ( $B = 0.051, p = 0.048$ ). Overall, there were no significant associations between social adjustment and hot or cold cognitive tests. However, increased T-scores on BRIEF-A BRI was significantly related to adverse outcomes on “stable income” ( $B = -0.77, p = 0.007$ ), “conflict with caregiver,” ( $B = 0.09, p = 0.007$ ), “stable housing” ( $B = -0.83, p = 0.002$ ).

A multiple linear regression analysis (enter method) predicting the number of previous treatment attempts was performed using the same independent variables. The overall model was significant, and more treatment attempts were predicted by increased score on Stroop interference ( $B = 0.09, p > 0.001$ ) and TMT part A ( $B = 0.04, p > 0.038$ ). The number of previous treatment attempts was also negatively related to a reduced BRIEF MI score ( $B = -0.07, p = 0.014$ ).

### 4. Discussion

Overall, the regression analyses in the present study found that the BRIEF-A inventory was a significant predictor of substance use status. The MI of BRIEF-A also predicted social adjustment scores, and the MI predicted number of previous treatment sessions within the SUD group. The contribution of the selected performance-based measures was sparse, although group comparisons showed that the control-group was faster on the three conditions from the Stroop test and the Trail Making Test part A.

#### 4.1. Group membership

The measures of cold EF distinguished between patients with SUD and controls. The controls were faster on the Stroop reading and naming tasks, and the Trail Making Test part A. These findings are in line with previous research, where SUD patients often exhibit impairments in inhibitory control, set shifting and reduced ability to suppress responses (Cardinal et al., 2004). This difference in cold EF is even evident in adolescents at risk for developing SUD when compared to peers (McNamee et al., 2008).

The SUD group performed slightly (but not significantly) better on the hot EF, measured by the IGT total score. A similar paradoxical effect on IGT performance and education has been documented in a previous study, but existing studies vary in their findings. Functional impairments based on IGT have been found in individuals with alcohol, cocaine, and opioid use disorders, relative to healthy controls (Bartzokis et al., 2000; Bechara & Damasio, 2002; Bechara et al., 2001). However, findings are not conclusive, and a number of studies have shown that groups of healthy controls do not learn to successfully select cards from the advantageous decks, and also showing high variance in anticipatory electro-dermal responses (Dunn, Dalgleish, & Lawrence, 2006). The contradicting findings from some studies, where controls perform poorly on IGT while not showing any deficiencies in real-life decision making, makes it unclear whether IGT performance have predictive value on real life functioning.

The demographic variables age, gender, education and WASI IQ predicted group membership better than the hot and cold EF measures. WASI provides a brief assessment of general intellectual abilities (Canivez, Konold, Collins, & Wilson, 2009), and these results are not surprising, given the impact of the *G factor*; IQ scores correlate with academic performance and performance in other areas of life (Kline,

**Table 3**  
Performance on cognitive tests for control and SUD groups.

	Controls (n = 32)	SUD patients (n = 126)	P- value <sup>#</sup>	Effect size <sup>*</sup>
<b>Stroop</b>				
Word reading	92.3 (13.9)	85.2 (12.8)	0.007	0.531
Color naming	69.0 (13.8)	62.3 (10.6)	0.013	0.545
Color/Word naming	43.8 (12.4)	38.9 (9.6)	0.019	0.441
Interference	4.3 (8.6)	5.9 (14.0)	0.524	0.137
<b>Trail Making Test</b>				
Part A	26.1 (9.2)	31.8 (12.3)	0.016	0.524
Part B	62.9 (32.2)	73.1 (43.6)	0.157	0.267
<b>Iowa Gambling Task</b>				
Total NET raw score	0.4 (18.6)	4.9 (26.0)	0.272	0.199
<b>BRIEF-A<sup>§</sup></b>				
Inhibit	51.1 (7.9)	64.4 (11.7)	0.001	1.332
Shift	50.9 (9.5)	62.2 (10.4)	0.001	1.134
Emotional control	40.3 (8.0)	59.0 (9.2)	0.001	2.169
Self-monitoring	50.6 (10.3)	59.8 (11.3)	0.001	0.857
BRI	50.3 (10.7)	63.4 (9.8)	0.001	1.276
Initiate	51.0 (10.7)	66.0 (11.2)	0.001	1.369
Working memory	53.7 (11.6)	65.2 (11.3)	0.001	1.004
Plan/Organize	53.2 (10.5)	63.0 (10.4)	0.001	0.937
Task monitoring	54.2 (10.6)	60.9 (11.2)	0.004	0.614
Organization of materials	50.1 (8.7)	55.2 (10.9)	0.019	0.517
Metacognition Index	52.8 (10.7)	64.0 (10.4)	0.001	1.061

BRI = Behavioral Regulation Index; All data are mean (SD), unless otherwise indicated. The analysis on BRIEF-A shown above is therefore based on a sample of n = 30 control and n = 116 SUD participants.

<sup>\*</sup> Student's *t*-test.

<sup>#</sup> Effect size reported as Cohen's *d*.

<sup>§</sup> Due to invalid BRIEF-A protocols, n = 2 control and n = 10 SUD participants were excluded from the analyses.

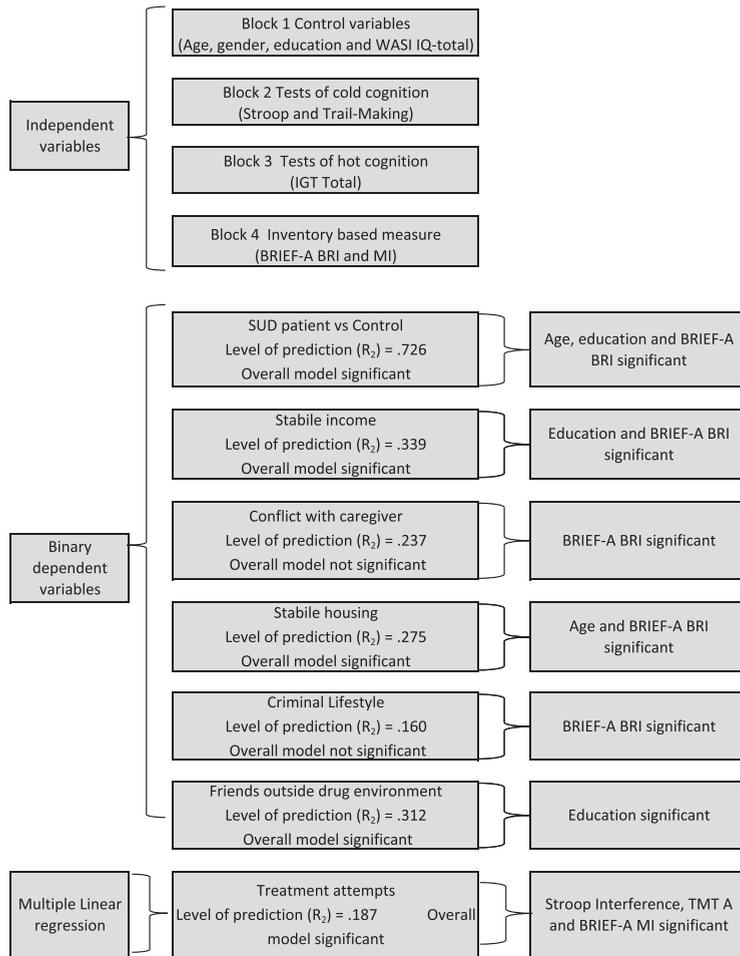


Fig. 1. Independent and dependent variables and results of the regression analyses. Level of prediction expressed as Nagelkerke's  $R^2$ .

2013b), and general intelligence can be understood as a broad reasoning ability that is useful in solving a wide variety of problems in life (Kline, 2013a).

Responses on BRIEF-A was significantly elevated on all the nine scales for SUD patients compared to the controls. Previous studies have found similar results, where current polydrug users report significantly more executive dysfunction on BRIEF-A, compared to non-users (Hadjiefthyvoulou, Fisk, Montgomery, & Bridges, 2012). Several studies have supported the validity of the BRIEF scales and other rating scales in assessing every-day executive functioning (Isquith et al., 2013). Moreover, there are established associations between BRIEF scores and corresponding neural substrates (P. Anderson, 2002), ecological validity with regard to predicting both every-day functioning (Isquith et al., 2013), and academic performance (Waber, Gerber, Turtios, Wagner, & Forbes, 2006).

Similar to our findings, it has proven difficult to establish associations between neuropsychological performance tests and rating scales of EF, and this has raised questions whether the two assessment strategies address different cognitive functions or different applications of cognitive skills (Isquith et al., 2013; McAuley, Chen, Goos, Schachar, & Crosbie, 2010). Isquith et al. (2013) offers a possible frame of explanation where neuropsychological performance tests are hypothesized to

assess cold aspects of EF, and rating scales address a hot emotional aspect of EF. With regard to the BRIEF-A, this hypothesis draws support from research that have applied confirmatory factor analysis of the BRIEF-A scales, and detected a distinct emotional regulatory factor, consisting of the Emotional Control and Shift scales (Gioia, Isquith, Retzlaff, & Espy, 2002). Previous studies have speculated that the BR index is in fact a measure of hot EF, in contrast to the less emotional items constituting the remaining scales (Egeland & Fallmyr, 2010). This distinct hot factor in BRIEF has been replicated in several studies (McCandless & O' Laughlin, 2007; Peters, Algina, Smith, & Daunic, 2012). On the other hand, a recent study, (Skogli, Egeland, Andersen, Hovik, & Øie, 2014) on hot and cold EF in ADHD found no correlation between any of the BRIEF scales and performance based measures of hot performance EF. The correlation matrix displayed marginally higher correlation between cold EF tests and cold BRIEF scales than with the hot BRIEF scales. Overall cold BRIEF scales reached moderate correlation with cold EF tests. To our knowledge the majority of these findings have been based on studies of with attention deficit hyperactivity disorder, and we have not succeeded in finding previous studies investigating associations between neuropsychological performance tests and rating scales of EF adult SUD samples.

#### 4.2. Social adjustment

BRIEF-A was associated with SUD as well as some indicators of social adjustment in SUD patients. Even when controlling for significant demographic variables, the BRI in BRIEF-A was associated with several domains of social adjustment, where increased scores on the BRI of the BRIEF-A were related to both substance abuse and lower social functioning. The BRI consists of four subscales crucial for real-life adaptive social behavior, which offers a plausible explanation for our findings. The Inhibit scale assesses the ability to assert impulse control (*go/no-go*), and to what extent one is able to inhibit, stop or adjust one's behavior when called for by the circumstances. The Shift scale assesses one's ability to flexibly change from alternating situations, tasks or aspects of challenges. The Emotional control scale assesses one's ability to regulate the expression of emotional responses, while the Self-Monitor scale assesses interpersonal awareness and to which extent one understands how one's behavior affects others (Roth et al., 2005). The BRIEF-A questionnaire measure participant's subjective evaluation about their function in real-life situations, and our findings suggest that the BRIEF-A have a higher ecological validity than results obtained on performance based tests.

We did not find any association between performance-based assessment of hot or cold EF and SUD, or social adjustment in the SUD group.

There is a scarceness of literature detailing the link between performance based measures of hot and cold EF in SUD, and their relation with social adjustment. However, regarding neurocognitive predictors of social adjustment, studies of patients with closed brain injury indicates that impairments in overall social adjustment (occupational status, leisure activities, social contacts and family life), are closely linked to the severity of the damage and subsequent cognitive sequela (Oddy, Coughlan, Tyerman, & Jenkins, 1985).

Our findings suggest that typical and commonly used neurocognitive performance based assessments might render a false negative outcome in an initial evaluation, while a questionnaire-based self-evaluation might predict impaired social adjustment associated with substance abuse.

The lack of relationships between self-rating measures and performance based measures of EF could imply that they are measuring different aspects of executive functions, and some suggest that performance measures are particularly sensitive to components of executive functions in isolation, while rating scales assess application of those skills, (Isquith et al., 2013). It has been argued that traditional neuropsychological tests artificially fractionate an integrated functional network (Burgess, 1997), and that the operationalization and types of methods used to measure EF impacts the conclusions and interpretations we can make. Our results indicate that IGT and BRIEF-A BRI assess two different cognitive constructs. IGT is presumably sensitive to subtle, unconscious perceptions of somatosensory feedback or "hunches" to guide decision-making, whereas the BR index from BRIEF-A captures the responder's own view of his or her ability to maintain appropriate control of their own behavior and emotional responses (Roth et al., 2005). This is supported by recent findings showing only minimal correlations between the two types of measures (Toplak, West, & Stanovich, 2013), providing further support for the hypothesis that there are separate EF pathways measured by IGT versus BRIEF-A (Sonuga-Barke, 2003).

#### 4.3. Strengths and limitations

The SUD participants were recruited from ten different treatment facilities within the Stavanger University Hospital region. The patients were asked by their counselor whether they wished to participate. We have no data describing the patients that declined research participation. A Norwegian study found a threefold increase in the rate of disability pensions among patients who chose not to participate in the Hordaland Health Study (Knudsen, Hotopf, Skogen, Øverland, & Mykletun, 2010). Furthermore, nonparticipants were characterized by

poorer lifestyle habits including smoking and drug and alcohol abuse (Korkeila et al., 2001; Shahar, Folsom, Jackson, & The Atherosclerosis Risk in Communities Study, I, 1996) and had lower scores on indicators of somatic and mental health (Drivsholm et al., 2006). It is therefore likely that the patients that declined research participation would have increased, rather than decreased, the group differences reported here.

The SUD and control groups were different on a number of demographic variables. Age, sex, education, and IQ were included as covariates in the statistical analyses to adjust for this limitation somewhat. The significant difference in education between the SUD and control group was challenging to avoid. It was almost impossible to find control participants with fewer than 10 years of education that did not have a substance abuse problem.

This research field faces a number of interpretive challenges as to the etiology of cognitive deficits associated with substance abuse. Psychiatric comorbidity, medical risk factors (e.g. head trauma, HIV, malnutrition, overdose), genetic predispositions, and premorbid vulnerability (e.g. genetic, psychosocial, and environmental) may all play significant causal roles leading to the current neuropsychological profile. Several psychiatric diagnoses are characterized by changes in EF, and psychiatric functioning was assessed with self-report, and not supplemented with observer-rated scales. To ensure validity and reliability in assessment of psychopathological symptoms, it is recommended that both subjective-, and observer rating are employed (Möller, 2009). Hence, it is possible that our findings could be impacted by comorbid psychiatric symptoms.

Furthermore, although there is marked evidence of an association between different aspects of SUD and cognitive impairment, the direct versus indirect roles of the various substances are not clear. Theoretically, a number of cognitive deficits could be viewed as antecedents to the onset of SUD, especially those involving EF connected to decision-making and impulsivity (Nigg, Blaskey, Huang-Pollock, & Rappley, 2002; Nigg et al., 2006).

## 5. Conclusions

The BRIEF-A inventory was the most sensitive measure of EF in patients with substance use disorder, followed by measures of cold EF. Evaluation with BRIEF-A should thus be considered as an integral part of the clinical routine when dealing with assessment of patients with SUD. Assessment of EF may contribute to the scientific and clinical effort of understanding the cognitive and behavioral aspects of SUD, and could prove vital in tailoring SUD treatment programs, particularly considering the high dropout numbers at early treatment stages. However, it is well known that neurocognitive assessment services are scarce, costly, and generally unavailable to SUD patients. Hence, it is crucial to develop, evaluate, and apply testing procedures that could be made more readily available in busy clinical settings and that could also be administered by a broader array of professions. Our data indicate a promising potential for inventory-based EF assessment in SUD patients as measured by BRIEF-A. Self-report measures of EF can be valuable, cost-effective, and accurate at an initial clinical evaluation, providing important complementary measures to performance based tests.

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#### Competing interests

The authors declare that they have no competing interests. We certify that there is no conflict of interest with any financial organization or nonfinancial competing interests regarding the material discussed in the manuscript.

