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Working memory subsystems are impaired in chronic drug dependents

Soliman AM, Gadelrab HF, Elfar RM. Working memory subsystems are impaired in chronic drug dependents.

Background: A large body of research that has investigated substance dependence and working memory (WM) resources, yet no prior study has used a comprehensive test battery to examine the impact of chronic drug dependence on WM as a multi-component system.
Objectives: This study examined the efficiency of several WM components in participants who were chronic drug dependents. In addition, the functioning of the four WM components was compared among dependents of various types of drugs.
Method: In total, 128 chronic drug dependents participated in this study. Their average age was 38.48 years, and they were classified into four drug-dependence groups. Chronic drug dependents were compared with a 36-participant control group that had a mean age of 37.6 years. A WM test battery that comprised eight tests and that assessed each of four WM components was administered to each participant.
Results: Compared with the control group, all four groups of drug dependents had significantly poorer test performance on all of the WM tasks. Among the four groups of drug users, the polydrug group had the poorest performance scores on each of the eight tasks, and the performance scores of the marijuana group were the least affected. Finally, the forward digit span task and the logical memory tasks were less sensitive than other tasks when differentiating between marijuana users and the normal participants.
Conclusion: The four components of WM are impaired among chronic drug dependents. These results have implications for the development of tools, classification methods and therapeutic strategies for drug dependents.

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Keywords: drug dependence; verbal; visuospatial working memory; working memory

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Significant outcomes

- Compared with drug-free participants, drug dependents had functional impairments in all of the working memory (WM) components that we tested.
- Among the groups of drug dependents that we studied (heroin, cocaine, marijuana and polydrug users), polydrug dependents had the most severe performance impairments in tests of the four WM components that we studied compared with the test results of drug-free participants.
- The type of drug dependence in which an individual engages has a differential and negative impact on the functioning of WM components.

Limitations

- Causality cannot be inferred from our cross-sectional data. Thus, we cannot conclude that drug dependence causes the impairment of WM.
- The findings of this study are limited to chronic drug dependents who used certain types of drugs for prolonged periods of time.
- Interpretation of the non-significant differences between the marijuana users and the drug-free participants in our study that were observed in tests of specific WM components should be made with caution.

Introduction

WM plays a key role in the service of performing complex cognitive tasks by means of maintaining and processing various types of information (i.e. verbal and visuospatial). Previous research has suggested that WM is positively correlated with a large number of cognitive processes, including thinking (1,2), reasoning (3–5), decision making (6,7), attention (1,2) and planning (8,9).

A number of models have been proposed that attempt to explain the WM functions (10–12). The most widely investigated and influential model was initially presented by Baddeley and Hitch (13). According to their model, WM comprises three distinct components that have interdependent functions: (1) the visuospatial component, which comprises the visual cache and the inner scrip and which accounts for the maintenance and processing of visual and spatial information; (2) the phonological component, which encompasses the phonological store and inner speech and is responsible for managing verbal and acoustic information and (3) the central executive component, which is considered to be the cornerstone of the WM system. This component is dedicated to coordinate the functioning of the verbal and visuospatial components of WM by monitoring, attending to and retrieving relevant information from these two components while simultaneously prohibiting the storage of irrelevant information and its retrieval from long-term memory. It is conceptualised as the executive manager of WM.

Recently, Baddeley (14) added the so-called episodic buffer as a fourth component of WM. He posited that the episodic buffer component of WM links verbal, spatial and visual information with a chronological order that is presumably involved in the development of associations between long-term memory and semantic meaning. Baddeley and colleagues established this component based on the observation that amnesic patients could retrieve short memories that exceeded the capacity of the phonological loop despite having limited abilities to encode recent information in long-term memory (13,14).

