patient's healed epithelium remained stable even after the end of treatment with the substance-P-derived peptide. Perhaps presence of the sensory neural signal is required only to start the healing process.

The clinical application of the eye drops containing of FGLM and IGF-I was approved by the Internal Review Board of Yamaguchi University Hospital. Written informed consent was obtained from the patient.

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Low-dose MDMA ("ecstasy") induces vasopressin secretion

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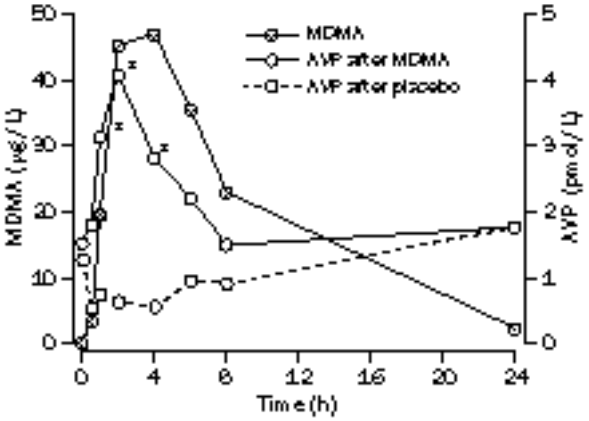
Abuse of 3,4-Methylenedioxymethamphetamine (MDMA, commonly called ecstasy) has been associated with acute symptomatic hyponatraemia with the syndrome of inappropriate antidiuretic-hormone secretion (SIADH).[1] In one case, raised antidiuretic-hormone (arginine vasopressin; AVP) concentration was found.[2] We investigated whether the hyponatraemic effect of MDMA is a direct effect of AVP secretion.

Approval was obtained from the UK Home Office for the purchase and administration of MDMA, and from King's College London Ethics Committee. Eight normally hydrated healthy male volunteers aged 22–32 years, were each given 47·5 mg MDMA hydrochloride (Sigma; equivalent to 40 mg MDMA base) in capsule form with 200 mL water at 1000 h. Three acted as untreated controls at least 2 weeks later. Blood was taken before ingestion and at 30 min, 1 h, 2 h, 4 h, 6 h, 8 h, and 24 h after. Samples were analysed for MDMA by GC-MS and for AVP by RIA.[3] Cortisol and sodium concentrations were also measured. Statistical analysis between before and after data was by repeated-measures ANOVA or by paired *t* test.

Plasma AVP concentrations reached a maximum between 1 h and 2 h after drug administration. Baseline AVP concentrations (range 1·14–1·88 pmol/L) increased significantly at 2 h (range 2·46–9·16 pmol/L; paired *t* test p=0·006, one tail), mean AVP concentrations (figure) contrasting with the small decrease observed on control occasions. Despite increases in AVP and MDMA, a correlation was not shown (Spearman *r*=0·2, p=0·1), probably because of the rapid clearance of AVP, the initial elimination half-life of which is about 6 min,[4] compared with that of MDMA, which is measured in hours. Sodium concentrations changed significantly, ranges at baseline and 2 h after drug administration were 139–145 mmol/L and 140–142 mmol/L respectively; seven of eight volunteers showed a decrease of 1–3 mmol/L, whereas the remaining volunteer showed an increase of 1 mmol/L (paired *t* test p=0·025, one tail). Mean initial cortisol concentration was 331·4 nmol/L (range 208·8–603·4 nmol/L), which increased, although not significantly (p>0·05), to 377·2 nmol/L (range 268·4–583·3 nmol/L) at 2 h.



Plasma concentrations of AVP after MDMA (n=8) or placebo (n=3) in healthy volunteers. Concentrations of MDMA are also shown (n=8)

Results are exressed as geometric means; repeated measures ANOVA*, p<0·05 for AVP values for each subject compared with basal concentrations.

Street "ecstasy" frequently contains more than 100 mg of MDMA. In this study, a single relatively small dose caused an acute rise in AVP concentration at a time of day when it would not be expected to change. The rise in AVP was accompanied by a small fall in plasma sodium concentrations. The hyponatraemic illness experienced by some users is thus likely to be linked to the drug's ability to stimulate secretion of AVP. Hence, if fluid intake is excessive, even a relatively small dose of MDMA could lead to symptoms of hyponatraemia. The rise in AVP does not seem to be part of a generalised stress response because there was no significant change in plasma cortisol concentration. It therefore seems that MDMA-induced hyponatraemia is unlikely to be due to a rare and idiosyncratic reaction, but results from a pharmacological effect compounded by excessive fluid ingestion. Animal studies show that MDMA stimulates the output of serotonin by serotonergic neurones, and AVP secretion is regulated by serotonergic pathways.[5]

The message is that those who take "ecstasy" or similar drugs may be at risk of hyponatraemia and should, therefore, avoid drinking fluid in excess of the body's requirements. This may be difficult for users to estimate because MDMA reduces perception of thirst and impairs judgment.

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