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Visual and auditory perceptual rivalry in migraine

Allison M McKendrick[1], Josephine Battista[1], Joel S Snyder[2] and Olivia L Carter[1]

Abstract

Introduction: Recent evidence demonstrates that perceptual rivalry rate can be modulated by perturbation of the serotonergic system. Specifically, pharmacologically lowering the availability of serotonin results in slower rivalry rates. As it has been suggested that brain serotonin is low during the interictal phase of migraine, we hypothesized that perceptual rivalry rates would be reduced in individuals with migraine.

Methods: Visual and auditory perceptual rivalry measures were obtained for a group of 30 participants with migraine (15 migraine with aura, 15 migraine without aura) and 20 non-headache control individuals.

Results: Our experiments reveal fewer perceptual rivalry switches within both visual and auditory domains for our migraine without aura group, while the with-aura group performed similarly to non-headache controls. Dividing the data by headache frequency rather than headache subtype classification revealed fewer perceptual switches in those with more frequent headaches.

Conclusions: Our data provides further support for interictal differences in brain sensory reactivity in migraine, with the observed effects being in the same direction as those caused by pharmacologically reducing brain availability of serotonin in normal observers.

Keywords

Audition, migraine, perceptual rivalry, psychophysics, vision

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Introduction

There is considerable evidence for altered sensory responses in people with migraine, both during attacks and in between. Patient symptoms suggest heightened sensory sensitivity, for example, resulting in photophobia and phonophobia during migraine events (1,2). These symptoms form part of the diagnostic criteria for migraine (2). Between migraine events, some people with migraine report elevated discomfort when viewing striped grating patterns and visual illusions (3,4). The neural mechanisms underpinning these symptoms are not established, but are generally assumed to result from some sort of ill-defined neural hyperexcitability. Of substantial debate in the migraine literature is whether such hyperexcitability is primary, or arises secondarily to reduced inhibitory mechanisms (for review see 5,6).

The majority of psychophysical studies designed to explore perceptual consequences of alterations to cortical excitability or inhibition in migraine have concentrated on visual processing. Visual symptoms are a key feature of migraine, both for those who experience visual aura, and also those who do not but have symptoms such as photophobia (2). Auditory involvement in migraine is also demonstrated by the common symptom of phonophobia (7), as well as recent evidence for interictal differences in sound aversion (8). The most consistent evidence for interictal differences within the auditory system has been provided by electrophysiology, where a key feature of migraine revealed by evoked potential studies is an impairment of habituation to repeated stimulation. This difference is manifest in both auditory and visual domains (9–11). The neural mechanism of aberrant habituation is not fully elucidated, however one suggested explanation is that

[1]University of Melbourne, Australia.
[2]University of Nevada Las Vegas, USA.

Corresponding author:
Allison M McKendrick, Department of Optometry and Vision Sciences, The University of Melbourne, Parkville 3010, Australia
Email: allisonm@unimelb.edu.au

reduced habituation could arise if migraine involves lower pre-activation levels of sensory cortices relative to non-headache controls (6). According to this theory, lower pre-activation levels of sensory cortices will result in a wider range of supra-threshold stimulation prior to habituation being initiated.

A longstanding theory regarding a possible mechanism for lower cortical pre-activation levels in migraine involves a central neurochemical imbalance within the serotonergic system, such that between migraine events the available serotonin is low (12–14). A sudden increase in availability of serotonin in the brain has been linked to the acute migraine event (15), and it has been suggested that lower circulating serotonin levels in between migraines results in an environment where responses to increasing levels of serotonin at the time of the migraine are up-regulated. Serotonin has a range of different effects in the central nervous system, including altering levels of conscious brain activity related to arousal and attention (16–18).

An interesting recent observation is that serotonin levels can influence the rate at which perceptual rivalry occurs. Perceptual rivalry refers to the regular fluctuations between 'competing' perceptual states that can be induced by ambiguous stimuli – stimuli that can be validly perceived in more than one way. The most commonly studied examples of perceptual rivalry such as the face/vase illusion, Necker cube and binocular rivalry are visual (19). However, perceptual rivalry also exists in the auditory (20,21) and tactile domains (22). Because these phenomena involve fluctuations in awareness and perceptual suppression without any changes to the sensory input, perceptual rivalry has been traditionally used as a tool to investigate the neural correlates of awareness and attention (19). More recent studies have looked at the effect of serotonergic hallucinogens on perceptual rivalry to investigate the link between serotonin and consciousness more directly (23,24). Psilocybin, a 5-$HT_{1A\&2A}$ receptor agonist, was found to dose-dependently slow the rate of switching between perceptual states during rivalry in a healthy human population (24). A further two studies – one using psilocybin after pretreatment with the 5-HT_{2A} antagonist ketanserin (23), the second using the HT_{1A} receptor agonist tandospirone alone (25) – suggests a possible role of the 5-HT_{1A} receptor in mediating the observed slowing of rivalry switch rate in parallel to subjective changes in arousal and vigilance levels. As one of the primary consequences of 5-HT_{1A} receptor activation is suppression of the raphe neurons responsible for serotonin release throughout the cortex (26,27), these findings suggest a link between reduced brain serotonin levels and slower rivalry switching rate. While other effects of 5-HT_{1A} receptor activation – and indeed other neurotransmitter systems – may also be involved in determining perceptual rivalry switch rate, the importance of the serotonergic system is further supported by the finding of faster switching in anxious individuals (28). Nagamine and colleagues (28) concluded that the increased switch rate may be due to elevated serotonergic neural activity in the raphe nucleus in individuals with high anxiety.

