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Exploration of anomalous perceptual experiences in migraine between attacks using the Cardiff Anomalous Perceptions Scale

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Abbreviations: CAPS: Cardiff anomalous perceptions scale; VDS: Visual discomfort scale; PCA: principal components analysis; MA: migraine with aura; MO: migraine without aura; M: migraine; C: control; VT: visual trigger; SD: standard deviation; SE: standard error; N: number.

Abstract
Distortions in sensory experiences that precede a migraine attack have been extensively documented, the most well-known being the visual aura. Distortions in the experience of other senses are also reported as part of an aura, albeit less frequently, together with changes in the perception or ownership of the body or body parts. There are many examples of differences in aspects of *visual* perception between migraine and control groups, between attacks, but not as much on unusual experiences involving other senses, the sense of the body or the experience of the environment. Seventy-seven migraine (33 with aura) and 74 control participants participated. Anomalous perceptions were experienced by both migraine and control groups, but more with migraine experienced them and rated them as more distressing, intrusive and frequent. Associations with reports of visual triggers of migraine and visual discomfort are presented. This study is the first to show relationships between these factors.

These data have not been published elsewhere previously.

Keywords: migraine; anomalous perceptual experience; visual aura; non-visual aura; visual discomfort; visual triggers; CAPS

1. Introduction

Migraine is a severe, recurrent headache that can be accompanied by sensory disturbances before and during the headache phase. The World Health Organisation (2004) estimated that it affects one in nine (11% overall, 15-18% females, 6-8% males, based on American and European epidemiological studies). This is likely to underestimate the actual prevalence, however, as many do not seek medical advice, particularly when there is a family history of migraine.

Often the sensory disturbances before the headache (the aura) are visual, such as the classic fortification spectra, which describes a crescent shaped set of zig-zag lines that starts centrally and grows slowly through one quadrant or hemifield, leaving a scotoma in its wake. Other visual aura symptoms include twinkling dots or phosphenes, again often in one quadrant or hemifield; seeing the scene as if through running water, tunnel vision; double vision or a loss of vision. The fortification spectra has long been attributed to a wave of spreading depression that traverses the primary visual cortex (Milner, 1958; Hardebo, 1991; Major et al., 2019). The positive visual symptoms (the fortifications) are attributed to a transient rapid rise in neuronal excitation involving depolarisation and the scotoma to a subsequent hyperpolarisation and electrical silence. The underlying neural locus or loci for aura involving other positive visual symptoms is less clear, probably including primary and higher visual cortical areas, those involving double vision are likely to involve activity in the brainstem. Aura symptoms usually last for approximately half an hour. During the headache stage, most people report photophobia and some report continuing aura symptoms [International Headache Society (IHS), 2018].

Visual stimuli such as stripes, flicker and glare, are also reported to trigger an attack (Debney, 1984; Wilkins et al., 1984; Shepherd, 2000, 2010; Harle et al., 2006). These features of migraine have prompted studies of visual perception both during (Boles, 1993; Schott, 2007) and between migraine attacks (reviewed in Chronicle & Mulleners, 1996; Shepherd, 2007; 2010; 2019). Various techniques have been used including psychophysics (McKendrick et al., 2001; Antal et al., 2005; Shepherd, 2006, 2007; Tibber et al., 2006; Tibber & Shepherd, 2006; Shepherd et al., 2011, 2012, 2013; Karanovic et al., 2011; Singh & Shepherd, 2016; Shepherd & Joly-Mascheroni, 2017), electrophysiology (Oelkers et al., 1999; Ambrosini et al., 2003; de Tommaso et al., 2014; Magis et al., 2016; Major et al., 2019; Marucco et al., 2019; Fong et al., 2020), transcranial magnetic stimulation (Schoenen et al., 2003; Brigo et al., 2012; Cosentino et al., 2014;) and functional imaging (Hadjikhani et al., 2001; Huang et al., 2006; Datta et al., 2013; Wei et al., 2019). Several aspects of visual perception have been shown to differ between people with and without migraine, between attacks, such as the perception of motion, contrast, colour, orientation and visual discomfort. Some of the above cited articles have also reported interactions and correlations between these aspects of visual perception, and between these aspects and reports of visual migraine triggers.

The term visual discomfort refers to the illusions, distortions and aversion that some people experience when viewing high contrast, repetitive, geometric patterns, such as stripes, dotty images or checkerboards, or when viewing flickering light. People can report seeing shadowy shapes or lattices; washes or flashes of colour; a sense of motion in the background; the patterns may appear to rotate; or they may have impressions of elements in the patterns standing out in depth, either stationary or undulating, as if the patterns were breathing (Shepherd, 2000, 2007). Visual discomfort has also been called pattern sensitivity, pattern glare or visual stress, hereafter just the term visual discomfort will be used. Both the number of illusions seen and aversion are greater in migraine compared to control groups (Wilkins et al., 1984; Chronicle & Mulleners, 1986; Shepherd, 2000, 2007; 2010).

Apart from experiencing visual discomfort from the environment or encountering visual triggers, the consequences of the cited differences in the other aspects of visual perception, do not, in general, affect a person's day to day life. They are often measured by determining detection or discrimination thresholds: the feintest grating that can be perceived, or the smallest contrast difference between two gratings that can be reliably discriminated, for example. This line of research has, nevertheless, been used to refine models of neurological function in migraine, in particular, the debate between cortical hyper- vs hypo-excitability and to understand the variety of visual pathways that may be affected, both sub-cortical and cortical.

A model of cortical hyperexcitability in migraine has been discussed for over 30 years and is usually attributed to a lack of inhibition (Wilkins *et al.,* 1984; Chronicle and Mulleners, 1996; Antal *et al.,* 2005). A lack of cortical excitation has also been discussed, however (Shepherd, 2001, 2006) as have hybrid models combining elements of both hypo- and hyper-excitability e.g. low cortical pre-activation combined with heightened responsiveness [Schoenen, 1996a,b; 1996b; 1998; Shepherd, 2001, 2006; Ambrosini *et al.,* 2003; Schoenen *et al.* 2003; Coppola *et al.,* 2005; 2007]. Further elaboration of the arguments for either model can be found in Antal *et al.* (2005), Shepherd (2007), Coppola *et al.* (2007), Cosentino *et al.* (2014) and Magis *et al.* (2016).

Various authors have drawn attention to the importance of developing models that consider differences in migraine at all levels of the visual system, even as early as the retina (McKendrick *et al.,* 2001; McKendrick and Badcock, 2004; Karanovic *et al.,* 2011; Tibber and Shepherd, 2006; Shepherd *et al.,* 2012; Magis *et al.,* 2016; Singh and Shepherd, 2016; Shepherd and Joly-Mascheroni, 2017). An overview of the studies that have tailored their tasks to particular stages within the visual system has led to the suggestion that one general model of neurological function in migraine may be inappropriate as different stages within the visual pathways may be affected in distinct ways (for an early review, see Shepherd, 2007; for later discussions see Shepherd *et al.,* 2012; Singh and Shepherd, 2016; Shepherd and Joly-Mascheroni, 2017; Shepherd, 2019).

An alternative way to examine group differences is by the use of questionnaires. The study by Wilkins *et al.* (1984) entitled "A neurological basis for visual discomfort", for example, was largely based on a diverse series of questionnaires. Over a series of 15 experiments, they asked for ratings of pleasantness of different gratings, preference for the same gratings, the number of illusions seen in these gratings from a given checklist (blurring, shimmering, flickering, bending of the lines, shadowy shapes, red, yellow, green, blue, fading of the pattern), headache susceptibility, headache frequency, characteristics associated with headache (including weakness, numbness, loss of appetite, nausea, photophobia, unilateral pain, change in vision, blood pressure, unsteadiness, throbbing pain, pain location, light-headedness, tinnitus, time of day of headache onset). In each experiment involving participants with self-reported migraine, the migraine group had greater discomfort than participants in other groups. They suggested the group differences may result from a failure of cortical inhibition in migraine.

This early study has influenced many of the headache questionnaires that have been developed since. For example, it influenced the development of the visual discomfort scale (Conlon *et al.* 1999); several of the questionnaires used in the studies by Shepherd and colleagues (e.g. Shepherd, 2000; Harle *et al.,* 2006; Shepherd *et al.,* 2013); the pattern glare test (Wilkins and Evans, 2001; Evans and Stevenson, 2008); the Cortical Hyperexcitability Index versions I and II (Braithwaite *et al.,* 2015; Fong *et al.,* 2019) and the search for a single-item migraine screening test (Yuan *et al.*, 2016). All of these questionnaires focus principally on vision.

