ELSEVIER

Pharmacology, Biochemistry and Behavior 73 (2002) 491–504

PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR

www.elsevier.com/locate/pharmbiochembeh

Chronic drug use and cognitive impairments

Robert I. Block[a,*], Wesley J. Erwin[b], M.M. Ghoneim[a]

[a]*Room 5140, Westlawn Building, Department of Anesthesia, University of Iowa, Iowa, IA 52242, USA*
[b]*Department of Counseling and Student Affairs, Minnesota State University Moorhead, Moorhead, MN 56563, USA*

Received 15 June 2001; received in revised form 4 January 2002; accepted 29 March 2002

Abstract

Reports regarding the effects of chronic drug use on human cognition and comparisons of different drug user groups have been inconsistent. Methodological flaws may account for some inconsistencies. To determine the effects of chronic drug use on cognition, drug users ($n = 192$) were tested 17.1 ± 0.3 days (mean ± S.E.) and 99.4 ± 1.7 days on average after their last use of drugs before beginning treatment. Drug users were categorized as stimulant, alcohol, or polydrug users. Their performance on tests of academic achievement, verbal memory, and abstraction was compared to performance of community-dwelling controls ($n = 137$). The groups were matched on selected demographic and psychiatric characteristics. Historical records of achievement test scores were used to attempt to control for premorbid intellectual ability. Drug users showed impairments on each of the achievement tests ($P < .001$), as well as poorer total recall ($P < .01$) and abstraction ability ($P < .05$). Stimulant users performed worse on several tests relative to the other drug use groups. Only one of six tests demonstrated improvements following about 3 months of abstinence. Thus, chronic drug use is associated with cognitive impairments that do not improve substantially even after several months of abstinence.

Keywords: Abstinence; Achievement tests; Alcohol; Cognition; Drug use; Human; Memory; Stimulants

1. Introduction

Studies of the chronic effects of drug abuse on cognition have produced inconsistent findings. Although certain studies have found deficits in memory, attention, abstraction, decision-making, and visuospatial abilities (Bauer, 1996; Beatty et al., 1995, 1997; Mittenberg and Motta, 1993; Rogers et al., 1999; Rosselli and Ardila, 1996), others have failed to find deficits in some of the same functions (Bolla et al., 1999; Gillen et al., 1998; Hoff et al., 1996; O'Malley et al., 1992; Robinson et al., 1999). For example, contrasting findings that cocaine users performed poorer than, or equivalent to, controls have been reported on the Logical Memory subtest of the Wechsler Memory Scale (Bolla et al., 1999; Rosselli and Ardila, 1996), the California Verbal Learning Test (Gillen et al., 1998; Mittenberg and Motta, 1993), Trail Making Tests A and B (Beatty et al., 1995; Bolla et al., 1999; O'Malley et al., 1992), and the Block Design subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Beatty et al., 1995; Gillen et al., 1998; O'Malley et al., 1992).

Stimulant users actually performed better on certain measures than controls in a few studies (Bolla et al., 1999; Hoff et al., 1996; Manschreck et al., 1990; McKetin and Mattick, 1998; O'Malley et al., 1992). Cocaine users, relative to controls, completed mazes more quickly (Manschreck et al., 1990) and performed better on the Rey Auditory Verbal Learning Test, Trial 1 (Bolla et al., 1999), the Oral Fluency part of an abbreviated version of the Benton Multilingual Aphasia Exam (O'Malley et al., 1992), and the number of correct categories on the Wisconsin Card Sorting Test and the Controlled Oral Word Association Test (Hoff et al., 1996). Amphetamine users who were assessed as being in a low-dependence group performed better than controls on the verbal memory index of the Wechsler Memory Scale-Revised (McKetin and Mattick, 1998).

Studies comparing the severity of cognitive deficits associated with different drugs have also shown discrepant results. One study (Selby and Azrin, 1998) found that

* Corresponding author. Tel.: +1-319-335-8975; fax: +1-319-335-8996.
E-mail address: robert-block@uiowa.edu (R.I. Block).

0091-3057/02/$ – see front matter
PII: S0091-3057(02)00816-X

cocaine users performed better than alcohol and polydrug users, whereas several other studies found that cocaine users generally performed worse than alcohol and polydrug users (Bauer, 1994, 1996; Beatty et al., 1995; Robinson et al., 1999; Rosselli and Ardila, 1996).

Methodological flaws in studies may account for some of the inconsistencies mentioned above. Virtually no studies have included measures of premorbid cognitive function, raising the possibility that differences between drug users and controls, or differences among classes of drug users, existed before the onset of drug use, rather than being caused by drugs. Although a few studies attempted to estimate premorbid cognitive function (Beatty et al., 1995; Berry et al., 1993; McKetin and Mattick, 1997, 1998; McKetin and Solowij, 1999), such estimates have limited validity. A number of studies have not included a control group of nonusers (Ardila et al., 1991; Dafters et al., 1999; Horner, 1997; Krystal and Price, 1992; McKetin and Mattick, 1997; Strickland et al., 1993). To convincingly demonstrate cognitive deficits in drug users, comparison with an appropriately matched control group is essential. Many studies have involved small sample sizes, for example, as few as eight (Strickland et al., 1993) drug users. In the present study, we avoided these methodological flaws by retrieving historical records of achievement test scores to measure premorbid cognitive function, including a control group, and using a large sample size.

We compared three primary categories of drug users — stimulant, alcohol, and polydrug users. These broad categories provided sufficiently large group sizes to afford adequate power. We also conducted more fine-grained analyses, for example, comparing cocaine and amphetamine users within the stimulant group. These more fine-grained analyses provided justification for the pooling of subjects into the primary categories, as did other considerations, for example, with respect to cocaine and amphetamine, both drugs stimulate the central nervous system at many levels, have prominent effects on dopamine and other monoaminergic neurotransmitters, and produce similar patterns of intoxication and clinical problems (Schuckit, 2000, pp. 120–121).

2. Method

2.1. Subjects

The study was conducted with the understanding and consent of each subject, following approval of the experimental protocol by the University of Iowa institutional review committee for the use of human subjects.

2.1.1. Drug users

Drug users were recruited from drug treatment programs — almost exclusively (97%) inpatient or residential programs — in nine Iowa communities. They were reimbursed for participation. In an initial session conducted following admission and attenuation of major withdrawal effects (mean ± S.E. of 11.9 ± 0.3 days after subjects' last use of drugs and 9.4 ± 0.3 days after beginning treatment), information about subjects were collected in a structured interview using the Addiction Severity Index (McLellan et al., 1992), portions of the Quick Diagnostic Interview Schedule III-R (Marcus et al., 1991), and locally developed instruments that included additional questions concerning subjects' demographic characteristics and drug use, medical, legal, employment, educational, and childhood histories.

Subjects were 18–49 years old and had to have learned English before age 5, completed at least part of the tenth grade, and attended the fourth grade in Iowa so that fourth grade Iowa Tests of Basic Skills (Hieronymus et al., 1982) scores could be retrieved to attempt to measure premorbid cognitive function. Volunteers with serious, uncorrected visual or hearing problems or histories of schizophrenia, childhood mental retardation, or brain disease unrelated to drug use were excluded.

2.1.2. Controls

Control subjects were paid volunteers recruited by random digit telephone dialing, mailings, and advertisements. Volunteers were excluded if they had used any categories of illegal drugs in the last 30 days or more than nine times in their lifetime; had a history of dependence on alcohol or illegal drugs; or reported a year or more of regularly feeling the effects of alcohol, or having three or more alcoholic drinks per day on average in the last 2 years. In addition, volunteers had to meet the inclusion/exclusion criteria for drug users stipulated above.

Efforts were made to match the groups of drug users and controls on selected demographic characteristics (such as age and education) and psychiatric characteristics (current mood and anxiety disorders). This was done by periodically reviewing the characteristics of the subjects recruited to date and preferentially recruiting additional subjects whose inclusion would narrow any discrepancies between the groups. To justify our interpretation of fourth grade Iowa Test scores as measures of premorbid cognitive function, it was deemed important to match the groups on socioeconomic status (Stevens and Cho, 1985) of their parents during the subjects' childhood and percentages of Caucasians, because of the influence of socioeconomic factors on performance on such tests. The groups were successfully matched on a number of characteristics, as described in Section 3 (see Table 1). Because the drug users were highly atypical of the general population in several respects (e.g., disproportionately high percentages of men, minority group members, and individuals with mood and anxiety disorders), in order to match them with controls on a number of characteristics, it was not possible to also match them on gender. Therefore, gender was entered into the analyses as a statistical control.

