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### Article

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## RESEARCH ARTICLE

# A pilot study assessing the brain gauge as an indicator of cognitive recovery in alcohol dependence

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## Abstract

Alcohol dependence (AD) is associated with multiple cognitive deficits, which can affect treatment outcomes. Current measures of tracking brain recovery (e.g., functional magnetic resonance imaging) can be less accessible for practitioners. This study pilots a novel device (the brain gauge; BG) to assess its utility, and track recovery of cognitive function in residential alcohol treatment. Methods: A repeated measures design assessed changes in cognitive function during detoxification. Twenty-one participants with AD (16 Male; Mean age  $43.85 \pm 6.21$ ) completed a battery of alcohol and memory questionnaires and BG tasks at two time-points (~days 4 and 10) during a single managed detoxification episode. Results: Repeated measures ANCOVA revealed that some BG metrics significantly improved, with medium to large effect sizes - processing speed, focus, temporal order judgement and overall cortical metric. However, differences in subjective cognitive function were non-significant after controlling for depression and anxiety change scores. Anxiety change emerged as a significant factor in subjective cognitive function. Conclusions: We conclude it is possible that the prefrontal cortex (PFC) recovers more slowly compared to other brain areas, and there are compounding effects of improvements in anxiety and depression, and metacognitive deficits on subjective EF assessments. Future research should seek to validate the clinical utility of the BG by comparing against established neuroimaging methods.

## KEYWORDS

alcohol dependence, brain health, cognitive function, cortical metrics

## 1 | INTRODUCTION

Alcohol dependence (AD) is associated with multiple cognitive deficits, which can affect treatment outcomes (Brion et al., 2017). The functions that are most impaired include executive functions (EFs), learning, impulsivity, memory, attention, visuospatial abilities,

processing speed and verbal fluency (Stavro, Pelletier & Povtin, 2013). The integrity of EF in particular is important in AD (Dominguez-Salas et al., 2016; Goldstein & Volkow, 2002; Oscar-Berman et al., 2014) and is predictive of treatment outcomes. Impaired inhibitory control has been shown to predict relapse (Noël et al., 2002; Petit et al., 2014). Similarly, higher scores on a

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test used to measure task shifting are associated with treatment adherence (Desfosses et al., 2014). Furthermore, memory updating predicts both relapse and treatment adherence (Dean et al., 2009; Noël et al., 2002).

These findings are logical, as these cognitive deficits impact an individual's ability to learn, retain, and apply strategies for relapse prevention (Dawson & Grant, 2000; Pitel et al., 2007), and to maintain goal-directed behaviours (De Wilde et al., 2013). Maintaining abstinence is important as extended abstinence leads to cognitive recovery (Stavro et al., 2013). This suggests that if an individual can be supported appropriately through the initial treatment stages, their cognitive function may improve to a point at which relapse is less likely. In the UK, the National Institute for Health and Care Excellence (NICE) alcohol treatment guidance recommends including brief measures of cognitive functioning to help establish treatment planning goals, but formal assessment should only be performed if impairment persists after abstinence or reduction in alcohol use (NICE, 2011). There is evidence that some types of rehabilitation interventions can improve cognitive deficits in some patient groups with AD, although it is uncertain whether these also lead to improved treatment outcomes (Bates et al., 2013). While economic resources often limit the intensity and duration of treatment that can be offered, assessing cognitive function and how it relates to treatment outcomes could allow services to offer suitable treatment for individuals who are at higher risk (Brion et al., 2017).

Positron emission tomography (PET) studies show that acutely, alcohol causes an increase in dopamine turnover in the ventral striatum (Boileau et al., 2003) and increased metabolism in the striatum, amygdala and mesencephalon (Volkow et al., 2008). However, decreased whole-brain glucose metabolism is observed following acute administration (Volkow et al., 2008; Wang et al., 2003) suggesting that alcohol inhibits top down control of behaviour and primes reward-driven, alcohol seeking behaviours (Gilman et al., 2008). Chronic alcohol use in AD is associated with atrophy of the prefrontal cortex (PFC) and parietal cortex, when measured with functional magnetic resonance imaging (fMRI; Harris et al., 2008; Oscar-Berman et al., 2009). Furthermore, fMRI shows that AD is related to abnormal activation of these areas during working memory tasks (Desmond et al., 2003; Tapert et al., 2001), and low cognitive performance correlates with PFC and parietal degradation (Chanraud et al., 2007). fMRI also indicates that the medial PFC plays a large role in relapse (Charlet et al., 2014), and overcoming craving (Goldstein & Volkow, 2011). It is therefore possible that PFC dysfunction could have a significant impact on the cognitive deficits observed in AD (Moselhy et al., 2001), and consequently could affect treatment outcomes.

Whilst fMRI can assess the health and function of these brain regions and has been used to track recovery of neurological dysfunction after acquired brain injury (e.g., Munoz-Cspedes et al., 2005) it is a costly, immobile, time-consuming, and highly technical activity. Therefore, a device that is cheap, portable, and

quick to administer would be useful in assessing brain function in AD patients and in recovery planning. The present study aims to use the *Brain Gauge* (BG) to test somatosensory reaction time, which can be mapped on to cortical functions, and used to infer the functional status of various cortical pathways. These 'cortical metrics' are thus the perceptual correlates of interactions between groups of neurons (Tommerdahl, 2017). The BG tracks cortical health by recording responses to the stimulation of two adjacent fingertips, and using these to infer the integrity of cortical processes. This is based on the premise that the somatosensory system is organised so that adjacent skin regions (e.g., fingertips) project to adjacent cortical areas (Saladin, 2012). These adjacent areas react to vibrotactile stimuli in predictable patterns that affect perception of the stimuli; thus responses can be used to infer and quantify the functioning of the relevant mechanisms (Favorov et al. 2017a). If these mechanisms are disrupted, they affect higher-level cognitive processes<sup>1</sup>.

