Cerebral venous sinus thrombosis induced by 'ecstasy'  

Abuse of the synthetic amphetamine deriva-
tive, 'ecstasy' (3,4-methylenedioxyamphetamine, MDMA) causes convulsions and sudden cardiac death,1 hyperpyrexia, acute renal failure,2 psychosis,3 and cerebral haemorrhage.4 We report a previously unrecognized, serious neurological complication.

After ingestion of a single tablet of MDMA at a dance party, a 22 year old woman spent eight hours dancing without drinking any fluids. Twelve hours after tak-
ing the MDMA she developed throbbing headache, nausea and photophobia, fol-
lowed by visual fortification spectra, expres-
sive dysphasia and right hemisensory loss. After 2 hours the sensory loss and dysphasia resolved, and photophobia, nausea and headache, remained. There was no past history or family history of migraine. She smoked 10 cigarettes per day, had no regular medication, and had never previ-
ously taken illegal substances. She was seen by a neurologist because of persistent headache, and a transient recurrence of right hemisensory loss. Examination was normal and a diagnosis of probable migraine was made. She was treated with aspirin and metoclopramide. Twelve days after ingesting 'ecstasy' she was reviewed because of persistent headache, and was found to have bilateral papilloedema.

Brain CT with and without contrast enhancement was normal. Lumbar puncture revealed clear CSF with an opening pressure of 32 cm (normal under 16 cm). The CSF contained 52 × 106 red blood cells per litre and 2·21 × 106 white blood cells per litre (90% lymphocytes). No organisms were seen, no viral or bacterial organisms were detected, and the culture was negative. CSF protein level was elevated at 2·97 g/l, and CSF glucose was normal. Four vessel cerebral angiography demonstrated a delayed venous phase with filling of all of both transverse sinuses. Coagulation studies, including lupus anticoagulant, anti-
cardiolipin antibodies, proteins S and C, and antithrombin III, were normal. A diag-
nosis of cerebral venous sinus thrombosis was made. CSF was proteinated with intravenous heparin and repeated lumbar puncture for four weeks until her symptoms resolved. On review three months later she was asympto-
matic with no papilloedema.

Cerebral venous sinus thrombosis has not previously been reported as a complication of MDMA abuse, although disseminated intravascular coagulation is recognised in amphetamine toxicity.5 MDMA causes increased hepatic proteination and swelling,6 and can lead to dehydration,7 a recognised cause of cerebral venous sinus thrombosis.8 It is customary to drink large volumes of liquids after taking MDMA, but in this case no fluids were taken. The combination of volume depletion and the thrombogenic effect of an amphetamine might explain the development of the condition.

Cerebral venous sinus thrombosis has a mortality of approximately 10%, and a con-
siderable risk of neurological disability in survivors.9 Although abuse of MDMA should be discouraged, the importance of maintaining adequate hydration following ingestion of the drug, should be emphas-
sised.

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5 Harris DF, De Silva R. Ecstasy and intra-
6 Ginsberg MD, Hortzman M, Schmidt-
7 Greer GT, Tolbert JR. Subjective and objective responses of the effects of 3,4-methylenedioxyamphetamine ('ecstasy') in normal volunteers. J Psychoactive Drugs 1986;18:313–27.

Some observations on the aetiology of progressive hemifacial atrophy ("Parry–Romberg syndrome")  

Although clinical reports of progressive hemifacial atrophy (HFA) have appeared for over 150 years,1 the causes of the condition remain unknown. Various theories, some underpinned with experimental evidence, have been advanced, including a genetically determined disturbance of facial development, possibly inherited as an auto-

dosomal dominant condition with incomplete penetrance; a localised manifestation of idiopathic progressive facial atrophy; or a disturbance of facial autonomic innervation, either central or peripheral. The discovery of a further patient with HFA allowed us to address some of these theories.

A 23 year old left handed white male complained of progressive wasting of the right side of his face. He was the second of identical twins, delivered per vaginum without instrumental or comp-
lication. His developmental milestones occurred at appropriate times. He first noticed thinning of the face at age 17, par-

ticularly around the chin and later around the cheek. These changes were noticed, but not investigated, by contemporaneous photographs.