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EH initiated the project, wrote the manuscript and contributed to project design, analysis, and interpretation; AHE contributed to statistical analyses, interpretation and manuscript revision; KPH contributed with writing and revising the manuscript and interpretation of the analyses; SMN, JRM and AL contributed to revision of the manuscript; and EW contributed to manuscript revision and overall supervision of this research. All authors read and approved the final manuscript.

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## Paper II



## One-year sobriety improves satisfaction with life, executive functions and psychological distress among patients with polysubstance use disorder



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### ABSTRACT

**Introduction:** Polysubstance use disorder is prevalent in treatment-seeking patients with substance use disorder (SUD), with a higher risk of developing comorbid psychiatric symptoms, more pervasive deficits in cognitive functions, and inferior treatment results. The present study investigates if individuals with polysubstance use disorder who achieve at least one year of abstinence show greater improvements in satisfaction with life, executive functions, and psychological distress, compared to relapsers and controls. The prospective recovery from polysubstance use disorder assessed with broad output indicators remains understudied. A better understanding of the pattern of recovery of the chosen output indicators could shed light on the recovery process for this group of patients.

**Material and methods:** We investigated changes in satisfaction with life, executive functions and psychological distress over a period of 12 months in patients who remained abstinent and in those who relapsed. Subjects with polysubstance use disorder (N = 115) were recruited from outpatient and residential treatment facilities; healthy controls (N = 34) were recruited by posters exhibited at social welfare and GP offices. Executive functions were assessed by the Behaviour Rating Inventory of Executive Function-Adult self-report version (BRIEF-A), psychological distress by the Symptom Checklist-90-R (SCL-90-R), and satisfaction with life by the Satisfaction With Life Scale (SWLS). Substance use was assessed by self-reports on the Alcohol Use Disorders Identification Test (AUDIT) and the Drug Use Disorders Identification Test (DUDIT). Participants were categorized as “relapsers” if they had AUDIT score  $\geq 8$ , or DUDIT score  $\geq 2$  for women and  $\geq 6$  for men.

**Results:** Results indicated that the abstinent group had the greatest improvement on all the indicators compared with relapsers and controls. Participants who successfully quit substance use for one year showed improved satisfaction with life, executive functions, and psychological distress compared to participants who relapsed and controls.

**Conclusions:** Our study provides support for the view that there is a clinically and statistically significant recovery of satisfaction with life, executive functions, and psychological distress for SUD patients following one-year of abstinence. This knowledge highlights the importance of time and continued abstinence.

Our findings suggest that a gradual and careful step-up of learning requirement should be adopted, and SUD treatment should initially focus on stabilizing the patient and achieving abstinence, while interventions for comorbid problems and more cognitively demanding treatment components are more likely to succeed later in the treatment sequence.

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**Abbreviations:** SUD, substance use disorder; EF, executive function; BRIEF-A, Behaviour Rating Inventory of Executive Function-Adult version; SWLS, Satisfaction With Life Scale; SCL-90-R, Symptom Checklist-90-R; AUDIT, Alcohol Use Disorders Identification Test; DUDIT, Drug Use Disorders Identification Test; WASI, Wechsler Abbreviated Scale of Intelligence; MI, Metacognition Index; BRI, Behavioral Regulation Index; GEC, Global Executive Composite.

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## 1. Introduction

Polysubstance use disorder is the most common diagnosis among patients seeking treatment for substance use, and polysubstance use is also associated with several challenges (Andrade, Carroll, & Petry, 2013). Compared with single-drug users, polydrug users have an earlier onset of drug use and a higher rate of dropout (King & Canada, 2004; Preti, Prunas, Ravera, & Madeddu, 2011), and they report higher levels of general psychological distress (Andreas, Lauritzen, & Nordfjærn, 2015; Quek et al., 2013; White et al., 2013). This group reports more symptoms of anxiety and depression (Booth et al., 2010; G. W. Smith, Farrell, Bunting, Houston, & Shevlin, 2011), which is clinically relevant because psychiatric comorbidity increases risk of relapse (Flynn & Brown, 2008). Furthermore, polysubstance use disorder is associated with pervasive deficits in cognitive functions, and significant impairments have been reported on neuropsychological tests of working memory, inhibition, cognitive flexibility, self-regulation, and decision-making (Moreno-López et al., 2012). Cognitive impairments and psychological distress thus place users with polysubstance use disorder at preeminent risk of impaired recovery and more treatment dropout (Preti et al., 2011). Consequently, treatment approaches for polysubstance use disorder are less effective compared with treatments for use of single substances (Connor, Gullo, White, & Kelly, 2014; Williamson, Darke, Ross, & Teesson, 2006).

A number of studies have found a co-occurrence between mental distress and dose-related polydrug use, and also a reduction of mental distress among abstinent patients (Andreas et al., 2015). However, efforts that focus on a broad spectrum of output indicators are needed to shed light on the recovery process for this important and highly vulnerable subgroup of SUD patients. Polydrug users constitute a high risk group compared with other SUD patients, with more distinct depressive and suicidal symptomatology at treatment admission (Riehmman, Iguchi, & Anglin, 2002), and also more social anxiety (Bakken, Landheim, & Vaglum, 2005). Studies have shown that impaired psychiatric and cognitive functions greatly diminish satisfaction with life (Burgess et al., 2000). Satisfaction with life is also reduced among SUD patients, although it has not been thoroughly investigated in patients with polysubstance use disorder. (Donovan, Mattson, Cisler, Longabaugh, & Zweben, 2005; K. Smith & Larson, 2003). As satisfaction with life is described as a core motivator for and predictor of successful treatment, it should be included as a key outcome indicator when evaluating the success of SUD treatment (De Maeyer, Vanderplasschen, & Broekaert, 2010).

Previous treatment studies of impaired executive functions in SUD patients have several limitations. They have primarily dealt with the acute and subacute effects of chronic alcohol and drug use (Fernandez-Serrano, Perez-Garcia, & Verdejo-Garcia, 2011; Vik, Cellucci, Jarchow, & Hedt, 2004; Yucel, Lubman, Solowij, & Brewer, 2007), and studies of long-term recovery do not always require a 14-day drug-free period prior to baseline testing (Fernandez-Serrano et al., 2011). Other studies have small sample sizes, often with a focus on patients with one primary addiction (Badiani, Belin, Epstein, Calu, & Shaham, 2011; Buelow & Suhr, 2009; Stavro, Pelletier, & Potvin, 2013). In addition, many studies have used cross-sectional designs and are therefore unable to track changes in individual patients over time (van Holst & Schilt, 2011). There is also considerable variability in the follow-up rates, ranging from 40% to 98% (Cottler, Compton, Ben-Abdallah, Horne, & Claverie, 1996; Desmond, Maddux, Johnson, & Confer, 1995; Stinchfield, Niforopoulos, & Feder, 1994), and some studies have not included a follow-up procedure for a control group (Schulte et al., 2014).

We have not been able to find other studies that have focused on satisfaction with life, executive functions, and psychological distress during the course of recovery for people with polysubstance use disorder, even though a consideration of all these variables could prove important to understand the course of recovery for these patients. The present study features a prospective design and a control group, and was used

to address the following question: Will individuals with polysubstance use disorder who achieve at least one year of abstinence show greater improvements in satisfaction with life, executive functions, and psychological distress, compared to relapsers and controls?

## 2. Material and methods

### 2.1. Participants

One hundred fifty SUD patients were recruited from 10 outpatient and residential treatment facilities within the Stavanger University Hospital catchment area (Norway) between March 2012 and May 2013. We employed broad inclusion criteria focusing on polysubstance use disorder because polysubstance use disorder is common in a clinical setting (Badiani et al., 2011; Stavro et al., 2013). The main inclusion criteria at baseline were: (a) evidence of SUD polysubstance use, operationalized as the use of more than one drug on a single occasion, or a history of abusing multiple drugs; (b) enrolled in a new treatment sequence by the substance use treatment service; and (c) at least 16 years of age.

The control group ( $N = 38$ ) was a convenience sample recruited by posters exhibited at social welfare and GP offices. Controls and SUD patients were compensated with NOK 400 (≈\$US 50) for the baseline testing. During the one-year follow-up period, 13 SUD patients and four in the control group withdrew or dropped out of the study. The final group included 115 SUD patients and 34 controls. This study was reviewed and approved by the Regional Ethical Committee (REK 2011/1877) and conducted according to its guidelines and those of the Helsinki Declaration (1975). Signed informed consent was obtained from all the participants.

### 2.2. Procedures

The study is part of a prospective cohort study of a sample of SUD patients in the Stavanger University Hospital catchment area. To minimize contamination from drug withdrawal and acute neurotoxic effects from psychoactive substances, baseline assessment was performed after two weeks of abstinence (Miller, 1985) by experienced and trained staff. Information on substance use was assessed using the Alcohol Use Disorders Identification Test (AUDIT) (Bohn, Babor, & Kranzler, 1995) and the Drug Use Disorders Identification Test (DUDIT) (Voluse et al., 2012). At the one-year follow up, patients were defined as relapsing to a significant level of use if they had an AUDIT score  $\geq 8$  or DUDIT score  $\geq 2$  for women and  $\geq 6$  for men (Bohn et al., 1995; Voluse et al., 2012).

### 2.3. Satisfaction with life

Satisfaction with life was assessed baseline and one year later with the Satisfaction With Life Scale (SWLS) (Diener, Emmons, Larsen, & Griffin, 1985). This is a self-report questionnaire including five items measuring the global life satisfaction experienced by the respondent. The SWLS has demonstrated good psychometric characteristics (Pavot & Diener, 2008). The five items are all set in a positive direction, and the total SWLS score (range = 5–35) was included in the present study. A score of 20 represents a neutral point on the scale; scores between 5 and 9 indicate that the respondent is very dissatisfied with life, while scores ranging between 31 and 35 indicate that the respondent is very satisfied with life (Pavot & Diener, 2008). In this study two patients did not complete the SWLS at the 1-year follow up, yielding a response rate was 98.2% for patients and 100% for controls.

### 2.4. Executive functions

This study assessed executive functions by asking the participants to complete the Behaviour Rating Inventory of Executive Function-Adult version (BRIEF-A) (Gioia, Isquith, Guy, Kenworthy, & Baron, 2000; Roth, Isquith, & Gioia, 2005) at baseline and one year later. The BRIEF-

A has been shown to have high ecological validity (Gioia et al., 2000; Roth et al., 2005), and to be associated with substance use status as well as several social adjustment indicators in patients with a history of polysubstance use disorder (Hagen et al., 2016). The BRIEF-A includes three composite scores including sets of subscales. A Behavioural Regulation Index (BRI-index) is calculated from the Inhibit, Shift, Self-Monitor and Emotional Control subscales. The BRIEF-A Metacognition Index (MI) is calculated from the Initiate, Plan/Organize, Working Memory, Organization of Materials, and Task Monitor subscales. In this study one patient and one control did not complete the BRIEF-A at the 1-year follow up, yielding a response rate was 99.1% for patients and 97.1% for controls. Validity scales of the BRIEF-A were examined, using the cut-off scores proposed by the original authors (Gioia et al., 2000). Invalid response style led to exclusion of one control and nine SUD participants at baseline, and three controls and five SUD participants at the one-year follow up. The final sample included the 30 controls and 101 SUD patients with valid BRIEF-A protocols.

The Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) was used to estimate intellectual function (IQ) by including two tests of verbal crystallized abilities (Vocabulary and Similarities) and two tests of nonverbal fluid-visual abilities (Block Design and Matrices) (Canivez, Konold, Collins, & Wilson, 2009).

### 2.5. Psychological distress

Psychological distress was measured at baseline and one year later using the Symptom Checklist-90-R (SCL-90-R) (Derogatis, 1994). This is a 90-item self-report symptom inventory that yields measures of nine symptom domains of psychological distress: (1) Somatization; (2) Obsessive compulsion; (3) Interpersonal sensitivity; (4) Depression; (5) Anxiety; (6) Hostility; (7) Phobic anxiety; (8) Paranoid ideation, and (9) Psychoticism. This study includes the nine subscales and the summary score; Global Severity Index (GSI) (Derogatis, 1994). In this study three patients did not complete the SCL-90-R at the 1-year follow-up, yielding a response rate was 97.4% for patients and 100% for controls.

### 2.6. Statistical analyses

Data were analyzed using IBM SPSS v22 for Mac. Statistical significance was interpreted at  $p < 0.05$  (two-tailed). Group differences were analyzed using  $t$ -tests, Mann-Whitney  $U$  tests, and Pearson's chi square-tests when appropriate. Levene's test was used to select the appropriate  $p$ -values based on whether the assumption of equal variances within groups was met. Histograms, Q-Q plots, Kolmogorov-Smirnov tests, and Shapiro-Wilk tests were used to investigate normality.

The research question was analyzed using mixed between-within subjects' ANOVA to compare changes in abstainers, relapsers and controls from the baseline to the one-year follow-up. Variables where the three groups have similar patterns of change from baseline to one year will not have a statistically significant interaction effect (the null hypothesis). Variables where one group has a different pattern of change from the other two groups are expected to show an interaction. To determine the cause of interaction effects, Wilcoxon signed rank tests were used to evaluate median change from baseline to one year within each group. Effect sizes were calculated as Cohen's  $r$  for nonparametric data, where 0.3 is considered a medium and 0.5 is considered a large effect (Cohen, 1988). Main effects were not interpreted in the presence of a statistically significant interaction (Bordens & Abbott, 2002).

## 3. Results

### 3.1. Group characteristics

At baseline, patients and controls were similar according to age, but controls were more often female (chi square = 5.8,  $p = 0.016$ ), had higher level of education ( $Z = 4.1$ ,  $p < 0.001$ ), and higher IQ score at

**Table 1**

Baseline demographic and clinical variables for participants, grouped according to drug use status after one year.

	Abstinent (N = 51)	Relapsers (N = 64)	Controls (N = 34)
Age	28.7 (7.5)	27.1 (8.1)	30.9 (12.9)
Male gender, n (%)	35 (68.6%)	42 (65.6%)	15 (55.9%)
Years of education	11.9 (1.8)	11.6 (1.7)	14.2 (3.1)
AUDIT score at baseline	12.3 (9.8)	15.2 (10.5)	5.4 (3.8)
DUDIT score at baseline	36.6 (9.6)	35.3 (8.7)	0.3 (1.2)
WASI IQ	100.7 (11.5)	95.8 (12.1)	105.5 (13.6)

AUDIT = Alcohol Use Disorder Identification Test; DUDIT = Drug Use Disorder Identification Test; WASI = Wechsler Abbreviated Scale of Intelligence. All data are means (SD), unless otherwise indicated.

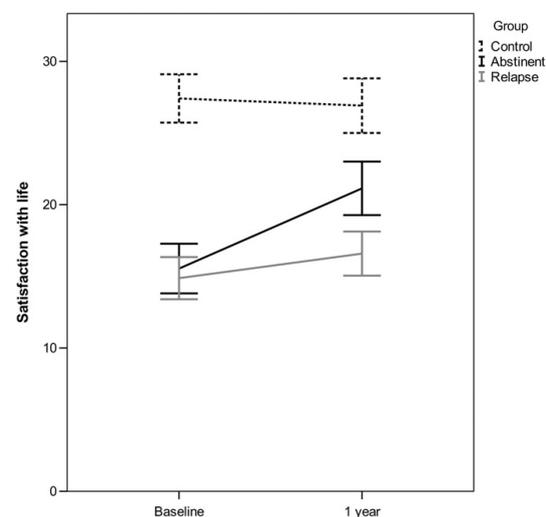
baseline ( $t = 3.2$ ,  $p < 0.001$ ). Clinical and demographic variables after one year for patients who remained abstinent ( $N = 51$ ), relapsers ( $N = 64$ ), and controls ( $N = 34$ ) are summarized in Table 1. Although there were no differences in baseline demographic variables between the two SUD groups, the abstinent group obtained a higher score on WASI IQ ( $t = 2.2$ ,  $p = 0.030$ ). Baseline levels of substance abuse, as measured by mean AUDIT/DUDIT score, did not differ between the two SUD groups.

### 3.2. Satisfaction with Life Scale (SWLS)

Analysis of SWLS showed a significant main effect of group [ $F(2,144) = 59.8$ ,  $p < 0.001$ ] and time [ $F(1,144) = 16.9$ ,  $p < 0.001$ ], and a significant group  $\times$  time interaction [ $F(2,144) = 9.84$ ,  $p < 0.001$ ]. Follow-up analyses showed that the interaction could be attributed to the significant improvement in the abstinent group ( $Z = -4.86$ ,  $P < 0.001$ ), with a medium to large effect size ( $r = 0.49$ ). The relapse and control group did not have statistically significant improvement. See Fig. 1 and Table 2.

### 3.3. Executive functions in everyday life (BRIEF-A)

Analysis of the BRIEF-A Global Executive Composite (GEC) showed a significant main effect of group [ $F(2,125) = 20.4$ ,  $p < 0.001$ ] and time



**Fig. 1.** Satisfaction with life "Satisfaction with life baseline and one year later measured with the Satisfaction With Life Scale (SWLS). Mean value for the control group, the participants that remained abstinent and the participants that relapsed to drug use. Error bars: 95% Confidence interval."

**Table 2**  
Self-reported executive functioning, psychological distress and life quality during the 1 year follow up period.

	Abstinent group (N = 51)			Relapse group (N = 64)			Control group (N = 32)		
	Baseline	1 year	Z value <sup>a</sup>	Baseline	1 year	Z value <sup>a</sup>	Baseline	1 year	Z value <sup>a</sup>
SWLS sum	15.7 (6.1)	21.1 (6.6)	-4.9**	14.9 (5.8)	16.6 (6.1)	-1.9	27.4 (4.8)	26.9 (5.5)	-0.4
BRIEF-A GEC	64.8 (11.8)	55.0 (12.3)	-4.5**	66.4 (9.4)	64.7 (10.2)	-1.5	52.3 (10.4)	48.7 (12.7)	-2.0*
BRIEF-A BRI	63.3 (11.2)	53.5 (11.5)	-4.4**	64.0 (12.5)	63.3 (10.2)	-0.2	51.0 (9.3)	49.3 (11.0)	-1.9
BRIEF-A MI	64.0 (11.6)	55.3 (11.9)	-4.5**	63.7 (13.1)	63.9 (11.0)	-1.5	53.1 (10.7)	50.1 (10.3)	-1.1
SCL-90-R GSI	1.0 (0.7)	0.5 (0.6)	-4.5**	1.3 (0.6)	1.1 (0.6)	-2.4*	0.4 (0.4)	0.4 (0.5)	-0.1
Somatization	0.87 (0.8)	0.43 (0.5)	-3.8**	1.10 (0.7)	1.09 (0.8)	-0.1	0.41 (0.5)	0.49 (0.5)	-1.4
Obsessive compulsive	1.44 (0.8)	0.85 (0.8)	-4.9**	1.61 (0.7)	1.43 (0.8)	-2.1*	0.58 (0.6)	0.52 (0.6)	-1.0
Interpersonal sensitivity	1.22 (0.9)	0.59 (0.8)	-4.5**	1.30 (0.7)	1.01 (0.7)	-3.2**	0.38 (0.4)	0.41 (0.6)	-0.6
Depression	1.23 (0.8)	0.66 (0.7)	-4.5**	1.49 (0.7)	1.26 (0.8)	-0.4*	0.43 (0.5)	0.45 (0.5)	-0.8
Anxiety	1.13 (0.9)	0.47 (0.6)	-5.2**	1.42 (0.8)	1.26 (0.8)	-2.1*	0.32 (0.4)	0.35 (0.5)	-0.7
Hostility	0.64 (0.8)	0.30 (0.5)	-3.7**	0.91 (0.8)	0.81 (0.9)	-1.2	0.20 (0.2)	0.23 (0.5)	-0.8
Phobic anxiety	0.79 (0.9)	0.35 (0.6)	-3.9**	1.10 (0.9)	0.84 (0.8)	-2.1*	0.17 (0.4)	0.19 (0.4)	-0.2
Paranoid ideation	0.97 (0.9)	0.48 (0.7)	-3.9**	1.21 (0.9)	1.10 (0.9)	-1.2	0.35 (0.4)	0.35 (0.6)	-0.7
Psychoticism	0.63 (0.7)	0.24 (0.4)	-4.7**	0.71 (0.6)	0.52 (0.5)	-2.55*	0.14 (0.3)	0.24 (0.5)	-1.8

All data are means (SD), unless otherwise indicated.  
 BRIEF-A GEC = Behaviour Rating Inventory of Executive Function-Adult Version Global Executive Composite; SCL-90-R GSI = Symptom Checklist-90-Revised Global Severity Index; SWLS = Satisfaction With Life Scale; AG = Abstinent group; RG = Relapse group; CG = Control group.  
 \*  $P < 0.05$ .  
 \*\*  $P < 0.001$ .  
<sup>a</sup> Results of Wilcoxon signed rank test. This measures improvement in median score in this group from baseline until one year later.

[ $F(1125) = 17.5, p < 0.001$ ], in addition to a significant group  $\times$  time interaction [ $F(2125) = 4.4, p = 0.015$ ]. The interaction is mainly attributed to the improvement in the abstinent group ( $Z = -4.52, P < 0.001$ ), with a medium to large effect size ( $r = 0.45$ ), but some of the interaction-effect could also be carried by an improvement in the control group ( $Z = -2.04, P < 0.05$ ), but this effect was small ( $r = 0.2$ ). The relapse group did not show a statistically significant improvement. See Fig. 2 and Table 2.

The BRIEF-A Behavioral Regulation Index (BRI) showed a significant group  $\times$  time interaction [ $F(2126) = 4.9, p = 0.009$ ]. The interaction could be attributed to the improvement in the abstinent group ( $Z = -4.5, P < 0.001$ ), with a large effect size ( $r = 0.6$ ). Relapsers and controls did not show a statistically significant improvement from baseline to one year. BRIEF-A Metacognition Index (MI) showed a significant group  $\times$  time interaction [ $F(2126) = 4.0, p = 0.020$ ]. The interaction

could be attributed to the improvement in the abstainers ( $Z = -4.5, P < 0.001$ ), with a large effect size ( $r = 0.6$ ). Relapsers and controls did not have statistically significant improvement. See Table 2.

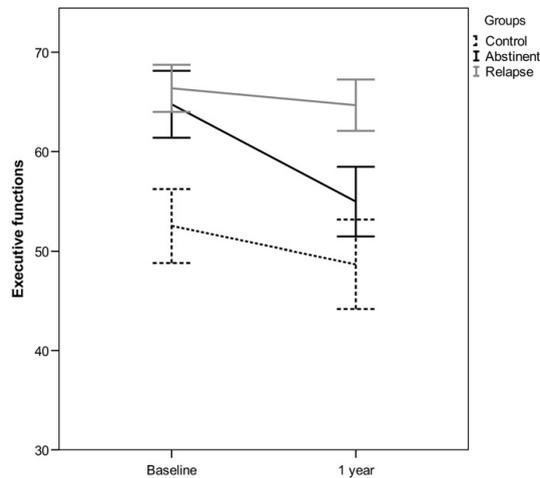
3.4. Symptom Checklist-90-R (SCL-90-R)

Analysis of psychological distress as measured by SCL-90-R Global Severity Index (GSI) showed a significant main effect of group [ $F(2143) = 24.7, p < 0.001$ ] and time [ $F(1143) = 23.8, p < 0.001$ ], in addition to a significant group  $\times$  time interaction [ $F(2143) = 11.0, p < 0.001$ ]. The interaction is mainly attributed to the improvement in the abstinent group ( $Z = -4.50, P < 0.001$ ), with a medium to large effect size ( $r = 0.45$ ), but some of the interaction-effect could also be carried by an improvement in the relapse group ( $Z = -2.44, P < 0.05$ ), but this effect was small ( $r = 0.2$ ). The control group did not have statistically significant improvement. See Fig. 3 and Table 2.

All nine SCL-90 subscales showed significant interactions at  $p < 0.05$ . The abstinent group improved from baseline to one-year on all nine subscales ( $p < 0.001$ ). The relapse group improved on the subscales; Obsessive compulsive, interpersonal sensitivity, depression, anxiety, phobic anxiety and psychoticism at a  $p < 0.05$  level, but showed no significant change on the subscales somatization, hostility, paranoid ideation. The control group had no change from baseline to one year on any of the SCL-90 subscales. See Table 2.

3.5. 3.4 abstinent vs. controls at baseline and one year

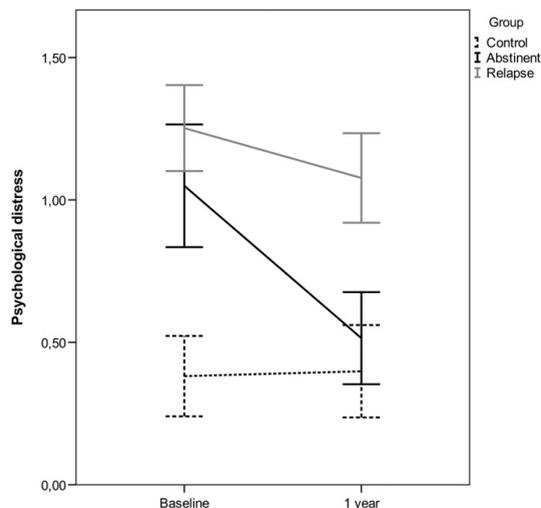
At baseline the abstinent group had significantly worse SWLS score ( $Z = -6.6, p < 0.001$ ), BRIEF-A GEC score ( $Z = -4.6, p < 0.001$ ) and SCL-90-R GSI score ( $Z = -5.0, p < 0.001$ ) compared to the control group. Comparing the scores at the 1-year follow-up between the abstinent and control group demonstrated a significant difference in scores on SWLS score ( $Z = -3.91, P < 0.001$ ) and BRIEF-A GEC score ( $Z = -2.21, P < 0.05$ ), but no evident difference between these groups on SCL-90-R GSI score. Although the abstinent group performed slightly worse compared to the control group (see Fig. 3), this difference was insignificant and indicates a normalization of psychological distress following one year of abstinence.



**Fig. 2.** Executive functions “Executive functions at baseline and one year later measured with the Global Executive Composite (GEC) from the Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A). Mean value for the control group, the participants that remained abstinent and the participants that relapsed to drug use. Error bars: 95% Confidence interval.”

3.6. Summary

Significant interactions with group and time were shown for all outcome variables, with the abstainers showing the highest improvement



**Fig. 3.** Psychological distress “Psychological distress at baseline and one year later measured with the Global Severity Index (GSI) from the Symptom Checklist 90 – Revised (SCL-90-R). Mean value for the control group, the participants that remained abstinent and the participants that relapsed to drug use. Error bars: 95% Confidence interval.”

on all variables (see Table 2). Overall, participants that successfully quit substance use for one year show improved satisfaction with life, executive functions and psychological distress compared to participants that relapse and controls.

#### 4. Discussion

This study compared the change from baseline to follow-up one year later on self-reported satisfaction with life, executive functions and psychological distress. The participants were patients with polysubstance use disorder who remained abstinent during the course of one year, patients who relapsed to substance use, and healthy controls. The abstinent group showed a significant improvement in perceived life quality, executive functions, and psychological distress compared with the relapsers and controls.

##### 4.1. Improvement of satisfaction with life, executive functions and, psychological distress.

Executive functions (EF) improved in the group of abstinent patients between baseline and one-year, but this was not the case with the patients that relapsed. Improvement of EF is very promising, considering that maladaptive, impulse-driven behaviour is strongly associated with a substance using lifestyle (Crews & Boettiger, 2009). Impulsivity and impaired EF have been associated with almost all stages of the SUD life cycle (Stevens et al., 2014): with increased probability of initiating use, more aggressive escalation of use, failure to reduce consumption and higher numbers of relapses after treatment (Jentsch, 2009; Robbins, Gillan, Smith, de Wit, & Ersche, 2012; Winstanley, Olausson, Taylor, & Jentsch, 2010). Notably, despite the improvement in EF in the abstainers, they still had somewhat impaired function compared with controls, which indicates that they still had some degree of vulnerability related to impaired EF, even after a year of abstinence.

Psychological distress decreased in the abstinent group. At the one-year follow up, the disparity between the abstinent group and the controls almost disappeared, suggesting a normalization of psychological distress following one year of abstinence. Together with the differences

between the relapsers and abstinent patients on almost all SCL-90 subscales, these results offer a promising view regarding initial recovery from psychological distress in SUD patients. This finding is in line with previous research that have found a reduction of psychological distress among patients who stopped using multiple drugs (Andreas et al., 2015), however it should be emphasized that the present study focused on a broader spectrum of output indicators than previously reported.

There was a significant difference in perceived satisfaction with life as measured by SWLS between the abstinent and relapse groups after one year. The importance of this finding is substantiated by previous studies showing an association between satisfaction with life and subsequent symptoms in recovery, where satisfaction with life increases through early recovery to stable abstinence (Laudet, Morgen, & White, 2006). Furthermore, a longer period of sobriety is shown to predict higher levels of satisfaction with life one year later, and satisfaction with life at the end of SUD treatment predicts commitment to sobriety (Laudet et al., 2006).

The multimodal improvement of satisfaction with life and executive functions with a decrease of psychological distress following one year of abstinence is compelling. Most therapeutic interventions for SUD, including, cognitive behavioral therapy, motivational interviewing, and 12-step programs, are verbally based interventions requiring extensive cognitive processing to facilitate cognitive, motivational, and behavioral change (Roehrich & Goldman, 1993). For instance, a common feature of most treatment initiatives involves learning the harmful effects of various drugs, as well as teaching of programme rules and overarching treatment philosophy (Grohman & Fals-Stewart, 2003), thus representing a distinct learning requirement at the onset of therapy. Our findings suggest that a gradual and careful step-up of learning requirements should be adopted, and emphasize that SUD treatment should initially focus on stabilizing the patient and achieving abstinence, while interventions for co-morbid problems and more cognitively demanding treatment components are more likely to succeed later in the treatment sequence, as cognitive functioning improves. Moreover, these results raise possibility that interventions specifically designed to improve cognitive function, such as memory training (Bickel, Yi, Landes, Hill, & Baxter, 2011), might facilitate somewhat more rapid recovery of cognitive function in this population.

##### 4.2. Strengths and limitations

Many studies in this field have used cross-sectional designs (van Holst & Schilt, 2011), and thus cannot track changes over time. We have used a prospective design for the patient and control groups to enable control of training effects by repeated testing and reports on the same questionnaires (Schulte et al., 2014). The mean IQ score of the control group (104) was within the normal range for the population. However, there was a significant difference in years of education, gender distribution and work experience between the patient groups and the controls (Table 1). These disparities are anticipated when comparing a healthy control group and a clinical sample of patients with polysubstance use disorder with a vast number of risk factors. With regard to education, all Norwegian citizens have compulsory education from five to 16 years old. It was difficult to recruit age-matched participants with fewer than 10 years of education who did not use drugs. The skewed gender distribution, with the SUD group being 67% male and the control group 55.9% male, may be explained by a factual gender difference in the prevalence of SUD between men and women; males are more likely to suffer from lifetime and 12-month use and dependence on drugs (Warner, Kessler, Hughes, Anthony, & Nelson, 1995). There was no significant age difference between patients and controls, which was a strength of the study as age is known to significantly impact neurocognitive functions.

To ensure a diverse picture of the dimensions underlying recovery, we broadened the scope of interest to satisfaction with life, executive functions and psychological distress. By testing participants after

14 days of detoxification, we aimed to exclude the possible subacute effects of the drug use (Fernandez-Serrano et al., 2011).