An example of one mechanism that is measured by the BG metrics is lateral inhibition (activated neurons suppressing neurons in neighbouring areas; Cohen, 2011), a factor that modulates response inhibition and EF (Friedrich et al., 2017). The integrity of lateral inhibition is a key factor in learning, memory and plasticity, thus measuring it can help us infer the functional status of the cortex; however, neurophysiological paradigms for measuring lateral inhibition are rather invasive, making them unsuitable for most studies (Mountcastle, 1957; Tommerdahl et al., 1993). The BG measures lateral inhibition by requiring that participants discriminate the amplitudes of two stimuli (which is strongest) when they are delivered first sequentially, and then simultaneously to adjacent fingertips. If lateral inhibition is functioning robustly, performance on the simultaneous and sequential tasks does not differ significantly. However, if something has compromised the process, a significant difference between the sequential and simultaneous task would be observed (see Zhang et al., 2008 for analysis of method). For example in concussed individuals, the difference between sequential and simultaneous amplitude discrimination was double that of healthy controls (Favorov et al. 2017a), indicating that lateral inhibition, or contrast enhancement of the activation of adjacent groups of neurons in the cortex, is significantly impaired (Tommerdahl et al., 2019). Consequently, the BG does not require a baseline for each participant to measure this metric, as the sequential task acts as a baseline for the simultaneous task (Tommerdahl et al., 2019). Other tasks to assess the BG metrics were designed in a similar manner; for brevity, the other metrics are not described in detail here, though further information on their calculation is displayed in Table 2, and in the following articles. Other metrics that are derived from the test battery include temporal order judgement (Tommerdahl et al., 2007), feedforward inhibition (Favorov et al. 2017b, pp. 383–397; Zhang et al., 2011), adaptation (Puts et al. 2013, 2014), and duration discrimination

<sup>1</sup>Further information about brain gauge metrics and their relation to executive function, alcohol dependence, and brain areas is displayed in Table 1.

TABLE 1 Mood, alcohol use and background variables

	N	%
Male	16	76.20
Medication status time 1		
Benzodiazepines	16	76.20
Other	5	25.00
Medication status time 2		
Benzodiazepines	3	14.30
Other	18	85.70
	M	SD
AUDIT	35.10	4.76
SADQ	42.24	14.87
HADS anxiety time 1	18.67	5.18
HADS anxiety time 2	16.38	5.29
HADS depression time 1	15.14	4.80
HADS depression time 2	12.48	4.38
Anxiety change	2.61	3.88
Depression change	2.57	3.59
TLFB-A		
6 Day Unit Total	224.36	98.66
Length of stay (days)		
Time 1	5.24	2.32
Time 2	9.00	2.21

Abbreviations: AUDIT, alcohol use disorders identification test; HADS, hospital anxiety and depression scale; SADQ, severity of alcohol dependence questionnaire; SD, mean; TLFB-A, Timeline Followback of Alcohol Use.

(Francisco et al., 2015). Interestingly for the current study, the effect of conditioning stimuli (delivered prior to the standard stimuli) on discriminative capacity is the 'adaptation metric', which remains constant in healthy participants (Zhang et al., 2011). However, a study of heavy drinkers (college students drinking over 60 drinks per month) showed a reduction in this metric, likely due to decreased cognitive function (Nguyen et al., 2013). Furthermore, in subjects with mild brain injury, cortical metrics have been used to track recovery (Favorov et al., 2017a).

This study piloted the use of the BG in a population undergoing residential detoxification treatment for AD. The aim of the study was to assess the utility of the BG in assessing recovery of cognitive function in alcohol dependent inpatients. We predicted that cognitive function (as measured by BG) would improve significantly from time 1 (T1—around 4 days after admission (range 2–13 days) to time 2 (T2—around 10 days after admission (range 4–15 days)). It was also predicted that subjective cognitive function (as measured by Behaviour Rating Inventory of

Executive Function—Adult [BRIEF-A]) would improve significantly from T1 to T2.

## 2 | METHOD

### 2.1 | Design

A repeated measures design was used to assess changes in cognitive function. The independent variable was time, with two levels - start of residential detox—T1 (day 4<sup>2</sup>), and discharge—T2 (~day 4–10). The dependent variables were the scores on the BG tasks and the subjective measures of EF.

### 2.2 | Participants

Twenty-eight participants (21 males; Mean age  $45.14 \pm 6.52$ ), referred for residential alcohol detoxification at an NHS inpatient unit in a city in North West England took part. Participants were referred from the community alcohol service, and received 6 sessions of Brief Intervention and Advice prior to referral and admission. Participants were eligible for the study if they were aged 20–55 years and had a current AD diagnosis. They were not eligible if they had a current diagnosis of a substance use disorder other than alcohol, a neurological impairment or a condition affecting the feeling/sensation in their arms; this was confirmed by self-report and clinical diagnosis. Seven datasets were removed due to; self-discharge between testing points (three males; one female), unrelated cerebral damage (male), and distractions during testing (one male; one female) leaving 21 full datasets for analysis (see Table 1 for demographic information). Of the remaining 21 participants, 16 were male and the sample had a mean age of  $43.85 \pm 6.21$ .

### 2.3 | Measures

#### 2.3.1 | Executive function

Subjective EF was measured using the BRIEF-A, a 75-item questionnaire that measures nine aspects of EF (see Roth et al., 2005 for full description).

#### 2.3.2 | Mood state

Mood state was measured using the Hospital Anxiety and Depression Scale (HADS; see Zigmond & Snaith, 1983), a 14-item scale assessing anxiety (e.g., 'I feel tense or wound up') and depression (e.g., 'I feel cheerful') respectively.

<sup>2</sup>Some participants were given benzodiazepines (chlordiazepoxide or oxazepam) to alleviate withdrawal symptoms on day 0 and 1, so for these participants, testing began on day 4.

