

# MIGRAINE IN SYNAESTHETES AND NON-SYNAESTHETES: A PREVALENCE STUDY

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## **Abstract**

Synaesthesia is a neurological condition in which an inducer stimulus in one sense leads to a concurrent percept in a second sense. The immune hypothesis of synaesthesia links synaesthesia to immune-related conditions such as migraine. More specifically, migraine with aura may be linked to grapheme-colour synaesthesia as both involve cortical hyperexcitability. In this study, 188 synaesthetes and 121 non-synaesthetes completed an online questionnaire about synaesthesia and migraine. We found no general link between migraine and synaesthesia, nor between migraine with aura and grapheme-colour synaesthesia. Exploratory analyses, however, showed that certain types of synaesthetic inducer (significant: scent, emotion, and personality; trends: pain, non-lexical visual experiences, taste, and touch) were associated with visual disturbances in headache among female participants. Based on our exploratory analyses we hypothesise that specific subtypes of synaesthesia are related to migraine. The relationship between these two conditions is likely to become clearer as research on the underlying causes of synaesthesia and migraine progresses.

Keywords: headache; hyperexcitability; synaesthesia

## 1. Introduction

Migraine is a neurological condition characterised by debilitating headache attacks accompanied by nausea and in some cases visual disturbances, known as aura (Goadsby, Lipton, & Ferrari, 2002). In men, migraine has a prevalence of about 6%, while in women the prevalence is 15-17% (Stewart, Shechter, & Rasmussen, 1994). The criteria for diagnosing migraine require at least five attacks of a lateralised, pulsating headache, lasting four or more hours, which disrupts daily activity and is aggravated by physical activity (Headache Classification Subcommittee of the International Headache Society, 2004). The headache is also to be accompanied by at least one of the following: nausea, photophobia (a heightened sensitivity to light) or phonophobia (a heightened sensitivity to sounds). In approximately 40% of cases, people with migraine also experience sensory disturbances, known as aura, which develop over a period of five to twenty minutes, and last for around an hour (Schürks, Buring, & Kurth, 2010). While they can occur in any modality, the most common aura are visual (Steiner et al., 2003).

Synaesthesia is also a neurological condition but is otherwise markedly different from migraine. Synaesthesia is usually reported by synaesthetes to be pleasant or neutral, rather than aversive, and is characterised by the presence of unusual extra perceptions (concurrents) in response to particular stimuli (inducers). These extra experiences may occur in the same sensory modality (e.g. a letter printed in black may elicit an experience of another colour; Jäncke, Beeli, Eulig, & Hänggi, 2009) or in a different sensory modality (e.g. hearing a word may elicit a sensation of taste; Simner & Haywood, 2009). In most cases, synaesthetes report that they have had their synaesthesia for as long as they can remember.

In the current study, we investigated whether the prevalence of migraine is greater in people who experience synaesthesia. Such an increase might be predicted for two reasons. Firstly, the immune hypothesis of synaesthesia links synaesthesia to immune-related conditions such as migraine. Secondly, both migraine with aura, and grapheme-colour synaesthesia, have both been associated with a hyperexcitability of the visual cortex.

### **1.1.      *The immune hypothesis of synaesthesia***

Recently, Carmichael and Simner (2013) have suggested that the development of synaesthesia may be determined by genes that influence both immune function and the development of the central nervous system. This hypothesis is motivated by current models of synaesthesia, which have focussed either on excessive connectivity between cortical areas or on disinhibited feedback, leading to a failure to suppress irrelevant cortical activity (Bargary & Mitchell, 2008). The immune system also plays a role in the development of cortical connectivity. Variation in immune-related genes could result in both the excessive connectivity and/or the disinhibited feedback proposed to underlie synaesthesia. Consequently, Carmichael and Simner hypothesise that synaesthesia is likely to be linked with many disorders related to immune function, such as irritable bowel syndrome, multiple sclerosis and migraine.

The role of immune system function has been assessed in a number of studies. Kemper, Meijler, Korf and Ter Horst (2001) reviewed the literature up to 1999 and concluded that there was no evidence for a well-defined disorder immunological disorder in migraine, due to methodological limitations of the available results. More recent studies have however suggested a role of the immune system, in particular inflammatory cytokines, in migraine (Perini et al., 2005; Bruno, 2007; Bockowski, Sobaniec and Zelazowska-

Rutowska, 2009; Yilmaz et al., 2010). Carmichael and Simner (2013) also proposed that cytokines might play a role in synaesthesia.

### **1.2. *Cortical hyperexcitability in synaesthesia and migraine***

An association between synaesthesia and migraine might also be predicted from a consideration of the mechanisms underlying the two conditions, as well as their possible shared root cause in immune system dysfunction. Both conditions have been linked to the ideas of hyperexcitability of the visual cortex, and evidence for this has been provided using transcranial magnetic stimulation (TMS). TMS can be used to excite the visual cortex, causing illusory visual percepts known as phosphenes. Cortical excitability in individuals has been assessed in terms of both whether it is possible to induce phosphenes at all and the threshold level of magnetic stimulation required for a phosphene to occur.

Brigo et al. (2012) performed a meta-analysis of TMS phosphene thresholds in migraine, finding that a greater proportion of people with migraine with aura experienced phosphenes than a control group. Moreover, phosphene thresholds tended to be lower in migraine with aura. Their analysis provided no evidence for any difference in phosphene thresholds in migraine without aura compared to the control group. These data suggest that the visual cortex is hyperexcitable in migraine with aura, but not in migraine without aura. TMS phosphene thresholds are also lower in grapheme-colour synaesthesia, again demonstrating increased excitability in the visual cortex (Terhune, Tai, Cowey, Popescu, & Cohen Kadosh, 2011). Since phosphene thresholds have not been measured in other types of synaesthesia, it is not known whether this effect is specific for grapheme-colour synaesthesia, or whether this is an example of a more widespread phenomenon.