Table 1
Demographic and psychiatric characteristics

	Completed first session		Completed first session			Completed second session		
	Controls	All drug users	Stimulant users	Alcohol users	Polydrug users	Controls	Abstinent drug users	Nonabstinent drug users
Continuous variables (means ± S.E.)								
Age (years) *	32.5 ± 0.7	32.8 ± 0.6	31.0 ± 1.0	35.5 ± 0.8	29.4 ± 1.3	32.9 ± 0.8	33.9 ± 1.1	32.9 ± 1.3
Education (years)	12.7 ± 0.1	12.5 ± 0.1	12.4 ± 0.2	12.6 ± 0.1	12.2 ± 0.2	12.7 ± 0.1	12.5 ± 0.2	12.6 ± 0.2
Parents' Duncan's socioeconomic index (Stevens and Cho, 1985)	33.9 ± 1.5	32.6 ± 1.2	34.1 ± 2.1	31.5 ± 1.7	32.6 ± 3.0	34.1 ± 1.6	32.7 ± 2.4	31.1 ± 2.8
Dichotomous variables (percentage)								
Men[†,‡,§]	50	75	59	85	73	50	83	70
Caucasian *	83	83	66	92	85	87	88	72
Current anxiety disorder	19	21	21	18	33	18	14	22
Current mood disorder[¶]	18	20	14	18	36	17	12	24

Of the drug users who completed the first session, 94% could be categorized based on their major problem drugs as stimulant, alcohol, or polydrug users and are listed in these categories above. See the text for discussion of this categorization and definitions of abstinent and nonabstinent drug users. Significant differences, evaluated by analyses of variance for continuous variables and Fisher's exact tests for dichotomous variables, are indicated as: controls and all drug users differ in first session, [†]$P<.001$; stimulant, alcohol, and polydrug users differ in first session, [¶]$P<.05$, [‡]$P<.01$, * $P<.001$; controls, abstinent drug users, and nonabstinent drug users differ in the second session, [§]$P<.001$.

2.2. First session

The first session was usually conducted 2–3 weeks after drug users' last use of drugs (17.1 ± 0.3 days on average). In this session, which lasted up to about 3 h and 15 min, subjects were administered standardized tests assessing basic, general intellectual skills, and abilities in verbal and mathematical areas, along with tests of abstraction ability and verbal memory.

2.2.1. Verbal and mathematical skills and abilities

Four tests from the eleventh/twelfth grade versions of the Iowa Tests of Educational Development, Level II (Iowa Testing Programs, 1987a,b), were administered. These were multiple-choice paper-and-pencil tests assessing reading comprehension (Ability to Interpret Literary Materials), verbal expression (Correctness and Appropriateness of Expression), mathematics (Ability to Do Quantitative Thinking), and vocabulary (Vocabulary) (Block and Ghoneim, 1993).

2.2.2. Abstraction ability

The computer-administered abstraction test, Concept Formation (Block and Ghoneim, 1993), involved schematic faces (Martin and Caramazza, 1980; Reed, 1972) with varying features. The subject studied a card depicting five members of each of two families. Then 20 new schematic faces, half from each family, were shown on the monitor and the subject tried to classify each into the correct family. This procedure was done twice. Of the two cards defining the families, one portrayed a well-defined concept and the other portrayed a "fuzzy" concept. Further procedural details have been described previously (Block and Ghoneim, 1993).

2.2.3. Verbal memory

The computer-administered memory test, Buschke's Test (Block and Ghoneim, 1993; Buschke, 1973), involved a list of 16 nouns, half of which were "high-imagery" words that were easy to visualize (e.g., "lemon" and "policeman") and the remainder "low-imagery" words (e.g., "fate" and "permission") (Paivio et al., 1968). The list was presented on the monitor. The subject recalled as many words as possible. Seven learning and test trials on the 16-word list were given consecutively. The subject tried to recall the whole list each time, but on learning trials after the first, the subject was reminded only of the words missed on the immediately preceding trial. This procedure allowed scoring of several aspects of memory, including total recall, long-term storage, short-term retrieval, long-term retrieval, and consistent long-term retrieval (Buschke, 1973). Further procedural details have been described previously (Block and Ghoneim, 1993).

2.3. Second session

Subjects participated in a second session, which took the same form as the first session. The second session was usually conducted 11–15 weeks after drug users' last use of drugs prior to beginning treatment (99.4 ± 1.7 days on average, disregarding relapses to drug use following the first session). The interval between the two sessions did not differ significantly between drug users and controls (means of 82.4 ± 1.7 and 86.1 ± 1.2 days, respectively).

2.4. Counterbalancing

Two alternate forms of each test were available, and their order of use in the two sessions was varied among subjects within each group. Two different orders of the tests within each session were used. Approximately equal numbers of subjects received each possible combination of orders of alternate forms, orders of tests within sessions, and orders of testing the well-defined and fuzzy concepts in Concept Formation. Subjects were assigned to these combinations based on randomized lists at the time of acceptance into the study.

Five of the tests were allocated to two parts of the test battery. One part included Ability to Interpret Literary Materials, followed by Correctness and Appropriateness of Expression. The other part included Concept Formation, Ability to Do Quantitative Thinking, and Buschke's Test, in the indicated order. The different orders of the tests within each session were defined by the order in which these two parts were administered. The Vocabulary test, which was expected to be the most resistant to effects of chronic drug use, was administered after completion of both parts and omitted if time was short.

2.5. Additional testing

Following the first and second sessions, some subjects with sufficient education were administered portions of the ACT Assessment (American College Testing Program, 1988) on subsequent days. These data will be reported separately.

2.6. Verification of abstinence

Urine specimens for drug screening were obtained, and breath tests for alcohol were conducted, during screening and the first and second sessions. Self-reports concerning drug use were obtained at the same times and during telephone interviews (up to four times between the first and second sessions). At the time of the first session, all drug users were abstinent and agreed to remain abstinent until the second session. However, they were tested in the second session even if they did not remain continuously abstinent between sessions, and were classified as continuously "abstinent" or as "nonabstinent." Subjects were classified as "nonabstinent" if they reported any use of alcohol or other drugs between sessions, or showed any positive urine screening or breath test. Subjects who showed acute drug effects or acknowledged recent drug use were excluded.

2.7. Categorization of drug users

Different categories of drug users were defined based on the Addiction Severity Index item, "Which substance is the major problem?" This categorization is denoted "major problem drugs" below. The subject was initially classified into one of 11 groups of drugs or two categories of polydrug use (i.e., with or without alcohol as one of the major problem drugs) by the interviewer after collection of a detailed drug use history. After examining the results of additional analyses (discussed below), three primary categories (stimulant, alcohol, and polydrug users), which included almost all drug users, were defined by pooling these groups together.

2.8. Statistical analyses

Matching of drug users and controls on demographic and psychiatric characteristics was checked by analyses of variance for continuous variables and Fisher's exact tests for dichotomous variables. Differences between groups in fourth grade Iowa Test scores were examined by analyses of covariance, controlling for gender. Similar analyses were done for other groupings, for example, to compare subjects who completed the second session to dropouts.

Test performance of drug users and controls in the first session was compared by analyses of covariance, controlling for intellectual ability before the onset of drug use (composite scores on the fourth grade Iowa Tests), gender, and which of the two alternate forms of each test was administered in the first session. Within-subjects factors included in the analyses of Buschke's Test and Concept Formation represented experimental manipulations, such as the imagery of the words and successive trials in Buschke's Test. Adjusted least-squares means were computed (SAS Institute, 1996).

Changes between the two sessions in subjects who completed the second session were examined by analyses similar to those described in the previous paragraph, but including session as an additional factor. Drug users were classified as "abstinent" or "nonabstinent," as defined above.

Analyses parallel to those described above were also conducted to compare different categories of drug users based on their major problem drugs (stimulant, alcohol, and polydrug users). Tukey tests on the adjusted least-squares means were done to determine which categories of drug users differed in performance from one another. Analyses comparing test performance of different categories of drug users controlled for differences among them in demographic and psychiatric characteristics.

Other supplementary analyses examined whether performance in the first session differed: (a) between subjects who completed the second session and dropouts; or (b) among drug users who completed the second session, between those who did and did not remain abstinent between sessions.

Stepwise discriminant analyses were done to examine differences among the different categories of drug users in usage of the 11 groups of drugs.

A significance level of $P < .05$ was used in all analyses.

3. Results

3.1. Demographic, psychiatric, and drug use characteristics

3.1.1. Drug users versus controls

The first session was completed by 192 drug users and 137 controls. The percentage of men was greater among the drug users than the controls. The two groups did not differ in mean age, education, or socioeconomic status (Stevens and Cho, 1985) of their parents during the subjects' childhood; percentages of Caucasians; or prevalences of current mood or anxiety disorders (Table 1, columns 2–3).

