Research Report

Cognitive processing of visual images in migraine populations in between headache attacks

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Abstract

Background and objective: People with migraine headache have altered interictal visual sensory-level processing in between headache attacks. Here we examined the extent to which these migraine abnormalities may extend into higher visual processing such as implicit evaluative analysis of visual images in between migraine events.

Methods: Specifically, we asked two groups of participants—migraineurs (N=29) and non-migraine controls (N=29)—to view a set of unfamiliar commercial logos in the context of a target identification task as the brain electrical responses to these objects were recorded via event-related potentials (ERPs). Following this task, participants individually identified those logos that they most liked or disliked. We applied a between-groups comparison of how ERP responses to logos varied as a function of hedonic evaluation.

Results: Our results suggest migraineurs have abnormal implicit evaluative processing of visual stimuli. Specifically, migraineurs lacked a bias for disliked logos found in control subjects, as measured via a late positive potential (LPP) ERP component.

Conclusions: These results suggest post-sensory consequences of migraine in between headache events, specifically abnormal cognitive evaluative processing with a lack of normal categorical hedonic evaluation.

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1. Background

Migraine is a headache disorder characterized by moderate to severe throbbing pain, with sensitivity or intolerance to light and sound during the headache, and is often accompanied by nausea and vomiting (Headache Classification Subcommittee of the International Headache Society, 2004). For a sufferer, what it is to be a migraineur often goes well beyond the headache itself. A migraineur may feel that he/she is impacted in daily activities, even when not suffering from an attack, during what is called the interictal period. Migraine has been considered to be a form of sensory processing disturbance, with evidence building to support the idea that migraineurs have abnormal responses to normal interictal sensory events (Goadsby, 2007). For example, migraineurs show reduced sensory habituation to repetitive visual stimulation as measured via visual evoked potentials. Specifically, the amplitude of the visual evoked components in response
to checkerboard reversals normally decrease over time, but migraineurs show no such evidence of this sensory habituation (Coppola et al., 2009; Sniatchkin et al., 2003). Less characterized is the post-sensory impact of migraine, with recent evidence suggesting that migraineurs have subtle interictal cognitive abnormalities aligning with attentional deficits (Demarquay et al., 2011; Mickleborough et al., 2011a, 2011b). Collectively, these findings indicate that migraineurs show a hypersensitivity to both sensory and attentional visual processing of visual events. Given the altered interictal visual sensory and cognitive functioning in migraineurs, the objective of this study was to examine the extent to which migraine may extend into higher visual processing such as evaluative analysis of visual images.

Specifically, we wanted to advance our understanding of potential post-sensory anomalies in how migraineurs implicitly process visual images, and in particular, the natural and automatic process of evaluating images at a hedonic level. Our methodological approach was based on a recent ERP study in normal populations examining implicit aesthetic evaluative analysis of common everyday visual images, and in this case, commercial branding logos (Handy et al., 2010). To do this, we measured migraineurs and non-migraine controls responses using event-related potentials (ERPs) as they viewed a serial stream of unfamiliar visual objects (232 distinct, different logos) in the context of a target identification task. In each trial block, each of these 232 logos was presented once. After completing 10 trial blocks, participants were then asked to identify the 15 logos they liked most and which 15 they disliked most. Importantly, they were not explicitly asked to think about or evaluate the logos in any way prior to this point of the study.

Using this paradigm, we wanted to examine whether migraineurs might show altered implicit hedonic analysis of visual images. In particular, making a like or dislike judgment of visual images is such a normal part of human behavior that it can be generated without conscious intent (Dijksterhuis and Aarts, 2003; Chen and Bargh, 1999). Moreover, even emotionally neutral images such as logos are implicitly evaluated at a hedonic level, and specifically manifest a bias for disliked logos, akin to emotional negativity biases (Handy et al., 2010; Dijksterhuis and Aarts, 2003). The ERP components measured for assessing implicit hedonic processing were the frontal/central N2 and the frontal/central LPP. The N2 and LPP components were chosen because they have been found to be sensitive to implicit hedonic analyses in previous studies (Handy et al., 2010).

Specifically, previous research suggests LPP amplitudes reflect the depth of evaluative analyses (Cacioppo et al., 1996; Crites et al., 1995; Cuthbert et al., 2000), such as increased evaluative categorization (Cacioppo et al., 1996; Crites et al., 1995) as well as activation of motivational and affective systems (Cuthbert et al., 2000). The LPP is also noted for being modulated by directing attention to emotional stimuli (Dunning and Hajcak, 2009). Using the N2 and LPP components, we asked whether migraineurs might show an altered pattern of implicit evaluative analysis at the hedonic level, and in particular we hypothesized that migraineurs might show anomalies in their responses to liked logos, disliked logos, or both, as compared to controls.

