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Illegal drug use and prospective memory: A systematic review

Adnan Levent*, Eddy J. Davelaar

Department of Psychological Sciences, Birkbeck, University of London, UK

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ABSTRACT

Illegal drug use is proposed to interfere with neurobiological functioning by damaging the neurotransmitter communication systems that are believed to be responsible for cognitive abilities, including perception, attention, and memory. This review specifically examined effects of illegal drug use on prospective memory (PM) – memory for future actions. Twenty- seven studies spanning 14 years were included in this review which were divided into two broad categories based on testing methods used: self-report and lab-based testing methods.

The quality of the included studies was assessed across five categories: sample type, sample size, abstinence period, testing methods and control for confounding factors. The overall quality of evidence was good for six studies and moderate for sixteen studies and low for five studies. The results from the studies employing self-report were inconsistent as illegal drug users exhibited PM deficits in some studies, but not in others. However, the studies with lab-based testing methods demonstrated more consistent findings with illegal drug users scoring worse than non-users on various PM tests. There were also consistent findings on the link between the dosage of drug taken and level of PM deficit. Based on the literature, there is moderate evidence that illegal drug use impairs PM ability. We recommend that further lab-based studies be conducted to assess dose-response effects on drug-specificity.

1. Introduction

In the last 25 years, much research has demonstrated the negative consequences of a number of illicit substances, such as 3,4-Methylenedioxymethamphetamine (MDMA), cocaine and cannabis. These drugs affect the communication system of the brain by interfering with the natural circulation of neurotransmitters, such as dopamine (DA), serotonin (5-HT), norepinephrine (NE), glutamate (Glu), and gamma-aminobutyric acid (GABA) that have been thought to be responsible for a wide range of processes, including perception, attention, memory, emotion, appetite, sleep, and more. As a result of illicit drug use, some biological and behavioral abnormalities have been observed in humans. For example, individuals who regularly use MDMA showed a reduction of cortical 5- hydroxytryptamine (5-HT) transporter binding compared to a non-user group (Semple et al., 1999). Furthermore, Volkow et al. (2009) demonstrated that cocaine and methamphetamine reduced dopamine release and dopamine D2 receptors in drug users. Behavioral consequences of illegal drugs use (e.g., MDMA, cocaine and more) are varied, including motor skill deficits (Klugman and Gruzelier, 2003), paranoia (Morton, 1999), tachypsychia (Atakan et al., 2012), and executive dysfunctions (Fox et al., 2001; Madoz-Gúrpide et al., 2011). Different types of memory are also influenced by illicit drug use. For instance, ecstasy users scored significantly lower on the verbal memory test compared to non-user controls (Schilt et al., 2007) and illegal poly-drug users had more difficulties in accessing semantic memory and autobiographical memory compared to non-users (Oliveira et al., 2007).

Another type of memory that suggested to be negatively affected by illegal drug use is prospective memory (Heffernan et al., 2001a). Prospective memory (PM) is the ability to remember to carry out a particular behavior at some future point in time which maybe in the short- or long-term (Henry et al., 2004). PM plays a very important role in everyday life as it governs our ability to organize our time in an efficient and independent way. The failures of PM can be irritating (e.g., forgetting to buy bread on the way home from work) as well as life threatening (e.g., forgetting to take daily medications; Terrett et al. 2014). For example, Nelson et al. (2006) found that people who reported forgetting to take their blood pressure medication were more likely to have a heart attack or die than people who did remember to take their medication. It can also influence an individual's reputation and self-esteem, such that one might be perceived as being organized and conscientious or as being unorganized and unreliable (Walter and Meier, 2014). PM is a multi-phase, complex cognitive ability that includes the following characteristics (McDaniel and Einstein, 2007).

* Corresponding author at: Department of Psychological Sciences Birkbeck, University of London, Male Street, London, WC1E 7HX, UK.
E-mail address: aleven01@mail.bbk.ac.uk (A. Levent).

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There must be a deliberately formed goal or plan that should be performed in the future. The PM task must be combined with an ongoing activity that needs attentional resources. Therefore, an individual has to consciously interrupt the ongoing task to perform their aimed action. There are five stages of PM: the formation of intention, a temporarily extended interval during which the intention is not attended to, the detection of a cue that triggers retrieval of the intention, recall of the intention and, lastly, execution of the intention (Zogg et al., 2012). There are two forms of PM: time- based and event-based. Time-based PM involves remembering to perform a planned action at a particular future time point, for example, attending a lecture at 12 pm, taking medication at 8 pm or drinking milk at 11 pm. Event-based PM involves remembering to perform a planned action when a particular event occurs. For instance, taking medication after dinner or buying a loaf of bread when passing the bakery on the way home. Event-based tasks are usually considered less cognitively demanding than time-based tasks as it is mostly likely that external cues trigger intended actions. By contrast, time-based tasks require more self- initiation and monitoring, thus they are more demanding and more sensitive to memory deficits (Sellen et al., 1997; Einstein et al., 1995). It is also worthy of note that PM relies on various cognitive processes, including executive functioning. Planning takes part in the formation and encoding of an intention (Kliegel et al., 2002) and working memory is responsible for storing the postponed intention while carrying out the ongoing task (Marsh and Hicks, 1998). Furthermore, attentional monitoring of the external world is important to recognize the convenient time or event to start the PM action (Landsiedel et al., 2017). Lastly, inhibitory control/cognitive flexibility is also required for PM as a person has to shift their attention away from the ongoing task in order to perform a planned intention (Kliegel et al., 2002).

The aim of this review was to examine research reporting the presence or absence of impairments in PM associated with the use of illicit drugs. The rationale for this review is two-fold. First, there is an increase in illegal drug use across the world. For example, according to the Crime Survey 2015/16, around 1 in 5 young adults aged 16 to 24 had taken an illicit drug in 2014 in England and Wales, which equates to around 1.1 million people (Home Office Statistical Bulletin, 2016). Globally, it is estimated that 1 in 20 adults, or a quarter of a billion people, aged 15-64 years, used at least one illicit drug in 2014 (United Nations Office on Drugs and Crime, 2016). Second, most studies on human memory have been retrospective in nature, referring to memory of words, people and events experienced or encountered in the past. While there is an increase in the number of researches on PM, the research on the impact of illicit drug use on PM is lagging.

2. Method

2.1. Identification of Studies

A computer-based search involving Science Direct, PubMed, PMC and Birkbeck Library databases was conducted. The key conceptual terms used as search parameters were prospective memory, everyday memory, prospective memory questionnaire, prospective memory task, virtual reality prospective memory task, cognition, drug, drug abuse, recreational drug, illicit drug, illegal drug, MDMA, cocaine, cannabis, amphetamine, methamphetamine, ketamine, heroin, opioids, methadone, magic mushroom, d-Lysergic Acid Diethylamide (LSD) and different combinations of these words. Furthermore, a backwards citation search was conducted (i.e., references in each of the journal articles retrieved were checked). There was no limitation on publication date.

2.2. Inclusion/Exclusion Criteria

The search was limited to English-language publications with human participants. Conference presentations, dissertations were excluded from the review. Studies had to report new findings, including replications, but those that examined subjects under the influence of any drugs were also excluded.