While serotonin is unlikely to be the only neuromodulator that influences rivalry rates, these findings suggest that perceptual rivalry might prove to be a useful indirect tool to study brain neuromodulatory status in individuals with migraine. Based on the above literature, if people with migraine have lower interictal circulating levels of serotonin, one would predict a slower rivalry rate in this population during interictal periods.

We could find only one previous study of visual binocular rivalry in migraine (29). That study showed a trend towards slower rivalry rates in migraine that did not reach statistical significance. Here we revisit the concept of perceptual rivalry in migraine and study both visual and auditory systems. Our visual rivalry method is quite different from the previous published report (29), because we use the bistable plaid motion stimulus (rather than presenting rivalrous static stimuli to the two eyes). The plaid motion stimulus consists of two superimposed gratings that are perceived as either a plaid pattern moving in a single direction, or as two superimposed transparent gratings sliding over each other in opposite directions (orthogonal to the plaid motion) (30). When observers view this stimulus for a prolonged period, they generally report experiencing switches between the coherent plaid percept and sliding grating percept, every few seconds (see Figure 1A and 1B) (31). To induce auditory rivalry, we used the auditory 'streaming' paradigm which consists of a series of low tones (A), high tones (B), and silences (–) presented in a repeating ABA– pattern (32). When the A and B tones differ to the appropriate degree, listeners typically report switching, every few seconds, between hearing a single coherent ABA– 'galloping' pattern or two separate streams of tones, each in a metronome-like rhythm (i.e. A–A–A–A–. . . and B–B–. . .) (see Figure 1C and 1D). This ambiguous auditory streaming has now been demonstrated to show rivalry properties that are equivalent to those observed with the visual plaid rivalry stimulus (20,21).

The visual plaid motion stimulus was selected for a number of reasons. Firstly, a variety of psychophysical studies have identified differences in various aspects of motion perception in individuals with migraine (33–36), hence the use of a moving stimulus might enhance the ability to find differences between groups. A binocularly presented bistable stimulus also avoids potential difficulties in matching the exact salience of the stimuli between eyes and will allow us to extend previous

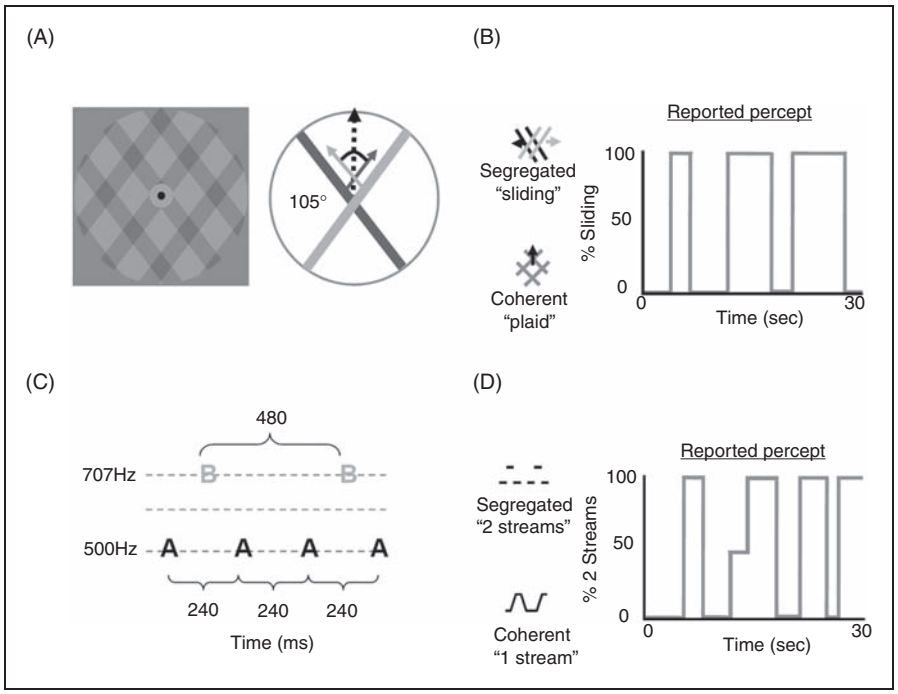

Figure 1. Perceptual rivalry stimuli. (A) Visual rivalry was induced using a plaid stimulus consisting of two transparent gratings with motion direction differing by 105°. (B) During prolonged viewing observers typically report switching every few seconds between perception of a single coherent plaid pattern or two segregated gratings sliding past each other in opposite directions. (C) Auditory rivalry was induced using the auditory streaming paradigm consisting of tone triplet sequences with a 500 Hz low tone repeated every 240 ms and a 707 Hz high tone or a silent period presented between alternative low tones. (D) When listening to this stimulus for prolonged periods, observers generally report alternating every few seconds between the perception of a single coherent galloping stream or separate low and high tone streams.

studies investigating changes associated with migraine, which have been demonstrated using a binocular rivalry stimulus that involves incompatible monocular patterns presented to each eye (29). However, the most important reason motivating our choice of stimulus was the fact that the auditory 'streaming' stimulus (32,37) was available to provide an auditory analogue to visual plaid motion stimulus (20,21). Hence, we were able to study both visual and auditory sensory systems using analogous methods in the same cohort of individuals. If a central mechanism of neuromodulator alteration is present in migraine, it should presumably result in alterations across multiple sensory modalities. The current experiments were designed to test the hypothesis that people with migraine manifest slower perceptual rivalry switching between migraine events relative to non-headache controls.