However, the present study has a number of limitations. First, it did not incorporate a randomized design. Relapsers and abstainers self-selected into their groups based on self-reports, and baseline or time-varying variables that were not assessed may have influenced our outcome variables. Thus, we cannot conclude that the differences in these outcomes observed at 12 months were caused only by changes in substance use status. Furthermore, in this study we only addressed a follow-up period of 12 months with only one follow-up wave, and the control group was relatively small. It is possible that a larger control group would have shown statistically significant improvements on EF. It is however, unlikely that a large control group would change the overall impression that participants achieving one year of abstinence show greater improvements compared to the other groups.

Finally, we were not able to determine the patterns of polydrug use in our sample; that is, whether different substances were used concurrently, or before or after another drug. This information would be beneficial to understand better the issues of polydrug use.

## 5. Conclusions

To date, few studies have investigated the natural progression of recovery in terms of this particular combination of outcome indicators in patients with polysubstance use disorder. Our study provides support for the view that there is a clinically significant recovery in satisfaction with life, executive functions and psychological distress for polysubstance using SUD patients following one-year of abstinence. This improvement from admission to one-year, suggests that a gradual progression of treatment should be adopted to ensure that the patients have the prerequisites for receiving treatment in a broad array of dimensions. By this, our findings could shed light on the recovery process for this group of patients. It highlights the necessity of an ongoing diagnostic approach as the clinical picture at the admission of treatment could be dramatically improved for patients suffering for polysubstance use disorder. This knowledge could provide hope for patients, as well as therapist, simply by highlighting the importance of time and continued abstinence. This might subsequently reduce dropout numbers and improve the recovery process for these patients. Future research should consider the timing and sequence of interventions in SUD treatment.

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## Competing interests

The authors declare that they have no competing interests. We certify that there is no conflict of interest with any financial organization or nonfinancial competing interests regarding the material discussed in the manuscript.

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EH initiated the project, wrote the manuscript, and contributed to project design, analysis, and interpretation; AHE contributed to statistical analyses, interpretation, and manuscript revision; KPH contributed to the writing and revision of the manuscript and interpretation of the analyses; SMN, JRM, and AJL contributed to the revision of the manuscript; and EW contributed to manuscript revision and overall supervision of this research. All authors read and approved the final manuscript.

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## Paper III



## One-year abstinence improves ADHD symptoms among patients with polysubstance use disorder



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### ABSTRACT

**Introduction:** Attention-deficit/hyperactivity disorder (ADHD) is a common comorbid disorder in patients suffering from substance use disorder (SUD). Individuals with co-occurring SUD and ADHD are more likely than SUD patients without ADHD to have developed SUD at a younger age, be polysubstance users, and need inpatient treatment more often. The present study investigates whether individuals with polysubstance use disorder who remain abstinent for a year after entering treatment have a more substantial reduction in ADHD symptoms than those who relapsed and controls.

**Material and methods:** Subjects were SUD patients (N = 115) and healthy controls (N = 34). ADHD symptoms were assessed using the adult ADHD Self-Report Scale (ASRS). Substance use was assessed by self-reports on the Alcohol Use Disorders Identification Test (AUDIT) and the Drug Use Disorders Identification Test (DUDIT). Participants were defined as having relapsed if they had an AUDIT score  $\geq 8$  or a DUDIT score  $\geq 2$  for women and  $\geq 6$  for men.

**Results:** Patients who remained abstinent for one year reported a substantial reduction of ADHD symptoms compared to patients who relapsed and controls.

**Conclusions:** Abstinence alleviates ADHD symptoms among patients with polysubstance use disorder. We suggest that confirmation of an ADHD diagnosis should follow a period of abstinence to avoid identification of false-positive cases.

### 1. Introduction

One of the most common disorders associated with substance use disorder (SUD) is attention-deficit/hyperactivity disorder (ADHD) (Brook, Whiteman, Cohen, Shapiro, & Balka, 1995; Kessler et al., 2006; Wilens & Spencer, 2010). Nearly 25% of the adults between 18 and 44 years old who have been diagnosed with SUD in the United States have also been diagnosed with ADHD (Kessler et al., 2006). Other studies show that 40% of clinical SUD samples in different countries screened positive for ADHD (Glind et al., 2013; van Emmerik-van Oortmerssen et al., 2012).

ADHD has an adverse effect on the course of SUD (McAweeney, Rogers, Huddleston, Moore, & Gentile, 2009; Wilens et al., 2011). Relative to SUD patients without ADHD, SUD patients with ADHD are more likely to have developed SUD at a younger age, become polysubstance users, and need inpatient treatment more often (Arias et al., 2008; Tamm et al., 2013). Also, SUD patients who screen for a concurrent adult ADHD diagnosis have been shown to have more severe and chronic SUD (Young et al., 2015), and a childhood ADHD diagnosis in SUD patients is associated with higher relapse rates after treatment termination (Carroll & Rounsaville, 1993).

ADHD is manifested in childhood, and it persists into adolescence in

**Abbreviations:** SUD, substance use disorder; ADHD, attention deficit hyperactivity disorder; ASRS, ADHD Self-Report Scale; AUDIT, Alcohol Use Disorders Identification Test; DUDIT, Drug Use Disorders Identification Test; WASI, Wechsler abbreviated scale of intelligence; GP, general practitioner; REK, Regional Ethical Committee; DSM, Diagnostic and Statistical Manual of Mental Disorders; ANOVA, analysis of variance

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almost 75% of the cases, and into adulthood in close to 50% (Wilens & Spencer, 2010). Most studies have focused on how the onset of ADHD, often in combination with conduct or bipolar disorders, increases the risk of later SUD (Wilens et al., 2011).

Comorbid ADHD place patients with SUD at risk of impaired recovery, with longer duration of substance use and slower remission rate (Wilens, Biederman, & Mick, 1998).

SUD complicates the diagnostic process, particularly for clients identified with ADHD in adulthood and for those with symptoms below the diagnostic threshold (Levin, Evans, & Kleber, 1998). Diagnosing ADHD in adult patients with SUD requires accurate retrospective information, and this is often difficult to obtain because of inadequate anamnestic data (Faraone et al., 2007; Levin et al., 1998). Consequently, there is a group of adults who meet all the criteria for an ADHD diagnosis except age at onset (Faraone et al., 2007). However, studies have found that this group has similar forms of psychiatric comorbidity, neurocognitive impairment, and familial transmission as the group with a confirmed diagnosis, only differing on the childhood onset requirement of the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) (Faraone et al., 2006; Faraone et al., 2006). Furthermore, because SUD often emerges in adolescence, the apparent late onset of ADHD may reflect the onset of SUD rather than ADHD, and although subthreshold ADHD may be a milder form of the disorder (Norén Selinus et al., 2016), it could also reflect nonspecific risk characteristics for SUD rather than symptoms of ADHD (Faraone et al., 2006). Taken together, this means that improvement of SUD symptoms may also lead to an improvement of problems associated with ADHD symptoms.

The present study investigates how 12 months of sobriety following the onset of treatment affects the presence of self-reported ADHD symptoms in a clinical sample of polysubstance users. Polysubstance use disorder is frequent in clinical SUD samples (Andrade, Carroll, & Petry, 2013). Comorbid ADHD place patients with SUD at risk of impaired recovery, with longer duration of substance use and slower remission rate (Wilens et al., 1998).

To our knowledge, this is the first study to report changes in self-reported ADHD symptoms in people with polysubstance use disorder during the 12-month period after initiation of treatment. Using a prospective design and a control group, we addressed the following question: Will individuals with polysubstance use disorder who remain abstinent for one-year show a greater improvement in ADHD symptoms compared with those who relapsed and controls?

## 2. Material and methods

### 2.1. Participants

One hundred and fifty SUD patients were recruited from 10 outpatient and residential treatment facilities within the Stavanger University Hospital catchment area (Norway) between March 2012 and May 2013. We employed broad inclusion criteria focusing on polysubstance use disorder because it is common in clinical settings (Badiani, Belin, Epstein, Calu, & Shaham, 2011; Stavro, Pelletier, & Potvin, 2013). The main inclusion criteria at baseline were: (a) evidence of SUD with polysubstance use, operationalized as the use of more than one drug on a single occasion, or a history of abusing multiple drugs; (b) enrolled in a new treatment sequence by the substance use treatment service; and (c) at least 16 years of age. At baseline, 22 patients were excluded because they did not meet the inclusion criteria (four had no substance use addiction and 18 did not report polysubstance use), leaving 128 patients in the study.

The control group ( $N = 38$ ) was a convenience sample recruited by posters exhibited at social welfare and GP offices. Controls and SUD patients were compensated with NOK 400 (~USD 50) for the baseline testing. During the one-year follow-up period, 13 SUD patients and four people from the control group withdrew or dropped out of the study.

The final group included 115 SUD patients and 34 controls. The retention rate was 89.8% for patients and 89.5% for controls. This study was reviewed and approved by the Regional Ethical Committee (REK 2011/1877) and conducted according to its guidelines and those of the Helsinki Declaration (1975). Written informed consent was obtained from all participants.

### 2.2. Procedures

The study is part of a prospective cohort study of a sample of SUD patients in the Stavanger University Hospital catchment area. To minimize contamination from drug withdrawal and the acute neurotoxic effects of psychoactive substances, baseline assessment was performed after two weeks of abstinence (Miller, 1985) by experienced and trained staff. Information on substance use was assessed using the Alcohol Use Disorders Identification Test (AUDIT) (Bohn, Babor, & Kranzler, 1995) and the Drug Use Disorders Identification Test (DUDIT) (Voluse et al., 2012). At the one-year follow-up, patients were defined as relapsing to a significant level of use if they had an AUDIT score  $\geq 8$ , or a DUDIT score  $\geq 2$  for women and  $\geq 6$  for men (Bohn et al., 1995; Voluse et al., 2012).

### 2.3. Adult ADHD self-report scale (ASRS)

The ASRS is a frequently used screening instrument for ADHD (Kessler et al., 2005). It is composed of 18 items that reflect the symptoms used to define ADHD according to the fifth edition of the Diagnostic and statistical manual of mental disorders (DSM-V) (Association, 2013). The results from this scale assess the presence of ADHD symptoms, but on its own, it is not an adequate diagnostic tool.

Symptoms are rated on a 5-point Likert-type scale (0–4 = never, rarely, sometimes, often, and very often), with a range of 0 to 72 for the 18-item instrument. This instrument has previously been validated in SUD populations (Dakwar et al., 2012; Van de Glind et al., 2013).

In the present study, we included a sum score across all the 18 ASRS items, a sum score for the ASRS items that assess inattention (items 1–4 and 7–11), and a sum score for the items that assess hyperactivity/impulsivity (items 5, 6, and 12–18).

In order to highlight the severity of individual items in the ASRS, we dichotomized responses to the ASRS items into “severe/not severe” according to recommendations by Kessler et al. (Kessler et al., 2005). Lastly, we used the “severe/not severe” dichotomized items to identify clinically significant ASRS profiles. The ASRS profile was dichotomized as “clinically significant” if  $\geq 9$  items were dichotomized as “severe”, and “not clinically significant” if  $< 9$  items were dichotomized as “severe”. This method is commonly used in clinical practice, and in line with the original recommendations by Kessler et al. (Kessler et al., 2005).

### 2.4. Statistical analyses

All analyses were performed using IBM SPSS v24 for Mac. Two-tailed  $p$ -values  $< 0.05$  were considered statistically significant. Data were assessed for normality with histograms, Q-Q plots, Kolmogorov-Smirnov tests, and Shapiro-Wilk tests. Visual inspection of histograms and Q-Q-plots revealed that ASRS-scores at baseline and 1 year follow up did not deviate from normality. This was also evident from the Kolmogorov-Smirnov test ( $D_{(149)} = 0.05$ ,  $p = 0.200$ ; and 1 year  $D_{(149)} = 0.06$ ,  $p = 0.200$ , respectively) and Shapiro-Wilk test (baseline  $W_{(149)} = 0.99$ ,  $p = 0.651$ ; and 1 year  $W_{(149)} = 0.99$ ,  $p = 0.327$ ). Sub-analysis of normality for each participant group yielded similar results (data not shown). As the data was normally distributed, parametric statistics were used throughout. The statistical procedures of the demographic variables have been published in a previous paper (Hagen et al., 2017).

Mixed ANOVA was used to compare changes in abstainers,

relapsers, and controls from baseline to the one-year follow-up. Variables for which one group's responses differed from those of the other two groups were expected to show a significant interaction. To determine the cause of interaction effects, a paired samples *t*-test was used to evaluate mean change from baseline to one-year within each group. Effect sizes were calculated as Cohen's *d* for paired samples and parametric data, where 0.5 was considered a medium effect and 0.8 was considered a large effect (Cohen, 1988). Main effects were not interpreted in the presence of a statistically significant interaction (Bordens & Abbott, 2002).

Lastly, the frequency of individual items dichotomized as severe was estimated for each group (i.e., abstinent, relapsed, and control), and changes in frequency during the one-year follow-up were investigated for each item using a repeated measures ANOVA. As multiple comparisons were made, Bonferroni adjusted *P*-values ( $0.05/18 = 0.003$ ) were used to establish statistical significance.

### 3. Results

#### 3.1. Group characteristics

We presented data for the clinical and demographic variables for patients who remained abstinent for a year (*N* = 51), patients who relapsed (*N* = 64), and controls (*N* = 34) in a previous paper (Hagen et al., 2017). In short, patients and controls did not differ in age, but controls were more often female (44% vs. 33%) and had a higher mean level of education (14.2 vs. 11.8 years) and a higher mean IQ score (105.5 vs. 98.2) at baseline. Three patients and five controls were < 18 years of age at the time of inclusion. Although there were no differences in baseline demographic variables between the two SUD groups, the abstinent group obtained a higher mean WASI IQ score (100.7 vs. 95.8). As measured by the mean AUDIT/DUDIT score, baseline levels of substance abuse did not differ between the two SUD groups.

#### 3.2. ASRS total score

At baseline, there was a significant difference ( $t = 6.4, p < 0.001$ ) in ASRS total score between patients ( $m = 34.7, SD = 10.7$ ) and controls ( $m = 21.2, SD = 11.4$ ). At baseline, patients who relapsed during the follow-up period had a higher ASRS total score than patients who remained abstinent, but this difference was not statistically significant (Table 1). Repeated measures ANOVA showed a significant effect of group [ $F(2,146) = 18.0, p < 0.001$ ] and time [ $F(1,146) = 25.7, p < 0.001$ ], and a significant group  $\times$  time interaction [ $F(2,146)$

**Table 1**  
ASRS scores at baseline and one-year follow-up.

	Abstinent group ( <i>N</i> = 51)		Relapse group ( <i>N</i> = 64)		Control group ( <i>N</i> = 34)	
	Baseline	1 year <sup>a</sup>	Baseline	1 year <sup>a</sup>	Baseline	1 year <sup>a</sup>
ASRS Part 1:	18.5	12.4	18.7	16.8	10.6	10.6
inattention	(6.8)	(8.0)***	(6.3)	(6.0)*	(6.1)	(6.2)
ASRS Part 2:	15.5	10.8	16.5	14.7	10.8	10.3
hyperactivity	(6.5)*	(7.4)***	(5.5)	(5.8)*	(5.2)	(5.3)
ASRS Total score <sup>b</sup>	34.0	23.3	35.6	31.6	21.2	21.0
	(11.8)	(14.4)	(9.6)	(9.6)	(11.4)	(9.3)
	[18]	[9]***	[25]	[19]*	[3]	[2]

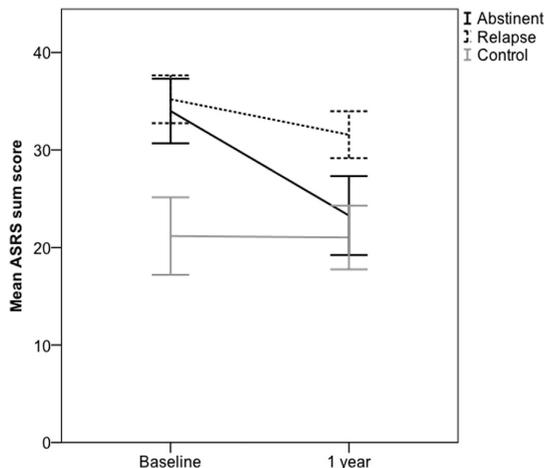
All data are means (SD).

