







ORIGINAL ARTICLE

Predictors of cognitive functioning in presentations to a community-based specialist addiction neuropsychology service

James R. Gooden^{1,2,3,4*} , Catherine A. Cox¹, Vanessa Petersen¹ , Ashlee Curtis⁵ , Paul G. Sanfilippo¹, Victoria Manning^{1,4} , Georgia L. Bolt¹  and Dan I. Lubman^{1,4} 

¹Turning Point, Eastern Health, Richmond, VIC, Australia, ²The National Centre for Clinical Research on Emerging Drugs (NCCRED), University of New South Wales, Sydney, NSW, Australia, ³National Drug and Alcohol Research Centre, University of New South Wales, Sydney, NSW, Australia, ⁴Monash Addiction Research Centre, Eastern Health Clinical School, Monash University, Box Hill, VIC, Australia and ⁵Centre for Drug Use, Addiction, and Anti-Social Behaviour Research, School of Psychology, Deakin University, Geelong, VIC, Australia

*Corresponding author. Email: jamesg@turningpoint.org.au

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Abstract

Introduction: Cognitive impairment is common in individuals presenting to alcohol and other drug (AOD) settings and the presence of biopsychosocial complexity and health inequities can complicate the experience of symptoms and access to treatment services. A challenge for neuropsychologists in these settings is to evaluate the likely individual contribution of these factors to cognition when providing an opinion regarding diagnoses such as acquired brain injury (ABI). This study therefore aimed to identify predictors of cognitive functioning in AOD clients attending for neuropsychological assessment.

Methods: Clinical data from 200 clients with AOD histories who attended for assessment between 2014 and 2018 were analysed and a series of multiple regressions were conducted to explore predictors of cognitive impairment including demographic, diagnostic, substance use, medication, and mental health variables.

Results: Regression modelling identified age, gender, years of education, age of first use, days of abstinence, sedative load, emotional distress and diagnoses of ABI and developmental disorders as contributing to aspects of neuropsychological functioning. Significant models were obtained for verbal intellectual functioning (Adj $R^2 = 0.19$), nonverbal intellectual functioning (Adj $R^2 = 0.10$), information processing speed (Adj $R^2 = 0.20$), working memory (Adj $R^2 = 0.05$), verbal recall (Adj $R^2 = 0.08$), visual recall (Adj $R^2 = 0.22$), divided attention (Adj $R^2 = 0.14$), and cognitive inhibition (Adj $R^2 = 0.07$).

Conclusions: These findings highlight the importance of careful provision of diagnoses in clients with AOD histories who have high levels of unmet clinical needs. They demonstrate the interaction of pre-morbid and potentially modifiable comorbid factors such as emotional distress and prescription medication on cognition. Ensuring that modifiable risk factors for cognitive impairment are managed may reduce experiences of cognitive impairment and improve diagnostic clarity.

Keywords: Neuropsychology; addiction; acquired brain injury; drugs and alcohol; cognition

Introduction

Delays in treatment seeking for individuals with alcohol and other drug (AOD) use disorders are well recognised and often by the time addiction treatment is sought, individuals present with a high level of psychosocial and medical complexity (Lubman et al., 2016). These biopsychosocial factors can have significant implications for treatment and management and importantly, the

presence of such factors may contribute to cognitive impairment. For instance, in other populations medical conditions including Hepatitis C (Barreira, Marinho, Bicho, Fialho, & Ouakinin, 2019; Yarlott, et al., 2017) and mental health conditions including depression, anxiety, post-traumatic stress disorder, and complex trauma are well known to impact cognitive functioning (Cohen et al., 2013; Goodall et al., 2018; Gould et al., 2012; Robinson, et al., 2013; Rock, et al., 2014). In AOD populations, acute cognitive impairments have been well documented as a result of active or recent substance and polysubstance use (Bruijnen et al., 2019; Mann, et al., 1999; Schmidt, Pennington, Cardoos, Durazzo, & Meyerhoff, 2017) and commonly prescribed and misused psychotropic medications (Crowe & Stranks, 2018; Tannenbaum, Paquette, Hilmer, Holroyd-Leduc, & Carnahan, 2012). Furthermore, individuals with neurodevelopmental disorders, including attention deficit hyperactivity disorder (ADHD) and specific learning difficulties, may also be more likely to engage in substance use (Beitchman, Wilson, Douglas, Young, & Adlaf, 2001; Carroll, et al., 2014; Wilens et al., 2011), and the presence of these conditions can further contribute to experiences of cognitive difficulty (Severtson, et al., 2012). Weak performances on formal neuropsychological examination can also arise, in part, due to limited educational attainment, which, by virtue of a dynamic interplay between aforementioned factors, is common in individuals with extensive AOD histories (Abad, et al., 2016; Gooden et al., 2021). Consideration of a range of biopsychosocial risk factors is therefore critical to ensuring accurate neuropsychological formulations and guiding functional outcomes when working with AOD populations (Gooden et al., 2021).

