Reviewer's report

Title: Synesthesia and Migraine: Case Report

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Reviewer: Michael Marmura

Reviewer's report:

This article describes an unusual association between migraine and a highly unusual type of aura best characterized as gustatory synesthesia in association with the visual experience of bright light. The experience lasted about the same amount of time as a typical migraine aura and was stereotyped, and was followed by migraine.

Because I was not able to find similar case descriptions in recent literature I feel this case is highly interesting.

Major Compulsory Revisions

1. I feel the most important way to improve the article would comment on why you think synesthesia could be a migraine aura as this would change the way we think about the disease.

The genetics of synesthesia are not well known, in fact less so than migraine with aura which is probably autosomal dominant with variable expression (at least in the case of hemiplegic migraine). From what I know, synesthesia may be seen in cases of temporal lobe epilepsy, autism and many individuals have creative talents. I am not aware of an association of migraine or psychiatric disorders and synesthesia.

More importantly - synesthesia as you mention is felt to be a disorder of abnormal association area processing or cross wirings - or that these individuals have a lack of inhibition of normal feedback. In contrast migraine aura is probably caused by cortical spreading depression with oligemia. Migraneurs with aura have a lower threshold for CSD and may have other predisposing factors such as low cerebral magnesium levels. The hypothesis here would be then that CSD/aura caused this acquired synthetic response in response to a light, which often exacerbates migraine.

2. Mention more clearly that the symptoms developed at the time of her visual scintillations - which is a common migraine aura. Light sensitivity is an associated symptom of migraine and might be part of prodrome but is not considered aura.

3. Did the patient use the petidine before the aura or only after headaches developed? If she used this medication before/during aura this could make the case harder to accept.
4. Please state if this patient had other type of synesthesia or not.

Minor Essential Revisions

Instead of importunate (a very uncommon word in English) just state the patient developed severe photo and phonophobia, or severe light and sound sensitivity.

I would remove the sentence that atypical perceptual experiences in migraine may be related to co-morbid (I would guess you mean psychiatric) disease. This may be true but I don't know that patients with affective disorders have more unusual auras than those who do not. The studies that you mention are quite small and clinic-based.

Please remove the italics from the article.

I think the discussion about the fact that the patient was a poor metabolizer could be removed.

Discretionary Revisions

Feel free to speculate more about how migraine aura and synesthesia could be related in this patient.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests