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Cognitive performance amongst recreational users of “ecstasy”

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Abstract *Rationale:* Previous work has suggested that memory impairments have been associated with the recreational use of “ecstasy”. This previous work, however, has not taken into consideration the additional use of cannabis amongst those examined. Cannabis use has also been associated with memory impairment. There is therefore a clear need to explore the impact of both of these illicit substances upon memory ability. *Objectives:* To determine whether recreational use of ecstasy impairs memory and attentional ability and to explore the impact of the concomitant use of cannabis upon these cognitive functions. In addition, an exploration of subjective accounts of cognitive ability was undertaken to determine whether objective impairments were perceived by users in everyday functioning. *Methods:* Cognitive functioning was examined in three groups of young people: 15 regular users of ecstasy; 15 regular users of cannabis who had never taken ecstasy and 15 control subjects who had never taken any illicit substances. The Weschler Memory Scale (revised) and a computerised reaction time task were administered on a day when the subjects claimed to be drug free. In addition, subjects completed a biographical questionnaire and the Cognitive Failures Questionnaire (CFQ) in order to assess subjective accounts of cognitive slips. *Results:* Performance was similar across all three groups for measures of visual reaction time, auditory reaction time, complex reaction time, visual memory and attention and concentration. Significant impairment was found on measures of verbal memory in both cannabis users and ecstasy users. A significant impairment in performance was found on measures of delayed memory for the ecstasy users compared to both the cannabis group and the control group. Despite these findings, no differences in subjective ratings of cognitive failures were found between the groups. *Conclusions:* The present study provides additional evidence for long-

term neuropsychological sequelae associated with the use of ecstasy, particularly with regard to delayed memory ability.

Key words Ecstasy · Cannabis · MDMA · Memory · Attention · Recreational drug · Cognition

Introduction

3,4-Methylenedioxymethamphetamine (MDMA) or “ecstasy” is the drug of choice for a growing number of recreational drug users in the UK, the rest of Europe and the USA. Current estimates indicate that between 200 000 and 5 million tablets of ecstasy are taken each weekend in the UK (Saunders 1997). The widespread use of ecstasy first became apparent in the late 1980s with the rise of the “rave” culture and warehouse parties, and since then ecstasy use has grown to become a central part of a complex and sophisticated sub-culture (Collin 1997).

MDMA, which is a ring-substituted amphetamine, was first patented in 1912 by Merck but was never marketed. The first reported use of the substance was in 1953 when it was tested as a potential chemical weapon by the US army (Saunders 1997). MDMA is a psychoactive drug and is more precisely classified as a catecholamine-like psychedelic (Julien 1998). Since the early 1970s, ecstasy has been regarded as a suitable adjunct to psychotherapy by some therapists due to its euphoria inducing properties and capability of inducing intense episodes of self awareness and empathy without concomitant psychotic effects or visual hallucinations (Greer 1992).

Concerns regarding the potential toxicity of MDMA resulted in the substance being made illegal in the UK and the USA, mainly as a consequence of laboratory based animal studies reporting high levels of neurotoxicity associated with the compound (Ricaurte 1992; Frederick and Paule 1997). During these studies, MDMA was shown to cause the release of serotonin and also acute depletion of serotonin from most axon termi-

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nals in the forebrain and to produce irreversible destruction of serotonin terminals. The evidence from animal studies coupled with the popularity of ecstasy as a recreational drug indicates the need for an exploration of the long-term psychological effects of the substance in humans.

A growing body of research indicates that memory impairments are a central characteristic of individuals who use ecstasy on a recreational basis (Curran and Travill 1997; Morgan 1998, 1999; Parrott et al. 1998). Previous research, however, provides little specific consideration of the use of other forms of drugs by ecstasy users. This is perhaps particularly significant when considering the use of cannabis. A number of reports have suggested that habitual use of cannabis may alter cognitive functioning, particularly memory ability (Block and Ghoneim 1993; Millsaps et al. 1994). It is likely that those individuals who have participated in previous research examining the deleterious effects of ecstasy are also regular users of this substance, given that cannabis is regarded by users as a useful substance for ameliorating the midweek low associated with ecstasy use, and is a further popular drug of choice in the "rave" sub-culture (Collin 1997).