2. Results

The N2 and LPP components were chosen because they have been found to be sensitive to implicit hedonic analyses in previous studies (Handy et al., 2010). Because of the waveform variability between migraineurs and controls, the components were captured in a series of 50 ms windows from 225–575 ms designed to capture the peak of the two components in each group, comprising electrodes F3, FZ, F4, C3, CZ, and C4. Statistical interrogation included a repeated measures ANOVA with group (control vs. migraine) as a between-subjects factor and preference (like vs. dislike vs. all non-target logos), electrode location, and time window (50 ms windows from 225–575 ms) as within-subjects factors. Separate ANOVAs within each group were planned to follow-up any significant interactions including group and preference. Grand-averaged ERP waveforms for Liked, Disliked, and All logos are shown in Fig. 1 as a function of headache classification and scalp location and in Table 1 as a function of group, preference and time window.

2.1. Frontal/central N2 & LPP

As can be seen in Fig. 1, it appeared that the post-sensory preference effects differed between groups across time windows, and this was confirmed statistically. We found a main effect of preference (F(2,56) = 14.92; p < 0.001), qualified by a group by window by preference interaction (F(2,56) = 1.94; p < 0.05). Planned ANOVAs within each group revealed that controls had a main effect of preference (F(1,28) = 8.55; p < 0.001), and an interaction of preference and time window (F(1,28) = 2.74; p < 0.01). Specifically, within the control group the mean amplitude of the disliked logos was less positive than the mean amplitude of all logos in all but the first time window (from 275–575 ms; all F(1,28) > 12.50; p < 0.01) and disliked logos was less positive in magnitude than the mean amplitude of liked logos in the two last windows (from 475–575 ms; all F(1,28) > 4.43; p < 0.05), while the mean amplitude of liked logos was less positive in magnitude than the mean amplitude of all logos only in two time windows (from 325–425 ms; all F(1,28) > 4.59; p < 0.05). These results reflect hedonic preference differences specifically in the LPP (275–575) components, but not in the N2 component (225–275).

In contrast, migraineurs showed no such effect of preference (F(1,28) = 3.03; p = 0.06) or for preference by time window (F(1,28) = 1.81; p = 0.05). To be sure these null effects were not a result of greater variability in the migraineur ERPs, we compared the average variance of the two groups and found that they do not differ significantly (t(56) = 1.244, p = 0.218).

2.2. Control analyses

2.2.1. Lateral occipital P1 peak

Because migraineurs are known to show altered sensory responses, including the P1 ERP component (Mickleborough et al., 2011b), we added a control analysis of the lateral occipital P1, which is known to index the sensory-evoked excitability of extrastriate visual cortex (Heinze et al., 1994). The P1 encompassed scalp electrodes OL & OR, using
a 95–105 ms post-stimulus time window centered on the latency of the peak in the grand-averaged waveforms. As can be seen in Fig. 1, it appeared that the amplitude of the P1 had a preference effect for controls but not migraines, and this was confirmed statistically. We found no main effect of preference ($F(1,56)=1.98; p=0.1430$), but a group by preference interaction ($F(1,56)=3.11; p<0.05$). Planned ANOVAs within each group revealed that controls had a main effect of attention in the P1 ($F(1,28)=5.86; p<0.01$), such that the mean amplitude of the disliked logos was more positive in magnitude than the mean amplitude of liked logos ($t(28)=2.84, p<0.01$) and of all logos ($t(28)=2.69, p<0.05$).

![Grand-averaged ERP waveforms as a function of group, preference, and scalp location. The N2 and LPP components were measured at 225–575 ms (in 50 ms windows) across electrodes F3, FZ, F4, C3, CZ, and C4. The P1 component (control analysis) was measured at 95–105 ms across electrodes O1 and O2. (a) Control Group (N=29), (b) Migraineur Group (N=29).]
while there was no significant difference between liked logos and all logos ($t(28)=0.71$, $p=0.48$). Migraineurs showed no such effect of preference in the P1 ($F(1,28)=0.06; p=0.94$).