### **1.3. *Visual processing in migraine and synaesthesia***

The immune hypothesis of synaesthesia, and the hyperexcitation found in both grapheme-colour synaesthesia and migraine with aura, could potentially link to a single underlying commonality between the two conditions. The immune hypothesis is related to either excessive connectivity between cortical areas or to disinhibited feedback in synaesthesia, and a failure to suppress irrelevant cortical activity (Bargary & Mitchell, 2008). In a similar way, reduced inhibition (Palmer, Chronicle, Rolan & Mulleners, 2000), and an inability to ignore irrelevant sensory stimuli (Tibber, Kelly, Jansari, Dakin & Shepherd, 2014) have also been argued to be attributes of migraine.

Terhune et al. proposed that hyperexcitability in grapheme-colour synaesthesia is related to increased excitability during development, which contributes to the establishment of atypical binding across modalities through Hebbian learning. In adulthood, they argued that increased excitability leads to a reduction in the signal-to-noise ratio in sensory signals, through the creation of neural noise. Such a decrease in signal-to-noise ratio could potentially contribute to the experience of migraine, since migraine has been associated with higher levels of noise in sensory processing (Wagner et al., 2010).

There are a number of reasons to suppose that the nature of hyperexcitability differs between migraine and synaesthesia, however. From a theoretical point of view, hyperexcitability in migraine could be a response to, rather than a cause of, increased sensory noise (Aurora & Wilkinson, 2007). It is important here to maintain a clear distinction between the *responsiveness* of the visual system to incoming stimuli (reflecting the magnitude of the response to stimuli) and its *sensitivity* (how reliably it can detect, or distinguish between, stimuli). All other things being equal, sensitivity will tend to increase with increasing responsiveness. However, sensitivity is also limited by the level of random variability in neural activity. Thus, for a given level of responsiveness, the signal-to-noise

ratio, and thus sensitivity, will reduce with increases in this neural noise. If, for example, there were a greater degree of random variability in the responses of neurons in the visual cortex of those with migraine than those without migraine, this would tend to reduce the signal-to-noise ratio, and thus reduce visual sensitivity. One way to counteract this reduced sensitivity would be to amplify the incoming signal, which could be achieved through increasing the responsiveness of cortical neurons to visual inputs.

Empirical studies also show clear differences in perceptual sensitivity between the two conditions. In synaesthesia, enhanced perceptual sensitivity is found in relevant modalities (Banissy, Walsh, & Ward, 2009) while in migraine, sensory processing tends to be worse across the board. For example, grapheme-colour synaesthesia is associated with enhanced ventral stream processing but impaired dorsal stream processing (Banissy et al., 2013; Barnett et al., 2008). Sensory processing in migraine is reduced in measures of contrast sensitivity, colour, and motion processing, and is not confined to either the dorsal or ventral stream (De Marinis, Rinalduzzi, & Accornero, 2007; McKendrick, Badcock, & Gurgone, 2006; McKendrick & Sampson, 2009). Again, it is important to appreciate that this reduced perceptual sensitivity is not incompatible with an increased perceptual responsiveness, since neural noise (which can vary independently of perceptual sensitivity) is also a limiting factor in performance.

#### **1.4. *Are migraine and synaesthesia associated?***

While cortical hyperexcitability is common to both grapheme-colour synaesthesia and migraine with aura, the consequences for sensory processing in the two conditions differ, and the association between the two, if any, is unclear.

Direct evidence of a link between synaesthesia and migraine is limited. Visual-gustatory and auditory-visual synaesthesia occurring specifically during migraine with aura have previously been reported in isolated case studies (Alstadhaug & Benjaminsen, 2010; Podoll & Robinson, 2002), and one synaesthete has reported that synaesthetic concurrents can trigger migraine (Tyler, 2005). Another case study has reported migraine without aura followed by the acquisition of visual disturbances in headache (i.e. migraine with aura) and acquired auditory-visual synaesthesia (Afra et al., 2012). More generally, migraine sufferers have been hypothesised to have unusual styles of multisensory integration (Schwedt, 2013; see also Yang et al., 2014).

One large-scale study (219 participants with migraine and 161 without) assessed the prevalence of *sensory and neurological symptoms* (SNS) in migraine. These included transient visual illusions, hallucinations and, of relevance to our study, synaesthesia. They found an increased rate of synaesthesia in migraine, and particularly so with migraine with aura (Jürgens, Schulte, & May, 2014). However, since the study was used to assess the extent of SNS in general in migraine, they did not record the specific sensory/conceptual categories of inducers and concurrents in any detail. Also, the authors discussed the possibility that the use of a limited numbers of questions, and recruitment of participants via a headache centre, who were likely therefore to be severely affected, could both potentially have contributed to an overestimation of the phenomena.

Another large-scale study by Rich, Bradshaw and Mattingley (2005) found that self-reported migraine was no more common in synaesthetes than in non-synaesthetes. However, they did not distinguish between migraine with and without aura, nor between different types of synaesthesia. The aim of our study was to break down these subgroups to

analyse the potential relationship between the conditions in more depth than has previously been achieved.