Traditional measures of the functioning of various WM components require that participants are presented with a series of items (e.g. digits, letters or blocks) about which they are subsequently asked questions that probe the degrees to which the items were able to be stored and manipulated (15). Thus, measuring the functioning of the central executive component requires that a participant perform tasks that require inhibition and/or switching attention, such as backward digit recall and counting (16–18). However, these types of tasks rely partially on the phonological loop component of WM and may not test the central executive component alone (19). In this study, we used two tasks that depend on executive functioning (the spot-the-word task and the verbal *n*-back task) to investigate this component of WM. These tasks depend on the concurrent storage and manipulation of information; they require that participants switch between tasks, such as retrieval and encoding, or they require that participants selectively retrieve information from long-term memory while suppressing the retrieval of irrelevant information (20).

A regular measure of the visuospatial component of WM involves showing participants visual and spatial stimuli, such as figures or shapes that must be remembered and processed. The participant is then instructed to report the identity and location of the stimulus that differs from the others. Phonological loop measures employ a serial recall technique in which the participants are instructed to repeat a series of spoken items in the order in which the items were originally presented. These testing methods are thought to test two subsystems of the phonological loop component of WM (storage and subvocal rehearsal).

Measuring the episodic buffer requires accessing information that exceeds the storage capacities of the visuospatial and phonological components in a manner that is independent of both central executive functioning and direct retrieval from long-term memory (21). A typical test of the episodic buffer should evaluate the degree to which visual and verbal codes are combined and linked to multidimensional representations in long-term memory. Because

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there are no completely accepted measures of the episodic buffer at present, we attempted to identify tasks that require combining different types of information from different memory sources (i.e. long-term memory, visual short-term memory and phonological short-term memory) as has been suggested by Baddeley and colleagues (14,19,22). In this study, we used two tasks (a logical memory task and a cross-modal task) that measure the episodic buffer in a manner that is independent of other WM subsystems. These tasks require combining the activities of different memory systems to bind information that has been obtained via different modalities into the representation of a coherent array of objects.

The model described above has been used extensively in examining both patients and healthy adults. To date, however, it has not been used to examine WM functions in individuals with various patterns of disordered behaviour (e.g. chronic drug dependence, personality disorders and dually diagnosed children).

A large number of studies have suggested that the chronic dependence of psychoactive substances results in poor cognitive functioning (23–28). These studies varied in their specific objectives; some studies were interested in examining the extent to which cognitive impairment that is associated with chronic drug dependence is linked to specific brain regions, whereas other studies focused on the way in which chronic drug dependence affects general brain function. In a comprehensive review, Lundqvist and colleagues (29) reported that chronic drug dependence resulted in disruptions in the neuropsychological network that caused remarkable deficits in short-term memory, attention and executive functioning. Their conclusion was based on the fact that drug dependence dramatically impacts the activity of most neurotransmitters by modulating the normal functioning of the forebrain and of broader brain regions. Consequently, poor cognitive performance can be predicted as a function of chronic psychoactive drug dependence.

According to previous literature, behavioural, neuropsychological and functional magnetic resonance imaging studies have shown that participating in drug abuse for a prolonged period of time resulted in performance impairments on tasks that measure various WM functions and resources, including the general capacity of WM (30–32), visual WM (33), spatial WM (34), processing speed (35), verbal recall (36), visuospatial WM (37), executive functions (38–40) and the ability to encode information into long-term memory (22). Nonetheless, to the best of our knowledge, no single study has examined all four of the components of WM in drug dependence, nor has one study evaluated the impact of chronic drug dependence on any or all of the WM components with respect to the identities of drugs, e.g. heroin, cocaine, marijuana or the simultaneous dependence of two or more psychoactive substances (polydrug use).

In this study, we were interested in examining the efficiency of each of the four main WM components in participants who were chronic drug dependents and in comparing WM performance in chronic drug dependents in WM performance with a carefully matched control population. We were also interested in comparing the functioning of the four WM components among users of several different drugs of dependence (i.e. heroin, cocaine, marijuana and polydrug users).

