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DOI
10.1177/0333102417719573

Publication date
2017

Document Version
Final published version

Citation (APA)
Perenboom, M., Yang, Y., Carpay, J., van der Helm, F., Ferrari, M., Schouten, A., & Tolner, E. A. (2017). *Nonlinear visual processing is faster in migraine with aura*. 56-57. Poster session presented at IHC 2017: 18th International Headache Congress, Vancouver, Canada. https://doi.org/10.1177/0333102417719573

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Headache Pathophysiology - Imaging and Neurophysiology

PO-01-008

Altered brainstem anatomy in migraine

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Objectives: Migraine is a common and debilitating neurological disorder characterised by unilateral throbbing, severe headaches, and often accompanied by nausea and photophobia. The exact mechanisms responsible for migraine remain unknown, although it has been proposed that changes in brainstem anatomy and function, even between attacks, may contribute to the initiation and maintenance of headache during migraine attacks. The aim of this investigation is to use brainstem-specific analyses of anatomical and diffusion weighted images to determine if the trigeminal system displays altered structure in individuals with migraine.
Methods: Using a 3 Tesla MRI scanner (Philips) we collected a high resolution T1-weighted anatomical (TR = 5.6 sec., TE = 2.5 ms, raw voxel size $0.9\times0.9\times0.9$ mm) and 2 diffusion tensor images (32 directions, b0, b1000, raw voxel size $2\times2\times2.5$ mm) in 24 migraineurs and 57 control subjects. All migraineurs were scanned during their interictal phase, i.e. at least 72 hours after a migraine and not within 24 hours of a migraine attack. All images were processed using Matlab and SPM12 software. In each individual, mean diffusivity maps were created using the DTI image sets. Using the SUIT toolbox, the brainstem region of the T1-weighted anatomical images and the mean diffusivity (MD) images were isolated and normalized to a brainstem specific template in Montreal Neurological Institute space and smoothed using a 3 mm FWHM Gaussian filter. Significant differences in regional brainstem volume and mean diffusivity were then determined using a random effects procedure ($p < 0.05$, small volume corrected).
Results: We found grey matter volume decreases in migraineurs in the region of the spinal trigeminal nucleus and dorsomedial pons. In addition, reduced grey matter volume and increased free water diffusivity occurred in areas of the descending pain modulatory system, including midbrain periaqueductal gray matter, dorsolateral pons, and medullary raphe. These changes were not correlated to migraine frequency, duration, intensity or time to next migraine.
Conclusion: This data revealed that when compared to controls, interictal migraineurs show decreased grey matter volume within key brainstem areas know to be activated during migraine attacks in addition to areas involved in endogenous pain modulation. Additionally, increased free water diffusivity occurred in areas of the descending pain modulation system. These data suggest that brainstem anatomy changes may underlie changes in activity that result in activation of the ascending trigeminal pathway and the perception of head pain during a migraine attack.

Disclosure of Interest: None Declared

Headache Pathophysiology - Imaging and Neurophysiology

PO-01-009

Nonlinear visual processing is faster in migraine with aura

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Objectives: Visual system abnormalities in migraine are linked to symptoms like photophobia and the visual aura. Little is known about the mechanisms contributing to these visual system alterations. Processing of visual input by the brain is a highly nonlinear operation, involving complex interactions among cortical and subcortical neuronal networks. Timing of this process can be estimated by analysing the cortical response to external light input at different frequencies. Using a sum-of-sinusoid light signal, instead of the classic pulse train, as input and novel EEG analyses it is possible to assess the time delay and frequency domain response. Here we investigate nonlinear visual processing in subgroups of migraine patients and headache-free participants.
Methods: Migraine patients with aura, without aura and healthy participants (N = 10/group) were subjected to bi-sinusoidal light stimulation for 320 1 sec-epochs, while scalp EEG was recorded at the occipital, parietal and frontal lobes. Light stimulus frequencies were chosen to guarantee no overlap of their harmonic and intermodulation frequencies for different orders of nonlinearity. Nonlinear interactions and time delay from stimulus to cortical EEG response were analysed in the frequency domain using novel phase clustering measures and amplitude spectral measures.

