Real world memory and executive processes in cannabis users and nonusers.

John E. Fisk,
University of Central Lancashire,
Preston PR1 2HE, United Kingdom

Catharine Montgomery
Liverpool John Moores University,
Liverpool L3 2ET, United kingdom

Running head: Real world memory and executive processes

Keywords: separable executive processes, everyday memory, prospective memory, cognitive failures, cannabis.

Corresponding author:
Dr John E Fisk
Department of Psychology
University of Central Lancashire
Preston PR1 2HE
United Kingdom
Tel 44 (0) 1772 894465
Fax 44 (0) 1772 892925
e-mail: jfisk@uclan.ac.uk

Abstract.

The relationships between executive processes, associative learning and different aspects of real world memory functioning were explored in a sample of cannabis users and nonusers. Measures of executive component processes, associative learning, everyday memory, prospective memory, and cognitive failures were administered. Relative to nonusers, cannabis users were found to be impaired in several aspects of real world memory functioning. No other group differences were apparent. The absence of cannabis related deficits in those executive component processes and aspects of learning that are believed to support real world memory processes is surprising given that cannabis related deficits were obtained in real world memory. The present results are discussed within the context of neuroimaging evidence which suggests that cannabis users may exhibit different patterns of neural activation when performing executive tasks while not always exhibiting deficits on these tasks.

Keywords: Cannabis, executive processes, prospective memory, cognitive failures

The focus of the present paper is real world memory functioning in abstinent cannabis users. More specifically we intend to explore the basis of cannabis-related deficits in prospective memory, everyday memory, and cognitive failures, and the extent to which these impairments are underpinned by deficits in pre-frontal executive processes. Given that cannabis is clearly the most popular illicit drug in North America, Europe and in other parts of the world (Andersson et al, 2005) it is of considerable importance to investigate whether consumption of the drug is associated with cognitive deficits.

Cannabis contains a number of chemical compounds collectively known as cannabinoids. The psychoactive properties of cannabis are mainly due to one of these cannabinoids, Δ^9 tetrahydrocannabinol, (THC). Animal studies have revealed that chronic administration of THC causes hippocampal damage and impairs maze learning in rats (Fehr et al, 1976; Lawston et al, 2000). In humans, cannabinoids may be neurotoxic or neuroprotective depending on their concentration, the timing of delivery and the cell type (Doble, 1999; Guzman et al, 2001; Hubert & Doble, 1998). It has been suggested that even small residual amounts of cannabinoids have the potential to cause neurotoxicity (Sarne et al, 2005; Sarne & Keren 2004). This raises the possibility that even occasional cannabis users might be at risk of neurological and consequent cognitive impairment.

Consistent with this possibility, Verdejo-Garcia et al (2006) reported that cannabis users might be impaired in aspects of executive functioning such as planning, working memory, and mental flexibility. Recall seems to be one area of cognition that is subject to cannabis-related deficits. Schwartz (1991) found that daily cannabis users exhibited impaired immediate recall on the Wechsler Memory Scale (WMS). Although slightly attenuated at 6-week retest, the cannabis-related deficit remained apparent. Similarly deficits among cannabis users were found on aspects of the Rey Auditory Verbal Learning Test (Solowij et al, 2002), verbal memory (Messinis et al, 2006), the retrieval of certain types of word stimuli (Block & Ghoneim, 1993), and visuo-spatial recall (Varma et al, 1988). More generally, performance on a range of cognitive tasks appeared to deteriorate with increasing years of heavy frequent cannabis use (Messinis et al, 2006). Impairments appeared to persist for at least at least 6 weeks following last ingestion of cannabis (Schwartz, 1991) and were especially evident in female (but not male) heavy users (Pope et al, 1997).

The existence of these laboratory-based deficits in basic memory processes raises the possibility that aspects of real world memory functioning including everyday memory, prospective memory, and the propensity for cognitive failures might be adversely affected among cannabis users. For example cannabis users might be more likely to forget the location of familiar objects around the house, forget to take essential objects when leaving the home or office, fail to recognise acquaintances, or forget important events that occurred the previous day, etc. These are all capacities that are assessed in established measures of everyday memory (Sunderland et al, 1983) or cognitive failures (Broadbent et al, 1982). An additional aspect of memory that is of relevance beyond laboratory contexts is prospective memory. This involves remembering to execute a particular behavior at some future point in time which may be in the short term or more long term, for example remembering to turn off the lights when leaving a room or remembering to attend a meeting, meet a friend or pass on a message. Measures of this construct have also been developed (e.g., Hannon et al, 1995). However, these aspects of real world memory remain under-investigated among cannabis users. Clearly the cannabis-related recall impairments evident in laboratory contexts are likely to be manifested outside the laboratory in real world situations. However, cognitive failures and prospective memory are also dependent on prefrontal executive processes as well as the medial temporal-hippocampal processes which support memory functions (Goldstein & Polkey 1992; Kliegel et al 2005; West, 1996). Planning and monitoring are important aspects of real world memory and clearly also draw on executive resources. Indeed, clear evidence of prefrontal involvement in real world memory tasks has been obtained (Marsh & Hicks, 1998; McDaniel et al, 1999; Whyte et al, 2006).

Thus cannabis-related deficits in real world memory may arise from traditional memory processes and/or as a result of pre-frontal impairments. A key aim of the present paper is to establish whether the cannabis-related deficits in memory processes that have been documented in the laboratory generalise to real world contexts. If so, the present paper will also seek to establish whether cannabis-related deficits in executive processes might also affect real world memory performance. Thus a range of laboratory based measures of executive functioning and learning, as well as self report measures of aspects of real world memory were administered. The

performance of cannabis users (with no history of other illicit drug use) on these measures was compared with that of drug naïve individuals.

