

## Posterior Cerebral Hypoperfusion in Migraine without Aura

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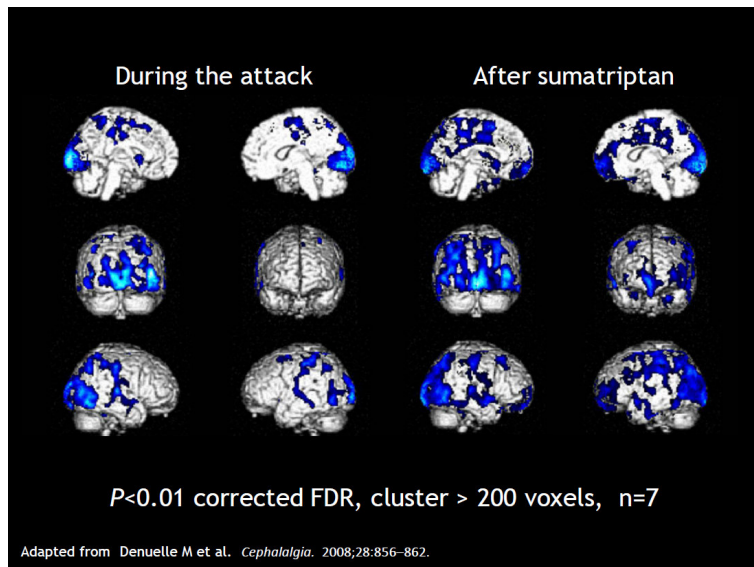
Most of the cerebral blood flow (CBF) studies in migraine have introduced the concept of a pattern different in migraine with aura (MA) and migraine without aura (MoA).

MA is characterized by a focal reduction of regional CBF in the posterior part of one hemisphere that usually, but not always, corresponds to the topography and timing of the reported symptoms.<sup>1-5</sup> The hypothesis of cortical spreading depression (CSO) during MA was suggested by Milner in 1958.<sup>6</sup> Recently, blood oxygen level-dependent (BOLD) functional magnetic resonance imaging (fMRI) has shown cerebrovascular changes in the cortex of migraineurs while experiencing a visual aura that closely resemble CSD.<sup>7</sup> In this study, a clear temporal and spatial correlation was established between the visual symptoms of the aura and the BOLD signal changes.

In MoA, no blood flow changes were noticed in several studies.<sup>8-10</sup> However, Woods and colleagues have reported a bilateral decrease in regional CBF (rCBF) spreading forward from visual associative cortex to parietal and occipitotemporal areas in a patient from the start of a spontaneous attack of MoA.<sup>11</sup> Since the initial positron emission tomography (PET) study performed by Weiller and colleagues,<sup>12</sup> further studies have shown activation in brainstem structures during MA and MoA.<sup>13-16</sup> Then brainstem nuclei may participate in migraine pathogenesis, probably in a dysfunctional mode of the anti-nociceptive network and cerebrovascular control.

In a previous publication using PET,<sup>17</sup> we have reported hypothalamic and brainstem activation in spontaneous migraine attacks recorded as soon as possible after onset. The aim of the present study, using the same design and the same patients, was to focus on cerebral relative hypoperfusion.<sup>18</sup> We used H<sub>2</sub><sup>15</sup>O PET to study seven patients (six female, one male, mean age 38.1 years) during a spontaneous migraine attack. None of the patients was receiving prophylactic treatment.

Mean time from attack onset to PET scan was 3 h 8 min (range 2 h 15 min to 3 h 50 min). The postpain relief PET scan was done within 6 h of headache onset for all patients (from 4 hours 20 minutes to 6 hours, mean time 5 hours 9 minutes). During MoA attacks, a relative hypoperfusion was found bilaterally in the occipital cortex and the posterior temporal and parietal cortex compared with the headache-free interval. The adjusted rCBF decrease was 10.34%. This relative hypoperfusion was significant when the patients are considered as a group as well as individuals (in five out of seven patients). After pain relief by sumatriptan, 4-6 h after onset, the relative hypoperfusion persisted. The adjusted rCBF decrease was 12.32% after sumatriptan.<sup>18</sup>



After flipping the images of left-sided headaches, so that six of seven migraines were on the right side, the relative posterior hypoperfusion remained bilateral before and after sumatriptan. Comparison between “flipped” and “unflipped” data revealed no significant differences. Second-order analysis demonstrated that hypoperfusion after sumatriptan compared with hypoperfusion before sumatriptan was even more important in the occipital region and appeared in the frontal lobe.<sup>18</sup>

When compared with the headache-free period, a decrease in posterior cortical rCBF was found during the headache phase. How can these modifications be interpreted? Considering that posterior hypoperfusion is present at the beginning of MoA as well as MA, two hypotheses could be advanced to explain this hypoperfusion: (i) hypoperfusion is a consequence of CSD; (ii) hypoperfusion is a primary neurovascular event.

Recent research in animals has shown that CSD could induce posterior hypoperfusion and would be able to activate the trigeminal meningeal afferents consistent with the development of headache.<sup>19</sup> However, this is much debated.<sup>20</sup> In our study, the hypoperfusion after sumatriptan is even more important in the occipital region and appears in the frontal lobe. CSD could not explain this frontal area of hypoperfusion, since CSD classically does not cross prominent sulci. However, a direct effect of sumatriptan cannot be ruled out.<sup>18</sup>

A primary brainstem dysfunction has been proposed as the origin of migraine attacks. Experimental work in animals has shown how brainstem nuclei disturbance could initiate the vascular changes seen in migraine.<sup>3</sup> Activation of noradrenergic neurons in the locus coeruleus would be expected to produce bilateral reductions in cortical blood flow<sup>21-23</sup> that would be more prominent in the occipital region,<sup>24</sup> the part of the brain affected by hypoperfusion during migraine attacks. Some arguments from neuroimaging studies in migraineurs are in favor of a primary brainstem dysfunction responsible for posterior hypoperfusion.<sup>25</sup> Concerning the absence of visual symptoms

during the hypoperfusion phase, a primary vascular event below the ischemic level seems to us a better explanation than an asymptomatic CSD.

In conclusion, we found in MoA a posterior hypoperfusion similar to the changes found in other studies in MA. If this hypoperfusion is specific to migraine, it favors the same pathophysiology in MA and MoA. However, the significance of this hypoperfusion needs to be specified.<sup>18</sup>

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