

## **Mechanisms of Pharmacological Action of Ecstasy Substances, Consequences of Episodic and Chronic Use and Expected Complications**

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The word ecstasy is used to describe a strong, euphoric feeling in a conversational language. According to psychologists definition, it is a special mental state, when a person is completely focused on the subject of interest and beyond it, he or she sees no time, no pain, no fatigue. More often, ecstasy contains MDMA (Methylenedioxymethamphetamine), which is a synthetic substance with a hallucinogenic and psychostimulant effect. As a result of its chemical and pharmaceutical processing, colored tablets and capsules are made. Other slang names of Ecstasy are the following: X, XTC, Adam, Molly, E, etc.. [2,4].

There are various methods of achieving ecstasy as a special mental state: dance, meditation, music, religious ritual, sex, and in the last 30 years, amphetamine, called MDMA[4].

Ecstasy is taken by perorally, rarely by inhalation; Its excitational and hallucinogenic action are manifested in a feeling of love, closeness and happiness; Warm and close relationships with those around them; In a sense of calm and complacency [3].

MDMA - this variety of amphetamine was created in 1912 by the German pharmaceutical company -MERCK, presumably as an appetite suppressant (anorexic), but it was not remembered by anyone until the 1970th. From that time on, psychotherapists began to use MDMA, believing that it helped people break through barriers and “get into each other’s souls”; MDMA was often offered to couples to deal with their marriage problems, but the medication soon left medical area and it has become a recreational drug - an integral attribute at discotheques and mass parties, so called raves. Since 1984, it has been spread out in students; but in 1985, the use

of ecstasy was deemed illegal since it was a threat to society, and the ecstasy moved underground, but its consumption increased. Since 1987, it has been widely distributed as a party drug [6]. Ecstasy is considered as heavy drug and nowadays, its manufacturing, storage or realization is forbidden in all countries of the world, including Georgia. Internationally, it is regulated by the UN Convention on Psychotropic Substances. Ecstasy is produced in illegal laboratories and it is never known how pure its chemical composition is. Often, ecstasy contains various additives that modify MDMA’s activity in different ways [4]. In 2015, by the Ministry of Internally Displaced Persons from the Occupied Territories, Labour, Health and Social Affairs of Georgia, National Center for Disease Control and Public Health with the financial support of European Union, the first national-level study on alcohol, tobacco and other drugs use among young people was conducted, and on the basis of this study, an annual report was published in 2016 - Drug Abuse in Georgia [1].

10th academic year students – young people born in 1999 were recruited for the study from different regions of Georgia. Two-stage (school and class) proportional simple random sampling was used for selection; 2477 completed questionnaires were analysed during the study [1].

The results of the study showed that in Georgia, the rate of consumption of ecstasy (MDMA) in young people is high throughout their lives as well as during past 12 months, more higher than other Amphetamines, especially in men (aged – 18-40 years) [1].

Ecstasy exists in tablet and capsule forms. It looks like vitamins of children: some are pink, some – blue, some - yellow or purple; There is either a smiley face depicted on them, or - a Mercedes mark, or another result of manufacturer’s fantasy; The tablet is sometimes triangular, sometimes round, and sometimes heart-shaped [4,5].

Amphetamines, including MDMA, are the derivatives of receptive phenylisopropilamines, which have strong stimulating effect on CNS; They represent sympathomimetics of indirect actions, that release serotonin, dopamine and other monoamines in the CNS; In case of taking ecstasy on fasting, it needs 15 minutes to reach the brain. MDMA enhances the activity of three transmitters in the brain: Dopamine, Norepinephrine, Serotonin. The latter is responsible for the “fight or run” reaction; In addition, they stimulate the ways of so-called “self-preservation”. These transmitters are characterized by the following effects [2,3]:

### Amphetamines, ecstasy consumption rates in young people in lifetime and during past 12 months

Lifetime	Boys	Girls	Total
Amphetamines	3.1	0.6	3.0
Methamphetamines	2.0	0.1	1.1
Ecstasy	7.2	1.1	4.4

Past 12 months	Boys	Girls	Total
Amphetamines	1.8	0.3	1.1
Methamphetamines	1.2	0.1	0.7
Ecstasy	3.3	0.6	2.7