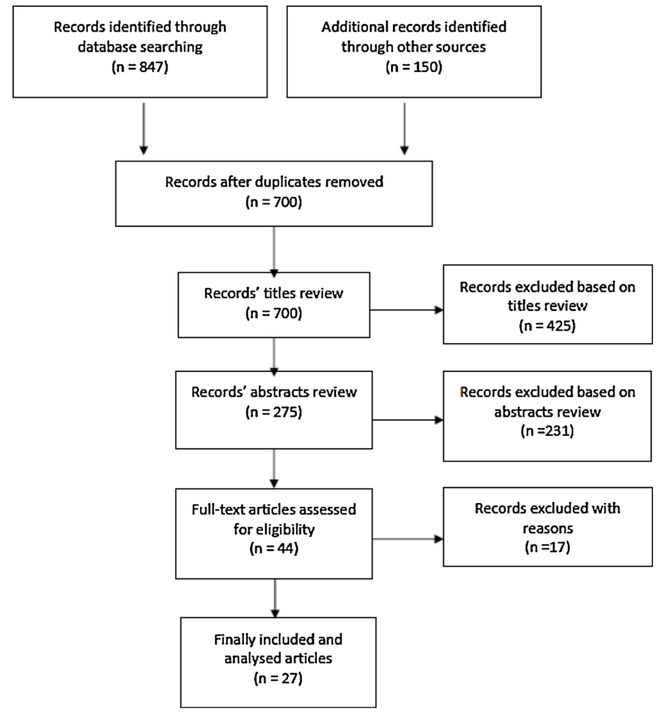

Fig. 1. Systematic review search results and flow chart.

2.3. Data Extraction

As Fig. 1 shows, twenty-seven studies met the inclusion criteria. There were a number of cases where an article consisted of more than one study (Heffernan et al. 2001b; Gallagher et al., 2014; Cuttler et al., 2012). In these cases, each study was assessed individually. Some studies used self-report PM tests as well as lab-based PM tasks and were reviewed twice, once under each appropriate subtitle.

Most participants from the drug user groups were ecstasy/poly-drug users, since they reported taking a range of other recreational compounds (e.g., cannabis, cocaine, amphetamine, heroin etc.) with the exception of the six studies in which participants were only cannabis users (Fisk and Montgomery, 2008; Arana et al., 2011; McHale and Hunt, 2008; Montgomery et al., 2012; Bartholomew et al., 2010; and Cuttler et al., 2012).

Furthermore, most studies compared drug users with non-users, with the exception of four studies (Zakzanis et al., 2003; Montgomery et al., 2010; Hadjiefthyvoulou et al., 2011a; Gallagher et al., 2014 study 1) that compared ecstasy/poly-drug users with no ecstasy poly-drug users (there was no non-user group).

2.4. Systematic Evaluation

The included studies were assessed on the following categories: sample size, sample type, testing methods, abstinence period, control for potential confounds. Each category was defined as good, moderate or low based on the information that was supplied in the article. Overall, studies with three and more categories that were defined as good met requirements for good quality of evidence; studies with three or more categories defined as at least moderate provided moderate quality of evidence. The rest of the studies were classed as providing low quality of evidence.

2.4.1. Population Representativeness

2.4.1.1. Sample Type. There were three classifications "good," "moderate," and "low" in this subcategory. A sample from the general population was defined as good in population representativeness when it included individuals of different ages, educational level, economic status and geographical locations. A sample from the student population was defined as moderate in population representativeness as they include individuals with similar age range and education background. A sample from the clinical population was defined as low in population representativeness as they include individuals with mental disorders that might directly affect the result of a study.

2.4.1.2. Sample Size. There were three classifications "good," "moderate," and "low" in this subcategory. Good sample size was defined as 100+ participants; moderate sample size was defined as 50-100 participants; and low sample size was defined as 0-50 participants.

2.4.1.3. Abstinence Period. There were three classifications "good," "moderate," and "low" with 7+ days, 3-7 days and less than 3 days of drug abstinence respectively. Studies in which the abstinence period was not given were also defined as low. It is very important that participants who take part in a study are not under influence of any drug as acute effects can interfere with individuals' cognitive functions (Garavan et al., 2008). There are also comedown effects that occur when the effects of drugs wear off. It lasts 3 to 7 days (McGregor et al., 2005) during which, the brain is readjusting the chemical imbalance. Therefore, ideally, it is recommended that subjects should be drug-free for at least 7 days (Miller and Gold, 1998).

2.4.1.4. Testing Methods. There were three classifications "good," "moderate," and "low" in this category. Good testing method was defined as both self-report and lab-based tests. Moderate testing method was defined as only lab-based tests. Low testing method was defined as only self- report tests. Self-report information obtained from individuals with a history of illegal substance use may not be accurate as it relies on participants' abilities to recall their past memories correctly which might be impaired due to drug use (Cuttler et al., 2012). By contrast, it is believed that lab-based tests are more objective and reliable as they offer real- world function testing through the use of a controlled setting (Montgomery et al., 2012).

2.4.1.5. Control for Confounding Factors. There were three classifications "good," "moderate," and "low" in this category. There are some factors that can contribute to PM performance, such as age (Henry et al., 2004), depression (Li et al., 2013), sleep quality (Grundgeiger et al., 2014), IQ (Uttl et al., 2013) and more. Therefore, studies that controlled for three or more of these factors were defined as good. Studies that controlled two of these factors were defined as moderate. Studies that controlled for only one factor or did not control for any potential confound at all or did not give any information about the controlling of confounding were defined as low.

3. Result

A summary of the twenty-seven studies included in the systematic review and overview of their results with the quality assessment are provided in Appendix A and B respectively. As Table 1 presents, of these, six studies met the requirements for good quality of evidence, sixteen studies met the requirements for moderate quality of evidence, and five studies met the requirement for low quality of evidence. This section consists of two parts on the basis of testing methods of PM: self-report questionnaires and lab-based tasks; and each part is broken down into three subtitles: the types of PM test, the studies using a between-groups design and studies with a correlation design.

3.1. The Studies with Self-Report PM Questionnaires

3.1.1. The Self-Report PM Questionnaires

Two types of self-report PM questionnaires were used in the studies; the Prospective Memory Questionnaire (PMQ; Hannon et al., 1995) and the Prospective and Retrospective Memory Questionnaire (PRMQ; Piauilino et al., 2010). The PMQ is a self-reported measure of PM that provides measures of three aspects of PM (short-term habitual, long-term episodic and internally cued) on a 9-point Likert scale (Hannon et al., 1995). There are fourteen questions that assess short-term habitual PM, (e.g., "I forgot to lock the door when leaving my apartment or house"); fourteen items assess long-term episodic PM, (e.g., "I forgot to return books to the library by the due date"); and ten items assess internally cued PM, (e.g., "I forgot what I wanted to say in the middle of a sentence"). Responses on the three subscales of PM range from 1(little forgetting) to 9 (a great deal of forgetting).

The PM subscale of the Prospective and Retrospective Memory Questionnaire (PRMQ) is also another type of self-report PM questionnaire which contains 8 PM complaints; four environmentally cued (e.g., "How often do you forget to buy something you planned to buy, like a birthday card, even when you see the shop?") and four self-cued (e.g., "How often do you forget appointments if you are not prompted by someone else or by a reminder, such as a diary or a calendar?") PM complaints (Piauilino et al., 2010).

3.1.2. The Studies Using Between Groups Design

There were twelve studies that used self-report questionnaires in order to examine perceived problems concerning PM (Heffernan et al., 2001a, b study 1, study 2; Montgomery and Fisk, 2007; Weinborn et al., 2011a, b; Bartholomew et al., 2010; Ciorciari and Marotte, 2011; Fisk and Montgomery, 2008; Cuttler et al., 2012 study 2; Hadjiefthyvoulou et al., 2011a, b).

As seen in Table 2, most studies with self-report testing methods had a moderate or above rating on the confounding control, sample type and size categories. In contrast, a low rating on the abstinence period category. The overall of quality of evidence was good for four studies, moderate for six studies and low for two studies.

In Table 3, the findings of the nine studies that used the PMQ are summarized. There were also three studies employing the PRMQ: the first two studies (Weinborn et al., 2011b; and Hadjiefthyvoulou et al. 2011b) showed that illicit drug users made significantly more complaints on Environmentally and Self-Cued PM compared to non-drug users. Whereas, the third study (Weinborn et al., 2011a) did not find significant differences between the groups on PM complaints.

Overall, the main finding is that there is no clear association between illegal drug use and PM deficits as some studies found PM deficits in drug user groups, but others did not.