<sup>a</sup> Results of paired samples *t*-test. This measures improvement in mean score from baseline to one-year later within the group.

<sup>b</sup> Number with clinical score is indicated by [N].

\*  $p < 0.05$ .

\*\*\*  $p < 0.001$ .



**Fig. 1.** Mean ASRS sum score for each group at baseline and one-year follow up. Footnote: Changes in mean ASRS sum score from baseline to one-year for each group. Standard deviation indicated by error bars.

= 10.2,  $p < 0.001$ ] (illustrated in Fig. 1). Follow-up analyses showed that the interaction could be attributed to the significant alleviation of ADHD symptoms in the abstinent group ( $t = 5.5, p < 0.001$ ), with a large effect size ( $d = 0.82$ ), and significant symptom improvement in the relapse group ( $t = 2.4, p = 0.017$ ), with a moderate effect size ( $d = 0.37$ ). In the control group, the ASRS total score did not change from baseline to one year later ( $m = 21.2, SD = 11.4$  vs.  $m = 21.0, SD = 9.4$ ). At both time-points, the total score in the control group was slightly lower than that at follow-up in the SUD patients who were abstinent ( $m = 23.3, SD = 14.4$ ), and considerably lower compared with those who relapsed ( $m = 31.6, SD = 9.6$ ).

#### 3.3. Inattention symptoms

At baseline, there was a significant difference ( $t = 6.4, p < 0.001$ ) in inattention symptoms between patients ( $m = 18.6, SD = 6.4$ ) and controls ( $m = 10.6, SD = 6.1$ ). The patient groups (abstained and relapsed) did not differ at baseline on the ASRS inattention subscale. Repeated measures ANOVA showed significant main effects of group [ $F(2,146) = 18.0, p < 0.001$ ] and time [ $F(1,146) = 21.1, p < 0.001$ ], and a significant group  $\times$  time interaction [ $F(2,146) = 10.2, p < 0.001$ ]. Follow-up analyses showed that the interaction could be attributed to the significant improvement in the abstinent group ( $t = 5.5, p < 0.001$ ), with a medium to large effect size ( $d = 0.82$ ), and a significant improvement in the relapse group ( $t = 2.3, p = 0.025$ ), with a small effect size ( $d = 0.31$ ). The ASRS inattention score in the control group did not change over time.

#### 3.4. Hyperactivity-impulsivity symptoms

At baseline, there was a significant mean difference ( $t = 6.4, p < 0.001$ ) between patients ( $m = 16.1, SD = 5.9$ ) and controls ( $m = 10.6, SD = 6.2$ ) on the ASRS hyperactivity/impulsivity subscale. The patient groups did not differ on this score at baseline, but the repeated measures ANOVA showed significant main effects for group [ $F(2,145) = 10.8, p < 0.001$ ] and time [ $F(1,145) = 17.9, p < 0.001$ ], and a significant group  $\times$  time interaction [ $F(2,145) = 5.4, p = 0.006$ ]. Follow-up analyses showed that the interaction could be attributed to significant improvement in the abstinent group ( $t = 4.5, p < 0.001$ ), with a moderate effect size ( $d = 0.66$ ), and significant improvement in

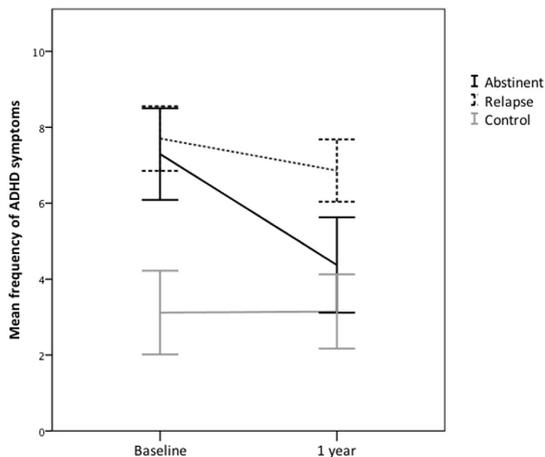


Fig. 2. Mean frequency of severe ADHD symptoms (in total) for each group. Footnote: Changes in frequency of severe ADHD symptoms from baseline to one-year for each group.

the relapse group ( $t = 2.4$ ,  $p = 0.021$ ), with a small effect size ( $d = 0.31$ ). The change in the hyperactivity-impulsivity subscale was not statistically significant for the control group.

### 3.5. ASRS scores indicating severe ADHD symptoms

The frequencies of number of severe ADHD symptoms (in total) for each group are presented in Fig. 2. Overall, patients reported a significantly higher number of severe symptoms than controls at baseline ( $t = 6.1$ ,  $p < 0.001$ ). The frequency of severe symptoms did not differ between the two patient groups at baseline ( $t = 0.6$ ,  $p = 0.570$ ). The abstinent group demonstrated a significant decrease ( $t = 4.4$ ,  $p < 0.001$ ) in severe symptoms from baseline ( $m = 7.3$ ,  $SD = 4.3$ ) to 1 year ( $m = 4.3$ ,  $SD = 4.5$ ), whereas the changes in the relapse group ( $t = 2.0$ ,  $p = 0.054$ ) and the control group ( $t = -0.1$ ,  $p = 0.937$ ) were not statistically significant.

The percentages of severe symptoms are presented for each group on each ASRS item in Table 2. The control group had no statistically significant change from baseline on any items of the ASRS. The relapse group had significant change on two symptoms, but these did not withstand Bonferroni correction for multiple comparisons. For the abstinent group, eight items demonstrated a significant improvement from baseline to the one-year follow-up, but only three items were considered statistically significant following Bonferroni correction: Item 8: sustained attention ( $F[1, 50] = 14.8$ ,  $p < 0.001$ ), Item 9: concentration when listening ( $F[1, 50] = 24.3$ ,  $p < 0.001$ ), and Item 13: Restlessness ( $F[1, 50] < 27.3$ ,  $p < 0.001$ ).

## 4. Discussion

This study compared patients with polysubstance use disorder who remained abstinent, patients who relapsed, and healthy controls on changes in self-reported ADHD symptoms from baseline to follow-up assessment one year later. The abstinent group showed a substantial reduction of ADHD symptoms compared with the relapse and control groups. In fact, the scores of the abstinent group at follow-up were only slightly higher than those of the healthy controls, who were in the normal range for ADHD symptoms at both baseline and follow-up. The improvements in the abstinence group were particularly prominent on the ASRS items that reflect problems related to sustained attention, concentration, and restlessness.

### 4.1. Improvement of self-reported ADHD symptoms

SUD complicates diagnostic procedures and accuracy for patients with comorbid ADHD symptoms of hyperactivity, impulsivity, and inattention. These symptoms are, however, not restricted to individuals with an ADHD diagnosis. Patients with SUD can develop impulsivity and hyperactivity, and have difficulty with attention as a result of the neurotoxic effects of the drugs that they use and the lifestyle associated with SUD (Yuan et al., 2009). Impulsivity and executive dysfunctions have been associated with almost all stages of SUD (Stevens et al., 2014), as individuals with these characteristics have an increased probability of starting to use drugs, more destructive intensification of use, and more relapses after treatment (Jentsch, 2009; Robbins, Gillan, Smith, de Wit, & Ersche, 2012; Winstanley, Olausson, Taylor, & Jentsch, 2010).

Systematic use of screening tools to identify ADHD in childhood is rare, which creates a risk of leaving cases undetected (Wilens et al., 2011). If these individuals later develop SUD, their attentional and impulsivity problems may be addressed for the first time as part of the initial diagnostic work in the SUD. Our findings suggest that active SUD and the associated lifestyle could account for some of the problems related to sustained attention, concentration, and restlessness, as these ADHD symptoms were substantially reduced in our clinical sample after one year of abstinence. The clinical importance of this result is strengthened by previous studies with the same cohort that have demonstrated improved executive functions, increased satisfaction with life, and reduced psychological distress (Hagen et al., 2017). Thus, our findings support the recommendation from previous research that there should be a “treatment hierarchy” that begins with treatment of the most prominent SUD symptoms and stabilization of the drug addiction (Wilens, 2004).

The reduction in ADHD symptoms in the two polysubstance use disorder groups in this study was compelling. The abstinence group showed a more profound reduction in severe ADHD symptoms, but the relapse group also showed some improvements. It is possible that, on average, SUD treatment improves ADHD symptomatology because it introduces a period of stability and reduces substance use. Several psychosocial treatments are recommended for SUD and comorbid mental disorders, including motivational interviewing, cognitive-behavioral therapy, contingency management, relapse prevention, case management, and social skills training (Horsfall, Cleary, Hunt, & Walter, 2009). To make behavioral changes, these treatments for SUD require cognitive processing and learning abilities (Roehrich & Goldman, 1993). This could involve learning about program rules, treatment philosophy, and the negative effects of different drugs (Grohman & Fals-Stewart, 2003), all of which represent a substantial learning requirement at the onset of therapy. However, the present results suggest that a slow, careful, stepwise approach to learning requirements should be adopted in treatment, one that initially focuses on stabilizing the patient, providing structure, and supporting abstinence from substance use.

Diagnosing ADHD with active SUD is challenging. The risk of false-positive ADHD diagnoses in patients assessed by ASRS has been reported (Lugoboni et al., 2017; Roncero et al., 2015). Thus, our finding is a reminder that a period of abstinence, preferably evident by urine tests or other means of substance monitoring, should be in place before providing conclusions regarding an ADHD diagnosis.

### 4.2. Strengths and limitations

Many studies in this field have used cross-sectional designs (van Holst & Schilt, 2011), and thus they were unable to track longitudinal changes. We used a prospective design for the patient and control groups, which allowed us to monitor possible training effects through repeated testing and reports on the same questionnaires (Schulte et al., 2014). However, there was a significant difference in years of

**Table 2**  
Percentage of severe scores on ASRS items at the one-year follow-up.

ASRS items	Abstinent group (N = 51)		Relapse group (N = 64)		Control group (N = 34)		
	Baseline % <sup>a</sup>	1 year %	Baseline % <sup>a</sup>	1 year %	Baseline % <sup>a</sup>	1 year %	
<b>Part 1 Inattention</b>							
1	Finishing	33.3	21.6	37.5	34.4	5.9	8.8
2	Organization	25.5	13.7	29.7*	14.1	2.9	2.9
3	Remembering	52.9 <sup>a</sup>	33.3	54.7	59.4	8.8	17.6
4	Initiation	70.6 <sup>a</sup>	51.0	76.6	71.9	26.5	38.2
7	Careless	33.3 <sup>a</sup>	13.7	29.7	21.9	11.8	14.7
8	Attention	52.9 <sup>***b</sup>	21.6	53.1	42.2	23.5	11.8
9	Listening	70.6 <sup>***b</sup>	31.4	64.1	62.5	23.5	20.6
10	Finding things	21.6	17.6	23.4	25.0	2.9	2.9
11	Easily distracted	68.6 <sup>**</sup>	45.1	76.6	67.2	38.2	47.1
<b>Part 2 Hyperactivity</b>							
5	Fidgets	76.5	62.7	89.1 <sup>a</sup>	75.0	61.8	58.8
6	Overactive	29.4	21.6	28.1	26.6	26.5	11.8
12	Staying seated	3.9	0.0	10.9	4.7	0.0	0.0
13	Restless	58.8 <sup>***b</sup>	23.5	59.4	53.1	14.7	8.8
14	Relaxing	35.3	27.5	34.4	35.9	11.8	11.8
15	Talks excessively	21.6 <sup>**</sup>	5.9	23.4	23.4	11.8	14.7
16	Blurts out answers	45.1	41.2	46.9	48.4	32.4	35.3
17	Waiting turn	17.6	9.8	21.9	14.1	2.9	8.8
18	Interrupts	11.8	5.9	10.9	6.25	2.9	2.9

% = percentage of participants with self-reported severe symptoms within this group. ASRS, Adult ADHD Self-Report Scale.

<sup>a</sup> Comparison between baseline and one-year follow-up.

<sup>b</sup> Significant after Bonferroni correction.

\*  $p < 0.05$ .

\*\*  $p < 0.01$ .

\*\*\*  $p < 0.001$ .

education, gender, and work experience between the patients and controls. Regarding education, all Norwegian citizens receive compulsory education from 5 to 16 years of age. Hence, it was difficult to recruit age-matched participants with fewer than 10 years of education who did not use drugs.

The present study has several other limitations. First, the patients in the relapse and abstinence groups were self-selected (based on their self-reports), and time-sensitive variables that we did not assess may have influenced our outcome variables. Thus, we cannot conclude that the differences in the outcomes observed at 12 months were only caused by changes in substance use status. Furthermore, we only assessed ADHD symptoms at baseline and one-year follow-up; therefore, we cannot determine when the abstinence group's improvements in ADHD symptoms occurred during the follow-up period. In addition, the assessment of ADHD symptoms with ASRS does not constitute a full diagnostic procedure. Without historical anamnestic data in our study, it is difficult to suggest whether the alleviation of symptoms only applies to a subthreshold group of patients or if it is also associated with late-onset ADHD diagnosis.

Future research should include longitudinal prospective cohort studies with repeated measures of the trajectories of ADHD symptomatology in SUD patients. The presence or absence of ADHD should be assessed at baseline or collected from hospital journal data whenever possible. Cohort studies assessing ADHD in childhood, focusing on the participants developing SUD later in the trajectory, could provide valuable information and possibly explain the mechanism behind the findings presented here.

## 5. Conclusions

To our knowledge, this is the first study to report improvement of ADHD symptoms for people with polysubstance use disorder during a 12-month treatment sequence. Our data suggest that there is a clinically (as well as a statistically) significant reduction in self-reported ADHD symptoms for SUD patients following one year of abstinence. This is useful knowledge for patients suffering from comorbid SUD and ADHD,

as well as for clinicians. Our finding is a reminder that the assessment of ADHD should follow a period of abstinence to avoid false-positive ADHD diagnoses. Instead of focusing on ADHD as a persistent disorder, treatment should focus on how supporting stable abstinence may reduce ADHD-like symptoms.

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<b>Region:</b>	<b>Saksbehandler:</b>	<b>Telefon:</b>	<b>Vår dato:</b>	<b>Vår referanse:</b>
REK vest	Arne Salbu	55978498	01.12.2011	2011/1877/REK Vest
			<b>Deres dato:</b>	<b>Deres referanse:</b>
			09.11.2011	

Vår referanse må oppgis ved alle henvendelser

Egon Hagen  
Regionalt kompetansesenter for rusmiddelbruk i Helse Vest  
Lågardsveien 78  
4010 STAVANGER

### **2011/1877: nevropsykologiske endringsprosesser ved rusmiddelbruk**

Vi viser til ditt e-brev datert 09.11.11 med svar på komiteens merknader.

Først vil vi påpeke at en skal bruke det fastsatte skjema for tilbakemelding i slike saker. REK Vest har likevel behandlet saken.

Saken er vurdert på nytt av komiteens leder.

Med unntak av punktet om bruk av SMS i kontakten med deltakerne, har REK Vest ikke ytterligere merknader eller spørsmål.

Når det gjelder bruk av SMS så er det mer problematisk. SMS er en *usikret kanal* og man kan ikke vite verken hvem som sender eller mottar meldinger. For REK Vest, er det uakseptabelt at helseopplysninger (se definisjon i Helseforskningsloven § 4d) formidles via SMS i og med at denne løsningen ikke utgjør en forsvarlig sikring av helseopplysninger. I praksis betyr dette at REK Vest godkjenner at en bruker SMS til å tilpasse avtaler og møtetidspunkt men at REK avslår ønsket om å bruke SMS til "å få et dynamisk tilstandsbilde på rusbruk og hvorvidt vedkommende er i eller utenfor behandling", i den grad dette innebærer utveksling av helseopplysninger/taushetsbelagte opplysninger. REK Vest har da også tatt i betraktning at det synes som om at det kun er deltaker som rapporterer til prosjektledelsen og ikke også motsatt vei, og mener dette ikke likevel ikke er akseptabelt da en ikke har garantier for hvem som faktisk rapporterer.

