Research Article

Differences in attention between methadone patients and abstinent problem heroin drug users frequenting a drug rehabilitation programme.

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Summary: *Cognitive deficits of attention have been associated with substance abuse. The present study assessed the degree to which the ability to concentrate and to sustain and shift attention is impaired in methadone patients and recovering heroin addicts who were all frequenting the same drug rehabilitation programme but were at different levels of their rehabilitation process. Test scores indicated a decrease in the ability to shift attention and to focus and tap on a sequential display of digits in the IED subtest and the RVIP subtest respectively of the Cambridge Automated Neuropsychological Test Battery (CANTAB) in the methadone group. Additionally, this decrease in performance ability was also visible in the more recently heroin addicts compared to the group who had been abstinent for a longer period of time. These findings indicate a progressive improvement in selective attention functions relative to drug-state and length of abstinence.*

Keywords: Attention, cognitive functions, methadone, heroin, abstinence

Introduction

Poly-drug use and abuse is a major societal problem. The cognitive deficits associated with the chronic abuse of drugs have important theoretical and clinical significance. They reflect changes in underlying cortical, sub-cortical and neuromodulatory mechanisms that underpin cognition and consequently have an impact on rehabilitative programs. (Rogers and Robbins, 2001).

Cognitive Impairment and different drugs of abuse

Chronic misuse of stimulant drugs, such as cocaine or amphetamine, or of opiates such as heroin has been shown to lead to long-lasting impairments in brain function (Ricaurte et al. 1984; Miller 1985). Heavier use of opiates in long-term users has been shown to be associated with greater likelihood of neuropsychological impairment when assessed by a battery including the WAIS, aphasia tests, and the Halstead battery (Grant et al. 1978).

Hill and Mikhael (1979) who studied opiate abusers with an almost exclusive drug preference for heroin found that they were impaired on Tactual Performance for memory and location and Tapping Tests, but not on the Category Test, a measure of abstract reasoning ability. They concluded that, since performance on the Category Test is thought to be related to damage to the frontal lobes, this brain region might be less affected by opiate abuse. This conclusion is supported to some extent by results from studies that have failed to detect a difference between opiate users and controls on other measure of neuropsychological functioning thought to correlate with frontal lobe damage (Bruhn et. al., 1975; Rounsaville, 1982).

Several studies have assessed cognitive function in stimulant (cocaine) abusers (Washton and Gold 1984; Ardila et al. 1991; Mittenberg and Motta 1993). In an extensive study of cocaine abusers and poly-abusers, Rosselli and Ardila (1996) found significant impairments in short-term memory and attention. Abstracting ability as tested by the Wisconsin Card Sorting Test and non-verbal short-term memory, were less impaired, while verbal fluency and long-term memory were un-impaired. Test scores were found to correlate with lifetime cocaine abuse, suggesting a relationship between drug abuse and cognitive dysfunction.

Although a substantial amount of evidence strongly indicates the impairment of cognitive functioning in different types of substance abusers, the specific type of cognitive impairment varies according to the type of drug used, the amount used per day, the duration of use and the recency of use. A 1992 study comparing twenty chronic cocaine abusers with age and education matched controls using standardized neuropsychological assessment procedures showed that in the cocaine abuser sample, neuropsychological performance was related to the amount and recency of cocaine use, suggesting a direct role of cocaine on cognitive functioning (O'Malley et. al., 1992). Additionally, a report published in the Journal of Neuropsychiatry and

Clinical Neurosciences (1999) revealed that heavy cocaine users show slower reaction times, more problems with attention and concentration, and perform worse on tests of mental flexibility and planning. The author attributed the amount and the recency of use as being the factors most closely related to a poor performance (Bolla, 1999).

A comparison of the cognitive functioning between amphetamine and heroin abusers and age- and IQ-matched control subjects, found qualitative differences, as well as some commonalities, in the profile of cognitive impairment between groups (Ornstein et. al., 2000). The chronic amphetamine abusers were significantly impaired in performance on the extra-dimensional shift task (a core component of the Wisconsin Card Sort Test) whereas in contrast, the heroin abusers were impaired in learning the normally easier intra-dimensional shift component. Whereas both groups were impaired in some tests of spatial working memory the amphetamine group, unlike the heroin group, was not deficient in an index of strategic performance on this test. The two groups were profoundly, but equivalently impaired on a test of pattern recognition memory sensitive to temporal lobe dysfunction. The results of this study support current literature and are indicative of chronic drug use leading to distinct patterns of cognitive impairment, with differences in the exact nature of the cognitive deficit according to the type of drug used (Ornstein et. al., 2000).

