



Short communication

## Premorbid and current neuropsychological function in opiate abusers receiving treatment

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### ABSTRACT

**Background:** There is an established corpus of evidence linking substance abuse with neuropsychological impairment, particularly implicating frontal lobe functions. These could potentially be premorbid to, rather than consequences of, direct effects of substance abuse.

**Methods:** A matched pairs design was employed in which currently abstinent opiate abusers in treatment were matched to 22 healthy control individuals. These were compared for premorbid and current neurobehavioral abnormalities with the self-report Frontal Systems Behavior Scale (FrSBe). Estimated premorbid and current IQ scores were also ascertained.

**Results:** There was no difference between the groups regarding socioeconomic background. There was no evidence for an alteration in cognitive function as measured by current IQ associated with opiate abuse, nor evidence of premorbidly lower IQ. However, with the FrSBe, the opiate abusers reported overall higher levels of apathy. They also had raised FrSBe total scores, indicating the presence of neurobehavioral features associated with frontal lobe impairment. Furthermore, the opiate abusers reported higher levels of these neurobehavioral abnormalities compared to their matched controls, even in the period preceding substance abuse.

**Conclusions:** The results suggest that some substance abusing individuals in treatment demonstrate raised levels of neurobehavioral abnormalities, independently of general intellectual functioning. Furthermore, the results imply that these abnormalities may have already been present prior to the effects on the nervous system of substance abuse.

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### 1. Introduction

Substance abuse is linked to neuropsychological impairments. Evidence from epidemiological studies suggests that low IQ is a risk factor for later-life substance dependence (Batty et al., 2005) and poor executive function has been described in a range of substance dependent samples (Hester et al., 2010; Lundqvist, 2005). Working memory (Verdejo-Garcia et al., 2010) and information process speed impairments are also commonly observed (Latvala et al., 2009; Verdejo-Garcia et al., 2010). This implies that substance abuse is closely linked to frontal lobe impairment. Furthermore, evidence suggests a link between decision making impairments and substance abuse (Bechara and Damasio, 2002; Bechara et al., 2002; Verdejo-Garcia et al., 2006a). The brain regions thought to

underlie these impairments are also primarily in the frontal lobes (Xi et al., 2010).

This recent emphasis on decision making has raised the issue of whether the frontal impairment is actually acquired. Alternatively, some people may show 'frontal' symptoms predisposing them to substance dependence (Bechara, 2005; Verdejo-Garcia et al., 2006b). Supporting this, a recent study demonstrated alterations in frontal lobe connectivity that are identifiable in individuals at risk for substance abuse (Herting et al., 2010). Together these factors imply neuropsychological function may be altered premorbidly in individuals who later develop substance dependence. Such hypotheses are difficult to test, however, there are neuropsychological tools that offer estimates of past functioning which can be applied to the premorbid period.

We used a self-report measure of frontal lobe function, the Frontal Systems Behavior Scale (Grace and Malloy, 2001), in a group of substance abusers and a control sample. This validated index of neurobehavioral abnormalities can be completed for present status and for a premorbid period. We also estimated premorbid IQ and measured current IQ in the same participants. We

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hypothesized that substance abusers would show lower premorbid IQ and higher FrSBe scores when compared to healthy controls.

## 2. Methods

### 2.1. Participants and matching procedure

Twenty-two individuals with histories of chronic substance abuse and 22 healthy controls participated. The 22 substance abuse participants were selected from a group of 40 who were recruited while attending a treatment clinic in northern England. Of these 40, 12 were excluded because a urine screen revealed recent drug use and five were excluded due to poor performance on the Wechsler Test of Adult Reading (WTAR; Wechsler, 2001). A low score on the WTAR prohibits estimation of function. A group of 70 controls were screened to be relatively drug-free, and demographically matched to the substance abuse group. From these 70 control and 23 substance abuse participants 22 pairs were matched. Each pair contained a substance abuse individual and a gender and age matched control. Although the 22 control participants were not completely drug and alcohol naïve, when screened with DSM-IV criteria (American Psychiatric Association, 2000) none had a past history which would reach criteria for substance abuse. In contrast, all of the substance abuse participants reached the criteria for both DSM-IV past substance abuse and dependence.

Of the 22 substance abuse participants all were being treated for opiate addiction, indeed when asked to identify their drug of choice 20 reported heroin and the remaining reported morphine. The most frequent method of use was injection (12/22), followed by inhalation (9/22), and tablet form (1/22). Twenty were being treated with methadone (administered at least once daily), one patient was treated with buprenorphine and one with diamorphine. The dependence was chronic in all cases. The mean number of months since commencement of daily illicit opiate use was 171 (SD = 81), and the mean reported current abstinence period in months was 32 (SD = 42).