METHOD

Participants. Those participating in the Study were selected from an existing database containing a range of measures for substance abusers and drug naïve individuals. Cannabis users were selected on the basis that cannabis was the only illicit substance used. Thus polydrug users who consumed cannabis and other illicit drugs such as cocaine and ecstasy were excluded. Non users were those who indicated that they had never used any illicit drug. Both groups included individuals who consumed alcohol and tobacco. As the database was constructed over a period of years the number of users and nonusers completing the various measures varied. Sample sizes for each of the measures are included in Table 1. Members of the database were recruited via direct approach to university students, and the snowball technique. The mean ages for the different samples ranged between 20 to 22 years for non users and consistently 21 years for users. Participants were requested to refrain from cannabis use for at least 24 hours prior to testing. The mean and median periods of abstinence for cannabis users in each sample are set out in Table 1. The samples contributing to the different measures overlapped to a substantial degree. For example, all participants completing the everyday memory and cognitive failures tasks also completed the updating and inhibition executive tasks.

<Insert Table 1 about here>

Materials

History of Drug Use. Patterns of drug use and other relevant lifestyle variables were investigated via means of a background questionnaire. The questionnaire gauged the use of cannabis and other drugs, as well as age, years of education, general health and other relevant lifestyle variables. In relation to illicit drugs, participants were asked a range of questions including frequency and duration of use and the last time that they had used each drug. Participants were also questioned concerning their history of drug use and these data were used to estimate total lifetime use of cannabis. Average weekly dose and the amount consumed within the previous 10 and 30 days were also assessed. Consumption of legal substances was also assessed. Participants were asked how many units of alcohol they consumed per week. Examples of what constituted a unit were provided, e.g., 1 glass of wine, a single measure of spirit, and

half pint of beer. Participants were also asked if they smoked and if so how many cigarettes per day they consumed.

Measures of Executive functioning (Fisk & Sharp, 2004).

Computation Span involved two elements, firstly participants were required to solve a simple arithmetic problem, for example, 7+3 = ?, by selecting the correct answer from among three alternatives; and secondly they were asked to recall the second digit of the problem (i.e., in the above example: 3). As the task proceeded, the number of problems that had to be solved, while recalling the last digit of each, gradually increased. Once all of the problems in a given set had been processed, the participant was asked to recall all of the second digits in the order in which they occurred. The task commenced with three trials containing just a single problem, this was followed by three trials with two problems presented consecutively, and then three trials with three consecutive problems, and so on. Span was defined as the maximum number of second digits successfully recalled in serial order. This level had to be achieved in at least two of the three relevant trials and the corresponding arithmetic problems had to be answered correctly.

Random letter generation task. Participants were asked to speak aloud a letter each time they heard an auditory signal. They were asked to avoid generating alphabetical sequences and repeat sequences such as AB or BBC. They were also asked to try and produce each letter with the same overall frequency. Each participant produced three sets of 100 letters, at the rate of one per second, one every two seconds and one every four seconds. The order in which the sets were produced was randomised for each participant. The experimenter recorded participants' responses. This task yields four separate measures for each generation rate. These are the total number of letters produced, the number of alphabetically ordered pairs, the number of times that any given letter pair is repeated, and redundancy, which is a measure of the extent to which each letter of the alphabet is produced equally often. Sequences containing relatively few letters that are repeated often, produce high redundancy. For each of these measures, the scores were standardised and averaged over the three generation rates thereby producing mean standardised scores for alphabetical sequences, repeat sequences, redundancy, and the total number of letters generated. For the first three of these a high score is associated with poor performance, for total number of letters a high score is indicative of efficient performance.

Fluid intelligence was measured via Raven's Progressive Matrices (Raven et al, 1998), and premorbid intelligence was assessed via the National Adult Reading Test (NART, Nelson, 1982).

Semantic Fluency: In the semantic fluency task, participants were required to produce as many animal names as they could think of. This could be different species, or breeds within species. Participants were given four minutes for this task.

Chicago Word Fluency Test. Participants were instructed not to write any place names, peoples name or plurals in this test. Firstly participants were given five minutes to write down as many words as they could, beginning with the letter "S". Secondly, they were given four minutes to write down as many four-letter words beginning with "C" as they could. As plurals were not allowed, words such as "cats", and repetitions of words were excluded. Scores for all three fluency tasks were the number of appropriate words generated in each case.

Plus-minus task. The plus-minus task, adapted from Miyake et al (2000) consists of three lists of 30 two-digit numbers (the numbers 10-99, randomised). On the first list, participants were instructed to add three to each number, and write their answer in the box next to it. On the second list, participants were instructed to subtract three from each number. On the third list, participants were required to alternately add and subtract three from the list (i.e. add three to the first number, subtract from the second, and so on). List completion times were measured with a stopwatch. The cost of shifting between adding and subtracting was calculated as the ratio between the time for list three and the average of the times for lists one and two.

Number-Letter task. In the number-letter task, adapted from Miyake et al (2000), a number letter pair (e.g.D4) is presented in one of four quadrants on a computer screen. If the target is in the top half of the screen, the task is to indicate if the letter is a vowel (A, E, I, O or U) or a consonant. If the target is in the bottom half of the screen, the task is to indicate if the number is odd or even. The practise version of the task comprises three sets. The target is presented in the top half of the screen for 12 trials, then the bottom half for 12 trials, and then in a clockwise rotation around all 4 quadrants for a further 12 trials. The main task follows the same structure, except there are 64 targets in each block. Therefore, the trials in the first two blocks required no switching, while the third set did. The shift-cost was the ratio between the average reaction times of the third block and the averages of the first two blocks.

Associative Learning. This was assessed via a verbal paired-associates task (Montgomery et al 2005a). Participants were presented sequentially with the same eight word pairs on a computer screen. For example,

DOOR CASE

YEAR PAGE

After each presentation, the participant was prompted with the first member of each pair and required to recall the second member. Eight such trials were administered. The order of presentation was randomised and changed for each trial. Measures included the number of correct responses in trial 1 (a measure of initial recall), forgetting, and the number of trials required to learn all associations.

Everyday memory: The Everyday Memory Questionnaire (EMQ, Cornish, 2000; Sunderland et al. 1983) is an established self-report measure of memory lapses in everyday activities. It consists of 27 statements, and in each case, participants respond on a 9-point scale ranging from "not at all in the last 6 months" to "more than once a day". Statements include: "forgetting where you put something"; "finding a television story difficult to follow"; a total score for everyday memory is calculated by summing the responses to all items.

