Cognitive impairment as a predictor of outcomes in SUD rehabilitation

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Thesis for the degree of Philosophiae Doctor (PhD)
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Scientific environment

This thesis was completed in collaboration with the Center for Alcohol and Drug Research, Stavanger University Hospital, Norway and the Department of Biological and Medical Psychology, University of Bergen, Norway. The research and thesis were supervised by Aleksander H. Erga, Helse Stavanger HF, and Astri J. Lundervold at the University of Bergen. The work was funded by Helse-Vest, Strategic Initiative for Substance use research.

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Within the purview of my professional engagements spanning various public and health sectors, I have been afforded the privilege of closely working with individuals grappling with substance use problems. I hold a deep conviction that people pursue happiness and meaning with sincerity and strive to escape the clutches of their self-defeating patterns. However, despite the collective endeavours of patients, healthcare professionals, researchers, and policymakers to address the complexities of substance use disorders, a disconcerting paradox persists – that several individuals experience relapses and the reversion to the harmful cycles that trap them, imposing a tremendous burden for the individual, their families and society. While notable progress has been achieved within the realms of clinical practice, research and policies, treatment effectiveness for substance use disorders remains an area for improvement. With a healthy dose of humility, my aspiration is that this project could potentially make a small but meaningful contribution to the evolution of treatment approaches and research directions in the times ahead.

I would like to express my heartfelt appreciation to the participants of the STAYER study, as well as the dedicated research staff and participating clinics involved in the project. This thesis builds upon the excellent groundwork laid by the STAYER research group at the Center for Alcohol and Drug Research. I am especially grateful to Thomas Svendsen, Anne-Lill Mjølhus Njaa, and Janne Årstad for their meticulous efforts in obtaining the STAYER data. Your creativity and persistence have made this project possible and have set a solid foundation for years of forthcoming research endeavours into the recovery processes of individuals with substance use disorders.

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Abbreviations

APA	American Psychiatric Association
BID	Borderline intellectual disability
BIF	Borderline intellectual impairment
BRI	Behavioral Regulation Index
BRIEF-A	Behavior Rating Inventory of Executive Function - Adult version
DSM	Diagnostic and statistical manual of mental disorders
DSM-III	Diagnostic and statistical manual of mental disorders, 3rd Edition
DSM-5	Diagnostic and statistical manual of mental disorders, 5th Edition
DUDIT	Drug Use Identification Test
DUDIT-C	Drug Use Identification Test – Consumption items
FSIQ	Full Scale Intelligence quotient
GEC	Global Executive Composite
GSI	Global Severity Index
ICD-10	International Classification of Diseases 10th Revision
ICD-11	International Classification of Diseases 11th Revision
ID	Intellectual disability
IQ	Intelligence quotient
KVARUS	National Quality Register for Substance Abuse

MBID	Mild to borderline intellectual impairment
MI	Metacognitive index
MoCA®	Montreal Cognitive Assessment®
pSUD	Polysubstance Use Disorder
PTSD	Post-Traumatic Stress Disorder
SCL-90-R	Symptom Checklist 90-Revised
STAYER	Stavanger Study of Trajectories of Addiction
SUD	Substance Use Disorder
SD	Standard Deviation
SWLS	Satisfaction With Life Scale
WASI	Wechsler Abbreviated Scale of Intelligence
WHO	World Health Organization

Abstract

Background

Research has repeatedly demonstrated that cognitive impairment among patients with substance use disorder (SUD) is high and associated with poorer SUD treatment outcomes. Identifying cognitive impairment may be pivotal in tailoring the delivery of treatment for this patient cohort. Clinicians typically rely on short screening instruments measuring broad cognitive domains for the identification of cognitive impairment. However, the ecological validity for such instruments in terms of predicting long-term clinically relevant outcomes in patients with an SUD is not well established. This PhD project examines the prevalence rates of cognitive impairment derived from frequently used short assessment instruments. It also assesses these instruments' ability to predict long-term substance use and psychological distress among patients with polysubstance use disorder (pSUD). Additionally, it examines the characteristics of patients with pSUD with coocurring borderline intellectual impairment (BIF).

Aims

Paper I. To examine the prevalence rate and demographic and clinical features of patients with a pSUD and cooccurring BIF.

Paper II. To investigate the predictive value of measures from common cognitive screening instruments on long-term substance use among patients with pSUD.

Paper III. To investigate the predictive value of measures from common cognitive screening instruments on long-term psychological distress and interactions between substance use, cognitive impairment and psychological distress among patients with pSUD.

Method

The project featured a prospective longitudinal cohort design. A total of 208 patients with SUD were recruited at convenience across 10 outpatient and residential enrolment sites within the specialized SUD treatment services in the Stavanger University Hospital catchment area. The sample of patients with pSUD comprised 164 participants. Cognitive impairment was measured with the Wechsler Abbreviated Scale of Intelligence (WASI), the Montreal Cognitive Assessment® (MoCA®), and the Behaviour Rating Inventory of Executive Function – Adult version (BRIEF-A). Psychological distress was measured by the Symptom Checklist 90-Revised (SCL-90-R), and substance use was measured by the Drug Use Identification Test – Consumption items (DUDIT-C). We conducted frequency analysis to establish prevalence rates of cognitive impairments according to the specific cognitive screening instruments and described differences in characteristics between the BIF and non-BIF groups. We performed logistic regression analyses to examine the predictive value of the specific cognitive screening instruments with substance use and psychological distress at the one- and five-year follow-ups as the dependent variables.

Results

Prevalence rates of cognitive impairment. In Paper I we found a prevalence rate of BIF of 13.6%. Only one participant scored within the IQ range of intellectual disability (IQ 50–70). In Paper II, we identified MoCA® and BRIEF-A derived cognitive impairment prevalence rates of 33% and 60%, respectively.

Characteristics of BIF. In Paper I, we found that participants with BIF displayed an elevated level of self-reported psychological distress compared to those without BIF, while other disparities were not observed. A post hoc regression analysis, controlling for possible confounders, confirmed the independent association between psychological distress and BIF.

Prediction of substance use. In Paper II, we found no association between results from WASI, MoCA® and BRIEF-A, and substance use outcomes one or five years after treatment initiation except for MoCA® and continuous DUDIT-C scores at year one. The WASI, MoCA® and BRIEF-A did not predict abstinence or heavy substance use one and five years after treatment initiation.

Prediction of psychological distress. In Paper III, MoCA® defined cognitive impairment proved to be a significant independent predictor of long-term psychological distress even after controlling for the effect of psychological distress at treatment initiation. However, BRIEF-A defined cognitive impairment lost statistical significance as a predictor of psychological distress at follow-ups when the effect of baseline psychological effect was controlled for. The relationship between WASI and psychological distress was equivocal, as it did not show a clear prediction pattern. When compared to baseline distress and substance use at one- and five-year follow-ups, the cognitive instruments exhibited limited explanatory power for long-term psychological distress.

Conclusion

The results in this PhD project indicate that there may be an overrepresentation of cognitive impairments, including BIF, among patients in SUD treatment. However, the utility of the WASI, MoCA® and BRIEF-A to predict long-term substance use and psychological distress in a clinical context appears to be limited. The project highlights the need to develop neuroscience-informed, viable and ecologically valid assessment procedures that can identify cognitive impairment in SUD populations.

Sammendrag

Gjentatte studier har vist at forekomsten av svekket kognitiv fungering blant pasienter med rusmiddellidelser er høy og assosiert med svakere behandlingsutfall i rusbehandling. Identifisering av svekket kognitiv fungering kan være avgjørende for å tilpasse behandlingen til denne pasientgruppen. Klinikere benytter oftest korte screeninginstrumenter som måler brede kognitive domener for å identifisere svekket kognitiv fungering. Imidlertid er den økologiske validiteten til disse instrumentene med henblikk på å kunne predikere langsiktig klinisk relevante behandlingsutfall ikke godt etablert. Dette PhD-prosjektet undersøker forekomsten av kognitive vansker definert ved vanlige korte kartleggingsinstrumenter. Prosjektet undersøker og disse instrumentenes evne til å predikere langsiktig rusmiddelinntak og psykologisk lidelsestrykk blant pasienter med rusmiddellidelse som bruker multiple rusmidler (pSUD). Videre undersøkes karakteristika til pasienter med pSUD og samtidig borderline intellektuell fungering (BIF).

Mål

Artikkel I. Å undersøke prevalens av samt demografiske og kliniske karakteristika til pasienter med pSUD og samtidig BIF.

Artikkel II. Å undersøke hvor godt resultater fra vanlige kognitive screeninginstrumenter kan predikere langtids rusmiddelinntak blant pasienter med pSUD

Artikkel III. Å undersøke hvor godt resultater fra vanlige kognitive screeningsinstrumenter kan predikere langtids psykisk lidelsestrykk samt interaksjon mellom rusmiddelbruk, kognitive vansker og psykisk lidelsestrykk blant pasienter med pSUD

Metode

Prosjektet benytter et prospektivt longitudinelt design. Totalt 208 pasienter med rusmiddellidelse ble rekruttert ved bekvemmelighet fra 10 poliklinikker og døgnenheter ved tverrfaglig spesialisert rusbehandling i Stavanger Universitetssykehus sitt opptaksområde. Utvalget av pasienter med pSUD utgjorde 164 deltakere. Svekket kognitiv fungering ble utledet fra Wechsler Abbreviated Scale of Intelligence (WASI), Montreal Cognitive Assessment® (MoCA®), og Behaviour Rating Inventory of Executive Function – Adult version (BRIEF-A). Psykisk lidelsestrykk ble utledet fra Symptom Checklist 90-Revised (SCL-90-R), og rusmiddelinntak ble utledet fra Drug Use Identification Test – Consumption items (DUDIT-C). Vi gjennomførte frekvensanalyse for å fastslå prevalensrate til svekket kognitiv fungering i henhold til de ulike kognitive screeninginstrumentene og beskrev forskjeller i karakteristika mellom BIF og ikke-BIF gruppene. Vi gjennomførte logistisk regresjonsanalyse for å undersøke den prediktive verdien til de ulike kognitive screeninginstrumentene med rusmiddelinntak og psykologisk lidelsetrykk ved ett- og femårs oppfølging som avhengig variabel.

Resultat

Prevalensrate for svekket kognitiv fungering. I Artikkel I fant vi en BIF prevalensrate på 13.6%. Kun én deltaker skåret i IQ-området til psykisk utviklingshemming (IQ 50–70). I Artikkel II og Artikkel III identifiserte vi prevalensrate av svekket kognitiv fungering utledet ved MoCA® og BRIEF-A på henholdsvis 33% og 60%.

BIF karakteristika. I Artikkel I fant vi at deltakere med BIF hadde forhøyet selvrapportert psykisk lidelsestrykk sammenliknet med deltakere uten BIF mens andre forskjeller ikke ble funnet. En post hoc regresjonsanalyse som kontrollerte for mulige konfunderende variabler bekreftet den uavhengige assosiasjonen mellom psykisk lidelsestrykk og BIF.

Prediksjon av rusmiddelbruk. I Artikkel II fant vi ingen assosiasjon mellom resultater fra WASI, MoCA® og BRIEF-A og rusmiddelinntak ved år en og fem ut over MoCA® og kontinuerlige DUDIT-C skårer ved år en. WASI, MoCA® and BRIEF-A predikerte ikke avhold fra eller omfattende rusmiddelbruk ett og fem år etter behandlingsoppstart.

Prediksjon av psykisk lidelsestrykk. I Artikkel III var svekket kognitiv fungering utledet ved MoCA® en signifikant uavhengig prediktor for langsiktig psykisk lidelsestrykk også etter at effekten av psykisk lidelsestrykk ved inklusjonstidspunktet var kontrollert for. Imidlertid mistet svekket kognitiv fungering utledet fra BRIEF-A statistisk signifikans som prediktor for psykisk lidelsestrykk ved senere målepunkter etter at effekten av psykisk lidelsestrykk ved inklusjonstidspunktet var kontrollert for. Forholdet mellom WASI og psykisk lidelsestrykk var uklart da det ikke fremkom et klart prediksjonsmønster. Sammenliknet med psykisk lidelsestrykk målt ved inklusjonstidspunktet og rusmiddelbruk ved ett- og femårs oppfølging, viste de kognitive instrumentene begrenset forklaringsverdi for langsiktig psykisk lidelsestrykk.

Konklusjon

Resultatene i dette PhD-prosjektet indikerer at svekket kognitiv fungering inkludert BIF kan være overrepresentert blant pasienter i rusbehandling. Imidlertid fremstår nytteverdien til WASI, MoCA® and BRIEF-A for å predikere langsiktig rusmiddelbruk og psykisk lidelsestrykk i en klinisk kontekst begrenset. Prosjektet understreker behovet for å utvikle nevrovitenskaplig informerte, hensiktsmessige og økologisk valide utredningsprosedyrer som kan identifisere svekket kognitiv fungering blant pasienter med rusmiddellidelse.

List of Publications

Hetland, J., Braatveit, K. J., Hagen, E., Lundervold, A. J., & Erga, A. H. (2021). Prevalence and characteristics of borderline intellectual functioning in a cohort of patients with polysubstance use disorder. Frontiers in psychiatry, 12, 1185. https://doi.org/10.3389/fpsyt.2021.651028

Hetland, J., Hagen, E., Lundervold, A. J., & Erga, A. H. (2023). Performance on Cognitive Screening Tests and Long-Term Substance Use Outcomes in Patients with Polysubstance Use Disorder. Eur Addict Res, 1-10. https://doi.org/10.1159/000528921

Erratum - Performance on Cognitive Screening Tests and Long-Term Substance Use Outcomes in Patients with Polysubstance Use Disorder. Eur Addict Res 2023; https://doi.org/10.1159/000533445

Hetland, J., Hagen, E., Lundervold, A. J., & Erga, A. H. (2023). Cognitive impairment as a predictor of long-term psychological distress in patients with polysubstance use disorders: A prospective longitudinal cohort study (In review)

Contents

Innhold

1. General introduction and theoretical framework

1.1 Background

The research field intersecting neurocognition and substance use disorder (SUD) has sharply advanced the understanding of the underpinning mechanics and clinical implications of cognitive impairments in recent decades (Kwako et al., 2016; Verdejo-García, 2018; Verdejo-García, Garcia-Fernandez, et al., 2019; Volkow & Boyle, 2018; Volkow et al., 2016). However, the translation of findings from neurocognitive research into clinical practice and guidelines has been slow (Verdejo-García, Lorenzetti, et al., 2019). Numerous national and international initiatives have highlighted the necessity of bridging the gap between neurocognitive research and clinical practice, including the National Brain Health Strategy (2018–2024) (HOD, 2017), initiatives paralleling the Research Domain Criteria developed by the US National Brain Health Strategy (Insel et al., 2010; Kwako et al., 2016; Litten et al., 2015), the Neuroscience Interest Group of the International Society of Addiction Medicine (Verdejo-García, Lorenzetti, et al., 2019), the Norwegian competence center for TSB (UiO, 2023) and expert clinical and research communities (Yücel et al., 2019).

The identification of both primary illness and coexistent cognitive or psychiatric conditions carries significance in the understanding and tailoring of treatment for patients with SUD (Braatveit et al., 2018b; Cardoso et al., 2016; Ciraulo et al., 2003; Daigre et al., 2019; Domínguez-Salas et al., 2016; Morisano et al., 2014; Najt et al., 2011; Santucci, 2012; Sofuoglu et al., 2016; Verdejo-García, Garcia-Fernandez, et al., 2019; Volkow & Blanco, 2023). However, there are major theoretical and practical obstacles that impede the assessment of cognitive function among individuals with SUD, and clinicians frequently must resort to short cognitive screening instruments. Moreover, currently available and viable cognitive assessment tools are not specifically developed for the SUD population and lack well-established validity for assessing long-term clinically relevant treatment outcomes.

The aim of the current PhD project is to further bridge the gap between the clinical field of SUD treatment and the research field of neurocognition by investigating the utility of brief cognitive assessment tools for patients with polysubstance use disorder (pSUD). This will be achieved by examining the predictive validity of clinically well-established cognitive screening tools as well as establishing prevalence rates of cognitive impairment among patients with pSUD. The aspiration is that insights gained from this project will serve as a foundation for guiding future research endeavours aimed at refining and developing assessment protocols specifically tailored for individuals with SUD.

1.2 Substance use disorder

1.2.1 Substance use disorder, definition and prevalence

Substance use disorder (SUD) is a pressing public health problem leading to considerable personal suffering, excess morbidity, mortality and considerable economic and social burden on society (Degenhardt et al., 2018; van Amsterdam et al., 2013; World Health Organization, 2019). Compared to other mental disorders, SUD is a leading cause of premature mortality (Whiteford et al., 2013). Globally, an excess of 35 million people are affected by drug addiction (World Health Organization, 2019), with annual deaths estimated to be approximately 0.5 million. The lifetime prevalence of SUD in Norway is estimated to be 10–20% (Grønholt et al., 2014), which is comparable to the Norwegian lifetime prevalence rates for other common psychiatric disorders, such as major depressive disorder, specific phobia and social anxiety (Reneflot et al., 2018). Moreover, the main causes of production loss in Norway are due to mental disorders and SUD (Kinge et al., 2023). In 2021, approximately 33,000 patients received treatment from the Norwegian multidisciplinary specialized addiction health services (Tverrfaglig Spesialisert Rusbehandling [TSB]), with 14,961 discharges from treatment (Bremnes & Indergård, 2022). The high prevalence rate and significant socioeconomic, health related, interpersonal and personal consequences of SUD underscore the pressing necessity for effective treatment options for this patient cohort. While there have been

advances in the prevention, treatment and long-term follow-up of SUD during the last 20 years, the results from SUD treatment are still unsatisfactory, particularly among adolescents and young adults (Belendiuk & Riggs, 2014).

SUD is nosologically categorized within the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) (APA, 2013) and encompasses the categories of substance abuse and dependence from previous DSM editions. The DSM-5 lists 11 symptoms related to loss of behavioural control, physical dependence, social problems and hazardous use. Individuals exhibiting two to three symptoms are considered to have a "mild" disorder, four to five symptoms constitute a "moderate" disorder, and six or more symptoms constitute a "severe" SUD – commonly characterized as addiction. The corresponding International Classification of Diseases 10th Revision (ICD-10) (WHO, 1992) diagnostic codes recommended by DSM-5 are F1x.10 - harmful use for the diagnosis of mild substance use disorder and F1x.20 - dependence syndrome for both moderate and severe substance use disorder (APA, 2013). In the International Classification of Diseases 11th Revision (WHO, 2022), harmful substance use and dependence remain separate nosological categories with minor modifications made to the diagnostic requirements. Participants in the research for the current thesis met the criteria for either a diagnosis of F1x.1 harmful use or F1x.2 dependency syndrome as delineated by the ICD-10. However, the term *SUD* will be used throughout the thesis when referring to substance-related disorders as described both by the ICD-10 and the DSM-5.

1.2.2 Polysubstance use

Polysubstance use is the consumption of more than one substance on separate occasions (sequential use) or at the same time (concurrent use) (Crummy et al., 2020). In this thesis, polysubstance use disorder (pSUD) refers to the use of multiple substances as part of a pattern of problematic substance use, in which the individual meets criteria for SUD for some, but not necessarily all substances used (Erga et al., 2021). The majority of clinical research on SUDs has been directed towards particular substances in isolation, with a history of polysubstance use typically considered an exclusion criterion (Crummy et al., 2020). However, polysubstance use

is common in both clinical and population samples (Bhalla et al., 2017; McCabe et al., 2017) and represents up to 91% of treatment-seeking patients, who consume an average of 3.5 substances (Onyeka et al., 2012). Moreover, polysubstance use is frequent in patients seeking treatment for monosubstance use disorders (Brooner et al., 1997; Choi & DiNitto, 2019; Nasreddine et al., 2005; Palamar et al., 2018; Staines et al., 2001; Timko et al., 2018).

Patients with polysubstance use display a more severe clinical profile than patients with monosubstance use. Polysubstance use is recognized as a growing public health concern associated with poorer outcomes, somatic comorbidities and higher mortality rates (Bhalla et al., 2017; Bourgault et al., 2022; Crummy et al., 2020; Timko et al., 2018). Polysubstance use is also associated with higher recidivism rates (Håkansson & Berglund, 2012). Compared to monosubstance users, individuals with polysubstance use tend to be male, are younger (Bhalla et al., 2017), have an earlier onset of substance use (Preti et al., 2011), have higher levels of psychological distress and personality disorders (Andreas et al., 2015; Booth et al., 2010; Landheim et al., 2003; Martinotti et al., 2009; Preti et al., 2011; Smith et al., 2011), more severe and persistent cognitive impairments (Bourgault et al., 2022; Hadjiefthyvoulou et al., 2012; Lewis et al., 2020; Selby & Azrin, 1998), and poorer social adjustment and lower socioeconomic status (Bhalla et al., 2017; McCabe et al., 2017; Quek et al., 2013). These characteristics are associated with an increased risk of treatment dropout and relapse (Agosti et al., 1996; Andersson et al., 2018; Brorson et al., 2013; Caldeiro et al., 2008; Daigre et al., 2019; Flynn & Brown, 2008; Şimşek et al., 2019; Stark, 1992). Thus, polysubstance use poses a considerable challenge for SUD treatment services, the overall mental health care system, and the criminal justice system (Andreas et al., 2015; Connor et al., 2014; Flynn & Brown, 2008; Håkansson & Berglund, 2012; Williamson et al., 2006).

1.3 The neurocognitive substrate of SUD

The development of SUD is related to a complex interplay between biological and environmental determinants comprising genetics, epigenetics, developmental

attributes, neurocircuitry, social and cultural systems, stress, trauma and exposure to alternative reinforcers (Agrawal & Lynskey, 2008; Belcher et al., 2014; Ewald et al., 2019; Volkow & Boyle, 2018; Yücel et al., 2007). However, neurocognitive models addressing substance use and its association with neural dysfunction and related cognitive deficits have received considerable attention in preclinical research and now considered a predominant perspective in the understanding of SUD pathogenesis (Bickel et al., 2018; Ochterbeck & Forberger, 2022; Yücel et al., 2019).

The brain disease model of addiction conceptualizes SUD as a chronically relapsing disorder of impulsivity and compulsivity that can be heuristically recognized as a three-staged composite addiction cycle of binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation (craving) (Koob & Volkow, 2010; Volkow et al., 2016). The compulsive substance intake characterizing severe SUD may be perceived as the endpoint of a sequence of transitions spanning from initial spontaneous or voluntary controlled use to progressive loss of control over substance-seeking and self-administration (Everitt, 2014; Everitt & Robbins, 2005; Everitt & Robbins, 2016; Yücel et al., 2019). Substances impact neurocognitive functioning directly by inducing alterations in neurochemistry and long-term plasticity in neurocircuitry across three functional systems: the incentive salience (or reward) system, negative emotionality (including the stress system), and the executive control system (Koob & Le Moal, 2005; Kwako et al., 2016; Yücel et al., 2019). Dysfunction in these neurocognitive domains forms core functional elements of SUD and closely maps to the stages in the addiction cycle, but is also viewed as concurrent contributors to SUD and relapse vulnerability (Kwako et al., 2016; Ramey & Regier, 2019).

During acute intoxication, the substance stimulates increased dopamine transmission in the mesocorticolimbic system (originating in the ventral tegmental area and projecting to the nucleus accumbens and associated ventral striatal areas as well as prefrontal cortex, orbito-frontal cortex and anterior cingulate). The sudden dopamine transmission flux in the mesolimbic pathway, particularly in the nucleus accumbens shell, drives the initial incentive salience and reward of substances that underlie cue-

induced drug-seeking and self-administration behaviour (Berridge & Robinson, 2016; Chiara & Bassareo, 2007; Koob & Volkow, 2016; Volkow & Boyle, 2018). Repeated substance administration induces mesolimbic sensitization, resulting in lasting incentive salience alterations responsible for reward sensitization and reward prediction errors, which renders the brain motivational systems hyperreactive to substance-related cues at the cost of reduced salience towards natural reinforcers (Berridge & Robinson, 2016; Goldstein & Volkow, 2002, 2011; Verdejo-García, 2020). Pavlovian and instrumental learning represent a key approach to understanding the transition from voluntary to compulsive substance use. In this context, initial substance administration is goal-directed and controlled by action–outcome mechanisms. After prolonged exposure to substances, drug-seeking shifts to a habitual stimulus–response behaviour that is insensitive to outcome devaluation (Corbit et al., 2014; Everitt & Robbins, 2016; López et al., 2016; Zapata et al., 2010). The transition is neurobiologically mediated by a shift from prefrontal cortical to striatal control over drug-seeking and drug-intake behaviour as well as a shift from ventral to dorsal striatum activation (Everitt & Robbins, 2016; Murray et al., 2012).

As behaviour shifts from impulsivity to compulsivity, the motivation of substance-related behaviour also shifts from positive to negative reinforcement and greater automaticity (Antons et al., 2020; Koob & Volkow, 2016). Obstruction of prolonged substance administration, acute or protracted, is associated with a withdrawal syndrome that may be understood in terms of motivational aspects and better characterized as a negative emotional state (e.g., dysphoria, increased sensitivity to stress, depression, anhedonia, irritability and anxiety) rather than physical symptoms of withdrawal, which are usually short-lived (Janiri et al., 2005; Koob, 2009; Koob & Le Moal, 1997; Koob & Volkow, 2010; Volkow & Boyle, 2018). Neural circuits underpinning the withdrawal phase comprise basal forebrain areas, including the extended amygdala and habenula, as well as decreased activity in the mesocorticolimbic dopamine system, and implicate neurotransmitters and neuropeptides such as corticotropin-releasing factor, norepinephrine and dynorphin (Batalla et al., 2017; Koob & Le Moal, 2005). In this context, it is proposed that substance-seeking and self-administration in severe SUD is driven by negative

reinforcement and instrumental avoidance learning by, at least transiently, removing or avoiding negative emotional states (Koob & Le Moal, 2005; Wikler, 1973). In addition, negative emotional states may influence habit learning by inducing insensitivity to outcome value and altering action-oriented contingencies (Everitt & Robbins, 2016). Koob (2008) posits that negative emotionality reflects a hedonic homeostatic dysregulation and change in the allostatic state, i.e., a chronic deviation of the hedonic regulatory system from its normal operation level following repeated substance administration. This hedonic allostatic shift is hypothesized to be underpinned by dysregulation of the reward system and recruitment of the brain stress system, leading to long-lasting increases in both reward thresholds (hedonic habituation and tolerance) and aversive anxiety-like responses that motivate and increase the propensity to initiate, sustain and escalate substance administration in efforts to maintain homeostasis.