3.2. Major problem drugs

Of the 192 drug users, 94% ($n = 180$) could be classified into three primary categories according to their major problem drugs: 56 stimulant users (26 amphetamines and 30 cocaine), 91 alcohol users, and 33 polydrug users (12 with and 21 without alcohol). These three categories were used in analyzing effects of major problem drugs. The few remaining drug users (6%; $n = 12$) with other major problem drugs (marijuana, barbiturates, and opiates other than heroin and methadone) were omitted from these analyses. Stimulant, alcohol, and polydrug users differed in some characteristics (Table 1, columns 4–6). Alcohol users were older than stimulant and polydrug users, and included more men and Caucasians than stimulant users. The prevalence of mood disorders was lower among stimulant than polydrug users.

Table 2 compares stimulant, alcohol, and polydrug users on average days of use per 30-day period of each of 11 drug groups during the 2 years preceding abstinence. Stepwise discriminant analysis indicated that use of alcohol, cocaine, and amphetamines (in that order) provided the best discrimination among the groups, consistent with their definitions. The average squared canonical correlation for the final model was $r = .46$. Alcohol users showed very limited use of drugs other than alcohol. Stimulant and polydrug users both used a variety of drugs, but could be distinguished by the more frequent use of stimulants by the former and other drugs by the latter.

Table 2
Monthly days of drug use during past two years categorized by subjects' major problem drugs

Drug group	Entry probability	Alcohol users	Polydrug users	Stimulant users
Alcohol	*	21.2 ± 1.0	12.2 ± 1.9	6.4 ± 1.1
Cocaine	*	0.5 ± 0.2	4.7 ± 1.2	8.5 ± 1.5
Amphetamines	*	1.0 ± 0.4	7.8 ± 1.5	11.1 ± 1.8
Marijuana	*	3.5 ± 0.9	16.5 ± 2.2	9.6 ± 1.7
Opiates	*	†	2.5 ± 1.1	0.1 ± 0.1
Barbiturates	‡	†	0.2 ± 0.1	†
Methadone	‡	†	†	†
Sedatives	§	†	4.3 ± 1.6	0.9 ± 0.6
Inhalants	¶	†	0.6 ± 0.6	†
Heroin	¶	†	0.2 ± 0.2	†
Hallucinogens	¶	†	0.3 ± 0.2	0.1 ± 0.0
Sums				
Stimulants		1.5 ± 0.4	12.5 ± 1.7	19.6 ± 2.0
All drugs except stimulants and alcohol		3.5 ± 0.9	24.7 ± 3.2	10.7 ± 2.0

Means ± S.E. are shown. Collection of drug use information conformed to the classification by the Addiction Severity Index of drugs of abuse into 11 groups. The drug groups are listed in order of entry into a stepwise discriminant model (with $P < .05$ levels for variables to enter and leave the model), or, for those that did not enter, in order of probability level for entry at the final stage. "Opiates" includes opiates other than heroin and methadone. "Sedatives" includes sedatives, hypnotics, and tranquilizers other than barbiturates. Entry probability is indicated as: * $P < .001$; ‡ $P < .01$; § $P < .05$; or ¶ not significant. Monthly days of use under .05 are indicated by †. The two rows at the bottom summarize use of stimulants (cocaine and amphetamines combined) and all drugs other than stimulants and alcohol combined.

3.3. Subjects completing the study

The second session was completed by 204 subjects (62%). Subjects who completed the second session did not differ from dropouts in any of the demographic and psychiatric characteristics listed in Table 1 or in scores on the fourth grade Iowa Tests (data not shown). Of drug users who completed the second session, 58% were abstinent. Gender differed among controls, abstinent drug users, and nonabstinent drug users who completed the second session (Table 1, columns 7–9). However, this was attributable to the greater percentage of men among drug users than controls at the outset. Abstinent and nonabstinent drug users who completed the second session did not differ in gender or other demographic or psychiatric characteristics. Nor did they differ in fourth grade Iowa Test scores (data not shown). Stimulant, alcohol, and polydrug users did not differ in percentages who completed the second session, and those who completed the second session did not differ in percentages who were abstinent.

3.4. Missing data

Apart from dropouts, the only important source of missing data was the omission of the Vocabulary test depending on time constraints, discussed above (32% missing for analyzing drug users vs. controls in first session, and 46% missing for analyzing changes between sessions). Missing data for other variables were infrequent, averaging 3%.

3.5. Relationship of fourth grade Iowa Test scores to drug use

Although drug users had not begun to use drugs when they took the fourth grade Iowa Tests, they obtained poorer overall composite scores than controls ($P < .001$ for Drug Use effect), and performed poorer on each test: Vocabulary, Reading, Language, Work-Study Skills, and Mathematics (Fig. 1a; $P < .01$, $P < .001$, $P < .001$, $P < .001$, and $P < .01$, respectively). Thus, these measures of premorbid intellectual abilities were predictors of subsequent drug use. Stimulant, alcohol, and polydrug users did not differ in fourth grade Iowa Test scores (Fig. 1b).

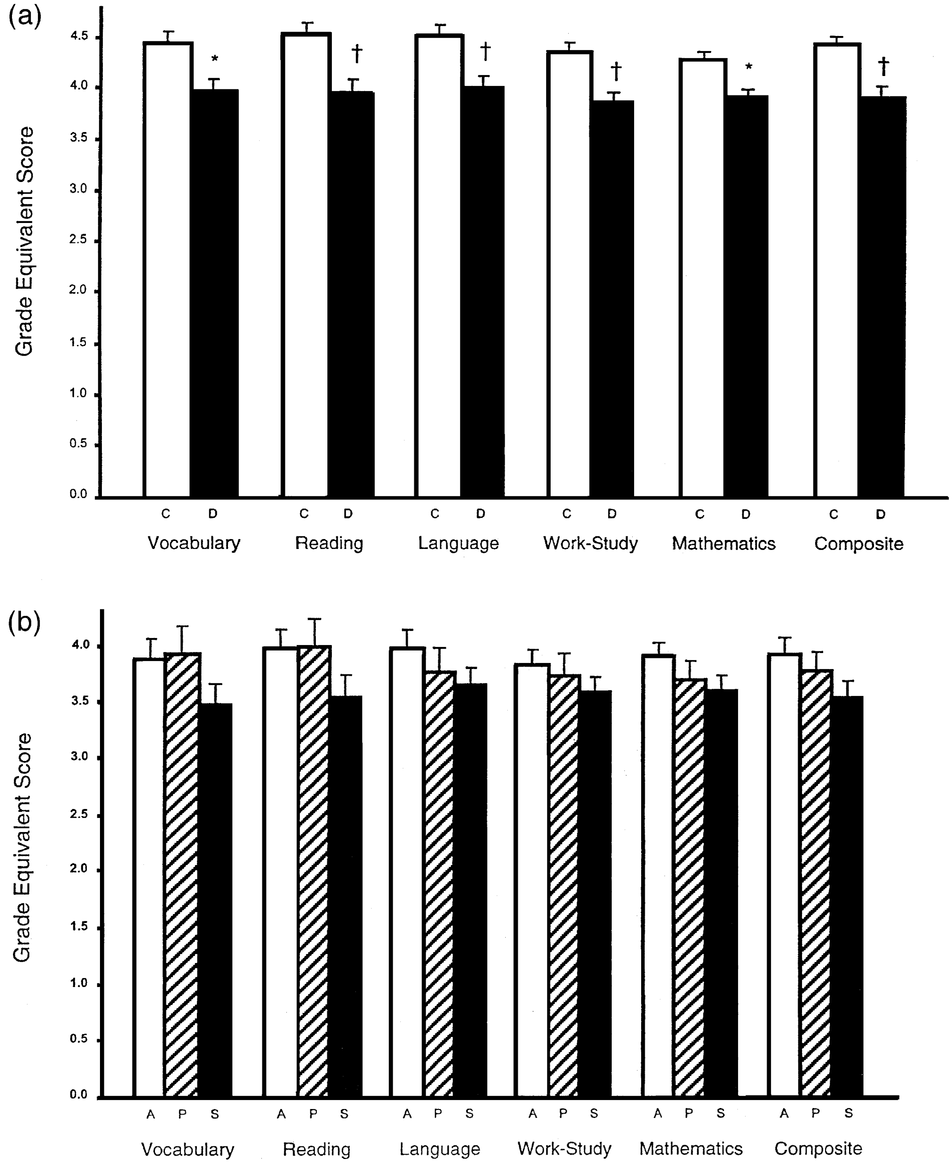

Fig. 1. Scores on the fourth grade Iowa Tests. Grade equivalent scores are shown. The values are adjusted least-squares means. Error bars indicate 1 S.E. (a) Drug users and controls. C = controls, D = drug users. $^{*}P<.01$, $^{\dagger}P<.001$ for Drug Use effect (see text). (b) Drug users classified according to their major problem drugs. A = alcohol users, P = polydrug users, S = stimulant users. No pairwise differences were significant.