One obvious difference between the two conditions is that migraine is much more common in women (Stewart et al., 2006) while there is no difference in the prevalence of synaesthesia across the sexes (Simner et al., 2006). While we would expect an association between migraine and synaesthesia to be reflected in a greater rate of synaesthesia in women, the size of this effect is expected to be modest. For example, if we take the prevalence of migraine to be 5% in men and 15% in women, and assumed a rate of synaesthesia in migraine that was, say, three times that in people without migraine, we can calculate the predicted relative prevalence of synaesthesia in men and women. These calculations are provided in Appendix 1. However, given the very low prevalence of synaesthesia, this would be unlikely to be detectable. For example, if the overall rate of grapheme-colour synaesthesia were 1% (Simner et al., 2006), this would result from a rate of 0.91% in men and 1.07% in women. Given the same assumptions, however, we predict the rate of migraine to be around 2.5 times what it is in the general public, and also a greater prevalence of migraine in women in both the synaesthete and non-synaesthete populations.

The immunological theory of synaesthesia outlined above indicates a possible link between migraine and synaesthesia generally, though one that has not been supported by previous research. Case studies, furthermore, suggest a link specifically between migraine with aura and synaesthesia, and larger-scale studies suggest that both grapheme-colour synaesthesia and migraine with aura are associated with hyperexcitability in visual cortex.

Thus, we hypothesised that while there would not be a higher incidence of migraine among synaesthetes, there would be a higher incidence of migraine with aura (but not

other types of headaches) in grapheme-colour synaesthesia (but not other kinds of synaesthesia). In addition to the strict criteria for the diagnosis of migraine with aura, we also hypothesised that grapheme-colour synaesthesia might also be more broadly associated with the experience of visual disturbances during headaches, since these may also reflect increased visual cortex excitability. We also explored whether particular kinds of inducer or concurrent in synaesthetes were associated with migraine, migraine with aura or visual disturbances in headaches, though we did not make any specific predictions about these possible associations.

## 2. Methods

Three hundred and nine participants<sup>1</sup> (mean age: 27.97 years; S.D. = 12.20, range = 18-82) were recruited via online communities of research volunteers and synaesthetes, and from among the personal contacts of the researchers, to fill out an online questionnaire on synaesthesia, personality characteristics (included as a check for response bias) and headache experiences (see Appendix 2 for full questionnaire). Participants were told the questionnaire was about “personal experiences in synaesthetes and non-synaesthetes”, and were aware prior to taking part that there were questions about health, but not about headaches specifically. The study was approved by the University of East London Research

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<sup>1</sup> Before analysis, nine rows of data from the automatically collected data file were removed because they were duplicates or near-duplicates of a previous row, and three rows because the contact email address the participant had provided was identical to a previous row (hence, we categorised these as technical errors); leaving us with 317 participants. Since men and women are known to have different prevalences of migraine, we removed three participants who stated their gender as ‘other’ and two who responded ‘prefer not to say’. One participant was removed because they had given all answers to the Big Five Inventory as ‘neither agree nor disagree’, indicating inattentiveness to the questionnaire. One participant was removed because they had not provided enough data in the headache questions to enable us to categorise the type of headaches they experienced. Finally, one participant was removed because they claimed to be a synaesthete but did not pass the consistency test.

Ethics Committee and is in accordance with the World Medical Association Helsinki Declaration (2008).

Of the participants, 56 were male and 253 were female. As we had so few male participants, and as there are known sex differences in self-reported rates of synaesthesia (Simner et al., 2006), we report results for female participants only. Participants were classified on the basis of self-reported synaesthesia (a subset of 23 had taken and passed the consistency test at [www.synesthete.org](http://www.synesthete.org) (Eagleman et al., 2007), but this number was not sufficient to analyse consistency-verified and non-verified synaesthetes separately, so we collapsed across the two groups). We also classified participants as being either headache free or having one of four headache types (migraine with aura, migraine without aura, tension, other) based on their answers to the questions, chosen as the most suitable for use in questionnaire-based studies (Köhler, Eisentraut, & Graeber, 1995; Wagner, 2011):

- *How often do you have a headache?* Possible answers: all the time, about once a day, several times a week, several times a month, once a month or less frequent, once a year or less frequent. Headache frequency over once a month was categorized as 'high', once a month or less frequent was categorized 'low'.
- *How bad are your worst headaches?* Possible answers: noticeable but not distracting, fairly distracting, bad enough to take time off work/cancel a social engagement, so severe you have to rest, almost unbearable. The answer 'noticeable but not distracting' was categorized as 'not bad', any other was categorized as 'bad'.
- *How many times have you experienced a headache attack that lasts 4-72 hours when it is left untreated (e.g. by pain medications)?* Possible answers: never, 1-2 times, 2-4

times, 5 times or more. Never was categorized as ‘low frequency’, 1 or more as ‘high frequency’.

- *Either before your headache or during it, do you notice any change in your vision?*

Possible answers: never, sometimes, usually, always, don’t know. Never, don’t know, and failure to respond to this question were categorized as ‘no’, other answers as ‘yes’.

- *During your headache, but not before, do you feel sick in the stomach? and During your headache, but not before, do you vomit?* Possible answers to both questions: strongly disagree, disagree a little, neither agree nor disagree, agree a little, strongly agree.

Strongly disagree, disagree a little and neither agree nor disagree were categorized as ‘no’, other answers as ‘yes’. Where participants provided a ‘no’ answer to one question and a ‘yes’ to the other, both answers were classed as ‘yes’.