Current trends in research on other stimulants such as ecstasy have resulted in the growing evidence of chronic, heavy, recreational use of ecstasy being associated with sleep disorders, depressed mood, persistent elevation of anxiety, impulsiveness and hostility, and selective impairment of episodic memory, working memory and attention (Morgan, 2000). A study by Parrott et al. (1998) reported that light to moderate ecstasy users whilst exhibiting selective deficits in memory performance, did not show impairments in other aspects of cognitive functioning, such as, simple reaction time, choice reaction time, vigilance performance and Sternberg task reaction time. In a recent study, (Gamma, et. al., 2000), mood and regional cerebral blood flow (rCBF) profiles between regular polytoxic Ecstasy users and Ecstasy-naive controls were compared. Brain activity was measured during cognitive activation by an attentional task using positron emission tomography (PET) and [H2(15)O]. Statistical parametric mapping revealed that brain activity did not differ between the two groups and. Significantly higher levels of depression were found in the Ecstasy-using subjects, however, both groups also performed equally on the cognitive task requiring sustained attention (Gamma, et. al., 2000).

The attentional aspect of cognitive impairments observed in drug abusers has also been investigated independently in a study comparing recently recovering substance abusers and subjects with attention deficit-hyperactivity disorder (Hoegerman, et. al., 1993). The results of this study showed intriguing educational and therapeutic implications of the similarities between cognitive impairments of newly sober substance abusers and adults with persistence of attention deficit-hyperactivity disorder (ADHD). In another study using only adolescent female substance abusers and female non-substance abusers as controls, the findings suggested that the female substance abuse group performed deficiently on tests requiring language skills, sustained attention and perceptual efficiency and scored lower than controls on standardized tests of intelligence and academic achievement (Tarter, et. al., 1995).

Similar to the effects observed in other drugs of abuse, methadone, an opiate, has also been found to exhibit a wide range of cognitive deficits. In a study comparing methadone patients with ex-substance abusers, poorer performance in tests of learning and recall were found in the methadone group compared to the abstinent ex-substance abuser group (Gritz et. al., 1975). In a more recent study by Darke et. al., (2000), the cognitive functioning between methadone-maintenance subjects and naïve controls was compared. The results of this study clearly show that almost half of the subjects in the methadone-maintenance group demonstrated to have cognitive impairment in the severely impaired range and moderate deficits were seen in both information processing and problem solving (Darke, S, et. al., 2000). The function of attention in methadone patients is illustrated in a study using a series of cognitive psychomotor performance tests to compare the ability of a number of cognitive functions between methadone patients and naïve controls. The results of this study demonstrated a decrease in performance ability especially on the attention tasks with the methadone group compared to controls (Specka et. al., 2000).

CANTAB - The Cambridge Neuropsychological Test Automated Battery

The Cambridge Neuropsychological Test Automated Battery (CANTAB), firstly developed by CeNeS in 1987, is a computerized battery of neuropsychological tests. It has been shown in more than 100 published studies to be sensitive to cognitive changes in a variety of brain disorders and normal subjects. Twelve tests form its 'Attention Battery', 'Visual Memory Battery' and 'Working Memory and Planning Battery'. It provides for the assessment of a variety of cognitive functions, including working memory, attention, learning and problem solving, as well as tests of executive function and vigilance (Pantelis & Maruff, 1988). CANTAB also has four Parallel Batteries where different versions of the tests in the main batteries can be used.

CANTAB is very easy to administer, running DOS 6.0 on a 486DX processor with 4MB RAM, using a touch

screen or a mouse. The version used in this study is version 2.35 released by CeNeS Cognition in August 1998. All twelve tests are language free, making CANTAB highly suitable in multinational studies. Data is stored automatically and then analysed and summarized in a simple easy-to use format.

CANTAB is especially sensitive to cognitive changes even when traditional cognitive measures have proven insensitive (Robbins, 1998). It can be used across all ages, with psychiatrically disturbed or dementing subjects, but also with normally healthy individuals (Harrison, 1998).

CANTAB has been used and validated in hospitals and neuroscientific research groups across four continents. Over 2,000 subjects have been tested with CANTAB and their data has been used to determine norms for both patients and normal control subjects. The norms commonly used are given by age, gender, and IQ (CeNeS Cognition, 1998). The major division is by age, with bands for subjects less than 35, age from 35-49, then by decade up to 70 and a band for 70 and over. In this research the participants all fell under the –under 35 age bands.