### 2.2. Assessments

To assess premorbid socioeconomic status (SES) participants were interviewed regarding childhood background with the UK socio-economic classification system (ONS, 2005). Classifications range from 1.1 for 'higher professional occupations' through 8 for 'never worked and long-term unemployed.' Estimation of premorbid IQ was performed with the WTAR (Wechsler, 2001) and measurement of current IQ with the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999). To assess neurobehavioral function the self-report Frontal Systems Behavior Scale (FrSBe) was used (Grace and Malloy, 2001). This provides an overall score of frontal impairment and sub-scale scores for the three frontal-behavioral syndromes; apathy, disinhibition and dysexecutive (Duffy and Campbell, 1994). The FrSBe is designed to be rated both for current function and retrospectively for a premorbid period. The substance abuse individuals were asked to identify the year prior to their becoming involved with drug use and complete the FrSBe for that period. For each substance abuse individual their matched control completed the FrSBe for that same age. Furthermore, using the Wechsler scales we were able to derive estimated scores of premorbid and current IQ.

### 2.3. Procedure

Participants were interviewed regarding demographics, SES, and cognitive and neurobehavioral function. To screen for recent drug use in the substance abuse individuals a urine sample was taken at the end of the interview. Urine screening was not available

**Table 1**

Demographic features of the substance abuser and control groups.

	Substance abusers (n = 22)	Controls (n = 22)
Age	38.8 (8.7)	38.8 (9.3)
Male:female	14:8	14:8
Education	11.5 (1.6)	12.4 (1.8)
SES	5 (1.1–7)	5 (1.1–7)

For age and education, the mean number of years (+SD) is shown. SES = childhood socioeconomic status on the ONS socio-economic classification system, shown is the median (+range).

for the control group, though, honesty was emphasized and they were paid for their participation regardless of reported drug use. For the substance abuse group, all testing was conducted within 3–15 h of the previous dose of methadone/buprenorphine/diamorphine. The data reported here is part of a larger neuropsychological study to be reported later. The entire assessment took approximately three hours. All participants gave informed consent and were paid £30 (approximately US\$ 45). The research was approved by an appropriate ethics committee.

### 2.4. Design and statistical analyses

Twenty-two pairs of matched cases were compared. Demographics were analyzed using  $\chi^2$  and *t*-tests (or non-parametric equivalents). To compare premorbid and current status for IQ and FrSBe scores repeated ANOVAs were employed with time (premorbid or current) as a within subjects factor. As the participants were matched pairs it was necessary to enter group membership as a within subjects factor (Howell, 1992). As the primary hypothesis was that there would be a between-group difference in premorbid function (irrespective of current function) planned contrasts were performed on premorbid scores on each measure between the groups. The correlation analysis used one-tailed Pearson bivariate statistics.

## 3. Results

Demographic features of the groups are shown in Table 1; there were no significant between-group differences on any of these variables. Mean IQ scores and mean FrSBe raw scores are shown in Table 2. Overall the substance abuse group scored higher on the FrSBe than the control group for total FrSBe ( $F(1,21) = 4.62, p = .043$ ) and apathy ( $F(1,21) = 6.04, p = .023$ ). However, there were no significant main effects of group for either dysexecutive problems or disinhibition. As revealed by the ANOVA main effects of time, scores were significantly lower in the current time frame compared to premorbid, for total FrSBe scores ( $F(1,21) = 5.48, p = .029$ ), disinhibition ( $F(1,21) = 9.59, p = .005$ ), and dysexecutive problems ( $F(1,21) = 9.16, p = .006$ ). However, this pattern was similar in both groups; indeed none of the time by group interactions were statistically significant.

**Table 2**

Mean (+SD) FrSBe scores of the substance abuse group rated for current behavior (present) and for pre-substance abuse (past) and scores for the control sample rated at the same time points. Also included are mean (+SD) estimated premorbid IQ (past) and actual current IQ (present).

Scale	Substance abusers n = 22		Controls n = 22	
	Past	Present	Past	Present
Apathy	35.3 (10.4)	35.9 (8.5)	30.5 (8.9)	29.0 (8.1)
Disinhibition	41.6 (9.9)	34.9 (7.4)	36.5 (10.1)	33.2 (7.3)
Dysexecutive	49.0 (9.2)	41.9 (8.6)	44.2 (13.4)	40.2 (10.2)
Total FrSBe	125.8 (22.2)	113.6 (21.9)	111.1 (28.8)	102.1 (23.4)
IQ	101.0 (8.0)	99.9 (15.2)	102.7 (9.8)	104.5 (17.1)

FrSBe scores can be compared to the *T* scores of the normative sample provided by the test publisher. Under their criteria many of the substance abusers scored in the 'clinically significant' range for current status; 14/22 (64%) for apathy, 11/22 (50%) for dysexecutive problems, 10/22 (45%) for disinhibition, and 14/22 (64%) for total FrSBe scores. However, many of the control sample also scored as 'clinically significant' for current status; 7/22 (32%) for apathy, 9/22 (41%) for dysexecutive problems, 8/22 (36%) for disinhibition, and 9/22 (41%) for total FrSBe scores.