- *Have you ever seen a doctor about headaches and/or migraine?* (Free response.)

Headache classification was determined as in Table 1. We summarise the number of female synaesthetes and non-synaesthetes in each category in Table 2 below.

*Table 1: Classification of headache types for participants in this study*

| Headache classification | Headache frequency                | Headache severity | Number of attacks | Vision changes | Nausea | Seen a doctor? |
|-------------------------|-----------------------------------|-------------------|-------------------|----------------|--------|----------------|
| Headache free           | Low                               | Not bad           | Low               | No             | No     | No/no response |
| Migraine with aura      | High                              | Bad               | High              | Yes            | Yes    | Any            |
| Migraine without aura   | High                              | Bad               | High              | No             | Yes    | Any            |
| Tension*                | Low/high                          | Not bad/bad       | Low/high          | No             | No     | Any            |
| Other                   | Any other combination of symptoms |                   |                   |                |        |                |

\*To be classified as having tension headaches, participants had to have *at least* one of high headache frequency, bad headache severity, or high number of attacks.

*Table 2: Frequency of particular headache types among female synaesthetes and non-synaesthetes (percentages by column in parentheses).*

| Headache classification | Synaesthetes<br>(N = 161) | Non-synaesthetes<br>(N = 92) |
|-------------------------|---------------------------|------------------------------|
| Headache free           | 17 (11%)                  | 9 (10%)                      |
| Migraine with aura      | 28 (17%)                  | 20 (22%)                     |
| Migraine without aura   | 23 (14%)                  | 11 (12%)                     |
| Tension                 | 37 (23%)                  | 22 (24%)                     |
| Other                   | 56 (35%)                  | 30 (33%)                     |

### 3. Results

All analyses were carried out separately for male and female participants because of the differing prevalence of migraine in men and women. As we had few male participants, we do not report results for this group.

We used the Big Five Inventory (John & Shrivastava, 1999) to assess whether synaesthete participants were more likely to agree with questions overall (i.e. as a test of response bias) we carried out an analysis on all subsets of personality variables together. We tested response bias in two ways. The first involved coding responses to each statement on a scale from 1 (strongly disagree) to 5 (strongly agree), regardless of whether the statement was reverse-scored or not<sup>2</sup>. We then summed the scores for all statements. If synaesthetes were prone to agree with questions overall, they should have higher summed scores than the non-synaesthetes. However, this was not the case (Mann-Whitney  $U$  (251) = 7065.00;  $Z = 0.61$ ,  $p = .54$ ; synaesthete median summed score = 155.0, non-synaesthete median summed score = 155.5).

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<sup>2</sup> Because this test was about agreement with statements, *not* about the extent to which a participant felt they had a certain personality characteristic.

Our second analysis was performed by recoding responses to reflect reverse-scoring and then performing Mann-Whitney tests on each personality characteristic. Compared to non-synaesthetes, synaesthetes were significantly less extraverted (Mann-Whitney  $U$  (251) = 6204.50;  $Z$  = -.215,  $p$  = .03; synaesthete median score = 24.0, non-synaesthete median score = 25.5) and significantly less agreeable (Mann-Whitney  $U$  (251) = 6272.00;  $Z$  = -2.03,  $p$  = .04; synaesthete median score = 34.0, non-synaesthete median score = 36.0). Synaesthetes were also more open to new experiences than non-synaesthetes (Mann-Whitney  $U$  (251) = 3738.50;  $Z$  = -6.59,  $p$  < .001; synaesthete median score = 42.0, non-synaesthete median score = 35.0). Synaesthetes were non-significantly less conscientious (Mann-Whitney  $U$  (251) = 6442.0;  $Z$  = -1.72,  $p$  = .09; synaesthete median score = 31.0, non-synaesthete median score = 33.0) and more neurotic (Mann-Whitney  $U$  (251) = 6730.0;  $Z$  = -1.21,  $p$  = .23; synaesthete median score = 27.0, non-synaesthete median score = 25.0) than non-synaesthetes.

Synaesthetes are known to be less agreeable and more open to new experiences than non-synaesthetes (Banissy et al., 2013) as we found here. In the remaining three characteristics, synaesthetes all report less socially desirable characteristics (significantly less extraversion, non-significantly less conscientiousness and more neuroticism) than non-synaesthetes, indicating that they are unlikely to be responding in accordance with social desirability bias. Since no response bias was found here, we assumed that none would be present in the headache questions.

Participants were given a short description of synaesthesia at the start of the questionnaire (see Appendix 2) and were asked to rate how well they understood the nature of synaesthesia on a Likert scale from 1 (no understanding) to 10 (understanding exactly what it is, even if it is not personally experienced). We split participants into those

who reported that they experienced at least one type of synaesthesia (synaesthetes) and those who reported no types of synaesthesia (non-synaesthetes). Both groups reported a good understanding of synaesthesia, though synaesthetes rated their understanding as better (median = 9) than non-synaesthetes (median = 8; Mann-Whitney  $U(251) = 5077.50$ ,  $Z = 4.30$ ,  $p < .001$ ). This difference in self-rated understanding is likely to be the result of synaesthetes' subjective knowledge of the experience of synaesthesia.

We first assessed whether any particular headache classification was associated with synaesthesia *in general* using chi-square analysis on the data in Table 2. No significant result was found ( $\chi^2(4) = 0.96$ ,  $p = .92$ ,  $\phi = .06$ ).

