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CHANGE IN FREQUENCY OF ACUTE AND SUBACUTE EFFECTS OF ECSTASY IN A GROUP OF NOVICE USERS AFTER 6 MONTHS OF REGULAR USE

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SUMMARY

Background: *Recent research trends are to specify the relation between patterns of ecstasy use and side effects, possibility of dependency, tolerance and long term neurocognitive damage. The objective of this study was to assess the impact of regular ecstasy use on its acute and subacute effects.*

Subjects and methods: *At the first stage, we recruited 120 subjects. If participants continued regular use of ecstasy in this period, they were asked to participate in the second stage of the research 6 months later. Thirty-five subjects attended the second stage of the study, 5 of which were excluded because they had less than 5 drug experiences during the last 6 months. At last, we recruited 30 novice ecstasy users by means of the snowball technique in Tehran, Iran. The pattern of use and experienced effects of ecstasy was documented at the beginning and after 6 months of regular consumption with a self administered questionnaire.*

Results: *Little or no change was observed in acute effects. Those subacute effects that had considerable increase in frequency were anxiety, depression, aggression, memory impairment, poor concentration and learning problems.*

Conclusion: *Small change in acute effects suggests low possibility of tolerance after at least 6 months of regular use. Our results support long term neurocognitive damage and mood impairment with ecstasy use.*

Key words: *acute effects – ecstasy - regular use - subacute effects*

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INTRODUCTION

MDMA (3, 4-methylenedioxy-N-methylamphetamine), known by its street name ecstasy, is an amphetamine derivative with both stimulant and hallucinogenic properties (Davison & Parrott 1997, Rogers et al. 2009). It was patented by Merck in 1914 and has been synthesized to be an anorectic. Nevertheless, the first uses were allocated to psychotherapeutic sessions around 1970 but the popularity of its recreational consumption coincided with the "Raves" in 1990s (Cohen 1995, Montoya et al. 2002). Despite being a schedule 1 illicit drug, its popularity and consumption is growing even up until now (El-Mallak & Abraham 2007, Rahnavard et al. 2011). This might arise from a belief among the users that ecstasy is a kind of recreational drug with insignificant or at least rare side effects (Montoya et al. 2002, Gamma et al. 2005, Rahnavard et al. 2011).

The acute physical effects in general are related to its sympathomimetic properties namely tachycardia, diaphoresis, mydriasis, dry mouth and thirst. Physical effects more exclusive to MDMA are trismus and altered body temperature regulation (Vollenweider et al. 2002, Baylen & Rosenberg 2006, El-Mallak & Abraham 2007, Rogers et al. 2009). Fatal consequences of hyperthermia and hyponatremia following excessive water intake are reported as well (Rogers et al. 2009).

MDMA is believed to modulate the serotonergic system. Shortly after consumption, it releases the preexisting serotonin from presynaptic neurons and inhibits serotonin reuptake. This will explain the psychological effects like elevated mood and energy, feeling intimate with others and sexual arousal in few hours after ingestion of ecstasy. Users also experience subtle hallucinatory perceptions as well as increased alertness and in some cases confused thought. The alleged "coming down" after the experienced "high" occurs 7 to 8 hours after ingestion and most apparently after 24 hours. Serotonin depletion from CNS explains this phase of depressed mood, anxiety and aggressive behavior, also known as "mid week blues", in few days after consumption (Curran & Travill 1997, Parrott 2002; Verheyden et al. 2003).

Toxicity to 5-Hydroxytryptophan (5-HTP) neurons is the main concern stated in the literature, regarding the long term side effects. Evidence for cognitive damage is so patchy that reviewers can just suggest a subtle damage to some aspects of memory following indeterminate pattern of ecstasy use (Gouzoulis-Mayfrank & Daumann 2006).

Recent research trends are to specify the relation between patterns of ecstasy use and side effects, possibility of dependency, tolerance and long term neurocognitive damage. There are some subjective reports of different drug experiences in novice versus

experienced users (Verheyden et al. 2003). However, to our knowledge, no study has compared the same user before and after a period of regular consumption and lack of any prospective studies is noticeable in this field. This study was designed to evaluate the impact of regular ecstasy use on its acute and subacute effects.

SUBJECTS AND METHODS

We approached our participants in so called Ecs-parties held underground in Tehran, Iran. We used the snowball technique (Solowij et al. 1992) to appeal to more subjects by requesting the existing participants to spread the word among their friends. This was a self-administered questionnaire based study. After obtaining a verbal informed consent from participants and reassuring the confidentiality of their information, investigators arranged an appropriate time and venue for them to fill out the questionnaire. The subjects filled out the questionnaire with a guide of a medical doctor (GP). In addition, each item in the questionnaire had a detailed explanation. Inclusion criterion was to have used ecstasy at least once but no more than 5 times. Subjects were requested not to take the drug for at least a week before filling out the questionnaire. At the first stage, we recruited 120 subjects. If participants continued regular use of ecstasy in this period, they were asked to participate in the second stage of the research 6 months later. Thirty-five subjects attended the second stage of the study, 5 of which were excluded because they had less than 5 drug experiences during the last 6 months.

Our questionnaire was comprised of 3 main parts. The first part included few demographic questions like age and gender. The questions in the second part were allocated to the pattern of ecstasy use. In the third part, participants were asked about their last experience with the drug. Subjects had to specify the effects in the first 24 hours after ingestion (which we consider acute effects) and during the next 3-4 days (subacute). For both questions, subjects were provided a list of effects that they could choose from. They could indicate as many as they needed to best describe their experience. These lists of effects were collected by the authors based on the most frequent reported health outcomes of ecstasy use. This study was approved by the ethics committee of Tehran University of Medical Sciences and was performed in accordance with the Declaration of Helsinki and subsequent revisions.