In retrospect, he could recall being bitten on the chin during a fight at age 14 but this did not sensibly explain the condition. There was no history of facial numbness, migraine, seizures, or symptoms of bulbar palsy, and family history was negative for similar conditions.

Clinical examination revealed wasting of subcutaneous tissues on the right side of the face, including platysma. There was no neu-
do
trophic deficit in the cranial nerves, in par-

ticular trigeminal. The cranial reflexes were normal; the limbs were symmetrical and neurologically intact. Thorough inspection of the skin showed no stigmas of sclero-

derma. Eyebrows and moustache were sym-
metrical with no achromia or hyperchromia, and no appreciable difference in facial sur-
face temperature or sweating, or a skel-
tal deformity were detected. The patient's right handed brother, the first born twin, was also exam-
ined and had neither facial nor limb hemi-
trophy, neurological and dermatological examination also normal.

Investigations of the proband showed no bony asymmetry in skull and facial radi-
ographs, and no cerebral asymmetry on a CT brain scan. An electromyograph was normal, as were serological and somatosensory evoked potential studies. Electromyographic studies of the right orbicularis oculi and orbicularis oris, right facial nerve and blink reflexes, were within normal limits.

DNA fingerprints were prepared from the blood of the proband and his twin (Celmark Diagnostics, Abingdon, UK) and normal identical bands, thus confirming monozygosity.3

Serology proved negative for antinuclear antibodies, anti double-stranded DNA anti-

bodies, anti-centromere antibodies, anti-

SCL70, anti-Ro, anti-La, extractable nuclear antigens, and anti-neu-
trophi cytoplasmic antibodies.

To investigate the possibility that facial hemiatrophy results from localized autonomic dysfunction, a sympathetic and sympa-

tomic function were performed on the proband. Both sides of the face were tested, the clinically normal side acting as an inter-

nal control. The autonomic function of pupillary reactions was investigated using the following eye drops: 2·5% metha-

choline, 4% cocaine, and 1 in 1000 adrena-

cline. All reactions were as expected for the normally innervated pupil with no evidence of parasympathetic or sympathetic denerva-

tion (central or peripheral). Lacrimation was investigated by the Schirmer tear test; this was found to be symmetrical and within normal limits. Sudomotor function was investigated by a standard sweat test with quinizarin staining; no asymmetry in response was detected. No evidence of pos-

tural hypotension was found and there was no alteration in heart rate by measuring carotid sinus massage or ocular pressure.

Hemifacial atrophy is a disorder of uncer-
tain aetiology. Because of the diversity of clinical features seen in various cases, the unifying pathogenesis has been ques-
tioned, prompting the suggestion of possi-
bile aetiological heterogeneity.

The occasional familial occurrence of HFA suggests the operation of a genetic factor in the causation of some cases. Reviewing such reports, McKusick10 came to the conclusion that HFA was inherited as an autosomal dominant condition with incomplete penetrance and variable expression. In support of this hypothesis, Lowry11 later cast doubt on the appropriate-

ness of considering HFA as an autosomal dominant condition. Having been unable to locate any previous reports, we believe this to be the first documentation of normal tests of autonomic function for HFA in a proven monozygotic twin pair, an observation which argues strongly against an autosomal pattern of inheritance.

A number of reports of HFA with scleroderma** and limb atro-

phy have appeared, leading to speculation that the conditions may be related with a shared pathogenesis. HFA represents a form of localised scleroderma.5

The recent description of a patient with scleroderma, facial hemiatrophy and anti
double-stranded DNA antibodies prompted speculation as to whether such antibodies, or other autoantibodies described in sclerodermia, might be found in patients with "idiopathic" HFA.

It has been suggested that lesions to the ipsilateral cervical sympathetic innervation, whether peripheral or central, may cause HFA. Moss and Crikelair reported a rat model of progressive HFA following cervical sympathectomy. However, autonomic function testing in patients with HFA has produced conflicting results: although some patients have clear evidence of concomitant autonomic dysfunction (for example, ipsilateral Horner's syndrome) others give normal responses to standard tests of autonomic function. Nonetheless, Archambault and Fromm came to the conclusion that the sympathetic theory alone could explain most cases of HFA, even though no overt evidence of autonomic dysfunction, a position which seems less tenable today. Only indefinite pathological changes have been found in the cervical sympathetic ganglia in the few patients examined thoroughly at post mortem. The evidence of autonomic dysfunction was found in our patient.