The migraine aura is not, however, exclusively visual. The IHS classification criteria (2018) includes symptoms such as pins and needles or numbness (typically unilateral, on the face or limbs); speech disruption (dysarthria or aphasia); buzzing in the ears or tinnitus; dizziness or vertigo; a lack of co-ordination or clumsiness (ataxia) and one sided paralysis (hemiplegia). Such a range of symptoms indicates that diverse and extensive sub-cortical and cortical areas may be affected before and/or during a migraine attack. There are additional research and clinical reports of more elaborate experiences, such as a disowning of body parts, unilaterally, reminiscent of unilateral neglect or asomatognosia; detachment from the environment or from people; and/or sensing another person nearby (Blau, 1992; Kew *et al.,* 1998; Podoll *et al.,* 1999; Schott, 2007) although these are not in the IHS (2018) criteria. These observations led to the question addressed in the present study: do people with migraine experience an extended range of unusual sensory experiences *between attacks*, other than altered visual experiences?

The Cardiff Anomalous Perceptions Scale (CAPS) was constructed to test the propensity to psychotic symptoms and hallucinations in the general population (Bell *et al.,* 2006). Bell *et al.* (2011) describe the CAPS as a tool to assess a comprehensive range of perceptual anomalies that includes the classic five senses (vision, hearing, touch, taste, smell) together with proprioception, time perception, somatosensory and/or body image distortion, sensory flooding and changes in perceptual intensity. It is based on observations from psychiatry and neurology and the questions are structured to delve into different forms of insight each person

may have about their experiences. Bell *et al.* (2006, 2011) constructed the questions to tease apart whether each experience is a subjectively anomalous or an 'unusual' experience, a non-shared sensory experience, or an experience that has no obvious environmental source. It includes items such as 'do you ever see shapes, lights, or colours even though there is nothing really there'; 'do you ever sense the presence of another being, despite being unable to see any evidence?' and 'do you ever notice sounds are much louder than they normally would be?' [see Section 3 (Results) for a complete list]. The CAPS has been used with both non-clinical (Bell *et al.,* 2006, 2011; Braithwaite *et al.,* 2013, 2014; Humpston *et al.,* 2016) and clinical groups including anxiety, depression and psychosis (Bell *et al.,* 2011), schizophrenia (Caputo *et al.,* 2012) and autism (Horder *et al.,* 2014; Milne *et al.,* 2017).

The main aim of the present study was to assess whether more CAPS items would be endorsed in a migraine group compared to a control group. A second aim was to assess whether the CAPS items endorsed by those with migraine with aura related to the type of aura experienced. Several other questionnaires were also completed: (i) a migraine/headache symptom inventory to check correct diagnosis (IHS, 2018); (ii) a migraine/headache trigger list, for consistency with previous studies (Shepherd, 2000, 2010; Harle *et al.,* 2006), and (iii) the visual discomfort scale (VDS, Conlon *et al.,* 1999). The questionnaires were completed on-line.

The data presented here form part of a larger on-going study that aims to develop non-invasive visual tasks that can be used to enable people to track their overall health and well-being. For participants prone to headache or who experience migraine, the aim is for them to be able to predict, and consequently take action to avoid, their headache/migraine attacks. It requires participants to complete the visual tasks multiple times. There are a number of reports that perceptual and electrophysiological measures can track both migraine periodicity and treatment outcome (Khalil, 1991; Kropp and Gerber,, 1998; Evers *et al.,* 1999; Siniatchkin *et al.,* 1999; Judit *et al.,* 2000; Sand *et al.,* 2008; 2009; Siniatchkin *et al.,* 2009; Magis *et al.,* 2016; Martins *et al.,* 2019; Syversten *et al,.* 2019). As much of this research uses high contrast stripes and/or electrophysiological measures that require specialist equipment, it has few practical applications.

Other studies have used visual tasks involving stripes to demonstrate changes in visual discomfort or photophobia before and after the onset of other conditions, such as following exposure to stress, sleep deprivation or viruses (Wilkins *et al.,* 1984; Smith *et al.,* 1992), or to assess the efficacy of drug treatments such as beta-blockers (Khalil, 1991). These cannot be extended for repetitive testing in people's own homes for ethical reasons.

The data from the visual tasks are not presented here as data collection is still on-going. To date, not all participants have completed sufficient sessions using the visual tasks and some have terminated early, nevertheless, they have all completed the questionnaires and those data are presented here. The extensive set of questions included in the questionnaires were designed to gain a thorough profile of each participant as there were no face-to-face interviews. Shepherd and Patterson (2020) includes preliminary data on the visual tasks.

Shepherd (2000, 2010) and Harle *et al.* (2006) assessed various migraine and headache triggers using a questionnaire that included food, beverages, stress (onset or offset), hormonal factors (in women), dehydration, smells, visual stimuli and an open ended question where participants could list other visual and/or non-visual migraine or headache triggers [see Sections 2 (Materials and Methods) and 3 (Results) for a complete list]. In a sample of 180 people (132 with migraine), 60% of the migraine group cited at least one visual stimulus as a migraine trigger, compared to 15% of the remainder, the control group, who reported visual stimuli as a headache trigger (Shepherd, 2010). A principle components analysis (PCA) on these potential triggers for the migraine group showed that visual triggers was the first component extracted, accounting for the highest amount of variance in the data. This questionnaire was included in the present study.

Visual discomfort can be triggered by text, which usually presents as a high contrast black on white striped pattern. The VDS (Conlon *et al.,* 1999) was developed to measure a range of distortions and psychosomatic

symptoms experienced while reading. Example questions include 'how often do you get a headache when working under fluorescent light?'; 'when reading, do the words on a page of clear text ever appear to fade into the background then reappear?'; 'do you ever have difficulty reading the words on a page because they begin to flicker or shimmer?'. Higher VDS scores have been reported in migraine, compared to control groups (Shepherd *et al.,* 2012, 2013; Datta *et al.,* 2013; Cucchiara *et al.,* 2015; Imaizumi *et al.,* 2018). The higher VDS scores in migraine reported by Shepherd *et al.* (2012,2013) did not reflect heightened reading difficulties *per se*, as there were no significant differences between people with and without migraine on scores from the Adult Dyslexia Checklist (Vinegrad, 1994). The VDS was included in the present on-line study, rather than presenting a series of high contrast striped patterns, as (i) the VDS is simple to complete and (ii) it would be unethical to display aversive striped patterns in an unsupervised on-line test session since they can trigger migraine and epilepsy (Wilkins *et al.,* 1984; Harding & Takahashi, 2004).

It was hypothesised that the migraine group would have higher CAPS scores. It was also hypothesised that those with aura may endorse CAPS items related to the type of aura they experience, on the assumption that those with aura experience hallucinatory symptoms as part of the attack and that a residual may continue between attacks. Based on previous research, it was also predicted that the migraine group would report more visual triggers of headache than the control group, and would have higher visual discomfort scores.

2. Materials and Methods
2.1. Participants
One hundred and fifty-eight participants were recruited from an existing migraine panel, advertisements in GP surgeries and hospital neurology clinics, using social media and from an on-line crowd-sourcing platform (Mechanical Turk). The exclusion criteria were (i) failing to answer the questions; (ii) providing information that was not consistent with a participant classifiable as with or without migraine according to the IHS criteria (2018); (iii) reporting poor eyesight in either eye; (iv) being under 18 years of age; (v) having a neurological or other condition that could affect visual acuity or day to day vision including photophobia. Examples were given for the latter: epilepsy, multiple sclerosis, diabetes, lupus and macular degeneration. Seven were excluded using criteria (i) to (v), which left 151 participants.

INSERT TABLE 1 HERE

The participants were asked whether or not they had migraine and, if so, whether it had been medically diagnosed by a GP or neurologist. Migraine classification, however, followed the IHS criteria (2018) as some people claim to have migraine when it is clear they do not. The headache needed to have the following characteristics: a duration between four and seventy-two hours unmedicated and at least two from the following four (i) pain so intense it interferes with or prohibits daily activity; (ii) pain that worsens with routine daily activities such as bending or climbing stairs; (iii) pain that has a throbbing or stabbing nature; (iv) pain that is located on one side of the head. Two pictures of a skull were included, one facing and one sideways, with six numbered regions that corresponded to occipital, parietal, temple, frontal and orbital areas and the crown/vertex. The skull was used so there would be no distraction from facial features and because it very clearly showed the differences between the locations of each region. Participants were then asked if the pain was on one side or both and, if one sided, whether it was always the same side. When asked about the nature of the pain they were asked if it was tightening, pressing, throbbing, stabbing, burning or something else: if something else there was a box where they could describe the pain in in their own words. The headache also needed to be associated with photophobia and phonophobia and/or with nausea. Finally, there needed to be no other identifiable causes (medication, alcohol or substance abuse) and other questions were included to rule out sinus, tension or cluster headache. This section of the questionnaire was developed in consultation with two neurologists, two psychologists and two optometrists all of whom had a specialist interest in migraine.

There were also questions that asked about triggers of migraine (for those with migraine) or headache (for those without). The trigger list included hormonal factors (for women), stress, noise, tiredness, smells, chocolate, cheese, other food, red wine, other alcohol, caffeine, flickering lights, regular visual patterns such as stripes, escalator treads or venetian blinds, alternate light and shade, a prompt for participants to specify

any other visual triggers and a prompt for them to list any other triggers not already mentioned. They were asked to specify whether each item commonly, occasionally or never triggered their migraine (for the migraine group) or headache (for the control group). This list has been used in previous research (Harle *et al.,* 2006; Shepherd, 2000; 2010). This section of the questionnaire was also developed in consultation with two neurologists and two psychologists with a specialist interest in migraine.