Cognitive Failures: The Cognitive Failures Questionnaire (CFQ) measures the relationship between attentional performance and general cognitive functioning. The questions relate to different aspects of cognitive functioning and failure, such as perceptual failures (e.g. do you fail to notice signposts on the road?), misdirected actions (e.g. do you bump into people?) and memory failures (e.g. do you forget what you came to the shops to buy?). The term "cognitive failure" is an umbrella term to cover all three types of slip. Each questionnaire item required a number (0-4 inclusive) to be circled. For each item, four corresponded to "very often" and 0 to "never". There were 25 items in total yielding a maximum score of 100.

To assess the accuracy of participants' responses the Cognitive Failures Questionnaire for Others was also administered. This was completed by a 'significant other', i.e., someone who possessed a reasonable knowledge of the participant's behavior in real world contexts. The participant's significant other was asked: 'During the last six months has your relative/partner/housemate seemed to be:' after which eight items were presented, including for example, 'Forgetful, such as forgetting where he/she has put things, or about appointments, or about what he/she has done?'

The participant's significant other responded on a 5 point scale with responses to half of the items beginning with "very often" and half with "never". Following reversal of the scores as appropriate a total score was obtained by summing the scores to the individual items. This yielded a maximum score of 40. In the original study, Broadbent et al. used family members or partners of the participant, but due to the nature of student populations, in the present study we adopted the same approach as Smith-Spark et al (2004) and added "housemate" to the list of significant others. Total scores and percentage of slips reported were calculated to enable comparison between the two measures.

Prospective memory (PM): This was assessed using the Prospective Memory Questionnaire (PMQ), which is an established self-report measure (Hannon et al., 1995). The PMQ provides measures of three aspects of PM on a scale of 1-9 for each aspect. Fourteen questions measure short-term habitual PM, e.g. "I forgot to turn my alarm clock off when I got up this morning". Fourteen items measure long-term episodic PM, e.g. "I forgot to pass on a message to someone". Ten questions measure internally cued PM, e.g. "I forgot what I wanted to say in the middle of a sentence". In addition, 14 questions make up the "techniques to remember" scale, which provides a measure of the number of strategies used to aid remembering. Responses on the PM scales ranged from 1 (never) to 9 (4 or more times a week/month/year) with the midpoint of the scale labelled '2 or more times a week/month/year'. For each of the 4 scales, a total score is calculated by summing the responses in each section, and dividing by the number of items in that section (14 for ST-habitual, LT-episodic and strategies, 10 for internally cued). Thus scores on all 4 scales ranged from 1-9 with high scores being indicative of much forgetting, and many strategies used to aid remembering.

Procedure

Participants were informed of the general purpose of the Study, and written informed consent was obtained. The tests were administered under laboratory conditions, and a computer running MS-DOS was used for the computer based tasks. Participants were fully debriefed, paid 15 UK pounds in store vouchers, and given drugs education leaflets. The study was approved by the Ethics Committee of the University, and was administered in accordance with the ethical guidelines of the British Psychological Society.

The tests were administered in the following order: background questionnaire, random letter generation, paired associates learning task, computation span, NART, Raven's progressive matrices, everyday memory, cognitive failures and the prospective memory questionnaires, the word fluency tests, and the number-letter and plus-minus tasks. Individual participants only completed a subset of the above measures.

Design. All measures were analysed using a between participant design with user group with two levels (cannabis users and non users) as the independent variable. In relation to cognitive failures an additional analysis was performed with the source of the ratings within participants and user group between. Dependent variables were respectively the intelligence, executive function, learning, and real world memory measures.

Statistics. Group differences in the background variables (intelligence, cigarettes consumed per day and units of alcohol per week) the executive function and learning measures were evaluated through ANOVA. Similarly ANOVA was used to evaluate group differences in the everyday memory and cognitive failures measures. In relation to prospective memory, MANOVA was utilised with the four measures as dependent variables. Subsequently ANOVAs were also conducted to evaluate group differences in the prospective memory individual measures.

Where statistically significant group differences are obtained on the dependent variables, in those cases where the samples in question also differ significantly on the background measures, ANCOVA will be conducted with the relevant background measures as covariates. If there are any instances where the groups differ significantly on any of the executive or learning measures, ANCOVA will be conducted with the real world memory variables as dependent variables and the relevant executive and learning measures as covariates. This will shed light on the extent to which any cannabis-related differences in real world memory are due to group differences in the executive or learning measures. ANCOVA will also be used in order to explore whether any group differences in the various measures of real world memory have a common basis.

RESULTS

Indicators of cannabis use may be found in Table 1. Over the different samples mean lifetime cannabis use ranged between 470 to 1208 joints. Average weekly dose

ranged between 2.6 and 6.7 joints. There were no significant group differences with respect to the NART, $F < 1$ for all samples. The Ravens measure did not differ significantly between cannabis users and non users for those individuals completing the associative learning and word fluency measures.[1] However cannabis users performed significantly better than non users on the Ravens measure for those samples completing the updating and inhibition executive tasks and the everyday memory and cognitive failures measures.[2] Again compared to non users, cannabis users achieved higher Ravens scores in relation to the switching executive function sample and prospective memory sample, however, the group difference was just short of significance in both cases.[3]

With regard to tobacco, Table 1 reveals that on average the number of cigarettes consumed each day was similar for both the cannabis user and nonuser groups. Only for the sample completing the switching executive function task was the group difference significant[4]. None of the other samples yielded significant group differences[5]. Cannabis users generally consumed more alcohol (units per week) compared to nonusers. The difference was statistically significant for the updating, everday memory/cognitive failures, and prospective memory samples[6]. For the samples completing the access and switching executive function task and for the sample completing the associative learning task, the group differences were not statistically significant[7]

Contrary to expectation inspection of Table 2 reveals that cannabis users did not differ significantly from nonusers on any of the measures of executive functioning. Neither were any group differences evident on the learning measures. Indeed generally the group means were in close proximity. Cannabis users exhibited slightly higher switch costs on the plus-minus and number-letter tasks. On the associative learning task cannabis users actually recalled more than non users on trial one. However, these differences failed to reach significance.