3.6. First session

3.6.1. Verbal and mathematical skills and abilities

Fig. 2a shows first session performance of drug users and controls on the eleventh/twelfth grade Iowa Tests. The values shown in this and subsequent figures are adjusted for effects of fourth grade Iowa Test composite scores and gender. Drug users showed poorer performance than controls on each test ($P<.001$ for Drug Use effect for all tests). Thus, drug users were cognitively impaired early in the abstinence period, even while controlling for their poorer premorbid cognition.

Fig. 2b shows first session performance of stimulant, alcohol, and polydrug users on the eleventh/twelfth grade Iowa Tests. The groups differed on Ability to Interpret Literary Materials ($P<.001$ for Major Problem Drugs effect). Stimulant users performed poorer than both polydrug and alcohol users ($P<.001$ and $P<.01$, respectively, for Tukey tests). Polydrug and alcohol users did not differ from one another. On Correctness and Appropriateness of Expression, stimulant users performed poorer than polydrug users ($P<.05$ for Major Problem Drugs effect; $P<.05$ for Tukey test). No other pairwise differences were significant. Vocabulary showed a marginally significant difference ($P=.09$ for Major Problem Drugs effect) among groups, with a similar pattern. Ability to Do Quantitative Thinking did not show differences among groups.

3.6.2. Abstraction ability

Drug users made fewer correct responses than controls in Concept Formation (Fig. 3a; $P<.05$ for Drug Use

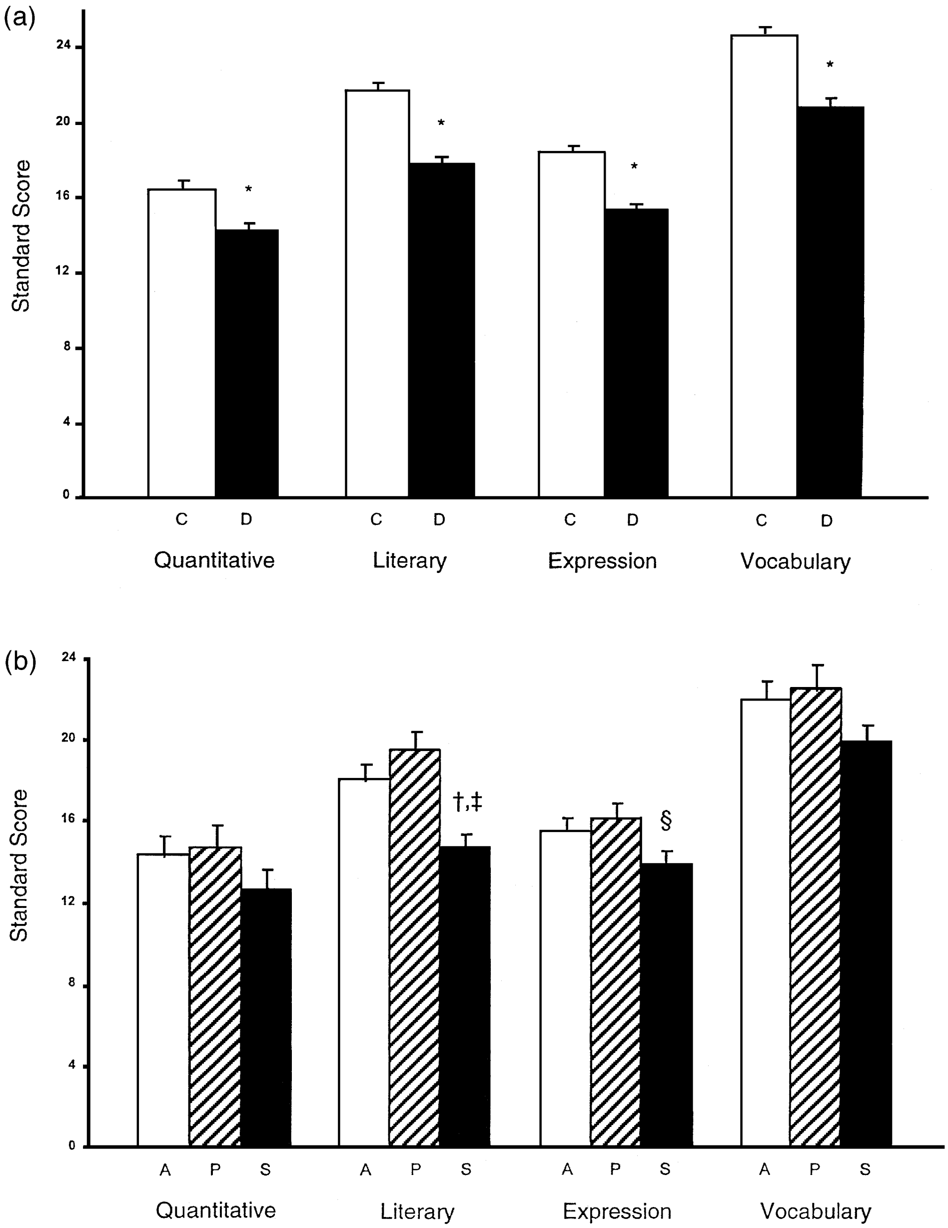

Fig. 2. Scores on the eleventh/twelfth grade Iowa Tests during the first session. Standard scores are shown. Quantitative = Ability to Do Quantitative Thinking, Literary = Ability to Interpret Literary Materials, Expression = Correctness and Appropriateness of Expression. The values are adjusted least-squares means. See Fig. 1 for abbreviations of the groups. Error bars indicate 1 S.E. (a) Drug users and controls. * $P < .001$ for Drug Use effect (see text). (b) Drug users classified according to their major problem drugs. † $P < .01$ for difference between stimulant and alcohol users; § $P < .05$, ‡ $P < .001$ for difference between stimulant and polydrug users (see text).

effect). Stimulant users performed poorer than polydrug users (Fig. 3b; $P < .05$ for Major Problem Drugs effect; $P < .05$ for Tukey test). No other pairwise differences were significant.

3.6.3. Verbal memory

In Buschke's Test, drug users, relative to controls, showed lower total recall, long-term storage, long-term retrieval, and consistent long-term retrieval (Fig. 4; $P < .01$, $P < .05$, $P < .01$, and $P < .01$, respectively, for Drug Use effects). The effects of drug use changed very little over trials. Both drug users and controls showed better performance with high- than low-imagery words, but the magnitudes of these imagery effects were smaller for drug users than controls (Fig. 4; $P < .05$, $P < .001$, $P < .001$, and $P < .001$ for Drug Use × Imagery effects for total recall, long-term storage, long-term retrieval, and consistent long-term retrieval, respectively; $P < .001$ for Imagery effects for all these variables). Drug users showed more impairment relative to controls for high- than low-imagery words.

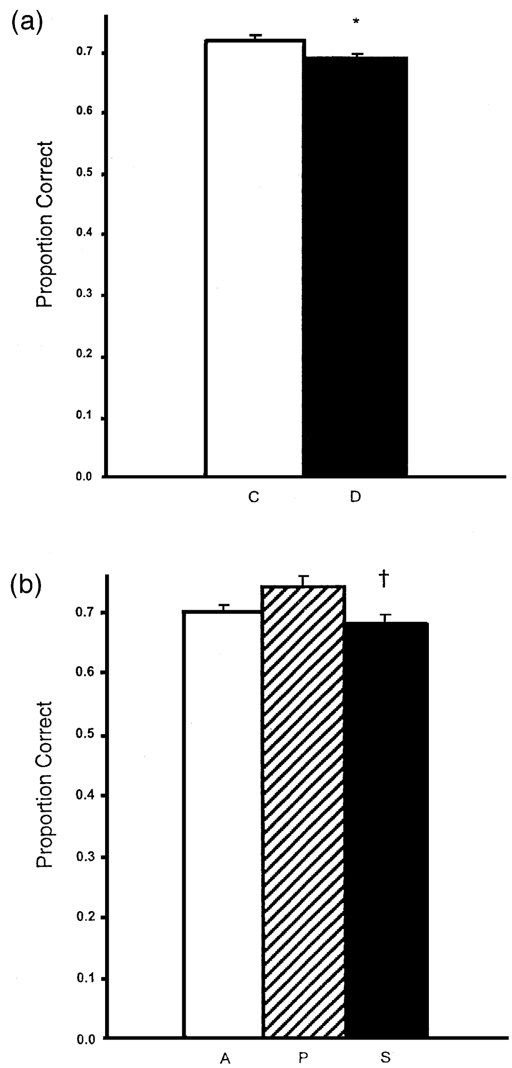

Fig. 3. Proportion correct in Concept Formation during the first session. The values are adjusted least-squares means, pooled over fuzzy and clear concepts (see text). See Fig. 1 for abbreviations of the groups. Error bars indicate 1 S.E. (a) Drug users and controls. * $P<.05$ for Drug Use effect (see text). (b) Drug users classified according to their major problem drugs. † $P<.05$ for difference between stimulant and polydrug users (see text).