Facial trauma is a recognised antecedent of HFA (in up to a third of cases) but the mechanism (s) whereby it might produce this condition remain to be clarified. Much remains to be learned of the aetiology of this condition, which probably should not be regarded as a uniform syndrome. Its clinical heterogeneity probably reflects an underlying aetiological heterogeneity. Some cases probably reflect a developmental abnormality, possibly with a genetic basis. Other cases may form part of the clinical spectrum of scleroderma, and others still may result from involvement of the cervical sympathetic chain. The suggestion has also been made that cases with prominent neurological manifestations may result from a slow viral infection.

We thank Dr R C Hughes for permission to report his patient.

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**Subarachnoid haemorrhage associated with MDMA abuse**

Over recent years the use of 'ecstasy' (3,4-methyldioxymethylamphetamine, MDMA), a synthetic amphetamine derivative, has become increasingly popular. In the United Kingdom organised abuse of 'ecstasy' often takes place at 'rave parties' involving several hundred participants in prolonged vigorous dancing.

MDMA is generally taken orally and in the only case that has been reported a peak plasma concentration of 0.106 mg/l was measured at two hours following a 50 mg oral dose (in a 74 kg adult male). The elimination half life in this case was estimated to be 7.6 hours with 65% of the dose excreted in the urine unchanged and 7% excreted as the metabolite methylendioxymethylamphetamine (MDMA) within three days. Whilst the potential for misuse has been recognised and it has been banned under UK legislation as a class 'A' drug since 1971, serious morbidity and mortality associated with MDMA has only recently been noted. Deaths following MDMA abuse have occurred in the presence of underlying pathology such as ischaemic heart disease, asthma and cardiac conduction defects but no precipitating cause is necessary; death has been reported due to ventricular fibrillation. In addition, significant morbidity has been noted including hyperthermia, disseminated intravascular coagulation and acute renal failure. Despite widespread abuse acute neurological complications from MDMA seem to be rare. Cocaine and amphetamine abuse are both well recognised causes of subarachnoid haemorrhage but we are unaware of any similar reports of subarachnoid haemorrhage associated with MDMA abuse.

A 25 year old female presented in the accident and emergency department at 11.20 am with a severe occipital headache of sudden onset at 6 am that morning. The headache was described as the "worst headache she had ever had" and was associated with vomiting. Between 00.30 and 05.00 she had taken 2 1/2 'ecstasy' tablets, while sitting at home with friends. Although she was a "regular user" and this amount was 'usual' for her, she denied the use of 'ecstasy' for the previous two months. There was no history of any other drug abuse and she had not consumed alcohol. Past medical history was unremarkable and there was no prescribed medication.

On clinical examination she was appyreal, alert, orientated, and responding appropriately to verbal commands. Motor responses and eye opening were normal; she had menigismus with a positive Kernig's sign on the right. Pupils were symmetrical and not dilated with normal direct and consensual reactions. Management and examination of the cranial nerves was normal. Reflexes were symmetrically brisk with normal tone and power and flexor plantar responses. Blood pressure on arrival 5 1/2 hours after the onset of symptoms was 120/60 mmHg with a regular heart rate of 80/min. The remainder of the physical examination was clinically normal as was routine haematology and biochemistry. The MDMA plasma concentration measured at the National Poisons Unit, Guy's Hospital, was 0.21 mg/l 13 – 18 hours after ingestion and the analysis excluded the presence of other stimulant drugs.

She received 60 mg of dihydrgcodeine orally as analgesia. A CT head scan was performed showing subarachnoid haemorrhage with blood in the sulci (fig 1a, b). Treatment was started with regular oral nimodipine 60 mg 4 hourly, before transfer to the regional neurosurgical centre. Carotid angiography revealed a left posterior communicating artery aneurysm (fig 2), which was subsequently clipped. Following surgery she made a complete recovery.

![Figure 1](http://jnnp.bmj.com/content/56/10/1036-1035.1)