Statistical analysis

We used descriptive statistics to analyze our data.

RESULTS

Despite having recruited 120 participants for the first phase of the study, only 30 showed-up for the second stage and were eligible to complete this part. Therefore, the latter 30 subjects comprised our study population.

The mean age of our participants was 25.31 (±4.88) years. Males made up 75% of our subjects. The most common mode of drug administration was taking tablets. Almost all of the cases consumed ecstasy in parties and with a group of friends but not alone. Two-thirds of subjects were poly drug users, cannabis and alcohol being the most reported drugs used concurrently with ecstasy. Reasons for repeated use were psychological needs (54%), peer pressure (27%), physical demand (11%) and being in the occasion (5%). Only 3 subjects reported increase in ecstasy dose in the following sessions after baseline. The frequencies of subjective acute and subacute effects of ecstasy both at baseline and after 6 months of regular use are presented in Table 1.

Table 1. Frequency of subjective acute and subacute effects of Ecstasy at baseline and after 6 months of regular use

Acute effects	Frequency at baseline (%)	Frequency After 6 months (%)	Subacute effects	Frequency at baseline (%)	Frequency After 6 months (%)
Increased alertness	56.7	66.7	Fatigue	66.7	80
Tachycardia	63.4	90	Decreased appetite	50	20
Diaphoresis	50	73.4	Muscle aches	43.4	50
Vertigo	16.7	13.4	Insomnia	36.7	43.4
Urinary retention	20	13.4	Flashbacks	36.7	33.4
Being extremely happy	86.7	90	Tachycardia	20	23.4
Activeness	73.4	80	Headache	20	20
Dry mouth	73.4	80	Anxiety attacks	10	30
Extremely tender	66.7	80	Nightmares	13.4	66.7
Tendency to have intimate contacts with others	43.4	46.7	Depressed mood	66.7	86.7
Nausea & vomiting	20	10	Loosing memory	30	60
Auditory hallucinations	23.4	20	Learning difficulties	20	73.4
Visual hallucinations	23.4	13.4	Poor concentration	33.4	60
Olfactory hallucinations	43.4	13.4	Confusion	20	16.7
Jaw muscle spasm	50	53.4	Skin irritations	6.7	13.4
Sexual arousal	36.7	33.4	Aggression	10	23.4
Decreased libido	20	16.7			

DISCUSSION

Our results showed little or negligible difference in the frequency of acute effects at baseline and after 6 months of regular use. Most of our subjects claimed that they continued using the same number of ecstasy tablets they used at the beginning of the study. Hence, this might pose the question whether tolerance has not become apparent (at least after 6 months of regular use) or whether the subjects used conjunctive drugs during the last session of ecstasy administration which might have mimicked or enhanced its acute effects.

Two thirds of our population was polydrug users and the most consumed drugs were alcohol and cannabis. Studies have shown concurrent administration of alcohol and ecstasy did not enhance any effects of the two drugs when consumed alone (Dumont et al. 2008). Meanwhile co-administration of cannabis makes a difference on the overall outcome of ecstasy use. It has been reported that concurrent cannabis consumption might attenuate the aggressive behaviors associated with ecstasy while highlighting the paranoid symptoms. It might also make subjects more susceptible for long term effects of ecstasy (Milani et al. 2005). One shortfall of this study was not recording the exact pattern of cannabis or other drug co-administration during the study period.

Variations in dose and chemical make-up of tablets sold under the name of ecstasy might also have a role in explaining this result. Tablets vary in the dose of MDMA and there is a possibility of co-existence of other substances such as MDA (3, 4 methylenedioxy-amphetamine) and MDEA (3,4-methy-lenedioxyethyl-amphetamine), which are stimulants and might enhance the acute effects of MDMA (Khajeamiri et al. 2011, Parrott 2004). The setting in which the drug is consumed can have an impact on its effects (Parrrott 2004, Bedi & Redman 2006). This is not the case for our participants because almost all took the drug in a party setting.

In regard to subacute effects, increases in concentration difficulty episodes, memory impairment and learning disabilities suggests possible long term neurocognitive damage which is the area of great controversy (Gouzoulis-Mayfrank & Daumann 2006, Hoshi et al. 2007, Kalechhstein et al. 2007). Among other subacute effects, there are also increases in the frequency of anxiety, depression and aggression. This is also in line with suspicions about the long term impact of ecstasy on mood (Verheyden et al. 2002, Montoya et al. 2002, Morton 2005).

The growth in ecstasy craving which was observed between the beginning and the end of our study implicated the possibility of dependency. This is in line with observations about higher dependency rate in heavy ecstasy users (von Sydow et al. 2002, Thomasius et al. 2005).

To best of our knowledge, this is one of the first studies to administer “before and after” prospective methodology to evaluate the impact of ecstasy on novice versus experienced users. We believe this methodology would reduce the group mismatch biases which might have confounded the existing evidence (Cole et al. 2002, Gouzoulis-Mayfrank & Daumann 2006). One of the limitations of this study is the majority of the subjects were polydrug users. However, they expressed their experiences with ecstasy.

Comparing the frequency of acute effects lets us evaluate the possibility of tolerance in an objective manner. Most other studies which assessed tolerance were participants’ subjective reports by answering direct questions (Verheyden et al. 2003).

CONCLUSION

Our results did not support the possibility of tolerance after at least 6 months of regular use. We also noted the probability of long-term cognitive and mood impairment with ecstasy use.

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Conflict of interest: None to declare.

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