2.2.2. Redistribution of logo selections
In addition, as a possible control issue, we wanted to determine whether the pattern of results we report with migraineurs lacking preference effects could be due to a differing selection criterion as opposed to an actual abnormal early sensory and later cognitive response to the stimuli. Specifically, perhaps being a migraineur causes one to pick particular images that are different than non-migraineurs select, such that the logo properties (symmetry, complexity, contrast, etc.) do not produce the same sensory response as those that controls select Table 2.

The logos selected by each group are presented in Table 3, which demonstrates a relatively even distribution of logo choices across groups. Nonetheless, in order to directly address this question, we paired each migraineur with a control and exchanged their 15 liked and 15 disliked choices.
and reanalyzed this new data. In this way, if the logos chosen by migraineurs somehow differed from those chosen by controls and the results were a consequence of the selection criterion, then we would expect to see a reversal of the original results, such that the migraineurs would have a preference effect in the sensory level P1 and cognitive-level N2 and LPP, but controls would not.

Statistical interrogation for the ERP components replicated the main hedonic analyses with the exception of using “swapped” logos (using like and dislike logos of a paired participant from other group). We found no significant preference effects or interactions for P1, N2, or LPP time windows (all F(2,56) < 0.72; all ps > 0.49). These null results are consistent with both groups responding to “random” logos as opposed to their personal liked and disliked logos, and discards the possibility that a group difference in logo selection bias could be producing the group by preference interactions.

### 3. Discussion

Our study was designed to examine post-sensory consequences of visual processing, specifically the extent to which migraineurs show altered implicit evaluative analysis of visual images. In this regard, we found that controls showed a bias for disliked logos, as measured via amplitude the LPP component, a negativity bias that was absent in migraineurs. In the following sections, we discuss functional implications of this finding and the possible relationship of this finding to known sensory abnormalities in migraineurs.

#### 3.1. Absent negativity bias

The primary result of our study was that migraineurs showed a lack of a negativity bias for their implicit hedonic analyses, relative to what was observed in controls. Specifically, we found a significant difference between migraineurs relative to non-migraine controls for hedonic preference effects, such that controls had decreased LPP amplitude for disliked logos (as compared to either liked or all logos), while migraineurs lacked this bias of disliked images. This corresponds with previous research that reveals that, in normal visual processing, images we dislike appear to stand out to us at a neurocognitive level (Handy et al., 2010). In addition, our control analysis revealed that migraineurs lacked the increased P1 component for disliked logos (as compared to liked or all logos) found in controls. An increased P1 has been linked to increased attention (Handy and Mangun, 2000; Handy et al., 2003), suggesting that controls, but not migraineurs, show early increased attention to disliked logos. This is consistent with a negativity bias, in which more weight is given to negative than positive evaluations (Cacioppo and Bernston, 1994; Dijksterhuis and Aarts, 2003; Ito et al., 1998). In contrast, migraineurs lack this negativity bias in early in visual cortex, as well as in later post-sensory processing in frontal/central cortex.

What might the impact of this be for migraineurs? An adaptive advantage of the negativity bias is that images can be assessed and attention can be quickly redirected to potentially threatening events (Cacioppo and Bernston, 1994; Ito et al., 1998). Controls show this bias as early as P1 processing, in this case suggesting that they initially put more emphasis on the disliked logos. Considering the
|   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   | CN | MG |   |
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negativity bias as an adaptation, migraineurs seem, to some degree, to be lacking this early motivational advantage of categorizing preference. This fits with previous data that shows that migraineurs have an abnormality for how attentional resources are allocated to environmental stimuli (Demarquay et al., 2011; Mickleborough et al., 2011a, 2011b, 2013). The current study extends this theory to suggest that migraineurs lack the normal negativity bias, perhaps suggesting migraineurs are not adequately categorizing the environment for quick allocation of attention.

3.2. Sensory contributions to altered evaluative analyses?

Given our findings about visual post-sensory anomalies, to what extent, if at all, might they be driven by or independent of known sensory abnormalities? Two key concepts suggest that our findings of migraineurs lacking normal negativity bias are not just a forward-cascade of the basic sensory abnormalities, but more likely another consequence of a more global cortical hyperexcitability in migraine. First, intercellular inhibitory processes are indicated in both the lack of habituation in migraineurs (Aurora et al., 2005; Brighina et al., 2009), and in the modulatory effects of spatial attention (Houghton and Tipper, 1996), so altered inhibition in migraine may be at the core of both effects. In addition, if it were a consequence of sensory abnormalities one would expect to see more evidence of these anomalies appearing throughout our waveforms, whereas they are distinct to specific components. While our data suggests a common pathophysiological link between our post-sensory effects and the sensory abnormalities in migraineurs, we can only surmise as it is beyond the scope of our paradigm. Either way, our study clearly suggests post-sensory consequences of migraine in between headache events, specifically abnormal cognitive evaluative processing with a lack of normal categorical hedonic evaluation.