Method

Participants

A total of 164 male participants took part in this study; 128 participants were drug dependents aged 38.48 ± 4.75 years. Drug dependents were compared with a drug-free control group that comprised 36 participants aged 37.61 ± 3.75 years. Participants were recruited by the Al-Amal Program at the Smoking Cessation Society (APSCS) in Al-qunfudah City, KSA. Across all of the drug dependents, the mean duration of drug dependence was 11.83 ± 1.09 years. The drug dependents self-reported their lifetime histories of drug dependence, and they were diagnosed by the medical board of the drug abstinence centre in KSA according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (41) criteria for the dependence of each specific drug (heroin, cocaine, marijuana and polydrug). The duration of dependence for each individual group of drug dependents was as follows: the heroin group had an average dependence duration of 11.67 ± 1.13 years, the cocaine group had an average dependence duration of 11.93 ± 1.29 years, the marijuana group had an average dependence duration of $11.61 \pm .83$ years and the polydrug group had an average dependence duration of 11.80 ± 1.08 years. All of the drug dependents except for polydrug have reported that they never use more than one drug. The poly drug dependents reported that they were using more than one drug during the reported drug-dependence duration.

Overall, there were no significant differences between the durations of drug dependence of the four groups of participants [$F(1, 163) = 0.58$, $p > 0.05$]. The participants reported a maximum of 15 days of abstinence from drug use prior to the assessment, and no significant effects of the duration of abstinence were noted for any of the tasks.

The drug dependents who met our inclusion criteria were divided into groups according to the type of drug(s) that they used as follows: heroin ($n = 36$), cocaine ($n = 30$), marijuana ($n = 28$) and

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polydrug ($n = 40$). All of the dependents disclosed information regarding whether they were regular users of a single drug (i.e. heroin, cocaine or marijuana) or two or more drugs (polydrug users), and their records with the APSCS were used to confirm their self-reports. All of the participants reported that they had not used any drugs after completing their treatment courses. The inclusion criteria for the experiment were as follows: all of the drug dependents were involved in recovery programs that used non-pharmacological approaches. All of the drug dependents were free from both drug use and substitution therapy, and they had negative urine toxicology assays. None of the participants had any indications of nicotine dependence according to the DSM-IV criteria. All of the control participants were screened by a clinician who was affiliated with the APSCS to establish any history regarding drug abuse, alcohol abuse and general health issues. None of the control participants had a history of systemic diseases, substance abuse, neurological disorders or psychological disorders.

All of the participants completed an average of 13.16 ± 1.83 years of schooling. The average education levels of the various groups were as follows: members of the control group had completed 16.34 ± 1.84 years of schooling, members of the heroin group had completed 13.12 ± 1.67 years of schooling, members of the cocaine group had completed 13.08 ± 1.88 years of schooling, members of the marijuana group had completed 13.39 ± 1.88 years of schooling and members of the polydrug group had completed 13.16 ± 1.82 years of schooling. Overall, there were no significant differences in the education levels of the five groups [$F(1, 163) = 3.81, < 0.05$]. All of the participants had intelligence scores that were within an average range; the clinical psychologist who was affiliated with the APSCS reported that the average Raven Progressive Matrices Test percentile of the cohort was 49.65 [standard deviations (SD) = 26.08] prior to the assessment of WM, and percentile rankings were based on the Saudi norms. All of the participants had lower middle class socioeconomic backgrounds; they had a mean socioeconomic score of 6.1 with a SD of 2.54 on an 8-point family income scale in which a score of 1 referred to the highest income bracket and a score of 8 referred to the lowest. The self-reports of all of the participants showed that they were drug dependents for more than 10 years, attended treatment programs at the APSCS, they were married and living with their families, and they were right-handed. All of the participants volunteered to take part in the experiment, but the Society administration offered each of them a small honorarium to encourage participation. The ethics committee at the Department of Psychology and Education at the University College, Umm Ala-qura University, KSA, has approved all of the tasks and procedures. Informed consent was obtained from each of the participants prior to the start of the experiment.

WM measures

Phonological loop functioning. The digit span forward subscale of the Wechsler adult intelligence scale (42) was used to measure the phonological loop component of WM. In this task, the participant listened to a series of digits (digits ranged from 1 to 9) that were read aloud by the experimenter, after which the participants were instructed to repeat the digits in the same order in which they had been presented. The number of correctly recalled digits represented the participant's score for the phonological loop component of WM. For more about using this test score as an indicator of phonological loop functioning (see for details 8,43,44).