#### **Vedtak:**

*Prosjektet godkjennes på betingelse av at ovennevnte villkår tas til følge.*

REKs vedtak kan påklages til Den nasjonale forskningsetiske komité for medisin og helsefag, jfr. helseforskningsloven § 10, 3 ledd og forvaltningsloven § 28. En eventuell klage sendes til REK Vest. Klagefristen er tre uker fra mottak av dette brevet, jfr. forvaltningsloven § 29.

Med vennlig hilsen,

Jon Lekven (sign.)  
komitéleder/dr.med.

Arne Salbu  
rådgiver

**Kopi til:** sverre.martin.nesvaag@sus.no, bronnick@gmail.com, Astri.Lundervold@psybp.uib.no



**Doctoral Theses at The Faculty of Psychology,**  
**University of Bergen**

<b>1980</b>	Allen, H.M., Dr. philos.	Parent-offspring interactions in willow grouse ( <i>Lagopus L. Lagopus</i> ).
<b>1981</b>	Myhrer, T., Dr. philos.	Behavioral Studies after selective disruption of hippocampal inputs in albino rats.
<b>1982</b>	Svebak, S., Dr. philos.	The significance of motivation for task-induced tonic physiological changes.
<b>1983</b>	Myhre, G., Dr. philos.	The Biopsychology of behavior in captive Willow ptarmigan.
	Eide, R., Dr. philos.	PSYCHOSOCIAL FACTORS AND INDICES OF HEALTH RISKS. The relationship of psychosocial conditions to subjective complaints, arterial blood pressure, serum cholesterol, serum triglycerides and urinary catecholamines in middle aged populations in Western Norway.
	Værnes, R.J., Dr. philos.	Neuropsychological effects of diving.
<b>1984</b>	Kolstad, A., Dr. philos.	Til diskusjonen om sammenhengen mellom sosiale forhold og psykiske strukturer. En epidemiologisk undersøkelse blant barn og unge.
	Løberg, T., Dr. philos.	Neuropsychological assessment in alcohol dependence.
<b>1985</b>	Hellesnes, T., Dr. philos.	Læring og problemløsning. En studie av den perseptuelle analysens betydning for verbal læring.
	Håland, W., Dr. philos.	Psykoterapi: relasjon, utviklingsprosess og effekt.
<b>1986</b>	Hagtvet, K.A., Dr. philos.	The construct of test anxiety: Conceptual and methodological issues.
	Jellestad, F.K., Dr. philos.	Effects of neuron specific amygdala lesions on fear-motivated behavior in rats.
<b>1987</b>	Aarø, L.E., Dr. philos.	Health behaviour and socioeconomic Status. A survey among the adult population in Norway.
	Underlid, K., Dr. philos.	Arbeidsløse i psykososialt perspektiv.
	Laberg, J.C., Dr. philos.	Expectancy and classical conditioning in alcoholics' craving.
	Vollmer, F.C., Dr. philos.	Essays on explanation in psychology.
	Ellertsen, B., Dr. philos.	Migraine and tension headache: Psychophysiology, personality and therapy.
<b>1988</b>	Kaufmann, A., Dr. philos.	Antisocial atferd hos ungdom. En studie av psykologiske determinanter.

	Mykletun, R.J., Dr. philos.	Teacher stress: personality, work-load and health.
	Havik, O.E., Dr. philos.	After the myocardial infarction: A medical and psychological study with special emphasis on perceived illness.
<b>1989</b>	Bråten, S., Dr. philos.	Menneskedyaden. En teoretisk tese om sinnets dialogiske natur med informasjons- og utviklingspsykologiske implikasjoner sammenholdt med utvalgte spedbarnsstudier.
	Wold, B., Dr. psychol.	Lifestyles and physical activity. A theoretical and empirical analysis of socialization among children and adolescents.
<b>1990</b>	Flaten, M.A., Dr. psychol.	The role of habituation and learning in reflex modification.
<b>1991</b>	Alsaker, F.D., Dr. philos.	Global negative self-evaluations in early adolescence.
	Kraft, P., Dr. philos.	AIDS prevention in Norway. Empirical studies on diffusion of knowledge, public opinion, and sexual behaviour.
	Endresen, I.M., Dr. philos.	Psychoimmunological stress markers in working life.
	Faleide, A.O., Dr. philos.	Asthma and allergy in childhood. Psychosocial and psychotherapeutic problems.
<b>1992</b>	Dalen, K., Dr. philos.	Hemispheric asymmetry and the Dual-Task Paradigm: An experimental approach.
	Bø, I.B., Dr. philos.	Ungdoms sosiale økologi. En undersøkelse av 14-16 åringers sosiale nettverk.
	Nivison, M.E., Dr. philos.	The relationship between noise as an experimental and environmental stressor, physiological changes and psychological factors.
	Torgersen, A.M., Dr. philos.	Genetic and environmental influence on temperamental behaviour. A longitudinal study of twins from infancy to adolescence.
<b>1993</b>	Larsen, S., Dr. philos.	Cultural background and problem drinking.
	Nordhus, I.H., Dr. philos.	Family caregiving. A community psychological study with special emphasis on clinical interventions.
	Thuen, F., Dr. psychol.	Accident-related behaviour among children and young adolescents: Prediction and prevention.
	Solheim, R., Dr. philos.	Spesifikke lærevansker. Diskrepanskriteriet anvendt i seleksjonsmetodikk.
	Johnsen, B.H., Dr. psychol.	Brain asymmetry and facial emotional expressions: Conditioning experiments.
<b>1994</b>	Tønnessen, F.E., Dr. philos.	The etiology of Dyslexia.
	Kvale, G., Dr. psychol.	Psychological factors in anticipatory nausea and vomiting in cancer chemotherapy.

	Asbjørnsen, A.E., Dr. psychol.	Structural and dynamic factors in dichotic listening: An interactional model.
	Bru, E., Dr. philos.	The role of psychological factors in neck, shoulder and low back pain among female hospitale staff.
	Braathen, E.T., Dr. psychol.	Prediction of excellence and discontinuation in different types of sport: The significance of motivation and EMG.
	Johannessen, B.F., Dr. philos.	Det flytende kjønnnet. Om lederskap, politikk og identitet.
<b>1995</b>	Sam, D.L., Dr. psychol.	Acculturation of young immigrants in Norway: A psychological and socio-cultural adaptation.
	Bjaalid, I.-K., Dr. philos	Component processes in word recognition.
	Martinsen, Ø., Dr. philos.	Cognitive style and insight.
	Nordby, H., Dr. philos.	Processing of auditory deviant events: Mismatch negativity of event-related brain potentials.
	Raaheim, A., Dr. philos.	Health perception and health behaviour, theoretical considerations, empirical studies, and practical implications.
	Seltzer, W.J., Dr.philos.	Studies of Psychocultural Approach to Families in Therapy.
	Brun, W., Dr.philos.	Subjective conceptions of uncertainty and risk.
	Aas, H.N., Dr. psychol.	Alcohol expectancies and socialization: Adolescents learning to drink.
	Bjørkly, S., Dr. psychol.	Diagnosis and prediction of intra-institutional aggressive behaviour in psychotic patients
<b>1996</b>	Anderssen, Norman, Dr. psychol.	Physical activity of young people in a health perspective: Stability, change and social influences.
	Sandal, Gro Mjeldheim, Dr. psychol.	Coping in extreme environments: The role of personality.
	Strumse, Einar, Dr. philos.	The psychology of aesthetics: explaining visual preferences for agrarian landscapes in Western Norway.
	Hestad, Knut, Dr. philos.	Neuropsychological deficits in HIV-1 infection.
	Lugoe, L.Wycliffe, Dr. philos.	Prediction of Tanzanian students' HIV risk and preventive behaviours
	Sandvik, B. Gunnhild, Dr. philos.	Fra distriktsjordmor til institusjonsjordmor. Fremveksten av en profesjon og en profesjonsutdanning
	Lie, Gro Therese, Dr. psychol.	The disease that dares not speak its name: Studies on factors of importance for coping with HIV/AIDS in Northern Tanzania
	Øygard, Lisbet, Dr. philos.	Health behaviors among young adults. A psychological and sociological approach
	Stormark, Kjell Morten, Dr. psychol.	Emotional modulation of selective attention: Experimental and clinical evidence.

	Einarsen, Ståle, Dr. psychol.	Bullying and harassment at work: epidemiological and psychosocial aspects.
<b>1997</b>	Knivsberg, Ann-Mari, Dr. philos.	Behavioural abnormalities and childhood psychopathology: Urinary peptide patterns as a potential tool in diagnosis and remediation.
	Eide, Arne H., Dr. philos.	Adolescent drug use in Zimbabwe. Cultural orientation in a global-local perspective and use of psychoactive substances among secondary school students.
	Sørensen, Marit, Dr. philos.	The psychology of initiating and maintaining exercise and diet behaviour.
	Skjæveland, Oddvar, Dr. psychol.	Relationships between spatial-physical neighborhood attributes and social relations among neighbors.
	Zewdie, Teka, Dr. philos.	Mother-child relational patterns in Ethiopia. Issues of developmental theories and intervention programs.
	Wilhelmsen, Britt Unni, Dr. philos.	Development and evaluation of two educational programmes designed to prevent alcohol use among adolescents.
	Manger, Terje, Dr. philos.	Gender differences in mathematical achievement among Norwegian elementary school students.
<b>1998</b>	Lindstrøm, Torill Christine, Dr. philos.	«Good Grief»: Adapting to Bereavement.
<b>V</b>	Skogstad, Anders, Dr. philos.	Effects of leadership behaviour on job satisfaction, health and efficiency.
	Haldorsen, Ellen M. Håland, Dr. psychol.	Return to work in low back pain patients.
	Besemer, Susan P., Dr. philos.	Creative Product Analysis: The Search for a Valid Model for Understanding Creativity in Products.
<b>H</b>	Winje, Dagfinn, Dr. psychol.	Psychological adjustment after severe trauma. A longitudinal study of adults' and children's posttraumatic reactions and coping after the bus accident in Måbødalen, Norway 1988.
	Vosburg, Suzanne K., Dr. philos.	The effects of mood on creative problem solving.
	Eriksen, Hege R., Dr. philos.	Stress and coping: Does it really matter for subjective health complaints?
	Jakobsen, Reidar, Dr. psychol.	Empiriske studier av kunnskap og holdninger om hiv/aids og den normative seksuelle utvikling i ungdomsårene.
<b>1999</b>	Mikkelsen, Aslaug, Dr. philos.	Effects of learning opportunities and learning climate on occupational health.
<b>V</b>	Samdal, Oddrun, Dr. philos.	The school environment as a risk or resource for students' health-related behaviours and subjective well-being.
	Friestad, Christine, Dr. philos.	Social psychological approaches to smoking.
	Ekeland, Tor-Johan, Dr. philos.	Meining som medisin. Ein analyse av placebofenomenet og implikasjoner for terapi og terapeutiske teoriar.

<b>H</b>	Saban, Sara, Dr. psychol.	Brain Asymmetry and Attention: Classical Conditioning Experiments.
	Carlsten, Carl Thomas, Dr. philos.	God lesing – God læring. En aksjonsrettet studie av undervisning i fagtekstlesing.
	Dundas, Ingrid, Dr. psychol.	Functional and dysfunctional closeness. Family interaction and children's adjustment.
	Engen, Liv, Dr. philos.	Kartlegging av leseferdighet på småskoletrinnet og vurdering av faktorer som kan være av betydning for optimal leseutvikling.
<b>2000 V</b>	Hovland, Ole Johan, Dr. philos.	Transforming a self-preserving "alarm" reaction into a self-defeating emotional response: Toward an integrative approach to anxiety as a human phenomenon.
	Lillejord, Sølvi, Dr. philos.	Handlingsrasjonalitet og spesialundervisning. En analyse av aktørperspektiver.
	Sandell, Ove, Dr. philos.	Den varme kunnskapen.
	Oftedal, Marit Petersen, Dr. philos.	Diagnostisering av ordavkodingsvansker: En prosessanalytisk tilnæringsmåte.
<b>H</b>	Sandbak, Tone, Dr. psychol.	Alcohol consumption and preference in the rat: The significance of individual differences and relationships to stress pathology
	Eid, Jarle, Dr. psychol.	Early predictors of PTSD symptom reporting; The significance of contextual and individual factors.
<b>2001 V</b>	Skinstad, Anne Helene, Dr. philos.	Substance dependence and borderline personality disorders.
	Binder, Per-Einar, Dr. psychol.	Individet og den meningsbærende andre. En teoretisk undersøkelse av de mellommenneskelige forutsetningene for psykisk liv og utvikling med utgangspunkt i Donald Winnicotts teori.
	Roald, Ingvild K., Dr. philos.	Building of concepts. A study of Physics concepts of Norwegian deaf students.
<b>H</b>	Fekadu, Zelalem W., Dr. philos.	Predicting contraceptive use and intention among a sample of adolescent girls. An application of the theory of planned behaviour in Ethiopian context.
	Melesse, Fantu, Dr. philos.	The more intelligent and sensitive child (MISC) mediational intervention in an Ethiopian context: An evaluation study.
	Råheim, Målfrid, Dr. philos.	Kvinneres kroppserfaring og livssammenheng. En fenomenologisk – hermeneutisk studie av friske kvinner og kvinner med kroniske muskelsmerter.
	Engelsen, Birthe Kari, Dr. psychol.	Measurement of the eating problem construct.
	Lau, Bjørn, Dr. philos.	Weight and eating concerns in adolescence.
<b>2002 V</b>	Ihlebak, Camilla, Dr. philos.	Epidemiological studies of subjective health complaints.

	Rosén, Gunnar O. R., Dr. philos.	The phantom limb experience. Models for understanding and treatment of pain with hypnosis.
	Høines, Marit Johnsen, Dr. philos.	Fleksible språkrom. Matematikklæring som tekstutvikling.
	Anthun, Roald Andor, Dr. philos.	School psychology service quality. Consumer appraisal, quality dimensions, and collaborative improvement potential
	Pallesen, Ståle, Dr. psychol.	Insomnia in the elderly. Epidemiology, psychological characteristics and treatment.
	Midthassel, Unni Vere, Dr. philos.	Teacher involvement in school development activity. A study of teachers in Norwegian compulsory schools
	Kallestad, Jan Helge, Dr. philos.	Teachers, schools and implementation of the Olweus Bullying Prevention Program.
<b>H</b>	Ofte, Sonja Helgesen, Dr. psychol.	Right-left discrimination in adults and children.
	Netland, Marit, Dr. psychol.	Exposure to political violence. The need to estimate our estimations.
	Diseth, Åge, Dr. psychol.	Approaches to learning: Validity and prediction of academic performance.
	Bjuland, Raymond, Dr. philos.	Problem solving in geometry. Reasoning processes of student teachers working in small groups: A dialogical approach.
<b>2003</b> <b>V</b>	Arefjord, Kjersti, Dr. psychol.	After the myocardial infarction – the wives' view. Short- and long-term adjustment in wives of myocardial infarction patients.
	Ingjaldsson, Jón Þorvaldur, Dr. psychol.	Unconscious Processes and Vagal Activity in Alcohol Dependency.
	Holden, Børge, Dr. philos.	Følger av atferdsanalytiske forklaringer for atferdsanalysens tilnærming til utforming av behandling.
	Holsen, Ingrid, Dr. philos.	Depressed mood from adolescence to 'emerging adulthood'. Course and longitudinal influences of body image and parent-adolescent relationship.
	Hammar, Åsa Karin, Dr. psychol.	Major depression and cognitive dysfunction- An experimental study of the cognitive effort hypothesis.
	Sprugevica, Ieva, Dr. philos.	The impact of enabling skills on early reading acquisition.
	Gabrielsen, Egil, Dr. philos.	LESE FOR LIVET. Lesekompetansen i den norske voksenbefolkningen sett i lys av visjonen om en enhetsskole.
<b>H</b>	Hansen, Anita Lill, Dr. psychol.	The influence of heart rate variability in the regulation of attentional and memory processes.
	Dyregrov, Kari, Dr. philos.	The loss of child by suicide, SIDS, and accidents: Consequences, needs and provisions of help.
<b>2004</b> <b>V</b>	Torsheim, Torbjørn, Dr. psychol.	Student role strain and subjective health complaints: Individual, contextual, and longitudinal perspectives.