Within the different age bands, the norms are divided into three bands of IQ: less than 110, 110 to 119 and 120+. In the standardized norms, IQ is estimated form the National Adult Reading Test (NART). This test would have proved inappropriate for this sample since most of the participants were not English speaking (but see accompanying paper). The minor division within each age/IQ band is gender. CANTAB tests, with the exception of some spatial measures have been shown to be insensitive to gender, however in this particular experiment only males were used. CANTAB has been shown to have test-re-test reliability and therefore the battery is reliable over time (Shah, 1998).

The two tests selected for this study were extracted from the Attention Battery section of the CANTAB:

1. The Intra/Extra Dimensional Shift (IED)
The IED is a test that measures the subject's ability to attend to the specific attributes of compound stimuli and to shift that attention when required. Two artificial dimensions are used in this test, colour-filled abstract shapes and white lines. Simple stimuli are made of just one of these dimensions, whereas compound stimuli are made-up of both, namely white lines overlying colour-filled shapes. Participants progress through the test by satisfying a set criterion of learning at each of nine stages (six consecutive correct responses). If at any stage the participant fails to reach this criterion after 50 trials, the test is terminated (CeNeS Cognition, 1998a).

2. The Rapid Visual Information Processing (RVP)
The RVP is a test of sustained attention with a small working memory component. This test has a 2-minute training period before the actual 4-minute test is run. On both training and actual test a white box appears in the center of the computer screen, inside which, digits from 2-9 appear in a pseudo-random order, at the rate of 100 digits per minute. Participants are required to monitor the changing digits for pre-defined number sequences and to respond by pressing a button at the presentation of the final digit of the sequence. The reaction time is not measured (CeNeS Cognition, 1998a).

Method and Materials

Participants
Participants (N=30) aged between 18 and 27 were selected from a drug rehabilitation programme (San Blas Therapeutic Community, Caritas, Malta). All participants were male, had a history of heroin drug use and had been or were currently being detoxified by use of methadone. Exclusionary criteria included those people who were currently on prescribed psychiatric medication and who had a psychiatric history. All the participants came from the same social background and none had completed secondary school education. Females were not used in this study because the available number of female problem heroin drug users was deemed to be too small to effectively have sufficient numbers in each of the different groups.

Procedure
Following a screening procedure where all participants were formally assessed on their drug-use history with a personal details questionnaire and a general drug use questionnaire resulted in three groups with ten participants in each group. Group 1 consisted of 'ex-problem heroin users who were currently on methadone'; Group 2 consisted of 'ex-problem heroin users who had been detoxified by use of methadone 1-3 months ago'; and Group 3 consisted of 'ex-problem heroin drug users who had been detoxified by use of methadone 6-12 months ago. All groups were matched according to age, social class and education. Prior to the experimental sessions, all the participants were debriefed together on the experimental procedure and were given a consent form to read and sign.

Experiment
The experiment was conducted in a room allocated for the test within the rehabilitation building. Testing was carried out on an individual basis, over four consecutive days, with a random allocation of participants to time of testing. Prior to each experiment, standardised instructions were used to explain each test . The sequence in which the two tests were administered was balanced between the groups to eliminate performance variance as a result of motivation and/or subjective difficulty on either one of the tests

The duration of each experiment was approximately 30 minutes. Testing commenced at 9.00am and the last test

on each day was conducted by not later than 3.00pm.

Materials

The Intra/Extra-Dimensional Shift and the Rapid Visual Information Processing tests from the Attention Battery section of The Cambridge Neuropsychological Test Automated Battery (CANTAB) were administered to each participant. These tests were selected for their accuracy in measuring the particular cognitive function (attention) relevant for this study and also for their avoidance of 'floor' and 'ceiling' effects.

Scoring

The main data items following each test from the CANTAB were automatically recorded and summarised. A summary table is given for each test where the score, standard score (Z score) and percentile of the main items being measured. In the Intra/ Extra Dimensional Shift Test the data items recorded were:

- Stage reached (maximum 9)
- Total errors
- Errors at ED-shift
- Errors up to ED-shift

In the Rapid Visual Information Processing Test, the data items recorded were:

- Probability of hit – this is the probability of the subject responding correctly, equal to the hits / (hits and misses).
- Probability of false alarm – this is the probability of a false alarm, equal to false alarms / (false alarm and correct rejection).

Data Analysis

The scores obtained from the CANTAB tests and the information obtained from the participants' checklist - age and type of group (1, 2 or 3) were inputted into a data file for SPSS Version 10.0 analysis.