In addition, previous research into the effects of ecstasy has concentrated on memory ability with little consideration given to attentional skills. Given that attention can be regarded as the fundamental building block for other forms of cognitive activity, clarification is needed as to whether it is memory which is impaired in ecstasy users or attentional precursors to memory performance.

A number of attempts have been made to determine whether ecstasy users perceive themselves to be experiencing negative side-effects associated with use of the drug (Peroutka et al. 1988; Krystal et al. 1992). Such survey-based reports have focused mainly on affective functioning and little systematic comparison of self-reports of specific aspects of cognitive ability has been undertaken between ecstasy users and control participants. This seems to be a crucial area of investigation given the evidence that is emerging to suggest that cognitive performance can be affected by the use of the drug.

The present study aims to examine the performance of recreational users of ecstasy, cannabis and a control group of drug-free individuals on a battery of tests of memory functioning and attentional ability, and to examine subjective reports of cognitive functioning amongst the three groups.

Materials and methods

Subjects

Three groups of subjects were assessed, all of whom were recruited via the "snowball" technique (Solowij et al. 1992). None of the subjects reported using prescribed psychoactive substances. All subjects were in employment and professional careers and were comparable in terms of number of years in education and socioeconomic status. The use of alcohol was low amongst the participants. All subjects described themselves as social drinkers con-

suming on average two units of alcohol per week in each group. None of the subjects reported a history of psychiatric illness. However, it was not possible to verify this.

Group 1 included 15 participants who were regular users of ecstasy (mean age 31 years, 5 months (SD=4 years, 2 months), age range 23 years, 5 months to 44 years, 0 months). Eight of the participants in this group were female. These participants had taken ecstasy an average of 20 times over a 5-year period. All reported that they had been ecstasy free for at least 2 months prior to testing. All of these participants were also habitual cannabis users, having smoked cannabis an average of 4 days per week over a 10-year period. Participant recruitment however was restricted to individuals who had decided to stop using cannabis, due to concerns relating to the confounding effect of recent cannabis use on the results of the study. All participants reported being cannabis free for 1 month prior to testing. It must be noted that participants in this group were therefore experiencing a period of cannabis withdrawal. It was not possible to verify abstinence via drug screening. The initial aim of the project had been to recruit individuals who had taken ecstasy but who did not use cannabis. However, the author found it impossible to identify individuals who met this criterion. A number of the subjects in this group had taken other forms of illicit drugs within the last 10 years. These drugs included LSD ($n=2$, on three and two occasions, respectively), amphetamine sulphate ($n=2$, on two occasions in both cases) and cocaine ($n=3$, on approximately four, five and one occasion, respectively). The use of these other drugs was very infrequent and at least 3 years prior to testing.

Group 2 included 15 individuals who were regular users of cannabis (mean age 30 years, 3 months (SD= 6 years, 3 months); age range 21 years, 7 months to 43 years, 3 months). Eight of the participants in this group were female. These individuals reported never having taken ecstasy or any other psychoactive substance. Participants in the cannabis group had taken the drug on average 4 days per week over an 11-year period. Participant recruitment, however, was restricted to individuals who had decided to stop using cannabis, due to concerns relating to the confounding effect of recent cannabis use on the results of the study. All participants reported being cannabis free for 1 month prior to testing. It was not possible to verify abstinence via drug screening. It must be noted that participants in this group were therefore experiencing a period of cannabis withdrawal.

Group 3 included 15 individuals who reported that they had never taken any illicit substance (mean age 32 years, 1 month (SD=4 years, 1 month); age range 26 years, 2 months to 39 years, 1 month). Nine of the participants in this group were female.

Ethical considerations and procedures

The author accepts that it is crucial when undertaking research into the effects of illicit drug use not to be seen to be providing implicit approval for the use of such substances. Each subject was therefore required to sign a written informed consent form prior to the onset of the assessments. The form detailed that the author acknowledged that MDMA and cannabis were illegal substances which may have adverse side-effects and that neither the researcher nor the University of Sunderland condoned their use and that participation in the current research should not be regarded as providing encouragement or approval for the use of these substances. Subjects were also informed that their participation was voluntary and they could withdraw from the study at any time and their anonymity was assured. Subjects were then informed of the aims of the study.