Methods

Participants

Fifty people participated in this study and were recruited via an advertisement within the University of Melbourne community, or from a database of previous study participants. Two separate advertisements were used, one that asked for volunteers with migraine and one asking for individuals who did not experience headaches. Participants were reimbursed A$20 for participation in the study to partially offset expenses incurred in attending. Participants attended for a single 2-hour session.

The migraine group consisted of 30 people: 15 who fulfilled the International Headache Society's 2004 criteria (2) for migraine with aura (MA) and 15 who met the criteria for migraine without aura (MO). Twenty approximately age-matched controls, who experienced fewer than four headaches per year and had never experienced a headache or migraine that fulfilled the International Headache Society criteria (2004) also participated. Participants in the migraine group were aged between 18 and 41 years (mean 29, SD 6), and control participants were aged from 23 to 45 years (mean 29, SD 7). There was no significant difference in mean age between these groups ($t_{(48)} = 0.20$, $p = 0.84$), nor between the two migraine groups ($t_{(28)} = 0.08$, $p = 0.14$).

All participants were required to have best corrected visual acuity of 6/7.5 or better and to have refractive errors less than ±5.00 D sphere and ± 2.00 D astigmatism. Participants were free from systemic disease

known to affect visual function, and had normal findings in a comprehensive eye examination (slit lamp biomicroscopy, ophthalmology, applanation tonometry) conducted as part of the study. All participants had self-reported normal hearing. With the exception of oral contraceptives, participants were taking no other systemic medications except for one individual who was being treated for mild hypertension. Written informed consent was provided prior to participation, in accordance with a protocol approved by our institutional human research ethics committee and in accordance with the tenets of the Declaration of Helsinki.

Participants in the migraine group were not permitted to be taking prophylactic medications for migraine and were assessed at a minimum of 4 days since the end of their last migraine in order to allow washout of any medications taken to relieve migraine symptoms and to ensure recovery from the episode. Current migraine features were recorded by clinical interview and questionnaire. Twenty-five of the 30 migraine participants reported a formal diagnosis of migraine from either their general medical practitioner or a neurologist. Four of the remaining five participants that had not received a formal diagnosis reported a first-degree relative with similar symptomatology that had received a medical diagnosis of migraine. Participants also completed the Migraine Disability Assessment (MIDAS) questionnaire, a validated tool that scores the impact of headaches over the past 3 months on tasks of daily living (38). MIDAS scores are typically interpreted as follows: grade 1, minimal or infrequent disability (score 0–5); grade 2, mild disability (score 6–10); moderate disability (score 11–20), and severe disability (score 21 +).

Stimuli and equipment

The visual and auditory rivalry measurements were conducted using a personal computer running Matlab R2008a with the Psychtoolbox Win 2.54 toolbox (39,40) and were presented on a ViewSonic G90fB 19-inch CRT monitor (85 Hz, 1024×768 pixels). Viewing was binocular with participants wearing their required refraction for a viewing distance of 57 cm, maintained with a chin and forehead rest. The computer contained a SoundMAX integrated digital audio card and the sounds were presented binaurally through Sennheiser HD205 headphones, at a clearly supra-threshold (but not aversive) volume. Responses were recorded using a standard computer keyboard.

Visual rivalry

Visual rivalry was measured using a drifting plaid pattern (see Figure 1A), which is comprised of two overlapping drifting gratings. Moving plaids can be seen as coherent motion (the motion of the two separate grating components is integrated into a single object) or transparency (the motion of the two components is segregated and the gratings appear to slide over each other) (30). With prolonged viewing, the percepts of coherence and segregation alternate, with the first percept almost always being that of coherence (31) (Figure 1B).

Our plaid was composed of rectangular-wave gratings with a duty cycle of 0.33 (one-third dark grey 14.5 cd/m^2, two-thirds light grey 21 cd/m^2) and a spatial frequency of 0.3 cycles/degree of visual angle (Figure 1). The plaid was presented within a circle of 13 degrees in diameter, on a grey background of 14.5 cd/m^2. The dark gratings moved at a speed of 2°/s. The intersections were a visibly darker 7 cd/m^2 grey. The stimulus was identical to the one reported previously (21). A red 0.2° fixation dot was presented in the centre of a dark grey 9 cd/m^2 exclusion zone of 3° in diameter. The purpose of the fixation spot was to minimize opto-kinetic nystagmus eye movements. In each trial the angle between the direction of motion for the two gratings was 105°, equivalent to the two gratings being tilted to the left and right from a vertical orientation by 52.5°. The orientation of the stimulus was such that the segregated components were seen as two overlaying gratings sliding over each other horizontally towards the left and right of the screen and the coherent plaid stimulus was perceived to move upwards.

Auditory rivalry

The auditory stimuli consisted of repeating patterns of low and high tones in an ABA–ABA–... pattern, where 'A' was always a 500 Hz tone, 'B' was always 707 Hz, and '–' was a silence (Figure 1C). The A and B tones were each presented for 50 ms, including 10 ms rise–fall times. The interval between adjacent tone onsets within each ABA– cycle was 120 ms, as was the silent period between the ABA triplets. Therefore, the duration of each ABA– cycle was 480 ms. Participants completed practice trials with a B tone of 1000 Hz, which is easier to hear as segregated. The tones were perceived either as coherent (galloping rhythm) or segregated, where they were perceived as two independent 'streams' of tones (Figure 1D).

