SHORT REPORT

Occipital activation in glyceryl trinitrate induced migraine with visual aura
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A case of migraine is presented with visual aura triggered on two separate occasions by glyceryl trinitrate (GTN). Positron emission tomography was carried out during the second triggering session. Activation in the primary visual area of the occipital cortex was demonstrated during the aura. This is the first published case of migraine aura triggered reproducibly by GTN.

Migraine is a common and disabling disorder with an estimated prevalence of 10–15%. A small but significant proportion of these have migraine with aura, most commonly in the form of visual disturbances, such as scintillating scotoma. Leao first described the phenomenon of spreading depression when he found that noxious stimulation of rabbit cerebral cortex produced a spreading decrease in electrical activity, moving at a rate of 2–3 mm/min. This rate corresponds well with the propagation of visual aura. It has been proposed that this cortical spreading depression represents the neurobiological basis for migraine whereby neuronal activation and suppression are followed by corresponding vascular changes.

It has been difficult to image patients with migraine aura because functional brain imaging is technically demanding and spontaneous attacks are unpredictable. While nitric oxide (NO) donors have long been recognised to trigger severe headache, and indeed to trigger migraine, they have generally not been recognised to trigger migraine aura, even in those who have had it spontaneously.

CASE REPORT

A 54 year old male with episodic migraine with aura volunteered to participate in a positron emission tomography (PET) study in migraine. He had a history of migraine with aura as defined by the International Headache Society (IHS) criteria since his teenage years, with a frequency of up to eight attacks per month, each lasting one to two days if left untreated. A typical attack would begin with visual aura in the form of bright, flashing zig-zag shapes moving around his visual field and rarely he experienced macropsia. The visual aura would last 10 to 20 minutes and would be followed by a left sided headache with associated nausea, photophobia, phonophobia, and aggravation by movement. His attacks were usually aborted within two hours with the use of zolmitriptan. He had no other significant medical conditions. His father also suffered with migraine with aura.

Glyceryl trinitrate triggering

An intravenous infusion of 0.5 μg/kg/min glyceryl trinitrate (GTN) was given over 20 minutes on two occasions separated by one week with the aim of inducing a migraine. On both occasions a migraine was successfully triggered, after 150 minutes and 165 minutes, respectively. The subject underwent PET scanning during the second session of GTN.

A visual aura typical of the subject’s previous attacks was also triggered during both sessions of GTN. He described flashing bright zig-zag patterns spreading across his visual field lasting 10 minutes. He was unable to describe any laterality of the visual symptoms. The aura remained unchanged by eye closure. This was then followed by a left sided migrainous headache. Subcutaneous sumatriptan (6 mg) was then given to the subject and the migraine attack was successfully aborted.

PET scanning and analysis

The subject was scanned before the infusion, while pain-free, and during the aura and headache phases of migraine. He described the onset of the aura, and scanning of the aura phase began immediately following this description. PET was carried out with an ECAT EXACT HR+ scanning system (CTI Siemens, Knoxville, Tennessee, USA) in three dimensional mode with septa retracted. He had his eyes closed throughout the scanning sessions. An antecubital vein cannula was used to give the tracer (350 mBq of H15O). The activity was infused into subjects over 20 seconds at a rate of 10 ml/min. The data were acquired in one 90 second frame beginning five seconds before the peak of the head curve. The subject had a total of 12 scans, two of which were during the aura. The aura subsided during the second of the scans. The interval between scans was eight minutes. Attenuation correction was carried out with a transmission scan acquired at the beginning of each study. Images were reconstructed by filtered back projection into 63 image planes (separation 2.4 mm) and into a 128×128 pixel image matrix (pixel size 2.1×2.1 mm2). SPM99 (Wellcome Department of Imaging Neuroscience, http://www.fil.ion.ucl.ac.uk/spm) was used for data analysis. Images were realigned with the first as the reference and then co-registered, and finally spatially normalised into the space defined by the atlas of Talairach and Tournoux. The normalised images were smoothed with a Gaussian filter of 10 mm full width at half maximum. Statistical parametric maps were derived using prespecified contrasts, comparing regional cerebral blood flow during aura versus rest. An uncorrected threshold of p<0.001 was chosen for tabular and graphical reporting.

Analysis of the PET data revealed right sided occipital activation when comparing the two scans taken during the visual aura with those taken immediately before the GTN infusion (fig 1). The activation was in the primary visual region (V1) of the occipital cortex (Brodmann area 17). This area has a very high degree of retinotopic precision and orientation selectivity. No significant activation was observed in the V1 region of seven other patients with IHS.

Abbreviations: GTN, glyceryl trinitrate; HIS, International Headache Society
Recent study by Sances and colleagues involving 197 subjects but failed to induce the aura in these. 10 However, in a previous fMRI study involving GTN triggering of migraine and was one of two patients in whom migraine aura was triggered. 15

In conclusion, we present evidence for the reproducibility of GTN as a trigger of migraine aura. While the number of patients who can have aura reliably re-triggered are small, such cases clearly exist and may offer insights into the neuroanatomical correlates of this fascinating clinical symptom.

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