However, these findings should be treated with some caution for the following reasons: first, in the study by Bartholomew et al. (2010), data were not normally distributed in terms of age, alcohol or nicotine consumptions and therefore non-parametric Mann-Whitney U tests were performed. Second, Hadjiefthyvoulou et al. 2011a compared ecstasy/poly-drug users with no ecstasy poly-drug users, so there was no non-drug user group. Third, Cuttler et al. (2012) study 2 used the more conservative alpha level of .01 rather than .05 to control for inflation of Type I error while performing multiple tests. Fourth, overall, most studies had low ratings on abstinence periods and testing methods.

3.1.3. The Studies Using Correlational Designs

There were six studies that used the self-report PM questionnaires to examine the relationship between the dose of drugs taken and severity of PM deficit (Rodgers et al., 2001, 2003, 2006; Arana et al., 2011; Ciorciari and Marotte, 2011; Cuttler et al., 2012 study 1)

As seen in Table 1, all studies were classified as good in the sample size category, but low in the testing method and abstinence period. Four studies included participants from the general population and two

Table 1
Quality assessment of the 27 studies included in the systematic review. The studies are ordered by overall quality of evidence.

No	Reference	Sample type	Sample Size	Testing Methods	Control for confounds	Abstinence Period	Overall Quality of Evidence
1	Bartholomew et al., 2010	M	M	G	G	G	G
2	Gallagher et al., 2014 study 1	M	G	M	G	G	G
3	Gallagher et al., 2014 study 2	M	G	M	G	G	G
4	Hadjiefthyvoulou et al., 2011a	M	M	G	G	G	G
5	Hadjiefthyvoulou et al., 2011b	M	M	G	G	G	G
6	Cuttler et al., 2012 study 2	M	G	G	G	L	G
7	Weinborn et al., 2011a	G	M	G	M	M	M
8	Weinborn et al., 2011b	L	M	G	G	L	M
9	Bedi and Redman, 2008	G	G	M	M	L	M
10	Heffernan et al., 2001a	G	M	L	M	L	M
11	Heffernan et al., 2001b study 1	G	M	L	M	L	M
12	Heffernan et al., 2001b study 2	G	M	L	M	L	M
13	Zakzanis et al., 2003	M	L	M	G	G	M
14	Montgomery and Fisk, 2007	M	M	L	G	G	M
15	Montgomery et al., 2010	M	L	M	G	G	M
16	Montgomery et al., 2012	M	L	M	G	M	M
17	McHale and Hunt, 2008	G	M	M	M	L	M
18	Rendell et al., 2007	G	M	M	G	L	M
19	Rendell et al., 2009	L	L	M	G	G	M
20	Terrett et al., 2014	G	M	M	G	L	M
21	Rodgers et al., 2001	G	G	L	M	L	M
22	Rodgers et al., 2006	G	G	L	M	L	M
23	Rodgers et al., 2003	G	G	L	L	L	L
24	Arana et al., 2011	M	G	L	L	L	L
25	Fisk and Montgomery, 2008	G	L	L	G	L	L
26	Ciorciari and Marotte, 2011	G	G	L	L	L	L
27	Cuttler et al., 2012 study 1	M	G	L	L	L	L

Table 2
The Studies with Self-Report Testing Methods. Each study was assigned a number, please check Table 1.

	Confounding Control	Sample Size <50: Abstinence Period <3	Sample Size <50: ≥3AND<7	Sample Size <50: ≥7	50<Sample Size<100: Abstinence Period <3	50<Sample Size<100: ≥3AND<7	50<Sample Size<100: ≥7	Sample Size >100: Abstinence Period <3	Sample Size >100: ≥3AND<7	Sample Size >100: ≥7
General Sample	≥3	15								
	2				10, 11, 12	7		21, 22		
	≤1							23, 26		
Student Sample	≥3						1, 4, 5, 14	6		
	2									
	≤1							24, 27		
Patient Sample	≥3				8					
	2									
	≤1									

studies from the student population (Arana et al., 2011; Cuttler et al., 2012 study 1). There were four studies that did not control for any potential confound and two studies controlled only for two potential confounds (Rodgers et al., 2001, 2006). Overall, of the six studies, two were classified as being of moderate quality of evidence and four studies as having low quality of evidence.

Rodgers et al. (2001) web-study included four groups: ecstasy and cannabis users, only ecstasy users, only cannabis users and non-users. This study showed that the amount of cannabis use predicted more self-reported errors on the PMQ short term (Beta = 0.109, $p < .05$) and internally cued (Beta = 0.121, $p < .05$) scales. Whereas, the level of ecstasy use predicted more self-reported errors on the PMQ long-term scale (Beta = 0.115, $p < .05$) and the number of errors made during the test (Beta = 0.108, $p < .05$). In another web-study by Rodgers et al. (2003), poly-drug users were tested and the result revealed that the level of ecstasy use, but not cannabis use, predicted worse score on the long-term scale of the PMQ (Beta = 0.147, $p \leq .001$) and the number of errors made (Beta = 0.112, $p \leq 0.01$) while completing the questionnaires. Rodgers et al. (2006) replicated and extended these findings with another web-based study in which ecstasy/poly-drug users were

Table 3
Overview of the findings of the nine studies employing the PMQ.

Reference	Short-Term PM Deficit	Long-Term PM Deficit	Internally Cued PM Deficit
Heffernan et al., 2001a	✓	✓	✓
Heffernan et al., 2001b, study 1	✓	✓	✓
Heffernan et al., 2001b, study 2	✓	✓	✗
Montgomery and Fisk, 2007	✗	✓	✓
Fisk and Montgomery, 2008	✓	✓	✓
Hadjiefthyvoulou et al., 2011a	✓	✗	✗
Bartholomew et al., 2010	✗	✗	✗
Ciorciari and Marotte, 2011	✗	✓	✗
Cuttler et al., 2012 study 2	✗	✗	✓

Keys: ✓ = present ✗ = not present

tested. These users were divided into groups based on the number of occasions they took ecstasy (e.g., group 1: users with 1-9 occasions ecstasy use; group 2: users with 10-99 occasions; and group 3: users with more than 100 occasions) and they found that there was significant relationship between the frequency of MDMA use and frequency of reporting a number of PM problems ((X^2 (2, N = 206) = 18.11, $p < .001$)). Moreover, Arana et al. (2011) examined cannabis users who were divided into groups based on the dose of cannabis use and what age they have started using cannabis. The result revealed that the earliest the year or the higher the cannabis dosage, the poorer was long term PM ($r = -.257$, $p < .01$) or internally cued PM ($r = -.334$, $p < .01$). Cuttler et al., 2012 study 1 also carried out an online study in which cannabis users (users with a high risk, a moderate risk, a low risk and no risk of cannabis abuse and/or dependence) were assessed. In order to test the relationships between cannabis consumption, problems with cannabis use, and self-reported PM failures, a series of correlation analyses were conducted. Significant correlations were detected between cannabis consumption and self-reported failures on the short-term internally-cued ($r = .12$, $p \leq .001$) and long-term episodic subscales of the PMQ ($r = .15$, $p \leq .001$) and the PM subscale of the PRMQ ($r = .11$, $p \leq .01$).

In contrast to these findings, Ciorciari and Marotte (2011) did not find any correlation between drug frequency and PM impairment after assessing MDMA users, MDMA-free cannabis users and controls who were naïve to illicit substance use.

Overall, the findings of five studies showed that there is a significant link between the amount of drug taken and level of PM deficit with higher amount of drug use being associated with poorer prospective memory.