The progressive mesolimbic sensitization, dorsolateral accumbens driven stimulus–response habit formation, and activation of the stress system is also concurrent with a weakening of top-down prefrontal control over striatal regions (Everitt & Robbins, 2016; Klugah-Brown et al., 2020; Koob & Volkow, 2010; Zilverstand et al., 2018). Several dual-process theories have been proposed highlighting the role of higher-order cognitive functions and emphasizing the interaction between bottom-up "drive" systems (e.g., the reward system or negative emotionality) and higher-order top-down cognitive "control" systems (Bechara, 2005; Bickel & Marsch, 2001; Bickel et al., 2018; Goldstein & Volkow, 2011; Sofuoglu et al., 2016; Verdejo-García & Bechara, 2009). The impaired Response Inhibition and Salience Attribution (iRISA) model posits that disruptions of top-down prefrontal cortex functioning and associated neural networks leads to attributing excessive salience to substances and substance-related cues, reduced sensitivity to nonsubstance reinforces and reduced ability to inhibit maladaptive or disadvantageous behaviours, e.g., substance intake (Goldstein & Volkow, 2002, 2011). Zilverstand et al. (2018) reviewed the evidence in the neuroimaging literature with respect to the iRISA model and identified impairment within six large-scale brain networks (referred to as the reward, habit, salience,

executive, memory and self-directed networks) underpinning substance cue reactivity, decision making, inhibitory control and social emotional processing. The identified impairments in these networks are consistent with all major theories of SUD (Berridge & Robinson, 2016; Everitt & Robbins, 2016; Goldstein & Volkow, 2011; Koob & Volkow, 2016; Redish et al., 2008; Verdejo-García & Bechara, 2009). Crucially, as predicted by the iRISA model, the severity of SUD is associated with a disengagement of the executive network (ventrolateral and dorsolateral prefrontal cortex) that supports the selection of possible behavioural responses, while abstinence and treatment upregulate it (Zilverstand et al., 2018).

1.4 Cognitive impairments and SUD

The nature and trajectories of SUD hinges on the interaction between individual-based factors, e.g., genetics, neuroadaptation, psychopathology, and environmental and social drivers. Cognition has been proposed to interface nature and nurture in SUD (Verdejo-García, 2020). Genetic and early environmental influences shape the cognitive traits that dynamically interact with the environmental contexts throughout development to determine the individual's vulnerability or resilience to develop an SUD (Kendler et al., 2012). Simultaneously, substance use directly and indirectly impacts neurocognitive functioning by producing alterations in neurochemistry that modify learning, cognitive control processes and environmental interactions (Everitt, 2014; Everitt & Robbins, 2016). Translating key notions of contemporary neurobiological models into a cognitive framework may provide a more comprehensive and integrative understanding of SUD and allow for the expansion of their scope and impact (Mathews & MacLeod, 2005; Verdejo-García, 2020).

Patients with SUDs often exhibit cognitive deficits that encompass domains including processing speed, selective and sustained attention, learning and memory, emotional processing, visuospatial and verbal abilities, executive functions, decision-making, social cognition, and emotional control (Bates et al., 2013; Bruijnen, Dijkstra, et al., 2019; Fernández-Serrano et al., 2011; Rogers & Robbins, 2001; Toledo-Fernández et al., 2020; Verdejo-Garcia et al., 2019). Prevalence estimates of cognitive impairment

among SUD populations vary considerably and range from 20 — 80%, which reflects the heterogeneity of the research populations, substance class studied, definition of and severity of cognitive impairments, and assessment protocols, e.g., instruments utilized and time from cessation to assessment (Bates, Bowden, et al., 2002; Beurmanjer et al., 2022; Bruijnen, Dijkstra, et al., 2019; Copersino et al., 2009; Fernández-Serrano, Pérez-García, Perales, et al., 2010). However, cognitive impairments among individuals with SUD are typically more subtle than those observed in populations with acquired brain injury (Caracuel et al., 2008). Nonetheless, the domains of speed/attention, executive functioning and decision-making have received particular attention as they are considered "meaningfully associated" with relevant SUD treatment outcomes such as treatment retention, relapse and quality of life (Verdejo-Garcia et al., 2019).

It is also extensively documented that long-term use of psychoactive substances causes functional and structural brain alterations and subsequent cognitive impairments in cognitive domains such as episodic memory, emotional processing, visuospatial abilities, learning and several executive functions such as working memory, inhibition and decision making (Fernández-Serrano et al., 2011; Holst & Schilt, 2011; Rogers & Robbins, 2001; Verdejo-García & Pérez-García, 2007; Vik et al., 2004; Yücel et al., 2007). Furthermore, studies show that substances may induce both generalized and substance-specific effects on neuropsychological performance. (Fernández-Serrano et al., 2011; Fitzpatrick et al., 2020; Holst & Schilt, 2011; Klugah-Brown et al., 2020; Rogers & Robbins, 2001; Verdejo-García & Pérez-García, 2007). It is subsequently suggested that sequential or simultaneous use of multiple substances may cause additive or synergetic neurocognitive effects, leading to greater impairment among polysubstance users compared to monosubstance users (Medina et al., 2006; Sung et al., 2013; Yücel et al., 2007).

Sustained abstinence has been shown to be associated with volumetric brain recovery in regions underpinning executive functions among both alcohol and cocaine users (Connolly et al., 2013; Zou et al., 2018) and higher self-reported executive functioning (Hadjiefthyvoulou et al., 2012; Hagen, Erga, Hagen, et al., 2017).

Although studies show some recovery of cognitive function after substance abstinence, neurocognitive alterations may be persistent, even after a substantial period of time (Bates et al., 2005; Czapla et al., 2015; Fernández-Serrano et al., 2011; Gouzoulis-Mayfrank & Daumann, 2006b; Holst & Schilt, 2011; Vik et al., 2004; Zhong et al., 2016). However, it is noteworthy that cognitive dysfunction does not necessitate clinically significant impaired adaptive functioning (Abramovitch et al., 2021; Arvidsson & Granlund, 2018; Berry et al., 2019; Bertelli et al., 2017; Braatveit et al., 2018b; Chaytor & Schmitter-Edgecombe, 2004; Spooner & Pachana, 2006; Tupper & Cicerone, 1990).

While a portion of the cognitive deficits associated with SUD may originate from neuroadaptations (Klugah-Brown et al., 2020; Verdejo-García, 2018) or neurotoxic effects (Gouzoulis-Mayfrank & Daumann, 2006b; Pfefferbaum et al., 1998; Sung et al., 2013; Yücel et al., 2008) from the substance itself, several associated influences may contribute to the neurocognitive impairment profile (Melugin et al., 2021; Toledo-Fernández et al., 2020), including head trauma (Fals-Stewart & Bates, 2003; Marceau et al., 2016), family history of substance intake (Bates, Labouvie, et al., 2002; Fals-Stewart & Bates, 2003), lower education (Bates, Labouvie, et al., 2002; Braatveit et al., 2018a; Latvala et al., 2009), congenital and premorbid impairments (Braatveit et al., 2018a; Fals-Stewart & Bates, 2003; Wilson et al., 2021; Yücel et al., 2007), cooccurring psychiatric disorders (Fals-Stewart & Bates, 2003; Moraleda-Barreno et al., 2020; Paelecke-Habermann et al., 2005; Shwartz et al., 2020; Sofuoglu et al., 2016; Yücel et al., 2007), cerebrovascular changes (ischemic and hemorrhagic events) or vasculitic disease (Rojas et al., 2005), hypoxia (Vik et al., 2004), HIV/AIDS (Norman et al., 2009) and malnutrition (Choi et al., 2021; Liu et al., 2003; Mahboub et al., 2021; Spencer et al., 2017). Thus, the cognitive impairments observed in the SUD population may originate from a complex interplay among a multitude of factors affecting multiple brain regions and cognitive domains.

1.4.1 Borderline intellectual functioning

Intelligence is the aggregate or global capacity of the individual to act purposefully, to think rationally and to deal effectively with the environment (Wechsler, 1944, p. 3). Conventional psychometric tests of intelligence typically yield an intelligence quotient (IQ), which serves as a measure of general cognitive functioning. IQ conforms to a Gaussian distribution within the general population with the mean set at 100 and a standard deviation (SD) of 15. An IQ score between one and two SDs below the population mean (approximately an IQ between 70 and 85) is considered borderline intellectual functioning (BIF) and encompasses 13.6% of the general population. Originally, the DSM (APA, 1952, 1968) recognized BIF as a mental disorder with both intellectual and functional impairments. During revisions, BIF was removed from the disorder chapters in DSM-III (APA, 1980) due to the general argument that individuals with BIF do not consistently manifest reduced adaptive skills or functional impairment (Wieland & Zitman, 2016). BIF was also considered overinclusive as a nosological category (Ferrari, 2009). BIF is now coded in the DSM-5 in the V-section as a condition that may have clinical implications. (APA, 2013) Correspondingly, the ICD-10 classifies BIF as R41.83, defined as a "symptom or sign involving cognitive functions and awareness" (WHO, 1992). BIF is therefore neither classified as a mental disorder nor typically considered a form of disability (Ferrari, 2009). However, studies show that individuals with BIF may exhibit difficulties in several aspects of life comparable to individuals with a diagnosis of intellectual disability (ID) and that individuals with BIF may need targeted support (Chen et al., 2006; Didden, 2017; Ferrari, 2009; Gigi et al., 2014; Hassiotis, 2015; Hassiotis et al., 2008; Lim et al., 2022; Melby et al., 2020; Nouwens, Lucas, Embregts, et al., 2017; Peltopuro et al., 2014; Snell et al., 2009).

Research has demonstrated that IQ as a model of intelligence may not adequately capture the nature of cognitive impairments found in ID (Bertelli et al., 2017; Greenspan, 2017). The DSM-5 has also deemphasized reliance on the IQ cut-off score as a diagnostic criterion for and subclassification of ID (Wieland & Zitman, 2016). Consequently, emphasis has been placed on adaptive functioning for the

diagnosis of ID. However, most studies identify BIF solely on measures of intellectual functioning, i.e., IQ ranging between 70 and 85 (Braatveit et al., 2018b).

The lack of terminological consensus of BIF and absence in the main diagnostic classification is reflected in the research literature where operationalization varies widely. Studies investigating BIF typically classify BIF within mild-to-borderline intellectual disability (MBID) with IQ ranging between 50 and 85 (encompassing 15.8% of the general population) or treat BIF as a control group (Peltopuro et al., 2014). The term borderline intellectual disability (BID) is also used by some to describe individuals who meet all ICD-10/DSM-5 criteria for intellectual disability but exhibit both intellectual and adaptive impairments between one and two SDs below the population mean, along with concurrent evidence for childhood learning difficulties (Braatveit et al., 2018b; Braatveit, 2018). For simplification, the term BIF will be used throughout this thesis, reflecting the emphasis on neuropsychological test performance when defining intellectual impairment, also when referencing literature on BID and MBID. However, instances of terminological differences that are relevant for the interpretation of research findings and discussion will be addressed when pertinent.

1.4.2 Prevalence of borderline intellectual functioning

There is a scarcity of studies examining the prevalence rates of BIF in SUD populations, with reported rates varying considerably from 3% to 39% (Braatveit et al., 2018a; Luteijn et al., 2017; VanDerNagel et al., 2014). Prevalence data for BIF are difficult to compare because of a lack of consensus on terminology (i.e., whether mild intellectual disability and measures of adaptive function are included in the definition), differences in group characteristics, level of disability, treatment settings, comorbid psychiatric disorders, assessment procedures, and definition and scope of substance use (Braatveit et al., 2018b; Carroll Chapman & Wu, 2012; Salvador-Carulla et al., 2013; van Duijvenbode & VanDerNagel, 2019).

1.4.3 Executive functioning

Executive functions refer to higher level top-down cognitive "control" processes that regulate goal-directed behaviour and are typically associated with complex cortical circuits that involve the prefrontal cortex and related regional neural networks (Friedman & Miyake, 2017; Friedman & Robbins, 2022). Executive functions are influenced by different internal and environmental factors, such as sleep, mood, and stress. As a result, the ability to regulate behaviour varies across situations and time (McKinney et al., 2020). Executive functions are sometimes considered separate from cognitive functions. Although distinct, several executive processes, e.g., working memory, inhibitory control, and cognitive flexibility, and neural systems are mobilized in response to complex task demands (Collette et al., 2005). Executive functions are also significant contributors to the so-called g-factor, which comprises cognitive capacities associated with fluid intelligence such as reasoning, problem-solving, and planning (Ardila, 2018; Arffa, 2007; Bertelli et al., 2017; Friedman et al., 2006; Valls-Serrano et al., 2016). Several studies have highlighted impaired executive functions as key risk factors for the initiation of substance use, while also impacting the pathogenesis and treatment trajectory of SUD by compromising the regulation of attention, thought, emotions, and behaviour (Balconi et al., 2022; Blume & Alan Marlatt, 2009; Diamond, 2013; Domínguez-Salas et al., 2016; Hofmann et al., 2012; Jordan & Andersen, 2017; Kräplin et al., 2022; Volkow & Boyle, 2018; Wilson et al., 2021; Zilverstand et al., 2018). Furthermore, substance intake is associated with impaired executive functions. The extent to which substances impair executive functioning is influenced by factors such as the type of substance, substance combinations, dosage, duration of use and debut age (Bjork et al., 2022; Fernández-Serrano, Pérez-García, Schmidt Río-Valle, et al., 2010; Fernández-Serrano et al., 2011; Hadjiefthyvoulou et al., 2012; Lopes et al., 2017; Verdejo-García et al., 2005). Impaired executive functioning, and in particular processes related to the cross-temporal organization of behaviour, is also considered a key transdiagnostic component in SUD (Kwako et al., 2016). The prevalence of mild executive dysfunction among treatment-seeking patients enrolled in a therapeutic community has been estimated to be between 70% for pSUD and 80% for alcohol mono-users.

However, this frequency dropped to 35% and 40%, respectively, when applying stricter criteria. Furthermore, working memory exhibited the highest impairment prevalence among the executive components analysed in both groups (Fernández-Serrano, Pérez-García, Perales, et al., 2010). Others have found impaired executive impairments in the range of 45—63% among treatment-seeking patients with an SUD (McKowen et al., 2017; Verdejo-García et al., 2005).

1.5 Cognition and SUD vulnerability in a developmental perspective

Cognitive disruptions may significantly contribute to the initiation, misuse and maintenance of substance use in SUD. Executive function deficits (e.g., heightened impulsivity) and novelty seeking are characteristics of normative adolescent development, partly due to differential development in neural circuits involved in reward processing relative to top-down control systems during that developmental period (Casey et al., 2008; Hester et al., 2010; Rose et al., 2019). The adolescent propensity for risk-taking behaviour is reflected by the fact that alcohol and illicit substance use is typically initiated mid-adolescence (Kelly et al., 2019; Pedersen & Skrondal, 1998).

Children and adolescents with poor impulse inhibition, externalizing disorders and attention-deficit hyperactivity disorder display neurocognitive characteristics including even higher impulsivity and reward sensitivity. These adolescents are more prone to engage in risk-taking behaviour compared to peers and represent subgroups with an augmented risk for later substance use and lifetime SUD (Elkins et al., 2007; Nigg et al., 2006; Rose et al., 2019; Squeglia et al., 2014). Furthermore, substance use during early adolescence interferes with neurodevelopment in a critical period for brain maturation, including the refinement of connectivity in the prefrontal cortex, to induce long-term neurocognitive changes that further exacerbate lifetime SUD risk (Crews et al., 2007; Hanson et al., 2011; Jordan & Andersen, 2017; Lisdahl, 2013; Lubman & Yücel, 2008; Salmanzadeh et al., 2020). However, executive functioning may play a more significant role in driving externalizing behaviour and leading to a

continuing loss of control over substance use in young adults with mild to moderate SUD, rather than being a vulnerability factor for SUD, which may be secondary and occurs after a prolonged period of hazardous use (Kräplin et al., 2022).

Studies investigating the relationship between childhood IQ and later substance use have produced mixed results. Adolescents with BIF may be more likely to use substances and to be at a higher risk for developing SUD than their average IQ peers (Gigi et al., 2014; van Duijvenbode & VanDerNagel, 2019). However, high childhood IQ may also increase the risk of substance use in later life, particularly among women (White & Batty, 2011). Early cannabis use debut age is associated with impaired executive functioning (Jacobus et al., 2015) but not reduced IQ (Jackson et al., 2016). One possible pathway, at least in the case of cannabis use, is that high IQ is associated with traits for sensation seeking (Raine et al., 2002) and openness to experience (Furnham & Cheng, 2016) and that these traits are associated with substance use (Barnum & Armstrong, 2019; Erevik et al., 2017; Terracciano et al., 2008).

1.6 Substance use and mental health

Findings from multiple epidemiological and clinical studies demonstrate a general cooccurrence between SUDs and mental illness, such as mood and anxiety disorders, attention-deficit hyperactivity disorder, psychosis, personality disorders as well as suicidality and general psychological distress (Andreas et al., 2015; Brady et al., 2013; Compton et al., 2007; Conway et al., 2006; De Alwis et al., 2014; Erga et al., 2021; Grant et al., 2004; Hjemsaeter et al., 2020; Langås et al., 2012b; Magidson et al., 2012; Merikangas et al., 1998; Morisano et al., 2014; Pennay et al., 2011; Ross & Peselow, 2012; Torrens et al., 2011). Moreover, individuals with polysubstance use exhibit higher levels of psychological distress and personality disorders compared to mono substance users (Andreas et al., 2015; Booth et al., 2010; Landheim et al., 2003; Martinotti et al., 2009; Preti et al., 2011; Smith et al., 2011). Overall, epidemiological studies indicate that approximately 50% of those with an SUD also have one or more comorbid mental disorders (Kessler et al., 1996). Among adults

receiving treatment from mental health care services, 30–50% have a comorbid substance use disorder (Sheidow et al., 2012; Toftdahl et al., 2016). The prevalence estimate of any mental illness among patients in SUD treatment settings is between 40–90% (Landheim et al., 2003; Verheul et al., 2000). A Norwegian study found that approximately 90% of patients receiving care from either an SUD or psychiatric service had a comorbid SUD and lifetime mental illness (Langås et al., 2012). Conversely, sustained cessation, reduction of substances used, and abstinence from specific substanes are associated with a decrease in psychological distress and symptom alleviation (Andreas et al., 2015; Bahorik et al., 2016; Booth et al., 2010; Deng et al., 2012; Erga et al., 2021; Hagen, Erga, Nesvåg, et al., 2017). Despite efforts to clarify the causal mechanisms underlying the observed associations between SUDs and other mental health disorders, the nature and directionality of the association remains a significant challenge to researchers (Langås et al., 2012b; Morisano et al., 2014; Quello et al., 2005; Santucci, 2012). It has been proposed that substance intake itself is a risk factor for or can exacerbate mental disorders (Andreas et al., 2015; Ross & Peselow, 2012; Swendsen et al., 2010). Mental disorders may also precipitate SUD (Bakken et al., 2003; Langås et al., 2012b). However, both SUD and mental disorders may be secondary to common risk factors (Santucci, 2012). Evidence also suggests a reciprocal influence between SUD and mental disorders in which having one increases vulnerability to develop the second or changes its clinical trajectory (Flórez-Salamanca et al., 2013; Morisano et al., 2014), including worsening treatment outcomes, craving intensity and relapse vulnerability (Clarke et al., 2009; Engel et al., 2016; Fatseas et al., 2018; Glasner-Edwards et al., 2010; Grella et al., 2001; Najt et al., 2011). Furthermore, negative emotionality is also understood as an integral transdiagnostic feature of SUD (Koob, 2009; Kwako et al., 2016) and is assessed by clinical inventories of depression, anxiety and anger (Kwako et al., 2019; Nieto & Ray, 2022; Votaw et al., 2020).

1.7 Cognition and mental health

Cognitive functions represent intermediate phenotypes that can be linked to disruptions of neural circuitry and functioning in psychiatric disorders (Goschke, 2014; Morris & Cuthbert, 2012; Nolen-Hoeksema & Watkins, 2011). Specific deficits in executive functioning and discrete neurocognitive domains are manifested in both psychological distress and several psychopathological conditions, such as psychosis, mood and anxiety disorders, attention-deficit hyperactivity disorders and personality disorders, as well as suicidality (Burton et al., 2022; Diamond, 2013; Garcia-Villamisar et al., 2017; Höijer et al., 2020; Kim et al., 2018; Marazziti et al., 2010; Millan et al., 2012; Nolen-Hoeksema & Watkins, 2011; Wood et al., 2019). Elevated levels of psychological distress are also associated with poorer IQ (Höijer et al., 2020; Keyes et al., 2017; Teasdale & Antal, 2016). Cognitive impairments are strongly related to disability in depression and schizophrenia and affect quality of life and effectiveness of therapy regardless of illness (Clarke et al., 2009; Kim et al., 2018; Millan et al., 2012; Van Rheenen et al., 2019). Cognitive dysfunction may also be present in several ostensibly remitted patient groups and suggests that such impairments could have a trait character (Millan et al., 2012; Paelecke-Habermann et al., 2005; Sofuoglu et al., 2016). Cognitive impairments may indeed serve as a transdiagnostic dimension in all psychopathologies, including SUDs (Abramovitch et al., 2021; Burton et al., 2022; Kwako et al., 2016; Yücel et al., 2007). Dual diagnosis may constitute an added risk for cognitive impairment among patients with SUD. Levy et al. (2008) found more severe executive functioning impairment among patients with a dual diagnosis of comorbid bipolar disorder and SUD compared to those without SUD. Conversely, executive functioning in patients with comorbid personality disorder and SUD may be comparable to those with a single diagnosis (Moraleda-Barreno et al., 2020). However, the relationship between mental illness and neuropsychological test performance might be mediated by factors other than latent cognitive functioning. Moritz et al. (2017) suggested that neuropsychological performance impairments among patients with depression were largely attributed to lower performance motivation and more negative momentary influences. Others have

demonstrated that motor abnormalities among patients with depression may influence task performance (Lohr et al., 2013; Tsourtos et al., 2002).

Some neurocognitive abilities, including executive functions, may be altered by existing psychological interventions, such as mentalization-based treatment, originally developed to promote intra- and interpersonal functioning (Thomsen et al., 2017). Several researchers have advocated for the assessment of cognitive functioning as a crucial target in treatment planning and suggested that the implementation of cognitive remediation therapies may serve as a promising intervention strategy for addressing psychopathology and dual diagnosis (Goschke, 2014; Kim et al., 2018; McGurk, 2016; Morris & Cuthbert, 2012; Nolen-Hoeksema & Watkins, 2011; Sofuoglu et al., 2016; Van Rheenen et al., 2019).

1.8 Cognition and SUD treatment

Benefiting from SUD treatment programs and achieving SUD recovery involves several prerequisite cognitive functions, including attention, memory, verbal skills, problem solving, and abstract reasoning. Cognitive deficits may produce loss of cognitive and behavioural flexibility and compromise the capacity to assimilate and engage in treatment programmes that often are cognitive taxing and typically place a strong emphasis on educative and cognitive interventions (Aharonovich, Brooks, et al., 2008; Bates et al., 2013; Desfosses et al., 2014; Fernández-Serrano, Pérez-García, Perales, et al., 2010; Stevens et al., 2014; Teichner et al., 2002). Indeed, research repeatedly demonstrates that cognitive impairments are associated with poorer SUD treatment outcomes and negatively impact treatment processes and therapeutic change mechanisms, including recognition of problem use (Rinn et al., 2002; Severtson et al., 2010), treatment adherence (Bates et al., 2006), outpatient therapy attendance (Copersino et al., 2012), aftercare attendance (Smith & McCrady, 1991) drop-out rate (Aharonovich et al., 2006; Brorson et al., 2013; McKellar, Kelly, et al., 2006; Steele et al., 2014; Streeter et al., 2008; Sømhovd et al., 2019), relapse proneness (Barreno et al., 2019; Beurmanjer et al., 2022; Braatveit et al., 2018b; Czapla et al., 2015; Hagen, Erga, Hagen, et al., 2017), self-efficacy (Bates et al.,

2006; Worley et al., 2014), disposition to change and desire for help (Blume & Alan Marlatt, 2009; Le Berre et al., 2012; Luteijn et al., 2017), treatment motivation (Katz et al., 2005), procrastination and productivity (Day et al., 2013) and commitment language (Aharonovich, Amrhein, et al., 2008). Conversely, protracted abstinence promotes the recovery of cognitive functions, which subsequently may reduce the risk of relapse (Hagen, Erga, Hagen, et al., 2017; Rolland et al., 2019; Rubenis et al., 2019; Stevens et al., 2014). Moreover, impaired executive functioning is also linked to worse treatment responsiveness in potential comorbid psychopathologies, such as depression (Groves et al., 2018) and obsessive–compulsive disorder (D'Alcante et al., 2012), which in turn may increase the risk of dropout (Andersson et al., 2018; Krawczyk et al., 2017) and relapse (Andersson et al., 2023; Lauvsnes et al., 2022).