Failure to consider the interaction and contribution of biopsychosocial factors to an individual's presentation could lead to misattribution biases where transient cognitive impairments are assumed to be permanent and misdiagnosed as an acquired brain injury (ABI), or more permanent cognitive deficits are minimised. This is problematic in that modifiable, potentially treatable factors may be left unmanaged, or alternatively, more permanent cognitive deficits can go unrecognised. Unmanaged comorbidities can also prevent or delay the provision of formal diagnoses if multiple aetiologies are considered to be contributing to an individual's cognitive difficulties (Gooden et al., 2021). This, in turn, can have profound implications for eligibility and timely access to necessary funding, disability support and services.

Taken together, these confounding variables, health inequities and stigma associated with AOD use (Birtel, et al., 2017; Room, 2005; Schomerus et al., 2010; van Boekel, et al., 2013), have significant potential to complicate the experience of cognitive impairment and presentations to treatment services. A challenge for neuropsychologists, psychologists and physicians working within addiction settings is to weigh up the likely individual contribution of these biopsychosocial risk factors when providing diagnostic opinions and recommendations. Unfortunately, previous research on cognitive impairment in AOD settings often lacks clinical applicability, for instance, by excluding those with high levels of complexity or polysubstance use (Liu, Williamson, Setlow, Cottler, & Knackstedt, 2018). As such there is a pressing need for research exploring the relative contributions of biopsychosocial factors upon cognitive function in clinical groups that are representative of treatment seeking individuals with AOD use. This study therefore aims to identify the individual contribution of commonly experienced biopsychosocial factors upon cognitive functioning in a sample of individuals who attended for neuropsychological examination at a specialist addiction treatment service. In addition to the expected contributions of reduced educational attainment, ABI and developmental disability, it was predicted that a final regression model for each cognitive domain would include significant contributions from the following independent variables in the direction described:

- i. The presence of a mental health history, greater emotional distress, and a history of trauma would all negatively impact measures of cognition.
- ii. Multiple sedating medications, as measured by the Sedative Load Index, would negatively impact measures of cognition.
- iii. The presence of untreated Hepatitis C would be associated with reduced performance on measures of cognition.

- iv. More extensive substance use histories, shorter abstinence durations, and current polysubstance use would also be related to reduced performances on measures of cognitive functioning.

Methods

Setting

The Statewide Addiction Specialist Neuropsychology Service is a government funded community-based service based at Turning Point, a national addiction treatment and research centre based in Melbourne, Victoria. Further information regarding the service model has been previously described (Gooden *et al.*, 2021).

Design

This study was a retrospective case file audit conducted following ethical approval from the Eastern Health Human Research Ethics Committee (Ref: LR88/2017).

Participants

Participants included 200 individuals who were referred for a neuropsychological assessment between August 2014 and June 2018 and consented to their data being used for research purposes. During the audit period, 14 individuals declined to provide this consent at the time of assessment. Inclusion and exclusion criteria for the study were determined by the referral criteria for the service which requires clients to be aged over 18, with a significant past or current AOD history and not referred for medico legal or decision making capacity purposes. Based on clinical observations, embedded and formal measures of effort, participants who were determined to have not provided appropriate effort during the assessment and yielded invalid test results ($n = 5$) were excluded from analyses.

Measures

A comprehensive history was obtained as part of standard clinical practice via interview and documented in the clients' neuropsychological report along with assessment findings and formulations. The following information was extracted from these reports: basic demographics including age, gender, years of formal education, Hepatitis C status, the presence of a diagnosed ABI, moderate or severe TBI (defined according to severity criteria set forth in Ponsford, *et al.*, 2013), or neurodevelopmental condition (e.g. intellectual, specific learning or language disabilities and ADHD), the history of complex trauma (from childhood or adulthood) or a diagnosed mental health condition and substance use histories. Sources for this information included self-reported histories of diagnoses that were conferred by a treating clinician such as a GP, psychologist, psychiatrist, or other specialist. Where available, source records and informant reports were reviewed to verify these histories and any further details. In a proportion of cases, diagnoses of neurodevelopmental conditions or ABI were conveyed as a result of their neuropsychological assessment. An evidence-based biopsychosocial approach to neuropsychological formulation and diagnosis is employed at the service, whereby information is drawn from a range of sources, including clinical history and observations, relevant medical documentation and cognitive examination. Developmental, psychological, medical, intrinsic, substance-related, cognitive, family, and social contextual factors are all considered and integrated into formulation.