Procedure

Participants were instructed to maintain fixation and to report by key press whether they perceived each stimulus (visual or auditory) as coherent or segregated. When the stimuli were perceived as a single coherent percept, participants were required to hold down the

Table 1. The number of 30s trial intervals excluded due to an absence of percept switches for each group

	Visual			Auditory		
	Number of runs excluded	Total runs measured	% data excluded	Number of runs excluded	Total runs measured	% data excluded
Non-HA	13	400	3.3	28	400	7
MA	13	300	4.3	12	300	4
MO	10	300	3.3	19	300	6.3

'down' arrow key. When the stimuli were perceived as segregated, participants held down the 'right' arrow key. Both keys were held down during periods when the percept was 'unclear' and could not be defined as either coherent or segregated, and all keys were released when no stimulus was presented. Perceptual switches were counted when there was a transition from coherent to segregated or vice versa (with or without an intervening period where the percept was unclear). A swap from unclear to either single percept was not counted as a switch in itself, nor was a switch from a single percept to unclear and back to the same percept (for example, coherent to unclear to coherent was not a switch).

The visual and auditory paradigms were investigated in separate, alternating blocks, within a single test session. Each experiment consisted of four blocks (two visual and two auditory) that were run alternately, commencing with the visual task. There were five trials in each block. Each trial lasted for 30 s, with a 10 s break between trials. All participants repeated the experiment. In other words, each participant completed a total of eight blocks (four of each paradigm).

All participants completed practice trials in order to familiarize themselves with the requirements of the task. Formal testing began after the participant perceived coherent and segregated stimuli for both the visual and auditory stimuli and expressed confidence in reporting these percepts and the switch between. The test session lasted about 90 minutes in total, with rest breaks permitted as required.

Data analysis

Statistical analysis was performed using SPSS v18.0 (SPSS Inc., Chicago, IL, USA). Between-group analysis was performed on two main measures: (a) the time until the first switch within a test interval; and (b) the total number of switches obtained within the 30 s time period. The duration of each percept (including the unclear state) was also investigated but showed no differences between groups and was not central to our hypothesis so is not reported further. The mean total period of the unclear percept for each group on each task varied between 210 ms and 517 ms.

A small number of 30 s trial intervals were excluded from further analysis because the observer did not report a switch within the entire period. For these trials it was not possible to calculate either of our outcome measures of interest (time to first switch and number of switches). A minority of observers (represented from each group) had several trials at the beginning of their first test series where this was the case, but then subsequently consistently reported switching for future trials. Despite receiving training and reporting switching during training, we expect that these individuals were not fully familiar with the task. The percentage of collected data that was excluded from analysis from each participant group is shown in Table 1.

We excluded one non-headache participant from further analysis as she did not experience auditory switching on 12 of her 20 trials. She had no other anomalies suggesting the likely presence of difficulty on the rivalry task; however, she was the only participant in any group that was pregnant at the time of testing. Consequently, the final sample size for analysis was 49 participants (19 non-headache; 15 migraine with aura; 15 migraine without aura).

Results

Headache history

Figure 2 shows box plots of the migraine characteristics of the two migraine groups. There was no statistically significant difference between groups for most of the headache characteristics. The migraine without aura (MO) group had more frequent migraines than the migraine with aura (MA) group in the 12 months prior to testing which approached statistical significance (Mann–Whitney rank sum test, $p = 0.05$). Inspection of Figure 2 (panel E) reveals that the MA group data was highly skewed (median of three migraines per annum, but two participants with 20 or more migraines per annum). Panel F shows the raw scores from the MIDAS questionnaire. This score is a tally of the number of days in the preceding 3-month