Thirty-three had migraine with aura (MA), all but one of whom had a visual aura. If a participant indicated they had visual symptoms associated with their migraine, a series of pop-up questions asked about their nature to ensure that it was an aura and not simply noticing floaters or experiencing photophobia. They were asked whether whatever they experienced appeared before or during the headache, if there was a time lapse between it ending and the headache starting, how many minutes it lasted for, whether it was visible with both eyes or only one, whether it was stationary or whether it moved (and, if it moved, in what sort of way and how far), if it grew over time (and, if so, in what way), if it was coloured, if it appeared in all areas of space, just on one side, or in a restricted area (and, if one-sided or in a restricted area, where it was), whether it formed lines, blobs or flashes, whether the component parts were joined up or spatially separate and, if joined up, what the overall shape was of all the joined up parts. They were asked if they could see objects through it/if it was transparent or whether it was superimposed on top of objects. Answers included seeing wavy lines, zig-zags, squiggles, radiating lines, a sparkly big wheel, black and silver lines, flashes of dots, a scintillating scotoma, moving bright blue and black swirls like a lava lamp. The majority of the descriptions included motion and the disturbances started small and centrally and then grew out to the periphery. The disturbances were mostly described as superimposed on objects, obscuring them.

Non-visual aura symptoms were also reported by those with visual aura: 12 experienced pins and needles or numbness, most commonly on one side of the face, or on the nose, lips and mouth. Less frequently they were reported on a hand or the fingertips, down one arm, leg or foot. Seven reported speech as being effortful (dysarthria), four reported difficulty in thinking and producing sensible speech (aphasia). Nine reported dizziness or vertigo, three had buzzing in the ears (tinnitus), two reported double vision (diplopia) and six said they became uncoordinated or clumsy before the headache (ataxia). The one participant in the MA group who did not have a visual aura reported pins and needles on one side of the face, buzzing in the ears, dizziness and lack of co-ordination or clumsiness. Forty-four had migraine without aura (MO) and the remaining 74 comprised the control (C) group (Table 1).

To assess good eyesight, the participants were asked whether they could read the text on the back of a compact disc case held at arm's length, with each eye separately. Wearing spectacles or contact lenses was allowed. These questions were included for two reasons. First, the participants were being asked about visual symptoms associated with migraine or headache, so people who had a deterioration or loss of vision not associated with migraine or headache needed to be excluded. Second, after the questionnaires, there were several visual tests, the results of which are not included here. Apart from the questions about the symptoms and characteristics of their migraines or headaches, the rest of the questions were answered about their experiences when migraine- or headache-free. Participants were also asked whether they took daily medication, but this was also not an exclusion criterion [nine did: three MA–Propranolol, Topiramate, Nortriptyline; six MO–Amitriptyline, Topiramate]. None of the control group reported taking any daily medication.

Frequency estimates were obtained by asking the participants to think back over the last three months and to estimate how many migraines (or headaches, for the control group) they had experienced. Then they were asked to think about whether their migraines or headaches had been more or less frequent than usual over the last few months and use this to estimate how many they had in the last year (after Wilkins *et al.,* 1984). The frequency estimates (Table 1) should be taken as a rough guide only as consecutive days with migraine may have been counted as separate attacks. For example, 28 reported that their attacks could last for more than a day, particularly when unmedicated. These estimates may also contain counts of headaches that were not migraine, although those with migraine were asked to count migraine only. For these reasons, modal frequencies are also included in Table 1 as a more representative summary of the majority within each group. All participants were invited to log on multiple times and were asked if they had migraine since the last time.

From those with aura who did and who had reported the highest frequencies, they tended to experience them in mixed bouts, having some attacks with aura and some without over several days, with days clear in-between each bout. This may have complicated their assessment of their migraine frequency and perhaps led to over-estimation of the number experienced in 12 months.

All participants had the chance to win a small monetary prize for their participation. Those recruited from the on-line crowd-sourcing platform (Mechanical Turk) received a small payment upon completion. Informed consent was obtained in accordance with the declaration of Helsinki (1991) and ethical approval was obtained from Birkbeck College's Department of Psychological Sciences ethics committee. Participants had to read background information to the study on the first on-line page and to manually tick multiple items on a consent checklist in order to proceed.

2.2 Procedure

The participants completed the questionnaires on their own computers. They were presented in the following order:

– The migraine and headache questionnaire (Chronicle, 1993; Shepherd, 2000; Harle *et al.,* 2006), to confirm that they could be classified as having migraine or not based on the IHS (2018) criteria.
– The list of common migraine and headache triggers (Shepherd, 2006). The participants specified whether each item commonly, occasionally or never caused headache; these were coded as 2, 1 or 0, respectively.
– The VDS (Conlon *et al.,* 1999), which contains 23 questions. Each question has a four-point rating scale ranked 0-3 to indicate the severity of the symptoms (0 being the least severe, 3 being the most).
– The CAPS (Bell *et al.,* 2006), which consists of 32 items. Each item is first presented as a simple yes/no question. If the participant answers 'yes' to a question, three subscales are presented: intrusiveness, distress, and frequency. These three subscales are rated using a 5-point Likert Scale (1 being the least intrusive, distressing or frequent, 5 being the most).

For both the VDS and the CAPS, participants were instructed to answer the questions about their experiences in-between migraine and headache attacks. They were asked to respond as honestly as possible. It was explained that the only experiences we were not interested in were those that may have occurred under the influence of drugs.

2.3 Statistical Analyses

Statistical analyses were conducted using SPSS version 26 (SPSS Inc., Chicago, IL, USA). The migraine and headache trigger data were analysed with exploratory principal components analyses (PCA) to determine general clustering between the variables (Kim *et al.,* 1978; Dunteman, 1989). Tests of multicollinearity (determinants greater than 0.00001), overall Kaiser-Meyer-Olkin measures of sampling adequacy (greater than 0.5) and significant Bartlett's tests of sphericity ($p<0.001$) indicated that the data were suitable for each PCA (Field, 2005). Following previous studies (Harle *et al.,* 2006; Shepherd, 2000; 2010), varimax rotation was used before interpreting the components and a cut-off correlation was selected (0.5) that resulted in all variables loading on only one component. Varimax rotates the components to find an optimum configuration of uncorrelated components.

Most of the CAPS total, distress, intrusiveness and frequency scores, the total VDS scores and the average visual trigger (VT) scores (averaged across the four visual trigger questions: flicker, repetitive visual patterns, alternate light and shade and the number of self-declared other visual triggers) differed significantly from a normal distribution for each group (Kolmogorov-Smirnov tests, $p<0.05$). Group differences were therefore assessed with Kruskal-Wallis one-way ANOVAs, followed by pairwise *a priori* Mann-Whitney U tests when significant group differences occurred in the ANOVA analyses.

Responses to the CAPS questions and the endorsement of different aura symptoms each yielded dichotomous data. VT scores were dichotomised by re-coding them as "any visual trigger" or not. VDS scores were dichotomised by dividing the data at the median score. Correlations between these measures were then assessed with the phi coefficient for dichotomous variables, r_ϕ.

3. Results

3.1. Triggers of migraine and headache

As the data collected came from on-line questionnaires, the first analysis was performed on the migraine and headache trigger items to confirm that the on-line responses were similar to those reported previously (Harle *et al.,* 2006; Shepherd, 2000; 2010). In these earlier studies, the migraine trigger variables were summarized by four components following a PCA: (i) visual stimuli, (ii) food, (iii) alcohol and (iv) stress and the general environment.

Seventy nine percent of the MA group cited at least one visual migraine trigger [flickering light, geometric or striped patterns, alternate light and shade, other visual stimuli such as computer screens, cinema (particularly 3-D), video games, bright flashes in the dark, scrolling on screens or mobile telephones, reading, transitions from dark to light]. Similar visual migraine triggers were reported by 73% of the MO group. Sixty per cent of the control group also endorsed similar items as headache triggers.

Two exploratory PCAs were conducted, one for the data from each group (migraine or control). As expected, four components were extracted with eigenvalues greater than 1, which, for both groups, accounted for 62% of the variance in the original variables. The correlations between each variable and the component to which it contributes are shown in Table 2. The trigger items are listed in decreasing order of their loadings on each component for the migraine group, to highlight the similarities and differences between the two groups.

INSERT TABLE 2 HERE

The components extracted from the migraine group's data were interpreted as (i) visual stimuli together with tiredness and stress; (ii) food; (iii) alcohol; (iv) stimuli from the environment: auditory, olfactory and visual (not including flicker, stripes and alternate light and shade). For the control group, the components were interpreted as (i) food; (ii) visual stimuli; (iii) alcohol; (iv) stress, tiredness and visual stimuli from the environment (not including flicker, stripes and alternate light and shade). Thus, while two of the extracted components from the two groups are the same (food and alcohol), the composition of the other two, and the order of the components (amount of variance explained), differs. For example, visual stimuli emerged as the first component from the migraine group's data, accounting for 26% of the variance, whereas it emerged as the second component in the control group's data and accounted for only 17% of the variance. These results agree with those reported previously (Harle *et al.,* 2006; Shepherd, 2000; 2010), which provides credibility to the participants' responses to the remaining questionnaires.