Sedative load index

The Sedative Load Index is a measure of the combined sedative load of prescribed medications based on classifications of their sedative properties (Hoban *et al.*, 2015; T. Linjakumpu *et al.*, 2003;

T. A. Linjakumpu et al., 2004). Prescribed medications are categorised into three groups each which have their own sedative rating; Group 1: Primary Sedatives (rating of 2); Group 2: Medications with a sedative component and medications with sedation as a prominent adverse effect (rating of 1); Group 3: Medications with sedation as a known potential adverse effect, and medications with no known sedative effect (rating of 0). A total score is then calculated by summing the ratings of each medication prescribed for each participant. Higher total scores are indicative of higher sedative loads and a score of ≥ 3 indicates the individual is using \geq two drugs with sedative properties (T. A. Linjakumpu et al., 2004).

Alcohol and substance use

Measures of alcohol and substance use included self-reported details regarding age of first use, the total number of alcohol or illicit substances used on a daily or near daily basis, and days of abstinence (i.e. difference between reported last substance use and day of assessment). Where available, additional records from other AOD services were reviewed to verify these self-reported histories.

Neuropsychological assessment

Assessment measures were selected at the time of assessment and at the discretion of the treating neuropsychologist. All measures are commonly administered in clinical practice, well validated, reliable, and sensitive to changes in cognitive functioning as indicated by their inclusion in neuropsychological test compendia (e.g. Lesak, et al., 2012; Strauss, et al., 2006). In order to ensure maximal participant data, only the most commonly administered measures were selected for inclusion in the current study. As such, test data for the following cognitive domains were extracted from client records: verbal and nonverbal intellectual functioning, verbal and visual memory, working memory, information processing speed, psychomotor speed, divided attention, and cognitive inhibition (Table 1). Emotional distress was measured using the Depression, Anxiety and Stress Scales (DASS) 21 Item version and the combined score from all three scales was used (Lovibond & Lovibond, 1995).

Procedure

Case files were reviewed by the clinic neuropsychologists, de-identified, and relevant data including client history, assessment results, and neuropsychological formulations were extracted into a database. To characterise neuropsychological assessment results, as per standard clinical practice, raw scores were compared to age corrected normative data and standardised using scaled scores or Z scores at the time of assessment. As such, the standardised scores for each cognitive domain were extracted and utilised in the current study with the selection of which normative data to utilise being made by the assessing clinician at the time of the assessment.

Data analysis

To evaluate hypotheses, a series of multiple regression models were conducted. Predictor variables for these models included: age, gender, years of education, presence of a diagnosed ABI, neurodevelopmental diagnosis, mental health diagnosis, DASS total score, trauma history, sedative load, Hepatitis C status, age of first AOD use, days of abstinence, and number of current substances used.

Outcome variables included performance on measures of verbal intellectual functioning, non-verbal intellectual functioning, working memory, information processing speed, verbal memory, visual memory, psychomotor scanning speed, divided attention, and cognitive inhibition (Table 1). In order to identify candidate variables for the multivariable models, each predictor variable was tested against the outcome variables independently in a univariate model. Predictor variables that were

Table 1. Neuropsychological assessment measures, variables used, and normative data

Cognitive domain	Test	Variable used	Normative data
Verbal intellectual functioning	Wechsler adult intelligence scale: fourth edition	VCI index (composite score)	(Wechsler, 2008a)
Nonverbal intellectual functioning	Wechsler adult intelligence scale: fourth edition	PRI index (composite score)	(Wechsler, 2008a)
Working memory	Wechsler adult intelligence scale: fourth edition	Digit span (scaled score)	(Wechsler, 2008a)
Processing speed	Wechsler adult intelligence scale: fourth edition	PSI index (composite score)	(Wechsler, 2008a)
Verbal memory (stories)	Wechsler memory scale: fourth edition	Logical memory II (scaled score)	(Wechsler, 2008b)
Visual memory	Rey complex figure test	30 min recall trial (z score)	(Meyers & Meyers, 1995)
Psychomotor speed	Trail making test	Part A time taken (z score)	(Tombaugh, 2004)
Divided attention	Trail making test	Part B time taken (z score)	(Tombaugh, 2004)
Cognitive inhibition	Stroop test (Victoria version)	Colour-word trial: time taken (scaled score)	(Troyer, et al., 2006)

Note. Normative data for all measures were age corrected with the exception of the Trail Making Test which was age and education corrected. Further details for each test can be located through source publishers or reference texts as follows: Wechsler Adult Intelligence Scale (WAIS-IV; Wechsler, 2008a); Wechsler Memory Scale (WMS-IV; Wechsler, 2008b); Trail Making Test (TMT; Reitan & Wolfson, 1988); Rey Complex Figure test (RCFT; Meyers & Meyers, 1995); Stroop Test (Strauss et al., 2006).

significant at the 20% level ($p < 0.2$) were deemed to be candidate variables and were included in the preliminary multivariable model.