Subjects were tested individually on a day when they reported they were drug-free. One researcher collected all data from the subjects and was therefore not "blind" to group membership. Each testing session took approximately 45 min.

Ethical clearance for the study was provided by the Ethics Committee at the University of Sunderland.

Assessment measures

The following battery of tests was administered in the order detailed below.

Computerised reaction time tasks

These tasks were developed specifically for the study and had not been used prior to this investigation. All tasks were presented using a Viglen Dossier lap-top computer with a Pentium processor and were written in Visual Basic and Turbo C++. All reaction time tasks had a 3-min duration. The mean response time and percentage of correct responses was automatically recorded. Three measures of reaction time were included: visual reaction time, auditory reaction time and complex reaction time.

Visual reaction time task Following a random delay, a white circle 2 cm in diameter appeared in the centre of the screen for 1 s. Subjects were required to press the spacebar as quickly as possible each time they saw the circle.

Auditory reaction time task Following a random delay, subjects were presented with a simple tone. They were required to press the spacebar as soon as possible each time they heard the tone.

Complex reaction time task Following a random delay single digits ranging from 1 to 9 appeared in the centre of the screen for a duration of 1 s. Subjects were required to press the corresponding number key from those across the top of the keyboard as quickly as possible each time they saw a number.

The Wechsler Memory Scale (revised)

Subjects were required to complete all sub-scales of the Wechsler Memory Scale (WMS) (revised) in accordance with the instruction manual. The Wechsler Memory Scale (revised) consists of a series of brief sub-tests, each measuring a different facet of memory performance. Eight of the sub-tests measure short-term learning and the recall of verbal and figural material. The verbally presented and visually presented materials are alternated to maintain interest. These sub-tests are immediately followed by a further four tasks which assess delayed recall. Two of these four assess the retention of verbally presented material and two, visually presented material. The full battery takes approximately 45 min to complete.

The eight tests of short-term memory contribute to two composite Scale Scores, General Memory (this has five sub-tests) and Attention and Concentration (three sub-tests). The General Memory Scale is further sub-divided into two additional sub-scales measuring specifically Verbal Memory and Visual Memory. The four delayed trials contribute to a sub-scale of Delayed Recall. Summary scores, described as "Indexes" are provided for these composites.

- **Figural Memory.** The participant is shown a set of abstract designs. After each set of designs is removed, the participant is required to identify the previously seen designs within a larger set of designs.
- **Logical Memory I.** The participant listens to two brief stories. After each one has been read aloud by the investigator, the participant retells the story from memory. The total score is derived from the total number of ideas recalled across both stories.
- **Visual Paired Associates I.** The participant is required to learn the colour associated with each of six abstract line drawings. The pairs are presented until the participant answers all six items correctly; only the first three presentations are scored.
- **Verbal Paired Associates I.** The participant is required to learn eight word pairs, four of which reflect common associations and four of which reflect uncommon associations. Up to six trials are provided in which to learn the pairs. Only the first three trials are scored.

- **Visual Reproduction I.** The participant is required to draw from memory simple geometric designs that they are exposed to for 10 s.
- **Digit Span.** The participant is required to repeat a series of digits, forward and backward.
- **Visual Memory Span.** The participant is required to touch a series of coloured squares in a predetermined order as demonstrated by the examiner. The number of squares included increases with each trial. The task is then repeated with the participant required to touch the squares in reverse order.
- **Logical Memory II.** This is the delayed trial of Logical Memory I administered 30 min after the first presentation of the stories. The participant is required to retell the stories once more without further exposure to them.
- **Visual Paired Associates II.** This is the delayed recall trial of Visual Paired Associates I.
- **Verbal Paired Associates II.** This is the delayed recall trial of Verbal Paired Associates I.
- **Visual Reproduction II.** This is the delayed recall trial of Visual Reproduction I.

Index scores were calculated for the following measures:

- **Verbal Memory.** This is derived from performance on the following sub-tests: Logical Memory I; Verbal Paired Associates I.
- **Visual Memory.** This is derived from performance on the following sub-tests: Figural Memory; Visual Paired Associates I; Visual Reproduction I.
- **General Memory.** This is a composite index score derived from performance on the following sub-tests: Logical Memory I; Verbal Paired Associates I; Figural Memory; Visual Paired Associates I; Visual Reproduction I.
- **Attention and Concentration.** This is derived from performance on the following sub-tests: Mental Control; Digit Span; Visual Memory Span.
- **Delayed Recall.** This is derived from performance on the following sub-tests: Logical Memory II; Visual Paired Associates II; Verbal Paired Associates II; Visual Reproduction II.

