Intranasal apomorphine: a new treatment in Parkinson's disease

Apomorphine, a directly acting dopamine agonist, has recently been used in the treatment of Parkinson's disease complicated by motor fluctuations. Benefit is seen rapidly and reliably following subcutaneous injection. We have sought alternative, more convenient routes of delivery for the drug. Effective mucosal absorption has been reported and we now describe the use of apomorphine delivered intranasally.

Eight patients with Parkinson's disease were studied. Their mean age was 58-1 years (48-70), duration of disease 12-9 years (5-22), and length of treatment with levodopa 11-8 years (4-19). All had severe on-off fluctuations which had already been shown to respond to intermittent subcutaneous injections of apomorphine.

Patients were assessed in an off period following withdrawal of usual medication using a modified Webster rating scale, timed walking over a 12 metre course and unilateral hand-tapping for 30 s on digital counters mounted 20 centimetres apart. Apomorphine solution (10mg/ml) was administered, intranasally, using a metered-dose device and the above assessments were repeated at regular intervals until motor performance returned to baseline.

In seven cases there was a prompt response to 6mg (0.6ml) intranasal apomorphine. No adverse effects were noted and the nasal spray caused no local irritation. In these seven patients the mean Webster scores improved from 21.8 to 10.9; walking times from 17.3 to 9.0 seconds; and tapping counts from 29 to 5.

In the seventh patient the motor response occurred after a mean interval of 8.9 minutes (6-15) and persisted for a mean duration of 44 minutes (36-55). Similar times were reported by the patients for subcutaneous use and equivalent improvements in the measures of Parkinsonism were also seen with both methods of administration. The onset and duration of response appeared to correlate with blood levels of apomorphine demonstrated in one case (fig). The intranasal dose was between 1.5 and twice the subcutaneous one. The patient who did not respond to 6mg did so following a larger dose of 8mg. She had a long history of nasal congestion, perhaps hindering the mucosal absorption of apomorphine.

This preliminary study suggests that intranasal delivery may offer an effective alternative to subcutaneous injection of apomorphine. The benefits of the latter, including the speed and quality of motor response, appear to be retained in most cases with this simpler technique, prompting further evaluation of its long-term use.


**Table**

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Age mean (SD)</th>
<th>Sex (female/male)</th>
<th>SIR mean (SD) pmol/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control patients</td>
<td>27</td>
<td>35 (3)</td>
<td>10/17</td>
<td>113.9 (6.3)</td>
</tr>
<tr>
<td>Epileptic patients</td>
<td>16</td>
<td>46 (8)</td>
<td>6/10</td>
<td>135.4 (9.3)</td>
</tr>
<tr>
<td>Subgroup with recent convulsion</td>
<td>6</td>
<td>52 (8)</td>
<td>2/4</td>
<td>166.6 (12.3)*</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>20</td>
<td>51 (8)</td>
<td>5/15</td>
<td>125.5 (11.3)</td>
</tr>
<tr>
<td>Subgroup with recent infarction</td>
<td>5</td>
<td>54 (6)</td>
<td>1/4</td>
<td>154.6 (21.4)**</td>
</tr>
</tbody>
</table>

*significant difference from epileptic patients (p < 0.01, Wilcoxon test)
**significant difference from cerebrovascular disease (p < 0.001)

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Autoscopy in hemianopic field

Autoscopy is the visual perception of oneself or part of one's body into the external visual space. Although this is the conventional definition, autoscopic phenomena need not always be visual. For instance, it can be perceived in front of the viewer. It has been described in normal subjects, in organic neurological, functional (migraine, epilepsy) and psychiatric disorders. Autoscopy in focal cerebral lesions is a classical case, and autoscopic images appearing in the hemianopic field are still rarer. Our case had a right occipital infarct with autoscopy in the left hemianopic field.

A sixty year old man was admitted with a history of bifrontal thrombosis headache which started suddenly two weeks before. About one week after the onset, the headache became worse and almost simultaneously the patient started seeing his own image in front of him on the left side. Five days later, at the time of admission he was able to give a detailed account of his experience. The image first appeared about a week after the headache, and for the first three to four minutes. He could identify the face and upper part of the body including the cloth of the shirt and the expression. The patient was admitted for a month, he had no other significant complaints. He was discharged and followed up by his own physicians.