The preliminary multivariable model for each outcome was tested with all candidate variables and then a stepwise procedure was followed where predictors with progressively highest p values were independently removed from the model and the fit of the model examined to see if the predictor made a meaningful contribution to each performance indicator, with R squared change scores at $p < 0.05$ as the criterion. Predictor variables were then reinserted into the model to cross check for any significant contribution. Plausible interaction terms among predictors were tested to generate a final regression model for each outcome variable. Age and gender were retained as predictor variables for all models. Analyses were conducted in Stata 16.0 (StataCorp., 2019) and SPSS Version 27 (IBM Corp., 2020) and were two-sided with a p -value < 0.05 considered to be statistically significant.

Results

Participant demographics and neuropsychological test performances are presented in Table 2. The majority of individuals in the sample were aged between 18 and 64, were male and had a Grade 10 level or less of education. Females ($M = 44.25$, $SD = 11.71$) were significantly older than males ($M = 38.18$, $SD = 8.97$), $t(71.85) = -3.37$, $p = 0.001$, and had completed significantly more years of education ($M = 11.49$, $SD = 1.99$) than males ($M = 10.88$, $SD = 1.74$), $t(190) = -2.06$, $p = 0.04$.

Across the sample, 71% had a formal mental health history. Inclusive of pre-existing and newly conveyed diagnoses, neurodevelopmental diagnoses including intellectual, learning and language disabilities and ADHD were present in 16% of cases while ABI including moderate to severe

Table 2. Participant characteristics and neuropsychological test performances

	<i>N</i> (%)	<i>M</i> (<i>SD</i>)	Range	Normal reference range
Age	195	39.77 (10.09)	19–64	
Gender				
Male	144 (73.8)			
Female	51 (26.2)			
Education (years)	192	11.04 (1.83)	7–18	
Mental health				
Formal diagnosis	139 (71.6)			
Trauma history	78 (40.6)			
DASS total score	148	53.19 (29.48)	0–126	
Medical				
Untreated hepatitis C	37 (19.3)			
Treated hepatitis C	16 (8.3)			
ABI diagnosis	48 (24.6)			
Developmental diagnosis	32 (16.4)			
Sedative load	195	1.51 (1.83)	0–8	
Substance use				
Age of first use	177	15.04 (4.46)	8–48	
Lifetime substances used ^a	195	3.56 (1.55)	0–8	
Current substances used daily ^b	195	0.35 (0.61)	0–3	
Days of abstinence	160	268.50 (805.52)	0–5840	
Neuropsychological test scores ^c				
Verbal intellectual function	174	89.01 (14.22)	61–130	90–110
Nonverbal intellectual function	170	92.22 (13.36)	69–127	90–110
Processing speed	175	86.25 (12.53)	56–117	90–110
Working memory	187	7.79 (2.30)	3–16	8–12
Verbal memory (stories)	183	7.38 (3.16)	1–16	8–12
Visual memory	134	–1.18 (1.39)	–5.05 to 2.10	–0.6 to 0.6
Psychomotor speed	176	–0.55 (1.41)	–6.77 to 1.69	–0.6 to 0.6
Divided attention	171	–2.03 (2.65)	–12.98 to 1.72	–0.6 to 0.6
Inhibitory control	163	8.15 (2.53)	0–17	8–12

Note. ABI, acquired brain injury; DASS, Depression, Anxiety and Stress Scale.

^aDefined as the lifetime number of alcohol and illicit substances used.

^bDefined as the number of alcohol and illicit substances currently used on a daily or near daily basis.

^cMeasures were administered based on clinical judgement and so not all clients completed each measure.

traumatic brain injuries and non-traumatic acquired brain injuries were present in 25% of cases. Overall 25% of the sample had a new diagnosis conveyed as a result of the assessment.

The most frequently prescribed medications that contributed to sedative load indices included diazepam ($n = 35$, 17.9%), methadone ($n = 21$, 10.8%), escitalopram ($n = 17$, 8.7%), quetiapine

($n = 16$, 8.2%), mirtazapine ($n = 16$, 8.2%), pregabalin ($n = 13$, 6.7%), and olanzapine ($n = 13$, 6.7%). Regarding sedative loads, 107 (55%) individuals had a score of one or more indicating the presence of a prescribed medication with sedative properties while 56 (29%) had a score of 3 or more indicating use of two or more medications with sedative properties. Twenty nine percent of individuals were maintaining daily use of alcohol or illicit substances, while the median duration of abstinence was 7 days. On average, the sample used between three to four different types of substances in their lifetime. The average age of onset of substance use was 15 years.