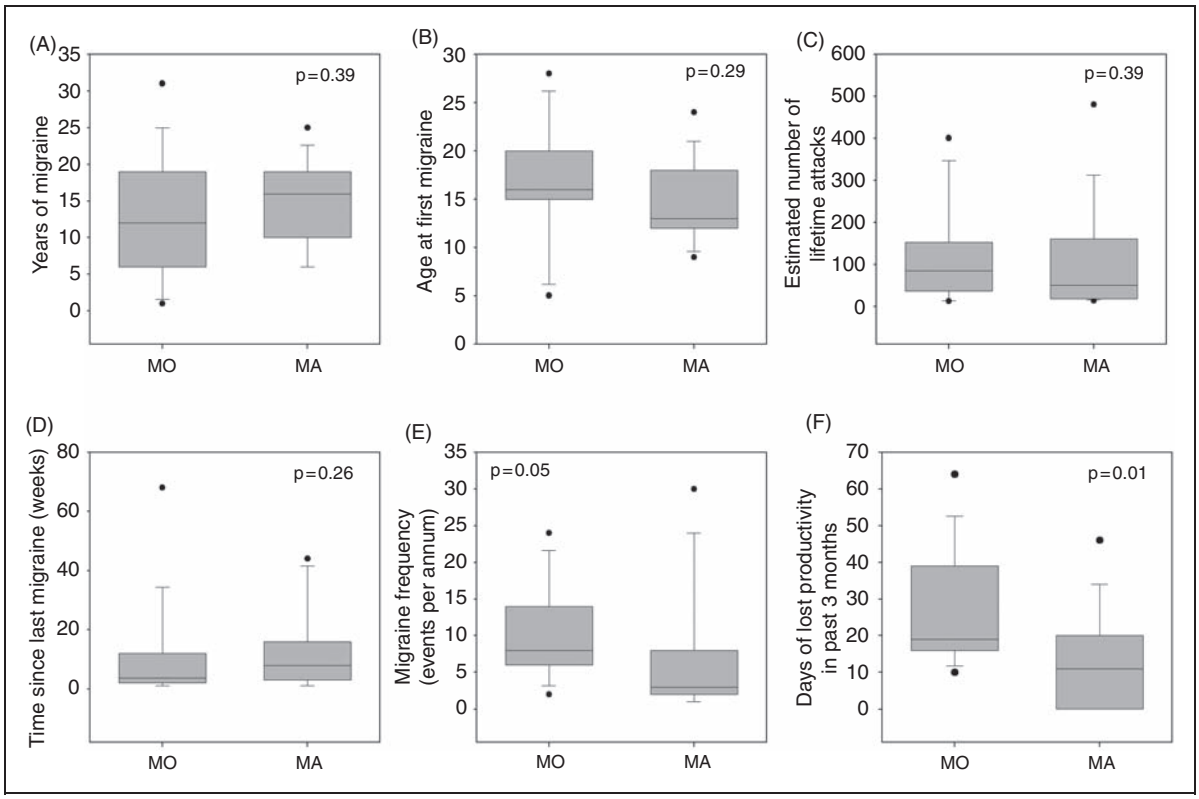

Figure 2. Comparison of headache features between the migraine without aura (MO) and migraine with aura (MA) groups. The boxes represent the 25th, 50th and 70th percentiles, with the whiskers showing the 10th and 90th percentiles. (A) Years of migraine (B) Age at first migraine (c) Number of lifetime attacks (D) Weeks since last migraine (E) Migraine frequency (F) MIDAS raw score.

period where headaches resulted in reduced productivity of employment, schooling, household duties, and family/social activities. The MO group reported significantly greater impact of their headaches on daily activities than the MA group (Mann–Whitney rank sum test, $p = 0.01$).

Rivalry – time to first perceptual switch

Figure 3 shows group mean results for the average time elapsed until the first reported perceptual switch. For all three groups, the first switch occurred slightly earlier on average for the auditory than the visual task (main effect of task: $F(1,46) = 4.52$, $p = 0.04$). There was no significant difference between groups for this measure ($F(2,46) = 1.91$, $p = 0.16$), and no significant interaction between group and modality (vision or auditory): $F(2,46) = 0.26$, $p = 0.77$).

Rivalry – number of switches within the 30 s time interval

Figure 4 shows the average number of switches within each 30 s trial period. Group means (±95% confidence intervals of the mean) are shown. There was a significant difference between groups for this measure ($F(2,46) = 4.12$, $p = 0.02$) with post hoc testing (Tukey) showing that the MO group performance differed from that of the other two groups ($p < 0.05$). There was no significant interaction between group and modality ($F(2,46) = 0.65$; $p = 0.52$), hence the between-group difference was of a similar magnitude for auditory and visual tasks.

Relationship between auditory and visual task performance

If a common central mechanism is at least partially responsible for influencing the number of switches in visual and auditory domains, then a relationship between the measures on the two tasks should be present within individuals. Table 2 shows correlation coefficients (Pearson product moment) between the auditory and visual tasks for all participants ($n = 49$), and the migraine ($n = 30$) and control groups ($n = 19$) separately. When the entire cohort is combined, all correlations are statistically significant at $p < 0.05$. It should be noted that the time to first switch and number of switches are non-independent, as the length of time remaining within the 30 s period for

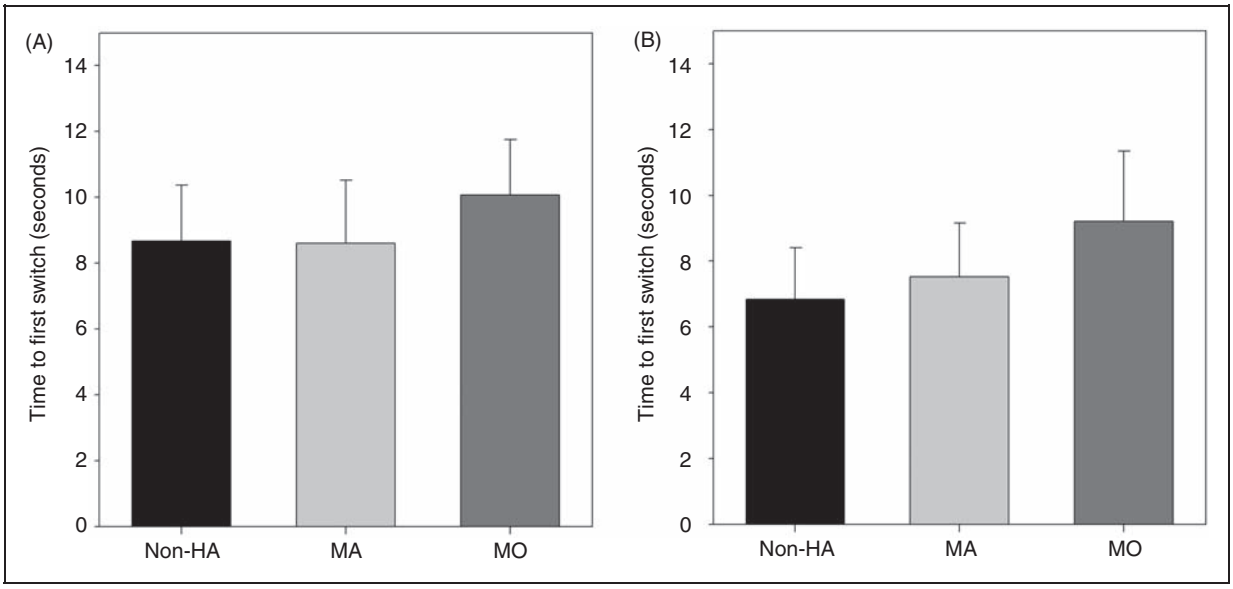

Figure 3. Mean time elapsed until the first perceptual switch (±95% confidence intervals of the mean) for (A) the visual task and (B) the auditory task.