3.2. The Studies with Lab-Based PM Tasks

3.2.1. Lab-Based PM Tasks

The lab-based PM tasks used in the reviewed research can be categorized into two groups: event-based and time-based. In event-based PM tasks, subjects are requested to remember to carry out a task when cued by appropriate information; it could be short-term or long-term. For example, in the Pattern Recognition task, participants are asked to press the "/" key when two patterns appearing on the computer screen are the same or the "z" key when they are different. After each ½ minute period, the patterns increase in complexity and for each complexity level the computer holds a record of the number of correct responses. In order to save their scores, the subjects are asked to remember to press the ‘F1’ key when the message “please wait a moment” appears on the computer screen at the end of each ½ minute period. This task is repeated three times and failure to press “F1” key is used to assess an event-based PM deficit (Hadjiefthyvoulou et al., 2011a; Gallagher et al., 2014 study 1). Another event-based PM task is the Belonging subscale of the Rivermead Behavioural Memory Test in which participants have to remember to ask for a belonging back at the end of the experiment (McHale and Hunt, 2008). Regarding time-based PM tasks, subjects are requested to remember to carry out a task at a certain point in time. For instance, in the Fatigue short-term PM test (Hadjiefthyvoulou et al., 2011a) participants are asked to indicate their fatigue level every 20 minutes throughout the experiment and in the Mail long-term PM test participants are asked to return a document via post a week or two later from the time of experiment (Gallagher et al., 2014 study 1).

There are also standardized tests, such as the Memory for Intentions Screen Test (MIST; Woods et al., 2008) and the Cambridge Prospective Memory Test (CAMPROMPT; Wilson et al., 2004). In the former, subjects are asked to complete a word- finder puzzle that serves as a distractor and carry out eight different PM tasks (time- and event-based), including four 2-min (short delay) and four 15-min (long delay) trials in 30 minutes. In the latter test, subjects are asked to complete some distractor tasks (e.g., word- search) for a twenty-minute period while they need to remember to carry out the PM tasks (three time-based and three event-based).

Another popular task is the Jansari-Agnew-Akesson-Murphy (JAAM; Jansari et al., 2004) test which is a virtual reality assessment where participants have to play the role of an assistant in an office setting. Their responsibilities include making the office ready for a meeting, turning on the coffee machine when the first person turns up for the meeting, noting the times of fire alarm, organizing chairs and tables for a meeting etc. The JAAM task consists of eight constructs: planning, adaptive thinking, selection, creative thinking, prioritization, together with action-based, event-based and time-based PM subscales.

Another virtual task that is used to measure PM is the Virtual Week task which is a board game where subjects move around the board by rolling a dice (Rendell and Craik, 2000). The starting point is the time when people wake up and each circuit of the board represents a day. The subjects are required to make choices and perform daily activities for a virtual week (7 days) throughout the game. There are ten PM tasks for each virtual day: four regular (time- and event-based) where normal daily duties are undertaken; four irregular (time- and event-based) in which occasional tasks are undertaken; and two time-check tasks where participants are requested to stop playing the game and monitor actual time on the stop-clock.

Lastly, in a video-based PM task participants are given a list of 17 specific locations, such as “at Starbucks” and associated actions that are either questions to be answered, such as “what color is the wall?” or tasks to be carried out at that location, such as “buy coffee.” This is followed by the presentation of a 10-minute long video depicting a shopping area and concentrating on fronts of shops and passers-by that give cues about the location that are to be used to recall the previously shown location-action combinations (Bartholomew et al., 2010).

3.2.2. The Studies Using Between Groups Design

Sixteen studies (McHale and Hunt, 2008; Rendell et al., 2007, 2009; Bartholomew et al., 2010; Montgomery et al., 2010, 2012; Weinborn et al., 2011a, b; Hadjiefthyvoulou et al., 2011a, b; Gallagher et al., 2014 study 1, study 2; Terrett et al., 2014; Zakzanis et al., 2003; Cuttler et al., 2012 study 2; Bedi and Redman, 2008) used lab-based tasks in order to examine participants’ performance on PM.

Table 4 shows the results of the quality assessment of the sixteen studies. As seen, most studies had a good rating on the control confounding factors category. As a sample type and size, most studies were rated as moderate or below. Overall, of the sixteen studies, six studies were classified as being of good quality of evidence and ten studies as having moderate quality of evidence.

In Table 5, the findings of the fifteen studies that assessed time- and event-based PM deficit were summarized. There was another study with a lab-based testing method that employed the video-based PM task to assess overall PM deficit. The result of this study also demonstrated that cannabis users performed significantly poorer than the controls on the video-based PM task (Bartholomew et al., 2010).

Table 4
The Studies with Lab-based Testing Methods. Each study was assigned a number, please check Table 1.

Sample	Confounding Control	Sample Size <50: Abstinence Period <3	Sample Size <50: ≥3AND<7	Sample Size <50: ≥7	50<Sample Size <100: Abstinence Period <3	50<Sample Size <100: ≥3AND<7	50<Sample Size <100: ≥7	Sample Size >100: Abstinence Period <3	Sample Size >100: ≥3AND<7	Sample Size >100: ≥7
General Sample	≥3				18, 20					
General Sample	2				17	7		9		
General Sample	≤1									
Student Sample	≥3		16	13, 15			1, 4, 5	6		2, 3
Student Sample	2									
Student Sample	≤1									
Patient Sample	≥3			19	8					
Patient Sample	2									
Patient Sample	≤1									

Table 5
The Overview of the findings of fifteen studies employing lab-based testing methods.

Reference	Event-based PM deficit	Time-based PM deficit
Zakzanis et al., 2003	✓	✓
McHale and Hunt, 2008	✗	✓
Terrett et al., 2014	✓	✓
Hadjiefthyvoulou et al., 2011a	✓	✓
Hadjiefthyvoulou et al., 2011b	✓	✓
Weinborn et al. 2011a	✓	✓
Weinborn et al. 2011b	✓	✓
Gallagher et al., 2014, study-1-	✓	✓
Gallagher et al., 2014, study-2-	✓	✓
Rendell et al., 2007	✓	✓
Rendell et al., 2009	✓	✓
Montgomery et al., 2010	✓	✗
Montgomery et al., 2012	✓	✓
Bedi and Redman, 2008	✗	✗
Cuttler et al., 2012 study 2	✗	✗

Keys: ✓ = present ✗ = not present

Overall, most lab-based studies found either event-based or time-based PM deficits or both in illegal drug user groups, in particular MDMA/poly-drug users compared to non-user groups apart from two exceptions: Cuttler et al. (2012) study 2 and Bedi and Redman (2008) failed to find significant differences between illicit drug users and non-illicit drug users on time-based PM or event-based PM. However, as mentioned earlier, Cuttler et al. (2012) study 2 used an adjusted alpha level of .01 to control for inflation of Type I error. While less conservative alpha (e.g., .05) would have revealed a significant effect on the event-based PM.

Most studies did not differentiate between short- and long-term PM while testing either time- or event-based PM apart from four studies (McHale and Hunt, 2008; Hadjiefthyvoulou et al., 2011a; Gallagher et al., 2014, study 1, study 2). These four studies tested participants on short- and long-term time-based PM and found that poly-drug users were impaired in both types of time-based PM.

3.2.3. The Studies Using Correlational Designs

Three of the aforementioned studies with lab-based testing methods also looked into the relationship between the dosage of drug use and PM impairment (Hadjiefthyvoulou et al., 2011a; Gallagher et al., 2014 study 2; Montgomery et al., 2012).

As seen in Table 1, most studies were classed as "good" for control of potential and abstinence period and "moderate" for sample type and testing methods. In term of sample size, one study was classed as "good" (Gallagher et al., 2014, study 2), one study as "moderate" (Hadjiefthyvoulou et al., 2011a) and one study as "low" (Montgomery et al., 2012). The overall quality of evidence was good for two studies and moderate for one study.