Across the cognitive domains measured, mean performances were largely within the low average range (9th to 24th percentile), one standard deviation below the average range (Wechsler, 2008a) with the exception of divided attention where mean scores were an average of more than two standard deviations below population norms (<2nd percentile). For each domain, a wide range of performances were observed ranging from extremely low (<2nd percentile) through to high average to superior (97th percentile).

Predictors of cognitive functioning

Results from the final exploratory regression models and included predictor variables for each outcome measure are presented in Table 3. Significant models were obtained for verbal intellectual functioning, $F(5, 126) = 7.09$, $p < 0.001$, $\text{Adj } R^2 = 0.19$; nonverbal intellectual functioning, $F(4, 162) = 5.42$, $p < 0.001$, $\text{Adj } R^2 = 0.10$; information processing speed, $F(5, 114) = 6.84$, $p < 0.001$, $\text{Adj } R^2 = 0.20$; working memory, $F(4, 143) = 3.02$, $p = 0.02$, $\text{Adj } R^2 = 0.05$; verbal recall, $F(5, 175) = 4.21$, $p = 0.001$, $\text{Adj } R^2 = 0.08$; visual recall, $F(5, 117) = 7.96$, $p < 0.001$, $\text{Adj } R^2 = 0.22$; psychomotor speed, $F(3, 136) = 4.89$, $p = 0.003$, $\text{Adj } R^2 = 0.08$; divided attention, $F(4, 132) = 6.72$, $p < 0.001$, $\text{Adj } R^2 = 0.14$; and cognitive inhibition, $F(5, 156) = 3.33$, $p = 0.007$, $\text{Adj } R^2 = 0.07$.

With regard to individual predictors, for verbal intellectual functioning, years of education strongly predicted better performance while having a diagnosis of a developmental disability was strongly associated with decreased performance. Heightened emotional distress was also associated with decreased performance. This model accounted for 19% of the variance. Gender was a statistically significant predictor of nonverbal intellectual functioning with males performing 5.88 points better (representing around one third of a standard deviation on this index), on average, than females. Years of education was also associated with better performance and having a diagnosis of ABI was associated with a predicted decrease of 6.27 points in composite scores for nonverbal intellectual functioning.

Age, gender and education significantly predicted information processing speed, with females processing information more efficiently than males, those with more years of education performing better and processing speed deteriorating with age. Heightened emotional distress was associated with processing efficiency while a relationship was observed between fewer days of abstinence and better performance.

For working memory, having a diagnosis of a neurodevelopmental disability was associated with 1.24 decrease in standard scores (representing almost half a standard deviation on this measure) while heightened emotional distress was also associated with reduced performances. For verbal memory, a significant interaction was found between developmental disability and years of education. Accordingly, although the presence of a developmental disability was associated with a decrease in performance, the impact of this was mitigated by each year of formal education completed. Thus, for an individual with 7 years of education and a developmental disorder, the model predicted a decrease in 4.18 points in verbal memory compared to an individual without a developmental disorder. Poor visual memory performance was significantly predicted by the presence of an ABI and higher sedative loads. In addition, age and age of first use were predictive of visual memory performance whereby being male, older and commencing substance use at a later age predicted better performance. Collectively this model accounted for 22% of the variance.