Next, we assessed whether grapheme-colour synaesthesia would be particularly associated with migraine with aura. Given that it is not clear whether grapheme-colour synaesthesia is the only type of synaesthesia associated with cortical hyperexcitability, we excluded synaesthetes without grapheme-colour synaesthesia from this analysis, but retained synaesthetes who reported other types of synaesthesia alongside grapheme-colour. We collapsed our headache classifications into those with migraine with aura and those without migraine with aura and our grapheme-colour synaesthesia classifications into those who self-reported letter-colour and/or number-colour synaesthesia, and those who reported no synaesthesia (Table 3). Tests on the data in Table 3 found no significant result ( $\chi^2(1) = 0.72$ ,  $p = .40$ ,  $\phi = -.06$ ).

*Table 3: Frequency of migraine with aura in headache among female grapheme-colour synaesthetes and non-synaesthetes (percentages by column in parentheses).*

| Migraine with aura? | Grapheme-colour synaesthetes<br>(N = 95) | Non-synaesthetes<br>(N = 92) |
|---------------------|--|------------------------------|
| Yes                 | 16 (17%)                                 | 20 (22%)                     |
| No                  | 79 (83%)                                 | 72 (78%)                     |

We also collapsed headache classifications into those who self-reported visual disturbances in headache and those who did not (Table 4). Again, there was no significant difference ( $\chi^2(1) = 1.50$ ,  $p = .22$ ,  $\phi = -.09$ ).

*Table 4: Frequency of visual disturbances in headache among female grapheme-colour synaesthetes and non-synaesthetes (percentages by column in parentheses).*

| Visual disturbances? | Grapheme-colour synaesthetes<br>(N = 95) | Non-synaesthetes<br>(N = 92) |
|----------------------|--|------------------------------|
| Yes                  | 33 (35%)                                 | 40 (43%)                     |
| No                   | 62 (65%)                                 | 52 (57%)                     |

Given that grapheme-colour synaesthesia co-occurs more often than expected by chance with day-colour and month-colour synaesthesia (Novich, Cheng, & Eagleman, 2011), we extended each of these analyses to cover the 15 synaesthetes who had day-colour or month-colour synaesthesia but not grapheme-colour synaesthesia (Tables 5 and 6). Neither of the findings was significant (migraine with aura:  $\chi^2(1) = 1.32$ ,  $p = .25$ ,  $\phi = -.08$ ; visual disturbances:  $\chi^2(1) = 2.46$ ,  $p = .16$ ,  $\phi = -.11$ ).

*Table 5: Frequency of migraine with aura in headache among female grapheme-colour, day-colour and month-colour synaesthetes and non-synaesthetes (percentages by column in parentheses).*

| Migraine with aura? | Synaesthetes<br>(N = 110) | Non-synaesthetes<br>(N = 92) |
|---------------------|---------------------------|------------------------------|
| Yes                 | 17 (15%)                  | 20 (22%)                     |
| No                  | 93 (85%)                  | 72 (78%)                     |

*Table 6: Frequency of visual disturbances in headache among female grapheme-colour, day-colour and month-colour synaesthetes and non-synaesthetes (percentages by column in parentheses).*

| Visual disturbances? | Synaesthetes<br>(N = 110) | Non-synaesthetes<br>(N = 92) |
|----------------------|---------------------------|------------------------------|
| Yes                  | 36 (33%)                  | 40 (43%)                     |
| No                   | 74 (67%)                  | 52 (57%)                     |

We found no evidence for an increased prevalence of migraine in synaesthetes, so we next calculated the strength of the evidence supporting this conclusion. We used a Monte Carlo approach to estimate firstly the probability that the rate of migraine with aura is greater in synaesthetes than non-synaesthetes, and secondly the odds ratio:

$$\frac{p_s / 1 - p_s}{p_n / 1 - p_n}$$

Where  $p_s$  is the probability of migraine with aura in the synaesthesia group, and  $p_n$  is the probability of migraine with aura in the non-synaesthesia group. In our case, the odds ratio represents the strength with which migraine with aura is associated with synaesthesia. A ratio greater than one indicates a positive association. We calculated 1000000 samples using a beta conjugate prior, and used the proportion of samples in which  $p_s > p_n$  as a measure of the probability that migraine with aura is more prevalent in synaesthetes with non-synaesthetes. We calculated that there was a 25% chance that the predicted increase in prevalence holds. There was a 95% chance that the odds ratio falls within the range (0.85-0.91).

### **3.1. Exploratory analyses in the synaesthete group**

For these analyses, we split synaesthete participants only into groups by reported inducer and concurrent<sup>3</sup>, analysing each inducer and each concurrent separately to assess whether any of them were associated with migraine (with and without aura), migraine with aura, or visual disturbances in headache. These results are presented in Tables 5-10. As we

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<sup>3</sup> Not including types of synaesthesia participants recorded in free-response boxes, nor pairings of sound-sound, scent-scent, taste-taste, emotion-emotion, personality-personality (these within-sense pairings may or may not be synaesthesia), nor any of the four possible pairings between pain and touch (these are likely to be *mitempfindung*, or referred itch, which is known to have an increased prevalence in synaesthetes (Burrack, Knoch, & Brugger, 2006).

have conducted multiple tests on the same data, we corrected the  $\alpha$ -level using false detection rate (FDR) control. This procedure involves ranking all p-values (i.e. every p-value in Tables 7-12 is included in one FDR calculation) from smallest to largest, and then calculating for each of them whether  $p_i \leq (\alpha/m)*i$  is true<sup>4</sup>. All p-values that meet this requirement are considered to be significant (see Benjamini & Hochberg, 1995, for details). In this case, the largest p-value for which this is true is .003. For significant results, we have reported which cell of the chi-square has the standardized residual furthest from zero and can therefore be considered to be driving the effect.