The predictors of treatment dropout or early relapse may differ from the predictors of long-term outcomes. Although cognitive impairments have been linked to worse outcomes from SUD treatment episodes, studies rarely exceed 12 months, and the ultralong-term outcome trajectories of patients with cognitive impairments are largely unknown. Treatment retention, considered a crucial predictor of SUD recovery, poses a considerable challenge in SUD treatment (Brorson et al., 2013; De Leon & Jainchill, 1986; Stark, 1992). However, remission with or without abstinence and treatment is common (Dawson et al., 2005; Tucker et al., 2020). Moreover, some studies have found a disconnect between treatment retention and substance use outcomes among patients with cognitive impairments (Aharonovich, Brooks, et al., 2008; McKellar, Harris, et al., 2006). According to McKellar, Harris, et al. (2006), cognitive impairment was a predictor of treatment dropout among patients with an SUD, but it did not predict substance use five years after dropout.

Recovery pathways between patients with and without cognitive impairment may differ. Informal treatment processes and social structures may take on increased salience in determining behavioural, psychosocial, emotional and vocational outcomes among patients with cognitive impairments (Bates et al., 2006; Buckman et al., 2008). Individuals with impaired intellectual functioning may also experience access barriers to substance abuse treatment (Gosens et al., 2021; VanDerNagel et al.,

2018). Compared to those with mental health issues in the general population, they are also more likely to be treated with psychotropic medications and less likely to receive psychotherapy (Hassiotis et al., 2008; Wieland et al., 2014).

1.9 Neuropsychological assessment

1.9.1 Ecological validity

After the advent of computerized tomography, the role of neuropsychology shifted from detecting and localizing brain damage to obtaining quantitative descriptions of the patients' cognitive status (Chaytor & Schmitter-Edgecombe, 2004; Farah, 1994). Additionally, emphasis was directed towards describing the implications of neuropsychological test results and utilizing this understanding to predict everyday functioning or life outcomes and to inform treatment planning (Kibby et al., 1998; Ruff, 2003; Spooner & Pachana, 2006). The term "ecological validity" refers to the extent to which the results of neuropsychological tests or research findings can be generalized to behaviours observed in a naturalistic environment (Andrade, 2018; Tupper & Cicerone, 1990). Conceptually, two approaches have been employed to establish ecological validity: verisimilitude and veridicality (Chaytor & Schmitter-Edgecombe, 2004; Drew Gouvier et al., 2010; Zimmerman, 2011). Versimilitude is related to construct and face validity and concerns the extent to which tasks performed during testing resemble real-life tasks. Veridicality is related to the constructs of concurrent validity and predictive validity and pertains to the empirical accuracy in predicting one or more environmental behaviour outcomes (Drew Gouvier et al., 2010; Franzen & Wilhelm, 1996). Consensus concerning the magnitude of the relationship between test results and outcome measures for the purpose of establishing ecological validity is lacking (Chaytor & Schmitter-Edgecombe, 2004). Nevertheless, within psychological research, correlations of .10, .30, and .50 are conventional benchmarks for "small", "medium" and "large" effects (Hemphill, 2003). Although some neuropsychological test results may moderately be related to everyday performance, much of the behavioural variance is unaccounted for (Chaytor & Schmitter-Edgecombe, 2004). Irrespective of the chosen approach to

establish ecological validity in SUD research (be it verisimilitude, veridicality, or a combination), decisions must be made pertaining to the selection of the criterion variable or outcome behaviour that should be associated with the neuropsychological test results and cognitive constructs. The selected outcomes must be pertinent to the individuals' ecological context and aligned with both the patients' goals and the treatment services' mandate. At a minimum, the justification of incorporating neurocognitive testing in SUD research and clinical practice lies in its capacity to predict target behaviour that may hold clinical, personal or relational significance in the patients' recovery process (Bjornestad et al., 2020; Donovan et al., 2012; Tiffany et al., 2012).

1.9.2 Neuropsychological assessment SUD

The main challenge to neuropsychological assessment of patients with an SUD in both research and clinical practice is posed by the interaction between neurocognitive measures and substance use. The accuracy of neuropsychological measures may be contaminated by potential substance withdrawal and acute effects from psychoactive substances (Manning et al., 2008; Miller, 1985). Furthermore, the varying duration between substance cessation and neuropsychological measurements in studies makes it challenging to compare research results (Fernández-Serrano, Pérez-García, Perales, et al., 2010). Polysubstance use is also prevalent in both clinical and population samples (Bhalla et al., 2017; Brooner et al., 1997; Choi & DiNitto, 2019; McCabe et al., 2017; Onyeka et al., 2012; Palamar et al., 2018; Staines et al., 2001; Timko et al., 2018) and has synergetic or additive neurocognitive sequelae. Conversely, some substances may even mask or protect against neurocognitive sequelae of other substances (Fernández-Serrano et al., 2011). Indeed, some have hypothesized that cannabinoids have neuroprotective properties that may preserve cognition in users of MDMA (Gouzoulis-Mayfrank & Daumann, 2006a) and methamphetamine (Gonzalez et al., 2004). Hence, isolating the impact of an individual substance on neuropsychological test performance proves challenging, and generalizing findings becomes problematic (Fals-Stewart & Bates, 2003). The potential pervasive cognitive impairment resulting from substance intake, coupled with the absence of data on premorbid cognitive functioning, poses a challenge in accurately differentiating

between premorbid characteristics and substance-related neurocognitive sequelae. Additionally, researchers frequently have to rely on proximal variables to infer premorbid cognitive abilities, such as self-reported learning difficulties or education attainment (Braatveit et al., 2018a). Furthermore, cognitive functioning may gradually improve spontaneously after cessation or reduction of substance intake, potentially diminishing the predictive value of the neuropsychological test results (Bates et al., 2013; Hagen, Erga, Hagen, et al., 2017; Hanson et al., 2010).

The impact of SUD, cognitive impairments and contextual factors, e.g., stigma, on the individual's adaptive function compounds methodological challenges. Concerns have been raised regarding the capacity of individuals with cognitive impairments to provide meaningful consent to participate in research (Smith et al., 2006). There are also theoretical concerns regarding the accuracy of the data obtained from subjects with SUD or cognitive dysfunction, e.g., problems with recollection, problem-denial or social desirable report styles (Ann Stoddard Dare & Derigne, 2010; Blume & Alan Marlatt, 2009; Dillon et al., 2005; Hindin et al., 1994; Smith et al., 2006; VanDerNagel et al., 2017). There are also limitations to how many tests that can be conducted, as overly exhaustive or time-consuming test batteries that cover all relevant cognitive domains can result in a loss of motivation to participate. This issue may be particularly relevant in studies with inaccessible clinical populations, such as individuals with SUD, who may lead unstable lifestyles and exhibit fluctuating motivation (Svendsen et al., 2021). Furthermore, the innate lifestyle for several patients with an SUD poses a multitude of practical obstacles to data acquisition and study retention, such as difficulties tracking down participants due to frequent changes in telephone number or address (Smith et al., 2006; Svendsen et al., 2017).

1.9.3 Cognitive assessment in a clinical context

The assessment of cognitive impairment within the SUD population has primarily been confined to research endeavours rather than a component of routine clinical practice (Berry, Shores, Nardo, et al., 2021). Nevertheless, efforts have been made to implement neuropsychological assessment and intervention practices informed by neuroscience-based approaches into the realm of SUD treatment (Berry, Shores,

Nardo, et al., 2021; Kwako et al., 2016; Oslo University Hospital, 2021a, 2021b, 2021c; Verdejo-Garcia et al., 2019). Although accurate identification of cognitive impairment may be key to enabling informed and personalized treatment, identifying such impairments poses a challenge in a clinical SUD treatment context. Cognitive decrements may be subtle and gradually, leaving the patient unaware of particular alterations in their cognitive functioning, especially if they have been present for an extended period of time (Hanson et al., 2011). Moreover, there may be discrepancies between performance on neuropsychological tests and the therapist's clinical evaluation of neurocognitive status (Fals-Stewart, 1997). Performance on cognitive screening tests and self-reported cognitive functioning may not provide an accurate indicator of neurocognitive status but rather reflect psychological distress (Hagen et al., 2019; Shelton & Parsons, 1987; Shwartz et al., 2020; Verdejo-García & Pérez-García, 2008). Moreover, symptoms of PTSD among patients with comorbid SUD may negatively alter the criterion validity of cognitive screening instruments (Kutash et al., 2023). Although a comprehensive neuropsychological assessment represents the gold standard, it is rarely a viable option due to time constraints and the availability of personnel with adequate neuropsychological training. The patient may also exhibit variable motivation, attendance, acute intoxication or substance withdrawal that impede assessment efforts. Consequently, clinicians are typically forced to rely on short screening instruments measuring broad cognitive domains. However, the criterion-related validity of such instruments, i.e., the veridicality-approach to ecological validity in terms of long-term clinically relevant outcomes in patients with an SUD, is not well established (Ko et al., 2021).

1.10 Aims and research questions

The main aim of this PhD project was to improve the knowledge on cognitive functioning, substance intake and psychological distress among patients with a pSUD. This includes establishing and comparing prevalence rates derived from clinically viable short cognitive assessment instruments and examining the instruments' ability to predict ultralong-term clinically relevant SUD treatment

outcome variables. Paper I aimed to examine the prevalence rate and demographic and clinical features of patients with a pSUD and cooccurring BIF. The main aim of Paper II was to investigate the predictive value of measures from common cognitive screening instruments on long-term substance use among patients with pSUD. Paper III aimed to investigate the predictive value of measures from common cognitive screening instruments on long-term psychological distress and interactions between substance use, cognitive impairment and psychological distress among patients with pSUD.

2. Methods

2.1 Design

The project used a prospective longitudinal cohort design. All data were obtained from the Norwegian Stavanger Study of Trajectories of Addiction (STAYER) examining neurocognitive, psychological and social recovery in patients with SUD (Helse Stavanger HF, 2023).

2.2 Procedure

The STAYER project aimed to ensure high retention rate and validity by implementing effective tracking strategies and participants engagement (Svendsen et al., 2017). Two research assistants were enlisted with the primary objective to track participants and conducting assessments. Each participant was assigned a primary research assistant throughout the project to ensure continuity and establish a working alliance. To ensure engagement in the study project, SMS-messages were delivered on special events relevant to the participants and they were also required to report their treatment status and substance intake at biweekly SMS follow-ups. Flexible visitation strategies were established which enabled follow-ups outside traditional office hours and in weekends. Additionally, ambulatory follow-up and assessment per telecommunication was offered. A comprehensive list of contact information for the participants was compiled and frequently updated. This list included contact information of friends, relatives, and other relevant individuals. Scheduling was done during the current follow-up with the use of SMS or telephone reminder one day prior to the next follow-up. In addition, communication strategies were employed to brand the study and ensuring high degree of community involvement from user organization, collaborating clinics and private organizations.

The participants were assessed irrespective of their treatment status or abstinence from substances over time. The baseline assessment in the STAYER project employed 16 instruments and self-report forms, while the quarterly and annual

assessments employed 8 and 14 instruments, respectively. The duration of assessments was between 45 to 250 minutes. Some participants reported strain from this examination schedule. Therefore, the volume of assessment inventories and assessment frequencies was reduced during the study progression to ensure study retention. In addition, biweekly monitoring SMS messages was delivered.

2.3 Study population

A total of 208 patients with SUD were recruited at convenience across 10 outpatient and residential enrolment sites within the specialized SUD treatment services in the Stavanger University Hospital catchment area between March 2012 and January 2016. To be eligible for treatment within the Norwegian specialized SUD treatment services, patients must meet the criteria for either a diagnosis of F1x.1 harmful use, F1x.2 dependency syndrome, or F63.0 pathological gambling as defined by the ICD-10 (World Health Organization, 1992). The inclusion criteria were a) patients enrolled in the treatment program within the specialized substance use treatment service to which they were admitted for at least two weeks; b) patients who met the diagnostic criteria for F1x.1 or F1x.2; c) patients over 16 years of age; d) patients who reported polysubstance use defined as the consumption of multiple substances within the last year before inclusion; and e) signed a written informed consent. Among the 208 patients in the STAYER cohort, 44 patients were excluded because of monosubstance use (alcohol N = 35, cannabis N = 1) or lack of substance-related disorders, e.g., gambling N = 8. The remaining sample of patients with pSUD comprised 164 participants. For Paper I, we additionally excluded one case because of missing IQ scores and one case because of an IQ score < 70; thus, the remaining sample in that study comprised 162 individuals. Papers II and III also utilized the pSUD cohort comprising 164 participants. Some participants had missing or invalid data for one or two cognitive measures. However, we opted not to exclude cases listwise to obtain optimal statistical power.

Baseline assessments were performed after a minimum of two weeks of self-reported abstinence to minimize contamination from drug withdrawal and the acute neurotoxic

effects from substances (Manning et al., 2008; Miller, 1985). Participants were compensated approximately NOK 400 for their participation. Data collection was carried out by trained research personnel from the STAYER research group, and clinicians treating the participants were naïve to the assessment results obtained in the current study.

2.4 Instruments and study variables

See Table 1 for an overview of all the instruments and variables used in the three papers. We used a preliminary version of the semistructured interview National Quality Register for Substance Abuse (KVARUS) (Center for Alcohol & Drug Research Helse Vest, 2018) to obtain demographic variables, substance administration, debut age, treatment and work history, vocational, and social adjustment.

2.4.1 Wechsler Abbreviated Scale of Intelligence

We employed the Norwegian version of the Wechsler Abbreviated Scale of Intelligence (WASI) in all papers to evaluate intellectual function (Brager-Larsen et al., 2001; Wechsler, 1999). The WASI was developed to provide a brief and reliable estimate of intellectual functioning. The test consists of four subtests. Two of these subtests are verbal measures of crystallized intelligence (Vocabulary and Similarities), which yield a Verbal Intelligence Quotient (VIQ), while the other two subtests are nonverbal measures of fluid intelligence (Block Design and Matrix Reasoning), which yield a Performance Intelligence Quotient (PIQ). In Paper I, participants with a full-scale IQ (FSIQ) score on the WASI between 70 and 85 were classified as having BIF. In Paper II and Paper III, participants with an FSIQ score of < 86 were defined as cognitively impaired, while those scoring ≥ 86 were classified as nonimpaired.

2.4.2 The Montreal Cognitive Assessment

We employed the Montreal Cognitive Assessment® (MoCA®) in Papers II and III to provide an overall measure of cognitive function by sampling behaviour across 14

performance tasks that engage aspects of attention, orientation, language, visuospatial abilities, executive function, and memory (Nasreddine et al., 2005). MoCA® is scored in integers with a total range of 0 to 30 and adjusted by +1 point if the test subject has less than 13 years of education. At a sum-score equal to or below 25, MoCA® has demonstrated high sensitivity and acceptable specificity in detecting mild cognitive impairment (Nasreddine et al., 2005). Furthermore, MoCA® has demonstrated good test-retest reliability and internal consistency, as well as sensitivity in detecting mild cognitive impairment in patients with SUD using this cut-off value (Copersino et al., 2009; Ko et al., 2021).

2.4.3 Behavior Rating Inventory of Executive Function - Adult version

We utilized the self-report questionnaire Behaviour Rating Inventory of Executive Function - Adult version (BRIEF-A) (Roth et al., 2005; Roth et al., 2013) in Papers II and III to assess executive functioning in real-life scenarios. The BRIEF-A yields nine subscales and three composite scores. The Behavioral Regulation Index (BRI) comprises the subscales inhibit, shift, self-monitor and emotional control. The subscales initiate, plan/organize, working memory, organization of materials, and task-monitor compose the Metacognition Index (MI). The BRI and MI can be merged to produce the overall Global Executive Composite (GEC). We applied the BRIEF-A cut-off scores, age norms and validation criteria proposed by the original authors (Roth et al., 2005). A t-score of ≥ 65 on the GEC was used to identify participants with cognitive impairment.

2.4.4 Symptom Checklist 90-Revised

We utilized the Norwegian version of Symptom Checklist 90-Revised (SCL-90-R) (Derogatis, 1994) in Papers I and III to assess psychological symptoms and distress. The SCL-90-R is a 90-item self-report measure widely used in clinical practice and research. The norms of the Norwegian version of SCL-90-R are derived from the general Norwegian population. SCL-90-R has been validated for patients with SUD as well as individuals with intellectual disability (Bergly et al., 2013; Kellett et al., 1999). Respondents rate each item on a five-point Likert scale, reflecting the level of

distress experienced in the past seven days, ranging from 0 (not at all) to 4 (severely). The checklist yields nine symptom dimension subscales: Somatization, Obsessive–Compulsive Disorder, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism, as well as a Global Severity Index (GSI), which was utilized as a measure of overall psychological distress. For Paper III, we also defined "caseness", i.e., a self-reported level of psychological distress that warrants further assessment, as a GSI standardized t score ≥ 63 or t score ≥ 63 on two or more symptom scales (Derogatis, 1994).

2.4.5 Satisfaction With Life Scale

We employed the Satisfaction With Life Scale (SWLS) (Diener et al., 1985) in Paper I to measure life satisfaction. The SWLS is a self-report questionnaire containing five items with a Likert-type format ranging from 1-strongly disagree to 7-strongly agree. A score of 20 represents a neutral point on the scale, while scores between 5 and 9 indicate dissatisfaction with life, and scores ranging between 31 and 35 indicate a high degree of life satisfaction (Pavot & Diener, 2008). SWLS has demonstrated robust psychometric characteristics (Pavot & Diener, 2008) and has also been validated for individuals with intellectual disability (Lucas-Carrasco & Salvador-Carulla, 2012).

2.4.6 The Drug Use Identification Test

The Drug Use Identification Test (DUDIT) is a self-report screening tool to assess substance consumption, substance behaviours, and substance-related problems (Voluse et al., 2012). It comprises 11 items that are reported on a five-point Likert scale ranging from "never" to "four or more times a week". For Paper II and Paper III, we used the four consumption items from the DUDIT (DUDIT-C) to gauge substance intake (Berman et al., 2015) and the DUDIT-C continuous scores when investigating the association between substance intake and cognitive performance. In paper II, we also defined two substance intake categories: total abstinence (DUDIT-C score = 0) and heavy substance use (DUDIT-C score ≥ 7). In the original DUDIT protocol, subjects reported substance use past 12 month; however, in Paper II and Paper III. participants reported substance use within the previous four months.

Table 1. Variables and instruments employed in the three papers.

	Variable	Instrument
Paper I	FSIQ (Cognitive status)	WASI
	GSI	SCL-90-R
	Life satisfaction	SWLS
	Age	KVARUS
	Gender	KVARUS
	Income from work or meaningful daily activity	KVARUS
	Work experience	KVARUS
	Education	KVARUS
	Treatment attempts	KVARUS
	In/out patient	KVARUS
	Debut age	KVARUS
	Years of substance use	KVARUS
	Lifetime injection	KVARUS
Paper II		
	FSIQ (Cognitive status)	WASI
	GEC (Cognitive status)	BRIEF-A
	Sum score (Cognitive status)	MoCA®

	Substance use (DUDIT consumption items)	DUDIT
	Age	KVARUS
	Gender	KVARUS
Paper III		
	FSIQ (Cognitive status)	WASI
	GEC (Cognitive status)	BRIEF-A
	Sum score (Cognitive status)	MoCA®
	GSI, Caseness	SCL-90-R
	Substance use (DUDIT consumption items)	DUDUT
	Age	KVARUS
	Gender	KVARUS

BRIEF-A: Behavior Rating Inventory of Executive Functioning – Adult version; DUDIT: The Drug Use Identification Test; GEC: Global Executive Composite; GSI: Global Severity Index; FSIQ: Full Scale IQ; KVARUS: National Quality Register for Substance Abuse; MoCA®: Montreal Cognitive Assessment; SCL-90-R: Symptom Checklist 90-Revised; SWLS: Satisfaction With Life Scale WASI: Wechsler Abbreviated Scale of Intelligence

2.5 Statistical method

In Paper I, we conducted a frequency analysis for the BIF and non-BIF groups. To compare between-group means, we performed independent-sample t-tests, while the chi-squared test of independence was used to determine group associations for the categorical variables. We also performed a post hoc analysis to explore the

association between BIF and SCL-90-R GSI scores by conducting a multiple regression analysis (forward selection) with SCL-90-R GSI score as the dependent variable and BIF status, age, gender, years of education, age of onset of substance use, history of injecting drugs, and SWLS sum score as independent variables.

In paper II, Mann–Whitney U tests were performed to evaluate between-group differences, and the chi-squared test of independence was used to analyse group differences for the categorical variables. To address multiple comparisons, Bonferroni-adjusted p-values were utilized to determine the statistical significance of study dropout and outcome variables of abstinence and heavy use at the one- and five-year follow-ups. We conducted logistic regression analyses with abstinence and heavy use at the follow-ups as the dependent variables and cognitive impairment defined according to the specific cognitive screening tool (MoCA®, WASI, or BRIEF-A), age and gender as predictors.

In paper III, Mann–Whitney U tests were performed to evaluate between-group differences, and the chi-squared test of independence was used to analyse group differences for the categorical variables. We conducted three-step hierarchical logistic regression analyses with SCL-90-R caseness at the one- and five-year follow-ups as the dependent variable and cognitive impairment defined according to the specific cognitive screening instrument (MoCA®, WASI, or BRIEF-A) as predictor in block 1, DUDIT-C score from the corresponding time point of interest in block 2 and baseline SCL-90-R GSI in block 3. We also used Nagelkerke's R2 to measure the goodness of fit of the logistic regression models.

2.6 Ethics

This study protocol was reviewed and approved by the Regional Ethics Committee West, University of Bergen, approval reference REK 2011/1877. The research was conducted according to its guidelines and those of the Helsinki Declaration (1975). All participants gave written informed consent. The STAYER project emphasized end user involvement and was initiated in partnership with end user organizations.

Participants are also invited to annual information meetings where they are updated on project developments from initiation to 2020. Due to the COVID-19 pandemic, these meetings were suspended until March 2023.

3. Results

3.1 Paper I: Prevalence and characteristics of BIF

Paper I examined the prevalence rate and demographic and clinical features of patients with a pSUD and cooccurring BIF. Among the participants included in the analysis, frequency analysis showed that 18% were classified as having BIF. Patients with BIF had elevated SCL-90-R GSI scores compared to patients without BIF. We did not find any statistically significant disparities between the BIF and non-BIF groups with regard to age, gender, income from work or other meaningful daily activities, years of work experience, years of education, treatment attempts, in- or outpatient status, SWLS sum score, age of substance debut, years of substance use, injected substances and age of first injection. A multiple regression analysis was computed to further investigate the association between the presence of BIF and SCL-90-R GSI scores. The procedure yielded a significant regression equation with BIF status, age and SWLS sum score as significant predictors of the SCL-90-R GSI scores.

3.2 Paper II: Predicting substance use outcomes

Paper II examined the ability of the MoCA®, WASI and BRIEF-A to predict long-term substance use outcomes. The associations of these instruments with long-term substance use were also established. A statistically significant association between continuous DUDIT-C scores and the respective cognitive measures was found only for MoCA® at the 1-year follow-up. Moreover, the results of the MoCA®, WASI and BRIEF-A did not predict substance abstinence or heavy substance use at the one- and five-year follow-ups. Although the investigation of cognitive impairment rates was not a specified aim in Paper II, frequency analyses unveiled that 33% exhibited cognitive impairment defined by MoCA®, while 60% displayed cognitive impairment defined by BRIEF-A GEC.

3.3 Paper III: Predicting psychological distress.

Paper III examined the associations between cognitive impairments and long-term psychological distress and the ability of cognitive screening tools to predict caseness. The results from the selected cognitive screening instruments showed associations with psychological distress and predicted later psychological distress.

At treatment initiation, there was no association between scores on MoCA® and psychological distress. However, MoCA®-defined impairment was associated with an increase in caseness at years one and five. Additionally, MoCA proved to be a significant independent predictor of long-term caseness in all regression modes. Importantly, even after accounting for the influence of baseline psychological distress, MoCA still served as an independent predictor of caseness. In all analyses, BRIEF-A defined impairment displayed a consistent positive association with elevated psychological distress and caseness. However, contrary to MoCA®, BRIEF-A lost statistical significance as a predictor variable when the effect of baseline psychological distress was controlled for. The relationship between WASI and psychological distress was equivocal, as WASI did not show a clear prediction pattern. WASI defined cognitive impairment was associated with psychological distress at baseline and caseness at year five, also when controlling for baseline psychological distress. Baseline psychological distress was associated with caseness at both one- and five-year measurements. Furthermore, it predicted caseness at both timepoints, even after controlling for the effect of substance use and cognitive impairment according to the respective instruments.

4. Discussion

4.1 Main findings

4.1.1 Prevalence rates of cognitive impairment

One main objective in the current project was to investigate the prevalence of cognitive impairments in general, with particular attention to individuals defined as BIF in a representative SUD population. The 18% prevalence rate of BIF among patients with SUD is somewhat higher than the expected 13.6% defined according to the Gaussian distribution of the general population norms. However, the estimate is also slightly lower than the 23% reported in Braatveit et al. (2018b). For Papers II and III, cognitive impairment was defined as an FSIQ <86, which classifies both participants with borderline intellectual functioning and those in the IQ range of mild intellectual impairment (IQ 50–70) as cognitively impaired (van Duijvenbode & VanDerNagel, 2019). Surprisingly, the STAYER pSUD cohort consisted of only a single participant with an IQ score below 70 (IQ=67). Thus, the subgroup with intellectual impairment reported in Paper II and Paper III effectively comprised participants with BIF, not MBID. In this context, the frequency of MBID in the current study is close to the 15.8% expected in the general population but considerably lower than the MBID rates of 30–39% previously reported among inpatient SUD populations (Braatveit et al., 2018b; Luteijn et al., 2017).

A secondary finding from Paper II indicates that the prevalence rate of MoCA® defined cognitive impairment was 33%. This frequency is comparable to the previously reported prevalence in SUD populations utilizing an identical MoCA® cut-off value (Bruijnen, Dijkstra, et al., 2019; Copersino et al., 2009; Fjærli et al., 2021; Sømhovd et al., 2019). The frequency of BRIEF-A GEC derived cognitive impairment was 60% and is comparable to the 63% reported in (McKowen et al., 2017).