	Haugland, Bente Storm Mowatt Dr. psychol.	Parental alcohol abuse. Family functioning and child adjustment.
	Milde, Anne Marita, Dr. psychol.	Ulcerative colitis and the role of stress. Animal studies of psychobiological factors in relationship to experimentally induced colitis.
	Stornes, Tor, Dr. philos.	Socio-moral behaviour in sport. An investigation of perceptions of sportpersonship in handball related to important factors of socio-moral influence.
	Mæhle, Magne, Dr. philos.	Re-inventing the child in family therapy: An investigation of the relevance and applicability of theory and research in child development for family therapy involving children.
	Kobbeltvedt, Therese, Dr. psychol.	Risk and feelings: A field approach.
<b>2004</b>	Thomsen, Tormod, Dr. psychol.	Localization of attention in the brain.
<b>H</b>	Løberg, Else-Marie, Dr. psychol.	Functional laterality and attention modulation in schizophrenia: Effects of clinical variables.
	Kyrkjebø, Jane Mikkelsen, Dr. philos.	Learning to improve: Integrating continuous quality improvement learning into nursing education.
	Laumann, Karin, Dr. psychol.	Restorative and stress-reducing effects of natural environments: Experiential, behavioural and cardiovascular indices.
	Holgersen, Helge, PhD	Mellom oss - Essay i relasjonell psykoanalyse.
<b>2005</b>	Hetland, Hilde, Dr. psychol.	Leading to the extraordinary? Antecedents and outcomes of transformational leadership.
<b>V</b>	Iversen, Anette Christine, Dr. philos.	Social differences in health behaviour: the motivational role of perceived control and coping.
<b>2005</b>	Mathisen, Gro Ellen, PhD	Climates for creativity and innovation: Definitions, measurement, predictors and consequences.
<b>H</b>	Sævi, Tone, Dr. philos.	Seeing disability pedagogically – The lived experience of disability in the pedagogical encounter.
	Wiiium, Nora, PhD	Intrapersonal factors, family and school norms: combined and interactive influence on adolescent smoking behaviour.
	Kanagaratnam, Pushpa, PhD	Subjective and objective correlates of Posttraumatic Stress in immigrants/refugees exposed to political violence.
	Larsen, Torill M. B. , PhD	Evaluating principals` and teachers` implementation of Second Step. A case study of four Norwegian primary schools.
	Bancila, Delia, PhD	Psychosocial stress and distress among Romanian adolescents and adults.
<b>2006</b>	Hillestad, Torgeir Martin, Dr. philos.	Normalitet og avvik. Forutsetninger for et objektivt psykopatologisk avviksbegrep. En psykologisk, sosial, erkjennelsesteoretisk og teorihistorisk framstilling.
<b>V</b>		

	Nordanger, Dag Øystein, Dr. psychol.	Psychosocial discourses and responses to political violence in post-war Tigray, Ethiopia.
	Rimol, Lars Morten, PhD	Behavioral and fMRI studies of auditory laterality and speech sound processing.
	Krumsvik, Rune Johan, Dr. philos.	ICT in the school. ICT-initiated school development in lower secondary school.
	Norman, Elisabeth, Dr. psychol.	Gut feelings and unconscious thought: An exploration of fringe consciousness in implicit cognition.
	Israel, K Pravin, Dr. psychol.	Parent involvement in the mental health care of children and adolescents. Empirical studies from clinical care setting.
	Glasø, Lars, PhD	Affects and emotional regulation in leader-subordinate relationships.
	Knutsen, Ketil, Dr. philos.	HISTORIER UNGDOM LEVER – En studie av hvordan ungdommer bruker historie for å gjøre livet meningsfullt.
	Matthiesen, Stig Berge, PhD	Bullying at work. Antecedents and outcomes.
<b>2006</b>	Gramstad, Arne, PhD	Neuropsychological assessment of cognitive and emotional functioning in patients with epilepsy.
<b>H</b>	Bendixen, Mons, PhD	Antisocial behaviour in early adolescence: Methodological and substantive issues.
	Mrumbi, Khalifa Maulid, PhD	Parental illness and loss to HIV/AIDS as experienced by AIDS orphans aged between 12-17 years from Temeke District, Dar es Salaam, Tanzania: A study of the children's psychosocial health and coping responses.
	Hetland, Jørn, Dr. psychol.	The nature of subjective health complaints in adolescence: Dimensionality, stability, and psychosocial predictors
	Kakoko, Deodatus Conatus Vitalis, PhD	Voluntary HIV counselling and testing service uptake among primary school teachers in Mwanza, Tanzania: assessment of socio-demographic, psychosocial and socio-cognitive aspects
	Mykletun, Arnstein, Dr. psychol.	Mortality and work-related disability as long-term consequences of anxiety and depression: Historical cohort designs based on the HUNT-2 study
	Sivertsen, Børge, PhD	Insomnia in older adults. Consequences, assessment and treatment.
<b>2007</b>	Singhammer, John, Dr. philos.	Social conditions from before birth to early adulthood – the influence on health and health behaviour
<b>V</b>	Janvin, Carmen Ani Cristea, PhD	Cognitive impairment in patients with Parkinson's disease: profiles and implications for prognosis
	Braarud, Hanne Cecilie, Dr. psychol.	Infant regulation of distress: A longitudinal study of transactions between mothers and infants
	Tveito, Torill Helene, PhD	Sick Leave and Subjective Health Complaints

	Magnussen, Liv Heide, PhD	Returning disability pensioners with back pain to work
	Thuen, Elin Marie, Dr.philos.	Learning environment, students' coping styles and emotional and behavioural problems. A study of Norwegian secondary school students.
	Solberg, Ole Asbjørn, PhD	Peacekeeping warriors – A longitudinal study of Norwegian peacekeepers in Kosovo
<b>2007</b>	Søreide, Gunn Elisabeth, Dr.philos.	Narrative construction of teacher identity
<b>H</b>	Svensen, Erling, PhD	WORK & HEALTH. Cognitive Activation Theory of Stress applied in an organisational setting.
	Øverland, Simon Nygaard, PhD	Mental health and impairment in disability benefits. Studies applying linkages between health surveys and administrative registries.
	Eichele, Tom, PhD	Electrophysiological and Hemodynamic Correlates of Expectancy in Target Processing
	Børhaug, Kjetil, Dr.philos.	Oppseding til demokrati. Ein studie av politisk oppseding i norsk skule.
	Eikeland, Thorleif, Dr.philos.	Om å vokse opp på barnehjem og på sykehus. En undersøkelse av barnehjemsbarns opplevelser på barnehjem sammenholdt med sanatoriebarns beskrivelse av langvarige sykehusopphold – og et forsøk på forklaring.
	Wadel, Carl Cato, Dr.philos.	Medarbeidersamhandling og medarbeiderledelse i en lagbasert organisasjon
	Vinje, Hege Forbech, PhD	Thriving despite adversity: Job engagement and self-care among community nurses
	Noort, Maurits van den, PhD	Working memory capacity and foreign language acquisition
<b>2008</b>	Breivik, Kyrre, Dr.psychol.	The Adjustment of Children and Adolescents in Different Post-Divorce Family Structures. A Norwegian Study of Risks and Mechanisms.
<b>V</b>	Johnsen, Grethe E., PhD	Memory impairment in patients with posttraumatic stress disorder
	Sætrevik, Bjørn, PhD	Cognitive Control in Auditory Processing
	Carvalho, Susana Fonseca, PhD	Prevention of bullying in schools: an ecological model
<b>2008</b>	Brønnick, Kolbjørn Selvåg	Attentional dysfunction in dementia associated with Parkinson's disease.
<b>H</b>	Posserud, Maj-Britt Rocio	Epidemiology of autism spectrum disorders
	Haug, Ellen	Multilevel correlates of physical activity in the school setting
	Skjerve, Arvid	Assessing mild dementia – a study of brief cognitive tests.

	Kjønniksen, Lise	The association between adolescent experiences in physical activity and leisure time physical activity in adulthood: a ten year longitudinal study
	Gundersen, Hilde	The effects of alcohol and expectancy on brain function
	Omvik, Siri	Insomnia – a night and day problem
<b>2009 V</b>	Molde, Helge	Pathological gambling: prevalence, mechanisms and treatment outcome.
	Foss, Else	Den omsorgsfulle væremåte. En studie av voksnes væremåte i forhold til barn i barnehagen.
	Westrheim, Kariane	Education in a Political Context: A study of Knowledge Processes and Learning Sites in the PKK.
	Wehling, Eike	Cognitive and olfactory changes in aging
	Wangberg, Silje C.	Internet based interventions to support health behaviours: The role of self-efficacy.
	Nielsen, Morten B.	Methodological issues in research on workplace bullying. Operationalisations, measurements and samples.
	Sandu, Anca Larisa	MRI measures of brain volume and cortical complexity in clinical groups and during development.
	Guribye, Eugene	Refugees and mental health interventions
	Sørensen, Lin	Emotional problems in inattentive children – effects on cognitive control functions.
	Tjomsland, Hege E.	Health promotion with teachers. Evaluation of the Norwegian Network of Health Promoting Schools: Quantitative and qualitative analyses of predisposing, reinforcing and enabling conditions related to teacher participation and program sustainability.
	Helleve, Ingrid	Productive interactions in ICT supported communities of learners
<b>2009 H</b>	Skorpen, Aina Øye, Christine	Dagliglivet i en psykiatrisk institusjon: En analyse av miljøterapeutiske praksiser
	Andreassen, Cecilie Schou	WORKAHOLISM – Antecedents and Outcomes
	Stang, Ingun	Being in the same boat: An empowerment intervention in breast cancer self-help groups
	Sequeira, Sarah Dorothee Dos Santos	The effects of background noise on asymmetrical speech perception
	Kleiven, Jo, dr.philos.	The Lillehammer scales: Measuring common motives for vacation and leisure behavior
	Jónsdóttir, Guðrún	Dubito ergo sum? Ni jenter møter naturfaglig kunnskap.
	Hove, Oddbjørn	Mental health disorders in adults with intellectual disabilities - Methods of assessment and prevalence of mental health disorders and problem behaviour
	Wageningen, Heidi Karin van	The role of glutamate on brain function

	Bjørkvik, Jofrid	God nok? Selvaktelse og interpersonlig fungering hos pasienter innen psykisk helsevern: Forholdet til diagnoser, symptomer og behandlingsutbytte
	Andersson, Martin	A study of attention control in children and elderly using a forced-attention dichotic listening paradigm
	Almås, Aslaug Grov	Teachers in the Digital Network Society: Visions and Realities. A study of teachers' experiences with the use of ICT in teaching and learning.
	Ulvik, Marit	Lærerutdanning som danning? Tre stemmer i diskusjonen
<b>2010</b>	Skår, Randi	Læringsprosesser i sykepleieres profesjonsutøvelse. En studie av sykepleieres læringserfaringer.
<b>V</b>	Roald, Knut	Kvalitetsvurdering som organisasjonslæring mellom skole og skoleeigar
	Lunde, Linn-Heidi	Chronic pain in older adults. Consequences, assessment and treatment.
	Danielsen, Anne Grete	Perceived psychosocial support, students' self-reported academic initiative and perceived life satisfaction
	Hysing, Mari	Mental health in children with chronic illness
	Olsen, Olav Kjellevoid	Are good leaders moral leaders? The relationship between effective military operational leadership and morals
	Riese, Hanne	Friendship and learning. Entrepreneurship education through mini-enterprises.
	Holthe, Asle	Evaluating the implementation of the Norwegian guidelines for healthy school meals: A case study involving three secondary schools
<b>H</b>	Hauge, Lars Johan	Environmental antecedents of workplace bullying: A multi-design approach
	Bjørkelo, Brita	Whistleblowing at work: Antecedents and consequences
	Reme, Silje Endresen	Common Complaints – Common Cure? Psychiatric comorbidity and predictors of treatment outcome in low back pain and irritable bowel syndrome
	Helland, Wenche Andersen	Communication difficulties in children identified with psychiatric problems
	Beneventi, Harald	Neuronal correlates of working memory in dyslexia
	Thygesen, Elin	Subjective health and coping in care-dependent old persons living at home
	Aanes, Mette Marthinussen	Poor social relationships as a threat to belongingness needs. Interpersonal stress and subjective health complaints: Mediating and moderating factors.
	Anker, Morten Gustav	Client directed outcome informed couple therapy

	Bull, Torill	Combining employment and child care: The subjective well-being of single women in Scandinavia and in Southern Europe
	Viiig, Nina Grieg	Tilrettelegging for læreres deltakelse i helsefremmende arbeid. En kvalitativ og kvantitativ analyse av sammenhengen mellom organisatoriske forhold og læreres deltakelse i utvikling og implementering av Europeisk Nettverk av Helsefremmende Skoler i Norge
	Wolff, Katharina	To know or not to know? Attitudes towards receiving genetic information among patients and the general public.
	Ogden, Terje, dr.philos.	Familiebasert behandling av alvorlige atferdsproblemer blant barn og ungdom. Evaluering og implementering av evidensbaserte behandlingsprogrammer i Norge.
	Solberg, Mona Elin	Self-reported bullying and victimisation at school: Prevalence, overlap and psychosocial adjustment.
<b>2011</b>	Bye, Hege Høivik	Self-presentation in job interviews. Individual and cultural differences in applicant self-presentation during job interviews and hiring managers' evaluation
<b>V</b>	Notelaers, Guy	Workplace bullying. A risk control perspective.
	Moltu, Christian	Being a therapist in difficult therapeutic impasses. A hermeneutic phenomenological analysis of skilled psychotherapists' experiences, needs, and strategies in difficult therapies ending well.
	Myrseth, Helga	Pathological Gambling - Treatment and Personality Factors
	Schanche, Elisabeth	From self-criticism to self-compassion. An empirical investigation of hypothesized change processes in the Affect Phobia Treatment Model of short-term dynamic psychotherapy for patients with Cluster C personality disorders.
	Våpenstad, Eystein Victor, dr.philos.	Det tempererte nærvær. En teoretisk undersøkelse av psykoterapeutens subjektivitet i psykoanalyse og psykoanalytisk psykoterapi.
	Haukebø, Kristin	Cognitive, behavioral and neural correlates of dental and intra-oral injection phobia. Results from one treatment and one fMRI study of randomized, controlled design.
	Harris, Anette	Adaptation and health in extreme and isolated environments. From 78°N to 75°S.
	Bjørknes, Ragnhild	Parent Management Training-Oregon Model: intervention effects on maternal practice and child behavior in ethnic minority families
	Mamen, Asgeir	Aspects of using physical training in patients with substance dependence and additional mental distress
	Espevik, Roar	Expert teams: Do shared mental models of team members make a difference
	Haara, Frode Olav	Unveiling teachers' reasons for choosing practical activities in mathematics teaching

<b>2011</b> <b>H</b>	Hauge, Hans Abraham	How can employee empowerment be made conducive to both employee health and organisation performance? An empirical investigation of a tailor-made approach to organisation learning in a municipal public service organisation.
	Melkevik, Ole Rogstad	Screen-based sedentary behaviours: pastimes for the poor, inactive and overweight? A cross-national survey of children and adolescents in 39 countries.
	Vøllestad, Jon	Mindfulness-based treatment for anxiety disorders. A quantitative review of the evidence, results from a randomized controlled trial, and a qualitative exploration of patient experiences.
	Tolo, Astrid	Hvordan blir lærerkompetanse konstruert? En kvalitativ studie av PPU-studenters kunnskapsutvikling.
	Saus, Evelyn-Rose	Training effectiveness: Situation awareness training in simulators
	Nordgreen, Tine	Internet-based self-help for social anxiety disorder and panic disorder. Factors associated with effect and use of self-help.
	Munkvold, Linda Helen	Oppositional Defiant Disorder: Informant discrepancies, gender differences, co-occurring mental health problems and neurocognitive function.
	Christiansen, Øivin	Når barn plasseres utenfor hjemmet: beslutninger, forløp og relasjoner. Under barnevernets (ved)tak.
	Brunborg, Geir Scott	Conditionability and Reinforcement Sensitivity in Gambling Behaviour
<b>2012</b> <b>V</b>	Hystad, Sigurd William	Measuring Psychological Resiliency: Validation of an Adapted Norwegian Hardiness Scale
	Roness, Dag	Hvorfor bli lærer? Motivasjon for utdanning og utøving.
	Fjermestad, Krister Westlye	The therapeutic alliance in cognitive behavioural therapy for youth anxiety disorders
	Jenssen, Eirik Sørnes	Tilpasset opplæring i norsk skole: politikeres, skolelederes og læreres handlingsvalg
	Saksvik-Lehouillier, Ingvild	Shift work tolerance and adaptation to shift work among offshore workers and nurses
	Johansen, Venke Frederike	Når det intime blir offentlig. Om kvinners åpenhet om brystkreft og om markedsføring av brystkreftsaken.
	Herheim, Rune	Pupils collaborating in pairs at a computer in mathematics learning: investigating verbal communication patterns and qualities
	Vie, Tina Løkke	Cognitive appraisal, emotions and subjective health complaints among victims of workplace bullying: A stress-theoretical approach
	Jones, Lise Øen	Effects of reading skills, spelling skills and accompanying efficacy beliefs on participation in education. A study in Norwegian prisons.