### 2.3.3 | Alcohol use status

Alcohol use was assessed using a number of validated questionnaires: The Alcohol Use Disorders Identification Test (AUDIT) assessing harmful/hazardous drinking (see Saunders, Aasland, Babor, De la Fuente, & Grant, 1993), The Severity of Alcohol Dependence Questionnaire (SADQ-C; Stockwell et al., 1994) and the Timeline Follow-back of Alcohol Use (TLFB-A; Sobell & Sobell, 1992) assessing recent drinking behaviour.

### 2.3.4 | Cognitive function

Brain Gauge Pro (version 3) was used to assess cognitive function. BG runs on a personal computer and is the same size and shape as a computer mouse, so is easily portable. The current study used a customised test battery comprised of tests that target PFC function. Two cylinders (5 mm diameter) on the BG deliver vibrotactile stimulation (in the flutter range; 25–50 Hz) to the index and middle finger of the non-dominant hand. The BG software running on the laptop provides participants with instructions on each task, and consists of a series of practice trials and five sequential trials. Participants have to respond correctly, by clicking the computer mouse with their dominant hand, to three consecutive practice trials to proceed, and all participants in the present study were able to proceed to the main task after the practise trials. Specific tasks are detailed below:

*Reaction Time (1 & 2—normative range 150–200 ms).* Participants are required to click on a ‘bullseye’ target as soon as they feel a tap on their fingers, using a computer mouse.

*Sequential Amplitude Discrimination* (normative range 20–70 microns). Vibrations are delivered to each fingertip sequentially, and participants have to decide which vibration was more intense (left or right finger) by clicking on the computer screen with the mouse.

*Simultaneous Amplitude Discrimination* (normative range 20–70 microns). Vibrations are delivered to each fingertip simultaneously, and participants have to decide which vibration was more intense (left or right finger) by clicking on the computer screen with the mouse.

*Temporal Order Judgement* (normative range 15–35 ms). Participants must determine which of two vibrations (left or right) delivered to the fingertips came first.

*Duration Discrimination* (normative range 30–80 ms). Participants must determine which of two vibrations (left or right) lasted longer.

*Reaction Time Variability* (normative range 0–20 or 10% of Reaction Time). This is the composite score created from variability on reaction time one and two.

See Table 2 for a description of the metrics derived from these tasks and how they are calculated.

### 2.3.5 | Procedure

Potential participants were informed of the study by staff at the treatment centre. If patients indicated an interest, a meeting with

the researcher was arranged. Posters were also placed around the facility with contact details of the researcher. All testing occurred in a small IT room in the treatment centre. In the first testing session (T1; a mean of  $5.39 \pm 2.60$  days after treatment entry), participants gave informed consent and completed all assessments. The BG test battery was completed on an ASUS X555L laptop with a 15.6" screen, using a standard computer mouse to respond. Participants completed the HADS, BRIEF-A, and BG tasks again at T2 (mean of  $9.22 \pm 2.35$  days after treatment entry). The variation in follow up days was due to availability of participants, with some participants progressing through detoxification more slowly/rapidly than expected, which shortened/lengthened the duration of their stay. Participants were given a £10 online shopping voucher as compensation.

### 2.3.6 | Ethical considerations

Written informed consent was obtained from all participants. The study received approval from Liverpool John Moores University Research Ethics Committee, and the local NHS Health Research Authority Research Ethics Committee.

### 2.3.7 | Statistical analyses

Data were entered in to IBM SPSS (version 25). Repeated measures ANOVA was used to investigate changes in anxiety and depression from time 1 to time 2. A series of repeated measures ANCOVAs with time point (two levels: time 1, time 2) as the repeated measures factor, were used to analyse changes in the BG and BRIEF-A scores over time. In all analyses, depression and anxiety change scores (time 1–time 2) were included as covariates.

## 3 | RESULTS

Demographic information and mean scores for anxiety and depression are displayed in Table 1. Inspection of the means shows that there were significant reductions in anxiety and depression from time 1 to time 2. Repeated measures ANOVAs revealed that this improvement was significant for anxiety  $F(1,20) = 8.56, p = 0.008, \eta^2 = 0.30$ , and also for depression  $F(1,20) = 11.12, p = 0.003, \eta^2 = 0.36$ .

Mean scores for the BG metrics are presented in Table 3. To investigate which metrics showed improvements over time, a series of repeated measures ANCOVAs were performed on each individual metric. There were 4 metrics which showed significant improvement over time - for brevity, only significant effects are reported below (see Table 3 for full analysis). For the focus metric, there was a significant effect of time indicating an improvement in focus from time 1–time 2  $F(1,18) = 20.66, p = 0.001, \eta^2 = 0.53$ , with a large effect size. Inspection of Table 3 shows that mean focus score increased from 47.90 at time 1 to 81.33 at time 2. For the speed metric, there

TABLE 2 Description of brain gauge metrics (adapted from King et al., 2018)