4.1.2 Characteristics of BIF

In Paper I, we aimed to investigate the demographic and clinical features of BIF among patients with pSUD. The findings indicated that participants with BIF displayed elevated levels of self-reported psychological distress compared to those without BIF, while other disparities were not observed. A post hoc regression analysis, controlling for possible confounders, confirmed the independent association between psychological distress and BIF. These findings align with previous studies indicating that BIF is a risk factor for mental problems and psychiatric comorbidities (Chen et al., 2006; Gigi et al., 2014; Hassiotis, 2015; Hassiotis et al., 2008; Lim et al., 2022; Melby et al., 2020; Peltopuro et al., 2020). The research design of the current project did not allow us to determine the causal relationship between BIF and psychological distress. Surprisingly, and contrary to previous findings and discussions (Emerson, 2011; Gigi et al., 2014; Hassiotis et al., 2008; Nouwens, Lucas, Smulders, et al., 2017; Peltopuro et al., 2020; Snell et al., 2009), our study did not provide evidence of impairment in adaptive functioning among individuals with BIF. This finding aligns with previous studies that have suggested that IQ is a poor predictor of general everyday functioning in individuals with mild and borderline intellectual disability (Arvidsson & Granlund, 2018).

4.1.3 Prediction of substance use

Our main objective in Paper II was to examine how well the MoCA®, WASI and BRIEF-A predicted substance use one and five years after treatment initiation. We expected to observe a negative outcome among patients defined as cognitively impaired according to at least one of the screening instruments due to the well-documented link between cognitive impairments and adverse treatment outcomes such as relapse (Barreno et al., 2019; Beurmanjer et al., 2022; Braatveit et al., 2018b; Czapla et al., 2015; Hagen, Erga, Hagen, et al., 2017) and drop-out (Aharonovich et al., 2006; Brorson et al., 2013; Steele et al., 2014; Streeter et al., 2008; Sømhovd et al., 2019), which in turn may increase the risk of relapse (De Leon & Jainchill, 1986; Kast et al., 2021; Simpson et al., 1997; Simpson et al., 1999). Surprisingly, we could not establish any association between results from the cognitive assessment instruments and substance use outcomes one or five years after treatment initiation

except for the continuous DUDIT-C scores and MoCA® results at year one. However, the existing body of literature examining the impact of cognition on substance use treatment outcomes is predominantly restricted to periods of 12 months or less. The findings align with McKellar, Harris, et al. (2006), who reported that cognitive impairments predicted dropout from residential SUD treatment programs but not problematic substance use five years after dropping out from treatment (McKellar, Harris, et al., 2006). However, others have also reported a disconnect between treatment retention and later substance use in shorter study designs (Aharonovich, Brooks, et al., 2008). Furthermore, remission, with or without substance abstinence, is common (Dawson et al., 2006; Dawson et al., 2005; Newcomb et al., 2001; Tucker et al., 2020; Walters, 2000).

Several explanations for the lack of associations between cognitive status and substance use outcomes may be proposed. The treatment services may effectively have addressed the specific needs of patients with cognitive impairments. However, it is improbable that the majority of the study participants underwent comprehensive cognitive assessments that informed the treatment services to tailor their approach to accommodate cognitive deficits. With respect to this, it is noteworthy that the clinicians involved in patient care were naïve to the cognitive test results obtained in the study. Nonetheless, SUD treatment in Norway is a comprehensive undertaking that involves extensive cooperation and support from various governmental and private organizations. The provision of care is commonly a joint effort between the hospital trust, municipalities, Norwegian labor and welfare services and private community organizations to ensure a wide range of cost-free services, including therapy, access to private and public informal aftercare services, daily activities, practical assistance, housing and benefits to secure economic stability (Helsedirektoratet, 2012, 2017, 2020). The comprehensive nature of these integrated services may have the potential to compensate for certain aspects of adaptive function impairments due to cognitive deficits and mitigate disparities related to cognitive status.

The predictive value of the results from cognitive assessment may be attenuated in patients with pSUD. Individuals with pSUD often face profound social burdens and limited access to psychosocial resources. The confluence of these factors may severely compromise treatment and support efforts, consequently diminishing the role of cognition in recovery and reducing the predictive value of cognitive assessments.

Predictors of short-term relapse or problematic substance use may not correspond to long-term substance use outcomes. The Betty Ford Institute Consensus Panel (2007) posited three distinct stages in SUD recovery, reflecting the level of stability and resilience to relapse: early recovery (1-12 months), sustained recovery (1-5 years), and stable recovery (5 years or more). Individuals in long-term recovery generally experience fewer issues pertaining to housing, criminal activities, and substance abuse, and they are more likely to be employed or pursuing education compared to those in the early stages of recovery (Martinelli et al., 2020). Moreover, early abstinence is characterized by cognitive impairments (Fernández-Serrano et al., 2011; Hagen, Erga, Hagen, et al., 2017; Holst & Schilt, 2011; Verdejo-García & Pérez-García, 2007; Yücel et al., 2007), withdrawal (Li et al., 2015) and the need for change in nutrition and physical exercise (Jeynes & Gibson, 2017; Weinstock et al., 2017). This likely renders certain aspects of cognition (e.g., impulsivity) and physical capacity a salient feature of early recovery but not at later stages.

4.1.4 Prediction of psychological distress

Our main objective in Paper II was to determine the ability of the MoCA®, WASI and BRIEF-A to predict psychological distress one and five years after treatment initiation. The main finding of the study was that the results from the BRIEF-A and MoCA® emerged as significant predictors of long-term distress. However, the results from BRIEF-A lost statistical significance as a predictor after controlling for the effect of baseline psychological distress. This finding aligns with research that has demonstrated that results from the BRIEF-A are intimately linked to psychological distress and psychopathology across a wide range of clinical and nonclinical populations (Arellano-Virto et al., 2021; Braun et al., 2021; Geiger et al., 2019; Hagen et al., 2021; Kaiser et al., 2019; Løvstad et al., 2012; Løvstad et al., 2016;

Meltzer et al., 2017; Shwartz et al., 2020). The results for WASI were equivocal, as it did not function as a significant predictor in the regression models at year one, but showed significance in the year five models. A possible explanation for the association between results from the WASI and, to an extent the MoCA®, on long-term psychological distress may be found in their ability to provide measures of multiple and diverse cognitive domains (Royall et al., 2007). A more general impairment profile may hold greater significance in later stages of recovery when the individual has to cope with the intricacies and complex requirements of work and social life compared to early phases of recovery where goals are more demarked and the support network is more active and involved. In this context, cognitive impairment may increase the risk of psychological distress when interfering with the individuals' coping with the demands of daily life. Nevertheless, when compared to baseline distress and substance use at one- and five-year follow-ups, the instruments exhibited limited explanatory power for long-term psychological distress.

4.2 Methodological concerns

4.2.1 Selection bias

The study applied a convenience sampling method across 10 diverse in- and outpatient clinics. This strategy may have provided a heterogeneous and clinically relevant sample. However, convenience sampling is vulnerable to ascertainment biases that may limit the generalization of the current findings. The STAYER project has not obtained data on the characteristics of patients who declined participation. Nevertheless, nonparticipation in health studies has been linked to low socioeconomic status, living in socially deprived areas, lower education, unemployment and receiving disability pensions (Knudsen et al., 2010; Koopmans et al., 2012; Korkeila et al., 2001; Vo et al., 2023). SUD, psychotic disorders, and personality disorders are also particularly overrepresented among nonparticipants (Knudsen et al., 2010). This risk profile is relevant for the current research questions. For example, the prevalence of personality disorder among treatment-seeking patients with SUD is high (Landheim et al., 2002; Langås et al., 2012a), particularly among

patients with pSUD (Preti et al., 2011). Moreover, personality disorders are associated with cognitive impairment (Abramovitch et al., 2021; Bates, Labouvie, et al., 2002; Mortensen et al., 2005) but also greater functional impairment (Langås et al., 2012a; Skodol et al., 1999) and worse prognosis (Hasin et al., 2011; Verheul, 2001). Thus, a potential undersampling of patients with personality disorders may have resulted in reduced disparities in group differences pertaining to cognitive impairment, social adjustment and treatment outcomes and subsequently contributed to driving the null findings in Paper I and Paper II.

4.2.2 Missing data and study drop-out

The primary design concern in the present project revolves around the issues of low statistical power due to drop-out and missing data, specifically at the 5-year follow-up. Despite the STAYER research group's utilization of elaborate tracking and follow-up strategies to mitigate issues of missing data and drop out (Svendsen et al., 2021; Svendsen et al., 2017), we were unable to obtain data from several participants at follow-ups. The combination of a modest sample size, the high level of missing data and attrition undermines the internal and external validity of the current study and places constraints on statistical approaches in the study design (Austin et al., 2021; Gustavson et al., 2012; Morgan, 2017; Tipton et al., 2016).

The low data granularity in Papers II and III complicates the interpretation of the results. Participants may have undergone several transitions from substance use and abstinence periods between follow-up measurement points (Moe et al., 2021) and potential fluctuating psychological distress and mental health (Erga et al., 2021; Patel et al., 2015). Clinical recovery involves achieving a state of enduring behavioural stability (Bjornestad et al., 2020; Moe et al., 2021). However, the measures used in the present study reflect status at a particular moment in time and fail to capture the dynamic nature of long-term recovery. This issue is partly inherent to the STAYER design due to the selected frequency of measurements after year one but also stems from decisions made to reduce the volume of assessment inventories and assessment frequencies to alleviate strain on the participants and minimize study drop-out.

Consequently, the most complete and adequate datasets following the initial year were acquired at the annual follow-ups.

4.2.3 Measurements

Several studies share the limitation that participants are classified as cognitively impaired on the basis of performance on single tests or use of a single aggregated cut-off score from neuropsychological assessment batteries designed to evaluate a wide range of abilities (Fals-Stewart & Bates, 2003; Ko et al., 2021). However, numerous brain regions and information-processing operations contribute to the neuropsychological profile in patients with SUD (Fernández-Serrano, Pérez-García, Schmidt Río-Valle, et al., 2010). Converging evidence identifies a similar latent structure of neuropsychological abilities as risk factors for poor test performance in individuals with SUD. These encompass executive functioning, verbal ability, psychomotor and information-processing speed, and memory (Bates, Labouvie, et al., 2002; Fals-Stewart & Bates, 2003). As such, the current studies risk oversimplifying neuropsychological functioning and abilities underpinning test performance, thereby threatening ecological validity (Chaytor & Schmitter-Edgecombe, 2004; Fals-Stewart & Bates, 2003). However, while some dismiss brief measures of general cognition as mere “screening” tools, they may account for significantly more variance in functional outcomes than formal tests of attention, executive control, memory, verbal or visuospatial functioning (Royall et al., 2007). Crucially, in both research and clinical contexts, brief measures of general cognition may also be the only viable option for cognitive evaluation in SUD populations with severe functional impairment, as they are short, easy to administer, cost-effective and require minimal training.

Inferences from the results derived from the WASI warrant caution and limit the ability to draw robust conclusions. The frequency estimate of BIF derived from WASI was considerably lower than that reported in previous research on SUD populations (Braatveit et al., 2018b; Luteijn et al., 2017). Previous research has also shown that WASI norms are prone to overestimate the FSIQ in Norwegian samples (Bosnes, 2009; Siqveland et al., 2014), which may have resulted in the

underestimation of the BIF frequency rate. A skewed cut-off value may mask true disparities between the BIF and non-BIF groups in Paper I as well as drive the null findings in Paper II. This may occur due to the inclusion of non-BIF patients within the BIF group and/or lower statistical power caused by the small size of the low-scoring group. Severe alcohol use may also result in a greater reduction of performance IQ among individuals with intellectual functioning in the normal range compared to individuals with MBID, adding complexity to the interpretation of group differences (van Duijvenbode et al., 2016). Moreover, the criterion validity of the WASI with respect to correspondence with performance on the Wechsler Adult Intelligence Scale-III may be poor (Axelrod, 2002).

Strikingly, MoCA® proved to be an independent predictor for future caseness in Paper III but failed to predict later substance use in Paper II. However, MoCA® has been shown to be a poor predictor of impairments on later neuropsychological tests (Bruijnen, Jansen, et al., 2019) and may be sensitive to a range of mental illnesses (Blair et al., 2016; D'Hondt et al., 2018; Wood et al., 2019). Furthermore, PTSD symptomatology among patients with comorbid SUD may threaten the validity of the MoCA® results (Kutash et al., 2023). The elevated level of PTSD symptomatology among participants in the STAYER cohort (Belfrage et al., 2022) is therefore a cause for concern.

The STAYER study lacks detailed data regarding the specific type of substance used by the participants. Nor does it contain the participants' ICD-10 diagnosis. Although DUDIT is commonly employed in clinical practice, DUDIT-C is rarely utilized in research, which makes comparisons to previous findings difficult and the generalization of findings questionable. Moreover, the current project did not incorporate baseline DUDIT data due to concerns about the validity of the measure. This decision was made based on clear indications that participants had interpreted the instructions differently at the baseline measurement, whereby they reported substance use from different time frames. In subsequent follow-ups, the instruction of the DUDIT-C was underlined to increase data accuracy. Moreover, the KVARUS self-report questionnaire and the items intended to measure social adjustment have

not been validated; for example, the phrase “having other meaningful activity” lacks specificity.

Including gender among the predictor variables or performing gender-stratified analysis in Paper III would have been advantageous for elucidating the interplay of cognition, substance use and psychological distress. The use of an SCL-90-R T-score to delineate caseness in Paper III may be discriminatory to women because women tend to report more psychological distress than men. A higher average GSI for women than for men is reflected in the norms (Siqveland et al., 2016). This bias may hold significance due to the association between psychological distress and cognitive impairments (Blair et al., 2016; Hagen et al., 2021; Teasdale & Antal, 2016). Moreover, PTSD symptomatology and depression are overrepresented among women (Belfrage et al., 2022; Farré et al., 2017) and linked to cognitive impairments (Kutash et al., 2023; Stordal et al., 2004; Sumner et al., 2017). Women may also be more susceptible to substance-induced cognitive impairment than men (Bourgault et al., 2022). Thus, the study may fail to identify potential gender-specific disparities in the interaction between cognition, substance use and psychological distress. However, due to the low number of events per variable, we opted to exclude gender to minimize the risk of overfitting the logistic regression models. Some have suggested the use of a GSI raw score >1 as an alternative to delineate caseness to circumvent the issues with the SCL-90-R gender-specific norms (Siqveland et al., 2016). However, we decided to define caseness in accordance with the original author of the SCL-90-R (Derogatis, 1994) to increase the generalizability of the findings and their clinical utility.

4.2.4 Neuropsychological testing and SUD

The requirement of two weeks of substance abstinence prior to the neuropsychological assessments in the current studies falls at the lower end of the duration for psychometric testing after cessation in SUD research (Fernández-Serrano et al., 2011). Cognitive functioning typically shows significant improvement after 2-6 weeks (Vik et al., 2004), and withdrawal or other short-term effects might have influenced test performance for some participants in the current studies (WHO,

2009). However, the results from the MoCA® and BRIEF-A were comparable to existing findings in SUD populations (Bruijnen, Dijkstra, et al., 2019; Copersino et al., 2009; Fjærli et al., 2021; McKowen et al., 2017; Sømhovd et al., 2019). This correspondence may enhance the external validity of the findings, allowing for generalization to the broader SUD population.

Regarding WASI, intellectual functioning is often regarded as a relatively stable construct with trait-like characteristics (Deary, 2014; Whitaker, 2008). In the context of SUD, vocabulary may be resistant to the effects of substance use and maintain stability despite the presence of cognitive impairment. Indeed, studies indicate that the negative effect of substance use on IQ scores may be limited to 4-8 points (Fried et al., 2005; Manning et al., 2008; Meier et al., 2012) or be nonexistent (Braatveit et al., 2018a). The presence of a single participant with WASI performance in the intellectual disability range in the pSUD cohort also contradicts the notion that substance use has significantly decreased WASI scores in the current studies.

5. Concluding remarks and clinical implications

This thesis provides a theoretical framework for describing the interplay between substance use disorders, cognition and psychological distress in the context of assessment in SUD treatment services. The triple comorbidity of SUD, other mental disorders and cognitive impairment is widespread in clinical samples and remains a significant challenge for the delivery of effective health-care services. To date, few studies have examined long-term outcomes of cognitive impairments among individuals with an SUD. The project utilized instruments and inventories readily available in treatment services, thereby facilitating translation of the findings to a clinical context.

The findings in the current project indicate that there may be an overrepresentation of cognitive impairments, including borderline intellectual functioning, among patients in mainstream SUD treatment. Surprisingly, the ability of cognitive instruments such as the BRIEF-A, MoCA®, and WASI to predict long-term outcomes in a clinical context appears to be limited. Specifically, the cognitive status of patients defined by these instruments accounted for a small variance in terms of abstinence, heavy substance use and psychological distress. These findings are striking given the considerable body of evidence that highlights the negative effect of cognitive impairments on therapeutic processes and outcomes among patients with SUD.

The limited utility of the instruments used in the current project may be attributed to their specific biases and limitations. The MoCA® may not adequately measure executive functions, which are the primary cognitive domains that are impaired among patients with SUD and which have been shown to negatively impact treatment processes and outcomes (Blume & Alan Marlatt, 2009; Kwako et al., 2016; Le Berre et al., 2017; Verdejo-García & Bechara, 2009; Verdejo-García, Lorenzetti, et al., 2019). The results from the BRIEF-A are intimately linked to psychological distress (Shwartz et al., 2020) and may be better understood as a measure of psychopathologically derived functional impairments. The WASI-norms are skewed, and test results may not provide an accurate reflection of latent intellectual

impairments. Moreover, the instruments did not measure other potential relevant cognitive domains, such emotion-driven response inhibition and decision making, which might be key in predicting substance use among patients with SUD (Barreno et al., 2019; Verdejo-García, 2017). Alternatively, the extensive health and social services provided by the Norwegian welfare system may potentially mitigate some of the challenges faced by patients with cognitive impairments.

Nevertheless, the present project confirms a high prevalence of cognitive impairment among patients with pSUD. This necessitates the implementation of routine screening for cognitive impairment in SUD treatment, which should be reflected in treatment guidelines, strategic policies, and resource allocation. The project findings highlight the need to develop assessment procedures that can both identify patients with cognitive impairments relevant for SUD treatment and differentiate between transient and persistent neurocognitive impairments. Although some patients may experience spontaneous recovery or significant amelioration of cognitive functions after substance cessation, several may have enduring needs that surpass the scope of standard in- or outpatient health services. This underscores the importance of a multidisciplinary and multifaceted approach to SUD treatment, encompassing a wide array of governmental bodies and community players. Similarly, patients with pSUD exhibit a high rate of mental health problems, emphasizing the necessity for a routine, comprehensive diagnostic assessment tailored to this population. Ascertaining the mental health status of patients with SUD may be important when evaluating cognitive functioning, particularly in cases where clinicians must rely on short cognitive screening instruments and self-report inventories.

6. Future research

Studies aimed at establishing neuroscience-informed, viable and ecologically valid assessment procedures for patients with SUD are strongly warranted. The Research Domain Criteria for Mental Disorders was previously complemented with an alcohol addiction domain criteria-based framework (Insel et al., 2010; Kwako et al., 2016; Litten et al., 2015; Yücel et al., 2019), and initiatives have been made in neurofunctional phenotyping to understand the heterogeneity in SUD (Kwako et al., 2016; Kwako et al., 2019; Nieto & Ray, 2022). A pivotal step in translating new neuroscientific insights to clinical practice is to develop clinically viable neurocognitive assessment protocols with well-established ecological validity in terms of predicting therapeutic processes, change mechanisms, and treatment outcomes. In the context of these developments, efforts must be made to disentangle the effects of psychological distress and substance use on self-reported cognitive functioning, test performance and treatment outcomes. Although promising assessment instruments have been developed to target executive functions in patients with SUD (Berry, Shores, Lunn, et al., 2021; Berry, Shores, Nardo, et al., 2021), further validation is still needed. It is also crucial to examine the potential mediating and moderating effects of environmental and social factors on the association between cognitive impairments and treatment outcomes, as these factors may further elucidate patient heterogeneity, have prognostic value, and be incorporated into assessment and treatment protocols.

Given the well-documented high prevalence of cognitive impairments, including impaired intellectual functioning, there is a pressing need for the development of new treatment protocols, as well as iterations of existing ones, that are tailored to meet the needs of patients with cognitive impairments (Mistler et al., 2021). Potential interaction effects between cognitive impairments and treatment programs in terms of modality (e.g., group or individual therapy, motivational interview or mentalization-based therapy), level of care (in- or outpatient), and treatment services (e.g., specialized treatment service and/or vocational training) (Merkx et al., 2007) may be of pivotal importance to treatment planning and execution. Some evidence suggests

that the negative effects of cognitive impairments can be mitigated during treatment in a residential setting (Passetti et al., 2011; Rychtarik et al., 2000; Rychtarik et al., 2017) or through the use of a less cognitive demanding treatment modality (Carroll et al., 2011). Studies matching treatment intervention to patient characteristics have yielded mixed results (Cooney et al., 1991; Hser et al., 1999; UKATT Research Team, 2008). However, matching based on neuroscientific phenotyping (Kwako et al., 2016) is opening up exciting new avenues for research into novel treatment modalities, including cognitive remediation therapies, and accompanying clinically valid neurocognitive assessment procedures.

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Prevalence and Characteristics of Borderline Intellectual Functioning in a Cohort of Patients With Polysubstance Use Disorder

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Objective: To determine the prevalence and associated demographic and clinical features of borderline intellectual functioning (BIF) among individuals with polysubstance use disorder (pSUD).

Methods: We applied a cross-sectional analytical design to data from the Norwegian STAYER study (n = 162), a cohort study of patients with a pSUD from the Stavanger University hospital catchment area. We used Wechsler Abbreviated Scale of Intelligence Full Scale IQ (FSIQ) to define BIF (FSIQ = 70–85) and non-BIF (FSIQ = >85) and collected demographic and clinical data using semi-structured interviews and self-reports on the Symptom Checklist 90-Revised (SCL-90-R) and the Satisfaction With Life Scale (SWLS).

Results: The prevalence of BIF was 18% in the present study. The presence of BIF was associated with higher SCL-90-R GSI scores than in the non-BIF group. There were no significant differences between the BIF and non-BIF groups regarding age, gender, participation in meaningful daily activity, years of work experience, years of education, satisfaction with life, level of care, treatment attempts, age at substance-use onset, years of substance use, history of injecting drugs, or age of onset of injecting drugs.

Conclusion: The present study confirmed a higher prevalence of BIF among patients with pSUD than expected from the distribution of IQ scores in a general population. Elevated SCL-90-R GSI scores suggested that BIF is associated with increased psychological distress in patients receiving treatment for pSUD. Further studies on this association, and its effect on treatment procedure and outcomes are strongly warranted.

Keywords: polysubstance use disorder, borderline intellectual functioning, symptom check list-90-R, satisfaction with life scale, intelligence quotient, prevalence, substance use disorder

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INTRODUCTION

Intellectual functioning in patients with substance use and abuse has received increased attention during the last decade (1, 2). This follows the fact that intellectual functioning (e.g., reasoning, planning, problem solving, judgement, and abstract thinking) is a core predictor of a variety of life outcomes, with the most severe impairments observed in patients with an intelligence quotient

(IQ) two standard deviations below the population mean (IQ < 70) (3–5). In the present study, we focused on the impact of borderline intellectual functioning (BIF), which is defined as an intelligence quotient ranging between one and two standard deviations below the population mean (IQ = 70–85). Based on previous studies, we know that adults with BIF have an increased vulnerability for developing psychiatric disorders, including a substance use disorder (SUD) (2, 6–12). Assessment of intellectual function should therefore be considered an important component of clinical examination and treatment planning of SUDs.

According to the normal distribution of IQ scores (Bell Curve), approximately 13.6% of individuals in the general population would be allocated to a subgroup defined with BIF, with elevated rates commonly observed in clinical populations (13). Nevertheless, the frequency estimates within clinical groups are uncertain because of methodological differences between studies (ascertainment biases, the choice of diagnostic tools, service configurations, and entry criteria). In addition, there is a historical lack of terminological consensus and classification of BIF (14, 15) and non-agreed-upon diagnostic criteria in diagnostic manuals like the DSM-V and ICD-10 (16, 17). Nevertheless, studies have shown that individuals with BIF exhibit difficulties in several aspects of life, that these difficulties may occur at a similar level as for individuals with a diagnoses of intellectual disability (ID), and that individuals with BIF may need targeted support (1, 4, 6, 9, 10, 14, 18–21).

Individuals with BIF may not only be severely impaired; they are also less likely to receive adequate treatment for mental health issues, less likely to receive psychotherapy, and more likely to be treated with psychotropic medication than individuals with mental health problems in the general population (10, 22). This is obviously the case in individuals with co-occurring BIF and SUD; they tend to show adverse rehabilitation outcomes when offered mainstream SUD treatment, because of factors such as reduced disposition to change and desire for help (23, 24), lower treatment compliance (25), high drop-out rate (26–28), relapse during treatment (29), and negative treatment experiences (30). Therefore, it is alarming to realize that impaired intellectual functioning is often overlooked in treatment programs for patients with SUD, even though it can be a key clinical factor in predicting treatment needs and prognosis (24, 29, 31–34).

There is a dearth of research on BIF in general, and BIF in SUD populations in particular. When included in studies, BIF is typically classified broadly as mild-to-borderline intellectual disability (MBID) with IQ ranging between 50 and 85, or treated as a control group (4). The major thrust of research on the co-occurrence of BIF and SUD originate from the field of ID services and target substance use in individuals with a known ID diagnosis. Subsequently, findings are mainly published in journals in that field, rather than in journals in the field of medical addiction (2). Initiatives to develop a framework around the clinical and adaptive needs of patients with co-occurring SUD and BIF have been sporadic and uncoordinated (14).