3.2. Group differences for the CAPS scores, visual trigger scores and visual discomfort

As mentioned in Section 2.2, the CAPS has four outcome measures: first, the total score, which is a tally of the number of items endorsed, for each participant, giving a possible range of 0 to 32. When an item is endorsed, participants are then given rating scales from 1 to 5 to assess distress, intrusiveness and frequency. The proportion of participants who endorsed each CAPS item is shown in Figure 1A. Clearly, the MA group had the highest proportion of participants endorsing the most frequent items [1, 23, 4, 18, 20, four of which refer to sensory intensity (auditory, visual, olfactory and tactile or somatosensory), and one to unexplained visual experiences, Table 3], followed by the MO group and, lastly, the control group. The MA group also had the highest proportion of participants endorsing several other items [27, 30, 14, 29, 12, 16, 32, six of which refer to distorted, unexplained or non-shared sensory experiences (gustatory, olfactory, auditory, tactile, Table 3)].

INSERT FIGURE 1 AND TABLE 3 HERE

Average distress, intrusiveness and frequency ratings are depicted in Figures 1B–1D for each CAPS item, and overall ratings are given in Table 4A. Bell *et al.* (2006) summed the distress, intrusiveness and frequency ratings for all endorsed CAPS items, and gave non-endorsed items a rating of 0, leading to a possible range from 0 to 160 for each dimension. This was necessary for their PCA, where every variable needed to have an equal number of responses. Here, however, that constraint was not required for the assessment of *group differences*. Furthermore, allocating a participant a rating of 0 for distress or intrusiveness associated with a

non-endorsed item would be qualitatively different to a distress or intrusiveness rating of 0 given by a participant who had endorsed that item had they been given the opportunity to select 0: the latter participant may like the experience of that item, for example (the scales go from 1 to 5, they do not include 0). Distress, intrusiveness and frequency ratings for items that were not endorsed were, therefore, omitted from the group comparisons. Non-endorsed items were retained for the group comparisons of the *total* scores as a response of 0 for that question meant that the item was not experienced. Items were endorsed by 31/33 (94%) of the MA group, 29/44 (66%) of the MO group and 45/74 (61%) of the C group.

As expected, the CAPS total scores differed between the three groups, MA, MO and C [Kruskal-Wallis one-way analysis of variance (KW): $\chi^2_{(2)}$=9.8, *p*<0.01]. Planned pairwise comparisons revealed that the difference between the MA and C groups differed significantly, but there were no significant differences between the MO and C groups nor between the MA and MO groups (Mann-Whitney *U* tests, Table 4B).

Ratings for distress, intrusiveness and frequency for endorsed CAPS items also differed between the three groups (KW distress ratings: $\chi^2_{(2)}$=9.7, *p*<0.01; intrusiveness: $\chi^2_{(2)}$=12.2, *p*<0.005; frequency: $\chi^2_{(2)}$=6.8, *p*<0.05). Planned pairwise comparisons revealed a similar pattern of results as for the CAPS total scores: the distress and frequency ratings were significantly higher in the MA than in the C group but there were no significant differences between the ratings from the MO and C groups nor between the MA and MO groups after adjusting for multiple comparisons, apart from MA vs MO and intrusiveness ratings (Mann-Whitney *U* tests, Table 4B).

INSERT TABLE 4 HERE

Also included in Table 4 are the group averages for the VT scores (the average number of visual items endorsed from the migraine/headache trigger inventory listed in Table 2). As expected, the migraine groups endorsed significantly more visual triggers than the control group, but the group differences were not statistically significant ($\chi^2_{(2)}$=4.9, *p*=0.085). The average VDS scores were also larger in the MA group, compared to the MO and C groups, but the differences were not statistically significant ($\chi^2_{(2)}$=3.0, *p*=0.2).

Cucchiera *et al.* (2015) divided VDS scores into sub-scales reflecting movement or fading; blur or diplopia; headache or eye soreness; glare; re-reading of words or lines, and slow-reading (after Borsting *et al.,* 2007). They also created a revised VDS score using only those items that differed between groups (Qs 1, 2, 9, 14, 16–18, 20, 21, 23) and again reported differences between both MA and MO and the control groups.

In the present study, Kruskal-Wallis one-way ANOVAs on each of the 6 sub-scales and their revised VDS produced only one significant difference between the groups: glare (VDS item 19: $\chi^2_{(2)}$=14.7, *p*<0.005). Pairwise comparisons revealed that the glare ratings were significantly higher in the migraine than in the control groups. The differences were statistically significant for the MA and C groups comparison (Mann-Whitney *U* test=1739, mean ranks 69.7, 47.0, *N*=107, *p*<0.001) and for the MA and MO comparison (Mann-Whitney *U* test=497, mean ranks 46.9, 33.8, *N*=77, *p*<0.05, Bonferroni adjusted). The MA group had the highest ratings to the glare question: when reading under fluorescent lighting or in bright sunlight, does the glare from bright, glossy pages cause you to continually move the page around so that you can see the words clearly?

3.3 Correlations
Whether the nature of aura symptoms experienced in MA, or their VDS and VT scores, correlated with individual CAPS items involving the same sensory systems was assessed with correlation for dichotomous variables (r_ϕ). Experiencing a visual aura was not included in the correlations as all but one participant with aura experienced a visual aura.

INSERT TABLE 5 HERE

As may be expected, the aura symptoms correlated significantly with themselves, with the exception of language difficulties, which did not correlate significantly with any other aura symptom (Table 5). For the remainder, the highest correlation was between dizziness and pins and needles (r_ϕ=0.81, p<0.001), and the lowest significant correlation was between diplopia and tinnitus (r_ϕ=0.36, p=0.04).

There were only two significant correlations between the type of aura experienced and individual CAPS items: experiencing language difficulties as part of the aura correlated with experiencing sounds more loudly than usual between migraine attacks (r_ϕ=0.40, p=0.02). Tinnitus as part of the aura correlated with experiencing one's skin to be more sensitive to touch between migraine attacks (r_ϕ=0.45, p=0.01).

In the MA group, VT scores correlated significantly only with the VDS (r_ϕ=0.56, p=0.001): those who cited more visual triggers experienced greater visual discomfort than those who cited fewer. The VDS also correlated significantly with ataxia as part of the aura (r_ϕ=0.39, p=0.02) and the following CAPS items, between attacks: having days where lights or shapes seem brighter or more intense than usual (CAPS item 23, r_ϕ=0.45, p=0.009); experiencing dramatic changes of time (item 27, r_ϕ=0.39, p=0.02); seeing shapes, lights or colours even though there is nothing really there (item 4); hearing noises or sounds when there is nothing about to explain them (item 6); detecting smells that do not seem to come from the surroundings (item 8); experiencing unexplained tastes (item 14)—for each of these, r_ϕ=0.36, p=0.04.

Including those with migraine without aura as well as those with aura in the correlations between VDS, VT and CAPS items yielded a broadly similar pattern, although more of the sensory CAPS items correlated significantly with VDS: seeing shapes, lights or colours even though there is nothing really there (item 4, r_ϕ=0.43, p<0.001); having days where colours or lights seem brighter or more intense than usual (item 23, r_ϕ=0.40, p<0.001); hearing noises or sounds when there is nothing about to explain them (item 6, r_ϕ=0.31, p=0.006); noticing sounds are louder than normal (item 1, r_ϕ=0.33, p=0.004); finding sensations happen all at once and flood you with information (item 15, r_ϕ=0.23, p=0.04); feeling that someone is touching you but nobody is there (item 12, r_ϕ=0.23, p=0.04); experiencing unexplained tastes (item 14, r_ϕ=0.36, p=0.001); experiencing dramatic changes of time (item 27, r_ϕ=0.33, p=0.003). VT correlated significantly with VDS (r_ϕ=0.27, p=0.02) and noticing sounds are louder than normal (item 1, r_ϕ=0.32, p=0.005).

Running the same correlations on the control group's data resulted in significant correlations only between VDS and (i) VT (r_ϕ=0.36, p=0.002); (ii) finding your skin is more sensitive to touch (item 20, r_ϕ=0.29, p=0.014); (iii) finding your face looks different when looking in the mirror (item 22, r_ϕ=0.26, p=0.03); (iv) experiencing dramatic changes of time (item 27, r_ϕ=0.23, p=0.04).

