Pearls & Oy-sters: Dynamics of altered cerebral perfusion and neurovascular coupling in migraine aura

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CASE REPORT A 37-year-old woman presented 90 minutes after acute onset of mild motor aphasia with word-finding difficulties and hypesthesia of the right arm. MRI was immediately performed as she presented within the 3-hour time window for IV thrombolysis. Diffusion-weighted images (DWI) were normal, but perfusion MRI (dynamic susceptibility contrast) sequences showed marked hypoperfusion in the left hemisphere affecting both middle cerebral artery and posterior cerebral artery (PCA) territories. These findings were considered compatible with migraine aura. The patient subsequently developed a mild left-sided headache. Clinical symptoms gradually improved to full recovery after 6 hours without specific treatment.

Follow-up MRI perfusion scans were obtained 24 hours and 2 months after the episode. Functional transcranial Doppler (fTCD) from the P2-segments of the PCA during visual stimulation was performed at the same time points as MRI (figure). The first follow-up MRI showed only mild residual hypoperfusion in the left hemisphere, and in the asymptomatic state 2 months later, no perfusion abnormality was detected. Correspondingly, initial severe changes of neurovascular coupling on fTCD were found with nearly no response to visual stimulation in the acute phase. After 24 hours, neurovascular coupling improved with a normal response on the asymptomatic right side and persisting changes in the left PCA, whereas at 2-month follow-up, a normal cerebrovascular response was observed.

DISCUSSION We describe consecutive magnetic resonance perfusion imaging and fTCD findings at 3 different time points during and after migraine aura in a 37-year-old patient. This longitudinal observation demonstrates reversible perfusion abnormalities on MRI during migraine aura. Simultaneously, fTCD showed impaired cerebrovascular responses of

both PCAs to visual stimulation which later gradually normalized.

Transient perfusion changes during migraine aura have been described in several studies, some using perfusion-weighted MRI.^{1,2} These changes may persist beyond the acute aura phase. In addition, altered neurovascular coupling has been reported³ and we have recently detected such vasomotor changes in patients with migraine with aura in fTCD studies.⁴

The neurovascular coupling is the adaptation of the regional cerebral blood flow (rCBF) based on local vasodilatation evoked by neuronal activity.⁵ Assessment of neurovascular coupling is a complementary tool to study the dysfunction of the cerebral vasculature related to migraine aura. Furthermore, fTCD may demonstrate a subclinical affection of the contralateral hemisphere indicating that the underlying pathophysiologic processes of migraine aura are not restricted to a single hemisphere, as has been suggested previously.⁶ The mechanism of bilateral cortical spreading depression has not yet been ascertained. Early animal studies have proposed a propagation of cortical spreading depression through the corpus callosum,⁷ but this has not been verified in humans. As an alternative explanation, a bilateral affection may also be linked to diaschisis, which could cause contralateral reduction of rCBF and glucose metabolism as described after ischemic stroke.⁸ Such a mechanism may play a role in the development of aura-related contralateral hypoperfusion.

Recent observations that cerebral microemboli are able to trigger cortical spreading depression underline a potentially ischemic mechanism of migraine aura.⁹ It is still a matter of debate whether perfusion changes observed during an aura could cause acute ischemic stroke. Clinical differentiation between migraine aura and migrainous infarction is difficult especially when severe headache is absent.¹⁰ Early MRI diffusion- and perfusion-weighted imaging may aid in differentiating these entities.

Figure MRI and functional transcranial Doppler (fTCD) at 3 different time points in a patient with migrainous aura

MRI (upper row) and fTCD (bottom row) on day 1, day 2, and after 2 months: the delay of contrast bolus arrival on perfusion MRI in the posterior part of the left hemisphere is reversible over time, whereas vasomotor reactivity of the posterior cerebral arteries as measured by fTCD first improved in the contralateral hemisphere and completely normalized after 2 months.

AUTHOR CONTRIBUTIONS

Dr. Wolf: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, acquisition of data. Dr. Held: drafting/revising the manuscript, acquisition of data. Dr. Förster: drafting/revising the manuscript, acquisition of data. Dr. Griebel: drafting/revising the manuscript, analysis or interpretation of data, acquisition of data, study supervision. Dr. Gass: drafting/revising the manuscript. Dr. Hennerici: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, study supervision. Dr. Kern: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, study supervision.

DISCLOSURE

Dr. Wolf, Dr. Held, Dr. Förster, Dr. Griebel, and Dr. Szabo report no disclosures. Prof. Gass serves on the editorial board of *Cerebrovascular Diseases*. Prof. Hennerici serves on a scientific advisory board for SERVIER; serves as Editor-in-Chief of *Cerebrovascular Diseases*, on the editorial board of the *Journal of Neuroimaging*, and Consulting Editor for the *International Journal of Stroke*; receives publishing royalties for *Vascular Diagnosis with Ultrasound: Clinical References With Case Studies* (Thieme Medical Publishers, 1998) and *Case Studies in Stroke: Common and Uncommon Presentations* (Cambridge University Press, 2006); has received speaker honoraria from SERVIER, Otsuka Pharmaceutical Co., Ltd., and Boehringer Ingelheim; and receives research support from BMBF, DFG SFB, and the European Union. Dr. Kern serves on the editorial board of *Cerebrovascular Diseases*; received a speaker honorarium from Philips Medical Systems; and has received research support from BMBF.

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Neurology 2011;77:e127-e128

DOI 10.1212/WNL.0b013e31823a0ceb

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