4. Experimental procedures

4.1. Participants

Fifty-eight paid volunteers participated; 29 were in the non-migraine control group (19 women and 10 men; age 25.9, SD 11.4) and 29 were in the migraine group (18 women and 11 men; age 26.1, SD 8.6). The study size was chosen based on previous isolation of the ERP components of interest (Handy et al., 2010). The migraineurs had 25.1 (SD 33.0) headaches a year, with each headache lasting 16.4 h (SD 33.0). In order to focus on the interictal period, all migraineurs had not had a migraine within 48 h prior and 48 h after the testing period. The study was advertised via posters in the University of British Columbia community and participants were paid an honorarium for their time. All participants gave their informed consent and all testing procedures were approved by the University of British Columbia Clinical Review Ethics Board. Data were collected at the University of British Columbia in Vancouver, Canada.
4.2. **Headache classification**

All migraine participants were required to meet the migraine criteria (with aura or without aura) specified by the International Headache Society (Headache Classification Subcommittee) and determined by an interview. In addition to our headache classification criterion, migraineurs were excluded if they were taking any form of migraine prophylactics.

4.3. **Stimuli**

This stimuli set was adapted from previous studies (Handy et al. 2010; Mickleborough et al. 2013). A total of 232 non-target logos were used as the primary stimulus set, plus an additional target logo; all logos can be viewed at [http://attention.psych.ubc.ca/Site/Downloads.html](http://attention.psych.ubc.ca/Site/Downloads.html). The logos were drawn from sources publicly available on the Internet and criteria for inclusion in this set included that the logo contained no verbal/lexical information (i.e., no words or letters) and that it was not a widely known or familiar image (e.g., such as the Nike “swoosh”).

4.4. **Procedures**

Each trial block began with the presentation of the target logo for 2s as a reminder of which logo required a manual response to be made; the same logo was used as the target across all trial blocks and participants. Within each trial block, this target was presented 20 times and each of the 232 non-target logos was presented once, with the order of presentation randomly varied between 10 trial blocks. The duration of each stimulus was 200 ms, and the inter-stimulus interval was randomly varied between 1300–1500 ms. Stimuli were presented on a VGA monitor controlled by a Pentium PC using the VAPP stimulus presentation system ([http://nilab.psychiatry.ubc.ca/vapp/](http://nilab.psychiatry.ubc.ca/vapp/)), and manual responses to the target were made by pressing a button on a hand-held joystick, with the thumb of response (left vs. right) counterbalanced between participants.

Initial instructions to the participants asked them to simply observe the logos on the screen and make a manual response as fast as possible whenever the target logo was presented. No instructions were given to think about or explicitly evaluate the non-target logos. After completing the task and removal of the EEG/EOG recording equipment, each participant was asked to identify 30 non-target logos based on hedonic preference (15 most liked, 15 most disliked), from one of four sheets of paper randomly displaying all 232 non-target logos.

4.5. **Electrophysiological recording**

Scalp potentials were recorded from 64 Ag/AgCl active electrodes via a Biosemi Active-Two ERP amplifier system. To ensure proper eye fixation and allow for the removal of events associated with eye movement artifacts, vertical and horizontal electro-oculograms (EOGs) were also recorded – the vertical EOG from an electrode inferior to the right eye, and the horizontal EOG from an electrode on the right outer canthus. Two additional electrodes were used to record from the left and right mastoids. EEG data was recorded relative to Active-Two’s CMS/DRL feedback loop (Common Mode Sense [CMS] and Driven Right Leg [DRL]), using a bandpass filter of 0.1–30 Hz, with a gain of 0.5 and with a digitized on-line sampling rate of 256 samples-per-second. Offline, all scalp electrodes were referenced to the average of the left and right mastoid signals. Automated artifact rejection was then used to eliminate trials with detectable eye movements, blinks, muscle potentials or amplifier blocking. For each participant, EEG time-locked to the remaining events of interest was epoched into 800 ms segments, beginning 200 ms before stimulus onset until 600 ms post-stimulus. These single-subject waveforms were then used to generate the group-averaged waveforms for display and analysis. A –200 to 0 ms pre-stimulus baseline was used for all ERP waveform measurements and displays.

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**References**