Table 3. Regression models for predictors of cognitive performance

Outcome variable	Predictors	Coef	Std err	<i>t</i>	<i>p</i>	95% CI	Adj R ²
Verbal intellectual functioning	Age	0.15	0.12	1.26	0.21	−0.10 to −0.38	0.19
	Gender (female)	−2.33	2.55	−0.91	0.36	−7.37 to 2.73	
	Education	2.31	0.59	3.89	<0.001	1.13–3.48	
	Developmental dx.	−8.41	3.66	−2.30	0.02	−15.66 to −1.17	
	DASS	−0.08	0.04	−2.18	0.03	−0.16 to −0.01	
Nonverbal intellectual functioning	Age	−0.13	0.10	−1.25	0.22	−0.33 to 0.08	0.10
	Gender (female)	−5.88	2.30	−2.55	0.01	−10.42 to −1.34	
	Education	1.29	0.53	2.44	0.02	0.25–2.34	
	ABI dx.	−6.27	2.31	−2.72	0.007	−10.83 to −1.71	
Information processing speed	Age	−0.24	0.11	−2.32	0.02	−0.45 to −0.04	0.20
	Gender (female)	7.17	2.34	3.07	0.003	2.54–11.90	
	Education	1.59	0.55	2.92	0.004	0.51–2.68	
	Days of abstinence	−0.004	0.002	−2.21	0.03	−0.008 to 0.00	
	DASS	−0.09	0.04	−2.63	0.01	−0.16 to −0.02	
Working memory	Age	−0.01	0.02	−0.57	0.57	−0.05 to 0.03	0.05
	Gender (female)	−0.19	0.42	−0.45	0.65	−1.03 to 0.65	
	Developmental dx.	−1.24	0.60	−2.06	0.04	−2.43 to −0.05	
	DASS	−0.02	0.01	−2.70	0.008	−0.03 to −0.004	
Verbal memory	Age	−0.003	0.02	−0.15	0.88	−0.05 to 0.04	0.08
	Gender (female)	1.00	0.53	1.89	0.06	−0.04 to 2.04	
	Education	0.15	0.14	1.13	0.26	−0.11 to 0.42	
	Developmental dx.	−9.85	3.93	−2.51	0.01	−17.61 to −2.09	
	Developmental dx. × education	0.81	0.37	2.21	0.03	0.09–1.53	
Visual memory	Age	0.03	0.01	2.30	0.03	0.004–0.052	0.22
	Gender (female)	−0.94	0.25	−3.67	<0.001	−1.44 to −0.43	
	ABI Dx.	−0.85	0.26	−3.27	0.001	−1.36 to −0.34	
	Sedative load	−0.17	0.06	−2.87	0.005	−0.29 to −0.05	
	Age of first use	0.09	0.04	2.30	0.02	0.01–0.16	
Psychomotor speed	Age	−0.002	0.01	−0.23	0.82	−0.02 to 0.02	0.08
	Gender (female)	0.76	0.25	3.09	0.002	0.27–1.25	
	DASS	−0.01	0.004	−2.12	0.04	−0.02 to −0.001	
Divided attention	Age	−0.01	0.02	−0.71	0.48	−.05 to 0.03	0.14
	Gender (female)	0.56	0.45	1.26	0.21	−0.32 to 1.45	
	Sedative load	−0.33	0.11	−2.96	0.004	−0.54 to −0.11	
	DASS	−0.02	0.01	−2.84	0.005	−0.03 to −0.01	

(Continued)

Table 3. (Continued)

Outcome variable	Predictors	Coef	Std err	<i>t</i>	<i>p</i>	95% CI	Adj R ²
Cognitive inhibition	Age	−0.04	0.02	−2.08	0.04	−0.08 to −0.002	0.07
	Gender (female)	0.47	0.46	1.03	0.30	−0.43 to 1.37	
	Education	0.13	0.12	1.11	0.27	−0.10 to 0.36	
	Developmental dx.	−7.84	3.15	−2.49	0.01	−14.06 to −1.61	
	Developmental dx. × education	0.67	0.29	2.27	0.02	0.09–1.25	

Note. ABI, acquired brain injury; DASS, Depression Anxiety and Stress, Scale; Dx, Diagnosis.

Divided attention was significantly predicted by sedative load and emotional distress, with the model accounting for 14% of the variance. This indicates that higher sedative load scores and increased symptoms of emotional distress were negatively impacting the efficiency with which individuals could rapidly switch and divide their attention.

Finally, better performance on a measure of cognitive inhibition was predicted by younger age and an interaction effect between developmental disability and years of education, similar to what was observed for verbal memory. Taking the average years of education for the sample, having a developmental disability was associated with a 0.47 point decrease in scaled scores for cognitive inhibition. Predictor variables for the presence of a mental health diagnosis, complex trauma history, untreated hepatitis C, and current substance use were not found to have made a meaningful contribution to any of the outcome measures assessed.

Discussion

This study aimed to evaluate the unique contribution of biopsychosocial factors to cognitive functioning in a group of community-based individuals presenting to a specialist neuropsychology addiction treatment service. In partial support of our hypotheses we found that higher sedative loads from prescribed medications strongly predicted worse performance on measures of divided attention and visual memory, while greater symptoms of emotional distress predicted worse performance on measures of divided attention, verbal intellectual functioning, information processing speed and working memory. As would be expected, gender, years of education, the presence of an ABI, and neurodevelopmental diagnoses also predicted aspects of cognitive functioning either independently or through interactions, while age, age of first use, and shorter abstinence durations were also identified as predictors in some domains. Current daily substance use, mental health diagnoses, trauma histories, and the presence of untreated hepatitis C were not independently associated with cognitive impairment in the current sample.

A primary finding from this study was an index of medication sedative load being predictive of reduced performance on measures of divided attention and visual memory, suggestive of individuals with larger sedative loads experiencing deteriorations in their ability to efficiently switch their attention between competing demands and recall complex visual information. The contribution of higher sedative loads to these domains observed in this clinical sample is concerning given these sedatives tend to be highly prescribed in AOD populations (Foulds *et al.*, 2018). The use of sedating medications is already associated with increased risk of overdose and death, particularly among opioid users (Australian Bureau of Statistics, 2017; Sun *et al.*, 2017) and these findings demonstrate that further caution is warranted in addition to this risk.