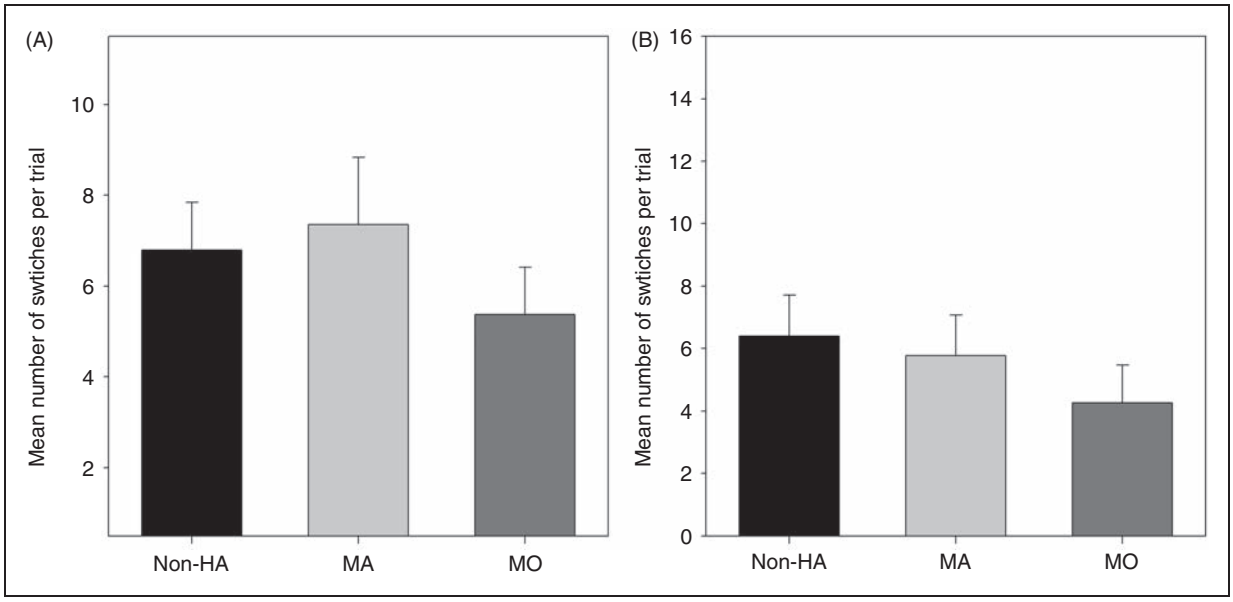

Figure 4. Group average number of perceptual switches per 30 s experimental trial period (±95% confidence intervals of the mean) for (A) the visual task and (B) the auditory task.

switching to occur is dependent on how many seconds expired prior to the first switch in a given trial (minus any time where the percept was 'unclear', however this was minimal for all observers). As previous studies have failed to find significant correlations between switch rate for these two tasks (20), it is worth noting that the relationship between the auditory and visual time to first switch approached significance for both the migraine and control groups analysed separately (both $p = 0.07$).

Relationship of rivalry switching to headache features

Figure 4 shows a significantly reduced number of switches in the MO group compared to the other two

Table 2. Pearson product moment correlations between visual and auditory rivalry parameters for the entire cohort (listed as 'All' $n = 49$), the migraine participants (M, $n = 30$) and the controls (C, $n = 19$)

	Visual	Auditory	Auditory
	Number of switches	Time to first switch	Number of switches
Visual	All: $r = -0.74$, $p < 0.01$	All: $r = 0.44$, $p < 0.01$	All: $r = -0.41$, $p < 0.01$
Time to first switch	M: $r = -0.72$, $p < 0.01$	M: $r = 0.33$, $p = 0.07$	M: $r = -0.39$, $p = 0.03$
	C: $r = -0.80$, $p < 0.01$	C: $r = 0.41$, $p = 0.07$	C: $r = -0.33$, $p = 0.17$
Visual	–	All: $r = -0.32$, $p = 0.02$	All: $r = 0.38$, $p < 0.01$
Number of switches	–	M: $r = -0.29$, $p = 0.12$	M: $r = 0.32$, $p = 0.08$
	–	C: $r = -0.16$, $p = 0.45$	C: $r = 0.33$, $p = 0.17$
Auditory	–	–	All: $r = -0.73$, $p < 0.01$
Time to first switch	–	–	M: $r = -0.82$, $p < 0.01$
	–	–	C: $r = -0.61$, $p < 0.01$

Table 3. Spearman rank order correlations between the number of switches for the auditory task and migraine features

Migraine feature	Correlation coefficient	*p*-value
Weeks since last migraine	0.159	0.402
Age at first migraine	−0.077	0.687
Years of migraine	0.069	0.715
Average frequency of migraines over past 12 months	−0.388	0.034*
Raw MIDAS score	−0.44	0.014*

*indicates $p < 0.05$.

groups. As shown in Figure 2, the MO group experienced on average more frequent migraines (although this difference did not quite reach statistical significance, $p = 0.05$) and had a statistically significant increase in the number of days of missed work/school/home duties caused by their headaches (as indicated by the MIDAS questionnaire result). The MIDAS questionnaire scores are considered to reflect whether headaches are well managed, hence our data indicates that our MO group had poorer headache management. To explore the possibility that the switching behaviour related to a headache feature other than the obvious presence or absence of aura, correlation coefficients were determined between the number of switches on the auditory task and the headache features shown in Figure 2 for the entire migraine cohort grouped together ($n = 30$). A statistically significant relationship was present between the number of auditory switches and both the migraine frequency (events in the past 12 months) and raw MIDAS score.