<Insert Table 2 about here>

Means and standard deviations for the everyday memory and cognitive failures measures may be found in Table 2. Given that a high score is indicative of real world memory problems, it is clear that cannabis users performed worse on both measures. In fact users' scores were roughly 20% higher on both measures. Given the significant difference on the Raven's measure and in the level of alcohol consumed, ANCOVA was conducted for both memory measures with the Raven's score and

units of alcohol consumed as covariates in both cases. The cannabis-related group difference remained significant with $F(1,57) = 4.72$, $p = .034$ for everyday memory and $F(1,57) = 4.91$, $p = .031$ for the cognitive failures measure. To investigate the basis of group differences on both memory measures two further ANCOVAs were conducted both with user group between participants. In the first analysis everyday memory was the dependent variable and the cognitive failures measure was the covariate. In the second analysis the measure of cognitive failures was the dependent variable and the everyday memory measure was the covariate. In both cases the cannabis group-related effect was reduced to below statistical significance, $F < 1$, with everyday memory as the dependent variable, and $F(1,59) = 1.46$, $p = .232$ with cognitive failures as the dependent variable. Thus it appears that the cannabis-related deficit in both measures may have some common basis.

With regard to the CFQ-for-others, participants were given the questionnaire and asked to give it to their relative, partner, or housemate to complete. A pre-paid addressed envelope was provided for the participant's significant other to return the questionnaire. In the event questionnaires were returned for 18 of the 29 nonusers and 20 of the 33 users. Table 2 reveals that according to their significant others users were judged as producing more cognitive failures compared to nonusers. This difference approached significant, $p = .065$ (two tailed), and given that the prediction was directional, the outcome was significant on a one-tailed basis.

For each participant the CFQ and the CFQ for-others scores were converted into proportions by dividing by the maximum possible score in both cases. On this basis the level (s.d.) of cognitive failures self reported by cannabis users and non users was respectively 41.65% (8.29) and 35.56% (10.95). However, the level (s.d.) of cognitive failures reported by significant others of cannabis users and non users was respectively 29.38% (9.06) and 24.17% (7.67). Thus in percentage terms significant others rated participants more favourably than the participants rated themselves. This was reflected in a significant effect of the source of the ratings, $F(1,36) = 48.31$, $p = .000$. However irrespective of the source of the ratings, in percentage terms, cannabis users exhibited a greater propensity for cognitive failures compared to nonusers, resulting in a significant effect of user group $F(1,36) = 5.54$, $p = .024$. The relationship between self ratings and ratings by significant others was virtually identical for both groups. Thus although there was a discrepancy between self and other ratings this discrepancy was similar in magnitude for both groups. Consistent

with this, ANOVA revealed that the interaction between the source of the ratings and user group was non significant, $F < 1$. Thus while all participants may overestimate the extent of their memory problems, there is no indication in the present results that users are less accurate than nonusers in assessing their propensity for cognitive failure.

Switching the focus to prospective memory, means and standard deviations for the different aspects may be found in Table 2. MANOVA with user group between participants and the four prospective memory component measures as dependent variables yielded a significant main effect of group, Wilks' lambda = .733, $F(4,42) = 3.82$, $p = .010$. From inspection of Table 2, it is clear that cannabis users scored significantly lower on all four component measures. However, it is noteworthy that the mean scores were in the lower half of the range indicating that on average the magnitude of the problem was not excessive for either group. Nonetheless, cannabis users did exhibit a significant deficit on all dimensions especially on the techniques component subscale indicating that they felt the need to use far more memory aids so as to avoid forgetting. Thus to an extent, the scores on the other component subscales are bolstered by the application of the various techniques and strategies that are employed and so may understate the underlying level of the deficit among cannabis users.

As noted above for those participants completing the prospective memory measure, cannabis users consumed significantly more alcohol compared to nonusers and the group difference on the Raven's measure approached significance. In order to control for these group differences, a MANCOVA was conducted with the prospective memory component measures as dependent variables, group between participants, and the Raven's scores and units of alcohol consumed as covariates. The multivariate effect was intensified following inclusion of the covariates, Wilks' lambda = .654, $F(4,40) = 5.29$, $p = .002$. With regard to the component measures, following inclusion of the covariates, univariate analyses revealed that the group differences remained significant for the PM short term, Internally Cued and Techniques subscales, $F = 9.25$, $p = .004$; $F = 9.44$, $p = .004$; and $F = 17.34$, $p = .000$ respectively on 1, 43 d.f. < 1, and $F(1,42) = 1.35$, $p = .252$, respectively. For the PM Long Term subscale, the group difference approached significance $F(1,43) = 3.70$, $p = .061$.

In order to explore the relationship between the prospective memory scale and the measures of everyday memory and cognitive failures, the last two of these were included as covariates and a further MANCOVA was conducted with the prospective memory component measures as dependent variables and group between participants. The multivariate effect was reduced to a trend following inclusion of the covariates, Wilks' lambda = .808, $F(4,39) = 2.32$, $p = .074$. With regard to the component measures, univariate analyses revealed that the group differences were no longer significant for the PM long term and Internally Cued components, $F < 1$, and $F(1,42) = 1.35$, $p = .252$, respectively. The cannabis-related deficit remained significant for the Short Term Habitual and the Techniques subscales, $F = 4.26$, $p = .045$ and $F = 8.98$, $p = .005$, respectively on 1, 42 d.f. Thus there appears to be some commonality between those factors giving rise to the everyday memory problems, the cognitive failures, and some aspects of the prospective memory deficiencies. However, the univariate ANCOVA results suggest that the deficits on the short term habitual and the techniques subscales might in part relate to some other functionally separate factor.

DISCUSSION

The results obtained failed to reveal cannabis-related deficits in executive component processes and associative learning. However, cannabis use did appear to adversely affect real world memory functioning. Cannabis users were impaired on all three measures, everyday memory, cognitive failures, and prospective memory. The cannabis-related deficits in everyday memory and cognitive failures appeared to have a common basis in that the significant group effect in each was reduced to below statistical significance following inclusion of the other as a covariate. However, following the inclusion of the everyday memory and cognitive failures measures as covariates, the multivariate group effect in prospective memory although reduced, approached significance and the univariate outcomes for the PM Short Term Habitual and the PM Techniques measures remained statistically significant. Thus it appears that the cannabis-related group deficits in prospective memory are in some way distinct from those in everyday memory and cognitive failures.