Although the number of our patients is small, we conclude preliminarily that 1) lumbar levels of SIR increase after generalised convulsions in epileptic patients; 2) this increase is non-specific with respect to seizure generating mechanisms and similar to increases induced by other conditions of acute tissue hypoxia, for example, cerebral infarction; 3) the negative findings of Pitkänen et al could be explained by sampling "ictal" and "interictal" levels at inadequate time intervals.

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Figure Linear regression of CSF SIR levels and intervals between pathological event and collection of CSF in patients with generalised convulsion (A); and in patients with cerebral infarction (C). Correlation coefficients were calculated on a Hewlett-Packard 9825A. Pearson's correlation coefficient was 0.985 for patients with generalised convulsion and 0.909 for patients with cerebral infarction. Horizontal line and shaded area represent mean (SD) level in control patients without proven neurological disease.

CVD (table). However, the subgroup of epileptic patients with convulsions, occurring within a period of several hours to three days preceding the lumbar puncture showed a significantly enhanced mean level of SIR. Linear regression of values with time interval between convulsion and lumbar puncture revealed that CSF levels were negatively correlated with intervals (tig). Both, slope of decline and regression coefficient where quite similar in a subgroup of CVD patients, studied within five days of a hemispheric infarction.

Our findings contrast with the negative results of Schröter et al., who compared "ictal" levels (one to two hours after generalised convolution) with "interictal" levels (one to four days after convolution) in the same patients. Interictal levels of SIR in the lower normal range were reported earlier by Kohler et al in lumbar fluid and by Wolf in ventricular fluid of epileptic patients. In convulsing rats cisternal CSF levels of SIR increased within five minutes and decreased after 30 minutes, an increase in lumbar levels in humans can only be expected after the ventriculo-lumbar transport time of about two hours, and an alteration of release of SIR may show a much more protracted time course due to postictal depression or other metabolic factors. According to our observations, normal lumbar levels of SIR can be expected within three to five days after the acute event.

Although the number of our patients is small, we conclude preliminarily that 1) lumbar levels of SIR increase after generalised convulsions in epileptic patients; 2) this increase is non-specific with respect to seizure generating mechanisms and similar to increases induced by other conditions of acute tissue hypoxia, for example, cerebral infarction; 3) the negative findings of Pitkänen et al could be explained by sampling "ictal" and "interictal" levels at inadequate time intervals.

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Autoscopy is defined as a "complex psychosensorial hallucinatory perception of one's own body image projected into the external visual space". Autoscopy is seen in organic and psychiatric autopsies. The body image is our concept of the shape, size and mass of our body and its parts. The concept of body schema is not an instinct. As a child grows, there is creation of a tridimensional model of the body and its surrounding external space. Internal and external stimuli contribute to the creation of this model which is dynamic and fluctuates according to circumstances. In addition to the organs, certain other attributes are also represented in this model, such as, ego or possessiveness. The conventional body image is not confined to the physical body alone but includes the clothes and objects of daily use.

The body schema concept is a global function of the brain and requires processing at different parts for its expression. Various names and classifications have been suggested for body schema disorders. The following classification is based on the tridimensional model. Changes in body schema are classified into those affecting its shape, size, mass and position in space. According to this classification the autoscopic is a disturbance of body schema affecting the shape. Autoscopy experience involving senses other than vision have been described in which autoscopic phenomena and auditory characteristics. The image involves the whole body or part of it, but it always includes the face. It may be transparent, opaque or coloured and may show expressions.

Autoscopy may be associated with infecions and intoxications, especially chronic alcoholism and typhoid fever; psychoses; epilepsy; migraine, and diffuse and focal cerebral lesions.

There is no satisfactory explanation for this phenomenon. But it is likely that autoscopy is due to abnormalities in a high level system which is responsible for the representation of the body in its environment. The malfunction of this system may result in misinterpretation of the body in space. Although autoscopy does not have any localising value, it may be an early manifestation of a focal cerebral disease.

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Letters to the Editor
Somatostatin in cerebrospinal fluid after generalised convulsions or cerebral infarction in humans.

H Cramer and K M Heitzelmann

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