LETTER TO THE EDITOR

Migraine headache is not associated with cerebral or meningeal vasodilatation—a 3T magnetic resonance angiography study

Antoinette Maassen VanDenBrink,1 Dirk Jan Duncker2 and Pramod R. Saxena1

1 Erasmus MC - Division of Pharmacology, Vascular and Metabolic Diseases, Department of Internal Medicine
2 Erasmus MC - Department of Experimental Cardiology

Correspondence to: Antoinette Maassen VanDenBrink, Erasmus MC - Division of Pharmacology, Vascular and Metabolic Diseases, Department of Internal Medicine, PO Box 2040, Rotterdam 3000 CA, The Netherlands E-mail: a.vanharen-maassenvandenbrink@erasmusmc.nl

Sir, with great interest, we read the article by Schoonman et al. (2008), who claim that ‘in contrast to widespread belief, migraine attacks are not associated with vasodilatation of cerebral or meningeal blood vessels’ and, therefore, ‘future anti-migraine agents may not require vasoconstrictor action’. Whereas the methodology used in this investigation is elegant, we disagree with their claim for the following reasons.

First, it may be noted that Schoonman et al. (2008) did observe vasodilatation during nitroglycerin (NTG; 0.5 μg/kg/min over 20 min) infusion in all blood vessels investigated (middle meningeal, internal and external carotid, middle cerebral, basilar and posterior cerebral arteries), but not during the migraine-like headache provoked 1.5–5.5 h after cessation of NTG infusion. However, these initial vasodilator changes can trigger a chain of events leading to headache. Cranial vasodilatation leads to enhanced blood volume following each cardiac stroke with consequent augmentation of vascular pulsations, which may be sensed by stretch receptors in the vessel wall; the resultant increase in perivascular (trigeminal) sensory nerve activity can provoke headache and other migraine symptoms (Fig. 2; Villalón et al., 2003). Admittedly, the magnitude of vasodilatation did not significantly differ between the 20 subjects later developing a migraine-like attack after NTG and the 7 subjects who did not or between the two sides in case of unilateral headache. This may, however, be due to differences in headache threshold.

Second, Schoonman et al. (2008) measured diameter changes in the proximal (extracranial) conducting section of the meningeal artery, but not during the migraine-like headache provoked 1.5–5.5 h after cessation of NTG infusion. However, initial vasodilator changes can trigger a chain of events leading to headache. Cranial vasodilatation leads to enhanced blood volume following each cardiac stroke with consequent augmentation of vascular pulsations, which may be sensed by stretch receptors in the vessel wall; the resultant increase in perivascular (trigeminal) sensory nerve activity can provoke headache and other migraine symptoms (Fig. 2; Villalón et al., 2003). Admittedly, the magnitude of vasodilatation did not significantly differ between the 20 subjects later developing a migraine-like attack after NTG and the 7 subjects who did not or between the two sides in case of unilateral headache. This may, however, be due to differences in headache threshold.

Second, Schoonman et al. (2008) measured diameter changes in the proximal (extracranial) conducting section of the meningeal artery, while the distal intracranial regions could not be studied due to technical reasons. The authors submit that ‘it seems likely that the large ‘conducting’ portions of the porcine-isolated meningeal artery are insensitive to the 5-HT1B/1D receptor agonist sumatriptan (Mehrotra et al., 2006), while others observed contractions when the whole meningeal arterial bed, including resistance vessels, was perfused (Bou et al., 2000). In addition, there is at least some evidence for the dilatation of cranial extracerebral arteriovenous anastomoses in migraine (Heyck, 1969) and these shunt vessels, which were not studied here, selectively and strongly constrict in response to ergot alkaloids as well as triptans in experimental animals (Saxena and Tfelt-Hansen, 2006).

Finally, one must keep in mind that this investigation concerns NTG-provoked (not spontaneous) migraine headaches and lacks measurements at the beginning of such headaches. To their credit, Schoonman et al. (2008) have acknowledged these potential limitations.
In conclusion, it is distinctly premature to ignore substantial evidence, derived from pharmacological studies in humans and experimental animals with vasoactive mediators and acutely active anti-migraine drugs, supporting cranial vasodilatation as being an integral part of the cascade of pathophysiological events in migraine (Villalón et al., 2003; Saxena and Tfelt-Hansen, 2006; Schoonman et al., 2008). We, therefore, refute the claim by Schoonman et al. (2008) that ‘migraine headache is not associated with cerebral or meningeal vasodilatation’. Notwithstanding, we not only praise these authors for undertaking the study, but also wholeheartedly share their hope that ‘future [acutely-acting] antimigraine drugs may not require vasoconstrictor action’. However, it should be borne in mind that the development of such drugs is quite independent of the question whether or not cranial vasodilatation is an integral part of migraine pathophysiology. Even we, who uphold this view, have stated that acutely acting anti-migraine drugs may owe their therapeutic efficacy to attenuation of (i) cranial vasodilatation; (ii) neuropeptide release from trigeminal neurons; (iii) plasma protein extravasation and/or (iv) central neuronal activity (Villalón et al., 2003).

References