Prior to the present paper, Rodgers et al (2001) was the only study that we are aware of to examine real world memory processes in illicit drug users. In an Internet based study of poly-substance abusers, regression analysis revealed that the frequency

of cannabis use was significantly associated with impairments in everyday memory and in aspects of prospective memory (PM). More specifically the PM short term and PM internally cued subscales were found to be adversely related to cannabis use while PM long term was significantly and adversely related to ecstasy use (Rodgers et al, 2001). The present results are broadly consistent with those of Rodgers et al. Everyday memory deficits were observed among cannabis-only users but unlike Rodgers et al our sample exhibited deficits in all aspects of prospective memory and in addition deficits in the CFQ measure were also observed. Furthermore on the CFQ-Others measure, the degree of impairment among users was judged to be greater than that among nonusers by their respective significant others. The differing pattern of prospective memory outcomes reported by Rodgers et al and the present paper might be a product of the different characteristics of the two samples. It may be that the effects of cannabis in the context of polydrug use are different than is the case for cannabis-only users.

Given that real world memory processes are known to be dependent on prefrontal executive resources (Marsh & Hicks, 1998; McDaniel et al, 1999; Whyte et al, 2006) cannabis-related deficits in real world memory might be taken as evidence of cannabis related deficits in executive functions. However, in this regard it is surprising that none of the laboratory measures of executive functioning and learning that were administered here were associated with cannabis-related deficits. It may be that while cannabis users are able to perform adequately in a laboratory setting, under the less controlled conditions that exist outside the laboratory, where there may be more distractions, users might demonstrate impairment. Thus it may be that were it possible to administer more ecologically valid executive function tasks in real world contexts cannabis-related deficits would be observed. Indeed other non-laboratory self-report measures have provided evidence of executive deficits. Verdejo-Garcia et al (2006) administered a multi-item rating scale measure which is believed to measure different aspects of prefrontal functioning including an executive component (planning, working memory, and mental flexibility) and an apathy component (loss of energy, poor initiation, blunted affective expression). The former is believed to rely on DLPFC resources and the latter on the anterior cingulate. It was found that the severity of cannabis use (an estimate based on the dose, frequency and length of use) significantly predicted outcomes on the executive and apathy subscales (Verdejo-Garcia et al, 2006).

Thus the absence of executive deficits in the laboratory context does not necessarily imply that these processes are entirely intact. Indeed although cannabis users performed normally in the laboratory tasks administered here this does not imply that THC has no effect on the neural structures supporting these tasks. Jager et al (2007) asked their participants to perform an associative learning task. Utilising fMRI, lower activation levels among frequent cannabis users were observed in the medial temporal structures (especially the para-hippocampal area) and the right DLPFC. However, task performance was unaffected and voxel based morphometry revealed no structural differences in the regions of interest (ROI). Analogous results were obtained in an earlier study by the same authors (Jager et at, 2006). Frequent but moderate cannabis users performed similarly to nonusers in tests of working memory and visuo-auditory selective attention. However, fMRI revealed that while there were no differences in terms of overall patterns of brain activity a more specific analysis focussing on ROI revealed differences in brain activity between users and nonusers in the superior parietal cortex. Although outside the prefrontal cortex, the parietal cortex is known to play a role in a range of executive tasks (Collette et al, 2006). The significance of these altered patterns of neural activation among cannabis users remains unclear although it is possible that they might result in impaired performance under more demanding conditions.

It is also possible that underlying deficits might have been apparent but that these were masked by other factors. For example Jacobsen et al (2007) note that most cannabis users also smoke tobacco and that the joint effects of these two psychoactive substances remains unclear. In a recent study they found that verbal memory and learning was impaired among adolescent cannabis users (but not nonusers) during a period of nicotine withdrawal. Through fMRI it was established that the impairment was associated with disrupted frontparietal connectivity. It is possible that nicotine and cannabis may interact in terms of their effects causing underlying memory impairments to be effectively masked in cannabis users (Jacobsen et al 2007).

While the range of outcomes reported above are potentially important, it is appropriate to acknowledge a number of limitations in relation to the present findings. With respect to real world memory, with one exception the measures used were self-report checklists. Clearly the results obtained must be viewed in the context of the reliability and validity of the instruments that were used. In this regard it is noteworthy that the results reported here from the CFQ-for-others demonstrated that

users were as accurate as nonusers in assessing their propensity for cognitive failures. This outcome is consistent with findings reported elsewhere for non clinical populations where a high level of agreement between self ratings and ratings by significant others has been obtained in relation to the real world memory (e.g., Hart et al, 2005; Olsson et al 2006; Smith-Spark et al, 2004). Beyond the issue of consistency with ratings by significant others, it has been demonstrated that the measure possesses internal consistency (Broadbent, et al 1982; Knight et al, 2004), retest reliability, face validity (Knight et al, 2004) and construct validity (Broadbent, et al 1982, Jones & Martin, 2003; Wallace, 2004; Wallace et al, 2002). The psychometric properties and construct validity of the everyday memory questionnaire (EMQ) have also been extensively explored in normal (Cornish, 2000) and clinical populations (Efklides et al, 2002; Koltai et al, 1996; Olsson et al, 2006; Schwartz & McMillan, 1989). Aspects of the EMQ were found to map onto discrete laboratory and real world memory measures and the utilisation of memory aids. Self ratings were highly correlated with ratings by significant others. Likewise the reliability and validity of Prospective Memory Questionnaire has been assessed (Hannon et al, 1995).

