Sir, We are grateful to Dr MaassenVanDenBrink and colleagues for their careful comments. Their critical analysis fully confirms and extends our summary and interpretation of the extant data on the putative role of vasodilatation in migraine (Schoonman et al., 2008). The available evidence, at best, is only circumstantial and primarily based on extrapolation of animal experiments and in vitro studies rather than on convincing findings in humans (Schoonman et al., 2008). In fact, this was the very reason for our study. We wanted to provide the first positive human evidence that migraine is indeed associated with cerebral or meningeal vasodilatation. Despite the use of highly sensitive imaging techniques, we failed to confirm that vasodilatation does occur during migraine headache. Dr MaassenVanDenBrink and colleagues raise some interesting alternative hypotheses to rescue the vascular hypothesis, but fail to provide any direct human evidence. It should be emphasized that experimental data, from even the most elegant in vitro and animal studies, merely are hypothesis generating rather than conclusive.

If vasodilatation would indeed be an important triggering mechanisms for migraine, all (not just some) vasodilators should trigger migraine attacks, non-vasodilators should not trigger migraine and all (not just some) vasoconstrictors should treat and prevent migraines. However, established vasodilators such as vasoactive intestinal peptide (Rahmann et al., 2008) and ethanol (Littlewood et al., 1988) are not known to induce migraine, sildenafil provokes migraine attacks without cerebral vasodilatation (Kruuse et al., 2003) and vasoconstrictors such as octreotide (Levy et al., 2005) and cocaine (Herning et al., 1999) have never been shown to either prevent or abort attacks.

Admittedly, it is virtually impossible in medicine to fully disprove a biological hypothesis. We, thus, cannot fully exclude that vasodilatation might be involved in the pathogenesis of migraine attacks in perhaps a subgroup of patients. However, the sobering fact is that, after nearly a century of investigations, direct positive human evidence for the vascular hypothesis is still lacking. Our findings have reinforced this conclusion. We would sincerely welcome novel studies testing the vascular hypothesis for migraine in humans.

References