<b>2012</b> <b>H</b>	Danielsen, Yngvild Sørebo	Childhood obesity – characteristics and treatment. Psychological perspectives.
	Horverak, Jøri Gytre	Sense or sensibility in hiring processes. Interviewee and interviewer characteristics as antecedents of immigrant applicants' employment probabilities. An experimental approach.
	Jøsendal, Ola	Development and evaluation of BE smokeFREE, a school-based smoking prevention program
	Osnes, Berge	Temporal and Posterior Frontal Involvement in Auditory Speech Perception
	Drageset, Sigrunn	Psychological distress, coping and social support in the diagnostic and preoperative phase of breast cancer
	Aasland, Merethe Schanke	Destructive leadership: Conceptualization, measurement, prevalence and outcomes
	Bakibinga, Pauline	The experience of job engagement and self-care among Ugandan nurses and midwives
	Skogen, Jens Christoffer	Foetal and early origins of old age health. Linkage between birth records and the old age cohort of the Hordaland Health Study (HUSK)
	Leveresen, Ingrid	Adolescents' leisure activity participation and their life satisfaction: The role of demographic characteristics and psychological processes
	Hanss, Daniel	Explaining sustainable consumption: Findings from cross-sectional and intervention approaches
Rød, Per Arne	Barn i klem mellom foreldrekonflikter og samfunnmessig beskyttelse	
<b>2013</b> <b>V</b>	Mentzoni, Rune Aune	Structural Characteristics in Gambling
	Knudsen, Ann Kristin	Long-term sickness absence and disability pension award as consequences of common mental disorders. Epidemiological studies using a population-based health survey and official ill health benefit registries.
	Strand, Mari	Emotional information processing in recurrent MDD
	Veseth, Marius	Recovery in bipolar disorder. A reflexive-collaborative exploration of the lived experiences of healing and growth when battling a severe mental illness
	Mæland, Silje	Sick leave for patients with severe subjective health complaints. Challenges in general practice.
	Mjaaland, Thera	At the frontiers of change? Women and girls' pursuit of education in north-western Tigray, Ethiopia
	Odéen, Magnus	Coping at work. The role of knowledge and coping expectancies in health and sick leave.
	Hynninen, Kia Minna Johanna	Anxiety, depression and sleep disturbance in chronic obstructive pulmonary disease (COPD). Associations, prevalence and effect of psychological treatment.

	Flo, Elisabeth	Sleep and health in shift working nurses
	Aasen, Elin Margrethe	From paternalism to patient participation? The older patients undergoing hemodialysis, their next of kin and the nurses: a discursive perspective on perception of patient participation in dialysis units
	Ekornås, Belinda	Emotional and Behavioural Problems in Children: Self-perception, peer relationships, and motor abilities
	Corbin, J. Hope	North-South Partnerships for Health: Key Factors for Partnership Success from the Perspective of the KIWAKKUKI
	Birkeland, Marianne Skogbrott	Development of global self-esteem: The transition from adolescence to adulthood
<b>2013</b>	Gianella-Malca, Camila	Challenges in Implementing the Colombian Constitutional Court's Health-Care System Ruling of 2008
<b>H</b>	Hovland, Anders	Panic disorder – Treatment outcomes and psychophysiological concomitants
	Mortensen, Øystein	The transition to parenthood – Couple relationships put to the test
	Årdal, Guro	Major Depressive Disorder – a Ten Year Follow-up Study. Inhibition, Information Processing and Health Related Quality of Life
	Johansen, Rino Bandlitz	The impact of military identity on performance in the Norwegian armed forces
	Bøe, Tormod	Socioeconomic Status and Mental Health in Children and Adolescents
<b>2014</b>	Nordmo, Ivar	Gjennom nåløyet – studenters læringserfaringer i psykologutdanningen
<b>V</b>	Dovran, Anders	Childhood Trauma and Mental Health Problems in Adult Life
	Hegelstad, Wenche ten Velden	Early Detection and Intervention in Psychosis: A Long-Term Perspective
	Urheim, Ragnar	Forståelse av pasientagresjon og forklaringer på nedgang i voldsrate ved Regional sikkerhetsavdeling, Sandviken sykehus
	Kinn, Liv Grethe	Round-Trips to Work. Qualitative studies of how persons with severe mental illness experience work integration.
	Rød, Anne Marie Kinn	Consequences of social defeat stress for behaviour and sleep. Short-term and long-term assessments in rats.
	Nygård, Merethe	Schizophrenia – Cognitive Function, Brain Abnormalities, and Cannabis Use
	Tjora, Tore	Smoking from adolescence through adulthood: the role of family, friends, depression and socioeconomic status. Predictors of smoking from age 13 to 30 in the "The Norwegian Longitudinal Health Behaviour Study" (NLHB)
	Vangsnes, Vigdis	The Dramaturgy and Didactics of Computer Gaming. A Study of a Medium in the Educational Context of Kindergartens.

	Nordahl, Kristin Berg	Early Father-Child Interaction in a Father-Friendly Context: Gender Differences, Child Outcomes, and Protective Factors related to Fathers' Parenting Behaviors with One-year-olds
<b>2014</b> <b>H</b>	Sandvik, Asle Makoto	Psychopathy – the heterogeneity of the construct
	Skotheim, Siv	Maternal emotional distress and early mother-infant interaction: Psychological, social and nutritional contributions
	Halleland, Helene Barone	Executive Functioning in adult Attention Deficit Hyperactivity Disorder (ADHD). From basic mechanisms to functional outcome.
	Halvorsen, Kirsti Vindal	Partnerskap i lærerutdanning, sett fra et økologisk perspektiv
	Solbue, Vibeke	Dialogen som visker ut kategorier. En studie av hvilke erfaringer innvandrerdommer og norskfødte med innvandrereforeldre har med videregående skole. Hva forteller ungdommenes erfaringer om videregående skoles håndtering av etniske ulikheter?
	Kvalevaag, Anne Lise	Fathers' mental health and child development. The predictive value of fathers' psychological distress during pregnancy for the social, emotional and behavioural development of their children
	Sandal, Ann Karin	Ungdom og utdanningsval. Om elevar sine opplevingar av val og overgangsprossessar.
	Haug, Thomas	Predictors and moderators of treatment outcome from high- and low-intensity cognitive behavioral therapy for anxiety disorders. Association between patient and process factors, and the outcome from guided self-help, stepped care, and face-to-face cognitive behavioral therapy.
	Sjølie, Hege	Experiences of Members of a Crisis Resolution Home Treatment Team. Personal history, professional role and emotional support in a CRHT team.
	Falkenberg, Liv Eggset	Neuronal underpinnings of healthy and dysfunctional cognitive control
Mrdalj, Jelena	The early life condition. Importance for sleep, circadian rhythmicity, behaviour and response to later life challenges	
Hesjedal, Elisabeth	Tverrprofesjonelt samarbeid mellom skule og barnevern: Kva kan støtte utsette barn og unge?	
<b>2015</b> <b>V</b>	Hauken, May Aasebø	« <i>The cancer treatment was only half the work!</i> » A Mixed-Method Study of Rehabilitation among Young Adult Cancer Survivors
	Ryland, Hilde Katrin	Social functioning and mental health in children: the influence of chronic illness and intellectual function
	Rønsen, Anne Kristin	Vurdering som profesjonskompetanse. Refleksjonsbasert utvikling av læreres kompetanse i formativ vurdering

	Hoff, Helge Andreas	Thinking about Symptoms of Psychopathy in Norway: Content Validation of the Comprehensive Assessment of Psychopathic Personality (CAPP) Model in a Norwegian Setting
	Schmid, Marit Therese	Executive Functioning in recurrent- and first episode Major Depressive Disorder. Longitudinal studies
	Sand, Liv	Body Image Distortion and Eating Disturbances in Children and Adolescents
	Matanda, Dennis Juma	Child physical growth and care practices in Kenya: Evidence from Demographic and Health Surveys
	Amugsi, Dickson Abanimi	Child care practices, resources for care, and nutritional outcomes in Ghana: Findings from Demographic and Health Surveys
	Jakobsen, Hilde	The good beating: Social norms supporting men's partner violence in Tanzania
	Sagoe, Dominic	Nonmedical anabolic-androgenic steroid use: Prevalence, attitudes, and social perception
	Eide, Helene Marie Kjærgård	Narrating the relationship between leadership and learning outcomes. A study of public narratives in the Norwegian educational sector.
<b>2015</b>	Wubs, Annegreet Gera	Intimate partner violence among adolescents in South Africa and Tanzania
<b>H</b>	Hjelmervik, Helene Susanne	Sex and sex-hormonal effects on brain organization of fronto-parietal networks
	Dahl, Berit Misund	The meaning of professional identity in public health nursing
	Røykenes, Kari	Testangst hos sykepleierstudenter: «Alternativ behandling»
	Bless, Josef Johann	The smartphone as a research tool in psychology. Assessment of language lateralization and training of auditory attention.
	Løvvik, Camilla Margrethe Sigvaldsen	Common mental disorders and work participation – the role of return-to-work expectations
	Lehmann, Stine	Mental Disorders in Foster Children: A Study of Prevalence, Comorbidity, and Risk Factors
	Knapstad, Marit	Psychological factors in long-term sickness absence: the role of shame and social support. Epidemiological studies based on the Health Assets Project.
<b>2016</b>	Kvestad, Ingrid	Biological risks and neurodevelopment in young North Indian children
<b>V</b>	Sælør, Knut Tore	Hinderløyper, halmstrå og hengende snører. En kvalitativ studie av håp innenfor psykisk helse- og rusfeltet.
	Mellingen, Sonja	Alkoholbruk, partilfredshet og samlivsstatus. Før, inn i, og etter svangerskapet – korrelerer eller konsekvenser?
	Thun, Eirunn	Shift work: negative consequences and protective factors

	Hilt, Line Torbjørnsen	The borderlands of educational inclusion. Analyses of inclusion and exclusion processes for minority language students
	Havnen, Audun	Treatment of obsessive-compulsive disorder and the importance of assessing clinical effectiveness
	Slåtten, Hilde	Gay-related name-calling among young adolescents. Exploring the importance of the context.
	Ree, Eline	Staying at work. The role of expectancies and beliefs in health and workplace interventions.
	Morken, Frøydis	Reading and writing processing in dyslexia
<b>2016</b> <b>H</b>	Løvoll, Helga Synnevåg	Inside the outdoor experience. On the distinction between pleasant and interesting feelings and their implication in the motivational process.
	Hjeltnes, Aslak	Facing social fears: An investigation of mindfulness-based stress reduction for young adults with social anxiety disorder
	Øyeflaten, Irene Larsen	Long-term sick leave and work rehabilitation. Prognostic factors for return to work.
	Henriksen, Roger Ekeberg	Social relationships, stress and infection risk in mother and child
	Johnsen, Iren	«Only a friend» - The bereavement process of young adults who have lost a friend to a traumatic death. A mixed methods study.
	Helle, Siri	Cannabis use in non-affective psychoses: Relationship to age at onset, cognitive functioning and social cognition
	Glambek, Mats	Workplace bullying and expulsion in working life. A representative study addressing prospective associations and explanatory conditions.
	Oanes, Camilla Jensen	Tilbakemelding i terapi. På hvilke måter opplever terapeuter at tilbakemeldingsprosedyrer kan virke inn på terapeutiske praksiser?
	Reknes, Iselin	Exposure to workplace bullying among nurses: Health outcomes and individual coping
	Chimhutu, Victor	Results-Based Financing (RBF) in the health sector of a low-income country. From agenda setting to implementation: The case of Tanzania
	Ness, Ingunn Johanne	The Room of Opportunity. Understanding how knowledge and ideas are constructed in multidisciplinary groups working with developing innovative ideas.
	Hollekim, Ragnhild	Contemporary discourses on children and parenting in Norway. An empirical study based on two cases.
		Doran, Rouven
<b>2017</b> <b>V</b>	Katise, Masego	The power of context in health partnerships: Exploring synergy and antagonism between external and internal ideologies in implementing Safe Male Circumcision (SMC) for HIV prevention in Botswana

	Jamaludin, Nor Lelawati Binti	The “why” and “how” of International Students’ Ambassadorship Roles in International Education
	Berthelsen, Mona	Effects of shift work and psychological and social work factors on mental distress. Studies of onshore/offshore workers and nurses in Norway.
	Krane, Vibeke	Lærer-elev-relasjoner, elevers psykiske helse og frafall i videregående skole – en eksplorerende studie om samarbeid og den store betydningen av de små ting
	Søvik, Margaret Ljosnes	Evaluating the implementation of the Empowering Coaching™ program in Norway
	Tonheim, Milfrid	A troublesome transition: Social reintegration of girl soldiers returning ‘home’
	Senneseth, Mette	Improving social network support for partners facing spousal cancer while caring for minors. A randomized controlled trial.
	Urke, Helga Bjørnøy	Child health and child care of very young children in Bolivia, Colombia and Peru.
	Bakhturidze, George	Public Participation in Tobacco Control Policy-making in Georgia
	Fismen, Anne-Siri	Adolescent eating habits. Trends and socio-economic status.
<b>2017 H</b>	Hagatun, Susanne	Internet-based cognitive-behavioural therapy for insomnia. A randomised controlled trial in Norway.
	Eichele, Heike	Electrophysiological Correlates of Performance Monitoring in Children with Tourette Syndrome. A developmental perspective.
	Risan, Ulf Patrick	Accommodating trauma in police interviews. An exploration of rapport in investigative interviews of traumatized victims.
	Sandhåland, Hilde	Safety on board offshore vessels: A study of shipboard factors and situation awareness
	Blågestad, Tone Fidje	Less pain – better sleep and mood? Interrelatedness of pain, sleep and mood in total hip arthroplasty patients
	Kronstad, Morten	Frå skulebenk til deadlines. Korleis nettjournalistar og journaliststudentar lærer, og korleis dei utviklar journalistfagleg kunnskap
	Vedaa, Øystein	Shift work: The importance of sufficient time for rest between shifts.
	Steine, Iris Mulders	Predictors of symptoms outcomes among adult survivors of sexual abuse: The role of abuse characteristics, cumulative childhood maltreatment, genetic variants, and perceived social support.
	Høgheim, Sigve	Making math interesting: An experimental study of interventions to encourage interest in mathematics