Studies examining the prevalence rates of BIF in SUD populations are scarce, and their prevalence rates vary considerably. Braatveit et al. found the prevalence rate of BIF among patients with SUD to be 23% (29), and Luteijn et al. reported a MBID prevalence rate of 39% (24). At the other end of the scale, VanDerNagel et al. reported a prevalence estimate as low as 3% (35). Furthermore, prevalence data for BIF and MBID are difficult to compare because of lack of consensus on terminology, differences in group characteristics, levels of disability, treatment settings, comorbid psychiatric disorders, and definition and scope of substance use (2, 13, 36). Taken together, studies of BIF based on standard instruments in well-characterized cohorts of patients with SUD are obviously warranted.

The lack of epidemiological data and findings showing that BIF may be vital for the broader understanding and treatment of patients with SUD motivated the present study to investigate the prevalence and characteristics of patients with BIF in a typical group of individuals receiving treatment for polysubstance use disorder (pSUD). Polysubstance use is common in both clinical, and population samples (37, 38). Moreover, polysubstance use patterns is frequent in patients seeking treatment for mono-substance disorders (39–43). In this context, pSUD refers to the use of multiple substances as part of a pattern of problematic substance use, in which the patient meets criteria for SUD for some, but not necessarily all substances used (44). Compared with mono-substance users, polysubstance users have an earlier onset of substance use (45), are younger (37), have higher levels of psychological distress and personality disorders (45–50), more persistent cognitive impairments (51), and poorer social adjustment (37, 46, 48, 52). Studies suggest that these characteristics are associated with increased risk of dropout and relapse (27, 53–57). Thus, patients with pSUD may have a more severe clinical profile than patients with mono-substance use and consequently pose a challenge for SUD-treatment services and the mental health care system (46, 53, 58, 59).

The aim of the present study is twofold: (1) to provide a prevalence estimate of BIF in patients with pSUD receiving mainstream SUD treatment (2) to investigate clinical and demographic features in subgroups of patients with and without co-existing BIF.

MATERIALS AND METHODS

Study Design and Patient Characteristics

The study used data from the Stavanger Study of Trajectories of Addiction (STAYER), an ongoing, prospective, longitudinal cohort study of the neurocognitive, psychological and social recovery in patients with polysubstance use who started a new treatment sequence in the Stavanger University Hospital catchment area (60, 61). See Andersson et al. (54) for more details regarding the structure of Norwegian SUD-treatment. To be eligible for specialized treatment for SUDs within the Norwegian public health service, patients must meet the criteria for a F1x.1 (harmful use) or F1x.2 (dependency syndrome) diagnosis, as defined by the ICD-10 (17). We performed baseline assessment after 2 weeks of abstinence, in an attempt to minimize contamination from drug withdrawal and the acute neurotoxic effects from psychoactive substances (62). Trained research personnel of the STAYER research group collected all data. In the

present study, polysubstance users were defined as patients with SUD who reported the use of multiple substances within the last year before inclusion. The project was approved by the Regional Ethics Committee (REK 2011/1877) and conducted according to its guidelines and those of the Helsinki Declaration (1975). All participants provided signed informed consent.

Participants

A total of 208 patients were recruited consecutively at convenience from 10 outpatient and residential treatment facilities within the Stavanger University Hospital catchment area between March 2012 and January 2016. All patients had been voluntary admitted for SUD-treatment.

Patients were included if they (1) signed a written informed consent, (2) were enrolled in a new rehabilitation sequence by the substance use treatment service, (3) reported use of multiple substances within the last year before inclusion, and (4) were 16 years or above. Patients received a compensation of NOK 400 for their time at the baseline testing. Of the 208 patients in the STAYER cohort, 44 patients were excluded from the present study because of mono-substance use (alcohol $N = 35$, cannabis $N = 1$) or lack of substance-related disorders (e.g., gambling $N = 8$). We excluded one case because of missing IQ scores and one case because of an IQ score <70; thus, the remaining sample of patients with pSUD comprised 162 individuals.

Assessment

We obtained demographic, neurocognitive, psychological, and social-functioning data using semi-structured interviews, cognitive tests, and self-reported measures at the baseline assessment. We used a preliminary version of the National Quality Register for Substance Abuse (KVARUS) (63), a semi-structured interview to obtain information on the type of substance intake, initial age at use, treatment and work history, and educational, vocational, and social adjustment.

Wechsler Abbreviated Scale of Intelligence

Wechsler Abbreviated Scale of Intelligence (WASI) (64) was used to assess intellectual function. WASI was created to establish a brief and reliable estimate of intellectual functioning and comprises four subtests, i.e., two verbal measures of crystalized intelligence (Vocabulary and Similarities), which yield a verbal intelligence quotient (VIQ), and two non-verbal tests of fluent intelligence (Block Design and Matrix Reasoning), which yield a performance intelligence quotient (PIQ). BIF was defined as a WASI Full-scale IQ (FSIQ) ranging between 70 and 85, and non-BIF was defined as a FSIQ > 85.

Satisfaction With Life Scale

Satisfaction with life was assessed using the Satisfaction With Life Scale (SWLS) (65). SWLS is a self-report questionnaire comprising five items to measure the respondent's global life satisfaction with a seven-point Likert-type format (ranging from 1-strongly disagree to 7-strongly agree). SWLS has demonstrated excellent psychometric characteristics (66) and also validated for individuals with ID (Cronbach's alpha = 0.79) (67). A score of 20 represents a neutral point on the scale; scores between 5 and 9 indicate dissatisfaction with life, while scores ranging between 31 and 35 indicate that the respondent is very satisfied with life (66).

Symptom Checklist 90-Revised

We used the Symptom Checklist 90-Revised (SCL-90-R), which is a 90-item self-report measure (68) assessing psychological symptoms and distress. SCL-90-R is widely used in clinical practice and research, and validated for patients with SUD and individuals with ID (68–70). Items are rated on a five-point Likert scale indicating the degree of distress, ranging from 0 (not at all) to 4 (severely) during the 7 previous days. The checklist comprises nine symptom dimension subscales: Somatization, Obsessive–Compulsive Disorder, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism, in addition to a global severity index (GSI), which was used here as a measure of psychological distress.

Statistics

The statistical software package SPSS version 26 (IBM Corp., released 2016) was used for all statistical analyses. Statistical significance was set at $P < 0.05$, and assumptions of normality evaluated based on Q–Q plots and by inspecting the residuals. A frequency analysis was run for the BIF and non-BIF groups. Independent-sample *t*-tests were performed to evaluate differences between-group means, and the chi-squared test of independence was used in case of categorical variables.

Because of an association between BIF status and SCL-90-R GSI score, we performed additional *post hoc* analyses to explore this association. As a result of the modest size of the BIF group, we opted not to use BIF status as a dependent variable in logistic regression analyses because of the risk of overfitting the regression model (71). Instead, we performed a multiple regression analysis (forward selection) with SCL-90-R GSI score as the dependent variable and BIF status, age, gender, years of education, age of onset of substance use, history of injecting drugs, and SWLS sum score as independent variables.

RESULTS

Among the 162 participants included in the analyses, 29 (17.9%) were classified as having BIF. **Table 1** shows the demographic and clinical features in the total sample and stratified according to intellectual functioning (i.e., the BIF and non-BIF group). Participants in the BIF group (M = 1.4, SD = 0.8) exhibited significantly higher SCL-90-R GSI scores than the non- BIF group [M = 1.1, SD = 0.6; $t_{(160)} = 2.5$, $p < 0.05$], indicating a higher degree of self-reported psychological distress in the former group. No further significant differences were detected between the BIF and non-BIF groups on any demographic or clinical feature.

Figure 1 shows that the distribution of IQ scores in the present cohort was comparable to the expected distribution in the general population, with a small shift toward the lower end of the scale.

Table 2 lists the WASI scores in the total sample and within the two groups. The mean WASI FSIQ in this BIF group was 80.3

TABLE 1 | Demographic and clinical features of the present sample stratified according to intellectual functioning.

	Total sample		BIF ($n = 29$)		Non-BIF ($n = 133$)		Statistics		
	n	Mean (SD)/*n* (%)	*n*	Mean (SD)	*n*	Mean (SD)	*t*(df)/Value (df)	Cohen's d	*P*-value
Age	162	27.6 (7.5)	29	26.1 (8.4)	133	27.9 (7.3)	−1.22 (160)	0.24	0.225
Male gender*	162	106 (65.4)	18 (62.1)		88 (66.2)		−0.18 (1)		0.674
Income from work or other meaningful daily activity*	162	101 (62.3)	17 (58.6)		84 (63.2)		0.21 (1)		0.648
Years of work experience	146[a]	5.6 (5.8)	26	4.0 (4.1)	120	5.9 (6.1)	−1.51 (144)	0.36	0.134
Education, years	162	11.6 (1.7)	29	11.2 (1.7)	133	11.7 (1.7)	−1.18 (160)	0.24	0.239
Treatment attempts	162	1.6 (2.4)	29	1.5 (2.0)	133	1.6 (2.4)	−0.29 (160)	0.06	0.776
In-patient*	161[a]	95 (58.6)	20 (71.4)		75 (56.4)		2.16 (1)		0.141
SCL-90-R GSI	162	1.1 (0.7)	29	1.42 (0.8)	133	1.1 (0.6)	2.48 (160)	0.46	0.014
SWLS sum score	162	15.4 (6.3)	29	14.8 (6.1)	133	15.5 (6.4)	−0.57 (160)	0.12	0.569
Age of drug debut	160[a]	13.1 (2.1)	29	12.7 (1.7)	131	13.1 (2.2)	−0.95 (158)	0.21	0.343
Years of drug use	160[a]	14.5 (7.5)	29	13.3 (8.1)	131	14.8 (7.4)	−0.95 (158)	0.18	0.343
Injected drugs*	161[a]	98 (60.5)	15 (51.7)		83 (62.9)		1.24 (1)		0.265
Age at first use of injected drugs	98[b]	19.7 (5.0)	15	18.2 (5.8)	83	20.0 (4.8)	−1.29 (96)	0.36	0.202

*Chi-squared test of independence.
[a]Numbers lower than 162 are caused by missing data.
[b]Participants with a history of injecting drugs.

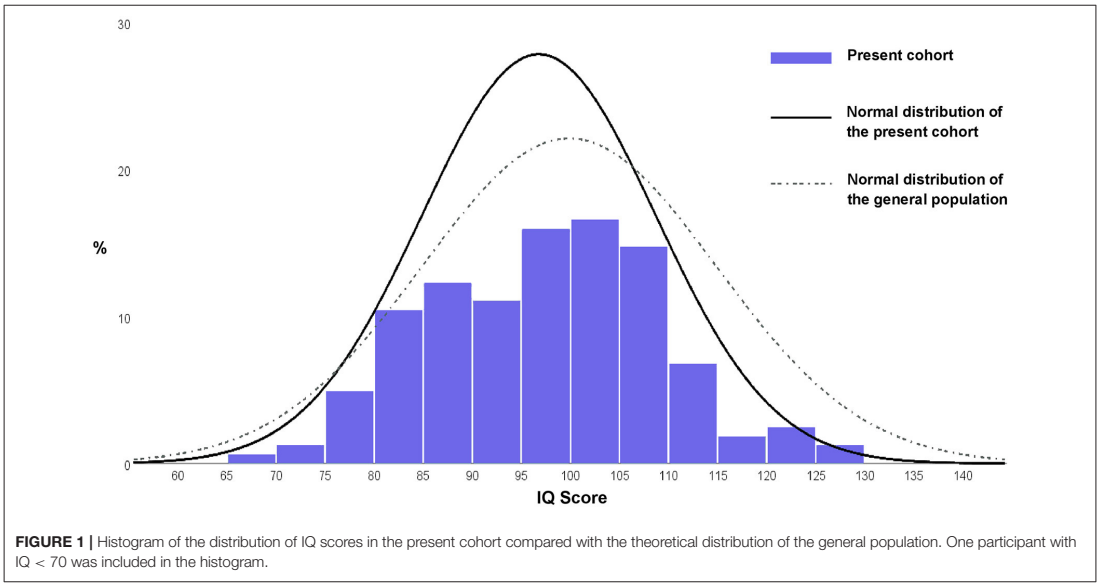

FIGURE 1 | Histogram of the distribution of IQ scores in the present cohort compared with the theoretical distribution of the general population. One participant with IQ < 70 was included in the histogram.

(SD = 3.8, 95% CI = 78.8–81.7), whereas the mean WASI FSIQ was 100.8 (SD = 9.4, 95% CI = 99.1–102.4) in the non-BIF group.

A multiple regression analysis using the SPSS' forward selection algorithm was computed to further investigate the association between the presence of BIF and the SCL-90-R GSI scores. The SCL-90-R GSI scores were included as the dependent variable and the BIF status as well as age, gender, years of education, age of onset of substance use, history of injecting drugs, and SWLS sum score as independent variables. This procedure yielded a significant regression equation $F_{(3,156)} = 14.882$, $P < 0.001$; $R^2 = 0.223$), leaving BIF status as well as age, and SWLS sum score as significant predictors of the SCL-90-R GSI scores (see **Table 3** for details).

DISCUSSION

The prevalence rate of BIF in patients with polysubstance use was 18% in the present study. There were few statistically significant

TABLE 2 | WASI scores in the total sample stratified according to intellectual functioning.

	Total sample		BIF (n = 29)		Non-BIF (n = 133)		Statistics		
	n	Mean (SD)	*n*	Mean (SD)	*n*	Mean (SD)	*t*(df)	d	*P* value
WASI FSIQ	162	97.1 (11.7)	29	80.3 (3.8)	133	100.8 (9.4)	−11.5 (160)	2.85	<0.001
WASI VIQ	162	95.1 (12.7)	29	82.5 (8.2)	133	97.8 (11.8)	−6.6 (160)	1.51	<0.001
WASI PIQ	162	99.9 (13.2)	29	82.0 (8.1)	133	103.8 (10.7)	−10.4 (160)	2.30	<0.001

TABLE 3 | Summary of the regression analysis with SCL-90-R GSI as dependent and BIF status, age, and SWLS sum as independent variables.

Variable	B	95% CI	β	*t*	*p*
(Constant)	2.533	[2.082, 2.983]		11.106	<0.001
SWLS Sum score	−0.039	[−0.054, −0.024]	−0.369	−5.219	<0.001
Age	−0.021	[−0.033, −0.008]	−0.233	−3.283	0.001
BIF-status	−0.256	[−0.499, −0.014]	−0.148	−2.086	0.039

BIF status is coded as 0 for BIF and as 1 for non-BIF.
CI, confidence interval for B.

differences between the BIF and non-BIF groups regarding demographic and clinical features. However, patients with BIF had significantly elevated SCL-90-R GSI scores, indicating a higher degree of psychological distress compared with the non-BIF group. A regression analysis confirmed the importance of BIF status, even when controlling for a range of demographic and clinical data.

The prevalence rate of BIF found in the current study was higher than that observed in the general population, but still somewhat lower than reported by some previous studies of patients selected from in-patient SUD populations (24, 29). However, the sample included in the study of Luteijn et al. (24) was selected from a forensic unit and gauged the prevalence rate of MBID, not BIF. Although it may be tempting to hypothesize that patients receiving in-patient treatment have more impaired intellectual functioning compared to patients receiving out-patient treatment, the results of the current study do not support this notion, as there were no significant differences in the prevalence rate of BIF between these two groups. The prevalence rate of BIF found in the present study was indeed higher than the 3% identified by VanDerNagel et al. (35). However, those authors relied on the identification of individuals with BIF through a review of caseloads and patient records. Because of the low recognition of MBID/BIF, those findings are expected to provide underestimations compared with the results of studies including direct assessment of intellectual functioning.

The regression model indicated independent negative associations between the independent variables SWLS sum score, age, and BIF-status and SCL-90-R GSI score among patients with pSUD. The association between SWLS sum score and SCL-90-R GSI score was expected, given the conceptual similarities between psychological well-being and life satisfaction in human functioning. In addition, age was negatively associated with SCL-90-R GSI scores, a finding that was expected based on previous studies (44, 72). A strong association between BIF and an elevated SCL-90-R GSI score among patients suffering from pSUD is a main finding of the present study. This finding is in accordance with previous studies reporting associations between psychological distress and impaired intellectual functioning (19, 73–76). Although causality of the association between SCL-90-R GSI score and BIF status in the present study is unknown, several direct and indirect paths may be suggested.

Individuals with impaired intellectual functioning may be susceptible to the development of psychological ill-health and impaired social adjustment due to reduced capacity for problem-solving, flexible adjustment and stress tolerance (77). Conversely, psychiatric disorders may induce temporary state-specific neurocognitive disruptions impairing cognitive performance (78–80). Finally, the selected measures may not reflect disparities in latent cognitive abilities as psychological distress may impede test performance indirectly through lack of performance motivation, low self-efficacy and increased engagement in distracting worrisome thoughts or task-irrelevant cognition.

The use of an IQ criterion in the diagnosis of ID is thought to reflect a relationship between intellectual and everyday functioning, and most studies identify borderline intellectual disability solely from intellectual functioning measures, i.e., BIF (29). While the current study found disparities in the associated clinical features between the BIF and non-BIF patients with pSUD, the differences were primarily reserved to the SCL-90-R GSI score. Surprisingly, the findings thus did not support the presence of a more global impairment in BIF compared to non-BIF patients with pSUD. e.g., educational attainment is typically shown to be associated with higher intellectual functioning (81–83). However, to access specialized treatment for SUDs within the Norwegian public health service, patients must exhibit severely debilitating substance use. Furthermore, both the BIF, and non-BIF groups share approximately the same early onset of substance use (13 years). Both early onset and subsequent severe substance use likely attenuate the predictive value of IQ by exerting a major detrimental influence on scholastic performance (84), attendance (85), drop out (86–89), and overall social adjustment.

The present study used the classification of BIF rather than borderline intellectual disability, as the latter relies on additional measures of adaptive functioning and onset before 18 years of age. In addition, several studies investigated the clinical features of co-occurring BIF and SUD by combining the IQ ranges of BIF and mild ID (2, 24, 35, 90, 91). The risk factors and associations identified in these studies may result from the inclusion of a proportion of individuals with ID. Alternatively, our results

may be used to argue that intellectual functioning, as measured by WASI or otherwise, may be less useful when accounting for differences in clinical features and everyday functioning in patients with SUD.

Strengths and Limitations

The current cohort was recruited from a multitude of specialized and diversified SUD rehabilitation services including both in- and out-patient units targeting different patient groups with regard to type and severity of comorbid psychiatric disorders, the severity of substance use, and degree of social adjustment and functioning, as well as the stage of the rehabilitation process. The universal access to health care in Norway allows the collection of a more comprehensive sample relative to countries where care is privatized and costly. Thus, the findings of the current study cannot necessarily be generalized to a specific clinical population (e.g., in-patients), but do elucidate the general state of intellectual functioning and associated clinical features among patients with pSUD.

Most previous studies investigated the clinical features of individuals with substance use among patients already identified as having ID (IQ $<$ 70) or MBID (IQ $=$ 50–85) (2). To the authors knowledge, this study is the first to examine the prevalence rates and associated demographic and clinical factors in individuals with previous unidentified BIF (IQ $=$ 70–85) in both in- and out-patients receiving mainstream SUD services for polysubstance abuse. The current study's main findings are consistent with the few other studies from a SUD population, who identify an over-representation of impaired intellectual function among patients with SUD (24, 29). The current study adds on to these results by controlling for the effect of age, gender, years of education, age of onset of substance use, history of injecting drugs and satisfaction with life, in the analysis of the association between BIF and psychological distress.

The main limitation of this study concerns the representativeness of the Norwegian WASI test norms. Previous studies have shown that WASI tends to overestimate the FSIQ IQ level in Norwegian samples (92, 93), which may have led to the underestimation of the prevalence rate of BIF in the current study. In addition, the clinical differences between the BIF and non-BIF groups in the sample may have been masked if a skewed cut-of value of BIF have led to inclusion of non-BIF patients within the BIF group. Furthermore, WASI has not explicitly been validated for patients with SUD with a high level of psychological distress, which may also have affected the results of the present study. Finally, the STAYER cohort was recruited using convenience sampling in a clinical setting, which is vulnerable to ascertainment biases by undersampling patients with lower intellectual functioning, low motivation for change and lower-functioning patients with BIF.

Clinical Implications

BIF among patients with SUD is common. Screening for intellectual functioning should therefore always be considered as part of the clinical practice, and treatment programs should account for a significant sub-population of patients with co-occuring SUD and intellectual impairments.

Clinicians should not only be wary of elevated levels of psychological distress in patients with SUD (54), but also that BIF may represent a potential added risk factor for detrimental treatment outcomes, drug-seeking behavior and relapse. Studies aimed at examining potential factors that mediate and moderate the relationship between psychological distress and intellectual functioning are therefore strongly warranted.

The current study could not establish a relationship between BIF status and social adjustment, which further highlights the importance of including data pertaining to everyday functioning in the assessment and diagnosis of ID, as well as the classification of borderline intellectual disability. Conjointly, measurements of general intellectual functioning may, to a lesser degree, predict social adjustment in patients with SUD. Furthermore, the associated risk factors as well as the long-term rehabilitation trajectories and prognosis of the co-occurrence of SUD and BIF are mostly unknown and warrant further investigation.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Regional Ethics Committee (REK 2011/1877). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

JH, EH, and AE: conceptualized and designed the study. JH: wrote the first draft and revised the manuscript. JH and AE: performed the analyses. AE, EH, KB, and AL: made critical revisions of the manuscript. AE and AL: supervised the study. All authors contributed to the article and approved the submitted version.

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Performance on Cognitive Screening Tests and Long-Term Substance Use Outcomes in Patients with Polysubstance Use Disorder

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Keywords
Cognitive impairment · Substance use · Outcomes · MoCA · IQ

Abstract

Introduction: Cognitive impairments among patients with substance use disorders are prevalent and associated with adverse treatment outcomes. However, knowledge of the predictive value of broad cognitive screening instruments on long-term treatment outcomes is limited. The present study aimed to examine the predictive value of measures from the Montreal Cognitive Assessment® (MoCA®), Wechsler Abbreviated Scale of Intelligence (WASI), and the Behaviour Rating Inventory of Executive Function – Adult version (BRIEF-A) on self-reported long-term substance use and abstinence in patients with polysubstance use disorders (pSUD). ***Methods:*** A cohort (N = 164) of patients with pSUD who started a new treatment sequence in the Stavanger University Hospital catchment area were recruited and followed prospectively for 5 years. Participants completed neurocognitive testing with the MoCA®, WASI, and BRIEF-A at inclusion and were categorized as cognitively impaired or non-impaired according to recommended cut-off values. The sum score of the items from the Drug Use Disorders Identification Test Consumption scale (DUDIT-C) was used as a measure of substance use outcome 1 and 5 years after inclusion. We defined substance abstinence (DUDIT-C = 0) and heavy substance use (DUDIT-C ≥7) to determine whether cognitive impairments measured by the respective instruments were associated with and could predict abstinence and heavy substance use 1 and 5 years after baseline. ***Results:*** At the 1-year follow-up, 54% of the total sample reported total abstinence from substances. Conversely, 31% presented heavy substance use. At 5 years, 64% of the total sample reported abstinence from substances, while 25% presented heavy substance use. The results showed a statistically significant association between cognitive impairment defined from MoCA® and higher continuous scores on DUDIT-C at 1-year follow-up. There were no differences in substance abstinence or heavy substance use between patients with and without cognitive impairment at the 1- and 5-year follow-ups. Furthermore, cognitive impairment did not explain substance abstinence or heavy substance use at the 1- and 5-year follow-ups. ***Conclusion:*** Generally, individuals with pSUD may be burdened and lack psychosocial resources to such an extent that cognitive functioning plays a subordinate role in long-term recovery. The present study suggests that results on screening tools assessing broad cognitive domains at treatment initiation have limited clinical value in predicting long-term substance use outcomes. There is a need to establish clinically viable instruments to assess cognitive functions with well-established clinical and ecological validity in the SUD population.

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Introduction

The prevalence of cognitive impairments among patients with substance use disorders (SUDs) is estimated to be between 30 and 80% [1, 2]. Such impairments may cause a loss of cognitive and behavioural flexibility and capacity to assimilate and engage in treatment programmes that often have an educative and cognitive emphasis [3, 4]. Indeed, previous findings suggest that cognitive impairments are associated with poorer SUD-treatment outcomes through lower recognition of problem use [5], lower treatment adherence [6], lower outpatient therapy attendance [7], a high dropout rate [8], relapse proneness [9], lower self-efficacy [10], and reduced disposition to change and desire for help [11, 12].

Abstinence is often considered a safe approach and the ultimate goal of SUD treatment [13]. Studies also suggest abstinence improves the quality of life, psychological distress, and executive function [14]. However, abstinence-based treatment may not be considered realistic for all patients with a SUD. For some, the primary clinical goal of treatment may rather be harm reduction, sustaining or improving daily life functioning, and preventing debilitating heavy substance use. In a clinical context, identifying long-term risk factors for abstinence and heavy substance use is paramount to tailor treatment to the patients' needs. Although cognitive impairments have been associated with adverse short-term treatment outcomes from SUD treatment, the ultralong-term outcome trajectories and recovery patterns of patients with cognitive impairments are still largely unknown. In fact, longitudinal studies investigating cognitive predictors rarely exceed 12 months.

Treatment retention is considered a key predictor of treatment outcome and constitutes a considerable challenge in treating patients with SUDs [15, 16]. Treatment may significantly reduce substance intake, but remission with or without abstinence and treatment is common [17, 18]. McKellar, Harris, and Moos [19] found that cognitive impairment predicted treatment dropout but not substance intake 5 years after dropping out of treatment. Thus, predictors of treatment dropout or early relapse may not correspond to predictors of long-term outcomes. Further longitudinal studies on associations between cognitive function and treatment outcome are therefore strongly called for.