The backward digit span task (45,46). In this task, the participants listened to a series of digits and were then required to recall the digits in reverse order. Each testing session began with trials in which participants were asked to recall two digits, and the number of digits that a participant was asked to recall was subsequently increased one digit at a time across several trials. For example, a participant might be given the digit series 2–7, then 3–8–1, and so on until there were 9 digits in the series. For further information about the application of this task as an indicator of phonological loop functioning (see for details 43,47).

Central executive functioning. A verbal two-back paradigm (8,48) was used to measure the functioning of the central executive component of WM. In this task, the participant was shown a series of 200 consonants on a computer screen. Consonants were presented one at a time for a period of 200 ms, and 2500 ms intervals elapsed between consonant presentations. Each participant was asked to determine which stimulus he had seen two screens prior to the present stimulus. A participant's central executive functioning score was determined as the total of correctly identified items divided by 10. For information about the application of this test as an indicator of central executive WM functioning (see for details 48).

The spot-the-word subtest of the speed and capacity for language processing test. In this task, the participants were asked to identify the real word in each of 60 pairs of items, each of which comprised one real word and one non-word. A participant's score on

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this task was the total number of correctly identified real words. For more information about the application of this test in the measurement of the central executive component of WM (see for details 49,50).

Visuospatial sketchpad functioning. *The block span forward subtest of the Wechsler memory scale* (48) was used to assess the visuospatial sketchpad component of WM. In this task, the participants were shown several series of visual blocks on a computer screen, each of which included between 2 and 8 blocks. For further discussion of the application of this test as an indicator of visuospatial sketchpad functioning (see for details 51,52).

The spatial span task (53,54). In this task, the participants were shown a sequence of two shapes, one of which had a red dot that moved around on top of the figure. After the two shapes were presented, an empty figure that contained three compass points appeared, and the participant was asked to first identify whether the two shapes were the same and then and to indicate the location of the moving red dot. The trials contained anywhere between one and nine set(s) of three shapes. A participant's score on this task was taken as the sum of the number of correctly identified dot locations and the number of correct identifications of whether the two shapes in the initial sequence were the same. For more detail about applying this task as an indicator of visuospatial sketchpad functioning (see for details 53–55).

Episodic buffer functioning. One way to assess the episodic buffer component of WM is by measuring a participants' ability to integrate information that has been stored in long-term memory with other WM content. The role of WM is to sustain the moment-to-moment processing of information in the service of other cognitive activity, and it accomplishes this by generating new episodic memories and by exploring semantic memory (13,29,56–58).

The logical memory subtest of the Wechsler memory scale (42). In this task, the participants listened to two short stories and were then asked to retell them (only the immediate recall condition of this subtest was used in our assessments). Raw scores are determined from the total number of story units that are recalled across the two stories and were used as indicators of the functional abilities of the episodic buffer component of WM.

Visual cross-modal task. In this task, the participants were presented with a series of pairs of unfamiliar words and unfamiliar shapes. A participant began with a pair of two items and was asked to identify the image that corresponded to a particular unfamiliar word from an array of four shapes. In subsequent trials, the participants were shown word-image pairs that were composed of two non-words and two nonsense shapes; the numbers of words and images in each pair were increased until a total span of nine non-words and nonsense shapes was reached (59,60). The assessment included a maximum of 10 pairs. A participant's score is the maximum number of pairs he/she can remember. The pairs continue until the performance of the participant is no longer better than the chance performance level. For more detail about using the results of this test as an indicator of episodic buffer functioning (see for details 58,59).

All of the tasks showed a good convergent validity; the results of these tests were significantly correlated with the results of well-known tests of WM (i.e. WM capacity, sentence span, random generation, visual digit span and prose recall). Correlation data are shown in Table 1. Alpha coefficients were used to determine the reliability of each task, and they ranged from 0.78 to 0.91.