With regard to the existence of cannabis-related differences, due to the quasi-experimental design of the study, it is possible that the two groups may have differed on some variable other than cannabis use. Some possibilities have been excluded such as intelligence (NART) and the use of other illicit drugs. Group differences in other variables such as general health, nutrition, or some premorbid condition predating drug use (Verheul, 2001) cannot be ruled out. Furthermore, due to limited resources we were unable to provide an objective measure of recent drug use (e.g. from hair or urine samples). While this is clearly a limitation it is not without precedent. For example other studies testing cognitive deficits among ecstasy and cannabis users have not used these techniques relying instead on self reports (e.g. Croft et al, 2001; Morgan, 1998; Morgan, 1999; Rodgers, 2000). Furthermore, the drug history questionnaire (Montgomery et al 2005b) used in the research reported here has been developed so as to provide a number of tests of internal consistency and we have no reason to doubt the integrity of the information provided by the participants. Nonetheless the results reported in the present paper need to be assessed within the context of the limitations that have been noted.

In conclusion, cannabis-related deficits in all aspects of real world memory were present. While no deficits were observed in laboratory tests of executive

function it remains possible that more ecologically valid tests of prefrontal processes might reveal cannabis-related differences. Further research is needed to explore the basis of cannabis related deficits in real world memory and their link with executive processes.

References

Andersson, M., Usiello, A., Borgkvist, A., Pozzi, L., Dominguez, C., Fienberg, A. A., Svenningsson, P., Fredholm, B. B., Borrelli, E., Greengard, P., & Fisone, G. (2005). Cannabinoid action depends on phosphorylation of dopamine- and cAMP-regulated phosphoprotein of 32 kDa at the protein kinase A site in striatal projection neurons. J Neurosci, 25(37), 8432-8438.

Block, R.I., & Ghoneim, M.M. (1993). Effects of chronic marijuana use on human cognition. Psychopharmacology (Berl), 110, 219-228.

Broadbent, D.E., Cooper, P.F., FitzGerald, P., & Parkes, K.R. (1982). The Cognitive Failure Questionnaire (CFQ) and its correlates. Br J Clin Psychol, 21, 1-16.

Collette, F., Hogge, M., Salmon, E., & Van Der Linden, M. (2006). Exploration of the neural substrates of executive functioning by functional neuroimaging. Neuroscience, 139, 209–221

Cornish, I. M. (2000). Factor structure of the Everyday Memory Questionnaire. Br J Psychol, 91, 427-438.

Croft R.J., Mackay, A.J., Mills, A.T.D., & Gruzelier, J.G.H. (2001). The relative contributions of ecstasy and cannabis to cognitive impairment. Psychopharmacology (Berl), 153, 373-379.

Doble A. (1999). The role of excitotoxicity in neurodegenerative disease: implications for therapy. Pharmacological Therapy, 81, 163-22.

Efklides, A., Yiultsi, E., Kangellidou, T., Kounti, F., Dina, F. & Tsolaki, M. (2002). Wechsler Memory Scale, Rivermead Behavioral Memory Test, and Everyday Memory Questionnaire in healthy adults and Alzheimer's patients. European Journal of Psychological Assessment, 18, 63-77.

Fehr, K.A., Kalant, H., & Leblanc, A.E. (1976). Residual learning deficit after heavy exposure to cannabis or alcohol in rats. Science, 192 (4245), 1249-1251.

Fisk, J.E., & Sharp, C. A. (2004). Age-related impairment in executive functioning: Updating, inhibition, shifting, and access. J Clin Exp Neuropsychol, 26, 874-890

Goldstein, L.H., & Polkey, C.E. (1992). Everyday memory after unilateral temporal lobectomy or amygdalo-hippocampectomy. Cortex, 28, 189-201.

Guzman, M,, Sanchez, C., Galve-Roperth, I. (2001). Control of cell survival/death decision by cannabinoids. J Mol Med, 78, 613-626.

Hannon, R., Adams, P., Harrington, S., Fries-Dias, C., & Gibson, M.T. (1995). Effects of Brain injury and age on prospective memory self-rating and performance. Rehabil Psychol, 40, 289-297.

Hart, T., Whyte, J., Kim, J., & Vaccaro, M. (2005). Executive function and self-awareness of 'real-world' behavior and attention deficits following traumatic brain injury. J Head Trauma Rehabil, 20, 333-347.

Hubert, J.P., & Doble, A. (1998). Neuroprotective compounds inhibit depoloarisation-evoked calcium transients in granule cells. Drug Dev Res, 45, 74-82.

Jacobsen, L.K., Pugh, K.R., Constable, R.T., Westerveld, M., & Mencl, W.E. (2007). Functional correlates of verbal memory deficits emerging during nicotine withdrawal in abstinent adolescent cannabis users. Biol Psychiatry, 61, 31-40.

Jager, G., Kahn, R.S., Van den Brink, W., Van Ree, J.M. & Ramsey, N.F. (2006). Long-term effects of frequent cannabis use on working memory and attention: an fMRI study. Psychopharmacology (Berl), 185, 358-368.

Jager, G., Van Hell, H.H., De Win, M.M.L., Kahn, R.S., Van den Brink, W., Van Ree, J.M., & Ramsey, N.F. (2007). Effects of frequent cannabis use on hippocampal activity during an associative memory task. Eur Neuropsychopharmacol, 17, 289-297.

Jones, G. V., & Martin, M. (2003). Individual differences in failing to save everyday computing work. Appl Cogn Psychol, 17, 861-868.

Kliegel, M., Phillips, L. H., Lemke, U., & Kopp, U. A. (2005). Planning and realisation of complex intentions in patients with Parkinson's disease. J Neurol Neurosurg Psychiatry, 76, 1501-1505

Knight, R. G., McMahon, J., Green, T. J., & Skeaff, C. M. (2004). Some normative and psychometric data for the geriatric depression scale and the cognitive failures questionnaire from a sample of healthy older persons. NZ J Psychol, 33, 163-170.

Koltai, D. C., Bowler, R. M., & Shore, M. D. (1996). The Rivermead Behavioural Memory Test and Wechsler Memory Scale- Revised: Relationship to everyday memory impairment. Assessment, 3, 443-448.

Lawston, J., Borella, A., Robinson J.K., & Whitaker-Azmitia, P.M. (2000). Changes in hippocampal morphology following chronic treatment with the synthetic cannabinoid WIN 55,212-2. Brain Res, 877, 407-410.

Marsh, R. L., & Hicks, J. L. (1998). Event-based prospective memory and executive control of working memory. J Exp Psychol Learn Mem Cogn, 24, 336-349.