Results

Analysis of the results revealed differences in attention and concentration between the three groups. In the IED subtest, the capacity to shift attention was poorest in the methadone group (Group 1). This capacity progressively improved between the 1-3 month group (Group 2) and the 6-12 month (Group 3) respectively. In the 'probability of a hit' task from the RVIP sub test, a similar progression in improvement in performance was observed. The three groups, however, did not differ significantly in the sustained attention task of the IED sub test. A table of means for all three groups (Table1.1 and figure 1) illustrate the differences in Group 2 (1-3 months 'clean') compared to Group 1 (methadone group) and similarly in Group 3 (6-12 months 'clean') compared to both Group 2 and Group 1.

Table 1.1: Comparison between groups on subtests.

Sub-tests	Group	Mean	Group	Mean	Group	Mean
Stage	1	-2.5	2	-0.5	3	0.17
Total Errors	1	-1.61	2	-0.37	3	-0.01
At ED	1	-1.15	2	-0.67	3	-0.065
Up to ED	1	-0.41	2	-0.068	3	0.033
Prob. of Hit	1	-2.28	2	-0.067	3	-0.037
Prob. of FA	1	0.1	2	0.1	3	0.4

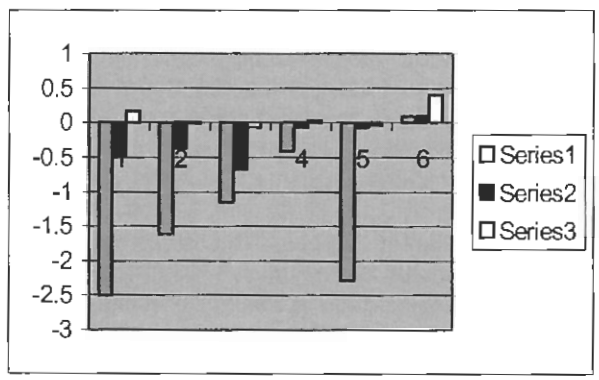

Fig.1. Series 1 = Group 1 (Methadone Group)
Series 2 = Group 2 (1-3 month Group)
Series 3 = Group 3 (6 month+ Group)

A multivariate ANOVA was used to reveal the differences between the three groups in some attention aspects of the sub-tests (table 1.2)

Table 1.2: Differences between groups on sub-tests

	df	F	Sig.
Stage	2	3.687	.038
Total Errors	2	5.438	.010
At ED	2	1.193	.319
Up to ED	2	0 .474	.628
Probability of a hit	2	12.599	.000
Probability of false alarm	2	0.309	.737

A series of Independent Samples T-test were used to investigate the differences between the groups. A comparison between the methadone group and the 1 to 3 months group, (Table 1.3), on the 'total errors' on the IED subtest and the 'probability of a hit' on the RVIP subtest reached significance $t(18) = -2.11$, $p < .05$; $t(18) = -4.94$, $p < .01$ respectively.

Table 1.3: Comparison on subtests between methadone group and 1-3 months group.

Subtests	T	df	Sig. (2-tailed)
Stage	-1.597	18	0.128
Total errors	-2.111	18	0.049
At ED	-0.58	18	0.569
Up to ED	-7.93	18	0.438
Probability of a hit	-4.943	18	0
Probability of F.Alarm	0	18	1.000

The same comparisons between the methadone group and the 6-12 months group, (Table 1.4) also yielded a significant difference t (18) = -3.16, $p<.01$; t (18) = -4.04, $p<.01$.

Table 1.4: Comparison on subtests between methadone group and 6-12 months group

Subtests	T	df	Sig. (2-tailed)
Stage	-2.279	18	0.035
Total errors	-3.159	18	0.005
At ED	-1.643	18	0.118
Up to ED	-0.719	18	0.481
Probability of a hit	-4.042	18	0.001
Probability of F. Alarm	-0.617	18	0.545

Comparisons between the 1-3 months group and the 6-12 months group, (Table 1.5) on the 'Total Errors' made on the IED subtest also revealed significant differences between the two groups, t (18) = -0.86, $p< .05$; however no significant difference was found between the two groups in the performance on the RVIP 'Probability of a hit' t (18) = 0.603, $p>.05$.