Short-term retrieval showed a different pattern than other aspects of memory, being better for low- than high-imagery words, presumably because subjects relied more on short-term retrieval for low- than high-imagery words (Fig. 4; $P<.001$ for Imagery effect). Drug users appeared to partially compensate for their memory impairments by relying more on short-term retrieval. Their short-term retrieval scores exceeded those of controls for high, but not low, imagery words ($P<.001$ for Drug Use × Imagery effect).

Overall performance of stimulant, alcohol, and polydrug users did not differ in Buschke's Test (data not shown). However, the groups differed in magnitudes of the imagery effects for total recall, long-term storage, and long-term retrieval ($P<.05$, $P<.001$, and $P<.01$, respectively, for Major Problem Drugs × Imagery effects). Stimulant and alcohol users showed larger imagery effects than polydrug users. There was also an interaction between major problem drugs and imagery for short-term retrieval ($P<.05$); but, as noted above, short-term retrieval showed a different pattern than other aspects of memory.

3.6.4. Effects of demographic and psychiatric differences among groups

In the analyses comparing drug users and controls, gender differences occurred for Ability to Do Quantitative Thinking, Ability to Interpret Literary Materials, and Vocabulary ($P<.001$, $P<.01$, and $P<.05$, respectively), with men performing better than women. In contrast, men performed poorer than women for four aspects of memory in Buschke's Test — total recall, long-term retrieval, consistent long-term retrieval, and long-term storage ($P<.01$, $P<.01$, $P<.05$, and $P<.01$, respectively). In the analyses comparing stimulant, alcohol, and polydrug users, the only effects of the demographic and psychiatric characteristics that were controlled in the analyses because they differed among categories of drug users (Table 1) were that men performed better than women in Ability to Do Quantitative Thinking ($P<.001$), and that age affected performance in Concept Formation ($P<.05$), Vocabulary ($P<.001$), and three aspects of memory in Buschke's Test — total recall, long-term retrieval, and consistent long-term retrieval ($P<.05$ for all). Our analyses controlled for the overall effects of these characteristics in order to assess the effects of drug use more accurately; we did not examine all possible interactions of these characteristics with each other, drug use, or experimental manipulations within Buschke's Test and Concept Formation.

3.7. Changes between sessions

Changes in performance between sessions were compared among three groups — controls, abstinent drug users, and nonabstinent drug users.

3.7.1. Tests on which groups differed in changes between sessions

3.7.1.1. Abstraction ability. The groups differed in changes in proportion correct in Concept Formation between sessions (Table 3; $P<.05$ for Group × Session effect). Proportion correct declined between sessions for nonabstinent drug users, whereas there was no change between sessions for controls and abstinent drug users.

3.7.1.2. Verbal memory. The groups differed in changes in Buschke's Test between sessions in total recall, long-term storage, long-term retrieval, and consistent long-term retrieval (Fig. 5; $P<.001$ for all Group × Session effects). Improvements between sessions were greater for abstinent drug users than controls or nonabstinent drug users.

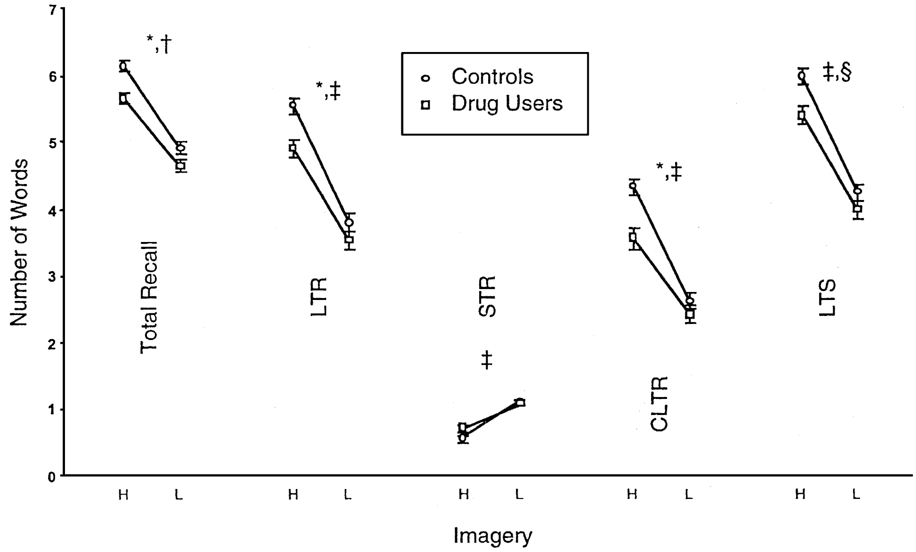

Fig. 4. Buschke's Test scores during the first session for high- and low-imagery words. Scores for total recall and four aspects of memory are shown. The values are adjusted least-squares means for numbers of words (maximum = 8), pooled over trials, and calculated separately for high- and low-imagery words. LTR = long-term retrieval, STR = short-term retrieval, CLTR = consistent long-term retrieval, LTS = long-term storage, H = high-imagery words, L = low-imagery words. Error bars indicate 1 S.E. Circles and squares represent controls and Drug Users, respectively. §$P<.05$, * $P<.01$ for drug use effect; †$P<.05$, ‡$P<.001$ for Drug Use × Imagery effect (see text).

The groups also differed in changes between sessions in short-term retrieval ($P<.001$ for Group × Session effect); but, as in other analyses, the pattern differed from that for other aspects of memory.

3.7.2. Tests on which groups did not differ in changes between sessions.

3.7.2.1. Verbal and mathematical skills and abilities. The eleventh/twelfth grade Iowa Tests showed no differences among groups in changes between sessions (Table 3). Scores on Ability to Interpret Literary Materials showed an overall decline between sessions ($P<.05$ for Session effect), while scores on the other tests showed no overall change.

3.8. Supplementary analyses

Factors that might be related to changes between sessions were examined in additional analyses. Initial cognitive status was somewhat predictive of continuous abstinence through the second session. Poorer performance in Concept Formation in the first session was a predictor of subsequent abstinence (Table 3; $P<.05$ for Abstinence effect), as were slower improvements over successive trials in some aspects of memory in Buschke's Test in the first session ($P<.01$, $P<.001$, and $P<.01$, respectively, for Abstinence × Trial effects for long-term retrieval, consistent long-term retrieval, and long-term storage).

Differences between abstinent and nonabstinent drug users in changes between sessions varied only incon-

Table 3
Changes between sessions of subjects who completed the second session

Test	Controls		Abstinent drug users		Nonabstinent drug users	
	First session	Second session	First session	Second session	First session	Second session
Concept Formation (proportion correct)*	0.72 ± 0.01	0.73 ± 0.01	0.67 ± 0.02	0.66 ± 0.02	0.73 ± 0.02	0.69 ± 0.02
Eleventh/twelfth grade Iowa Tests (standard scores)						
Ability to Do Quantitative Thinking	18.6 ± 0.6	18.4 ± 0.6	14.3 ± 0.9	15.3 ± 0.9	16.1 ± 1.0	15.1 ± 1.0
Ability to Interpret Literary Materials†	22.0 ± 0.5	21.4 ± 0.5	18.5 ± 0.8	16.2 ± 0.8	18.0 ± 1.0	17.4 ± 1.0
Correctness and Appropriateness of Expression	18.9 ± 0.4	18.7 ± 0.4	15.3 ± 0.7	16.0 ± 0.7	16.3 ± 0.8	15.9 ± 0.8
Vocabulary	25.1 ± 0.8	24.7 ± 0.8	22.2 ± 1.0	21.1 ± 1.0	21.1 ± 1.2	22.1 ± 1.2

Means ± S.E. are shown. See the text for definitions of abstinent and nonabstinent drug users. Changes between sessions shown by analyses of covariance and described in the text are represented as: * difference among groups in changes between sessions ($P<.05$), attributable to a decline between sessions for nonabstinent drug users, contrasting with no change between sessions for the other groups; †overall decline between sessions ($P<.05$), which did not differ among groups.