### Amphetamines, ecstasy consumption rates in general population in lifetime and during last 12 months

Life time	Man	Woman	Age 18-24	Age 25-29	Age 30-39	Age 40-49	Age 50+	Total
Amphetamines	1+ <sub>-0.4</sub>	0.1+ <sub>-0.0</sub>	0.2+ <sub>-0.1</sub>	1.1+ <sub>-0.7</sub>	0.5+ <sub>-0.3</sub>	0.7+ <sub>-0.4</sub>	0.3+ <sub>-0.2</sub>	0.5+ <sub>-0.2</sub>
Methamphetamines	0.8+ <sub>-0.5</sub>	0.1+ <sub>-0.0</sub>	0.3+ <sub>-0.1</sub>	1.0+ <sub>-0.5</sub>	0.4+ <sub>-0.2</sub>	0.6+ <sub>-0.3</sub>	0.3+ <sub>-0.1</sub>	0.4+ <sub>-0.2</sub>
Ecstasy	1.2+ <sub>-0.3</sub>	0	0.7+ <sub>-0.4</sub>	0.5+ <sub>-0.3</sub>	0.7+ <sub>-0.3</sub>	0.9+ <sub>-0.3</sub>	0.2+ <sub>-0.1</sub>	0.6+ <sub>-0.1</sub>

During past 12 months	Man	Woman	Age 18-24	Age 25-29	Age 30-39	Age 40-49	Age 50+	Total
Amphetamines	0	0	0	0	0	0	0	0
Ecstasy	0.1+ <sub>-0.1</sub>	0	0	0	0.2+ <sub>-0.2</sub>	0	0	0.1+ <sub>-0</sub>

**Dopamine** – produces an increased energy/activity and acts to enhance behavioural activities in the reward system;

**Norepinephrine** - Increases heart rhythm and blood pressure, which is especially dangerous for people with cardiovascular problems;

**Serotonin** - It affects the mood, appetite, sleep, also stimulates sexual arousal and strengthen confidence. High levels of serotonin can cause emotional closeness, elevated mood, and empathy in those who use MDMA.

Generally, amphetamines are characterized by high abuse potential; They represent recreational drugs and are characterized mainly by central rather than peripheral effects; Frequently, an ecstasy tablet with MDMA contains antihistamines and caffeine, and in the worst case, cocaine or ketamine [4].

MDMA enhances not only the release of serotonin, but also increases its consumption in the

body; It is also worth noting that hangover is usually accompanied by bad mood or depression, because, as mentioned above, high levels of serotonin are consumed throughout consumption of MDMA and during hangover the body suffers from lack of serotonin. Serotonin is known as a transmitter of good mood and pleasant feeling, which is mainly concentrated in the central nervous system and intestines [2,3].

Short and long-term effects of ecstasy on the brain [5,6]:

- Short-term effects of ecstasy on the brain include chemical and behavioural changes of the brain;
- Long-term effects of ecstasy include changes of brain structure, mood, memory, and behaviour.

Ecstasy, like other drugs, have an effect on the so-called “reward pathway” located in the limbic system of the brain, which explains its psycho-

stimulant and hallucinogenic action.

The effect of MDMA lasts from 3 to 6 hours. People after taking of MDMA:

- Have a positive attitude towards themselves and those around them;
- Energy increases;
- Self-limitations are diminished;
- The ego softens and emotional bonding empathogenic establishment even with a stranger becomes easier.

So, the majority of those taking this drug are euphorically happy, consequently, open and friendly towards the outside world. The main basis of the short-term effect of ecstasy, i.e., on the target in brain, is the serotonin system, in particular, it transports serotonin from neuronal terminals to the synaptic space along with other neurotransmitters, leading to an elevated mood, a feeling of empathy, and a sense of pleasure that may be accompanied by a vague thinking, agitating, and disruptive behaviour. Then there is the feeling of withdrawal from the body of drug and longing for repeated use of ecstasy and consequently, increasing the threshold of pleasure (i.e. decreased reaction). After 2 weeks of taking ecstasy, level of serotonin in the brain decreases dramatically, and after years, its level will not be completely restored, which disrupts the neuronal connections and it actually causes an abnormal change in mood, behaviour and memory [4,5,6].

During a week of moderate use of the drugs, a person may experience: anxiety, sleep problems, impulsivity, aggression, and depression; Decreased appetite; Memory and attention problems; Diminished interest and pleasure in sex, excessive thirst [4].

Persistent or prolonged use of ecstasy and after its withdrawal from the body causes: degeneration of nerve terminals which is primarily reflected in impaired memory (impaired verbal and visual memory) and behavioral impairment due to a sharp decrease in serotonin and its metabolites in the neocortex and hippocampus; Sleep disturbance; Depression [5,6].

Life-threatening effects after taking multiple doses:

Some people take multiple doses of ecstasy overnight; Increased doses of ecstasy increase the risk of developing side effects.

Clinicians have observed that episodic use of ecstasy in young people in the future develops alcohol dependence and chronic alcoholism, especially among young people with genetic predisposition.

Taking of repeated or high doses of ecstasy can result in hyperthermia, hypertension, cardiac arrhythmia, impairment of functional activity of muscles and kidney failure due to salt and fluid reduction. The development of these dangerous side effects may primarily be due to the impact of ecstasy on the brain, in particular the hypothalamus; Severe hyperthermia can cause brain damage or even death [2,3,4].