4. Discussion

4.1 Overview

This is the first study to look at anomalous perceptual experiences in migraine, between attacks, using the Cardiff Anomalous Perceptions scale (Bell *et al.,* 2006) and their associations with visual triggers, visual discomfort and, for those with aura, particular aura symptoms. The study developed from observations that performance on a broad range of *visual* tasks has been shown to differ between migraine and control groups, between attacks. The differences are usually more pronounced in those with visual aura, in those who experience visual discomfort between attacks and in those whose migraines can be triggered by visual stimuli (see Section 1, Introduction). The nature of the tasks used previously indicate distributed processing differences, between attacks, throughout the visual pathways from the retina to the primary visual cortex and extrastriate cortical areas. Given such distributed differences, the question asked in the present study was what other aspects of perception and experience might differ between attacks. There has, however, been limited assessment of other aspects of sensory experiences and perception. This study assessed diverse anomalous sensory experiences and distorted experiences of the body and the environment using the CAPS and found that all were experienced by some migraine and control participants, but more people with migraine experienced them, and rated them as more distressing and intrusive, than people in the control group (Figure 1, Tables 3 and 4).

4.2.Migraine and headache triggers
The first analysis used a PCA to summarise the trigger data and identify general clusterings between the trigger variables and confirm that the data collected in this on-line study agreed with those collected in a laboratory setting. Previously, Shepherd (2010) reported that 60% of a migraine group (number, N= 132) specified visual stimuli as migraine triggers. Here, 75% specified visual stimuli as migraine triggers (N=77; MA 79%, N=33; MO 73%, N=44) and, of all the various triggers, visual triggers accounted for the highest amount of the total variance in the PCA (26%, Table 2). Flickering lights, high contrast stripes or other repetitive patterns, and alternate light and shade, such as dappled sunshine, all correlated highly with the first extracted component. Visual stimuli also contributed to a general environment component (component four), which accounted for a further 9% of the variance. Cited examples included bright lights, computer over-use, reading, television (particularly excessive viewing), cinema, video games or other games (particularly 3-D), high contrast reflections, bright flashes in the dark, home theatre, office fluorescent lighting, scrolling when using a mobile telephone or tablet, bright lights on the road at night, recessed lighting, sunlight and abrupt transitions from dark to light. The other two components included food triggers and alcohol, which accounted for 15% and 12% of the variance, respectively.

In the control group, visual stimuli as headache triggers also contributed to two components from their PCA, the second and fourth, which accounted for only 17% and 8%, respectively, of the total variance for that group's data. Their second component was similar to the first from the migraine group: flickering lights, high contrast stripes or other repetitive patterns and alternate light and shade. The environmental visual stimuli that contributed to component four were similar to those that comprised component four for the migraine group, but there were fewer: cinema (particularly 3-D), computer or mobile telephone use (particularly excessive use), motion parallax, video games and bright flashes in the dark. The other two components were, as for the migraine group, food and alcohol, which accounted for 27% and 10% of the variance, respectively.

Finding that the potential triggers clustered into the four broad categories of visual stimuli, food, alcohol, and the environment may prompt sceptics to suggest that the analyses simply show associations between words in the English language. Two facts argue against this: first, the order of the components and the different order of the components for the migraine and control groups. If the extracted components simply reflected frequent word usage, the same components in the same order should emerge for the analyses on each group's data. Instead, visual stimuli emerged as the first component for the migraine group's data, but the second for the control group. Second, previous studies have found that performance on visual tasks differs when people who cite visual triggers are compared to those who do not (Conlon & Hine, 2000; Shepherd, 2006; Tibber & Shepherd, 2006; Shepherd *et al.,* 2013; Shepherd & Joly-Mascheroni, 2017). Visual discomfort from geometric visual patterns, for example, is heightened in migraine and is greatest in those who cite visual triggers (see Section 1, Introduction). A significant association between those who reported visual triggers of migraine or headache and those with high VDS scores was also found in the present study for all three groups (MA, MO, C, see Section 3.3, Correlations). These associations also suggest that the PCAs reveal more than common associations between words.

These results are similar to those presented previously (Shepherd, 2010), which lends credence to the responses to the other questionnaires. The results also confirm that visual stimuli are more prominent triggers of migraine than they are of headache in people without migraine, and a wider range of visual stimuli affect those with migraine than those without. Both groups, however, experience problems with headaches triggered by visual stimuli.

4.3 Group differences for CAPS total scores and CAPS sub-scales of distress, intrusiveness and frequency
The migraine participants had higher total CAPS scores and higher ratings for the three CAPS subscales (distress, intrusiveness and frequency). Eighty eight per cent of the MA group, 64% of the MO group and 57% of the control group reported anomalous perceptual experiences. This confirms the first question raised in the present study: would more people with migraine endorse the various CAPS items than people in the control group? The results indicate that unusual sensory experiences are quite common in the general population, but they are more common in migraine, particularly in MA (Figure 1A, Tables 3 and 4). Both migraine groups also found the anomalous perceptual experiences more distressing, intrusive and frequent than the control

group (Figures 1B–1D, Table 4), but the group differences were only statistically significantly different for the MA group compared to the control group. Intrusiveness scores were also higher in the MA group compared to MO. Evidently, the unusual phenomena experienced between migraine attacks can be unpleasant for all three groups between migraine or headache attacks, but they are particularly unpleasant for those with MA.

The average CAPS total scores and ratings for both the migraine and control groups were lower than those reported by Bell *et al.* (2006) in their non-clinical sample [Bell *et al.* (2006) reported averages for the CAPS total scores and the distress, intrusiveness and frequency ratings of 7.3, 15.5, 18.0 and 14.6, respectively; cf. Table 4]. These differences may reflect differences in the samples tested. Bell *et al.* (2006) tested mostly undergraduates and a younger sample (mean age 20 years, age range 18–44, 40% male), than in the present experiment (mean age 37 years, age range 22–72, 25% male). They commented that younger people, particularly young males, are more likely to report anomalous perceptual experiences. The only exclusion criterion they mentioned was failing to answer the questions. It is possible that not only did their sample include a higher proportion of young males than in the present study, but that some of their participants may have had neurological or other health conditions, or student life- and work-styles, which could affect their responses to the CAPS questions and lead to higher average CAPS scores. The present group included a larger age range and stricter exclusion criteria (see Section 2.1, Participants).

4.4 The three components of the CAPS
Bell *et al.* (2006) ran a Principal Components Analysis on their CAPS total scores, which resulted in three components labelled as temporal lobe experiences (TLE), chemosensation (CS) and clinical psychosis (CP). This was not performed in the current study as the focus was on group differences and whether particular items correlated with the different types of aura symptoms, visual discomfort, or visual triggers, not on assessing which CAPS items clustered together. Conversely, Fong *et al.* (2020) reported CAPS data for a migraine and control group using average scores for these three components. For each participant, they summed the ratings for each sub-scale (distress, intrusiveness and frequency), rather than used the total scores. They did not provide the scores for individual CAPS items nor differentiate between MA and MO. None of the three group comparisons were statistically significant, but the largest group difference was for the TLE component. Their migraine group (M) had larger scores than their control (C) group TLE: 24.0 (M) 15.3 (C); CS: 12.8 (M) 13.3 (C); CP: 5.5 (M) 4.3 (C).

For comparison with the results of Fong *et al.* (2020), average scores for these three components were calculated for the present study. The group differences were also greatest for the TLE component (M=24.1, C=15.0), then the CS (M=20.7, C=14.3), whereas the group averages for the CP component were comparable (M=5.0, C=6.1). This pattern held whether a combined migraine group was compared to the control group, or whether the MA and MO groups were compared to the control group separately. The difference in scores for the combined migraine and the control groups was statistically significant only for the TLE component (MWU=1901, mean ranks 62.2 (M), 45.9 (C), *p*=0.021, *N*=109, Bonferroni corrected).

4.5 Correlations
Contrary to one of the hypotheses, there were only two significant associations between the type of non-visual aura experienced and particular CAPS items: experiencing language difficulties as part of the aura correlated with experiencing sounds more loudly than usual between attacks and tinnitus as part of the aura correlated with experiencing one's skin to be more sensitive to touch between attacks (Section 3.3, Correlations). The lack of additional correlations between non-visual aura symptoms and relevant non-visual CAPS items, between attacks, was unexpected, and perhaps significant associations would emerge if a larger group of MA patients were recruited (here N=33).

In Figure 1, it is striking that the five most endorsed items all relate to primary sensations (perceiving sounds as louder than usual; seeing lights or colours as brighter than usual; seeing shapes, lights or colours when there is nothing there; experiencing smells as unusually strong and finding one's skin more sensitive to touch than usual). These five items also have the highest distress, intrusiveness and frequency ratings. Future research could clarify the content of these anomalous sensory experiences: which sounds are louder? Which colours brighter? What is seen? Which smells are enhanced? Where on the body is skin more sensitive?

Perhaps these five CAPS items may relate to the type of non-visual aura experienced if the questions were fine-tuned and a larger group recruited.

In the migraine group, there was a significant correlation between the VDS and reports of visual triggers, as expected from previous research (Shepherd *et al.,* 2012; 2013), which adds weight to the reliability of the other associations reported here. Associations with visual CAPS items may be expected as several of the VDS items could allude to hallucination, such as items 10 (when reading, do the words on a page of clear text ever appear to fade into the background and reappear), 13 (when reading, do the words on the page ever appear to move or float?), 18 (do you ever have difficulty reading the words on a page because they begin to flicker or shimmer?) and 21 (does the white background behind the text ever appear to move, flicker, or shimmer making the letters hard to read?).