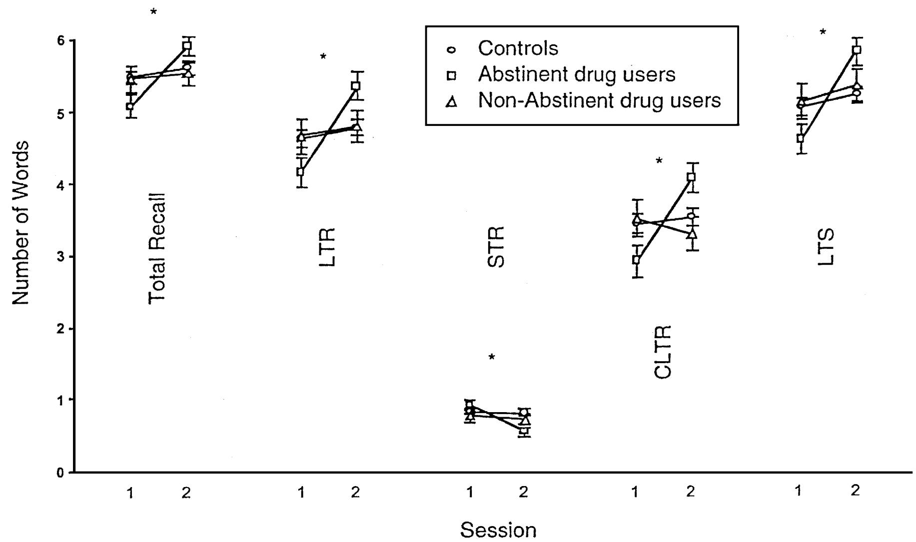

Fig. 5. Buschke's Test scores during the first and second sessions. Scores for total recall and four aspects of memory are shown. The values are adjusted least-squares means for numbers of words (maximum = 8), pooled over trials and high and low imagery words. 1 = first session, 2 = second session. See Fig. 4 for abbreviations of the memory scores. Error bars indicate 1 S.E. Circles, squares, and triangles represent controls, abstinent drug users, and nonabstinent drug users, respectively. See the text for definitions of abstinent and nonabstinent drug users. * $P < .001$ for Group × Session effect (see text).

sequentially among stimulant, alcohol, and polydrug users. There were no overall differences in first session performance between subjects who completed the second session and dropouts.

To increase group sizes, amphetamine and cocaine users were pooled in the analyses, as were polydrug users with and without alcohol as one of their major problem drugs. This pooling was appropriate because cognitive differences between the pooled subgroups were inconsequential. Analyses of covariance of performance in the first session showed no differences between the two subgroups of stimulant users or between the two subgroups of polydrug users. These analyses controlled for some differences between subgroups that were observed in the demographic and psychiatric characteristics listed in Table 1. For example, amphetamine users were younger than cocaine users, and more were Caucasian. Fourth grade Iowa Test composite scores did not differ between the two subgroups of stimulant users or between the two subgroups of polydrug users.

In analyses comparable to those shown in Table 1, several dichotomous characteristics related to early childhood and school experiences showed no significant differences among groups. Drug users and controls who completed the first session did not differ with respect to growing up in a home in which a language other than English was spoken; ever being evaluated for hyperactivity or learning, speech, or related problems; ever attending any special schools or special education classes all day long; or being required to repeat any grades in school. Thus, the poorer fourth grade Iowa Test scores of drug users, relative to controls, were not associated with differences in these other characteristics. These characteristics also showed no differences among stimulant, alcohol, and polydrug users who completed the first session; or among controls, abstinent drug users, and nonabstinent drug users who completed the second session.

4. Discussion

Early in the abstinence period, drug users showed impairments, relative to controls, in all the achievement, memory, and abstraction tests. These impairments were significant even while controlling for differences between drug users and controls in mental abilities during the fourth grade, before the drug users started using drugs. The greatest distinction of the present study from previous ones was its use of historical records of test scores to control for premorbid cognitive function. Other studies have used several methods to estimate premorbid cognitive function. One study (Beatty et al., 1995) used the Barona IQ, a method that predicts IQ from various demographic indices. Another study (Berry et al., 1993) used the New Adult Reading Test-Revised, whereas three studies (McKetin and Mattick, 1997, 1998; McKetin and Solowij, 1999) used both the New Adult Reading Test and the WAIS-R vocabulary subtest to estimate premorbid intelligence. However, these procedures have limited validity as estimates of premorbid intelligence.

We found that drug users performed poorer than controls in all the achievement tests administered during the fourth grade, suggesting that poorer intellectual abilities may be a predictor, as well as a consequence, of drug use. Performance on tests such as these is influenced by socioeconomic factors, but drug users and controls did not differ in the socioeconomic status (Stevens and Cho, 1985) of their parents during the subjects' childhood or percentages of Caucasians (Table 1), justifying our interpretation of the test scores as measures of premorbid intellectual abilities.

Our finding that poorer intellectual abilities may be a predictor of drug use implies that some of the cognitive impairments in drug users, relative to controls, which have been reported by other researchers, may have been due at least partially to premorbid differences. On the other hand, there have been some surprising reports of superior current performance on certain cognitive tests in some stimulant users relative to controls (Bolla et al., 1999; Hoff et al., 1996; Manschreck et al., 1990; McKetin and Mattick, 1998; O'Malley et al., 1992). In the absence of data on premorbid abilities, certain procedures for recruiting drug users and controls could conceivably lead to a bias in the direction of superior premorbid intellectual abilities in drug users, which could result in superior current performance on some tests. For example, such a bias might arise if drug users were intentionally or unintentionally matched with controls on some current characteristic that was positively associated with premorbid intellectual abilities, but negatively associated with drug use.

Early in the abstinence period in our study, stimulant users performed worse on several tests relative to the other drug use groups. Stimulant users performed worse than polydrug users on achievement tests that measured reading comprehension and recognition of appropriate forms of written expression, as well as a test of abstraction. Stimulant users also performed worse than alcohol users on reading comprehension.

To provide adequate power for our overall analyses comparing different categories of drug users, we pooled our cocaine and amphetamine users, inasmuch as analyses of covariance of performance in the first session showed no differences between them, and they did not differ in fourth grade Iowa Test composite scores. Future studies with larger samples of cocaine and amphetamine users should test for subtle differences in the cognitive effects of cocaine and amphetamine use, as well as separately comparing cocaine users and amphetamine users with users of other categories of drugs.

Most previous studies comparing stimulant users and users of other drugs have focused on cocaine users. Our findings that stimulant users showed some cognitive deficits relative to polydrug and alcohol users are consistent in the direction of differences with previous reports that cocaine users performed worse than polydrug users on several WAIS subtests (Robinson et al., 1999; Rosselli and Ardila, 1996) and worse than alcohol users with respect to attention (Bauer, 1996), memory (Beatty et al., 1995), intellectual ability (Beatty et al., 1995), and reaction time (Bauer, 1994). In contrast, one study (Selby and Azrin, 1998) found that cocaine users performed better than both polydrug and alcohol users on some tests.

Fewer cognitive studies have compared amphetamine users and users of other drugs. Studies comparing cognition of amphetamine and opiate users produced mixed results (Ornstein et al., 2000; Rogers et al., 1999). Users of 3,4-methylenedioxymethamphetamine, compared to polydrug users who had not used it, showed impairments on some tests but not others (Morgan, 1998, 1999). We observed no cognitive differences between polydrug and alcohol users, whereas previous studies reported that polydrug users performed worse than alcohol users on measures of memory, spatial abilities, and visual motor abilities (Beatty et al., 1997; Horner, 1997; Selby and Azrin, 1998).

The lack of any direct measures of premorbid intellectual abilities in past studies comparing different groups of drug users, variations among studies in the tests that were used, and the use of a special population (prisoners) in one study (Selby and Azrin, 1998) may contribute to differences in findings. The greater severity of cognitive impairments in stimulant users than polydrug or alcohol users in the present study, while controlling for premorbid intellectual abilities, could be due to distinctive patterns of impairments in brain function produced by use of different drugs. Neuroimaging studies would be desirable to seek direct evidence.

Over the period of about 3 months that we followed subjects, improvement in abstinent drug users relative to controls was observed in only one of six tests, Buschke's Test. This suggests that some of the drug-induced memory impairment may be transient and associated with withdrawal, but that many of the cognitive impairments associated with drug use may outlast the primary withdrawal period and may reflect persisting changes in brain function due to drug use. (An alternative interpretation, that some of the persisting changes in drug users could be due to failure to have acquired certain cognitive skills and abilities, is discussed in Section 4.1).