Accurate identification of cognitive impairments may be vital to enable personalized interventions. However, identifying such impairments is challenging in non-specialized clinical settings. Performance on cognitive screening tests or self-reports of cognitive functioning may not give an accurate impression of the patient's cognitive functioning and may even be more indicative of psychological distress than neurocognitive function [20–22]. In addition, there may be discrepancies between a therapist's clinical evaluation of neurocognitive status and performance on neuropsychological tests [23]. Although the gold standard entails a comprehensive neuropsychological examination, time constraints and the availability of personnel specialized in designing and interpreting results from these examinations are limited. Furthermore, anamnestic information may not be readily available, and patients may show variable motivation and attendance that impede the assessment efforts. As a result, service providers commonly rely on short screening instruments measuring broad cognitive domains. However, the criterion-related and, in particular, the ecological validity of such cognitive screening instruments in terms of long-term clinically relevant outcomes in patients treated for a SUD is not well established [24].

Aim

The overall objective of the present study was to evaluate the clinical value of including a set of well-known and commonly used cognitive screening instruments when patients with a polysubstance disorder (pSUD) are enrolled in a treatment program. Specifically, the present study aimed to (1) establish associations between cognitive impairments measured by the Montreal Cognitive Assessment® (MoCA®), Wechsler Abbreviated Scale of Intelligence (WASI), and Behaviour Rating Inventory of Executive Function – Adult version (BRIEF-A) and substance intake at follow-ups 1 and 5 years after enrolling in a treatment programme, and (2) examine the ability of the MoCA®, WASI, and BRIEF-A to predict substance abstinence and heavy substance use in patients with pSUD at the two follow-ups. Accordingly, we hypothesize that cognitive impairment according to at least one of the screening instruments will be associated with increased substance use and predict non-abstinence and/or heavy substance use at 1- and 5-year follow-ups after enrolment.

Materials and Methods

Design

This study is based on data from the Stavanger Study of Trajectories of Addiction (STAYER), a prospective longitudinal cohort study of neurocognitive, psychological, and social recovery in patients with SUD who started a new treatment sequence in the Stavanger University Hospital catchment area in Norway.

Setting

A total of 208 patients with SUD were recruited at convenience from 10 specialized outpatient and residential SUD-treatment facilities within the Stavanger University Hospital catchment area between March 2012 and January 2016. To be eligible for treatment in the Norwegian specialized SUD-treatment services, patients must meet the criteria for either a diagnosis of F1x.1 harmful use, F1x.2 dependency syndrome, or F63.0 pathological gambling as defined by the ICD-10 [25]. After a minimum of 2 weeks, a baseline assessment was performed to minimize contamination from drug withdrawal and acute neurotoxic effects from psychoactive substances [26]. Follow-up assessments were conducted after 1 and 5 years. Participants were compensated approximately EUR 40 for their participation. Trained research personnel of the STAYER research group collected all data. Clinicians working with the patient were naïve to the assessment results obtained in the current study.

Inclusion Criteria

The inclusion criteria were as follows: (a) patients enrolled in the treatment program to which they were admitted for at least 2 weeks; (b) patients who met the diagnostic criteria for F1x.1 or F1x.2; (c) patients over 16 years of age; and (d) patients who reported polysubstance use defined as the consumption of multiple substances within the last year before inclusion.

Measures

Demographic and neurocognitive data were obtained by conducting semi-structured interviews by asking the patients to fill out questionnaires and perform the selected cognitive tests at baseline. Substance intake was measured as part of the 1- and 5-year follow-up assessments [27].

The Montreal Cognitive Assessment (MoCA®) gives an overall measure of cognitive function [28]. It samples behaviour across 14 performance tasks that engage multiple cognitive domains and is scored in integers to obtain a total score between 0 and 30. MoCA® has demonstrated excellent sensitivity and acceptable specificity to identify mild cognitive impairment at a sum score equal to or below 25 [28]. MoCA® has demonstrated good test-retest reliability, good internal consistency, and sensitivity in detecting mild cognitive impairment according to this cut-off value among patients with SUD [2, 24].

The Wechsler Abbreviated Scale of Intelligence (WASI) was included to estimate intellectual function [29]. The WASI comprises four subtests, two verbal measures of crystallized intelligence (vocabulary and similarities) and two nonverbal tests of fluent intelligence (block design and matrix reasoning). WASI subtests are similar to their Wechsler Adult Intelligence Scale – Third Edition [30] counterparts but include different items. The full-scale IQ (FSIQ) was selected to reflect a general intellectual function ("g-factor"). Cognitive impairment was defined as a FSIQ <86, which classifies participants with borderline intellectual disability as cognitively impaired [31].

The BRIEF-A, a self-report questionnaire with high ecological validity, was included to assess executive functioning in real-life situations [32, 33]. The BRIEF-A comprises nine subscales and three composite scores. We examined the validity scales of the BRIEF-A and utilized the cut-off scores, age norms, and validation criteria proposed by the original authors [32]. Elevated scores are associated with substance use status and numerous social adjustment indicators in patients with SUDs [34]. A t-score of ≥65 on the BRIEF-A Global Executive Composite (GEC) score was used to identify participants with cognitive impairment.

The Drug Use Identification Test (DUDIT) is a self-report screening tool to assess substance consumption, substance behaviours, and substance-related problems [35]. The DUDIT comprises 11 items that are reported on a five-point Likert scale ranging from "never" to "four or more times a week." We used the four consumption items from the DUDIT (DUDIT-C) to gauge substance intake [27] and the DUDIT-C continuous scores when examining the association between substance intake and cognitive performance. In addition, we defined two substance intake categories: total abstinence DUDIT-C score = 0 and heavy substance use DUDIT-C score ≥7. In the original DUDIT protocol, subjects reported substance use over the past 12 months. In the current study, participants were enquired about substance intake pertaining to the past 3 months.

Statistical Methods

Assumptions of normality were evaluated by inspection of Q-Q plots and the Shapiro-Wilks test. To obtain optimal statistical power, we opted not to exclude cases listwise when some cognitive measures were missing or invalid. The DUDIT-C continuous scores were significantly skewed at the 1- and 5-year follow-ups (z-scores 4.56), and Mann-Whitney U test was performed to evaluate differences between-group means. The χ^2 test of independence was used to analyse group differences for the categorical variables. As multiple comparisons were made, Bonferroni adjusted p values were used to evaluate the statistical significance of study dropout and the outcome variables of abstinence and heavy use at the 1- and 5 year follow-ups. We ran separate logistic regression models with abstinence and heavy use at the follow-ups as the dependent variables and cognitive impairment defined according to the specific cognitive screening tool (MoCA®, WASI, or BRIEF-A), age, and gender as predictors. Statistics were conducted using the statistical software package SPSS version 26 (IBM Corp., released 2019).

Results

Of the 164 participants included in this study, 144 participants were available for the 1-year follow-up assessment, and 108 participants were available for the 5-year follow-up assessment. The flow of participants and available data are presented in Figure 1. Note, only one participant scored in the IQ range below 70 (IQ = 67).

Table 1 shows the demographic features of the sample at baseline, presented separately for the cognitively impaired and non-impaired groups. Patients with cognitive impairment were younger (Mdn = 24.0) than patients without cognitive impairment (Mdn = 27.0), U = 5,808.5, p = 0.028 when impairment was defined according to the GEC scale from BRIEF-A.

Regarding cognitive performance at baseline, 33% of the sample met the criterion for cognitive impairments

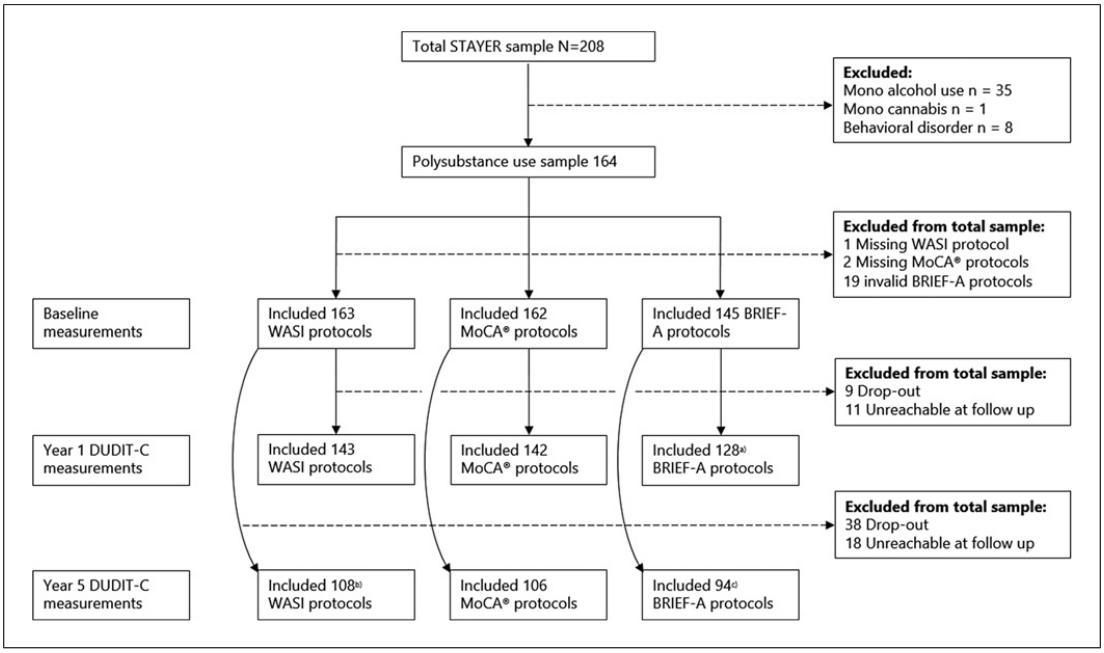

Fig. 1. Flow of participant inclusion, exclusion and missing data at baseline, 1-year, and 5-year follow-up measurements. Discrepancies between (i) excluded participants from the total sample and (ii) the number of included protocols at baseline and follow-up are due to overlap between protocols already excluded at baseline and participants who had dropped out or were unreachable at follow-up. Thus, **a)** 17 BRIEF-A protocols were excluded at 1-year follow-up measurements, and **b)** 55 WASI and **c)** 51 BRIEF-A protocols were excluded at 5-year follow-up measurements. MoCA®, Montreal Cognitive Assessment®; WASI, Wechsler Abbreviated Scale of Intelligence; BRIEF-A, Behaviour Rating Inventory of Executive Function – Adult version.

Table 1. Demographic features of the sample stratified according to cognitive impairment

	Total sample	MoCA® <26		WASI FSIQ		BRIEF-A GEC	
		Impaired[a] (*n* = 53)	Non-impaired[a] (*n* = 109)	Impaired[a] (*n* = 30)	Non-impaired[a] (*n* = 133)	Impaired[a] (*n* = 87)	Non-impaired[a] (*n* = 58)
Age at entry	27.6 (7.5)	27.6 (7.8)	27.6 (7.4)	26.0 (8.3)	27.9 (7.3)	27.6 (8.3)*	28.7 (5.6)
Male gender	107 (65.2)	35 (65.1)	71 (66.0)	18 (60.0)	88 (66.2)	60 (69.0)	36 (62.1)
Education at entry, years	11.6 (1.7)	11.6 (1.8)	11.6 (1.7)	11.3 (1.7)	11.7 (1.7)	11.5 (1.6)	11.8 (1.8)

MoCA®, Montreal Cognitive Assessment®; WASI, Wechsler Abbreviated Scale of Intelligence; BRIEF-A, Behaviour Rating Inventory of Executive Function – Adult version. Numbers indicate mean (standard deviation) for the variables age and education, and *n* (%) for gender. [a]Sample at baseline. *$p < 0.05$.

according to MoCA®, 18% according to WASI, and 60% according to BRIEF-A. At the 1-year follow-up, 54% of the sample reported total abstinence from substances. Conversely, 31% presented heavy substance use. At the 5-year follow-up, 64% of the sample reported abstinence from substances, while 25% presented heavy substance use. Nine (6%) participants dropped out of the study before the 1-year follow-up assessment, and 38 (23%)

Table 2. Substance use and study dropout measured at 1- and 5-year follow-ups stratified according to cognitive impairment

	Total sample	MoCA®		WASI FSIQ		BRIEF-A GEC	
		Impaired[a] (n = 53)	Non-impaired[a] (n = 109)	Impaired[a] (n = 30)	Non-impaired[a] (n = 133)	Impaired[a] (n = 87)	Non-impaired[a] (n = 58)
Year 1							
Study dropout	9 (5.5)	5 (9.4)	4 (3.7)	3 (10.0)	6 (4.5)	5 (5.7)	3 (5.2)
Total abstinence	78 (54.2)	19 (43.2)	57 (58.2)	12 (48.0)	66 (55.9)	37 (48.7)	32 (61.5)
Heavy substance use	45 (31.3)	17 (38.6)	28 (28.6)	8 (32.0)	36 (30.5)	27 (35.5)	13 (25.5)
Year 5							
Study dropout	38 (23.2)	13 (24.5)	25 (22.9)	11 (36.7)*	26 (19.5)*	21 (24.1)	16 (27.6)
Total abstinence	69 (63.9)	23 (66.7)	45 (61.6)	8 (50.0)	61 (66.3)	36 (62.1)	24 (66.7)
Heavy substance use	27 (25.0)	7 (21.2)	20 (27.4)	3 (18.8)	24 (26.1)	14 (24.1)	9 (25.0)

MoCA®, Montreal Cognitive Assessment®; WASI, Wechsler Abbreviated Scale of Intelligence; BRIEF-A, Behaviour Rating Inventory of Executive Function – Adult version. Numbers indicate n (%). At baseline, 162 MoCA® protocols, 163 WASI protocols, and 145 BRIEF-A protocols were analysed. At one-year follow-up, 142 MoCA® protocols, 143 WASI protocols, and 128 BRIEF-A protocols were analysed. At 5-year follow-up, 106 MoCA® protocols, 108 WASI protocols, and 94 BRIEF-A protocols were analysed. There were 20 missing DUDIT-C protocols at 1 year and 56 missing DUDIT-C protocols at 5 years. [a]Smple at baseline. *$p < 0.05$. **Bonferroni adjusted p values $p < 0.003$.

dropped out from the study before the assessment at the 5-year follow-up.

A statistically significant association between continuous DUDIT-C scores and overall cognitive performance measures was only found for MoCA® at 1-year follow-up, where a Mann-Whitney U test showed a significant difference between patients with cognitive impairment (Mdn = 4) and cognitively non-impaired patients (Mdn = 0), U = 25,777, p = 0.043. We found no differences in abstinence or heavy substance use between patients defined with and without cognitive impairments according to the included cognitive screening tests. At α = 0.05, patients with cognitive impairment measured by WASI were more likely to drop out of the study than patients without cognitive impairment at the 5-year follow-up measurement χ^2 (1, N = 163) = 4.1, p = 0.043. However, this result lost statistical significance after Bonferroni correction (0.05/18 = 0.003). Table 2 presents substance use and study dropout at 1- and 5-year follow-ups, stratified according to cognitive impairment measured by MoCA®, WASI, and BRIEF-A, and the total sample.

None of the predictors, including age and gender, were statistically significant in the logistic regression models exploring associations between the categorical substance use outcome variables (abstinence and heavy use at year 1 or year 5 follow-up) and cognitive impairment defined according to each of the cognitive screening tests (MoCA®, WASI, or BRIEF-A) (shown in Table 3).

Discussion

We examined the ability of three standard cognitive screening instruments to predict substance use 1 and 5 years after treatment initiation. As cognitive impairments are well-established risk factors for adverse SUD-treatment processes and outcomes [7, 8], we expected to find negative clinical outcome behaviour among patients defined as cognitively impaired according to at least one of the screening instruments. The present results partly confirmed this by showing a statistically significant association between cognitive impairment according to MoCA® and substance consumption at the 1-year follow-

Table 3. Summary of logistic regression analysis with substance use as the dependent variable and impairment defined by MoCA®, WASI, or BRIEF-A GEC, respectively, and age and gender as predictor variables

Dependent variable	Predictor	MoCA®			WASI FSIQ			BRIEF-A GEC		
		OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value
Year 1, abstinent	(Constant)	0.7	–	0.684	0.7	–	0.672	0.6	–	0.661
	Cognitive impaired	0.6	0.3–1.1	0.111	0.7	0.3–1.8	0.497	0.9	0.3–1.3	0.209
	Age	1.0	1.0–1.1	0.547	1.0	1.0–1.1	0.660	1.0	1.0–1.1	0.437
	Gender	1.3	0.6–2.6	0.522	1.3	0.6–2.6	0.485	1.3	0.6–2.9	0.501
Year 1, heavy substance use	(Constant)	1.3	–	0.765	1.3	–	0.759	1.2	–	0.847
	Cognitive impaired	1.5	0.7–3.2	0.271	1.0	0.4–2.6	0.980	1.5	0.7–3.4	0.303
	Age	1.0	0.9–1.0	0.358	1.0	0.9–2.6	0.421	1.0	0.9–1.0	0.242
	Gender	0.7	0.3–1.4	0.287	0.7	0.3–1.4	0.290	0.8	0.3–1.7	0.500
Year 5, abstinent	(Constant)	1.1	–	0.949	1.1	–	0.924	0.9	–	0.906
	Cognitive impaired	1.4	0.6–3.5	0.416	0.5	0.2–1.5	0.224	0.8	0.3–2.0	0.694
	Age	1.0	0.9–3.1	0.929	1.0	1.0–1.1	0.842	1.0	1.0–1.1	0.566
	Gender	1.3	0.5–3.1	0.574	1.4	0.6–3.2	0.477	1.3	0.5–3.2	0.603
Year 5, heavy substance use	(Constant)	0.5	–	0.611	0.5	–	0.555	0.7	–	0.817
	Cognitive impaired	0.7	0.2–1.9	0.491	0.6	0.2–2.5	0.518	0.9	0.4–2.5	0.883
	Age	1.0	0.9–1.1	0.937	1.0	0.9–1.1	0.897	1.0	0.9–1.1	0.739
	Gender	0.7	0.3–1.9	0.517	0.7	0.3–1.9	0.499	0.7	0.3–2.1	0.542

MoCA®, Montreal Cognitive Assessment®; WASI, Wechsler Abbreviated Scale of Intelligence; BRIEF-A, Behaviour Rating Inventory of Executive Function – Adult version. At baseline, 162 MoCA® protocols, 163 WASI protocols, and 145 BRIEF-A protocols were analysed. At 1-year follow-up, 142 MoCA® protocols, 143 WASI protocols, and 128 BRIEF-A protocols were analysed. At 5-year follow-up, 106 MoCA® protocols, 108 WASI protocols, and 94 BRIEF-A protocols were analysed. There were 20 missing DUDIT-C protocols at 1 year and 56 missing DUDIT-C protocols at 5 years. *$p < 0.05$.

up. Surprisingly, but in line with McKellar, Harris, and Moos [19], we did not find any disparities between cognitive impairment according to any of the cognitive screening instruments and any long-term clinically relevant substance use outcomes. Furthermore, according to MoCA®, WASI, and BRIEF-A scores, cognitive impairment did not predict substance abstinence or heavy substance use at the 1- and 5-year follow-ups.

In this study, the frequency of cognitive dysfunction varies between screening instruments. MoCA® identified a frequency rate of 33%, comparable to previous studies in SUD populations [2]. All participants with an impairment defined according to WASI had a FSIQ in the range of 50–85, labelled mild to borderline intellectual disability [31]. A frequency of 18% within this range is somewhat lower than prevalence rates of 30–39% reported in previous studies of patients with SUD [12, 31]. Lastly, the frequency of cognitive impairment defined according to BRIEF-A was 60%, comparable to the 63% frequency reported by McKowen et al. [36].

Abstinence was found to be common among all participants, regardless of cognitive impairment (54–64%). Conversely, 25–31% of all participants reported heavy substance use regardless of cognitive impairment. These findings align with some previous studies that have demonstrated a disconnection between cognitive impairment and behaviour considered relevant for successful SUD treatment, such as treatment retention, attendance, and substance use outcomes [19, 37].

Cognitive impairment is shown to be a risk factor for relapse during or shortly after treatment [31, 38, 39]. Furthermore, cognitive impairment has been shown to predict treatment dropout, which is a risk factor for relapse per se [8]. However, the current study suggests a limited value of using sum scores from standard screening instruments designed to assess broad cognitive domains, such as the WASI, MoCA®, and BRIEF-A, as predictors of long-term substance use. Moreover, the inability of MoCA® to predict long-term outcomes is of particular interest because it is commonly utilized in clinical settings, and studies are emphasizing its ability to detect cognitive impairments in SUD populations [24]. Other studies have suggested that performance on MoCA® can be used to predict several clinically relevant outcome variables, such as dropout from residential treatment facilities [40]. However, the MoCA® was not developed specifically to detect cognitive impairments in SUD populations. Some items may be redundant, and MoCA® may not adequately

test all cognitive functions relevant for SUD recovery. For example, the instruments utilized in the current study did not assess decision-making and emotion-driven response inhibition, although these cognitive components may be vital in predicting long-term substance intake [9, 41]. Indeed, this study classified participants as cognitively impaired or non-impaired based on a single aggregated cut-off which may have oversimplified the multidimensional nature of the neuropsychological functions and abilities required for SUD recovery [42]. Additional studies including more detailed information within MoCA®, and the two other instruments included in the present study are thus called for.

The predictive value of cognitive impairment may be attenuated in patients with pSUD as they may have a more severe clinical profile than patients with a mono-substance use disorder. Compared with mono-substance users, polysubstance users have an earlier onset of substance use [43], are younger [44], have higher levels of psychological distress and personality disorders [43, 45], poorer social adjustment [46], and lower socioeconomic status [47]. Studies suggest that these characteristics are associated with an increased risk of dropout and relapse [8, 48–52]. Generally, individuals with pSUD may be burdened and lack psychosocial resources to such an extent that cognitive functioning plays a subordinate role in long-term recovery. Alternatively, other psychosocial factors may play a more prominent role in later phases of the recovery process.

Strengths and Limitations

There are few screening instruments for cognitive impairment in adults with SUDs, and the predictive validity of current instruments related to key clinical variables is not sufficiently established [24]. SUDs are recognized as persistent diseases and limit the validity of outcome measurements from longitudinal studies of short duration. The current study is among the few studies examining long-term clinical outcomes among patients with co-occurring SUD and cognitive impairments. Moreover, this is the first study that has compared the predictive value of three standard clinical screening instruments on long-term substance intake in a representative cohort of patients with a SUD. The current study provides additional insight by utilizing clinically significant substance outcome categories.

The STAYER cohort represents a heterogeneous patient group recruited from several specialized and diverse SUD-treatment facilities. The universal access to health care in Norway allows for the collection of a more comprehensive sample relative to countries where care is privatized and costly. The study targets polysubstance users, representing up to 91% of treatment-seeking patients [53]. Thus, the study utilizes a highly representative and clinically relevant sample. This allows the results to be generalizable to the broader clinical SUD services. The STAYER research group has also been well funded and utilized elaborate tracking and follow-up strategies to ensure a high retention rate and few missing data entries [54].

The main limitation still concerns missing data, particularly at the 5-year follow-up. As with all longitudinal studies, missing data and a high attrition rate compromise the internal and external validity of the current study. Despite the efforts to ensure high retention, the research group could not obtain data on several participants at follow-up measurements, which adds to the study dropout attrition rate. This leaves a total of 34% of the patients without DUDIT-C results at the 5-year follow-up.

Although the cognitive assessments were performed a minimum of 2 weeks after substance cessation, the timeframe from detoxification to assessment may be too short for some participants to measure stable neurocognitive impairment. However, studies of long-term recovery have not always required 2-week substance abstinence [55]. In addition, the frequency of cognitive dysfunction according to MoCA® and BRIEF-A found in the current study is comparable to results reported in previous studies in SUD populations.

The current study does not include data on substance intake dynamics before and between the assessments. Thus, substance use measurements reflect the participants' substance intake only at a particular moment in time and may fail to capture the dynamic nature of recovery and relapse [56]. Although substance use may reflect a comprehensive understanding of recovery in substance use treatment, it is an insufficient requirement to conceptualize long-term recovery. Extensive changes pertaining to dimensions of connectedness, identity, meaning in life, occupation, and meaningful positive social relations are essential to handle the moderation of substance use [57] and should be considered a treatment goal per se.

We have not controlled for comorbid mental disorders. Affective states, such as dysphoria, depression, and anxiety, may be an integral and core functional element in SUDs [58]. Indeed, findings have shown that scores on WASI, MoCA®, and BRIEF-A are associated with psychological distress in SUD populations [21, 22, 59]. However, this issue is of limited relevance here, as the purpose of the current study was to determine the extent to which results on the cognitive screening instruments

can be used to predict long-term substance use outcomes, independent of aetiology.

The selected DUDIT-C cut-off score defining heavy substance use resulted in a modest sample size for that subsample. This might have contributed to driving the null findings at the 5-year follow-up. Furthermore, the sample included few patients with impaired intellectual functioning. The STAYER cohort was recruited using convenience sampling from a clinical setting, and is thus vulnerable to ascertainment biases by under-sampling patients in the lower end of intellectual functioning and with weak motivation for change. We did not find an increased dropout rate for participants with cognitive impairment according to WASI after Bonferroni correction. Nevertheless, it is still possible that a greater study dropout rate masks true differences in substance use behaviour in patients with impaired intellectual functioning due to low statistical power or that patients with impaired intellectual functioning and worse substance use outcomes had an increased risk of study dropout.