Gallagher et al. (2014 study 2) tested ecstasy/poly-drug users, cannabis-only users, and nonusers of illicit drugs and found that poorer performance on the event-based and short- term time-based PM tasks were associated with higher long-term average typical dose of ecstasy (respectively, $r = .295$, $p < .01$, $r = -.300$, $p < .01$). Montgomery et al. (2012) also reported this finding; the frequency of drug use was correlated with deficits in planning ($r = -.487$, $p < .001$), time-based ($r = -.394$, $p < .001$) and event-based PM ($r = -.521$, $p < .001$) on JAAM after assessing twenty cannabis-only users and non-illicit drug users. Furthermore, Hadjiefthyvoulou et al. (2011a) tested drug users (ecstasy/poly-drug users and non-ecstasy drug users) and demonstrated that increased total lifetime use of various drugs were related to increased real world memory impairment. For example, there was a correlation between event-based PM score and life time use of cocaine, ecstasy or cannabis (respectively, $r = -.408$, $p < .001$; $r = -.300$, $p < .01$; $r = -.233$, $p < .05$); time-based PM score and life time use of cannabis or cocaine (respectively, $r = -.276$, $p < .05$; $r = -.254$, $p < .05$).

Overall, the findings of three studies demonstrated that poorer PM performances were associated with a higher amount of illegal drug use.

4. Discussion

The aim of this review was to assess studies reporting the presence or absence of PM deficits that are associated with the use of illicit drugs. PM, the ability to remember to do something in the future, is a crucial component for successful execution of countless everyday tasks, including remembering to attend a meeting, paying the utility bill on time, buying bread on the way home. Multiple studies have demonstrated that PM errors account for more than half of all everyday memory problems (Schnitzspahn and Kliegel, 2009).Therefore, it is essential to keep track of the patterns of finding in this field in order to provide a comprehensive understanding of the potential impact of illicit drug use on PM.

The overall quality of evidence was good for six studies, moderate for sixteen studies and low for five studies. Most studies with self-report testing methods had a higher rating on the population representativeness categories (e.g., sample type and size) and lower rating on the abstinence period and confounding control categories compared to the studies with lab-based testing methods.

The studies employing self-report measures of PM, have shown mixed findings on the effect of illicit drug use on PM, but more evidence is in favor of illegal drugs being associated with time-based PM impairment (Heffernan et al., 2001a, b study1, b study 2; Montgomery and Fisk, 2007; Fisk and Montgomery, 2008; Ciorciari and Marotte, 2011; Weinborn et al., 2011b), also some deficits in short-term (Heffernan et al., 2001a, b study1, b study 2, Fisk and Montgomery, 2008; Hadjiefthyvoulou et al. 2011a) and internally cued PM (Heffernan et al., 2001a, b study 1; Montgomery and Fisk, 2007; Fisk and Montgomery, 2008; Cuttler et al., 2012 study 2). However, these findings may not necessarily reflect pure PM deficit as the PMQ and PRMQ rely on self-reports and it has been noted that drug users may not be able to accurately recall their past memories. Cuttler et al. (2012) study 2 compared three groups (chronic cannabis users, experimenter cannabis users and non-users) on the lab-based and self-report tests and found only significant differences on the internally cued PM subscale. However, the deficit was eliminated after controlling for self-reported problems with retrospective memory and deficits on the Rey Auditory Verbal Learning Test (RAVLT). Thus, it is possible that some of the impairments evident on the PMQ and PRMQ might be attributable to other memory components rather than the PM itself. Moreover, as mentioned earlier, most studies with the self-report testing method that found significant PM impairment in drug user groups did not control or report the abstinence period, thus participants might have been in the comedown period during testing where the brain tries to readjust the chemical imbalance, hence the result might not reflect their real long-term cognitive abilities.

To overcome this problem, researchers have started using lab-based testing methods that are very close to everyday life settings (e.g., the virtual week). There are some memory components that are involved in lab-based PM tasks as well, for example, the virtual week task relies on associative learning component of memory (Montgomery et al., 2005).However, they were designed to primarily test PM unlike the self-report PM measures. These researchers have demonstrated consistent findings with illicit poly-drug users scoring worse than non-users on either event-based or time-based PM tasks or both (Zakzanis et al., 2003; McHale and Hunt, 2008; Terrett et al., 2014; Hadjiefthyvoulou et al., 2011a, b; Weinborn et al. 2011a, b; Gallagher et al., 2014 study 1, study 2; Rendell et al., 2007, 2009; Montgomery et al., 2010, 2012) Although many different types of PM tasks were used in these studies, the results were consistent in that they found that drug users exhibited partial or complete PM deficits. It is unlikely that these findings are due to individual differences (e.g., age, gender, education level, IQ etc.), as the groups were well matched on these factors.

The body of work summarized in the current review also provided consistent results on the link between the amount of illicit drug consumption and PM deficit (Rodgers et al., 2001, 2003, 2006; Arana et al., 2011; Cuttler et al., 2012 study 1; Hadjiefthyvoulou et al., 2011a; Gallagher et al., 2014, study 2; Montgomery et al., 2010) apart from one study (Ciorciari and Marrotte, 2011) that failed to find the link. However, it should be noted that there was inconsistency in recording the level of illicit drug use (e.g., duration of use, average dose use, frequency of use, age at first use, total lifetime dose and usage etc.). Hence, it is hard to draw any firm conclusions based on a specific variable reflecting the level of drug use. There are findings that show that lifetime usage of both ecstasy and cannabis were related to either time-based or event-based PM measures or both indicating that as the lifetime usage goes up, the PM deficits increase in magnitude (Hadjiefthyvoulou et al., 2011a, 2011b; Montgomery et al., 2010, 2012; Rodgers et al., 2001; Arana et al., 2011; Gallagher et al., 2014, study 2; Weinborn et al., 2011a). With regard to frequency of use, cocaine and ecstasy use were significantly correlated with several of the PM measures including time- and event-based or short- and long-term (Hadjiefthyvoulou et al., 2011a; Rendell et al., 2007; Zakzanis et al., 2003). The frequency of cannabis use was also significantly associated with the two time-based PM measures (Gallagher et al., 2014, study 2). Furthermore, early users of cannabis displayed more deficits with long term PM and performed worse compared to the control group in the internally-cued PM strategy use (Arana et al., 2011). These indicators of the level of drug use may be correlated and moderated by the type and potency of the drug. Based on the available research it can be said that the amount of drugs taken is one of the greatest predictors in magnitude of PM impairment.

The findings from the range of studies demonstrated that excessive drinking can lead to impairments in everyday PM (Heffernan, 2008). Therefore, it is crucial to control for alcohol use while assessing PM performance. Most studies reviewed here found no significant differences due to alcohol use between drug user and control groups (Weinborn et al., 2011a; Heffernan et al., 2001a; Hadjiefthyvoulou et al., 2011b; Montgomery et al., 2012; Rendell et al., 2009; Bedi and Redman, 2008). However, in some studies the group of drug users consumed more alcohol than the control group (Montgomery et al., 2010; Arana et al., 2011; Hadjiefthyvoulou et al., 2011a; Heffernan et al., 2001b, study 1 and 2; Montgomery and Fisk, 2007; Gallagher et al., 2014, study -2; Bartholomew et al., 2010; and Fisk and Montgomery, 2008). After controlling for alcohol consumption, the illegal drug use-related differences in PM remained significant in these studies (Hadjiefthyvoulou et al., 2011a; Heffernan et al., 2001b, study 1 and 2; Montgomery and Fisk, 2007; Gallagher et al., 2014, study - 2; Bartholomew et al., 2010; Fisk and Montgomery, 2008). Therefore, in these studies, alcohol use does not appear to have an effect on PM deficits over and above the effect due to drug use.