Brain gauge metric	Description of metric and its relation to cognitive function and alcohol dependence
Speed	Computed from <i>Reaction Time</i> and <i>Reaction Time Variability</i> , simple measures of information processing speed the time required to process new information and retrieve stored information from memory (Iwasa et al., 2014). Speed is dependent on the integrity of white matter tracts in the brain (as white matter manages the speed of neuronal transmission; Conklin, et al., 2013) Turken et al., 2008).
Accuracy	Comprises the averaged <i>Amplitude Discrimination</i> scores ( <i>sequential and simultaneous</i> ). This metric reflects one's ability to accurately determine which of two stimuli is larger in size (amplitude). Lower scores reflect better performance, and in 'normative' function, both <i>Amplitude Discrimination</i> values should be similar. This measure is reliant on functional integrity of the parietal lobe, which is involved in executive function (EF; King et al., 2018). This metric also gives insight into lateral inhibition, which modulates response inhibition (Friedrich et al., 2017).
Temporal order judgement	Uses <i>Temporal Order Judgement</i> values. This measure is the smallest time difference (in ms) between two stimuli such that one can still identify which finger received the first stimulus, and measures the integrity of the fronto-striatal pathway (Meck & Benson, 2002). It is also a measure of temporal information processing (TIP), which is embedded in aspects of EF, such as in planning, evaluating previous actions/outcomes, and decision-making (Nowak et al., 2016).
Time perception	This is associated with <i>Duration Discrimination</i> task and the cortical-cerebellar pathway. The measure (in ms) is the smallest duration difference between two stimuli that one can perceive. Damage to the cerebellar lobe or the pathway to it results in impairments in time perception. Duration discrimination also reflects the role of the PFC in memory storage and recovery (Coull et al., 2011).
Focus	Focus measures the ability to attend to a task. Attention is crucial for maintaining goal-directed behaviour, and heavy alcohol use has been linked to significant impairments in attention. Attentional focus is also associated with the parietal cortex (Zeng et al., 2017).
Plasticity	Neuroplasticity is the ability of the brain to recover and restructure itself: Chronic alcohol use desensitises GABA receptors, which may be linked to central nervous system hyper-excitation (Kumar et al., 2009). Hyper-excitation negatively impacts plasticity (King et al., 2018) resulting in morphological changes in the brain (e.g., a decrease in dendritic connections, neurotrophic factors and brain size), all of which promote poor cognitive functioning.
Fatigue	Computed from the first and last reaction time tests ( <i>Reaction Time Variability</i> ). If performance declines between the first and second reaction time tests, the fatigue score will be low indicating impaired performance. Mental fatigue results in more demanding cognitive tasks, including EF, being compromised (van der Linden et al., 2003).
Cortical metric	A universal representation of brain health. This metric takes the information from every available test and computes an 'at a glance' view of total brain health.

was a significant effect of time, indicating that speed improved from time 1 (T1 35.00) to time 2 (T2 58.19)  $F(1,18) = 24.40, p = 0.001, \eta^2 = 0.58$ . Temporal order judgement also showed improvement from time 1 (41.81) to time 2 (50.81)  $F(1,18) = 4.50, p = 0.05, \eta^2 = 0.20$ . Finally, for the overall cortical metric score, there was a significant main effect of time indicating an improvement in performance from time 1 to time 2 (T1 60.00; T2 66.90)  $F(1,18) = 14.61, p = 0.001, \eta^2 = 0.45$ .

Mean scores for the BRIEF-A subscales are presented in Table 4.

To investigate which BRIEF-A subscales showed improvements over time, a series of repeated measures ANCOVAs were performed on each individual subscale. None of the BRIEF-A subscales showed significant improvements over time after controlling for anxiety and depression change scores (see Table 4 for full analysis). However,

inspection of Table 4 shows that the time  $\times$  depression change interaction was significant for the task switching, emotional control, planning and task monitoring subscales, while the time  $\times$  anxiety change interaction was significant for the inhibitory control, task switching, emotional control, self-monitoring, initiating, planning and organisation subscales of the BRIEF-A.

## 4 | DISCUSSION

The current study examined changes in cognitive function during early stages of alcohol treatment using a novel technology, the BG. We hypothesised that; (1) cognitive function (as measured by the BG) would improve significantly from T1 to T2, and (2) cognitive function

TABLE 3 Descriptive Statistics and repeated measure ANCOVA indices comparing Brain Gauge scores over time

	Time 1		Time 2		Time df (1,18)		Time × depression df (1,18)		Time × anxiety df (1,18)	
	M	SD	M	SD	F	p	F	p	F	p
Focus	47.90	30.40	81.33	23.65	20.66	<b>0.001</b>	0.03	0.87	0.60	0.59
Speed	35.00	21.11	58.19	19.04	24.40	<b>0.001</b>	0.00	0.99	0.30	0.59
Plasticity	73.62	16.52	69.10	18.19	3.36	0.08	0.06	0.81	0.15	0.71
Accuracy	73.52	23.60	68.90	26.80	2.88	0.11	1.02	0.33	0.001	0.98
Time perception	80.00	22.86	79.67	23.74	0.30	0.59	0.10	0.76	1.67	0.21
Fatigue	86.43	30.00	76.24	30.98	2.12	0.16	0.29	0.60	0.23	0.64
Temporal order judgement	41.81	41.88	50.81	42.91	4.50	<b>0.05</b>	1.60	0.22	0.48	0.50
Cortical metric	60.00	16.38	66.90	16.11	14.61	<b>0.001</b>	0.31	0.58	1.67	0.21

TABLE 4 Descriptive statistics and repeated measures ANCOVA indices comparing Behaviour Rating Inventory of Executive Function—Adult Subscales over time

	Time 1		Time 2		Time df(1,18)		Time × depression df (1,18)		Time × anxiety df (1,18)	
	M	SD	M	SD	F	p	F	p	F	p
Inhibition	16.95	4.01	14.71	4.54	0.27	0.61	1.45	0.24	16.05	<b>0.001</b>
Task-shifting	12.24	3.10	11.19	3.44	0.87	0.36	9.79	<b>0.006</b>	6.20	<b>0.02</b>
Emotional control	23.33	5.43	19.57	6.19	0.06	0.81	5.22	<b>0.04</b>	8.29	<b>0.01</b>
Self-monitoring	12.62	2.29	11.24	3.06	0.00	0.95	0.75	0.40	9.00	0.33
Initiating	16.10	3.39	14.14	4.63	0.11	0.75	1.19	0.29	11.14	<b>0.004</b>
Planning	18.52	4.45	16.90	4.77	2.96	0.10	11.67	<b>0.003</b>	11.70	<b>0.003</b>
Task-monitoring	11.33	2.37	9.76	3.00	0.82	0.38	3.96	<b>0.06</b>	0.29	0.60
Organisation of materials	13.29	4.03	11.95	4.35	0.01	0.92	0.18	0.68	6.72	<b>0.02</b>
Working memory	14.67	4.93	13.67	5.06	0.12	0.74	2.18	0.16	0.13	0.72

(as measured by BRIEF-A) would improve significantly from T1 to T2. Hypothesis 1 was mostly supported as four BG metrics showed significant improvement over time. However, Hypothesis 2 was not supported as there were no significant improvements in subjective cognitive function after controlling for changes in anxiety and depression.