The correlation analysis shown in Table 3 suggests that more frequent migraines are related to slower auditory switching. Our migraine groups were not balanced for migraine frequency. To explore this further, we split the migraine cohort differently: not according to the presence or absence of aura, but according to ranked reported frequency of migraine events. Due to tied ranks, the groups became: (a) the 16 people with 'less frequent' headaches (six or fewer per year: 10 MA, 6 MO), and (b) the 14 people with more frequent migraines (more than six per year: 5 MA, 9 MO). Performance on the rivalry tasks for these groups is shown in Figure 5. There was a statistically significant main effect of group for both the rivalry parameters (time to first switch: $F(2,46) = 5.29$, $p < 0.01$; number of switches: $F(2,46) = 6.14$, $p < 0.01$), with post hoc testing demonstrating a significant difference between the more frequent headache group and controls only (Scheffe's test: $p < 0.01$ for both the rivalry parameters). There was no significant interaction between modality (vision or audition) and group (time to first switch: $p = 0.61$; number of switches: $p = 0.24$).

Discussion

This experiment was designed to determine whether people with migraine have fewer perceptual switches than non-headache controls during the

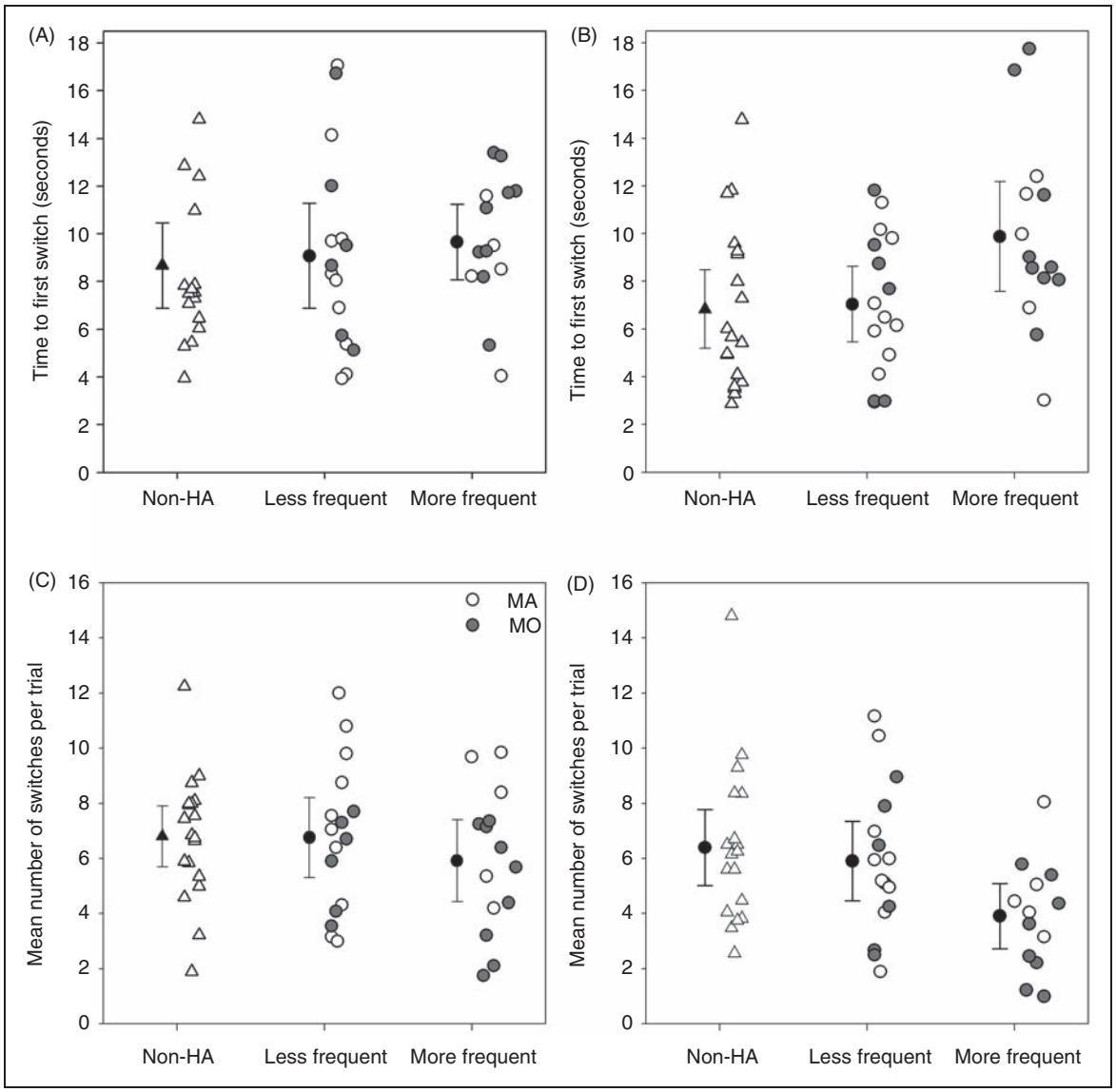

Figure 5. Rivalry parameters in which the migraine participants are split by migraine frequency rather than by presence/absence of aura. Data is presented as the mean ± 95% confidence interval of the mean in addition to showing all individual data, where unfilled triangles represent non-headache controls, unfilled circles represent migraine with aura individuals and grey filled circles represent migraine without aura individuals. (A) Time to first switch: visual (B) Time to first switch: auditory (C) Number of switches: visual (D) Number of switches: auditory.