The abstraction test, Concept Formation, also showed a difference among groups in changes over time. Performance of nonabstinent drug users became worse between sessions, which might possibly have been related to their resumption of drug use. However, there was no change between sessions for abstinent drug users or controls; abstaining from drug use did not lead to recovery of abstraction ability.

A longstanding viewpoint characterizes the abilities assessed by tests as falling along a continuum from "fluid" to "crystallized" (Cronbach, 1970, pp. 240, 281–282). Verbal and mathematical skills and abilities fall closer to the "crystallized" end than verbal memory and abstraction ability, because they rely relatively more on utilization of previously acquired information, including learning in school. Our finding that verbal memory and abstraction ability showed differences among groups in changes over time, whereas verbal and mathematical skills and abilities did not, may conceivably indicate that fluid abilities are more susceptible than crystallized abilities to change in drug users. However, this would not explain why verbal memory showed improvement in abstinent drug users, relative to controls, whereas abstraction ability did not. The differing changes over time in our memory and abstraction tests could reflect true differences in recovery of memory and abstraction ability following abstinence, or could be related to other differences between our specific tests, such as the greater importance of nonverbal elements in the abstraction test than the memory test.

Our finding of a lack of improvement in five of six tests over an abstinence period of about 3 months is consistent with several other studies of illegal drug users. Reaction time measures in attention tests showed no improvement in cocaine users over approximately 3 months of abstinence (Bauer, 1994, 1996); in another study, abstinent cocaine users' reaction times became slower, if anything, relative to controls, over a similar time period (Roberts and Bauer, 1993). Results from repeated tests of cocaine users earlier in the abstinence period were no more encouraging with respect to improvement (Berry et al., 1993). One study reported that cocaine users had scores in the normal range on tests of abstraction, attention, and memory after an average of 4 months of abstinence (O'Malley and Gawin, 1990); however, it is not clear whether these subjects improved during abstinence because they were not tested earlier in the abstinence period. Another study (Brown et al., 1994), which showed improvement in both polydrug and alcohol users over 4 weeks of treatment in performance on subtests of the WAIS, was limited by the lack of control for practice effects (i.e., absence of a control group), as well as inclusion of some users who relapsed. The most comprehensive previous series of studies of polydrug users showed improvements in neuropsychological functioning in some individuals, but a predominant pattern of persisting impairments after abstinence periods of 3 months (Grant et al., 1978) or 3–5 months (Judd et al., 1978).

More studies have examined cognitive recovery with abstinence for alcohol than other drugs, and the alcohol studies have provided generally more positive, albeit still mixed, findings (Parsons, 1987). Our finding in alcohol users (as well as stimulant and polydrug users) of memory improvement over an abstinence period of about 3 months, together with a lack of improvement in other tests, is generally consistent with this mixed pattern of findings in the literature. Our finding that these memory improvements involved long-term storage and retrieval, rather than short-term retrieval, contrasts with some evidence that recovery of memory with more prolonged abstinence in alcoholics is greater for short-term than long-term memory (Brandt et al., 1983). However, findings in the literature are mixed; another study that involved extensive memory testing observed no differences of long-term abstinent alcoholics from controls (Reed et al., 1992).

The long-term memory deficits in drug users early in the abstinence period were influenced by word imagery. Drug users, relative to controls, showed reduced imagery effects and more impairment for high- than low-imagery words. This pattern could reflect decreased or slowed development of elaborated memory representations among drug users, and is reminiscent of our previous findings using Buschke's Test with heavy, chronic marijuana users (Block and Ghoneim, 1993) and volunteers experiencing acute effects of benzodiazepines (Block and Berchou, 1984). Another observation in the present study — the tendency for short-term retrieval, compared to the long-term memory measures, to show different and somewhat compensatory changes associated with drug use — is also reminiscent of patterns in these previous studies.

4.1. Limitations

Our study had several limitations. Although the Iowa Tests used to measure premorbid cognitive functioning in the fourth grade show substantial correlations with eleventh/twelfth grade Iowa Test results (Block and Ghoneim, 1993), indicating the value of controlling for premorbid intellectual abilities, their value in this respect would be smaller for the tests of memory and concept formation, which assess distinct mental abilities. Our measure of premorbid cognitive functioning may not have been sensitive to other subtle premorbid cognitive differences between drug users and controls. Such subtle differences would then not have been controlled in our statistical analyses, and might have been partly responsible for the differences between groups in current cognitive functioning.

Furthermore, other premorbid noncognitive differences, which were not controlled could conceivably be responsible for the observed cognitive differences between groups. We matched drug users and controls on several demographic and psychiatric characteristics, and the one remaining major difference between groups, gender, was controlled statistically. Matching of drug users and controls on parental socioeconomic status during the subjects' childhood and percentages of Caucasians ameliorates concerns about interpreting the fourth grade Iowa Test scores as indicators of premorbid intellectual functioning, which might arise because of the influence of socioeconomic factors on performance on such tests. Differences among the groups of drug users in demographic and psychiatric characteristics were also controlled statistically. Nevertheless, more complete matching would have been ideal. These considerations illustrate some of the limitations of using premorbid intellectual abilities as a covariate; other, more general limitations of analysis of covariance are considered elsewhere (Adams et al., 1985; Jamieson, 1999; Winer, 1971, p. 753).

Impediments to cognitive development in the drug users that occurred following administration of the tests that provided our measure of premorbid cognitive functioning, but that were not directly caused by drug use, could also conceivably be responsible for the observed cognitive differences between drug users and controls. Children with lower cognitive function might have experienced negative feedback and labeling in school, and become increasingly alienated from school and study, particularly as they reached puberty. This could have resulted in increasing cognitive deficits over time, as well as dropping out of high school [in matching drug users and controls on education, we followed the standard convention, adopted by the Addiction Severity Index (McLellan et al., 1992), of counting a high school equivalency diploma as equal to 12 years of education]. This scenario could more plausibly explain the observed cognitive differences between groups for the tests that emphasized relatively more crystallized, as opposed to fluid, skills, and abilities. For tests that emphasized more crystallized skills and abilities, one might attribute the failure of the abstinent drug users to improve relative to the controls over the period of about 3 months that we followed subjects to a failure by the drug users to have acquired certain relevant cognitive skills and abilities in the first place. This would be an alternative to attributing their failure to improve to persisting changes in brain function due to drug use.

The groups of drug users were defined based on subjects' major problem drugs and did not capture the full spectrum of drug use. Stimulant users consumed other drugs, and polydrug users consumed stimulants, to varying degrees. Both groups used considerable marijuana. We previously reported that heavy, chronic users of marijuana (who were not in treatment) showed some cognitive deficits (Block and Ghoneim, 1993). In the present study, marijuana was the major problem drug for only 5% of drug users, too few to include it in our analyses based on major problem drugs.

5. Conclusion

Drug users showed impairments relative to controls on the memory, abstraction, and achievement tests that were administered. These impairments may reflect persisting changes in brain function associated with chronic drug use; after about 3 months of abstinence, recovery was evident on only one of six tests. Thus, chronic drug use is associated with cognitive impairments that do not improve substantially even after several months of abstinence. Chronic stimulant use may have particularly deleterious effects on cognition. Because drug users also showed cognitive impairments relative to controls before the onset of drug use, it is imperative to control for premorbid abilities in studies analyzing drug use and cognition.

Acknowledgments

This study was supported in part by the National Institute on Drug Abuse grant R01 DA03988. We wish to express our gratitude to C.K. Brown for the assistance with statistical analyses.

References

Adams KM, Brown GG, Grant I. Analysis of covariance as a remedy for demographic mismatch of research subject groups: some sobering simulations. J Clin Exp Neuropsychol 1985;7:445–62.

American College Testing Program. ACT assessment program technical manual. Iowa City (IA): American College Testing Program, 1988.

Ardila A, Rosselli M, Strumwasser S. Neuropsychological deficits in chronic cocaine abusers. Int J Neurosci 1991;57:73–9.

Bauer LO. Vigilance in recovering cocaine-dependent and alcohol-dependent patients: a prospective study. Addict Behav 1994;19:599–607.

Bauer LO. Psychomotor and electroencephalographic sequelae of cocaine dependence. In: Majewska MD, editor. Neurotoxicity and neuropathology associated with cocaine abuse. NIDA Res Monogr Ser, vol. 163. Rockville (MD): National Institute on Drug, 1996. p. 66–93.

Beatty WW, Katzung VM, Moreland VJ, Nixon SJ. Neuropsychological performance of recently abstinent alcoholics and cocaine abusers. Drug Alcohol Depend 1995;37:247–53.

Beatty WW, Blanco CR, Hames KA, Nixon SJ. Spatial cognition in alcoholics: influence of concurrent abuse of other drugs. Drug Alcohol Depend 1997;44:167–74.