Concerning the BG metrics—focus, speed, temporal order judgement and overall cortical metric showed a significant improvement over time. This suggests that within this cohort, brain areas related to attentional focus, information processing speed, time perception and overall cortical health improved over a relatively short time-period (average time between tests was 4.17 days), while the areas related to other metrics did not. This was unexpected, as it was hypothesised that all metrics would improve due to research showing that cognitive function improves after abstinence (Stavro et al., 2013). One possible reason for this discrepancy is the differential recovery rates of relevant brain areas following cessation. Interestingly, the four metrics that displayed significant improvement do not solely rely on the PFC. Speed and focus are also dependent on

the parietal cortex (Turken et al., 2008; Zeng et al., 2017), temporal order judgements activate the temporal-parietal junction (Davis et al., 2009) whereas overall cortical health reflects the integrity of the whole cortex (King et al., 2018). This is important as van Eijk et al. (2013) found partial recovery of grey matter volume in various areas including the parietal lobule, precuneus and cerebellum within the first two weeks of abstinence, but not in the precentral or frontal gyrus. In addition, Petit et al. (2017) suggest that compared to other brain regions, the PFC experiences more AD-related damage, and therefore recovers more slowly, with likely subtle differences in the specific networks associated with each cognitive function. The PFC experiences considerable damage as a result of AD, with research reporting atrophy (Harris et al., 2008; Oscar-Berman et al., 2009) and disruptions in function (Desmond et al., 2003; Tapert et al., 2001), correlated with low cognitive performance (Chanraud et al., 2007). Thus, it is possible that at such an early stage of detox, the PFC networks have not recovered to an extent that improvements in performance are detectable. It is also worthy of note that normative scores for all of the BG metrics should fall in the range 80–100. While

most of the metrics showed improvement from T1 to T2, only the focus metric was in the normative range at T2 indicating that while brain function has improved, a longer period of abstinence is required for function to approach normative performance.

The second hypothesis was not supported. While the means were in the direction of showing improvement from T1 to T2 for most subscales, after including anxiety change and depression change scores as covariates, none of these differences were statistically significant<sup>3</sup>. It is noteworthy that for task monitoring, emotional control and planning there was a significant interaction between time and depression change while there was a significant interaction between time and anxiety change for inhibitory control, task monitoring, emotional control, self-monitoring, initiation, planning and organisation of materials. In older adults, depression has been consistently linked to subjective memory complaints (Carrasco et al., 2017). Moreover, Marino et al. (2009) found that subjective memory complaints were related to mood state (as measured by the Profile of Mood States (POMS) questionnaire) while objective measures were not. Further research has found little relationship between subjective and objective assessments of cognitive function, with the former being more related to sub-clinical levels of anxiety and depression (Balash et al., 2013). Take together this suggests that improvements in subjective cognitive function could be mediated by decreases in state anxiety and depression between T1 and T2.

Thus the BRIEF-A results seem to be inconsistent with the BG results. In addition to the mediating effects of state anxiety and depression discussed above, one possibility is that these opposing results are due to other factors, specifically metacognitive deficits in the recovering AD patients. Indeed, AD may impair metacognition along with other cognitive functions (Le Berre et al., 2017). The BRIEF-A is self-report, relying on participants to evaluate their own EF, which makes the measure vulnerable to metacognitive impairments. For this cohort it may therefore be more appropriate for future studies to also use additional objective measures of EF for comparison with BG (such as validated neurocognitive performance-based tasks), though the impact of fatigue on BG measures after such tasks would need to be considered.

There were a number of limitations in the study. Firstly, it was not possible in the timescale to study the continuing improvements in cognitive function, or to assess whether initial cognitive function predicted relapse or recovery outcomes. Follow-up of participants after discharge was problematic, and future research should seek to provide additional assessments at 3 and 6 months following detoxification. The timescale of the project also limited the number of participants that could be recruited, which could limit the statistical power of the study, meaning the results should be interpreted with caution. Furthermore, we cannot eliminate the possibility that the sub-acute (pharmacological) effects of alcohol, not neurotoxic

damage, may have influenced the results. Participants should be abstinent for a minimum of two weeks prior to one of the testing periods to make this distinction (Fernández-Serrano et al., 2011), which was not possible in the current study. However, while it is clearly important to study longer-term changes, there has been comparatively less research on the recovery of cognitive function during the early stages of abstinence (Petit et al., 2017). The current study contributes to this lesser studied area. Another potential confound is the effects of residual benzodiazepine medication. On treatment entry (around 5 days prior to T1), many participants received benzodiazepines, prescribed to alleviate withdrawal symptoms. Short and long-term use of these drugs impairs cognitive function (Boeuf-Cazou, Bongue, Ansiau, Marquie & Lapeyre-Mestre, 2011; Snyder et al., 2005), and may have influenced either of the cognitive function measures. While this is unavoidable when testing participants during detox, it emphasises the necessity for a longer study with multiple follow-up points.

In conclusion, the current study assessed cognitive function during alcohol detox, and piloted the use of cortical metrics via the BG as markers of cognitive function in this cohort. It is possible that the differential BG metric results are due to slower recovery of the PFC compared to other brain areas, and that the BRIEF-A does not reflect this due to its relation to mood state and vulnerability to the effects of impaired metacognition. Future research should seek to implement multiple follow-ups over a longer time-period to study the predictive nature that metrics may have on relapse, and use validated measures of neurocognitive function to compare with the BG. Future research should also assess BG performance in comparison to well-validated measures of brain function such as functional Near Infrared Spectroscopy (fNIRS), fMRI and PET.

## CONFLICT OF INTEREST

MT is co-founder of Cortical Metrics, which has a licence from the University of North Carolina to distribute the Brain Gauge, the device used to conduct the study.