VDS scores did correlate significantly with not only visual CAPS items, but also with auditory, olfactory and gustatory items (seeing shapes, hearing noises and experiencing smells when there is nothing there, experiencing unexplained tastes) and with the sense of changes in the passage of time in each MA and MO group and with tactile sensations when the MA and MO groups were combined.

Visual discomfort has been studied quite extensively since the early study of Wilkins *et al.* (1984) (see Section 1, Introduction). There are a few reports of sound-induced discomfort, cutaneous allodynia and olfactory symptoms during and between migraine attacks in people with and without aura (Schrieber & Calvert, 1986; Main *et al.,* 1997; Lovati *et al.,* 2009; Coleman *et al.,* 2011), but they have not been examined in nearly as much detail. The pattern of associations between visual discomfort and CAPS items that involve other sensory modalities suggests a general heightened sensitivity across the senses, between attacks, in migraine with and without aura, which would warrant further investigation.

The link with visual discomfort may indicate that the sounds, smells, and tactile sensations experienced when there is nothing there are unpleasant. Equally, the higher distress and intrusiveness ratings for the endorsed CAPS items also indicate that the experiences are unpleasant (Figure 1, Table 4). The present results only show that visual discomfort is associated with, for example, hearing noises when there is nothing there. Are the sounds that produce discomfort similar to those that are heard when there is nothing there? Are the smells experienced when there is nothing there acrid or sweet? Are the tactile sensations like a soft brush or are they painful, similar to cutaneous allodynia? Finally, the types of smells and sounds that can trigger migraine could be elaborated upon in future research. Presumably if they can trigger migraine then they also elicit discomfort, much as visual triggers elicit visual discomfort. It may be that there is a general sensory discomfort condition in migraine, in addition to a general heightened sensitivity, which has been overlooked with the focus to date on visual discomfort. Such a condition could account for anomalous experiences between attacks and with the reports of various environmental triggers.

4.6 Questionnaire development
To address the issue of a general sensory discomfort condition, the set of questionnaires would need to be extended. The CAPS assesses a range of internal, external, and hallucinatory experiences of the body and the environment, whereas the current migraine/headache questionnaire focuses mainly on the visual aura, bodily sensations and speech. More precise questions could be included, to explore how people subjectively experience their internal and external environments. Questions could be added to explore the characteristics of (i) each endorsed CAPS items across the senses; (ii) environmental triggers (noise and smell as well as visual patterns). When an item is endorsed [for example: (i) smells that have no origin, (ii) smells as a trigger] there could follow prompts for specific details on the types of smells experienced. This would allow an assessment of the link between anomalous experiences between attacks, environmental migraine triggers and the general discomfort condition proposed above.

Shepherd *et al.* (2012; 2013), Datta *et al.* (2013), Cucchiara *et al.* (2015) and Imaizumi *et al.* (2018) have each used the VDS and reported significant differences between their migraine and control groups. In the original study, Conlon *et al.* (1999) also reported significant differences between those reporting severe headaches and those who did not. All of these studies recruited their participants from University or College campuses or

from school-leavers applying to University. As mentioned in the Introduction, the VDS was developed to measure distortions and psychosomatic symptoms experienced while reading. It is possible that the lack of significant group differences in the present study reflects differences in the people recruited. The reading habits of current or potential University students may differ to those recruited here. The present study also recruited a cohort with a wider distribution of ages and, presumably, backgrounds. There is some variability in the mean scores from each study, which is consistent with scores having been affected by sampling biases in the different studies (Cucchiera *et al.* 2015; Imaizumi *et al.,* 2018), such as education or gender. For example, the reported mean or median VDS scores for migraine or headache groups across these studies ranged from 8 to 25.4 and, for control groups, from 3 to 11.6.

Nevertheless, in the present study there were significant correlations between visual triggers, experiencing ataxia as part of an aura, several of the sensory CAPS items and the VDS. Shepherd *et al.* (2012; 2013) also reported significant correlations between reports of visual triggers and VDS scores. Shepherd *et al.* (2012) found VDS scores correlated significantly with a measure of relative motion discrimination: those with higher discomfort scores had higher relative motion thresholds. Cucchiera *et al.* (2015) reported VDS scores correlated with BOLD fMRI activation in the primary visual cortex during visual stimulation: increasing visual discomfort was associated with a greater BOLD signal change in MA (Datta *et al.* (2013) did not find a significant correlation between BOLD activation and VDS, however, their sample size was substantially smaller).

As mentioned in the Results section 3.2, Cucchiera *et al.* (2015) divided VDS scores into sub-scales reflecting movement or fading; blur or diplopia; headache or eye soreness; glare; re-reading of words or lines, and slow-reading (after Borsting *et al.,* 2007). Their MA and MO groups both had higher scores than the control group on most of the sub-scales, but the MA and MO groups did not differ from each other. They also created a revised VDS score and again reported differences between both MA and MO groups and their control group. This pattern was not replicated in the present study. The only group differences for the VDS sub-scales occurred for Q19, which asks about glare when reading under fluorescent or bright sunlight. The MA group had the highest proportion of people endorsing this item and the highest average ratings compared to the MO and C groups.

A comparison of the items that were endorsed by more than 10% of one group over the other in the present study revealed that those with migraine more frequently endorsed items relating to fluorescent lighting whereas the control group only endorsed one item more frequently. *Migraine group:* Q3 (Do your eyes ever feel watery, red, sore, strained, tired, dry or gritty, when working under fluorescent lights?); Q4 (How often do you get a headache when working under fluorescent lights?); Q19 (When reading under fluorescent lights or in bright sunlight, does the glare from the white glossy pages cause you to continually move the page around so that you can see the words clearly?) *Control group:* Q7 (Do you have to use a pencil or your finger to keep from losing your place when reading a page of text in a novel or magazine?)

On balance, the VDS appears to capture aspects of visual discomfort relevant to migraine, but it could be revised to widen its scope beyond discomfort elicited by reading. There are new questionnaires that assess aspects of visual discomfort, such as the 2nd version of the cortical hyperexcitability index, or CHi– II (Fong *et al.,* 2019) or the Leiden Visual Sensitivity Scale (Perenboom *et al.,* 2018). Twenty-six of the 28 items in the revised CHi-II refer to vision and all nine of the Leiden Scale refer to vision. Both studies reported positive significant correlations with the Evans and Stevenson (2008) pattern glare test.

Fong *et al.* (2019) performed a factor analysis on data from the CHi-II from a large University sample, excluding people with migraine. The data could be summarised by three factors labelled as: Heightened visual sensitivity and discomfort (including questions such as getting irritation form indoor lights, feeling dizzy or nauseous due to lights or patterns, experiencing visual discomfort from certain patterns); Aura-like hallucinatory experiences (including questions such as experiencing flashes of moving patterns, experiencing loss of visual information, experiencing flashes of colour); and Distorted visual perception (including questions such as having an out-of-body experience, experiencing the world draining in colour and vibrancy, visual perceptions seeming heightened or enhanced). They also included a measure of visual discomfort elicited by

high contrast striped patterns using the pattern glare (PG) test (Evans and Stevenson, 2008; Wilkins and Evans, 2001). In a second study, they included participants with migraine.

They reported three analyses relevant to the present study.
—First, they divided their control data into high and low PG groups (dividing at the 75th percentile resulted in N=79 and 237 for the high and low PG groups, respectively). Their high PG group had significantly higher average *CHi-II scores* for factor 2 (Aura-like hallucinatory experiences) than those in the low PG group. They conclude that this is consistent with a relationship between state-based PG scores and the presence of trait-based aura-like symptoms (factor 2) for their control group.
—Second, they compared PG scores from a group with migraine (N=27: 16 MA; 11 MO) to those without (N=316). The migraine group had significantly higher average *PG scores* than those without.
—Third, they found that the migraine group had significantly higher average *CHi-II scores* for factors 1 and 2 (Heightened visual sensitivity and discomfort and Aura like visual hallucinatory experiences) than the control group (a result that was replicated by Fong *et al.,* 2020).

Fong *et al.* (2019) concluded that people with migraine are more susceptible to PG, visual stress (factor 1) and aura-like hallucinations (factor 2) than those without, but the two groups' scores for factor 3 (distorted visual perception) did not differ. Unfortunately, they did not mention whether the migraine participants were instructed to respond to the CHi-II items for times when they were between attacks, or whether the responses from those with aura included symptoms experienced as part of their aura.

Questions on visual symptoms necessarily dominate migraine questionnaires, due to the visual aura, visual triggers, and visual discomfort. Future research could incorporate not only an extended migraine/headache questionnaire, trigger list, the CAPS and a version of the VDS, but also the CHi-II and the Leiden visual sensitivity scale. A comparison of responses to each of these questionnaires could determine which questions are relevant to migraine and which are not, leading to an assessment tool tailored to migraine symptomology. This would also lead to a better understanding of the range of sensory experiences that differ between people with and without migraine between attacks and their association with aura symptoms or trigger stimuli. Then it could be asked: is the prominence of sensory symptoms between attacks due to a general discomfort condition in migraine, or a change in neural function in specific sub-cortical and/or cortical areas associated with their aura, prodromal symptoms or migraine triggers? A tailored assessment tool would complement, and could help forge explanatory links between, the results from different disciplines if incorporated in future behavioural, electrophysiological, imaging or clinical studies.