Converting raw scores to index scores Each raw score is multiplied by a "weight" provided on the Record Form. The weighted raw scores are then summed to provide an overall score for each of the Index measures (Verbal Memory, Visual Memory, Attention and Concentration and Delayed Recall). The General Memory Score is calculated by adding the sums of the scores for Verbal Memory and Visual Memory. Index scores are then produced by converting the composite scores according to the age of the participant, using Table C-1 in the manual.

Cognitive Failures Questionnaire (Broadbent et al. 1982)

This questionnaire requires subjects to provide ratings of the perception of frequency of various cognitive slips over the past 4 weeks. Subjects are asked to rate their performance using a 5-point scale from never (0) to very often (4) on 25 statements relating to cognitive performance, giving a range of scores between 0 to 100.

Biographical questionnaire

The questionnaire was developed specifically for the study and included questions relating to age, occupation, and current and past drug use.

Results

Significant impairment was found on measures of verbal and general memory in cannabis users and ecstasy users compared to the drug-free control group. In addition, significant impairment was found for the ecstasy group on measures of delayed recall compared to both the cannabis group and the control group. No evidence of impairment was found on measures of visual memory, attention and concentration, visual reaction time, auditory reaction time or complex reaction time for either of the two groups of drug users.

All results were analysed using one-way analyses of variance and where appropriate Newman Keuls post-hoc analyses.

Memory performance

A significant difference was found on the Verbal Memory index [$F(2,42)=17.35$, $P<0.001$] (Table 1). Further analysis of the results of this index revealed a significant difference in performance during the Logical Memory sub-test [$F(2,42)=10.30$, $P<0.05$]. Post-hoc analysis revealed that both the drug groups were performing at significantly lower levels than the control group during this sub-test ($P<0.05$). No significant difference in performance was found between the groups during performance on the remaining task that comprises the Verbal Memory index, the Verbal Paired Associates task.

A significant difference was found on the General Memory index [$F(2,42)=10.60$, $P<0.001$] (Table 1). Post hoc analysis revealed that both drug groups were performing at significantly lower levels than the drug free control group ($P<0.05$). However, this index is a com-

posite measure of performance in both the Verbal and Visual Memory indices and this significant finding reflects the differences reported on the Verbal Memory index. No difference in performance was detected between the ecstasy and cannabis groups.

A significant difference was found on the Delayed Memory index [$F(2,42)=6.55$, $P<0.001$] (Table 1). Measures on the Delayed Recall index are derived from performance on the following sub-tests; Logical Memory II; Visual Paired Associates II; Verbal Paired Associates II; and Visual Reproduction II. Further analysis of the sub-tests which comprise this index (Table 2) revealed that there was a significant difference in performance during the Logical Memory II sub-test [$F(2,42)=15.4$, $P<0.001$], the Verbal Paired Associate II sub-test [$F(2,42)=13.5$, $P<0.05$] and the Visual Paired Associates II sub-test [$F(2,42)=15.6$, $P<0.05$]. Post-hoc analysis revealed that the ecstasy group and the cannabis group were performing at significantly lower levels than the control group during the Logical Memory II sub-test ($P<0.05$). The ecstasy group were found to be performing at a significantly lower level than both the cannabis group and the control group during the Verbal Paired Associates II sub-test ($P<0.05$) and the Visual Paired Associates II sub-test ($P<0.05$). No significant difference in performance between the groups was found during the Visual Reproduction II sub-test.

No significant differences were found between the groups on the Visual Memory index or on any of the sub-tests which comprise this index (Figural Memory; Visual Paired Associates I; Visual Reproduction I). Finally, no significant differences were found between the groups on the Attention and Concentration index or on any of the sub-tests which comprise this scale (Mental Control; Digit Span; Visual Memory Span).