## DATA AVAILABILITY STATEMENT

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

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## REFERENCES

- Balash, Y., Mordechovich, M., Shabtai, H., Giladi, N., Gurevich, T., & Korczyn, A. D. (2013). Subjective memory complaints in elders: Depression, anxiety, or cognitive decline? *Acta Neurologica Scandinavica*, 127, 344–350.
- Bates, M. E., Buckman, J. F., & Nguyen, T. T. (2013). A role for cognitive rehabilitation in increasing the effectiveness of treatment for alcohol use disorders. *Neuropsychology Review*, 23(1), 27–47.
- Boeuf-Cazou, O., Bongue, B., Ansiau, D., Marquie, J. C., & Lapeyre-Mestre, M. (2011). Impact of long-term benzodiazepine use on cognitive functioning in young adults: The VISAT cohort. *European Journal of Clinical Pharmacology*, 67(10), 1045.

<sup>3</sup>While not reported here, there were significant improvements in inhibition, self-monitoring, planning, task-shifting, initiating, task-monitoring, emotional control, and organisation of materials on the Behaviour Rating Inventory of Executive Function—Adult prior to inclusion of anxiety and depression change as covariates.



- Boileau, I., Assaad, J. M., Pihl, R. O., Benkelfat, C., Leyton, M., Diksic, M., et al. (2003). Alcohol promotes dopamine release in the human nucleus accumbens. *Synapse*, 49(4), 226–231.
- Brion, M., D'Hondt, F., Pitel, A.-L., Lecomte, B., Ferauge, M., de Timary, P., & Maurage, P. (2017). Executive functions in alcohol-dependence: A theoretically grounded and integrative exploration. *Drug and Alcohol Dependence*, 177, 39–47.
- Carrasco, P. M., Montenegro-Peña, M., López-Higes, R., Estrada, E., Crespo, D. P., Rubio, C. M., & Azorín, D. G. (2017). Subjective Memory Complaints in healthy older adults: Fewer complaints associated with depression and perceived health, more complaints also associated with lower memory performance. *Archives of Gerontology and Geriatrics*, 70, 28–37.
- Chanraud, S., Martelli, C., Delain, F., Kostogianni, N., Douaud, G., Aubin, H. J., & Martinot, J. L. (2007). Brain morphometry and cognitive performance in detoxified alcohol-dependents with preserved psychosocial functioning. *Neuropsychopharmacology*, 32(2), 429–438.
- Charlet, K., Schlagenhaut, F., Richter, A., Naundorf, K., Dornhof, L., Weinfurter, C. E., & Gutwinski, S. (2014). Neural activation during processing of aversive faces predicts treatment outcome in alcoholism. *Addiction Biology*, 19(3), 439–451.
- Cohen, R. A. (2011). Lateral Inhibition. In: J. S. Kreutzer, J. DeLuca & B. Caplan (Eds), *Encyclopedia of Clinical Neuropsychology*. Springer, New York. [https://doi.org/10.1007/978-0-387-79948-3\\_1379](https://doi.org/10.1007/978-0-387-79948-3_1379).
- Conklin, H. M., Ashford, J. M., Di Pinto, M., Vaughan, C. G., Gioia, G. A., Merchant, T. E., Ogg, R. J., Santana, V., & Wu, S. (2013). Computerized assessment of cognitive late effects among adolescent brain tumor survivors. *Journal of neuro-oncology*, 113(2), 333–340. <https://doi.org/10.1007/s11060-013-1123-5>
- Coull, J. T., Cheng, R. K., & Meck, W. H. (2011). Neuroanatomical and neurochemical substrates of timing. *Neuropsychopharmacology*, 36(1), 3.
- Davis, B., Christie, J., & Rorden, C. (2009). Temporal order judgments activate temporal parietal junction. *Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, 29(10), 3182–3188.
- Dawson, L. K., & Grant, I. (2000). Alcoholics' initial organizational and problem-solving skills predict learning and memory performance on the Rey-Osterrieth Complex Figure. *Journal of the International Neuropsychological Society*, 6(1), 12–19.
- Dean, A. C., London, E. D., Sugar, C. A., Kitchen, C. M., Swanson, A. N., Heinzerling, K. G., & Shoptaw, S. (2009). Predicting adherence to treatment for methamphetamine dependence from neuropsychological and drug use variables. *Drug and Alcohol Dependence*, 105(1), 48–55.
- Desfosses, M., Meadows, H., Jackson, M., & Crowe, S. F. (2014). The relationship between neuropsychological functioning and mental health outcomes of chronic alcohol users involved in counselling: Prediction of treatment outcome. *Australian Psychologist*, 49(5), 287–296.
- Desmond, J. E., Chen, S. A., DeRosa, E., Pryor, M. R., Pfefferbaum, A., & Sullivan, E. V. (2003). Increased frontocerebellar activation in alcoholics during verbal working memory: An fMRI study. *NeuroImage*, 19(4), 1510–1520.