Clinical Implications

According to our findings, cognitive impairment's predictive value for long-term treatment outcomes may be limited. In a clinical context, this is an optimistic outcome due to the high frequency of cognitive deficits in the SUD population. The results from screening with instruments assessing broad cognitive domains at treatment initiation should be interpreted with caution when informing treatment strategies. Conclusions must be supported by medical history, psychiatric and functional assessment, and a more comprehensive neuropsychological assessment. Recent efforts to develop cognitive screening instruments for the SUD population are promising [60]. However, the predictive validity of clinically relevant variables is not sufficiently established. Consequently, there is a need to establish clinically viable instruments with well-established clinical and ecological validity to assess cognitive functions in the SUD population. In addition, trajectories in SUD recovery among individuals with and without cognitive impairments warrant further investigation.

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Statement of Ethics

This study protocol was reviewed and approved by the Regional Ethics Committee West, University of Bergen, approval reference REK 2011/1877. The research was conducted according to its guidelines and those of the Helsinki Declaration (1975). All participants gave written informed consent.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Jens Hetland, Egon Hagen, and Aleksander Hagen Erga conceptualized and designed the study. Jens Hetland wrote the first draft and revised the manuscript. Jens Hetland and Aleksander Hagen Erga performed the analyses. Egon Hagen, Aleksander Hagen Erga, and Astri Johansen Lundervold made critical revisions of the manuscript. Aleksander Hagen Erga and Astrid Johansen Lundervold supervised the study. All authors contributed to the article and approved the submitted version.

Data Availability Statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation. Further enquiries can be directed to the corresponding author.

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Erratum

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In the article "Performance on Cognitive Screening Tests and Long-Term Substance Use Outcomes in Patients with Polysubstance Use Disorder" [Eur Addict Res 2023;29(2):150–159, DOI: 10.1159/000528921] by Hetland et al., the reported odds ratios for cognitive status and gender were incorrectly reported in Table 3. Following publication, the authors identified an error in the logistic regression analyses' predictor variables. The categorical predictor variables were mistakenly defined as scaled variables for the purposes of conducting the analysis. Consequently, the reported odds ratios for cognitive status and gender were presented in Table 3 as if they were scaled variables instead of categorical variables. To rectify this, the authors reanalyzed the data, ensuring the predictor variables were correctly defined.

The corrected Table 3 is shown here.

Table 3. Summary of logistic regression analysis with substance use as the dependent variable and impairment defined by MoCA®, WASI, or BRIEF-A GEC, respectively, age and gender as predictor variables

Dependent variable	Predictor	MoCA®			WASI FSIQ			BRIEF-A GEC		
		OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value
Year 1 Abstinent	(Constant)	0.6	–	0.483	0.8	–	0.804	0.7	–	0.585
	Cognitive impaired	1.8	0.9–3.7	0.111	1.4	0.6–3.2	0.497	1.6	0.8–3.3	0.209
	Age	1.0	1.0–1.1	0.547	1.0	1.0–1.1	0.660	1.0	1.0–1.1	0.437
	Gender	0.8	0.4–1.6	0.522	0.8	0.4–1.6	0.485	0.8	0.4–1.7	0.501
Year 1 Heavy substance use	(Constant)	0.9	–	0.845	0.6	–	0.496	1.1	–	0.937
	Cognitive impaired	0.7	0.3–1.4	0.271	1.0	0.4–2.5	0.952	0.7	0.3–1.5	0.303
	Age	1.0	0.9–1.0	0.356	1.0	0.9–1.0	0.421	1.0	0.9–1.0	0.242
	Gender	1.5	0.7–3.4	0.287	1.5	0.7–3.4	0.290	1.3	0.6–3.1	0.500
Year 5 Abstinent	(Constant)	2.5	–	0.272	1.1	–	0.945	1.2	–	0.852
	Cognitive impaired	0.7	0.3–1.7	0.416	1.9	0.7–5.7	0.224	1.2	0.5–2.9	0.694
	Age	1.0	0.9–1.1	0.929	1.0	1.0–1.1	0.842	1.0	1.0–1.1	0.566
	Gender	0.8	0.3–1.9	0.574	0.7	0.3–1.7	0.477	0.8	0.3–2.0	0.603
Year 5 Heavy substance use	(Constant)	0.2	–	0.089	0.2	–	0.090	0.4	–	0.294
	Cognitive impaired	1.4	0.5–3.8	0.491	1.6	0.4–6.0	0.518	1.1	0.4–2.8	0.883
	Age	1.0	0.9–1.1	0.937	1.0	0.9–1.1	0.897	1.0	0.9–1.1	0.739
	Gender	1.4	0.5–3.6	0.517	1.4	0.5–3.7	0.499	1.4	0.5–3.9	0.542

MoCA®, Montreal Cognitive Assessment®; WASI, Wechsler Abbreviated Scale of Intelligence; BRIEF-A, Behavior Rating Inventory of Executive Function – Adult version. At baseline, 162 MoCA® protocols, 163 WASI protocols, and 145 BRIEF-A protocols were analysed. At 1-year follow-up, 142 MoCA® protocols, 143 WASI protocols, and 128 BRIEF-A protocols were analysed. At 5-year follow-up, 106 MoCA® protocols, 108 WASI protocols, and 94 BRIEF-A protocols were analysed. There were 20 missing DUDIT-C protocols at 1 year and 56 missing DUDIT-C protocols at 5 years. *$p < 0.05$.

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Cognitive impairment as a predictor of long-term psychological distress in patients with polysubstance use disorders: A prospective longitudinal cohort study

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Running header: Predicting long-term psychological distress

Abstract

Background: The association between polysubstance use disorder (pSUD), mental illness, and cognitive impairments is well established and linked to negative outcomes in substance use disorder treatment. However, it remains unclear whether cognitive impairment predicts long-term psychological distress among treatment seeking patients with pSUD. This study aimed to investigate the associations and predictive ability of cognitive impairment on psychological distress one and five years after treatment initiation.

Methods: $N = 164$ treatment seeking patients with pSUD were sampled at treatment initiation. We examined associations between cognitive impairment according to Montreal Cognitive Assessment® (MoCA®), Wechsler Abbreviated Scale of Intelligence (WASI), and Behaviour Rating Inventory of Executive Function - Adult version (BRIEF-A) administered at treatment initiation and psychological distress defined by the Symptom Check List-90-Revised (SCL-90-R) at treatment initiation, one and five years later. We ran hierarchical logistic regressions to assess the predictive ability of the respective cognitive instruments administered at treatment initiation on psychological distress measured one and five years later including psychological distress at treatment initiation and substance intake at the measurements as covariates.

Results: The main results was that MoCA® and BRIEF-A predicted psychological distress at years one and five, but BRIEF-A lost predictive power when accounting for psychological distress at treatment initiation. Moreover, substance intake at follow-ups and psychological distress at treatment initiation were stronger predictors of psychological distress than cognitive impairment.

Conclusions: MoCA® may be less sensitive to psychopathology-driven cognitive impairments than BRIEF-A. The explanatory power of cognitive impairment at treatment initiation on later psychological distress is limited. Further studies should investigate the cost–benefit ratio of

implementing routine screening for psychological distress in patients with pSUD as opposed to conducting a comprehensive diagnostic assessment for all.

Keywords: MoCA, BRIEF-A, substance use disorder, cognitive impairment, mental illness, intellectual impairment

Background

Addressing mental health is pivotal to the treatment of substance use disorders (SUDs) due to its effect on quality of life, treatment retention and risk of relapse (1-8). Elevated psychological distress impedes individuals' capacity to engage in long-term objectives of psychosocial improvement and moderation of substance use (9) but also results in a perception of unmet treatment needs, particularly among male patients with SUDs (10). Therefore, it is imperative to identify risk factors influencing long-term mental health to optimize the efficiency of SUD treatment.

The relationship between SUDs, mental health and cognitive functioning is intricately intertwined (11-13). Epidemiological and clinical studies link SUD to a host of mental illnesses, such as mood and anxiety disorders, attention-deficit hyperactivity disorder, psychosis, personality disorders, suicidality and general psychological distress (12, 14-20). Executive dysfunction, and cognitive impairments in general, are suggested to be a transdiagnostic dimension in psychopathology (21). Indeed, psychological distress and several psychiatric disorders are associated with both specific deficits in executive function and general neurocognitive impairments, including impaired intellectual functioning. (22-32). The

manifestation of cognitive impairment in apparently recovered patient cohorts implies that some cognitive impairments associated with mental illness may possess trait-like qualities (23, 33, 34).

Psychological distress and executive deficits are also considered integral transdiagnostic components of SUD and map to the withdrawal/negative affect and preoccupation/anticipation stages in the addiction cycle (11, 35-37). Moreover, elevated psychological distress has also been linked with cognitive impairments in patients with SUD (38-40). This is noteworthy because cognitive impairments negatively affect several treatment processes and therapeutic change mechanisms (41-44) as well as treatment outcomes such as rates of drop-out (6, 45, 46) and relapse (47-49).

Despite the recognized link between SUD, psychological distress, and cognition, there is surprisingly little knowledge about the influence of cognitive functioning on long-term psychological distress among patients with SUD at treatment initiation.

Aim

This study aims to 1) establish associations between cognitive impairments measured by three screening instruments at baseline, the Montreal Cognitive Assessment® (MoCA®), Wechsler Abbreviated Scale of Intelligence (WASI) and Behaviour Rating Inventory of Executive Function - Adult version (BRIEF-A), and psychological distress measured according to self-reports on the Symptom Checklist 90 Revised (SCL-90-R) one and five years after enrolment in a treatment programme and 2) examine the ability of the MoCA®, WASI and BRIEF-A to predict psychological distress in patients with polysubstance use disorders at the two follow-up time points. Accordingly, we hypothesize that cognitive impairment according to at least one

instrument will be associated with increased substance use and predicted elevated distress at follow-ups one and five years after enrolment.

Methods

Design

This study is part of the Stavanger Study of Trajectories of Addiction (STAYER), a prospective longitudinal cohort study of neurocognitive, psychological and social recovery in patients with SUD who initiated a new treatment sequence in the Stavanger University Hospital catchment area in Norway.

Setting

Two hundred and eight patients were recruited at convenience from 10 specialized outpatient and residential SUD treatment facilities within the Stavanger University Hospital catchment area between March 2012 and January 2016. The eligibility criteria for treatment in specialized SUD-treatment services in Norway require patients to meet the diagnostic criteria for either F1x.1 harmful use, F1x.2 dependency syndrome, or F63.0 pathological gambling as defined by the ICD-10 (50). Participants were compensated approximately EUR 40 for their participation. Baseline assessment was performed after a minimum of two weeks of abstinence to minimize contamination from drug withdrawal and acute neurotoxic effects from psychoactive substances (51). Follow-up assessments were conducted after one and five years. Trained research personnel of the STAYER research group collected all data. Clinicians working with the patient were blinded to the assessment results obtained in the current study.

Inclusion criteria

Inclusion criteria were as follows: a) patients enrolled in the treatment program to which they were admitted for at least two weeks; b) patients over 16 years of age; c) patients who met the diagnostic criteria for F1x.1 or F1x.2; d) patients who reported polysubstance use defined as the consumption of multiple substances within the last year before inclusion.

Measures

Demographic and neurocognitive data were obtained by conducting semistructured interviews by asking the patients to complete questionnaires and perform the selected cognitive tests at baseline. Substance intake was measured at the one- and five-year follow-up assessments. At baseline, demographic and neurocognitive data were collected through semistructured interviews, questionnaires, and selected cognitive tests administered to the patients. Psychological distress was measured during baseline in addition to at the one- and five-year follow-up assessments.

The Montreal Cognitive Assessment (MoCA®) is a cognitive screening tool that measures overall cognitive function by sampling behaviour across 14 performance tasks that engage multiple cognitive domains (52). The test is scored in integers to obtain a total score between 0 and 30. We defined cognitive impairment (MoCA®+) at a sum score ≤ 25, where MoCA® has demonstrated excellent sensitivity and acceptable specificity in identifying mild cognitive impairment (52). A MoCA® nonimpaired group (MoCA®-) was defined at sum-score > 25. MoCA® has proven effective in detecting mild cognitive impairment among patients with SUDs, exhibiting good test-retest reliability, good internal consistency, and sensitivity when utilizing the specified cut-off value (53-55).

The Wechsler Abbreviated Scale of Intelligence (WASI) (56) comprises four subtests, two verbal measures of crystallized intelligence (Vocabulary and Similarities) and two nonverbal tests of fluent intelligence (Block Design and Matrix Reasoning). The subtests within the WASI correspond to the subtests found in the Wechsler Adult Intelligence Scale - Third Edition (57), although they feature different items. The full-scale IQ (FSIQ) was selected to reflect general intellectual function ("g-factor"). Cognitive impairment (WASI+) was delineated as an FSIQ < 86, thereby including participants with borderline intellectual functioning as cognitively impaired (39). We also defined a WASI nonimpaired group (WASI-) as FSIQ ≥ 86.

The Behavior Rating Inventory of Executive Function - Adult version (BRIEF-A) is a self-report questionnaire to assess executive functioning in real-life situations (58, 59). The BRIEF-A comprises nine subscales and three composite scores. We utilized the cut-off scores, age norms and validation criteria proposed by the original authors (58). Participants with cognitive impairment (BRIEF-A+) were identified by utilizing a standardized t score of ≥ 65 on the BRIEF-A Global Executive Composite (GEC) score. BRIEF-A GEC nonimpaired (BRIEF-A-) was defined as a GEC score < 65.

The Symptom Checklist-90-Revised (SCL-90-R) (60) is a 90-item self-report measure widely used in clinical practice and research. It has been validated for the assessment of psychological distress in patients with SUD (61), as well as in individuals with intellectual disabilities (62). A five-point Likert scale ranging from 0 (not at all) to 4 (severely) is used to assess the level of distress experienced by respondents in the past seven days. The checklist yields nine symptom dimension subscales: somatization, obsessive–compulsive disorder, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. The Global Severity Index (GSI) was employed to assess overall psychological distress. In accordance with Derogatis (60), we defined “caseness”, i.e., self-reported level of psychological distress that

warrants further assessment, as a GSI standardized t score ≥ 63 or t score ≥ 63 on two or more symptom scales.

The Drug Use Identification Test (DUDIT) is a self-report screening tool used to evaluate substance consumption, substance-related behaviours, and substance-related problems (63). The DUDIT consists of 11 items that are rated on a five-point Likert scale, ranging from "never" to "four or more times a week. We used the four consumption items from DUDIT (DUDIT-C) to gauge substance intake (64). As per the study's protocol, which mandated a period of abstinence from substances prior to baseline assessment, the DUDIT-C score was recorded as 0 at the baseline measurements.

Statistical procedure

Assumptions of normality were evaluated by inspecting histograms and the Shapiro–Wilks test. To obtain optimal statistical power, we did not listwise exclude cases when some cognitive measures were missing or invalid. The Shapiro–Wilks test indicated that the distribution of the SCL-90-R GSI scores departed significantly from normality at baseline ($W = 0.96$, $p < 0.001$), year 1 ($W = 0.92$, $p < 0.001$) and year 5 ($W = 0.89$, $p < 0.001$). This was the same for years of education ($W = 0.94$, $p < 0.001$) and age ($W = 0.92$, $p < 0.001$). Thus, a Mann–Whitney U test was applied to evaluate group differences. In accordance with Fritz et al. (65), we calculated effect sizes for these analyses. The chi-squared test of independence was used to analyse group differences for the categorical variables.

We ran separate three-step hierarchal logistic regression analyses with SCL-90-R caseness at years one and five as the dependent variable. Cognitive status defined according to the specific cognitive screening tool (MoCA®, WASI, or BRIEF-A) was entered in Block 1, DUDIT-C score from the corresponding time point of interest was added in Block 2, and baseline SCL-

90-R GSI score was added in block three. Nagelkerke's R^2 was used to measure the goodness of fit of the logistic regression models. Variance inflation factor diagnostics, utilizing a threshold of 2.50 (66), indicated that multicollinearity among the independent variables posed no issues in the regression models. Statistics were conducted using the statistical software package SPSS version 29 (IBM Corp., released 2022).

Results

Among the 164 participants included in this study, 145 were available for the one-year assessment, and 109 participants were available for the five-year assessment. Figure 1 presents the flow of participants and available data.

Insert Figure 1 about here

Table 1 shows the demographic characteristics of the sample at baseline, providing separate presentations of the cognitively impaired and nonimpaired groups. The BRIEF-A+ group was younger (*Mdn* = 24.0) than the BRIEF-A nonimpaired group (*Mdn* = 27.0), $U = 5808.5$, $p = .028$. The proportion of participants who met the criteria for caseness was approximately 76%, 58% and 52.3% at baseline, year one and year five, respectively.

Insert Table 1 about here

Association between cognitive impairment and SCL-90-R

Table 2 presents the SCL-90-R GSI and caseness at baseline, year 1 and five stratified by cognitive impairment. The proportion of SCL-90-R caseness was positively associated with MoCA®+ at year one χ^2 (1, N = 143) = 5.63, p =.018, V =.20 and year five χ^2 (1, N = 107) = 4.45, p =.035, V =.20.

At baseline, the WASI+ group (*Mdn* = 1.4) displayed a significantly higher SCL-90-R GSI score than the WASI- group (*Mdn* = 1.0), indicating elevated psychological distress U =2480, p =.038, r =.16. Similarly, at year five, the proportion of caseness was higher for the WASI+ group than for the WASI- group χ^2 (1, N = 109) = 6.30, p =.012, V =.24.

BRIEF-A+ demonstrated a positive association with all measures of SCL-90-R GSI and caseness. At baseline, the BRIEF-A+ group exhibited both a higher SCL-90-R GSI score (*Mdn* = 1.3) compared to the BRIEF-A- group (*Mdn* = 0.6), U =4200, p <.001, r =.56, and a higher likelihood of caseness χ^2 (1, N = 145) = 32.55, p <.0001, V =.47.

At year one, the BRIEF-A+ group displayed a significantly elevated SCL-90-R GSI score (*Mdn* = 0.8) compared to the BRIEF-A- group (*Mdn* = 0.4), $U = 2797$, $p < .001$ $r = .33$ in addition to a positive association with caseness χ^2 (1, $N = 129$) = 14.17, $p < .0001$, $V = .33$. Similarly, at year five, the BRIEF-A+ group demonstrated a significantly higher SCL-90-R GSI score (*Mdn* = 0.7) than the BRIEF-A- group (*Mdn* = 0.3), $U = 1448$, $p = .003$ $r = .30$. Additionally, the proportion of SCL-90-R caseness was also positively associated with BRIEF-A+ group χ^2 (1, $N = 95$) = 6.04, $p = .014$, $V = .25$.

Insert Table 2 about here

Prediction of SCL-90-R caseness by cognitive impairment

Table 3 and Table 4 summarize the test statistics and results obtained from the hierarchical logistic regression analysis conducted at years one and five, respectively. With the exception of WASI Model 1 at year one, all regression models yielded a significant solution. Nagelkerke R^2 increased from step 1 to step 2 and from step 2 to step 3 across the hierarchical regressions (either MoCA®, WASI or BRIEF-A as predictor) and was in the range of .056 –.425 at year 1 and .059 –.295 at year 5. MoCA®+ emerged as a significant independent predictor of long-term caseness in all models, except for Model 2 at year one, where it approached significance at an $\alpha = .05$ level ($p = .066$). Its odds ratios (ORs) ranged from 1.2 to 3.4. While WASI did not prove to be a significant predictor of caseness in the year one regression models, it gained significance in all models at year five, with ORs ranging from 4.5 to 5.2. BRIEF-A+ exhibited significant predictive ability for caseness in model 1 and model 2 at both year one and year five, with ORs

ranging from 1.7 to 5.2. However, the statistical significance of BRIEF-A as a predictor was lost in model 3 at both years one and five.

In addition, the DUDIT-C scores emerged as significant predictors of caseness in models 2 and 3 for both year one and year five, with ORs ranging from 1.1 to 1.2. Similarly, when baseline GSI was included in model 3 at both time points, it also demonstrated significant predictive value, with ORs ranging from 2.9 to 6.4.

Insert Table 3 about here

Insert Table 4 about here

Discussion

We established associations between three widely used cognitive screening tools and psychological distress and examined their ability to predict the occurrence of psychological

distress at levels warranting psychiatric assessment one and five years following treatment initiation. The main finding in the current study was that the results from the selected cognitive screening instruments showed associations with psychological distress and predicted later caseness in all regression models. However, the patterns of associations and predictive value varied across the included cognitive tests. MoCA® proved to be a significant independent predictor of long-term caseness. Notably, significance was sustained after controlling for the potential impact of baseline psychological distress. Thus, the MoCA® results may function as an independent predictor of long-term elevated psychological distress among patients with SUD. BRIEF-A+ was positively associated with elevated psychological distress and caseness according to SCL-90-R GSI at all time points, but contrary to MoCA®+, it lost statistical significance as a predictor variable for caseness when baseline psychological distress was controlled for. The baseline SCL-90-R GSI and DUDIT-C scores obtained from the one- and five-year follow-ups emerged as significant predictors of caseness in the regression models, even after accounting for cognitive impairment as assessed by the included cognitive screening instruments.

While the MoCA® was not specifically developed to detect cognitive impairments in patients with psychiatric illness or SUD, some subtests within the MoCA® are shown to be sensitive to deficits in executive functioning (67). These deficits are also recognized as hallmarks in both SUD (68) and other mental illnesses (21) but are also "meaningfully associated" with SUD treatment outcomes (69). Hagen et al. (38) suggest that MoCA® is dissociated from concurrent psychological distress among patients with SUDs. It is noted that the sample in Hagen et al. (38) shares a significant overlap with the sample used in the current study. Others have demonstrated an association between MoCA® and psychiatric comorbidities among patients with alcohol use disorder (40). Depressive symptomatology has also been shown to negatively impact MoCA® performance in a non-SUD population (70). Moreover, a total of 79% of

patients admitted to an acute psychiatric ward demonstrated cognitive impairment according to MOCA®, indicating that MoCA® is sensitive to a wide range of mental illnesses (71). Comorbid PTSD and SUD may also reduce the criterion-related validity of the MoCA® in terms of its correspondence with the Repeatable Battery for the Assessment of Neuropsychological Status (72). Notwithstanding, the current study suggests that MoCA® assesses some cognitive domains that 1) to a limited extent are affected by psychological distress measured with SCL-90-R and 2) contribute to the prediction of long-term caseness.

The mechanism by which MoCA® predicts long-term distress in the current study remains unknown. Previous studies have linked MoCA®-defined impairment to adverse treatment outcomes from isolated and formalized treatment settings (46, 73). However, patients with cognitive impairments may follow different recovery pathways than patients without such impairments, where informal treatment processes and social structures may gain prominence in determining behavioural, psychosocial, emotional and vocational outcomes (44, 74). Similarly, the link between MoCA®-derived cognitive impairments and psychological distress may partly be mediated by a complex interplay between treatment responsiveness and psychosocial factors (75). SUDs and mental health problems are associated with and share social risk factors such as lack of healthy and committed social relationships, financial strain, housing insecurity or poor quality housing, poor education, unemployment and exposure to violence (76-80). Moreover, individuals with SUD combat stigma and face barriers to social integration. These obstacles pose substantial challenges in their recovery or habilitation (81-83) and may contribute to sustaining or perpetuating mental health issues or substance use behaviour (84). Consequently, cycles of relapse and dropout out may impede or worsen social adaptation. The full burden of poor social, vocational, and community functioning as well as social exclusion may not become evident until several years after seeking treatment.

The results of the current study indicated that the BRIEF-A was intimately linked to psychiatric distress. However, the ability of BRIEF-A GEC to predict clinical outcomes in terms of long-term psychological distress beyond measures of baseline psychological distress at treatment onset appears limited. The association between psychological distress and elevated BRIEF-A self-reported executive impairments extends across diverse clinical and nonclinical cohorts, including veterans (85), patients with breast cancer, (86), adults with ADHD (32), patients diagnosed with mild or moderate depression (87), patients with neurological and neuropsychiatric conditions (88, 89), patients with brain tumors (90), older adults (91, 92), and controls (88). Improved BRIEF-A results are also linked to decreased psychological distress among patients with a SUD one year following cessation (49). Moreover, the BRIEF-A has shown questionable criterion-related validity pertaining to performance on objective tests of executive functioning. (87, 92-94) and clinically relevant SUD treatment outcomes (95). BRIEF-A may be particularly sensitive to latent executive deficits shared by SUD and psychiatric disorders, e.g., working memory impairments (13, 21, 96-102). Conversely, the BRIEF-A may gauge self-reported functional debilitation associated with psychological distress or mental disorders among patients with SUD rather than impaired executive functioning as defined from psychometric tests.

The relationship between WASI and psychological distress remains somewhat inconclusive. Measures of intellectual functioning have been associated with various mental illnesses (103, 104). The current findings partially align with Hunt et al. (105), who reported that higher WASI Matrix Reasoning scores predicted a greater reduction in depressive symptomatology among patients receiving treatment for problematic alcohol use. However, the theoretical basis for the seemingly random associations observed in the present study remains unclear. The study attrition rate may be higher among participants with cognitive impairments according to the WASI than among those without (95). The results from the current study could thus potentially

be explained by the presence of a subgroup within the sample with impaired intellectual functioning who are both treatment responsive and prone to study dropout, possibly driven by subjective improvement and a desire to disassociate from their past. This dropout profile has the potential to result in nonsignificant disparities over a shorter time span but reestablish an association between impaired intellectual functioning when the proportion of participants with lower treatment responsivity is significantly increased.

The study's results align with prior clinical and population-based research on the prevalence and developmental trajectories of mental illness, affirming that mental health problems among patients with SUD are substantial and that mental health problems act as a risk factor for later life mental health problems (14, 16, 106-108). It is also noted that in accordance with the recommended cut-off scores from SCL-90-R (60), a substantial proportion (76%) of the participants reported a level of psychological distress at treatment initiation, which warrants further assessment. This may suggest that screening for mental illness may be redundant for patients with pSUD and that a comprehensive diagnostic assessment of mental illness could represent a more cost-efficient approach in treatment planning for all patients with pSUD. Unsurprisingly, the study reinforces the well-documented association between substance intake and greater levels of psychological distress (14, 16, 109).