So, the brain predominantly is affected by ecstasy. For people taking ecstasy is especially dangerous: a sharp rise in body temperature (hyperthermia, even up to 42 degrees Celsius), dehydration, hypercoagulation and severe cardiovascular events. Studies conducted on monkeys made it clear that ecstasy mainly affects the brain [6].

Overdose causes: serotonin syndrome (muscle rigidity, hyperthermia, cardiovascular disorders, seizures), psychosis, hypertensive crisis [5,6].

Ecstasy tablets, capsules, or powder sold as MDMA-containing are likely to consist of other drugs instead of MDMA, or may be combined with MDMA; for example, such as cocaine, ketamine, methamphetamine, or synthetic cathinones (so-called "sea salt"); These substances can be very dangerous if the person does not know what he/she is taking. People who purposely or unknowingly mix such a mixture with other substances, such as marijuana and alcohol, may pose an even greater risk for their health [4].

Active self-administration of MDMA by experimental animals - was an important indicator of the potential for drug addiction, although it was expressed to a lesser degree than in the case of other drugs, e.g. such as cocaine. Some people observed symptoms of the drug addiction, which include the following symptoms: fatigue, loss of appetite, depression, difficulty in concentrating [4,6].

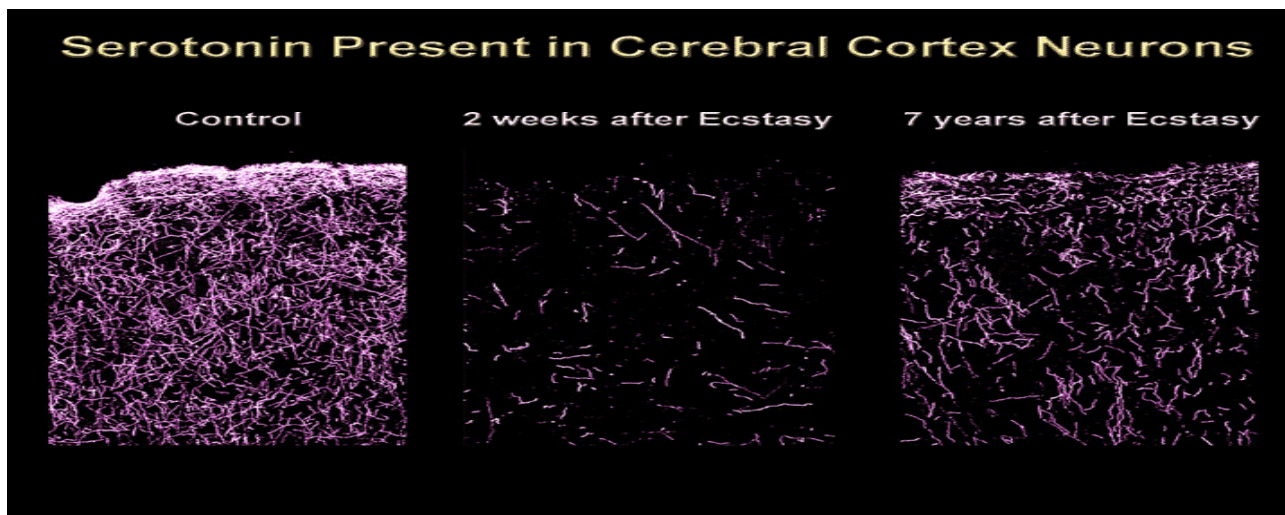
MDMA causes increased production of prolactin, oxytocin, adrenocorticotrophic hormone, Vasopressin [2,3].

Thus, the consumption of MDMA includes both pleasure and discomfort (rise in body temperature, abrupt change in blood pressure and heart rate, dry mouth and shivering, blurred vision, involuntary movement of muscles, especially the lower jaw muscle – causing clenching and damaged teeth, in some cases panic attack and hallucination) [2,3].

Unfortunately, there is no FDA-recommended medication or specific treatment available to deal with MDMA addiction. The most effective current treatment for patients with MDMA addi-



Level of serotonin in the neurons of cerebral cortex 2 weeks after and 7 years after of taking ecstasy (the image shows the segments from the neocortex of monkeys consuming ecstasy):



Short-term effects of ecstasy after leaving the body:



ction is cognitive-behavioural interventions designed to alter the patient’s thinking, expectations and behaviour, as well as increase their ability to cope with life’s stressful situations. Supportive healing groups can be effective in combination with behavioural interventions to support long-term recovery [6]. Hence, in the world, as well as in Georgia, dangerous club drug - Ecstasy, is quite popular among young people. In terms of drug use, the situation in Georgia is particularly serious; The main purpose of an anti-drug company is to bring the key message to all teens at an early age that “Ecstasy is not happiness, it’s a way out to nowhere.”

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