As mentioned in the introduction, PM relies on various cognitive processes, including executive functioning and working memory. Several studies have assessed the consistency between PM deficit and deficits in other memory and executive functions. For example, Rendel, et al. (2009) demonstrated that methamphetamine-induced PM deficit co-occur with deficits in retrospective memory, as ex-methamphetamine users scored worse than controls on the RAVLT, Digit Span, Phonemic Verbal Fluency and Hayling Sentence Completion Test in addition to PM. However, the literature does not support the claim that drug use affects all cognitive functions equally. For example, Hadjiefthyvoulou, et al. (2011b) did not find any effect on the RAVLT with ecstasy/poly drug users, whereas PM was impaired. It turns out that some non-PM tasks, such as computation span task (Montgomery and Fisk, 2007) show drug-related deficits, while other tasks, such as stem completion (Zakzanis et al., 2003) do not. This is even more striking when considering assessments of non-PM executive function, such as Random Letter Generation (Montgomery and Fisk, 2007), Behavioral Rating Inventory of Executive Function (Hadjiefthyvoulou, et al., 2011b), and even the Wisconsin Card Sorting Test (WCST, Arana, et al., 2011), all of which do not show drug- related deficits.

These results need to be interpreted with caution, however, as the reviewed literature on drug use and PM, did not use a standard battery of non-PM tasks. This necessarily means that not enough data has been published to assess whether the drug-related PM deficits reflect a deficit on all cognitive functions or is specific to functions underlying PM function. Based on the inconsistencies in the effects of drugs on non-PM functions, we take the view that there is some suggestion of cognitive specificity - some cognitive functions are specifically affected by drug use. We do acknowledge that in the limit, excessive drug use affects all cognitive functions. Therefore, the differential affect of drug use on PM and non-PM tasks may in part reflect the sensitivity of PM tasks to disruptions of cognitive sub-processes (e.g., recognizing a PM trigger) and in part the drug type, drug dosage, and drug tolerance of participants in the studies in the current literature. To adjudicate among the possibilities, future work on the impact of drugs on PM need to include non-PM memory tasks as well as well-established tasks of executive functions, such as the WCST or Tower of London (Shallice, 1982).

Interestingly, all the studies reviewed in this paper found significant PM deficit at least one PM measure with one exception (Bedi and Redman, 2008), suggesting the possibility of publication bias. For example, as seen in Table 2, there is a gap in the research literature of studies with a small sample size. This could be due to those studies not finding significant effects and therefore not published or submitted for publication. Even though a publication bias is not impossible, most studies with a large sample size reported significant findings.

The pattern of results found in the current review support previous empirical studies in which it has been reported that illegal drug use was associated with a range of neurotoxic effects. For example, Ramaekers et al. (2009) directly assessed the pharmacological effect of MDMA on PM and brain activity in a double-blind, placebo-controlled, cross-over study. Twelve recreational MDMA users received MDMA 75 mg and placebo and performed a lab-based PM task during functional imaging. The result showed that a single dose of MDMA increased PM failures and that MDMA concentration in plasma was positively correlated to number of prospective memory failures. Furthermore, ecstasy use has been linked to structural and functional damage to serotonergic cells in the frontal cortex of the brain that is believed to support PM (McCann et al., 2005; Urban et al., 2012). The medial temporal hippocampal structure is also linked to PM (Gordon et al., 2011). Abnormalities in these brain regions were observed with different types of drug users, such as Cannabis users (Jager et al., 2007), cocaine users (Nestler, 2005) and ecstasy users (Kish et al., 2010).

The included studies examined mostly poly-drug users who consumed a combination of different drugs. Thus, it is hard to associate PM impairment with a particular type of drug type (e.g., sedative and stimulant) or a specific drug (e.g., MDMA and cocaine). However, in most studies, ecstasy poly-drug users scored significantly worse than non-ecstasy users (Hadjiefthyvoulou, et al., 2011b; Gallagher et al., 2014, study 1; Zakzanis et al., 2003; Montgomery et al., 2010) or non-drug users (Heffernan et al., 2001a, 2001b; Montgomery and Fisk, 2007; Rendell et al., 2007; Weinborn et al., 2011a; Hadjiefthyvoulou et al., 2011a) on PM measures, specifically on the long-term PM subscales (Gallagher et al., 2014, study 1, 2; Heffernan et al., 2001a, 2001b; Montgomery and Fisk, 2007; Weinborn et al., 2011a; Rodgers et al., 2001, 2003; and Ciorciari et al., 2011). Furthermore, as mentioned earlier, Ramaekers et al. (2009) demonstrated MDMA-specific toxicity on PM performance, therefore it can be argued that the use MDMA associated with PM impairment. There might also be a possible link between cannabis use and PM impairment as in multiple studies cannabis use was associated with PM impairments (Hadjiefthyvoulou, et al., 2011b; Montgomery et al., 2012; McHale et al., 2008; Gallagher et al., 2014, study 2; Cuttler et al., 2012 study 2; Arana et al., 2011; Ciorciari et al., 2011), in particular with internally-cued PM deficits (Cuttler et al., 2012 study 1, 2; Arana et al., 2011; Fisk and Montgomery, 2008; Montgomery and Fisk, 2007; and Rodgers et al., 20011). However, these results need to be interpreted with caution as some studies fail to find a significant difference between cannabis user and non-user groups or a link between cannabis use and PM impairment. For example, in Gallagher et al. (2014, study 2) and Hadjiefthyvoulou et al. (2011b) studies, there were no significant differences between cannabis-only users and non-users even though there were significant differences between MDMA polydrug users and non-users. Moreover, Ciorciari and Marotte (2011) did not find any correlation between drug frequency and PM impairment in MDMA-free cannabis users. In addition to this, a few studies controlled for cannabis use while assessing the possible consequences of MDMA use on PM. After controlling for cannabis use, the results remained significant which shows that cannabis is not an important mediator of PM deficits in MDMA polydrug users (Heffernan et al., 2001a, 2001b study 1, 2).

Taken together, these results suggest that cannabis and MDMA differentially affected aspects of PM. Ecstasy use was associated with the long-term PM impairments, which could be related to storage and retrieval difficulties. In contrary, cannabis use was associated with reports of 'here-and-now' memory problems in the internally cued PM.

5. Strengths, Limitations, and Future Directions

This review was based on an extensive search of electronic databases, study selection, data extraction, study categorization and comprehensive quality of evidence assessments.

However, as mentioned earlier, our review might be limited by publication bias, whereby studies with non-significant results are less likely to be published.

The inclusion of only studies published in the English language might also be seen as a limitation of this review.

It is clear that further studies are needed to clarify the negative effect of illegal drug use on PM by employing lab-based testing methods rather than self-report testing methods (as Cuttler et al. (2012) demonstrated people with a history of drug use had self-report problems with retrospective memory), recruiting a greater sample size, better control of potential confounds (as there are many factors that might affect PM performance), recruiting a sample from the general population rather than the student or patient populations, requiring a longer abstinence period (at least a week), and using non-drug user participants as a control group. Future studies also should test particular drug users, such as only cannabis or MDMA users in order to understand the effects of a particular drug on PM. Moreover, in future studies, there should be consistency in recording the level of drug use. Lastly, most studies in this review were conducted by the same research group, therefore it is also necessary to carry out similar studies in different institutions and countries in order to maximize the generalizability of the findings.

6. Conclusion

To conclude, the present review intended to determine the impact of illicit drug use on PM, a crucial aspect of day-to-day cognitive functioning. The pattern of findings from studies with mostly moderate quality of evidence in this review suggests that PM is impaired in illegal drug users and should thus be included in the list of neuropsychological deficits resulting from illegal drug use.

Contributors

Authors A. Levent and E. J. Davelaar designed the study. A. Levent summarized previous related work. A. Levent and E.J. Davelaar managed the literature searches and realized the selection of references, extraction and evaluation of the data. A. Levent wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Summary of the 27 studies identified in this systematic review.

