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ORIGINAL ARTICLE

Plasma amino acids in ecstasy users

Hans Joerg Stuerenburg*[1], K. Petersen*[2], C. Buhmann*[1], M. Rosenkranz*[1], T. Baeumer*[1] & R. Thomasius*[2]

[1] Neurological Department and
[2] Department of Psychiatrie and Psychotherapy, University Hospital Hamburg Eppendorf, Martinistrasse 52, 20246 Hamburg, GERMANY.

Correspondence to: Hans Joerg Stuerenburg, M.D.
Neurological Department Median Clinic
Bad Suelze 18334 Bad Suelze, GERMANY
TEL: +49-3822972538
EMAIL: stuerenburg@uke.uni-hamburg.de

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Abstract

Recreational use of the illegal drug "ecstasy" has increased dramatically in recent years. We have measured 33 different plasma amino acids in ecstasy users and controls. Significant differences were found for phosphoserine, glutamate, citrulline, methionine, tyrosine and histidine. Resembling changes in the plasma aminoacids have been described in acute transient polymorphous psychosis. Thus, alterations in plasma – methionine and phosphoserine or other aminoacids could be involved in the psychical symptoms produced by MDMA.

Introduction

Recreational use of the synthetic methamphetamine derivative MDMA (3,4-methylenedioxymethamphetamine), the main constituent of the illegal drug "ecstasy", has increased dramatically in recent years. It is used primarily by adolescents and young adults. MDMA interferes with serotonin and catecholamine transporters in the central nervous system to increase synaptic monoamine levels and thereby mediate the majority of its central nervous effects. These range from wanted effects like euphoria and central nervous stimulation to mild hallucinations, impairment of cognition and psychotic episodes [1]. Acute transient polymorphous psychosis and delirium have been reported to be associated with alterations in plasma amino acids [2, 3]. As part of a comprehensive study of ecstasy users [4, 5] we have measured 33 different plasma amino acids.

Patients and methods

All subjects had been ecstasy-free (verified by toxicological analysis of the urine) for at least 3 days. In addition, information given by the subjects about their ecstasy intake and toxocological analysis of the hair ecstasy content were compared. A concordance of 91.3% was found between the self-reported data and levels detected in hair. We investigated 159 subjects (68 female, 91 male). 107 of them were ecstasy users, and they were grouped according to cumulative lifetime dose: group E1, <100 tablets (n = 34); group E2, 100 – 499 tablets (n = 42); group E3, 500 – 2500 tablets (n = 30). The ecstasy users in our random sample had taken ecstasy for four days up to eight years (on average, 5.3 months). In 49% of the users, the time that had elapsed since the last use of ecstasy was one month or less. We also investigated 11 abstinent subjects (group A), and 41 subjects who used other drugs but not ecstasy (group P). The

following amino acids were measured in plasma: alanine, arginine, asparagine, aspartate, alpha-alanine, citrulline, glutamate, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, ornithine, phenylalanine, phosphoserine, serine, taurine, threonine, tyrosine, valine, phosphoethanol, alpha-aminoadepsin, alpha-aminobutyric acid, dl-cystathionine, beta-aminobutyric acid, GABA, dl-allohydroxylysine, ornithine, 1-methylhistidine, 3-methylhistidine, anserine, and carnosine.

Results

Significant differences were found for phosphoserine: group PT (951.0 ± 105.2, mean ± S.D., pg/ml) differed significantly from group E3 (835.5 ± 125.9; $p<0.05$), and there was a significant negative correlation with the cumulative dose ($r = –0.32$, $p<0.01$; Spearman correlation coefficient). In the case of glutamate, group PT (44.5 ± 18.2) differed significantly from groups E1 (32.9 ± 12.4) and E2 (34.1 ± 12.8; $p<.05$), and we found a significant negative correlation with ecstasy consumption in the last 12 months ($r = –0.19$, $p<0.05$). For citrulline, group A (27.9 ± 4.6) differed significantly from group E2 (22.5 ± 4.8; $p<0.05$, and we found a significant negative correlation with consumption in the last 12 months ($r = –0.19$, $p<0.05$). In the case of methionine, group A (27.6 ± 7.1) differed significantly from groups E1 (20.0 ± 6.3) and E2 (19.2 ± 6.2; $p<0.05$), and we found a significant negative correlation with the cumulative dose ($r = –0.23$, $p <0.01$) and with consumption in the last 12 months ($r= –0.27$, $p<0.01$). In the case of lysine, group E3 differed significantly from groups PT, E1 and E2 ($p<.05$) and in the case of tyrosine we found a significant negative correlation with the cumulative dose ($r= –0.19$, $p < .05$). Finally, a significant difference in histidine concentration was found between group A (72.6 ± 13.0) and groups E1 (60.7 ± 8.5) and E3 (61.6 ± 9.5; $p<0.05$).

Discussion

The plasma concentrations of 33 amino acids in 159 ecstasy users and controls have been measured. We could demonstrate significant alterations in ecstasy users, phosphoserine, glutamate, citrulline, methionine and histidine were significantly reduced. Resembling changes have been described in acute transient polymorphous psychosis [2], in particular a fall in serine and methionine. Acute polymorphous psychosis is also possibly associated with ecstasy use, thus, alterations in plasma-methionine and phosphoserine or other aminoacids could also be involved in the psychical symptoms produced by MDMA. In particular, the association of these amino acids with serotonin [3, 6] with symptoms of delirium appears to be of interest. The fall in plasma glutamate which we could demonstrate here could also be associated with the psychopathology. In general, NMDA-receptor hypofunction is associated with memory impairments followed by other schizophrenia-like symptoms. Whether the altered plasma amino acid concentrations reflect alterations in the brain and cerebrospinal fluid is not clear. Therefore, a further analysis of excitatory, inhibitory and other amino acids in CSF would be of interest.

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