Though no inducers or concurrents are associated with migraine in general or migraine with aura, several inducers are associated with visual disturbances in headache: other (i.e. non-linguistic) visual experiences, scent, taste, emotion and personality. Further, touch as a concurrent is associated with migraine with aura.

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<sup>4</sup> Where  $i$  = the rank of the p-value,  $\alpha$  = the threshold p-value (i.e. 0.05) and  $m$  = the total number of p-values.

Table 7: Migraine (with and without aura) among female synaesthetes (N = 161), split by inducer types. Highlighted cells indicate largest unstandardised residual within a chi-square (for significant and near-significant results only; \* indicates standardized residual has a p-value of < .05), with a superscript + indicating that the cell has a higher value than expected and a superscript – indicating that the cell has a lower value than expected. P-values are two-tailed.

| Inducer type                      | Has inducer | Migraine? |          | $\chi^2$ | <i>p</i> | $\phi$ |
|-----------------------------------|-------------|-----------|----------|----------|----------|--------|
|                                   |             | Yes (%)   | No (%)   |          |          |        |
| Linguistic sequences <sup>5</sup> | Yes         | 42 (29)   | 101 (71) | 3.14     | .076     | .14    |
|                                   | No          | 9 (50)    | 9 (50)   |          |          |        |
| Spoken words                      | Yes         | 29 (29)   | 72 (71)  | 1.10     | .294     | .08    |
|                                   | No          | 22 (37)   | 38 (63)  |          |          |        |
| Written words                     | Yes         | 29 (30)   | 68 (70)  | 0.36     | .550     | .05    |
|                                   | No          | 22 (34)   | 42 (66)  |          |          |        |
| Other visual experiences          | Yes         | 13 (36)   | 23 (64)  | 0.42     | .516     | -.05   |
|                                   | No          | 38 (30)   | 87 (70)  |          |          |        |
| Sound                             | Yes         | 29 (29)   | 71 (71)  | 0.87     | .350     | .07    |
|                                   | No          | 22 (36)   | 39 (64)  |          |          |        |
| Scent                             | Yes         | 18 (32)   | 39 (68)  | 0.00     | .984     | .00    |
|                                   | No          | 33 (32)   | 71 (68)  |          |          |        |
| Taste                             | Yes         | 17 (32)   | 36 (68)  | 0.01     | .939     | -.01   |
|                                   | No          | 34 (31)   | 74 (69)  |          |          |        |
| Touch                             | Yes         | 15 (36)   | 27 (64)  | 0.43     | .513     | -.05   |
|                                   | No          | 36 (30)   | 83 (70)  |          |          |        |
| Pain                              | Yes         | 21 (42)   | 29 (58)  | 3.57     | .059     | -.15   |
|                                   | No          | 30 (27)   | 81 (73)  |          |          |        |
| Emotion                           | Yes         | 18 (32)   | 39 (68)  | 0.00     | .984     | .00    |
|                                   | No          | 33 (32)   | 71 (68)  |          |          |        |
| Personality                       | Yes         | 16 (32)   | 34 (68)  | 0.00     | .953     | -.01   |
|                                   | No          | 35 (32)   | 76 (68)  |          |          |        |

<sup>5</sup> Numbers, letters, days and/or months

Table 8: Migraine with aura among female synaesthetes (N = 161), split by inducer types. Highlighted cells indicate largest unstandardised residual within a chi-square (for significant and near-significant results only; \* indicates standardized residual has a p-value of < .05), with a superscript + indicating that the cell has a higher value than expected and a superscript – indicating that the cell has a lower value than expected. P-values are two-tailed.

| Inducer type             | Has inducer? | Migraine with aura? |          | $\chi^2$ | <i>p</i> | $\phi$ |
|--------------------------|--------------|---------------------|----------|----------|----------|--------|
|                          |              | Yes (%)             | No (%)   |          |          |        |
| Linguistic sequences     | Yes          | 23 (16)             | 120 (84) | 1.52     | .217     | .10    |
|                          | No           | 5 (28)              | 13 (72)  |          |          |        |
| Spoken words             | Yes          | 18 (18)             | 83 (82)  | 0.04     | .852     | -.02   |
|                          | No           | 10 (17)             | 50 (83)  |          |          |        |
| Written words            | Yes          | 18 (19)             | 79 (81)  | 0.23     | .631     | -.04   |
|                          | No           | 10 (16)             | 54 (84)  |          |          |        |
| Other visual experiences | Yes          | 8 (22)              | 28 (78)  | 0.75     | .385     | -.07   |
|                          | No           | 20 (16)             | 105 (84) |          |          |        |
| Sound                    | Yes          | 18 (18)             | 82 (82)  | 0.07     | .794     | -.02   |
|                          | No           | 10 (16)             | 51 (84)  |          |          |        |
| Scent                    | Yes          | 12 (21)             | 45 (79)  | 0.82     | .364     | -.07   |
|                          | No           | 16 (15)             | 88 (85)  |          |          |        |
| Taste                    | Yes          | 11 (21)             | 42 (79)  | 0.62     | .430     | -.06   |
|                          | No           | 17 (16)             | 84 (91)  |          |          |        |
| Touch                    | Yes          | 9 (21)              | 33 (79)  | 0.65     | .422     | -.06   |
|                          | No           | 19 (16)             | 100 (84) |          |          |        |
| Pain                     | Yes          | 13 (26)             | 37 (74)  | 3.74     | .053     | -.15   |
|                          | No           | 15 (14)             | 96 (86)  |          |          |        |
| Emotion                  | Yes          | 12 (21)             | 45 (79)  | 0.82     | .364     | -.07   |
|                          | No           | 16 (15)             | 88 (85)  |          |          |        |
| Personality              | Yes          | 10 (20)             | 40 (80)  | 0.34     | .558     | -.05   |
|                          | No           | 18 (16)             | 93 (84)  |          |          |        |