Procedures

All of the participants were given drug-dependence questionnaire, demographic and socioeconomic status surveys 2 weeks prior to their experiment sessions. The tasks were introduced to the participants, and they were then asked to sign informed

Table 1. Correlation coefficients between WM component tasks and other WM tasks

WM component	Task	WMC	SS	RG	VDS	PR
Phonological loop	Digit span forward	0.79**	0.80**	–	–	–
	Backward digit span	0.76**	0.64**	–	–	–
Central executive	Verbal two-back	0.87**	–	0.69**	–	–
	Spot-the-word	0.84**	–	0.66**	–	–
Visuospatial sketchpad	Block span forward	0.74**	–	–	0.74**	–
	Spatial span	0.87**	–	–	0.61**	–
Episodic buffer	Logical memory	0.78**	–	–	–	0.59**
	Cross-modal task	0.89**	–	–	–	0.50**

PR, prose recall; RG, random generation; SS, sentence span; VDS, visual digit span; WMC, WM capacity.
**Significant at the 0.01 level.

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consent forms and to provide general and demographic information. The testing sessions were individual. In a typical testing session, a participant was given a computerised task that had been programmed using the Superlab® software, and the task stimuli were displayed on a 15-inch computer screen. Three training trials were conducted at the beginning of each task. After ensuring that the participant fully understood the instructions and had completed the three training trails, the experimenter permitted him to begin the actual memory task. Three experienced psychologists oversaw the testing sessions. Participants were given 5–10-min intervals between tasks. All of the testing sessions were conducted in the mornings. The tasks were presented in the following order for all participants: backward digit span task, cross-modal task, block span forward task, digit span forward task, spatial span task, verbal two-back task, spot-the-word task and logical memory task. The mean duration of task administration was 15 ± 6 min for each task, and the average total administration time for all of the tasks was 116 ± 21 min.

Data analysis

We adopted a significance level of $p < 0.01$. All of the data were analysed using SPSS version 19.0 (SPSS, Inc., 2009, Chicago, IL, www.spss.com). Our data consisted of data from several WM tasks, in which chronic drug dependents were compared with matched controls and used a multivariate analysis of variance (MANOVA) followed by a series of analysis of variance (ANOVA) tests to examine the efficiencies of the various WM components. A MANOVA was also used to determine whether the patterns of the results of various WM component tasks (i.e. the visuospatial, phonological loop, central executive and episodic buffer tasks) differed by drug-dependence type (i.e. heroin, cocaine, marijuana, polydrug and drug-free controls). MANOVA is a statistical approach that is superior to either ANOVA or *t*-tests for the analysis of our data because it is likely that the task scores within each WM component will be correlated, and MANOVA takes these correlations into account when performing significance tests. Because we did not have the same number of cases in each group, the means that we reported were estimated marginal means.

Results

Table 2 shows the mean values of the eight WM component tasks along with MANOVA results in which these scores were assessed as functions of drug-dependence status (drug-free controls vs. drug dependents). The results of the MANOVA revealed that there were significant differences between the drug-free controls and drug-dependence participants in all eight of the WM component tasks and that these differences favoured the normal participants. The Wilks' Lambda values were also significant for all of the WM tasks. For example, the normal participants performed significantly better (MM = 7.36) than the drug dependents (MM = 5.31) in the verbal two-back test [$F(1, 162) = 61.57$, $p < 0.01$]. As shown in Table 2, the differences in results were more prominent in the case of the backward digit span [$F(1, 162) = 305.99$, $p < 0.01$], spot-the-word [$F(1, 162) = 217.53$, $p < 0.01$] and logical memory [$F(1, 162) = 1059.41$, $p < 0.01$] tasks. In addition, it is obvious from Table 2 that the performance scores of the drug-free participants on all of the WM component tasks were more homogenous than the performance scores of the drug dependents on the same tasks. For each WM task, the SD of the performance scores of the drug-free participants were smaller than the associated SD of the performance scores of the of the drug dependents (e.g. the SDs