Table 1.5: Comparison on subtest between 1-3 months group and 6-12 months group

Subtests	T	df	Sig. (2-tailed)
Stage	-1.5	18	0.151
total error	-0.865	18	0.398
at ED	-0.991	18	0.335
up to ED	0.088	18	0.931
Probability of a hit	0.603	18	0.554
Probability of F. Alarm	0.847	18	0.408

Discussion

The results obtained from this study show a progressive improvement in specific attention functions between Group 1 (methadone group) and Group 2 (1-3 months 'clean') and between Group 2 and Group 3 (6-12 months 'clean') respectively, both in the IED sub test as well as in the RVIP sub test. In the IED subtest the main difference observed between the groups was that of shifting attention when the rule of a given sequence was changed, reflected by the 'total errors' made, with Group 1 demonstrating to have the most problems. No differences however emerged in the IED sustained attention task between all the three groups. With regards to the 'probability of a hit' in the RVIP subtest, which is also reflective of sustained attention, the differences were significant between the methadone and the 1-3 months and the 6-12 months group respectively, however, there was no significant difference in this task between the 1-3 months group and the 6-12 months groups.

Research on methadone-maintenance patients' highlights the observation that these people show cognitive impairments in the moderate to severe range (Darke, 2000). The results that emerge from this study seem to reflect similar observations with the methadone group demonstrating a decreased capacity to shift attention and poorer concentration levels than the 1-3 months abstinent group and the 6-12 months abstinent group. On the other hand, the IED measure of sustained attention which showed no significant difference between groups has yielded similar results in other studies using matched controls and 3-5 week abstinent drug abusers, alcoholics, cocaine abusers (Beatty et. al., 1995) and ecstasy users (Gamma et. al., 2000).

The progressive improvement in performance on certain elements of the attention subtests with the 1-3 month group and the 6-12 month group respectively, compared to the methadone group, seems to demonstrate the increasing capacity of the recovering drug addict to concentrate, focus and shift attention to relevant cues with increasing drug-free time. This improvement is also highlighted by the fact that in the 'probability of a hit' RVIP subtest, no significant differences in performance emerged between the 1-3 months and the 6-12 months abstinent groups. Studies that have highlighted deficits in mental flexibility and attention and concentration problems in drug addicts have also found a relationship between the degree of cognitive impairment and the amount and recency of drug use (O'Malley, 1992; Bolla, 1999).

The results from this experiment, especially evident in the methadone group, translated into everyday function, may be reflected in slowness of response, failure to grasp the meaning of complex or rapid instructions and difficulty in shifting attention when necessary. These factors may be reflected as difficulties in thinking of adaptive solutions to problems that crop up in everyday routines, slowness in learning, and a tendency to fixate

on a pattern of events rather then shifting attention to other occurrences. Cognitive impairments may contribute to continued misuse and addiction in at least 2 ways. They may increase the likelihood of drug-seeking behaviour as a result of failure to control impulses, for example and in addition they may also interfere with the users capacity to assimilate and participate effectively in rehabilitation programs that often have an educational and cognitive component (Mc Crady et al., 1986). This finding is important for out-patient clinics or rehabilitation programmes that support a methadone-maintenance programme as non-compliance on the part of the patient or client with clinic routines and instructions may, therefore, reflect inability rather than motivational or personality characteristics.

Due to the methadone component in this study, no conclusions can be generated as to whether attention function improves as a result of the elimination of the methadone variable or as a result of the improved cognitive function due to drug abstinence in general. The only indications that may be drawn up from the results of this study are that ex-problem heroin users currently on methadone seem to show a decreased capacity in shifting attention and concentration relative to those who have been detoxified from methadone. This change is also progressive and improves as the time frame between methadone withdrawal and abstinence increases.

A methodological shortcoming in the study is the non-inclusion of a naïve control group which would have provided the possibility of comparing the performance between the 6-12 month abstinent group and the control group and thus enabling us to make inferences on the extent to which certain elements of attention improve in the abstinent problem heroin drug user compared to a the drug naïve person.

The possibility of pre-existing differences in individual cognitive capacity or intelligence cannot be ignored. Although the participants in this study all came from the same educational and social background and these two variables were balanced across all the three groups, this alone is not sufficient to ensure that the group is really homogeneous with regards to this factor. In addition to this, one cannot exclude the possibility that exposure to certain groups, educational courses and learning situations, which form part of the treatment in rehabilitation programmes, could have in some ways contributed to the improved capacity in certain attention functions with the 1-3 months group and even more so with the 6-12 months group.

A suggestion for future research would be to perform a longitudinal study on the same sample to re-assess and compare the performances across the different groups. Additionally, a baseline IQ test should also be administered to enable a correlation between performance and intelligence, thus eliminating pre-existing cognitive ability and intelligence as confounding variables. The addition of a group of naïve controls would introduce the possibility of investigating and comparing attention levels between the drugs exposed groups and the drug naïve group over the time frame in question.

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