- De Wilde, B., Verdejo-García, A., Sabbe, B., Hulstijn, W., & Dom, G. (2013). Affective decision-making is predictive of three-month relapse in polysubstance-dependent alcoholics. *European Addiction Research*, 19(1), 21–28.
- Domínguez-Salas, S., Díaz-Batanero, C., Lozano-Rojas, O. M., & Verdejo-García, A. (2016). Impact of general cognition and executive function deficits on addiction treatment outcomes: Systematic review and discussion of neurocognitive pathways. *Neuroscience & Biobehavioral Reviews*, 71, 772–801.
- Favorov, O. V., Francisco, E., Zai, L., & Tommerdahl, M. (2017). *Quantification of mild traumatic brain injury via cortical metrics: Analytical methods*. Military Health System Research Symposium.
- Favorov, O., Kursun, O., & Tommerdahl, M. (2017). *Role of feed-forward inhibition in neocortical information processing: Implications for neurological disorders* (pp. 383–397).
- Fernández-Serrano, M. J., Pérez-García, M., & Verdejo-García, A. (2011). What are the specific vs. generalized effects of drugs of abuse on neuropsychological performance? *Neuroscience & Biobehavioral Reviews*, 35(3), 377–406.
- Francisco, E. M., Holden, J. K., Nguyen, R. H., Favorov, O. V., & Tommerdahl, M. (2015). Percept of the duration of a vibrotactile stimulus is altered by changing its amplitude. *Frontiers in Systems Neuroscience*, 9, 77.
- Friedrich, J., Mückschel, M., & Beste, C. (2017). Somatosensory lateral inhibition processes modulate motor response inhibition—an EEG source localization study. *Scientific Reports*, 7(1), 4454.
- Gilman, J. M., Ramchandani, V. A., Davis, M. B., Bjork, J. M., & Hommer, D. W. (2008). Why we like to drink: A functional magnetic resonance imaging study of the rewarding and anxiolytic effects of alcohol. *Journal of Neuroscience*, 28(18), 4583–4591.
- Goldstein, R. Z., & Volkow, N. D. (2002). Drug addiction and its underlying neurobiological basis: Neuroimaging evidence for the involvement of the frontal cortex. *American Journal of Psychiatry*, 159(10), 1642–1652.
- Goldstein, R. Z., & Volkow, N. D. (2011). Dysfunction of the prefrontal cortex in addiction: Neuroimaging findings and clinical implications. *Nature Reviews Neuroscience*, 12(11), 652–669.
- Harris, G. J., Jaffin, S. K., Hodge, S. M., Kennedy, D., Caviness, V. S., Marinkovic, K., & Oscar-Berman, M. (2008). Frontal white matter and cingulum diffusion tensor imaging deficits in alcoholism. *Alcoholism: Clinical and Experimental Research*, 32(6), 1001–1013.
- Iwasa, H., Kai, I., Yoshida, Y., Suzuki, T., Kim, H., & Yoshida, H. (2014). Information processing speed and 8-year mortality among community-dwelling elderly Japanese. *Journal of Epidemiology*, 24(1), 52–59.
- King, D., Pa, H., & Tommerdahl, M. (2018). Use of the brain-gauge somatosensory assessment for monitoring recovery from concussion: A case study. *Journal of Physiotherapy Research*, 2(1), 13.
- Kumar, S., Porcu, P., Werner, D. F., Matthews, D. B., Diaz-Granados, J. L., Helfand, R. S., & Morrow, A. L. (2009). The role of GABA<sub>A</sub> receptors in the acute and chronic effects of ethanol: A decade of progress. *Psychopharmacology*, 205(4), 529.
- Le Berre, A.-P., Fama, R., & Sullivan, E. V. (2017). Executive functions, memory, and social cognitive deficits and recovery in chronic alcoholism: A critical review to inform future research. *Alcoholism: Clinical and Experimental Research*, 41(8), 1432–1443.
- Marino, S. E., Meador, K. J., Loring, D. W., Okun, M. S., Fernandez, H. H., Fessler, A. J., Werz, M. A. (2009). Subjective perception of cognition is related to mood and not performance. *Epilepsy and Behavior*, 14(3), 459–464.
- Meck, W. H., & Benson, A. M. (2002). Dissecting the brain's internal clock: How frontal-striatal circuitry keeps time and shifts attention. *Brain and Cognition*, 48(1), 195–211.
- Moselhy, H. F., Georgiou, G., & Kahn, A. (2001). Frontal lobe changes in alcoholism: A review of the literature. *Alcohol and Alcoholism*, 36(5), 357–368.
- Mountcastle, V. B. (1957). Modality and topographic properties of single neurons of cat's somatic sensory cortex. *Journal of Neurophysiology*, 20, 408–434.
- Munoz-Céspedes, J. M., Rios-Lago, M., Paul, N., & Maestu, F. (2005). Functional neuroimaging studies of cognitive recovery after acquired brain damage in adults. *Neuropsychology Review*, 15(4), 169–183.
- Nguyen, R. H., Gillen, C., Garbutt, J. C., Kampov-Polevoi, A., Holden, J. K., Francisco, E. M., & Tommerdahl, M. (2013). Centrally-mediated sensory information processing is impacted with increased