Table 2. Mean values and MANOVA results for WM components by drug abuse status

		Drug abuse status						
		Controls		Drug abusers				
WM component	Task	MM	SD	MM	SD	Wilks' Lambda	*F*-value*	Significance
Phonological loop	DSF	7.36	0.90	5.31	1.49	0.343	61.57	<0.01
	BDS	7.97	0.51	3.90	1.37		305.99	<0.01
Central executive	VTB	8.28	0.66	4.84	1.35	0.404	217.53	<0.01
	SW	7.83	0.70	4.43	1.40		197.97	<0.01
Visuospatial sketchpad	BSF	8.31	0.79	5.17	1.23	0.425	210.42	<0.01
	SS	7.06	0.979	4.36	1.50		103.15	<0.01
Episodic buffer	LM	26.28	0.889	17.98	1.46	0.133	1059.14	<0.01
	CM	6.08	0.879	4.15	1.32		69.51	<0.01

BDS, backward digit span; BSF, block span forward; CM, cross-modal task; DSF, digit span forward; LM, logical memory; SS, spatial span; SW, spot-the-word; VTB, verbal two-back.

*df = 1, 162.

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Table 3. Mean values and MANOVA results for WM components by type of drug abuse

		Drug abuse type												
		Control		Heroin		Cocaine		Marijuana		Polydrug				
WM component	Task	MM	SD	MM	SD	MM	SD	MM	SD	MM	SD*	Wilks' Lambda	*F*-value*	Significance
Phonological loop	DSF	7.36	0.90	5.00	1.43	5.22	1.01	6.94	1.21	4.48	1.11	0.106	43.35	<0.01
	BDS	7.97	0.51	4.16	0.74	4.32	0.74	5.35	0.95	2.38	0.77		282.18	<0.01
Central executive	VTB	8.28	0.66	4.77	0.74	5.06	0.84	6.44	1.01	3.63	0.95	0.176	161.05	<0.01
	SW	7.83	0.70	4.34	1.15	4.70	1.22	5.88	0.63	3.28	1.04		115.34	<0.01
Visuospatial sketchpad	BSF	8.31	0.79	5.18	0.85	5.61	0.81	6.38	0.63	4.00	0.99	0.194	135.75	<0.01
	SS	7.06	0.97	3.72	1.00	4.41	1.09	5.81	1.55	3.80	1.38		48.38	<0.01
Episodic buffer	LM	26.28	0.88	17.57	1.36	17.20	0.96	19.14	1.46	18.05	1.34	0.050	338.31	<0.01
	CM	6.08	0.87	4.31	0.77	4.63	0.96	5.40	0.88	2.78	0.83		78.27	<0.01

BDS, backward digit span; BSF, block span forward; CM, cross-modal task; DSF, digit span forward; LM, logical memory; SS, spatial span; SW, spot-the-word; VTB, verbal two-back.

*df = 1, 162.

for the digit span forward task were 0.90 and 1.49 for the drug-free controls and drug dependents, respectively).

Table 3 shows the mean values and MANOVA results for the eight WM component tasks as a function of drug-dependence type (heroin, cocaine, marijuana, polydrug and drug-free controls). The MANOVA results indicated that there were significant between-group differences in performance on all of the WM tasks that measured all of the WM components. It is clear that the performance of the drug-free controls on all of the WM tasks was significantly better than the performance of each group of drug dependents (see Tables 3 and 4 for *F*-values and their significances). Compared with the members of the various drug-dependence groups, the participants in the control group always performed better, and there was less variation in performance within the group, as indicated by the lower SD. This result is more obvious in the central executive and visuospatial tasks (see Tables 3 and 4 for *F* values and their significances). The polydrug group had the poorest performance of any of the groups on all of the WM tasks.