Table 1 Means (SD) during the Wechsler Memory Scale (revised), Cognitive Failures Questionnaire and Reaction Time Tasks

Measure	Ecstasy Mean (SD)	Cannabis Mean (SD)	Control Mean (SD)	P
Verbal Memory	86.40 (12.8)	88.07 (10.46)	109.67 (12.79)	<0.001
Visual Memory	113.33 (7.5)	110.33 (7.62)	109.53 (11.98)	>0.05
General Memory	94.00 (13.42)	93.87 (9.72)	111.47 (12.65)	<0.001
Attention	111.93 (9.38)	116.40 (13.76)	115.93 (8.84)	>0.05
Delayed Memory	96.53 (13.85)	108.47 (9.44)	111.93 (12.93)	<0.001
CFQ	45.20 (8.11)	40.80 (8.23)	45.13 (8.23)	>0.05
Visual Reaction Time (ms)	357.53 (71.78)	349.57 (96.97)	379.33 (75.96)	>0.05
Auditory Reaction Time (ms)	272.01 (77.49)	292.29 (95.47)	279.84 (67.35)	>0.05
Complex Reaction Time (ms)	1090.33 (261.72)	951.54 (122.76)	953.21 (120.86)	>0.05

Table 2 Mean weighted raw scores (SD) for the sub-tests of the Wechsler Memory Scale

Sub-test	Ecstasy	Cannabis	Control	P
Logical Memory I	30.1 (6.5)*	32.0 (5.4)*	48.4 (7.1)	<0.05
Verbal Paired Associates	21.5 (7.6)	23.3 (5.7)	24.5 (6.8)	>0.05
Figural Memory	4.0 (2.1)	6.2 (1.4)	6.6 (4.6)	>0.05
Visual Paired Associates I	17.5 (6.5)	12.7 (7.8)	18.1 (9.2)	>0.05
Visual Reproduction I	38.4 (10.3)	40.6 (12.4)	39.6 (13.9)	>0.05
Mental Control	4.9 (3.2)	5.3 (5.1)	5.4 (5.1)	>0.05
Digit Span	36.4 (6.8)	40.7 (7.1)	38.2 (5.2)	>0.05
Visual Memory Span	44.6 (20.1)	52.6 (14.2)	50.1 (16.3)	>0.05
Logical Memory II	18.4 (12.3)*	20.1 (8.9)*	38.2 (9.3)	<0.001
Visual Paired Associates II	6.3 (7.6)*	12.1 (4.3)	13.4 (2.6)	<0.05
Verbal Paired Associates II	8.5 (7.8)*	16.5 (4.8)	15.3 (7.6)	<0.05
Visual Reproduction II	38.7 (11.9)	39.0 (8.7)	36.9 (7.6)	>0.05

*Indicates significance during post-hoc analysis at $P < 0.05$

Subjective reports of cognitive functioning

No significant differences were found between the three groups with regard to subjective reports of cognitive functioning using the Cognitive Failures Questionnaire.

Reaction time performance

No significant differences were found between the three groups on the Visual Reaction Time task the Auditory Reaction Time task or the Complex Reaction Time task in terms of reaction time of number of errors of omission or commission.

Discussion

The findings support previous work investigating cognitive performance amongst chronic cannabis users indicating subtle impairments in verbal memory function with relatively intact performance on tasks of attention, concentration and visual memory (Millsaps et al. 1994).

Krystal et al. (1992) report a pattern of mild to moderate impairment on both initial and delayed sub-tests of the Wechsler Memory Scale as a feature of ecstasy users. In addition, Parrott et al. (1998) state "both memory measures, immediate word recall and delayed word recall, were significantly impaired in the MDMA subgroups". Neither of these studies discusses cannabis use amongst their participants making it difficult to identify the relative contribution of these substances to long-term sequelae. During the present study analysis of the sub-tests which comprise the Verbal Memory index reveals that both drug groups are impaired on the Logical Memory sub-test during immediate and delayed recall conditions. During this task, participants are required to listen to a short story and then retell the story as accurately as possible. The findings reported here are similar to Morgan (1999), who reported a deficit in immediate and delayed logical memory, as measured using the Rivermead Behavioural Memory Test, as a feature of MDMA use. However, unlike Morgan (1999), the current study indicates that this deficit is a feature of both ecstasy and cannabis users and cannabis users only, suggesting

that a deficit in logical memory maybe be associated with long-term cannabis use rather than ecstasy consumption.