The deleterious impact of commonly prescribed sedative medications to cognitive functioning is well established (Crowe & Stranks, 2018; Tannenbaum *et al.*, 2012). In particular, previous

literature has reported that short and intermediate acting GABAergic benzodiazepine drugs (e.g. midazolam) and first generation antihistamine and tricyclic antidepressant drugs can evoke amnesic and non-amnesic cognitive impairments (Tannenbaum et al., 2012). Furthermore, a meta-analysis of studies evaluating the long term use of benzodiazepines demonstrated persistent cognitive deficits in all domains explored with the exception of executive functioning, despite abstinence (Crowe & Stranks, 2018). Use of these medications in the long term therefore represents a wholly preventable contributor to cognitive impairment in an already vulnerable and at-risk client group. When prescribing these medications there needs to be consideration of the risks and benefits and specialist addiction medical input and monitoring may be appropriate. Combined with previous literature, the findings of the current study add to the public health concern regarding use of sedative medications and polypharmacy in AOD populations.

Previous studies have also recognised the contribution of mental health conditions to cognitive impairment in adult populations (Cohen et al., 2013; Goodall et al., 2018; Robinson et al., 2013; Rock et al., 2014). Our findings suggest current emotional distress is also a clear contributor to cognitive impairment in AOD settings: those with heightened emotional distress, including symptoms of depression, anxiety and stress at the time of assessment were experiencing difficulties on both higher and lower order aspects of cognitive functioning. This client group is often experiencing a range of stressors including legal issues, financial concerns, unstable accommodation, unemployment, family and relationship problems, including family violence (Lubman et al., 2016; Manning et al., 2017). Therefore, in this cohort it is critical that neuropsychologists are mindful of a client's emotional state and the presence of any psychosocial stressors in the lead up to and throughout the assessment process. For other clinicians this highlights the importance of considering the impact of such symptoms when facilitating interventions with a high cognitive load such as counselling or treatment discussions and adapting sessions accordingly. Highly complex clients would benefit from addiction psychiatry support to treat and provide emotional support, in addition to having practical needs addressed.

A consistent theme that emerged from these results was the impact of basic demographics including gender and years of education on cognitive outcomes in this group. The impact of educational attainment was most notably observed on verbally mediated tasks where increased years of education was associated with better performance on tasks such as verbal intellectual functioning which is consistent with previous research (Abad et al., 2016). Lower levels of educational attainment may also serve as a proxy for early adverse life events including experiences of childhood trauma, neurodevelopmental disability or poor psychosocial environments which could impact cognitive outcomes in adulthood through to old age (Livingston et al., 2020). One interesting pattern of findings was the interactions observed between neurodevelopmental disability and education. For each year of education, the impact of neurodevelopmental disability on verbal memory and cognitive inhibition was reduced. This may reflect the severity of the diagnoses where those with more severe conditions (e.g. intellectual disability), and therefore greater cognitive difficulty, may complete fewer years of education than those with less disabling conditions. Alternatively, access to education and appropriate supports may support the development of these cognitive skills despite the presence of disability.

Just as low levels of education may serve as a proxy for early life adversity, current findings suggest age may also serve as a proxy for cumulative impairment in some cognitive domains within this client group. Despite cognitive performances being normed for age, as per standard clinical practice, older individuals had slowed information speed and greater difficulty inhibiting a prepotent response, suggestive of a degree of cumulative impairment in these domains. This may reflect longer durations of substance use for instance or premature ageing secondary to the additive burden of cognitive risk factors and poor health (Bachi, Sierra, Volkow, Goldstein, & Alia-Klein, 2017).

A surprising finding also emerged where older age was a predictor of better visual memory recall. With normal age related declines being already corrected for in the standardisation process, it is possible this finding may reflect another element of this task such as different organisational

approaches or strategy use that may vary according to age, however, further investigation would be required to evaluate these factors more closely. Finally, gender was a predictor for multiple cognitive domains which is largely consistent with prior research (Herlitz, et al., 1997; Kramer, et al., 2003).

