123I-amphetamine-SPECT in classical migraine and migraine accompagnée

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Abstract
Migraine is considered to be a functional neurological disorder. In classical migraine (headache associated with prodromal visual field disturbances) and migraine accompagnée (headache associated with transient neurological symptoms), disturbances of cerebral blood flow and amine metabolism are thought to be pathogenetic factors. However, conventional methods of neuroimaging (CAT, NMR) usually do not yield any pathological findings in patients. Since 123I-iodoamphetamine (123I-IMP) crosses the intact blood brain barrier, 123I-IMP-SPECT is used for the assessment of cerebral perfusion in various neurological diseases, including functional disorders.

123I-IMP-SPECT was performed on 5 patients with classical migraine and 18 patients with migraine accompagnée. At the time of investigation, all patients were symptom-free. Cerebral blood flow was decreased in all patients with migraine accompagnée, and often corresponded to the site of headache as well as to the topography of transient neurological symptoms. This reduction was most obvious in a patient with persisting neurological symptoms. Most patients with classical migraine, however, did not show any alteration of cerebral perfusion.

It appears that migraine – and in particular migraine accompagnée – is characterized by a permanent alteration not only of cerebral blood flow but also of neuronal activity. Migraine attacks may occur in connection with exacerbations of preexisting metabolic alterations.

Keywords: Cerebral perfusion, migraine, SPECT.

1 Introduction
Radiolabeled amines such as 123I-iodoamphetamine are extracted by the brain in proportion to blood flow. In contrast to conventional radionuclides, 123I-iodoamphetamine crosses the intact blood brain barrier. 123I-iodoamphetamine imaging is therefore, used for the recording and assessment of cerebral perfusion in various neurologic diseases including functional disorders. The method provides physiologic information and complements anatomic and morphologic information provided by conventional methods of brain imaging [1, 2, 3].

Migraine, including classical migraine and migraine accompagnée, is considered to represent a functional neurological disorder. Classical migraine is clinically characterized by a migrainous headache associated with prodromal visual field disturbances. Migraine accompagnée is characterized by migrainous headache associated with transient neurological symptoms, i.e. hemiplegia. The pathogenesis of migraine is still obscure. Alterations of cerebral perfusion as well as disturbances of amine metabolism are considered to be pathogenetic factors.

Investigations of cerebral blood flow (CBF) in patients with migraine were generally performed during prodromal and/or headache phases using conventional methods. In spite of some remarkable exceptions, these investigations support the concept of a reduction of CBF during the prodromal stage of migraine headache [5–10, 12, 13]. Only few studies have been carried out on CBF in pain-free intervals [4, 9, 11, 12]. These studies do not show any changes of CBF between migraine attacks with the exception of one case with severe complicated migraine reported by Lauritzen and Olesen [4]. This patient demonstrated a minor low-flow region in the insula one week after an attack.

This paper reports on 123I-iodoamphetamine imaging of patients with classical migraine and migraine accompagnée in symptom-free intervals.

2 Patients and methods
The investigation included 23 patients with migraine (14 female and 9 male patients). The average age was 28.0 ± 10.4 S.D. years (range: 17 to 53 years of age). Five patients had classical migraine, while 18 patients were diagnosed as having migraine accompagnée.
pagnée (hemiplegic migraine: 15 patients, basilar artery migraine: 2 patients, 1 patient with persisting neurologic symptoms of hemiplegic as well as basilar artery migraine).

All subjects were patients of the headache ambulance of the Department of Neurology of the University of Münster. All patients received a neurological examination. $^{123}$I-IMP-SPECT and electroencephalography were performed in all patients during a headache-free interval. Additional investigations were performed when indicated by the results of the above examinations.

$^{123}$I-IMP-SPECT was performed according to the following method: 15 min. (occasionally 3 h.) following I.V. administration of 185 MBq $^{123}$I-IMP, 64 single images were obtained within a full circle of 360° using a rotating gamma camera (General Electric 400ACT). Imaging time was 30 sec per image; the examinations lasted 40 min. Tomographic slices of 12 mm width were reconstructed in sagittal, coronal, and horizontal projections by filter-back-projection employing a Butterworth filter with a cut-off frequency of 0,2 cm$^{-1}$ (STAR hard- and software by General Electric). Interpretation was qualitative.

### 3 Results

Table I summarizes the results of the investigation with $^{123}$I-IMP-SPECT. Only 1 of the 5 patients with classical migraine showed a reduction of perfusion, the other 4 patients showed no alterations. All 16 patients with hemiplegic migraine demonstrated a reduction of perfusion. In most of the patients a slight or marked correlation with the site of headache and the topography of the focal transient neurologic symptoms could be observed. The two patients with basilar artery migraine showed deficits of perfusion with marked correlations to the site of headache but with no correlations to the neurologic symptoms.

In the following, typical cases of the various diagnostic groups of migraine are described:

**Classical migraine:** This 21-year-old woman had had migraine attacks since the age of seven years. The attacks show a frequency of 5 times per month with an average duration of 2 to 3 days. The headache is always initiated by typical scintillating scotoma. Her brother and one cousin also suffer from classical migraine. Neurologic examination did not reveal any pathology. The EEG yielded an alpha rhythm with some paroxysmally generalized dysrhythmic groups without any signs of focal abnormalities. $^{123}$I-IMP-SPECT showed normal cerebral perfusion (Figure 1).

**Hemiplegic migraine:** This 25-year-old man experienced his first migraine attack one year ago. The headache is localized in the left temporoparietal region and is accompanied by a transient sensomotor paresis of the right arm and amnestic aphasia. Several attacks with the above symptoms have occurred. The mother of the patient and one brother also suffer from migraine accompagnée. The neurologic examination yielded normal results. Electroencephalography was performed one day after the first attack. It showed a focal delta activity in the left occipitotemporal area. Four days after this examination, the EEG revealed normal patterns. Doppler sonography, CAT, NMR, and cerebral angiography did not show any pathological findings. Conventional brain scan with $^{99m}$Tc-glucoperteonate performed 5 days after the attack was found to be normal. $^{123}$I-IMP-SPECT was carried out one month after the first attack. It showed a left-sided, occipitotemporal hypoperfusion corresponding to the localization of pain as well as to neurologic symptoms and EEG patterns (Figure 2). A repetition of the examination two months later still revealed a slight deficit of perfusion in this area.

**Basilar artery migraine:** This 53 year-old woman has been suffering from migraine for 35 years. The pain

### Table I. Correlation between cerebral hypoperfusion and topography of symptoms in various types of migraine.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
<th>Pathological SPECT findings (n)</th>
<th>Correlation to headache localization</th>
<th>Correlation to neurological symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>to headache marked</td>
<td>slightly none</td>
<td>marked</td>
</tr>
<tr>
<td>Classic migraine</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hemiplegic migraine</td>
<td>16*</td>
<td>6</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Basilar artery migraine</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* includes one patient with persisting neurologic symptoms. The symptoms indicate a combination of hemiplegic migraine and basilar artery migraine.