Authors, Year and Country and the finding*([t+, t-, r+, r-])	Sample Details: Number of participant (gender distribution, Mean age ((Standard Deviation or Range)) for each group	Combination of drugs taken	Test Batteries	Statistical controls for potential confounds	Abstinence period
Hadjiefthyvoulou et al., 2011a, UK [r+, t+]	42 ecstasy/polydrug users (14 males, Mean age: 21.67 (SD 3.61)) 31 non-users (5 males, Mean age:21.03(SD 3.25))	Ecstasy Amphetamine Cannabis Cocaine	PMQ Lab-based PM tasks	IQ Age Education	14 days
Weinborn et al., 2011a, Australia[t+]	31 Ecstasy/polydrug users (12 males, Mean age: 21.4 (SD 3.3)) 21 High risk alcohol users (9 males, Mean age: 19.5 (SD 2.1)). 31 Health adults (12 male, Mean age: 19.7 (SD 1.6))	Cannabis, Cocaine Ecstasy	MIST (Lab-based) and PRMQ	Sleep Age	3 days
Heffernan et al., 2001a, UK[t+]	30 Regular ecstasy/polydrug users (Mean age: 24.3 (range 18–43)) 31 non users (Mean age: 24.8 (range 19–37))	Cannabis Cocaine Ecstasy	PMQ	Age Gender	Not given
Heffernan et al., 2001b, study -1-, UK[t+]	46 Regular ecstasy/polydrug users (28 males, Mean age: 24.6 (range 18–43)) 46 Controls (17 males, Mean age: 26.1 (range 18–40))	Cannabis Cocaine Ecstasy	PMQ	Age Number of strategies used to remember	1 day
Heffernan et al., 2001b, study-2-, UK[t+]	30 Ecstasy/ polydrug users (17 males, Mean age:23.9 (range 19–40)) 37 Controls (10 males, Mean age: 25.5 (range 19–50))	Cannabis Cocaine Ecstasy	PMQ	Age Number of strategies used to remember	1 day
Rodgers et al., 2001, UK[r+]	155 Ecstasy and Cannabis Users 46 Ecstasy users only 108 Cannabis Users only 225 Non-users Overall 193 males, the modal age group 21–25	Ecstasy Cannabis	PMQ	Age Gender	Not given
Rodgers et al., 2003, UK.[r+]	199 Ecstasy/polydrug users 172 Only Cannabis users 309 Non-users Overall 298 males, the modal age 21–25	MDMA Cannabis Cocaine Amphetamine Magic mushroom LSD	PMQ	Gender	Not given
Montgomery and Fisk, 2007, UK.[t+]	43 Ecstasy/polydrug users (24 males, Mean age: 21.56(SD 1.68)) 51 Non-users (17 males, Mean age:21.51 (SD 1.70))	MDMA Cannabis Cocaine Amphetamine	PMQ	Sleep Alcohol use Age Gender IQ Education Heath Random Letter Generation	7 days
Hadjiefthyvoulou, et al., 2011b, UK.[t+]	29 Ecstasy/polydrug users (17 males, Mean age: 21.17 (SD 1.79)) 12 Cannabis Users (5 males, Mean age: 21.92 (SD 1.56)) 18 Non users (2 males, Mean age: 20.44(SD 2.28))	MDMA Cannabis Cocaine Ketamine Poppers LSD Amphetamine Magic Mushroom	CAMPROMPT (Lab-based)	Age Gender IQ Education Nicotine use Alcohol use	7 days
Montgomery et al., 2010, UK.[t+]	23 Ecstasy polydrug users (13 males, Mean age: 23.22(SD 4.56)) 26 Non-ecstasy polydrug users (9 males, Mean age: 21.92 (SD 2.27))	Ecstasy Cannabis Cocaine	JAAM (Lab-based)	Age Sleep IQ	7 days
Arana, et al., 2011, Spain.[r+]	113 Cannabis users (19 males, Mean age: 19.85(SD 2.21))	Cannabis Valium	PMQ Lab-based PM tasks	Not given	Not given
McHale et al., 2008, UK.[r+, t+]	18 Cannabis users (10 males, Mean age: 21.6(SD 1.1)) 20 Non-drug using controls (10 males, Mean age: 21.4(SD 1.6)) 20 Tobacco smokers (10 males, Mean	Cannabis	Lab-based PM tasks	Age	1 day
Montgomery et al., 2012, UK.[r+, t+]	20 Cannabis users (13 males, Mean age:21 (range 18–25)) 20 non-illicit users (7 males, Mean age: 20 (range 18–25))	Cannabis	JAAM (Lab-based)	IQ Alcohol use Mood Age	5 days
Weinborn et al., 2011b Australia.[t+]	53 individuals with substance use disorder (SUD) (30 males, Mean age: 39.9(SD 11.8)) 44 Heathy Adults (HA) (18 males, Mean age: 42.1(SD 14.2))	Cannabis Amphetamine Heroin	PMQ MIST (Lab-based)	Age Sex Ethnic Identity	Not being under influence of any drug during testing

Ciorciari et al., 2011, Australia. [r-, t+]	25 MDMA/ polydrug users (13 males, Mean age: 27.28(SD 6.30)) 37 Cannabis only users (9 males, Mean age: 27.70 (SD 7.65)) 43 Controls (12 males, Mean age: 27.72(SD 11.20))	Cannabis MDMA Methampheta mine Cocaine LSD Magic Mushroom	PMQ	Not given	Not being under influence of any drug during testing
Rendell et al., 2009, Australia. [t+]	20 ex-Methamphetamine Users (12 males, Mean age: 27.50(SD 5.21)) 20 Controls (12 males, Mean age: 28.20 (SD 5.00))	Cannabis Cocaine Methampheta mine	Virtual Week: A computerized version (Lab-based)	Age Gender Education IQ Depression Anxiety Heath Sleep	3 months
Rendell et al., 2007, Australia. [t+]	27 MDMA users (14 males, Mean age:21.3 (SD 1.96)) 34 controls (15 males, Mean age: 20.6 (SD 1.40))	MDMA Cannabis	Virtual Week: A Computerized version (Lab-based)	Age Education Vocabulary Health	2 days
Terrett et al., 2014, Australia. [t+]	26 opiate users (18 males, Mean age:31(SD 7.46)) 39 controls (17 males, Mean age: 39.47 (SD 7.94))	Heroin Methadone Cannabis	Virtual Week: A Computerized version (Lab-based)	Gender IQ Education	5 hours
Zakzanis et al., 2003, Canada.[t+]	15 MDMA/ polydrug users (12 males, Mean age:24.1 (SD 5.6)) 17 Polydrug no MDMA Controls (14 males, Mean age:23.4(SD 2.0))	Cannabis MDMA Opiates Amphetamine Cocaine LSD Magic Mushroom	Lab-Based PM tasks: Belonging Appointment Message	Education Gender Age	14 days
Gallagher et al., 2014, study -1-, UK. [t+]	65 Ecstasy/polydrug users (38 males, Mean age: 21.91(SD 2.40)) 85 non ecstasy/polydrug users (31 males, Mean age:20.89 (SD 2.38))	Cannabis MDMA Cocaine	Lab-based PM tasks: Pattern Recognition Fatigue Mail	Education Gender IQ Alcohol use Nicotine Use	7 days
Gallagher et al., 2014, study -2- UK. [r+, t+]	103 Ecstasy/polydrug users (51 males, Mean age:21.85(SD 2.98)) 38 Cannabis only users (17 males, Mean age: 21.47(SD 3.00)) 65 nonusers of illicit drugs (17 males, Mean age: 20.64(SD 2.23))	Cannabis MDMA Cocaine	Lab-based PM: Pattern Recognition Fatigue Mail	Education Gender IQ Alcohol use Nicotine Use	7 days
Bartholomew et al., 2010, UK. [t+]	45 Cannabis Users (20 males, Mean age:19 (SD 5)) 45 Non-users (17 males, Mean age:19 (SD 3))	Cannabis	PMQ Video-based task (Lab-based)	Depression Anxiety Alcohol use Nicotine use	10 days
Rodgers et al., 2006, UK. [r+]	209 Ecstasy/ polydrug users (124 males, the modal age 16-20)	MDMA Cocaine Cannabis Amphetamine	PMQ	Gender Age	Not being under influence of any drug during testing
Cuttler et al., 2012, Study 1, Canada. [r+]	805 Participants (291 males, Mean age: 20.44 (SD 2.34)) of those 376 cannabis users	Cannabis	PMQ	Not given	Not being under influence of any drug during testing
Cuttler et al., 2012, Study 2, Canada. [t+]	178 Participants (54 males, Mean age: 20.31(SD 2.62)) 48 non-users (who had never used cannabis), 48 experimenters (who had used cannabis five or fewer times in their lives), and 48 chronic users (who had used cannabis at least three times a week for one year)	Cannabis	PMQ Lab-based PM tests: the Fruit, Reminder and Call in	Education Level Gender IQ	Not being under influence of any drug during testing
Fisk and Montgomery, 2008, UK,[t+]	27 Cannabis users (Mean age: 21) 20 Non-users (Mean age:21)	Cannabis	PMQ	IQ Reading Alcohol use Nicotine use	2 days
Bedi and Redman, 2008, USA. [t-]	45 Ecstasy polydrug user 48 Cannabis polydrug users 40 Legal drug users	Cannabis Ecstasy Amphetamine Cocaine LSD Magic Mushrooms Ketamine	Lab-based tasks: Reminder and Belonging test	Age Gender IQ Sleep Mood	1 day