To further investigate the differences in the WM component task performance among the groups that we studied, the results of a multiple comparison analysis using Scheffé's method are presented in Table 4. It is clear from Table 4 that the performance score of each study group depended on both the particular WM component that was being tested and the specific task, but some generalisations can still be made. For example, the performance of drug-free controls was significantly better than that of all of the other drug-dependence groups in all of the WM component tasks with the notable exception of the group of marijuana users in the digit span forward and cross-modal tasks. No significant differences between the controls and the marijuana users were found for either of these two tasks. In addition, no significant differences in the performance scores of the cocaine and heroin groups were found for any of the WM components. The performance of the marijuana group was significantly better than that of both the heroin and polydrug groups in all WM

Table 4. Multiple comparison (Scheffé test) results for WM components by type of drug abuse

		Pair comparison*									
WM component	Task	N vs. H	N vs. C	N vs. M	N vs. P	H vs. C	H vs. M	H vs. P	C vs. M	C vs. P	M vs. P
Phonological loop	DSF	N	N	–	N	–	M	–	M	–	M
	BDS	N	N	N	N	–	M	H	M	C	M
Central executive	VTB	N	N	N	N	–	M	H	M	C	M
	SW	N	N	N	N	–	M	H	M	C	M
Visuospatial sketchpad	BSF	N	N	N	N	–	M	H	–	C	M
	SS	N	N	N	N	–	M	–	M	–	M
Episodic buffer	LM	N	N	N	N	–	M	–	M	–	M
	CM	N	N	–	N	–	M	H	–	H	M

BDS, backward digit span; BSF, block span forward; C, cocaine group; CM, cross-modal task; DSF, digit span forward; H, heroin group; LM, logical memory; M, marijuana group; N, normal (control group); P, polydrug group; SS, spatial span; SW, spot-the-word; VTB, verbal two-back.

Significant at the 0.01 level; letter indicates the direction of significance. –, not significant.

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components, and with the exception of the spatial span and cross-modal tasks, it was also better than the performance of the cocaine group on all of the measures of WM. Moreover, the polydrug group had significantly poorer performance than all of the other drug-dependence groups and the drug-free control group on most WM component tasks.

Discussion

In this study, we were interested in examining the performance of various types of drug dependents (i.e. heroin, cocaine, marijuana and polydrug) on tests of the four WM components that were established based on the multi-component model of WM that was initially suggested by Baddeley and Hitesh (61). This aim was specifically achieved by comparing the performance of a control group with the performances of matched groups of dependents of different types of drugs.

Our results indicated that the performance scores of drug dependents of all of the subtypes were poorer than those of the controls for all of the WM components. Cocaine and heroin had similar effects on performance in all of the WM tasks. Moreover, we found that members of the marijuana group performed significantly better than members of both the heroin and polydrug groups on tests of all four WM components, and they also performed better than members of the cocaine group on almost all tests of the various WM components. To ensure that the drug dependents were actually impaired on measures of the various WM components, their scores were examined with respect to the mean scores of the control group. For each test, a participant whose score was lower than 1.6 SD below the mean score of the controls was considered to be impaired, which is a well-recognised clinical criterion for establishing impairment (62).

The results of this study are consistent with previous reports that drug dependents have WM impairment (28,64–67). For example, Ilan et al. (64) found that marijuana use impacted both prolonged and temporary attentional processes and that it eventually resulted in diminished or impaired WM performance. Similarly, another group of researchers (65) hypothesised that heroin dependents would have significantly disrupted performance on the n-back task, which measures the central executive component of WM. Moreover, another study (68) examined the dose-dependent impact of cocaine on cell proliferation and neurogenesis in the dentate gyrus of the hippocampus in adult rats in addition to monitoring the effects of cocaine administration on WM. Their findings suggested that high doses of cocaine reduce both the production and development of new neurons in the hippocampus and worsen WM performance.

One group of researchers (69) was interested in the effects of polydrug dependence, and they examined the links between different types of drug dependence and the severity of neuropsychological performance impairment on tasks that are sensitive to the executive processes of WM, abstract reasoning, cognitive flexibility and inhibition. Their results revealed that the severity of 3,4-methylenedioxymethamphetamine dependence had serious effects on WM and on abstract reasoning, the severity of cocaine dependence had a serious effect on the degree of impairment in an inhibitory control index, and the severity of cannabis dependence had a profound effect on performance on a task that measured cognitive flexibility.