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Results: Higher harmonic and intermodulation interactions were detected between visual input and cortical responses. Amplitude spectrum and phase clustering responses differed per order and group. Migraine patients with aura showed a decreased time delay only at the occipital lobe compared to healthy controls and migraine patients without aura.

Conclusion: Visual processing is altered in migraine patients with aura compared to healthy controls and patients without aura. Furthermore, we demonstrated the potential of quantifying nonlinear interactions and temporal dynamics in the visual system using sum-of-sinusoid light stimulation. We are able to uncover alterations in visual processing in the context of neurological disease.

Disclosure of Interest: None Declared

Headache Pathophysiology - Imaging and Neurophysiology

PO-01-010

TRPA1 channel activation by cinnamaldehyde: Are migraine patients more susceptible than healthy subjects?

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Objectives: Previous studies have shown that some known triggers of migraine activate transient receptor potential (TRP) channels, in particular TRP Ankyrin subtype 1 (TRPA1), which makes this an interesting target for migraine therapy. TRPA1 is a nonselective cation channel functioning as a chemical nociceptor which is activated by cinnamaldehyde (CA). Cinnamaldehyde-induced dermal blood flow (CA-DBF) response has been established as a non-invasive, reproducible in vivo human model for TRPA1 activation in healthy volunteers[1]. The objective of this study is to determine whether the CA-induced DBF and pain response is different between female migraine patients, with and without aura, and healthy volunteers.

Methods: This was a single center, single-blinded, placebo-controlled study in 25 migraine patients (15 without and 10 with aura) and 25 healthy subjects matched for age, sex and BMI. Migraine patients suffered from moderate to severe migraine headache according to criteria from the International Headache Society (IHCD-3). Required migraine headache characteristics included: I) migraine with or without aura, II) one to six migraine attacks a month for at least the last three months prior to the study and III) a history of migraine of at least six months. To exclude influence of hormonal changes, all subjects were tested during their menstrual period. Three 10-mm rubber O-rings (8 mm inner diameter) were placed on the volar surface of the subject's dominant forearm. Topical doses of 20 μL of 10% cinnamaldehyde were applied to the two upper rings and one 20 μL placebo dose (i.e. vehicle) was applied to the lower ring. After a 30 minutes acclimatization period in a quiet, temperature controlled ($23 \pm 1^{\circ}C$) room in a semi-recumbent position, Laser Doppler scans of the subject's forearms were performed at baseline and at 5, 10, 15, 20, 30, and 40 minutes after CA application. At the same time points, pain scores were recorded using a numerical rating scale (NRS) −10.

Results: Topical application of 10% CA evoked an increase in DBF that did not differ between migraine patients (with and without aura) and healthy controls neither when expressed as Area Under the Curve ($AUC_{0–40\,min}$), nor when measuring the pain scores (table 1). The peak mean DBF response was observed 15 minutes post CA application in all groups.

Conclusion: Although preclinical literature suggests that TRPA1 plays an important role in migraine, we did not find a difference in the peripheral DBF response or pain response to CA-induced activation of TRPA1 between migraineurs and healthy subjects.

Abstract number: PO-01-010
Table

Parameter (mean ± SEM)	Healthy volunteers (n = 25)	Migraine patients (n = 25)	p-value (independent t-test)	Migraine with aura (n = 10)	Migraine without aura (n = 15)	p-value (ANOVA with post-hoc Bonferroni)
DBF $AUC_{0–40\,min}$ (PU*min)	17,272 ± 1,104	17,943 ± 5,364	0.665	15,918 ± 1,882	19,293 ± 1,202	0.287
Pain scores $AUC_{0–40\,min}$ (NRS-score*min)	8.2 ± 2.3	3.6 ± 1.6	0.104	2.3 ± 1.8	4.5 ± 2.5	0.232

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