Regarding IQ, all mean scores were around 100 which is the estimated population mean, indicating that both groups were essentially 'normal' in this respect. Furthermore, there was a difference of less than five IQ points between the highest and lowest mean IQ scores. Indeed, a repeated measure ANOVA revealed that neither the two main effects of time and group nor the interaction were statistically significant. For each of the ANOVA calculations an additional planned contrast was performed examining the premorbid scores only. IQ and FrSBe sub-scale scores by the substance abuse group were not significantly different from the control group. However, the substance abuse group had significantly higher total FrSBe scores in the premorbid period than the control group ( $F(1,21) = 4.58, p = .044$ ).

Finally, the WASI includes a verbal 'similarities' task. Performance on this task requires cognitive abstraction and is a measure of frontal lobe neurocognitive function (Miller and Cummings, 2007). It could be hypothesized that performance would be associated with substance abuse and severity of neurobehavioral symptoms. Although the control group had slightly higher means than the substance abuse group (47.7, *SD* = 11.1; 44.5, *SD* = 11.7), the difference was not statistically significant. To assess the relationship between WASI similarities scores and FrSBe scores correlations were performed. Within the substance abuse group similarities performance was significantly negatively correlated with dysexecutive scores ( $r = -.364, p = .048$ ). Similarly, in the full sample of 44 participants similarities scores negatively correlated with both dysexecutive ( $r = -.300, p = .024$ ) and total FrSBe scores ( $r = -.252, p = .049$ ). There were no significant correlations within the control group only, or with apathy or disinhibition scores in the substance abuse group only or full sample.

#### 4. Discussion

We found no evidence for lower premorbid or current IQ in the substance abuse group. However, we did find evidence that they scored generally higher for neurobehavioral problems. Apathy and total FrSBe scores were higher in the substance abuse group compared to the control group. Even premorbidly, they reported more problems as measured by the total FrSBe score. Supporting evidence that the FrSBe is measuring frontal function was provided by the observation that high FrSBe total and dysexecutive scores were associated with low performance on the WASI similarities task, a measure of frontal lobe mediated cognitive abstraction.

In addition, it was found that many of the substance abusers would be considered to be in the 'clinically significant' range of FrSBe scores, which is defined as scoring more than 1.5 standard deviations above the normative mean (based on a USA sample). However, it should be noted that several individuals in our UK control group also scored in this range. This finding highlights the importance of carefully matched and appropriate controls, as use of published normative data from different cultures can be misleading.

Our groups were carefully matched to be from family backgrounds of equivalent SES. This was performed in order to focus on premorbid function. Even with this carefully matched sample, it was found that FrSBe scores were raised premorbidly in the

substance abuse group. Our findings suggest that some individuals in treatment for substance abuse display neurobehavioral features of prefrontal dysfunction, and that this predates exposure to the direct effects of substance abuse. There are likely to be multiple and complex reasons for early manifestation of neurobehavioral problems. It has, for example, been demonstrated that childhood trauma is linked to neurobehavioral and cognitive function in homeless adults with high levels of substance abuse problems (Pluck et al., 2011). However, trauma is likely to be just one possible source of premorbid neurocognitive changes that later associate with substance abuse.

This research is based on retrospective self-ratings of behavior. Such information is not as reliable as longitudinally collected data and this is a limitation of the current research. However, there is evidence that such rating scales may have greater ecological validity than conventional neuropsychological tests in substance abuse research (Verdejo-Garcia and Perez-Garcia, 2008). The scale used was designed and validated for retrospective use in clinical groups (Grace and Malloy, 2001) and its reliability in abstinent substance abusers has been demonstrated (Verdejo-Garcia and Perez-Garcia, 2008). Our sample may have acquired neurocognitive changes due to chronic substance abuse, and this is a further consideration, as it may have influenced recall ability. However, we did not detect any cognitive changes indexed by IQ, and furthermore, it has been shown that assessments of own behavioral traits are remarkably unaffected by even advanced dementia (Klein and Gangi, 2010).

Overall, our findings agree with recent suggestions regarding the role of neurocognitive decision making functions in predisposing to substance abuse. They are also in accordance with evidence that alterations in frontal lobe physiology are present in individuals at risk for developing substance abuse problems (Herting et al., 2010).

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#### Contributors

All authors contributed to study design, identification and recruitment of appropriate clinical participants was performed by Drs Rele and Lagundoye. Recruitment of control participants was by Dr Parks. Data collection was performed by Drs Pluck and Sarkar and data analyses were performed by Drs Pluck, Parks and Lee. All authors contributed to preparation of the manuscript. Sadly, Professor Spence died before submission of this final version, but the other authors all approved it.

#### Conflict of interest

No conflict declared.

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