Table 9: Visual disturbances among female synaesthetes (N = 161), split by inducer types. Highlighted cells indicate largest unstandardised residual within a chi-square (significant and near-significant results only; \* indicates standardized residual has a p-value of < .05), with a superscript + indicating that the cell has a higher value than expected and a superscript – indicating that the cell has a lower value than expected. P-values are two-tailed.

| Inducer type             | Has inducer? | Visual disturbances? |         | $\chi^2$ | <i>p</i> | $\phi$ |
|--------------------------|--------------|----------------------|---------|----------|----------|--------|
|                          |              | Yes (%)              | No (%)  |          |          |        |
| Linguistic sequences     | Yes          | 49 (34)              | 94 (66) | 1.71     | .190     | .10    |
|                          | No           | 9 (50)               | 9 (50)  |          |          |        |
| Spoken words             | Yes          | 39 (39)              | 62 (61) | 0.79     | .375     | -.07   |
|                          | No           | 19 (32)              | 41 (68) |          |          |        |
| Written words            | Yes          | 39 (40)              | 58 (60) | 1.85     | .174     | -.11   |
|                          | No           | 19 (30)              | 45 (70) |          |          |        |
| Other visual experiences | Yes          | 21 (58)*+            | 15 (42) | 10.01    | .002     | -.25   |
|                          | No           | 37 (30)              | 88 (70) |          |          |        |
| Sound                    | Yes          | 39 (39)              | 61 (61) | 1.01     | .314     | -.08   |
|                          | No           | 19 (31)              | 42 (69) |          |          |        |
| Scent                    | Yes          | 30 (53)*+            | 27 (47) | 10.56    | .001     | -.26   |
|                          | No           | 28 (27)              | 76 (73) |          |          |        |
| Taste                    | Yes          | 28 (53)*+            | 25 (47) | 9.68     | .002     | -.25   |
|                          | No           | 30 (28)              | 78 (72) |          |          |        |
| Touch                    | Yes          | 22 (52)              | 20 (48) | 6.60     | .010     | -.20   |
|                          | No           | 36 (30)              | 83 (70) |          |          |        |
| Pain                     | Yes          | 24 (48)              | 26 (52) | 4.51     | .034     | -.17   |
|                          | No           | 34 (31)              | 77 (69) |          |          |        |
| Emotion                  | Yes          | 30 (53)*+            | 27 (47) | 10.56    | .001     | -.26   |
|                          | No           | 28 (27)              | 76 (73) |          |          |        |
| Personality              | Yes          | 27 (54)*+            | 23 (46) | 10.17    | .001     | -.25   |
|                          | No           | 31 (28)              | 80 (72) |          |          |        |

Table 10: Migraine (with and without aura) among female synaesthetes (N = 161), split by concurrent types. Highlighted cells indicate largest unstandardized residual within a chi-square (for significant and near-significant results only; \* indicates standardized residual has a p-value of < .05), with a superscript + indicating that the cell has a higher value than expected and a superscript – indicating that the cell has a lower value than expected. P-values are two-tailed.

| Concurrent type  | Has concurrent? | Migraine? |         | $\chi^2$ | <i>p</i> | $\phi$ |
|------------------|-----------------|-----------|---------|----------|----------|--------|
|                  |                 | Yes (%)   | No (%)  |          |          |        |
| Colour           | Yes             | 42 (32)   | 89 (68) | 0.05     | .827     | -.02   |
|                  | No              | 9 (30)    | 21 (70) |          |          |        |
| Shape            | Yes             | 28 (38)   | 42 (62) | 2.40     | .121     | -.12   |
|                  | No              | 23 (26)   | 64 (74) |          |          |        |
| Spatial location | Yes             | 25 (27)   | 66 (73) | 1.71     | .191     | .10    |
|                  | No              | 26 (37)   | 44 (63) |          |          |        |
| Sound            | Yes             | 13 (30)   | 30 (70) | 0.06     | .812     | .02    |
|                  | No              | 38 (32)   | 80 (68) |          |          |        |
| Scent            | Yes             | 15 (35)   | 28 (65) | 0.28     | .598     | -.04   |
|                  | No              | 36 (31)   | 82 (69) |          |          |        |
| Taste            | Yes             | 12 (27)   | 33 (73) | 0.72     | .395     | .07    |
|                  | No              | 39 (34)   | 77 (66) |          |          |        |
| Touch            | Yes             | 16 (46)   | 19 (54) | 4.07     | .044     | -.16   |
|                  | No              | 35 (28)   | 91 (72) |          |          |        |
| Pain             | Yes             | 7 (27)    | 19 (73) | 0.32     | .569     | .05    |
|                  | No              | 44 (33)   | 91 (67) |          |          |        |
| Emotion          | Yes             | 22 (31)   | 48 (69) | 0.00     | .953     | .01    |
|                  | No              | 29 (32)   | 62 (68) |          |          |        |
| Gender           | Yes             | 11 (28)   | 28 (72) | 0.29     | .592     | .04    |
|                  | No              | 40 (33)   | 82 (67) |          |          |        |
| Personality      | Yes             | 19 (30)   | 44 (70) | 0.11     | .740     | .03    |
|                  | No              | 32 (33)   | 66 (67) |          |          |        |