One possible explanation for these findings is that the proper functioning of the ventromedial cortical system relies heavily on the unity of neural systems that support the processing of WM material (70); most of these systems are implicated in the rewarding aspects of drug dependence (71). That is, chronic substance dependence disrupts the normal activity of the neuropsychological network by impacting the activity of most neurotransmitters throughout it and by subsequently impeding the functioning of the forebrain and of broader brain regions. This disruption results in a notable deficit in WM and executive functioning (72). That is, the dependence of either a single drug or of two or more drugs results in overtaxing WM resources by interfering with the normal functioning of the brain regions in which the WM resources are located. This interference may then diminish, if not impair an individual's ability to maintain and retrieve verbal and visuospatial information that can subsequently be used for behavioural or cognitive purposes (72) based on the notion that the prefrontal cortex plays a key role in a wide range of executive functions, including the management of WM resources (73). In addition, using cannabis for an extended period of time is associated with increased cortical activation that may subsequently result in suboptimal cortical efficiency during cognitive activities (74). In addition, the use of marijuana activates the inferior and middle frontal gyri, which are cortical regions that are related to visuospatial WM (75). Even the recent use of marijuana activates brain regions that are associated with the updating and inhibition functions of WM (76).

Our results revealed that there were no significant differences between the performance scores of the marijuana users and those of the drug-free participants on either the digit span forward task, which

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measures phonological loop functioning, or the logical memory task, which was used as a measure of the episodic buffer. This result is unexpected and an investigation of the reasoning behind it might exceed the scope of this study. However, it could be interpreted as partially resulting from exogenous variables in the abstinent period that may have resulted in the superior performance of the marijuana dependents compared to other drug dependents; it is also possible that recovering from a marijuana addiction requires that less time elapse before an individual returns to normal levels of WM performance than recovering from other drug addictions. This result needs further empirical investigation to be fully understood.

The apparent contradiction in results may result from the fact that the studies to which we have previously referred used a sample of participants who had only used drugs for recreational purposes whereas the participants in this study were drug dependent for more than 10 years.

More importantly, as we expected, we found that the performance of polydrug dependents was significantly worse than the performance of any of the other drug dependence groups or that of the drug-free controls on most WM tasks. This result is not surprising; the difficulties that arise as a result of drug dependence increase as more drugs are added to the mix because the additional drugs interfere more with neurotransmitter activities and consequently exacerbate any inhibition in performance on tasks that require WM resources. This notion is supported by the general agreement that all substance dependence creates dissonance in the neuropsychological network that then causes the levels of activity in cortical regions that support short-term memory, attention and executive functions to decrease (72).

In conclusion, this study found that chronic dependents of heroin, cocaine, marijuana and two or more drugs at the same time had impairment in all four of WM components that we studied, and impairment was measured on two tasks for each of the four WM components.

In addition, the heroin and cocaine users who participated in our study performed more poorly than the marijuana users on almost all of the tasks that involved WM resources. Almost all of the WM tasks that we used are sensitive for classifying drug dependents.

The findings of this study are limited to chronic drug dependents (individuals who have used a drug for 10 years or more) and to specific types of drug dependence, namely heroin, cocaine, marijuana and polydrug dependence. Our results are also limited to drug dependents who are not currently taking any type of medication and who have abstained from drug use for a maximum of 15 days. These findings have many implications for the development of tools and classification methods that can be used to assess drug dependence and for the development of therapeutic strategies for enabling recovery from drug dependence.

Despite the large body of research regarding the impact of drug use on the functionality of verbal and visuospatial WM, there is still a need to explore all four components of WM components using a comprehensive test battery. The episodic buffer, which is the most recently added component, is of particular interest. Future research should account for the experimental paradigm that is being used when examining effects of drug use on each of the four WM components. It is also important to examine the impact of drug dependence on a broader spectrum of cognitive processes, including processes that are associated with decision making, episodic memory, problem solving and reasoning. Finally, future research should also use functional brain imaging techniques to examine the neural bases of the WM deficits that are associated with drug dependence.

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