McDaniel, M. A., Glisky, E. L., Guynn, M. J., Routhieaux, B. C. (1999). Prospective memory: A neuropsychological study. Neuropsychology, 13, 103-110.

Messinis, L., Kyprianidou, A., Malefaki, S., & Papathanasopoulos, P. (2006). Neuropsychological deficits in long-term frequent cannabis users. Neurology, 66, 737-739.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A. & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to 'frontal lobe' tasks: A latent variable analysis. Cognit Psychol, 41, 49-100.

Montgomery C, Fisk JE, Newcombe R (2005a) The nature of ecstasy-group related deficits in associative learning. Psychopharmacology 180: 141-149

Montgomery, C., Fisk, J.E., Newcombe, R., & Murphy, P. (2005b). The differential effects of ecstasy/polydrug use on executive components: Shifting, inhibition, updating and access to semantic memory. Psychopharmacology (Berl), 182, 262-276.

Morgan, M.J. (1998). Recreational use of "ecstasy" (MDMA) is associated with elevated impulsivity. Neuropsychopharmacology, 19, 252-264.

Morgan, M.J. (1999). Memory deficits associated with recreational use of "ecstasy" (MDMA). Psychopharmacology (Berl), 141, 30-36.

Nelson, H.E. (1982). National Adult Reading Test (NART) Test Manual. Windsor, Berkshire, UK: NFER-Nelson

Olsson, E., Wik, K., Östling, A., Johansson, M., & Andersson, G. (2006). Everyday memory self-assessed by adult patients with acquired brain damage and their significant others. Neuropsychol Rehabil, 16, 257-271.

Pope, H. G., Jacobs, A., Mialet, J., Yurgelun-Todd, D., & Gruber, S. (1997). Evidence for a sex-specific residual effect of cannabis on visuospatial memory. Psychother Psychosom, 66, 179-184.

Raven, J., Raven, J.C., & Court, J.H. (1998). Manual for Raven's Progressive Matrices and Vocabulary Scales. Oxford, UK: Oxford Psychologists Press

Rodgers, J. (2000). Cognitive performance amongst recreational users of "ecstasy". Psychopharmacology (Berl), 151, 19-24.

Rodgers J, Buchanan T, Scholey AB, Heffernan TM, Ling J, Parrott A (2001) Differential effects of ecstasy and cannabis on self-reports of memory ability; a web-based study. Hum Psychopharmacol Clin Exp, 16, 619-625

Sarne, Y., & Keren, O. (2004). Are cannabinoid drugs neurotoxic or neuroprotective? Med Hypotheses, 63, 187-192

Sarne, Y., Tselnicker, B., Pick, C., & Keren, O. (2005). Dissociating between neuroprotective and neurotoxic effects of THC (delta-9 tetrahydrocannabinol). Paper presented at the International Association for Cannabis as Medicine (IACM) 3rd Conference on Cannabinoids in Medicine, Leiden University, 9-10th September, 2005.

Schwartz, A. F., & McMillan, T. M. (1989). Assessment of everyday memory after severe head injury. Cortex, 25, 665-671.

Schwartz, R. H. (1991). Heavy marijuana use and recent memory impairment. Psychiatr Ann, 21, 80-82.

Smith-Spark, J. H., Fawcett, A., Nicolson, R. I., & Fisk, J.E. (2004). Dyslexia and everyday cognitive performance. Memory, 12, 174-182.

Solowij, N., Stephens, R. S., Roffman, R. A., Babor, T., Kadden, R., Miller, M., Chriatiansen, K., McRee, B., & Vendetti, J. (2002). Cognitive functioning in long-term heavy cannabis users seeking treatment. JAMA, 287(9), 1123-1131.

Sunderland, A., Harris, J.E., & Baddeley, A.D. (1983). Do laboratory tests predict everyday memory? Journal of Verbal Learning and Verbal Behaviour, 22, 341-357

Varma, V. K., Malhotra, A. K., Dang, R., Das, K., & Nehra, R. (1988). Cannabis and cognitive functions: A prospective study. Drug Alcohol Depend, 21, 147-152.

Verdejo-Garcia, A., Rivas-Perez, C., Lopez-Torrecillas, F., & Perez-Garcia, M. (2006). Differential impact of severity of drug use on frontal behavioral symptoms. Addict Behav, 31, 1373-1382.

Verheul, R. (2001). Co-morbidity of personality disorders in individuals with substance use disorders. Eur Psychiatry, 16, 274-282.

Wallace, J. C. (2004). Confirmatory factor analysis of the cognitive failures questionnaire: Evidence for dimensionality and construct validity. Pers Individ Dif, 37, 307-324.

Wallace, J. C., Kass, S.J., & Stanny, C. J. (2002). The cognitive failures questionnaire revisited: Dimensions and correlates. J Gen Psychol, 129, 238-256.

West, R.L. (1996). An application of prefrontal cortex function theory to cognitive aging. Psychol Bull, 120, 272-292.

Whyte, J., Grieb-Neff, P., Gantz, C., & Polansky, M. (2006). Measuring sustained attention after traumatic brain injury: Differences in key findings from the sustained attention to response task (SART). Neuropsychologia, 44, 2007-2014.