Berry J, van Gorp WG, Herzberg DS, Hinkin C, Boone K, Steinman L, Wilkins JN. Neuropsychological deficits in abstinent cocaine abusers: preliminary findings after two weeks of abstinence. Drug Alcohol Depend 1993;32:231–7.

Block RI, Berchou R. Alprazolam and lorazepam effects on memory acquisition and retrieval processes. Pharmacol Biochem Behav 1984;20: 233–41.

Block RI, Ghoneim MM. Effects of chronic marijuana use on human cognition. Psychopharmacology 1993;110:219–28.

Bolla KI, Rothman R, Cadet JL. Dose-related neurobehavioral effects of chronic cocaine use. J Neuropsychiatry Clin Neurosci 1999;11:361–9.

Brandt J, Butters N, Ryan C, Bayog R. Cognitive loss and recovery in long-term alcohol abusers. Arch Gen Psychiatry 1983;40:435–42.

Brown TG, Seraganian P, Tremblay J. Alcoholics also dependent on cocaine in treatment: do they differ from "pure" alcoholics? Addict Behav 1994;19:105–12.

Buschke H. Selective reminding for analysis of memory and learning. J Verbal Learn Verbal Behav 1973;12:543–50.

Cronbach LJ. Essentials of psychological testing. 3rd ed. New York: Harper and Row, 1970.

Dafters RI, Duffy F, O'Donnell PJ, Bouquet C. Level of use of 3,4-methylenedioxymethamphetamine (MDMA or Ecstasy) in humans correlates with EEG power and coherence. Psychopharmacology 1999;145:82–90.

Gillen RW, Kranzler HR, Bauer LO, Burleson JA, Samarel D, Morrison DJ. Neuropsychologic findings in cocaine-dependent outpatients. Prog Neuropsychopharmacol Biol Psychiatry 1998;22:1061–76.

Grant I, Adams KM, Carlin AS, Rennick PM, Judd LL, Schooff K, Reed R. Neuropsychological effects of polydrug abuse. In: Wesson DR, Carlin AS, Adams KM, Beschner G, editors. Polydrug abuse: the results of a national collaborative study. New York (NY): Academic, 1978. p. 223–61.

Hieronymus AN, Lindquist EF, Hoover HD. Manual for school administrators, Iowa Tests of Basic Skills. Chicago: Riverside Publishing, 1982.

Hoff AL, Riordan H, Morris L, Cestaro V, Wieneke M, Alpert R, Wang GJ, Volkow N. Effects of crack cocaine on neurocognitive function. Psychiatry Res 1996;60:167–76.

Horner MD. Cognitive functioning in alcoholic patients with and without cocaine dependence. Arch Clin Neuropsychol 1997;12:667–76.

Iowa Testing Programs. ITED examiner's manual. Directions for testing, Iowa Tests of Educational Development, forms X-8 and Y-8. Iowa City (IA): Iowa Testing Programs, 1987a.

Iowa Testing Programs. ITED manual for teachers, administrators, and counselors, Forms X-8 and Y-8. Iowa City (IA): Iowa Testing Programs, 1987b.

Jamieson J. Dealing with baseline differences: two principles and two dilemmas. Int J Psychophysiol 1999;31:155–61.

Judd LL, Grant I, Bickford RG, Lee WG. Comparison of results from serially collected neuropsychological and EEG data. In: Wesson DR, Carlin AS, Adams KM, Beschner G, editors. Polydrug abuse: the results of a national collaborative study. New York (NY): Academic Press, 1978. p. 273–97.

Krystal JH, Price LH. Chronic 3,4-methylenedioxymethamphetamine (MDMA) use: effects on mood and neuropsychological function? Am J Drug Alcohol Abuse 1992;18:331–41.

Manschreck TC, Schneyer ML, Weisstein CC, Laughery J, Rosenthal J, Celada T, Berner J. Free base cocaine and memory. Compr Psychiatry 1990;31:369–75.

Marcus S, Robins LN, Bucholz K. Quick diagnostic interview schedule III-R. St. Louis (MO): Washington University School of Medicine, 1991.

Martin RC, Caramazza A. Classification in well-defined and ill-defined categories: evidence for common processing strategies. J Exp Psychol Gen 1980;109:320–53.

McKetin R, Mattick RP. Attention and memory in illicit amphetamine users. Drug Alcohol Depend 1997;48:235–42.

McKetin R, Mattick RP. Attention and memory in illicit amphetamine users: comparison with non-drug-using controls. Drug Alcohol Depend 1998;50:181–4.

McKetin R, Solowij N. Event-related potential indices of auditory selective attention in dependent amphetamine users. Biol Psychiatry 1999;45:1488–97.

McLellan AT, Kushner H, Metzger D, Peters R, Smith I, Grissom G, Pettinati H, Argeriou M. The fifth edition of the Addiction Severity Index. J Subst Abuse Treat 1992;9:199–213.

Mittenberg W, Motta S. Effects of chronic cocaine abuse on memory and learning. Arch Clin Neuropsychol 1993;8:477–83.

Morgan MJ. Recreational use of "ecstasy" (MDMA) is associated with elevated impulsivity. Neuropsychopharmacology 1998;19:252–64.

Morgan MJ. Memory deficits associated with recreational use of "ecstasy" (MDMA). Psychopharmacology 1999;141:30–6.

O'Malley SS, Gawin FH. Abstinence symptomatology and neuropsychological impairment in chronic cocaine abusers. In: Spencer JW, Boren JJ, editors. Residual effects of abused drugs on behavior. NIDA Res Monogr Ser, vol. 101. Rockville (MD): National Institute on Drug, 1990. p. 179–90.

O'Malley S, Adamse M, Heaton RK, Gawin FH. Neuropsychological impairment in chronic cocaine abusers. Am J Drug Alcohol Abuse 1992;18:131–44.

Ornstein TJ, Iddon JL, Baldacchino AM, Sahakian BJ, London M, Everitt BJ, Robbins TW. Profiles of cognitive dysfunction in chronic amphetamine and heroin abusers. Neuropsychopharmacology 2000;23:113–26.

Paivio A, Yuille JC, Madigan SA. Concreteness, imagery, and meaningfulness values for 925 nouns. J Exp Psychol Suppl 1968;76:1–25.

Parsons OA. Neuropsychological consequences of alcohol abuse: many questions—some answers. In: Parsons OA, Butters N, Nathan PE, editors. Neuropsychology of alcoholism: implications for diagnosis and treatment. New York (NY): Guilford, 1987. p. 153–75.

Reed SK. Pattern recognition and categorization. Cognit Psychol 1972;3:382–407.

Reed RJ, Grant I, Rourke SB. Long-term abstinent alcoholics have normal memory. Alcohol Clin Exp Res 1992;16:677–83.

Roberts LA, Bauer LO. Reaction time during cocaine versus alcohol withdrawal: longitudinal measures of visual and auditory suppression. Psychiatry Res 1993;46:229–37.

Robinson JE, Heaton RK, O'Malley SS. Neuropsychological functioning in cocaine abusers with and without alcohol dependence. J Int Neuropsychol Soc 1999;5:10–9.

Rogers RD, Everitt BJ, Baldacchino A, Blackshaw AJ, Swainson R, Wynne K, Baker NB, Hunter J, Carthy T, Booker E, London M, Deakin JF, Sahakian BJ, Robbins TW. Dissociable deficits in the decision-making cognition of chronic amphetamine abusers, opiate abusers, patients with focal damage to prefrontal cortex, and tryptophan-depleted normal volunteers: evidence for monoaminergic mechanisms. Neuropsychopharmacology 1999;20:322–39.

Rosselli M, Ardila A. Cognitive effects of cocaine and polydrug abuse. J Clin Exp Neuropsychol 1996;18:122–35.

SAS Institute. SAS/STAT® software: changes and enhancements through release 6.11. Cary (NC): SAS Institute, 1996. p. 556–60.

Schuckit MA. Drug and alcohol abuse: a clinical guide to diagnosis and treatment. 5th ed. New York: Kluwer Academic/Plenum, 2000.

Selby MJ, Azrin RL. Neuropsychological functioning in drug abusers. Drug Alcohol Depend 1998;50:39–45.

Stevens G, Cho JH. Socioeconomic indexes and the new 1980 census occupational classification scheme. Soc Sci Res 1985;14:142–68.

Strickland TL, Mena I, Villanueva-Meyer J, Miller BL, Cummings J, Mehringer CM, Satz P, Myers H. Cerebral perfusion and neuropsychological consequences of chronic cocaine use. J Neuropsychiatry Clin Neurosci 1993;5:419–27.

Winer BJ. Statistical principles in experimental design. 2nd ed. New York (NY): McGraw-Hill, 1971.