* [t+] Significant PM deficit in at least one PM measure, [t-] no group effect on PM.
* [r+] Significant correlation between at least one PM measure and drugs dosage, [r-] no correlation.

Appendix B. Overview of the Findings of 27 Studies with Quality Assessment.

Appendix B1: Studies Employing self-report testing methods

Reference	Sample type	Sample Size	Testing Methods	Control for confounds	Abstinence Period	Overall quality of the study
Significant Short-term PM deficit						
Heffernan et al., 2001a	G	M	L	M	L	M
Heffernan et al., 2001b study 1	G	M	L	M	L	M
Heffernan et al., 2001b study 2	G	M	L	M	L	M
Fisk and Montgomery, 2008	G	L	L	G	L	L
Hadjiefthyvoulou et al., 2011a	M	M	G	G	G	G
Non-significant Short-term PM deficit						
Montgomery and Fisk, 2007	M	M	L	G	G	M
Bartholomew et al., 2010	M	M	G	G	G	G
Ciorciari and Marotte, 2011	G	G	L	L	L	L
Cuttler et al., 2012 study 2	M	G	G	G	L	G
Significant Long-term PM deficit						
Heffernan et al., 2001a	G	M	L	M	L	M
Heffernan et al., 2001b study 1	G	M	L	M	L	M
Heffernan et al., 2001b study 2	G	M	L	M	L	M
Montgomery and Fisk, 2007	M	M	L	G	G	M
Fisk and Montgomery, 2008	G	L	L	G	L	L
Ciorciari and Marotte, 2011	G	G	L	L	L	L
Non-significant Long-term PM deficit						
Hadjiefthyvoulou et al., 2011a	M	M	G	G	G	G
Bartholomew et al., 2010	M	M	G	G	G	G
Cuttler et al., 2012 study 2	M	G	G	G	L	G
Significant Internally Cued PM Deficit						
Heffernan et al., 2001a	G	M	L	M	L	M
Heffernan et al., 2001b study 1	G	M	L	M	L	M
Montgomery and Fisk, 2007	M	M	L	G	G	M
Fisk and Montgomery, 2008	G	L	L	G	L	L
Cuttler et al., 2012 study 2	M	G	G	G	L	G
Non-significant Internally Cued PM Deficit						
Heffernan et al., 2001b study 2	G	M	L	M	L	M
Hadjiefthyvoulou et al., 2011a	M	M	G	G	G	G
Bartholomew et al., 2010	M	M	G	G	G	G
Ciorciari and Marotte, 2011	G	G	L	L	L	L
Significant Environmentally and Self-Cued PM Complaints						
Weinborn et al., 2011b	L	M	G	G	L	M
Hadjiefthyvoulou et al., 2011b	M	M	G	G	G	G
Non-significant Environmentally and Self-Cued PM Complaint						
Weinborn et al., 2011a	G	M	G	M	M	M
Significant relationship between drug usage and level of PM deficit						
Rodgers et al., 2001	G	G	L	M	L	M
Rodgers et al., 2006	G	G	L	M	L	M
Rodgers et al., 2003	G	G	L	L	L	L
Arana et al., 2011	M	G	L	L	L	L
Cuttler et al., 2012 study 1	M	G	L	L	L	L
Non relationship between drug usage and level of PM deficit						
Ciorciari and Marotte, 2011	G	G	L	L	L	L

Appendix B2: Studies employing lab-based testing methods

Reference	Sample type	Sample Size	Testing Methods	Control for confounds	Abstinence Period	Overall quality of the study
Significant Event-based PM deficit						
Zakzanis et al., 2003	M	L	M	G	G	M
Terrett et al., 2014	G	M	M	G	L	M
Hadjiefthyvoulou et al., 2011a	M	M	G	G	G	G
Hadjiefthyvoulou et al., 2011b	M	M	G	G	G	G
Weinborn et al., 2011a	G	M	G	M	M	M
Weinborn et al., 2011b	L	M	G	G	L	M
Gallagher et al., 2014 study 1	M	G	M	G	G	G
Gallagher et al., 2014 study 2	M	G	M	G	G	G
Rendell et al., 2007	G	M	M	G	L	M
Rendell et al., 2009	L	L	M	G	G	M
Montgomery et al., 2010	M	L	M	G	G	M
Montgomery et al., 2012	M	L	M	G	M	M
Non-significant Event-based PM deficit						
McHale and Hunt, 2008	G	M	M	M	L	M
Bedi and Redman, 2008	G	G	M	M	L	M
Cuttler et al., 2012 study 2	M	G	G	G	L	G
Significant Time-based PM deficit						
Zakzanis et al., 2003	M	L	M	G	G	M
McHale and Hunt, 2008	G	M	M	M	L	M
Terrett et al., 2014	G	M	M	G	L	M
Hadjiefthyvoulou et al., 2011a	M	M	G	G	G	G

Hadjiefthyvoulou et al., 2011b	M	M	G	G	G	G
Weinborn et al., 2011a	G	M	G	M	M	M
Weinborn et al., 2011b	L	M	G	G	L	M
Gallagher et al., 2014 study 1	M	G	M	G	G	G
Gallagher et al., 2014 study 2	M	G	M	G	G	G
Rendell et al., 2007	G	M	M	G	L	M
Rendell et al., 2009	L	L	M	G	G	M
Montgomery et al., 2012	M	L	M	G	M	M
Non-significant Time-based PM deficit						
Montgomery et al., 2010	M	M	M	G	G	M
Bedi and Redman, 2008	G	G	M	M	L	M
Cuttler et al., 2012 study 2	M	G	G	G	L	G
Significant Overall PM Deficit						
Bartholomew et al., 2010	M	M	G	G	G	G
Significant relationship between drug usage and level of PM deficit						
Hadjiefthyvoulou et al., 2011a	M	M	G	G	G	G
Montgomery et al., 2010	M	L	M	G	G	M
Gallagher et al., 2014 study 2	M	G	M	G	G	G

Population Representative: Sample type: General Population = Good(G); Student Population = Moderate (M); and Patient Population = Low (L) and Sample size: Sample size >100 = Good(G); Sample size > 50 and <100 = Moderate (M); and Sample size <50 = Low(L).

Abstinence period: Abstinence Period ≥7 days = Good(G); Abstinence Period < 7 days and ≤3 days = Moderate (M); and Abstinence Period <3 days or Abstinence period was not given = Low (L).

Testing Methods: Self-report + Lab-based tests = Good (G); Lab-based tests = Moderate(M); and Self-report tests = Low(L).

Control for Confounding Factors: Controlling for three or more confounding factors = Good (G); Controlling for two confounding factors = Moderate (M); and Controlling for only.

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