Cerebral venous sinus thrombosis induced by ‘ecstasy’

Abuse of the synthetic amphetamine derivatove, ‘ecstasy’ (3,4-methylenedioxymethamphetamine, MDMA) causes convulsions and sudden cardiac death, hyperpyrexia, acute renal failure, psychosis, and cerebral haemorrhage. 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 taking the MDMA, she developed a throbbing headache, nausea and photophobia, followed by visual fortification spectra, expressive dysphasia and right hemisensory loss. After 2 hours the sensory loss and dysphasia resolved, but the headache, photophobia and nausea remained. There was no past history or family history of migraine. She smoked 10 cigarettes per day, was on no regular medication, and had never previously 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 5-2 × 10⁶ red blood cells per litre and 2.21 × 10⁶ white blood cells per litre (90% lymphocytes). No organisms were seen, nor viral or bacterial antigens were detected, and the culture was negative. CSF protein was elevated (1.1 g/l), and CSF glucose was normal. Four vessel cerebral angiography demonstrated a delayed venous phase with absence of filling of both transverse sinuses. Coagulation studies, including lupus anticoagulant, antithrombin III and antithrombin III, were normal. A diagnosis of cerebral venous sinus thrombosis was made. CSF protease with intravenous heparin and repeated lumbar puncture for four weeks until her symptoms resolved. On review three months later she was asymptomatic 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. MDMA causes increased bleeding and coagulation and can lead to dehydration, a recognised cause of cerebral venous sinus thrombosis. 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 is a considerable risk of neurological disability in survivors. Although abuse of MDMA should be discouraged, the importance of maintaining adequate hydration following ingestion of the drug should be emphasised.

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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 autosomal dominant condition with incomplete penetrance; a localised manifestation of scleroderma; 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 suggestions.

A 23 year old left handed white male complained of progressive wasting of the right side of his face. He was the second born of identical twins, delivered per vagina without instrumentation or complication. His developmental milestones occurred at appropriate times. He first noticed thinning of the face at age 17, particularly around the chin and later around the cheek. The wasting was not noticed at home. His wasting was confirmed by contemporaneous photographs.

In retrospect, he could recall being bitten on the chin during a fight at age 14 but this did not result in any obvious trauma. 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 neuro- logical deficit in the cranial nerves, in particular trigeminal function was normal; the limbs were symmetrical and neurologically intact. Thorough inspection of the skin showed no stigmata of sclero- derma. Eyebrows and moustache were symmetrical with no achromia or hyperchromia, and no appreciable difference in facial surface temperature or skin blood flow were detected. The patient's right handed brother, the first born twin, was also examined and had neither facial nor limb hemiatrophy, neurological and dermatological examination was also normal.

Investigations of the proband showed no bony asymmetry in skull and facial radiographs, and no cerebral asymmetry on a CT brain scan. An electroencephalogram was normal, as were visual and auditory 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 (Celimark Diagnostics, Abingdon, UK) and normal identical bands, thus confirming monogyosity.²

Serology proved negative for antinuclear antibodies, anti double-stranded DNA antibodies, anti-centromere antibodies, anti-SSA, anti-SSB, anti-Ro, anti-La, anti-DNA, and anti-extractable nuclear antigens, and anti-neu- trophil cytoplasmic antibodies.

To investigate the possibility that facial hemiatrophy results from localised autonomic dysfunction, such a normal sympathetic function were performed on the proband. Both sides of the face were tested, the clinically normal side acting as an internal control. The autonomic function of the proband was investigated using the following eye drops: 2.5% metha- choline, 4% cocaine, and 1 in 1000 adrena- line. 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 evidence of sympathetic hypotension.

Hemifacial atrophy is a disorder of uncertain aetiology. Because of the diversity of clinical features seen in various cases, the uniformity of the syndrome has been questioned, prompting the suggestion of possible aetiological heterogeneity.

The occasional familial occurrence of HFA suggests the operation of a genetic factor in the causation of some cases. Reviewing such reports, McKusick³ came to the conclusion that HFA was inherited as an autosomal dominant condition with incomplete penetrance. The finding was made firm by contemporaneous photographs. In retrospect, he could recall being bitten on the chin during a fight at age 14 but this did not result in any obvious trauma. There was no history of facial numbness, migraine, seizures, or symptoms of bulbar palsy, and family history was negative for similar conditions.

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double-stranded DNA antibodies prompted speculation\(^2\) as to whether such antibodies, or other autoantibodies described in scleroderma, 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 Critchall reported a rat model of progressive HFA following cervical sympathectomy.\(^3\) 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.\(^4\) Nonetheless, Archambault and Fromm\(^5\) came to the conclusion that the sympathetic theory alone could explain most cases of HFA, even though no overt evidence of autonomic dysfunction was found in our patient.

Facial trauma is a recognised antecedent of HFA (in up to a third of cases)\(^6\) but the mechanism (in)whether it might produce the 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.\(^7,8\) 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 neuro-logic complications may result from a slow viral infection.\(^9\)

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Over recent years the use of 'ecstasy' (3,4-methylenedioxymethylamphetamine, 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 (MDA) within three days.\(^10\) 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 predisposing cause is necessary; death has been reported due to ventricular fibrillation.\(^11\) In addition, significant morbidity has been noted including hyperthermia, disseminated intravascular coagulation and acute renal failure.\(^12\) Despite widespread abuse acute neurological complications from MDMA seem to be rare.\(^13\) Cocaine and amphetamine abuse are both well recognised causes of subarachnoid haemorrhage\(^14\) but we are unaware of any similar reports of subarachnoid haemorrhage associated with MDMA.

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 "worse 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 appyral, alert, orientated, and responding appropriately to verbal commands. Motor responses and eye opening were normal; she had meningeal with a positive Kernig's sign on the right. Pupils were symmetrical and not dilated with normal direct and consensual 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/minute. The remainder of the physical examination was clinically normal as was the complete 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 dihydromocodeine 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/letters/jnnp_fullsize.png)  
**Figure 1** (A) (left) CT head without contrast showing blood in the cerebral sulci; (B) (right) CT head without contrast showing expansion of right lateral ventricle posteriorly.