5. Conclusion
This study is the first to show relationships between visual discomfort and anomalous sensory experiences, experiences of the self, of the environment, and of time, between attacks, in migraine (e.g. experiencing unexplained visual symptoms, noises, smells, touches and tastes, having a feeling of being touched when no-one is there). In addition, it has shown distortions in the perceived intensity of sensory stimuli, particularly visual, auditory, olfactory and tactile, between attacks. Answers to questionnaires clearly cannot provide evidence to tease apart the cause(s) of symptoms experienced between or during migraine attacks, or provide direct evidence for or against models of an underlying cortical hyper-, hypo-, or mixed hyper-and hypo-excitability of neuronal function in migraine (see Introduction). Nevertheless, the symptoms experienced and the pattern of associations between different measures can provide pointers. For example, finding that people with migraine experience distortions in the perceived intensity of *visual* stimuli between attacks was anticipated, given the research cited in Section 1 (Introduction), and they are likely to reflect fluctuations in activity in both subcortical and cortical visual areas that extend from the occipital to the parietal and temporal lobes. Finding distortions in the perceived intensity of auditory and tactile stimuli, in addition to visual stimuli is, by extension, likely to reflect fluctuating neural activity in more anterior areas of the temporal and parietal lobes. Feelings of being touched and finding time changes dramatically also implicate anomalous or fluctuating activity in more anterior parts of the temporal lobe. Thus, answers to questionnaires that demonstrate such a wide range of experiences can provoke novel ideas for research (and theory) that can be taken back into the laboratory, be it psychophysical, electrophysiological or imaging. Further research is

recommended to understand the exact experiences that can be experienced by people with migraine between attacks, when they appear ostensibly symptom free.

Data statement: The data can be made available in a spreadsheet.

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Figure 1: A The proportion of participants in each group who endorsed each CAPS item; B–D The average distress, intrusiveness and frequency ratings, respectively, from each group and for each CAPS item. Distress, intrusiveness and frequency were rated on scales ranging from 1–5.
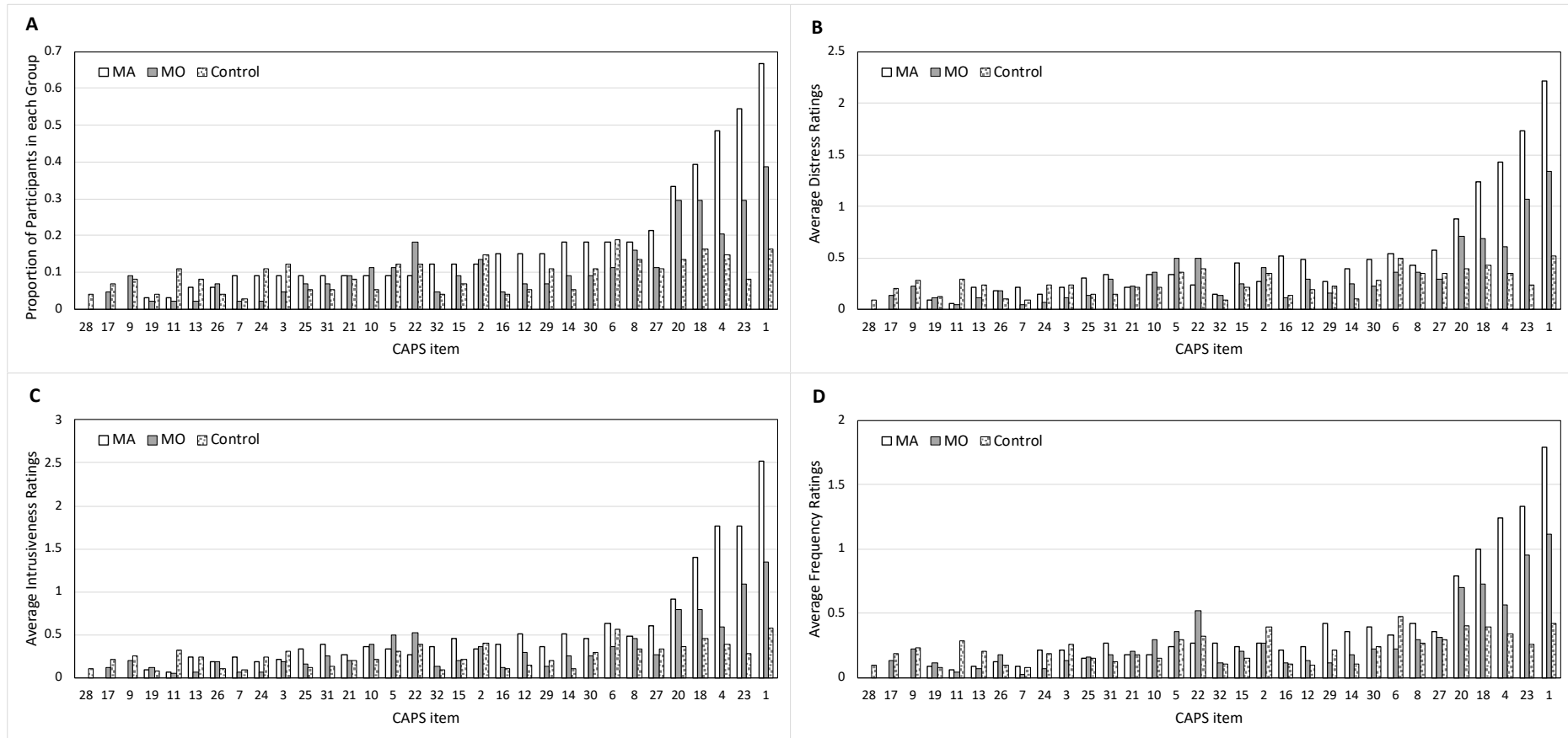
Group	Age (years)	Migraine duration (years experienced)	Migraine frequency (per year)
MA 24 F, 9M	39.2 ± 12.4 (22–72)	22.6 ± 14.7 (3–48)	44.2 ± 48.0 (1–100, mode=2)
MO 34 F, 10 M	36.1 ± 10.9 (22–70)	18.5 ± 13.5 (3–30)	32.2 ± 30.6 (5–100, mode=12)
C 30F, 44 M	31.9±8.1 (20–55)		

Table 1: Participant details (means ± one standard deviation, range of scores in parentheses) for age, migraine duration (years experienced) and migraine frequency. Modal migraine frequencies are also provided as those participants reporting very frequent attacks may have counted consecutive days with migraine as separate attacks, inflating the group means. MA: migraine with aura; MO: migraine without aura; C: control group; F: female; M: male.

QUESTIONNAIRE ITEMS FROM THE MIGRAINE/HEADACHE TRIGGER INVENTORY	MIGRAINE GROUP				CONTROL GROUP			
	C1 (26%)	C2 (15%)	C3 (12%)	C4 (9%)	C1 (27%)	C2 (17%)	C3 (10%)	C4 (8%)
Flickering lights: M=0.64, C=0.47	**0.78**	0.21	0.07	0.17	0.06	**0.72**	0.16	0.26
Repetitive visual patterns (stripes, geometric patterns): M=0.39,C=0.19	**0.77**	0.31	0.01	0.10	0.05	**0.76**	0.06	0.01
Tiredness: M=0.73, C=0.76	**0.68**	-0.05	0.18	-0.15	0.14	0.22	0.03	**0.69**
Alternate light & shade (dappled sunshine, sunshine & shadows): M=0.43, C=0.31	**0.67**	0.11	0.07	0.40	0.02	**0.68**	-0.02	0.21
Stress: M=0.88, C=0.86	**0.66**	-0.11	-0.01	0.12	-0.17	0.03	0.11	**0.74**
Other food: M=0.29, C=0.11	0.08	**0.79**	-0.06	-0.02	**0.78**	0.16	-0.09	0.08
Cheese: M=0.17, C=0.04	0.17	**0.79**	0.11	-0.16	**0.77**	0.06	0.03	0.09
Chocolate: M=0.17, C=0.07	-0.19	**0.71**	-0.09	0.35	**0.90**	0.13	0.01	-0.06
Caffeine: M=0.31, C=0.32	0.15	**0.62**	0.08	0.06	**0.77**	-0.13	0.12	0.12
Other alcohol: M=0.48, C=0.49	0.05	-0.07	**0.90**	0.14	-0.04	0.25	**0.84**	0.16
Red wine: M=0.43, C=0.32	0.14	0.15	**0.89**	-0.01	0.02	-0.06	**0.90**	0.03
Noise: M=0.45, C=0.50	0.23	-0.03	-0.15	**0.80**	0.13	0.49	0.48	0.29
Smells: M=0.32 C=0.31	-0.02	0.40	0.21	**0.56**	0.38	0.45	0.35	-0.18
Other visual (TV, cinema, computers, transitions from light to dark): M=0.62, C=0.51	0.22	-0.05	0.27	**0.55**	0.29	0.17	0.07	**0.62**

Table 2: The list of possible headache triggers and results from the PCAs for the migraine and control groups. Items with loadings greater than 0.5 are highlighted in bold. C1–C4=components 1–4. Numbers in parentheses in column headers show the amount of variance explained by each component. The numbers beside M (migraine) and C (control) show the proportion of participants in each group who endorsed that item. The items are listed in decreasing order of their loadings on each component for the migraine group, to highlight the similarities and differences between the two groups.