The absence of a relationship between abstinence and the majority of cognitive domains may be surprising given, at least partial, improvements in cognitive functioning have been well documented following abstinence from alcohol and other substances including amphetamine, heroin, and cannabis (Bates, et al., 2013; Mann et al., 1999; Schmidt et al., 2017; Schulte et al., 2014; Yücel, et al., 2007). Furthermore, contrary to expectations shorter abstinence durations were associated with better information processing speed in the current study. Collectively these findings might be reflective of selection bias, whereby individuals who are referred to our service for neuropsychological examination tend to be experiencing persisting cognitive difficulties, despite abstinence. Cognitive impairments which are not ameliorated with abstinence have been specifically observed following extensive alcohol and benzodiazepine use (Crowe, et al., 2019; Crowe & Stranks, 2018). Persistent impairments following abstinence from other illicit substances are less well established with the existing literature subject to many criticisms, such as the tendency to exclude or fail to consider implications of polysubstance use which is considered the norm rather than the exception in clinical settings (Liu et al., 2018; Schmidt et al., 2017). Furthermore, there are no available clinical practice guidelines for appropriate durations of abstinence prior to neuropsychological assessment. Finally, research on cognitive recovery with abstinence is unclear and compounded by difficulty elucidating what may be pre-existing cognitive weaknesses that pre-dispose individuals to substance use as compared to what weaknesses may be a consequence of substance use (Basterfield, et al., 2019).

The current study highlights the interplay between multiple biopsychosocial factors and cognition. While referral to neuropsychologists can assist in elucidating these factors and clarifying diagnostic questions, access to such services is often limited due to lengthy waitlists or prohibitive costs. For marginalised individuals with substance addiction, these are significant barriers and access to neuropsychological services with specific expertise in addiction is even further limited. In such a highly stigmatised group of individuals, neuropsychologists need to be mindful as to how neuropsychological assessments can be used to advocate for or deny access to services when much of the disability sector requires firm diagnoses in order to gain access, and simultaneously cautious in order to avoid unnecessary labels and additional stigma. Specialist addiction neuropsychology services, similar to Memory Clinics for older adults, would be an ideal solution given the high levels of complexity in the population.

Additionally, clinicians including general practitioners, addiction medicine specialists, psychiatrists, and psychologists need to be familiar with some of the presenting issues and potential for these factors to impact on or account for cognitive impairment. Our study indicates that a holistic approach to patient care is warranted. Timely management of these issues has the potential to either alleviate or reduce the severity of any cognitive complaints or in the event of persistent concerns, improve diagnostic accuracy of neuropsychological assessments.

Limitations

The findings of the current study must be interpreted in the context of a number of limitations. Firstly, this study was based on a convenience sample utilising retrospective data and so assessment measures and procedures were selected based on the needs of the client, the referral question and preferences of the clinician. Therefore, not all clients completed the same measures or the full battery of measures described, resulting in missing data throughout several variables. As such, for some outcome variables (most notably working memory) index scores were not available which may have impacted the results due to the reliance on a single test for this domain with a corresponding low R-squared value in this model. Similarly, some predictor variables also had missing data

as in some cases this information was not clearly documented in available reports. In view of this, applying a listwise deletion procedure to perform a complete case analysis of all of the variables tested in the models would have resulted in an overly restricted final sample that may not have been representative of the overall dataset. Consideration of statistical methods to mitigate the issue of missing data was also given including the use of multiple imputation methods, however, these were also not considered appropriate given the nature of the dataset (Jakobsen, et al., 2017).

Secondly, from the available data some aspects of individual's histories were difficult to quantify in variables appropriate for modelling such as the severity of ABI, neurodevelopmental conditions, Hepatitis C infection, or lifetime polysubstance use histories which may have prevented some associations from being detected. Some clinical information was reliant on self-report which may be subject to recall or nondisclosure bias. This was partially mitigated through the verification of available medical or other assessment records but nevertheless it remains a potential limitation.

As such, we cannot conclude that the relationships between these variables are limited to what was observed in the current study, and the factors related to optimal cognitive functioning are likely to be far more complex, multifaceted, and nuanced. The models in the current study should therefore be considered exploratory in nature. Prospective, longitudinal research systematically examining factors known to impact cognition, including polysubstance use, duration of use, number of detoxification admissions, and abstinence together with medication use, mental health and psychosocial stressors in real-world substance using populations would enable a more accurate understanding of this complex population.

Conclusions

In conclusion, the findings of the current study make an important contribution to the understanding of pre-existing and potentially modifiable biopsychosocial risk factors for cognitive impairment and reduced neuropsychological performance in individuals with alcohol and substance use disorders. Notwithstanding the acknowledged limitations associated with data from this real-world clinical sample, they highlight the importance of careful diagnostic formulation in clients with AOD histories who have high levels of unmet needs. At times, this may include adopting a conservative approach to clinical interpretation with consideration of the relevant biopsychosocial factors in cases where multiple unmanaged comorbidities are present in order to highlight treatable aetiologies and limit the impact of further labelling and stigmatisation in this cohort. Ensuring modifiable risk factors for cognitive impairment are managed, such as heightened experiences of emotional distress or the use of sedating medications, may reduce cognitive impairment, and improve diagnostic clarity.

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