Table 1. Intelligence and Indicators of Cannabis Use

	Updating and Inhibition Executive Functions: Computation Span and Random Generation Sample			Access Executive Function: Word Fluency Sample			Switching Executive Function: Plus/Minus-Number/Letter Task Samples		
	Mean	S.D.	n	Mean	S.D.	n	Mean	S.D.	n
Cannabis Users			46			24			20
Ravens Progressive Matrices	50.20	4.79	45	49.46	4.85	24	49.85	5.12	20
NART	29.67	5.54	46	28.96	5.65	24	28.40	5.28	20
Units of Alcohol per Week	16.39	11.31	46	14.35	8.34	24	15.10	7.74	20
Cigarettes per day	2.36	4.24	46	1.48	3.83	24	2.00	3.68	20
Total Use (joints)	742.73	1151.60	28	1098.05	1549.80	11	469.67	728.03	9
Frequency of Use (times per week)	0.75	1.04	28	0.76	0.95	11	1.11	1.52	9
Use During Previous 10 Days (joints)	1.11	3.04	46	0.71	1.83	24	1.15	3.38	20
Use During Previous 30 Days (joints)	6.79	24.29	40	4.25	9.81	18	12.16	37.82	16
Average Weekly Dose (joints)	4.17	8.23	28	6.10	12.34	11	2.61	3.90	9
Length of Use (weeks)	189.72	136.98	45	200.23	161.61	23	152.25	96.54	20
Abstinence period (weeks, Mean/Median/n)	28.73	4	45	12.55	3	23	36.15	6	20
Non-Cannabis Users			45			32			17
Ravens Progressive Matrices	47.18	5.32	45	47.21	5.05	32	46.65	5.15	17
NART	29.67	5.44	45	30.22	6.05	32	29.47	4.84	17
Units of Alcohol per Week	10.23	8.95	42	10.40	9.88	29	11.79	11.58	14
Cigarettes per day	1.33	3.90	45	1.88	4.53	32	0.00	0.00	17

Some users were unable or unwilling to quantify their previous patterns of use.

Table 1. Intelligence and Indicators of Cannabis Use (Continued)

	Everyday Memory and Cognitive Failures Sample			Prospective Memory Sample			Associative Learning Sample		
	Mean	S.D.	n	Mean	S.D.	n	Mean	S.D.	n
Cannabis Users			33			27			16
Ravens Progressive Matrices	50.09	4.78	32	50.30	4.63	27	49.19	4.20	16
NART	29.42	5.63	33	29.81	5.94	27	29.69	6.31	16
Units of Alcohol per Week	17.58	12.90	33	17.33	13.79	27	13.47	9.67	16
Cigarettes per day	2.17	4.26	33	1.89	4.27	27	2.22	4.56	16
Total Use (joints)	782.57	1241.55	22	784.45	1242.18	19	1207.65	1588.06	10
Frequency of Use (times per week)	0.64	0.85	22	0.55	0.72	19	0.84	0.96	10
Use During Previous 10 Days (joints)	0.94	2.54	33	0.96	2.78	27	0.94	2.17	16
Use During Previous 30 Days (joints)	3.82	8.06	30	2.69	5.54	24	5.46	10.89	14
Average Weekly Dose (joints)	4.51	9.13	22	4.28	9.54	19	6.70	12.84	10
Length of Use (weeks)	208.72	151.16	32	214.26	150.69	27	251.62	171.80	15
Abstinence period (weeks, Mean/Median/n)	19.65	4	32	21.07	4	27	5.58	2	15
Non-Cannabis Users			29			20			18
Ravens Progressive Matrices	47.07	5.02	29	47.65	4.39	20	46.94	4.72	18
NART	29.69	5.81	29	30.20	6.86	20	30.67	6.72	18
Units of Alcohol per Week	9.36	7.27	29	9.03	8.08	20	10.03	8.32	18
Cigarettes per day	2.07	4.73	29	3.00	5.48	20	3.33	5.69	18

Some users were unable or unwilling to quantify their previous patterns of use.

Table 2. Performance on Executive Function, Associative Learning, and Real World Memory Measures for Cannabis Users and Non Users.

	Cannabis Users		Non Users		F
	Mean	S.D.	Mean	S.D.	
Executive Function Tasks					
Random Letter Generation (standardised scores)					
Alphabetic Sequences	-0.04	0.67	-0.04	0.81	F < 1
Repeat Sequences	0.02	0.53	-0.06	0.72	F < 1
Redundancy	-0.06	0.91	-0.05	0.71	F < 1
Number of Letters	0.04	0.69	0.00	0.94	F < 1
Computation Span	4.43	1.41	4.58	1.63	F < 1
Word Fluency					
S letter	47.42	7.49	46.31	13.08	F < 1
C letter	15.79	4.70	16.56	6.26	F < 1
Semantic	44.63	11.08	43.09	8.92	F < 1
Switching Tasks					
Number – Letter ratio	1.70	0.35	1.58	0.34	F(1,35) = 1.04, p = .316
Plus-Minus Ratio	1.50	0.33	1.39	0.23	F(1,35) = 1.48, p = .233
Associative Learning Task					
Correct Trial 1	5.06	1.84	4.17	2.26	F(1,32) = 1.58, p = .217
Trials to Completion	3.94	1.39	4.33	1.33	F < 1
Forgetting	0.63	0.96	0.83	1.29	F < 1
Real World Memory Measures					
Everyday Memory	87.67	32.29	71.86	23.84	F(1,60) = 4.70, p = .034
Cognitive Failures	43.55	15.40	35.76	10.24	F(1,60) = 5.34, p = .024
Cognitive Failures-for-Others	11.75	3.63	9.67	3.07	F(1.36) = 3.61, p = .065
Prospective Memory					
Long Term Episodic	2.81	0.90	2.30	0.55	F(1,45) = 4.90, p =.032
Short Term Habitual	1.60	0.76	1.08	0.18	F(1,45) = 8.92, p = .005
Internally Cued	2.83	1.28	2.00	0.55	F(1,45) = 7.35, p = .009
Techniques	3.55	1.51	2.18	0.87	F(1,45) = 13.22, p = .001

[1] F(1,32) = 2.12, p = .155 and F(1,54) = 2.79, p = .100, respectively.
[2] F(1,88) = 8.01, p = .006 and F(1,59) = 5.81, p = .019, respectively.
[3] F(1,35) = 3.58, p = .067 and F(1,45) = 3.92, p = .054, respectively.
[4] None of the nonuser group smoked cigarettes. Thus ANOVA was inappropriate. Instead one-sample t test revealed that the number of cigarettes smoked by cannabis users differed significantly from zero, t (df=19) = 2.43, p = .025.
[5] F < 1 for all samples except those participants completing the updating executive task where F(1,89) = 1.44, p=.234.
[6] F(1,86) = 7.95, p=.006; F(1,60) = 9.18, p = .004; and F(1,45) = 5.77, p = .020. respectively.
[7] F(1,51) = 2.42, p=.126; F(1,32) = 1.01, p = ..324; and F(1,32) = 1.25, p = .272. respectively.