interictal period. A novel component of this study was the inclusion of comparable visual and auditory tasks (20,21) within the same migraine cohort. This methodology allowed comparison of perceptual switching across two sensory modalities known to show irregularities in people with migraine. Extending previous reports of a trend towards slower binocular rivalry (29), our data shows a significant reduction in the number of switches measured with both a visual plaid motion paradigm and an analogous auditory rivalry paradigm.

In this study we report the number of switches that occurred within the stimulus period. Within the rivalry literature, it is more common to report a switch rate or the same value expressed as average dominance duration (23–25,29). The short stimulus presentations used in our study, however, do not lend themselves to accurate calculation of true switch rate. As shown in Table 2, the time until the first switch was correlated with the number of switches. This arises in part because the length of time available for subsequent switching depends on the time used prior to first switch.

However, if we calculate a 'switch rate' for our participants by dividing the remaining time interval by the number of switches after the first switch, the mean performance of the control and the MO groups remain statistically different ($t(32) = -2.07$, $p = 0.04$). We chose not to use long duration stimuli to minimize potential issues with visual stimulus aversion and adaptation difference in the migraine groups to our striped and drifting patterns (3,4).

We introduced the idea of studying perceptual rivalry in migraine by summarizing evidence that switch rate can be modulated by perturbation of the serotonergic system (23,25). Serotonin has also been a point of focus in the migraine literature (12,13). One possible interpretation of our data is that MA and MO groups vary in the availability of serotonin. A recent Spanish population case control genetic study suggested differential involvement of serotonergic genes in MA and MO groups (41). Genetic association of a haplotype of tryptophan hydroxylase (the rate-limiting enzyme in serotonin availability) with MO has also been shown (42); however, serotonin transporter gene polymorphisms do not vary between MA and MO groups (43). While the existing literature provides support for this proposed role of serotonin in both rivalry switching and migraine, it is important to acknowledge that less is understood about potential contributions of other neurotransmitter systems. It is therefore possible that a series of complex interactions between multiple neurotransmitter systems is relevant.

The difference in the number of switches between our participant groups was relatively small; however, it should be kept in mind that our migraine cohort was relatively mild in terms of symptomatology. Participants were excluded if taking anti-migraine prophylaxis, and were recruited from a community sample rather than from a neurology clinic. It is possible that a more severe migraine cohort might reveal greater between-group differences. Furthermore, it may be useful for a future study to relate rivalry results to the length of time until the participants' next migraine event. Brain neuromodulator availability is predicted to alter with timing relative to migraine events, hence predicted to alter perceptual rivalry rates. Given that there is evidence for a sudden increase in availability of serotonin in the brain close to acute migraine events (15), and hypothesized lower circulating serotonin levels in between migraines, it is possible that perceptual switching rates will normalize immediately preceding and during the acute migraine event. A similar normalization in the immediate pre-migraine period has been shown for habituation abnormalities in migraine (44).

In a recent study by Wilkinson and colleagues (29), a trend towards slower perceptual transitions during binocular rivalry in a migraine population was explained in terms of a combination of enhanced cortical excitation and precortical differences in the eye's input strengths. Any such contribution of monocular differences in the two eyes' input strengths cannot account for the results of the current study as the visual stimuli used were presented binocularly and a similar reduction in the number of perceptual switches was found using an auditory paradigm. Our findings therefore extend the relevance of slower rivalry switches well beyond the primary visual cortex and suggest the involvement of a more general cortex-wide factor. While numerous extensive efforts have gone into developing neural models of binocular rivalry (generally depending on some level of mutual inhibition between monocular inputs coming from each of the two eyes), far less work has attempted to explain the nature of the inhibitory and excitatory network properties responsible for other forms of perceptual rivalry like those used here. Despite this fact, it is fair to say that reduced rivalry rate is most consistent with a general reduction in neural excitability. Our results are, therefore, consistent with a link between reduced levels of central serotonin and lower cortical pre-activation levels during the interictal phase of migraine (12–14). However, given the complexity and heterogeneous nature of serotonin receptor location and function (for review see 27), more directed experimental investigation will be required to understand the contribution that different pharmacological and physiological factors may play in migraine.

Perceptual testing is rapid, non-invasive and inexpensive. Despite considerable variability in the magnitude of perceptual measures between individuals (Figure 5), changes to perceptual status may yet prove to be clinically meaningful within an individual. An example is if measurements show a characteristic and repeatable alteration at different times relative to acute migraine events. Further study of rivalry at different time points in the migraine cycle, and in relation to other measures of presumed neuromodulator status (for example, electrophysiological measures of habituation (6)) will help unravel the links between the perceptual alterations and brain chemical imbalances in individuals with headache.

In conclusion, fewer auditory and visual perceptual switches were observed in individuals with more frequent migraines within our sample, which was largely comprised of people having migraines without aura. Our data provide further support for interictal differences in brain sensory reactivity in migraine, with the observed effects being in the same direction as those caused by pharmacologically reducing brain availability of serotonin in normal observers (24,25).

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Conflict of interest

The authors declare that there is no conflict of interest.

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