That is not to say, however, that the present study does not implicate ecstasy use as a possible contributory factor to long-term neuropsychological sequelae. The results of the present investigation suggest that those subjects in the ecstasy group are experiencing additional long-term impairments over and above those witnessed in the cannabis only group. Analysis of the sub-tests which comprise the Delayed Recall Index reveals that the ecstasy users were performing at significantly lower levels than both the control group and the cannabis group during the Verbal Paired Associates II task and the Visual Paired Associates II task. This suggests that whereas cannabis use may impact upon logical memory ability, the concomitant use of ecstasy has a more wide ranging impact on delayed recall ability, affecting a number of different sub-types of this cognitive skill.

This broad ranging impairment in delayed recall skills witnessed amongst ecstasy users and not in the cannabis group supports the growing body of work which suggests that use of ecstasy may result in serotonergic neurodegeneration. Animal based laboratory studies indicate that MDMA causes persistent degeneration of serotonergic terminals and this may underlie the memory impairment found here (Frederick and Paule 1997). Clearly, further work is required to provide an adequate explanation of the aetiology of these performance deficits.

Self-reports of cognitive functioning from the present study suggest that neither group of drug users perceived their cognitive performance to be impaired. It could be suggested that these results indicate the presence of a metacognitive deficit amongst drug users, which would render them unable to monitor and judge their own cognitive state accurately. Parrott (1998) suggests that subjects may have experienced a change in information processing strategies following drug use. However, the latter explanation appears to be unlikely, given that neither group of drug users reported impairment, and Parrott's explanation relates specifically to the phenomenological experiences associated with ecstasy use. The lack of subjective reports of cognitive impairment could result from the insensitivity of the Cognitive Failures Questionnaire and further work is needed to determine whether these findings can be replicated.

There are clearly a number of weaknesses in the present study characteristic of many investigations into recreational drug use. Research to date, including the present study, has involved the recruitment of individuals who describe themselves as ecstasy users. Based on findings from this often small and self-selected sample, researchers infer the deleterious effects of MDMA. Given the illegal status of the drug and the fact that the participants in such studies will have obtained their "pills" via the black-market, it is impossible to determine the level (if any) of MDMA they have ingested. It is notoriously easy to manufacture ecstasy and many of the pills available commercially are suggested to contain a number of other sometimes cheaper and more easily obtainable products in addition to, or instead of, MDMA including lysergic acid diethylamide (LSD)', amphetamine sulphate, heroin, ketamine and cocaine (Collin 1997), making it difficult to attribute any findings directly to the use of MDMA per se. Therefore, any such research can only confidently report findings in relation to tablets retailed as ecstasy rather than to MDMA specifically.

In addition, although the author did require the subjects to report on time since most recent drug use and to complete the testing whilst "drug-free", clearly the design of the study precludes any independent verification of the information provided by subjects with regard to this issue. All subjects in the present study reported that it was at least 2 months since the last time they had taken ecstasy. However, there is no clear cut guidance currently available regarding the neurochemical depletion rate following ecstasy use in human subjects, making it difficult to state with any certainty that following 2-month abstinence, the subjects were actually completely drug-free. In addition, although participants in both the ecstasy group and the cannabis group claimed to be cannabis free no verification of this drug-free state was possible. Also, it must be noted that recent withdrawal from cannabis after long-term use of the drug is a feature of participants in both of these groups. All of these issues are difficult to address however given the fact that placebo controlled laboratory based studies of the effects of MDMA in human volunteers remain extremely unlikely.

These cautionary notes highlight a number of issues. Firstly, it is clear that there is a need to consider the effects of cannabis in attempting to determine the neuropsychological sequelae associated with ecstasy. In addition, a more detailed and comprehensive exploration of subjective accounts of cognitive ability amongst recreational drug-users is necessary to provide further information regarding the lifestyle and personal experiences of this sector of the population. The present study provides further evidence that there may be deleterious effects associated with the use of ecstasy specifically relat-

ed to delayed memory function. Given the popularity of the drug and the growing evidence of associated neuropsychological impairment, one can only wonder what long-term impact will be on both the individual and society as users become older and the aging process takes its course.

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