QUESTIONNAIRE ITEMS FROM THE CAPS

1. Do you ever notice sounds are much louder than they normally would be? [Sensory intensity: MA=0.67 (22) MO=0.39 (17) C=0.16 (12)]

23. Do you ever have days where lights or colours seem brighter or more intense than usual? [Sensory intensity: MA=0.55 (18) MO=0.30 (13) C=0.08 (6)]

4. Do you ever see shapes, lights, or colours even though there is nothing really there? [Unexplained sensory: MA=0.48 (16) MO=0.20 (9) C=0.15 (11)]

18. Do you ever smell everyday odours and think that they are unusually strong? [Sensory intensity: MA=0.39 (13) MO=0.30 (13) C=0.16 (12)]

20. Do you ever find that your skin is more sensitive to touch, heat, or cold than usual? [Sensory intensity: MA=0.33 (11) MO=0.30 (13) C=0.14 (10)]

27. Do you ever find that your experience of time changes dramatically? [Temporal lobe: MA=0.21 (7) MO=0.11 (5) C=0.11 (8)]

8. Do you ever detect smells which don't seem to come from your surroundings? [Unexplained sensory: MA=0.18 (6) MO=0.16 (7) C=0.14 (10)]

6. Do you ever hear noises or sounds when there is nothing about to explain them? [Unexplained sensory: MA=0.18 (6) MO=0.11 (5) C=0.19 (14)]

30. Do you ever notice that food or drink seems to have an unusual taste? [Distorted sensory: MA=0.18 (6) MO=0.09 (4) C=0.11 (8)]

14. Do you ever experience unexplained tastes in your mouth? [Unexplained sensory: MA=0.18 (6) MO=0.09 (4) C=0.05 (4)]

29. Do you ever experience smells or odours that people next to you seem unaware of? [Non-shared sensory: MA=0.15 (5) MO=0.07 (3) C=0.11 (8)]

12. Do you ever feel that someone is touching you, but when you look nobody is there? [Unexplained sensory: MA=0.15 (5) MO=0.07 (3) C=0.05 (4)]

16. Do you ever find that sounds are distorted in strange or unusual ways? [Distorted sensory: MA=0.15 (5) MO=0.05 (2) C=0.04 (3)]

2. Do you ever sense the presence of another being, despite being unable to see any evidence? [Temporal lobe: MA=0.12 (4) MO=0.14 (6) C=0.15 (11)]

15. Do you ever find that sensations happen all at once and flood you with information? [Sensory flooding: MA=0.12 (4) MO=0.09 (4) C=0.07 (5)]

32. Do you ever hear sounds or music that people near you don't? [Non-shared sensory: MA=0.12 (4) MO=0.05 (2) C=0.04 (3)]

22. Do you ever look in the mirror and think that your face seems different from usual? [Distorted body: MA=0.09 (3) MO=0.18 (8) C=0.12 (9)]

5. Do you ever experience unusual burning sensations of other strange feelings in or on your body? [Distorted sensory: MA=0.09 (3) MO=0.11 (5) C=0.12 (9)]

10. Do you ever have the sensation that your limbs might not be your own or might not be properly connected to your body? [Distorted body, Temporal lobe: MA=0.09 (3) MO=0.11 (5) C=0.05 (4)]

21. Do you ever think that food or drink tastes much stronger than it normally would? [Sensory intensity: MA=0.09 (3) MO=0.09 (4) C=0.08 (6)]

31. Do you ever see things that other people cannot? [Non-shared sensory: MA=0.09 (3) MO=0.07 (3) C=0.05 (4)]

25. Do you ever find that common smells sometimes seem unusually different? [Distorted sensory: MA=0.09 (3) MO=0.07 (3) C=0.05 (4)]

3. Do you ever hear your own thoughts repeated or echoed? [Thought echo: MA=0.09 (3) MO=0.05 (2) C=0.12 (9)]

24. Do you ever have the feeling of being uplifted, as if driving or rolling over a road while sitting quietly? [Temporal lobe: MA=0.09 (3) MO=0.02 (1) C=0.11 (8)]

7. Do you ever hear your own thoughts spoken aloud in your head, so that someone near might be able to hear them? [Thought echo: MA=0.09 (3) MO=0.02 (1) C=0.03 (2)]

26. Do you ever think that everyday things look abnormal to you? [Distorted sensory: MA=0.06 (2) MO=0.07 (3) C=0.04 (3)]

13. Do you ever hear voices saying words or sentences when there is no one around that might account for it? [Verbal hallucination: MA=0.06 (2) MO=0.02 (1) C=0.08 (6)]

11. Do you ever hear voices commenting on what you are thinking or doing? [Verbal hallucination: MA=0.03 (1) MO=0.02 (1) C=0.11 (8)]

19. Do you ever find the appearance of things or people seems to change in a puzzling way, e.g., distorted shapes or sizes or colour? [Distorted body: MA=0.03 (1) MO=0.02 (1) C=0.04 (3)]

9. Do you ever have the sensation that your body, or a part of it, is changing or has changed shape? [Distorted body: MA=0 (0) MO=0.09 (4) C=0.08 (6)]

17. Do you ever have difficulty distinguishing one sensation from another? [Sensory flooding: MA=0 (0) MO=0.05 (2) C=0.07 (5)]

28. Have you ever heard two or more unexplained voices talking with each other? [Verbal hallucination: MA=0 (0) MO=0 (0) C=0.04 (3)]

Table 3. The proportion of participants in each group who endorsed each CAPS item. Raw frequencies are added in round parentheses after each proportion. MA: migraine with aura (N=33); MO: migraine without aura (N=44); C: control (N=74). Numbers at the start of each row are the question numbers from the CAPS. The items are listed in order of frequency (same order as in Figure 1). Category labels in square parentheses are those given by Bell *et al.*[31] for each of the 32 CAPS questions.

A	Group	CAPS Total	CAPS Distress	CAPS Intrusiveness	CAPS Frequency	VT	VDS
	MA	5.2±0.8 (0–17)	14.9±2.5 (0–63)	16.6±2.7 (0–63)	11.9±1.9 (0–36)	0.73±0.06 (0–2)	17.0±1.6 (0–57)
	MO	3.5±0.7 (0–20)	10.3±2.0 (0–47)	10.5±1.9 (0–47)	9.0±1.8 (0–47)	0.67±0.07 (0–2)	12.2±1.5 (0–61)
	Control	2.9±0.4 (0–16)	8.2±1.3 (1–51)	8.3±1.3 (0–45)	7.2±1.1 (0–48)	0.47±0.05 (0–2)	13.3±1.5 (0–48)
B	Comparison	MWU (N)	MWU (N)	MWU (N)	MWU (N)		
	MA, C	1671 (107)** (67.6, 47.9)	1676 (107)** (67.8, 47.9)	1734 (107)** (69.6, 47.1)	1608 (107)* (65.7, 48.8)		
	MO, C	1720 (118) NS (61.6, 58.3)	1739 (118) NS (62.0, 58.0)	1773 (118) NS (62.8, 57.6)	1732 NS (61.8, 58.1)		
	MA, MO	501 (77) NS (45.8, 33.9)	510 (77) NS (45.6, 34.1)	494 (77)* (46.0, 33.7)	556 (77) NS (44.2, 35.1)		

Table 4. A: Mean scores ± one standard error and range of scores (in parentheses) for the CAPS total score, the CAPS sub-scales of distress, intrusiveness and frequency, visual trigger (VT) scores and visual discomfort scale (VDS) scores. MA: migraine with aura; MO: migraine without aura. B: Significant differences between the groups are denoted by ** $p<0.01$, * $p<0.05$ (*a priori* Mann-Whitney U tests, Bonferroni adjusted for multiple comparisons). Numbers in parentheses denote the average ranks for each group in each analysis. N=number.

	Dizziness	Tinnitus	Diplopia	Ataxia	Aphasia
Pins & Needles	**0.81**	**0.42**	0.34	**0.62**	0.07
	$p<0.001$	$p=0.02$	NS	$p<0.001$	NS
Dizziness		**0.52**	**0.41**	**0.77**	0.18
		$p=0.002$	$p=0.02$	$p<0.001$	NS
Tinnitus			**0.36**	**0.67**	−0.16
			$p=0.04$	$p<0.001$	NS
Diplopia				**0.54**	0.18
				$p=0.001$	NS
Ataxia					0.33
					NS

Table 5. Correlations between migraine aura symptoms (r_ϕ). Significant correlations are highlighted in bold.