The examination of Nagelkerke R^2 across the regression models may suggest that 1) the contribution from baseline GSI and DUDIT-C to the models explanatory power is approximately equal, 2) the regressions where baseline GSI and DUDIT-C are included produce models with a moderate to strong relationship with long-term caseness, compared to a weak relationship when they are excluded, and 3) the difference in explanatory power between MoCA®, WASI FSIQ and BRIEF-A GEC in models including baseline GSI and DUDI-C is limited.

Strengths and limitations

The present study is one of few to investigate the long-term clinical outcomes in patients with cooccurring SUD and cognitive impairments. SUDs are recognized as enduring conditions, and data on long-term outcome measurements are of vital importance. The current study attempted to maximize ecological validity and sample heterogeneity. First, we utilized diverse widely used and viable instruments that facilitate generalizability to clinical practice. Second, the study targets polysubstance users, which is a clinically relevant sample, representing up to 91% of treatment-seeking patients (110). Third, the cohort is highly heterogeneous and was recruited from diverse SUD clinics. Norway's universal access to health care allows for the collection of a more comprehensive sample relative to countries where care is privatized and costly. Fourth, psychological distress represents a clinically relevant outcome measure, with clear implications for treatment planning and action.

The study dropout rate in the current cohort may be higher among participants with impaired intellectual functioning defined by the WASI than among those without (95). This may potentially modify the sample characteristics pertaining to hitherto unknown key variables accounting for temporal disparities in the association between intellectual impairment and psychological distress. Moreover, the sample size pertaining to participants with intellectual impairments is modest and may mask true differences in psychological distress between the WASI+ and WASI- groups. The size of the WASI+ group is modest, and fitting a regression model with three predictors exceeds the recommended number of events per variable in logistic regression analysis (111).

The results were not Bonferroni corrected and thus susceptible to type I error, i.e., the results may be spurious. However, there is little consensus on the conditions in which the results should be corrected. Due to the greater exploratory focus in the current study, an application of Bonferroni correction would also carry an inherent risk of committing Type II errors, which

was undesirable (112). Moreover, the consistent patterns observed in the results for MoCA® and BRIEF-A contribute to the strengthening of confidence in the obtained results.

The current study utilized a MoCA® cut-off score of ≤ 25 to detect cognitive impairment in accordance with previous recommendations to enhance comparisons and generalizability (52, 53, 55). However, the frequency of PTSD symptomatology in the STAYER cohort is high (113), and others have recommended lowering the MoCA® cut-off score to ≤23 to minimize the rate of false positives in SUD-PTSD populations (72).

Conclusions

Further studies should examine mediators between cognitive impairments and long-term psychological distress. Exploring potential mediators could provide valuable insights into the underlying mechanisms and potential targets for interventions aimed at reducing psychological distress in individuals with cognitive impairments. Research is needed to develop clinically viable short assessment tools with established criterion-related and ecological validity. Such instruments should aim to reliably differentiate between potential psychopathology-driven cognitive impairment and cognitive deficits derived from substance-related neuroadaptations or neurotoxic effects.

BRIEF-A may be sensitive to psychopathology-driven executive dysfunctions. Caution should be exercised when employing BRIEF-A within a clinical SUD context considering its potential limitations and biases. If utilized, it is crucial to corroborate the results with results from objective measures of executive functioning and a broader psychiatric evaluation. The utility of BRIEF-A may rather be evaluated and studied within the framework of being a viable tool assessing self-reported functional impairments associated with psychiatric conditions. Research

should be conducted to explore the potential of BRIEF-A in differentiating between patients with psychiatric disorders and SUD while also determining the feasibility of identifying distinct BRIEF-A profiles.

Considering the high frequency of mental health issues in patients with polysubstance use disorders, it is imperative to investigate the cost–benefit ratio of implementing routine screening for mental disorders in individuals presenting with polysubstance use, as opposed to conducting a comprehensive diagnostic assessment for all.

List of abbreviations

ADHD: Attention Deficit/Hyperactivity Disorder; BRIEF-A: Behaviour Rating Inventory of Executive Function - Adult version; CI: Confidence Interval; DUDIT: The Drug Use Identification Test; DUDIT-C: The Drug Use Identification Test - Consumption items; EUR: Euro; FSIQ: Full-scale IQ; GEC: Global Executive Composite; GSI: Global Severity Index; ICD-10: International Classification of Diseases, Tenth Revision; MoCA®: Montreal Cognitive Assessment®;OR: odds ratio; pSUD: poly substance use disorder; PTSD: Post Traumatic Stress Disorder; SCL-90-R: Symptom Check List-90-Revised; SUD: Substance Use Disorder; STAYER: Stavanger Study of Trajectories of Addiction; WASI: Wechsler Abbreviated Scale of Intelligence

Declarations

Ethics Approval and Consent to Participate

This study protocol was reviewed and approved by the Regional Ethics Committee West, University of Bergen, approval reference REK 2011/1877. The research was conducted according to its guidelines and those of the Helsinki Declaration (1975). All participants gave written informed consent.

Consent for publication

Not applicable.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

Jens Hetland and Aleksander Hagen Erga: conceptualized and designed the study. Jens Hetland: wrote the first draft and revised the manuscript. Jens Hetland and Aleksander Hagen Erga performed the analyses. Aleksander Hagen Erga and Astri Johansen Lundervold made critical revisions of the manuscript. Aleksander Hagen Erga and Astrid Johansen Lundervold supervised the study. All authors contributed to the article and approved the submitted version.

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Table 1. Demographic features of the sample stratified according to cognitive impairment.

	Total Sample	MoCA® < 26		WASI FSIQ		BRIEF-A GEC	
		Impaired [a] (n=53)	Nonimpaired [a] (n=109)	Impaired [a] (n=30)	Nonimpaired [a] (n=133)	Impaired [a] (n=87)	Nonimpaired [a] (n=58)
Age at baseline	27.6 (7.5)	27.6 (7.8)	27.6 (7.4)	26.0 (8.3)	27.9 (7.3)	27.6 (8.3)*	28.7 (5.6)
Gender							
Male	107 (65.2)	35 (33.0)	71 (67.0)	18 (17.0)	88 (83.0)	60 (69.0)	36 (62.1)
Female	57 (34.8)	18 (32.1)	38 (67.9)	12 (21.1)	45 (78.9)	27 (55.1)	22 (44.9)
Education at baseline, years	11.6 (1.7)	11.6 (1.8)	11.6 (1.7)	11.3 (1.7)	11.7 (1.7)	11.5 (1.6)	11.8 (1.8)

Note: MoCA®, Montreal Cognitive Assessment®; WASI FSIQ, Wechsler Abbreviated Scale of Intelligence Full Scale IQ; BRIEF-A GEC, Behaviour Rating Inventory of Executive Function – Adult version Global Executive Composite. Numbers indicate mean (standard deviation) for the variables age and education, and n (%) for gender. [a]Sample at baseline. *p <.05

Table 2. SCL-90-R scores stratified according to cognitive impairment assessed at baseline.

Baseline	Total Sample	MoCA® < 26		WASI FSIQ		BRIEF-A GEC	
		Impaired (n=53)	Nonimpaired (n=109)	Impaired (n=30)	Nonimpaired (n=133)	Impaired (n=87)	Nonimpaired (n=58)
SCL-90-R GSI	1.1 (0.7)	1.1 (0.7)	1.1 (0.7)	1.4 (0.8)*	1.1 (0.6) *a)	1.4 (0.6) ***	0.7 (0.5) ***a)
SCL-90-R Caseness	123 (75.9)	40 (75.5)	83 (76.5)	26 (86.7)	98 (73.7)	79 (90.8) ***	28 (48.3) ***
Year 1	Total Sample						
		Impaired (n=44)	Nonimpaired (n=99)	Impaired (n=25)	Nonimpaired (n=119)	Impaired (n=76)	Nonimpaired (n=53)
SCL-90-R GSI	0.8 (0.6)	1.0 (0.6)	0.8 (0.7)	0.9 (0.6)	0.8 (0.7)	1.0 (0.6) ***	0.6 (0.6) ***
SCL-90-R Caseness	84 (57.9)	32 (72.7)*	51 (51.5)*	17 (68.0)	66 (55.5)	54 (71.1) ***	20 (37.7) ***
Year 5	Total Sample						
		Impaired (n=33)	Nonimpaired (n=74)	Impaired (n=16)	Nonimpaired (n=93)	Impaired (n=59)	Nonimpaired (n=36)
SCL-90-R GSI	0.8 (0.7)	0.9 (0.7)	0.7 (0.6)	1.0 (0.8)	0.7 (0.7)	0.9 (0.7) **	0.5 (0.6) **
SCL-90-R Caseness	57 (52.3)	22 (66.7)*	33 (44.6)*	13 (81.3)*	44 (47.3)*	35 (59.3) *	12 (33.3) *

Note: MoCA®: Montreal Cognitive Assessment®; WASI FSIQ: Wechsler Abbreviated Scale of Intelligence Full Scale IQ; BRIEF-A GEC: Behaviour Rating Inventory of Executive Function – Adult version Global Executive Composite; SCL-90-:, Symptom Checklist-90-Revised; GSI: Global Severity Index. Numbers indicate the mean (standard deviation) for the variable Baseline SCL-90-R GSI and n (%) for SCL-90-R Caseness.

P values: *p ≤.05 ** p ≤.01 *** p ≤.001

Table 3 – Summary of hierarchical logistic regression analysis year one with SCL-90-R caseness as the dependent variable

Predictor	Model 1				Model 2				Model 3			
	Wald	*p*	OR	95% CI	*Wald*	*p*	OR	95% CI	*Wald*	*p*	OR	95% CI
MoCA®												
(Constant)	.041	.840	1.0	-	3.882	.049	.6	-	23.251	<.001	.9	-
MoCA®+	5.685	**.017**	2.6	1.2 – 5.4	3.388	.066	2.2	1.0 – 4.9	4.068	**.044**	2.7	1.0 – 7.0
DUDIT-C					14.415	**<.001**	1.2	1.1 – 1.3	11.738	**<.001**	1.2	1.1 – 1.3
Baseline GSI									22.393	**<.001**	6.4	3.0 – 13.9
	$\chi 2$ = 6.1, p = **.014**, R^2 = .056				$\chi 2$ = 24.0, p = **.<.001**, R^2 =.209				$\chi 2$ = 54.0, p = **<.001**, R^2 = .425			
	Correctly classified 70.6%				Correctly classified 70.4%				Correctly classified 73.9%			
WASI FSIQ												
(Constant)	1.216	.270	1.2	-	2.512	.113	.7	-	19.586	<.001	1.3	-
WASI+	1.385	.239	1.7	.7 – 4.3	1.144	.285	1.7	.6 – 4.5	.078	.780	1.2	.4 – 3.5
DUDIT-C					15.385	**<.001**	1.2	1.1 – 1.3	13.194	**<.001**	1.2	1.1 – 1.3
Baseline GSI									19.511	**<.001**	4.9	2.4 – 9.8
	$\chi 2$ = 1.4, p = .230, R^2 = .013				$\chi 2$ = 20.9, p = **< .001**, R^2= .182				$\chi 2$ = 45.6, p = **<.001**, R^2 = .367			
	Correctly classified 57.3%				Correctly classified 69.2%				Correctly classified 73.4%			
BRIEF-A												
(Constant)	3.123	.077	.606	-	9.650	.002	.3	-	20.707	**<.001**	.1	-
BRIEF-A+	13.168	**<.001**	4.0	1.9 – 8.4	11.124	**<001**	3.9	1.8 – 8.6	.305	.581	1.3	.5 – 3.5
DUDIT-C					12.663	**<001**	1.2	1.1 – 1,3	10.924	**<.001**	1.2	1.1 – 1.3
Baseline GSI									14.403	**<001**	6.0	2.4 – 15.1
	$\chi 2$ = 13.9, p = **< .001**, R^2 = .138				$\chi 2$ = 29.4, p = **<.001**, R^2 = .275				$\chi 2$ = 47.3, p = **<.001**, R^2 = .414			
	Correctly classified 67.2%				Correctly classified 71.1%				Correctly classified 74.2%			

Note: MoCA®: Montreal Cognitive Assessment; WASI: Wechsler Abbreviated Scale of Intelligence; BRIEF-A: Behavior Rating Inventory of Executive Function – Adult version; DUDIT-C: Drug Use Identification Test Consumption Items; Baseline GSI: Baseline Symptom Checklist-90-Revised; Global Severity Index; Model 1: Cognitive impairment as predictor variable; Model 2: Cognitive impairment + DUDIT-C score as predictor variables; Model 3: Cognitive impairment + DUDIT-C score + baseline SCL-90-R GSI score as predictor variables; OR: odds ratio; CI: confidence interval; $\chi 2$ = Omnibus test of model coefficient; R^2 = Nagelkerke R-squared. Significant p values at =α.05 in bold.

Table 4 – Summary of hierarchical logistic regression analysis year five with SCL-90-R caseness as the dependent variable

Predictor	Model 1				Model 2				Model 3			
	Wald	*p*	OR	95% CI	*Wald*	*p*	OR	95% CI	*Wald*	*p*	OR	95% CI
MoCA®												
(Constant)	1.104	.293	.8	-	5.470	.019	.5	-	15.258	**<.001**	.1	-
MoCA®+	4.612	**.032**	2.6	1.1 – 6.0	5.917	**.015**	3.1	1.2 – 7.5	5.956	**.015**	3.4	1.3 – 9.1
DUDIT-C					7.177	**.007**	1.1	1.0 – 1.3	6.180	**.013**	1.1	1.0 – 1.3
Baseline GSI									11.571	**<.001**	3.7	1.7 – 7.8
	$\chi 2$ = 4.8, p = **.028**, R^2 = .059				$\chi 2$ = 12.7, p = **.002**, R^2 =.151				$\chi 2$ = 26.5, p = **<.001**, R^2 = .295			
	Correctly classified 50.9%				Correctly classified 62.3%				Correctly classified 67.0%			
WASI FSIQ												
(Constant)	.391	.532	.9	-	3.492	.062	.6	-	13.658	**<.001**	.2	-
WASI+	5.618	**.018**	4.9	1.3 – 18.5	5.794	**.016**	5.2	1.4 – 19.8	4.322	**.038**	4.5	1.1 – 18.7
DUDIT-C					5.926	**.015**	1.1	1.0 – 1.2	4.917	**.027**	1.1	1.0 – 1.2
Baseline GSI									11.174	**<.001**	3.5	1.7 – 7.2
	$\chi 2$ = 7.0, p = **.008**, R^2 = .084				$\chi 2$ = 13.4, p = **.001**, R^2 = .155				$\chi 2$ = 26.6, p = **<.001**, R^2 = .291			
	Correctly classified 57.4%				Correctly classified 69.2%				Correctly classified 66.7%			
BRIEF-A												
(Constant)	3.844	.050	.5	-	6.377	.012	.4	-	11.712	**<.001**	.2	-
BRIEF-A+	5.532	**.019**	2.8	1.2 – 6.7	5.436	**.020**	2.9	1.2 – 7.0	.634	.426	1.5	.5 – 4.2
DUDIT-C					3.999	**.046**	1.1	1.0 – 1.2	3.195	.074	1.1	1.0 – 1.2
Baseline GSI									11.712	**.010**	2.9	1.3 – 6.7
	$\chi 2$ = 5.8, p = **.016**, R^2 = .079				$\chi 2$ = 10.0, p = **.007**, R^2 = .135				$\chi 2$ = 17.5, p = **<.001**, R^2 = .226			
	Correctly classified 61.7%				Correctly classified 66.0%				Correctly classified 66.0%			

Note: MoCA®: Montreal Cognitive Assessment; WASI: Wechsler Abbreviated Scale of Intelligence; BRIEF-A: Behavior Rating Inventory of Executive Function – Adult version; DUDIT-C: Drug Use Identification Test Consumption Items; Baseline GSI: Baseline Symptom Checklist-90-Revised; Global Severity Index; Model 1: Cognitive impairment as predictor variable; Model 2: Cognitive impairment + DUDIT-C score as predictor variables; Model 3: Cognitive impairment + DUDIT-C score + baseline SCL-90-R GSI score as predictor variables; OR: odds ratio; CI: confidence interval; $\chi 2$ = Omnibus test of model coefficient; R^2 = Nagelkerke R-squared. Significant p values at =α.05 in bold.

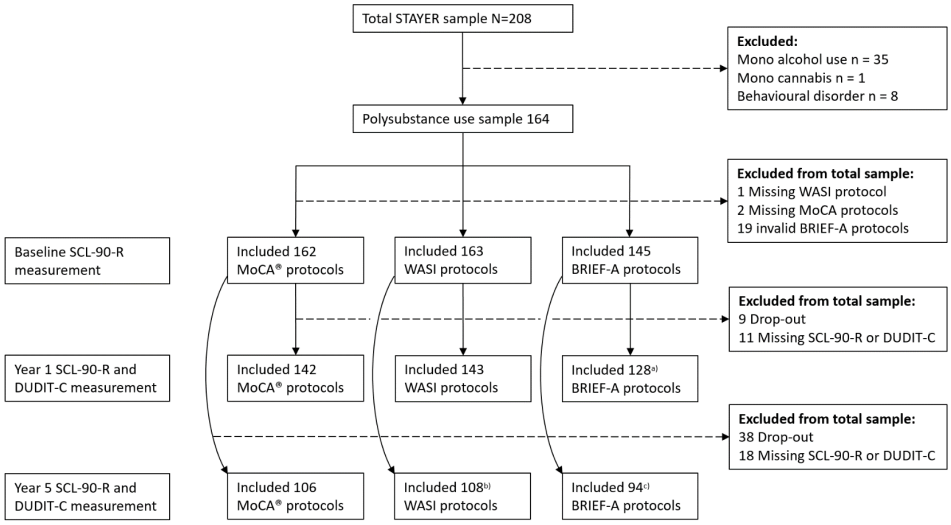

Figure 1. Flow of participant inclusion, exclusion and missing data at baseline, 1-year, and 5-year follow-up measurements. Discrepancies between (i) excluded participants from the total sample and (ii) the number of included protocols at baseline and follow-up are due to overlap between protocols already excluded at baseline and participants who had dropped out or had missing DUDIT-C or SCL-90-R entries at follow-up. Thus, a) 17 BRIEF-A protocols were excluded at the 1-year follow-up measurement, and b) 55 WASI and c) 51 BRIEF-A protocols were excluded at the 5-year follow-up measurement. MoCA®, Montreal Cognitive Assessment®; WASI, Wechsler Abbreviated Scale of Intelligence; BRIEF-A, Behaviour Rating Inventory of Executive Function – Adult version.

Doctoral Theses at The Faculty of Psychology, University of Bergen

1980	Allen, Hugh M., Dr. philos.	Parent-offspring interactions in willow grouse (Lagopus L. Lagopus).
1981	Myhrer, Trond, Dr. philos.	Behavioral Studies after selective disruption of hippocampal inputs in albino rats.
1982	Svebak, Sven, Dr. philos.	The significance of motivation for task-induced tonic physiological changes.
1983	Myhre, Grete, Dr. philos.	The Biopsychology of behavior in captive Willow ptarmigan.
	Eide, Rolf, 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, Ragnar J., Dr. philos.	Neuropsychological effects of diving.
1984	Kolstad, Arnulf, Dr. philos.	Til diskusjonen om sammenhengen mellom sosiale forhold og psykiske strukturer. En epidemiologisk undersøkelse blant barn og unge.
	Løberg, Tor, Dr. philos.	Neuropsychological assessment in alcohol dependence.
1985	Hellesnes, Tore, Dr. philos.	Læring og problemløsning. En studie av den perseptuelle analysens betydning for verbal læring.
	Håland, Wenche, Dr. philos.	Psykoterapi: relasjon, utviklingsprosess og effekt.
1986	Hagtvet, Knut A., Dr. philos.	The construct of test anxiety: Conceptual and methodological issues.
	Jellestad, Finn K., Dr. philos.	Effects of neuron specific amygdala lesions on fear-motivated behavior in rats.
1987	Aarø, Leif E., Dr. philos.	Health behaviour and sosioeconomic Status. A survey among the adult population in Norway.
	Underlid, Kjell, Dr. philos.	Arbeidsløyse i psykososialt perspektiv.
	Laberg, Jon C., Dr. philos.	Expectancy and classical conditioning in alcoholics' craving.
	Vollmer, Fred, Dr. philos.	Essays on explanation in psychology.
	Ellertsen, Bjørn, Dr. philos.	Migraine and tension headache: Psychophysiology, personality and therapy.
1988	Kaufmann, Astrid, Dr. philos.	Antisosial atferd hos ungdom. En studie av psykologiske determinanter.

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

	Bru, Edvin, Dr. philos.	The role of psychological factors in neck, shoulder and low back pain among female hospitale staff.
	Braathen, Eli T., Dr. psychol.	Prediction of exellence and discontinuation in different types of sport: The significance of motivation and EMG.
	Johannessen, Birte F., Dr. philos.	Det flytende kjønnet. Om lederskap, politikk og identitet.
1995	Sam, David L., Dr. psychol.	Acculturation of young immigrants in Norway: A psychological and socio-cultural adaptation.
	Bjaalid, Inger-Kristin, Dr. philos.	Component processes in word recognition.
	Martinsen, Øyvind, Dr. philos.	Cognitive style and insight.
	Nordby, Helge, Dr. philos.	Processing of auditory deviant events: Mismatch negativity of event-related brain potentials.
	Raaheim, Arild, Dr. philos.	Health perception and health behaviour, theoretical considerations, empirical studies, and practical implications.
	Seltzer, Wencke J., Dr. philos.	Studies of Psychocultural Approach to Families in Therapy.
	Brun, Wibecke, Dr. philos.	Subjective conceptions of uncertainty and risk.
	Aas, Henrik N., Dr. psychol.	Alcohol expectancies and socialization: Adolescents learning to drink.
	Bjørkly, Stål, Dr. psychol.	Diagnosis and prediction of intra-institutional aggressive behaviour in psychotic patients
1996	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.

1997	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.
1998 **V**	Lindstrøm, Torill Christine, Dr. philos.	«Good Grief»: Adapting to Bereavement.
	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.
H	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.
1999 **V**	Mikkelsen, Aslaug, Dr. philos.	Effects of learning opportunities and learning climate on occupational health.
	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.
H	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.
2000 V	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 tilnærmingsmåte.
H	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.
2001 V	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.
H	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.	Kvinners 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.
2002 V	Ihlebæk, 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.
H	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.
2003 V	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.
H	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.
2004 V	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 sportspersonship 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.
2004 H	Thomsen, Tormod, Dr. psychol.	Localization of attention in the brain.
	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: Experiencal, behavioural and cardiovascular indices.
	Holgersen, Helge, PhD	Mellom oss - Essay i relasjonell psykoanalyse.
2005 V	Hetland, Hilde, Dr. psychol.	Leading to the extraordinary? Antecedents and outcomes of transformational leadership.
	Iversen, Anette Christine, Dr. philos.	Social differences in health behaviour: the motivational role of perceived control and coping.
2005 H	Mathisen, Gro Ellen, PhD	Climates for creativity and innovation: Definitions, measurement, predictors and consequences.
	Sævi, Tone, Dr. philos.	Seeing disability pedagogically – The lived experience of disability in the pedagogical encounter.
	Wiium, 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.
2006 V	Hillestad, Torgeir Martin, Dr. philos.	Normalitet og avvik. Forutsetninger for et objektivt psykopatologisk avviksbegrep. En psykologisk, sosial, erkjennelsesteoretisk og teorihistorisk framstilling.
	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 consiousness in implicit cognition.
	Israel, K Pravin, Dr. psychol.	Parent involvement in the mental health care of children and adolescents. Emperical 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.
2006 H	Gramstad, Arne, PhD	Neuropsychological assessment of cognitive and emotional functioning in patients with epilepsy.
	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.
2007 V	Singhammer, John, Dr. philos.	Social conditions from before birth to early adulthood – the influence on health and health behaviour
	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
2007 H	Søreide, Gunn Elisabeth, Dr.philos.	Narrative construction of teacher identity
	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
2008 V	Breivik, Kyrre, Dr.psychol.	The Adjustment of Children and Adolescents in Different Post-Divorce Family Structures. A Norwegian Study of Risks and Mechanisms.
	Johnsen, Grethe E., PhD	Memory impairment in patients with posttraumatic stress disorder
	Sætrevik, Bjørn, PhD	Cognitive Control in Auditory Processing
	Carvalhosa, Susana Fonseca, PhD	Prevention of bullying in schools: an ecological model
2008 H	Brønnick, Kolbjørn Selvåg	Attentional dysfunction in dementia associated with Parkinson's disease.
	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
2009 V	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 Konwledge 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
2009 H	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
2010 V	Skår, Randi	Læringsprosesser i sykepleieres profesjonsutøvelse. En studie av sykepleieres læringserfaringer.
	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 Kjellevold	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
H	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
	Viig, 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.
2011 V	Bye, Hege Høivik	Self-presentation in job interviews. Individual and cultural differences in applicant self-presentation during job interviews and hiring managers' evaluation
	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 prosesses 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 psykoterapautens 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

2011 H	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-occuring 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
	Hystad, Sigurd William	Measuring Psychological Resiliency: Validation of an Adapted Norwegian Hardiness Scale
2012 V	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, skoleledereres 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.

2012 H	Danielsen, Yngvild Sørebø	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)
	Leversen, 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 samfunnsmessig beskyttelse
2013 V	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
2013 H	Gianella-Malca, Camila	Challenges in Implementing the Colombian Constitutional Court's Health-Care System Ruling of 2008
	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
2014 V	Nordmo, Ivar	Gjennom nåløyet – studenters læringserfaringer i psykologutdanningen
	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 pasientaggresjon 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
2014 H	Sandvik, Asle Makoto	Psychopathy – the heterogenety 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 innvandrerungdommer og norskfødte med innvandrerforeldre 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 overgangsprosessar.
	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.
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