- alcohol consumption in college-aged individuals. *Brain Research*, 1492, 53–62.
- NICE. (2011). *Alcohol-use disorders: Diagnosis, assessment and management of harmful drinking and alcohol dependence*. Retrieved from London, UK.
- Noël, X., Sferrazza, R., Van der Linden, M., Paternot, J., Verhas, M., Hanak, C., & Verbanck, P. (2002). Contribution of frontal cerebral blood flow measured by <sup>99m</sup>Tc-Bicisate SPECT and executive function deficits to predicting treatment outcome in alcohol-dependent patients. *Alcohol and Alcoholism*, 37(4), 347–354.
- Nowak, K., Dacewicz, A., Broczek, K., Kupisz-Urbanska, M., Galkowski, T., & Szelag, E. (2016). Temporal information processing and its relation to executive functions in elderly individuals. *Frontiers in Psychology*, 7, 1599.
- Oscar-Berman, M., Valmas, M. M., Sawyer, K. S., Kirkley, S. M., Gansler, D. A., Merritt, D., & Couture, A. (2009). Frontal brain dysfunction in alcoholism with and without antisocial personality disorder. *Neuropsychiatric Disease and Treatment*, 5, 309.
- Oscar-Berman, M., Valmas, M. M., Sawyer, K. S., Ruiz, S. M., Luhar, R. B., & Gravit, Z. R. (2014). Profiles of impaired, spared, and recovered neuropsychological processes in alcoholism. *Handbook of Clinical Neurology*, 125, 183.
- Petit, G., Cimochowska, A., Kornreich, C., Hanak, C., Verbanck, P., & Campanella, S. (2014). Neurophysiological correlates of response inhibition predict relapse in detoxified alcoholic patients: Some preliminary evidence from event-related potentials. *Neuropsychiatric Disease and Treatment*, 10, 1025.
- Petit, G., Luminet, O., Cordovil de Sousa Uva, M., Zorbas, A., Maurage, P., & de Timary, P. (2017). Differential spontaneous recovery across cognitive abilities during detoxification period in alcohol-dependence. *PLoS One*, 12(8), e0176638.
- Pitel, A. L., Witkowski, T., Vabret, F., Guillery-Girard, B., Desgranges, B., Eustache, F., & Beaunieux, H. (2007). Effect of episodic and working memory impairments on semantic and cognitive procedural learning at alcohol treatment entry. *Alcoholism: Clinical and Experimental Research*, 31(2), 238–248.
- Puts, N., Edden, R., Wodka, E., Mostofsky, S., & Tommerdahl, M. (2013). A vibrotactile behavioural battery for investigating somatosensory processing in children and adults. *Journal of Neuroscience Methods*, 218, 39–47.
- Puts, N. A. J., Wodka, E. L., Tommerdahl, M., Mostofsky, S. H., & Edden, R. A. E. (2014). Impaired tactile processing in children with autism spectrum disorder. *Journal of Neurophysiology*, 111, 1803–1811.
- Roth, R. M., Isquith, P. K., & Gioia, G. A. (2005). *Behavioral rating inventory of executive function - adult version*. Psychological Assessment Resources Inc.
- Saladin, K. (2012). *Anatomy and physiology*. McGraw Hill.
- Saunders, J. B., Aasland, O. G., Babor, T. F., De la Fuente, J. R., & Grant, M. (1993). Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. *Addiction*, 88(6), 791–804.
- Snyder, P. J., Werth, J., Giordani, B., Caveney, A. F., Feltner, D., & Maruff, P. (2005). A method for determining the magnitude of change across different cognitive functions in clinical trials: The effects of acute administration of two different doses alprazolam. *Human Psychopharmacology: Clinical and Experimental*, 20(4), 263–273.
- Sobell, L. C., & Sobell, M. B. (1992). Timeline followback: A technique for assessing self-reported alcohol consumption. In R. Z. Litten, & J. Allen (Eds.), *Measuring alcohol consumption: Psychosocial and biological methods* (pp. 41–72). Humana Press.
- Stavro, K., Pelletier, J., & Potvin, S. (2013). Widespread and sustained cognitive deficits in alcoholism: A meta-analysis. *Addiction Biology*, 18, 203–213.
- Stockwell, T., Sitharthan, T., McGrath, D., & Lang, E. (1994). The measurement of alcohol dependence and impaired control in community samples. *Addiction*, 89, 167–174.
- Tapert, S. F., Brown, G. G., Kindermann, S. S., Cheung, E. H., Frank, L. R., & Brown, S. A. (2001). fMRI measurement of brain dysfunction in alcohol-dependent young women. *Alcoholism: Clinical and Experimental Research*, 25(2), 236–245.
- Tommerdahl, M. (2017). *CAP corporation has partnered with cortical metrics to integrate their award-winning brain gauge Technology*. Retrieved from <https://insights.corticalmetrics.com/cap-corporation-has-partnered-with-cortical-metrics-to-integrate-their-award-winning-brain-gauge-technology/>
- Tommerdahl, M., Favorov, O., Whitsel, B., Nakhle, B., & Gonchar, Y. A. (1993). Minicolumnar activation patterns in cat and monkey SI cortex. *Cerebral Cortex*, 3, 399–411.
- Tommerdahl, M., Lensch, R., Francisco, E., Holden, J., & Favorov, O. (2019). The brain gauge: A novel tool for assessing brain health. *The Journal of Science and Medicine*, 1, 1–19.
- Tommerdahl, M., Tannan, V., Zachek, M., Holden, J., & Favorov, O. (2007). Effects of stimulus driven synchronization on sensory perception. *Behavioral and Brain Functions*, 3, 61.
- Turken, A. U., Whitfield-Gabrieli, S., Bammer, R., Baldo, J., Dronkers, N. F., & Gabrieli, J. D. E. (2008). Cognitive processing speed and the structure of white matter pathways: Convergent evidence from normal variation and lesion studies. *NeuroImage*, 42(2), 1032–1044.
- van der Linden, D., Frese, M., & Meijman, T. F. (2003). Mental fatigue and the control of cognitive processes: Effects on perseveration and planning. *Acta Psychologica*, 113(1), 45–65.
- van Eijk, J., Demirakca, T., Frischknecht, U., Hermann, D., Mann, K., & Ende, G. (2013). Rapid partial regeneration of brain volume during the first 14 days of abstinence from alcohol. *Alcoholism: Clinical and Experimental Research*, 37(1), 67–74. <https://doi.org/10.1111/j.1530-0277.2012.01853.x>
- Volkow, N. D., Ma, Y., Zhu, W., Fowler, J. S., Li, J., Rao, M., Mueller, K., Pradhan, K., Wong, C., & Wang, G.-J., et al. (2008). Moderate doses of alcohol disrupt the functional organization of the human brain. *Psychiatry Research Neuroimaging*, 162(3), 205–213.
- Wang, G. J., Volkow, N. D., Fowler, J. S., Franceschi, D., Wong, C. T., Pappas, N. R., Netusil, N., Zhu, W., Felder, C., & Ma, Y., et al. (2003). Alcohol intoxication induces greater reductions in brain metabolism in male than in female subjects. *Alcoholism: Clinical and Experimental Research*, 27(6), 909–917.
- Zeng, H., Weidner, R., Fink, G. R., & Chen, Q. (2017). Neural correlates underlying the attentional spotlight in human parietal cortex independent of task difficulty. *Human Brain Mapping*, 38(10), 4996–5018.
- Zhang, Z., Francisco, E., Holden, J. K., Dennis, R. G., & Tommerdahl, M. (2011). Somatosensory information processing in the aging population. *Frontiers in Aging Neuroscience*, 3, 18.
- Zhang, Z., Tannan, V., Holden, J., Dennis, R., & Tommerdahl, M. (2008). A quantitative method for determining spatial discriminative capacity. *BioMedical Engineering Online*, 7, 1–8.
- Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, 67(6), 361–370.

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