Table 11: Migraine with aura among female synaesthetes (N = 161), split by concurrent types. Highlighted cells indicate largest unstandardized residual within a chi-square (for significant and near-significant results only; \* indicates standardized residual has a p-value of < .05), with a superscript + indicating that the cell has a higher value than expected and a superscript – indicating that the cell has a lower value than expected. P-values are two-tailed.

| Concurrent type  | Has concurrent? | Migraine with aura?   |          | $\chi^2$ | <i>p</i> | $\varphi$ |
|------------------|-----------------|-----------------------|----------|----------|----------|-----------|
|                  |                 | Yes (%)               | No (%)   |          |          |           |
| Colour           | Yes             | 25 (19)               | 106 (81) | 1.40     | .236     | -.09      |
|                  | No              | 3 (10)                | 27 (90)  |          |          |           |
| Shape            | Yes             | 13 (18)               | 61 (82)  | 0.00     | 1.000    | .00       |
|                  | No              | 15 (17)               | 72 (83)  |          |          |           |
| Spatial location | Yes             | 12 (13)               | 79 (87)  | 2.58     | .109     | .13       |
|                  | No              | 16 (23)               | 54 (77)  |          |          |           |
| Sound            | Yes             | 7 (16)                | 36 (84)  | 0.05     | .822     | .02       |
|                  | No              | 21 (18)               | 97 (82)  |          |          |           |
| Scent            | Yes             | 9 (21)                | 34 (79)  | 0.51     | .475     | -.06      |
|                  | No              | 19 (16)               | 99 (84)  |          |          |           |
| Taste            | Yes             | 7 (16)                | 38 (84)  | 0.15     | .702     | .03       |
|                  | No              | 21 (18)               | 95 (82)  |          |          |           |
| Touch            | Yes             | 12 (34) <sup>*+</sup> | 23 (66)  | 8.89     | .003     | -.24      |
|                  | No              | 16 (13)               | 110(87)  |          |          |           |
| Pain             | Yes             | 5 (19)                | 21 (81)  | 0.07     | .787     | -.02      |
|                  | No              | 23 (17)               | 112 (83) |          |          |           |
| Emotion          | Yes             | 12 (17)               | 58 (83)  | 0.01     | .942     | .01       |
|                  | No              | 18 (18)               | 75 (82)  |          |          |           |
| Gender           | Yes             | 7 (18)                | 32 (82)  | 0.01     | .916     | -.01      |
|                  | No              | 21 (17)               | 101 (83) |          |          |           |
| Personality      | Yes             | 12 (19)               | 51 (81)  | 0.20     | .657     | -.04      |
|                  | No              | 16 (16)               | 82 (84)  |          |          |           |

Table 12: Visual disturbances among female synaesthetes (N = 161), split by concurrent types. Highlighted cells indicate largest unstandardized residual within a chi-square (for significant and near-significant results only; \* indicates standardized residual has a p-value of < .05), with a superscript + indicating that the cell has a higher value than expected and a superscript – indicating that the cell has a lower value than expected. P-values are two-tailed.

| Concurrent type  | Has concurrent? | Visual disturbances? |         | $\chi^2$ | <i>p</i> | $\phi$ |
|------------------|-----------------|----------------------|---------|----------|----------|--------|
|                  |                 | Yes (%)              | No (%)  |          |          |        |
| Colour           | Yes             | 45 (34)              | 86 (66) | 0.86     | .355     | .07    |
|                  | No              | 13 (43)              | 17 (57) |          |          |        |
| Shape            | Yes             | 24 (32)              | 50 (68) | 0.77     | .381     | .07    |
|                  | No              | 34 (39)              | 53 (61) |          |          |        |
| Spatial location | Yes             | 33 (36)              | 58 (64) | 0.01     | .943     | -.01   |
|                  | No              | 25 (36)              | 45 (64) |          |          |        |
| Sound            | Yes             | 15 (35)              | 38 (65) | 0.03     | .856     | .01    |
|                  | No              | 43 (36)              | 75 (64) |          |          |        |
| Scent            | Yes             | 19 (44)              | 24 (56) | 1.70     | .193     | -.10   |
|                  | No              | 39 (33)              | 79 (67) |          |          |        |
| Taste            | Yes             | 21 (47)              | 24 (53) | 3.07     | .080     | -.13   |
|                  | No              | 37 (32)              | 79 (68) |          |          |        |
| Touch            | Yes             | 17 (49)              | 18 (51) | 3.06     | .081     | -.14   |
|                  | No              | 41 (33)              | 85 (68) |          |          |        |
| Pain             | Yes             | 14 (54)              | 12 (46) | 4.27     | .039     | -.16   |
|                  | No              | 44 (33)              | 91 (67) |          |          |        |
| Emotion          | Yes             | 30 (43)              | 40 (57) | 2.51     | .113     | -.13   |
|                  | No              | 28 (31)              | 63 (69) |          |          |        |
| Gender           | Yes             | 11 (28)              | 28 (72) | 1.37     | .243     | .09    |
|                  | No              | 47 (39)              | 75 (61) |          |          |        |
| Personality      | Yes             | 25 (40)              | 38 (60) | 0.60     | .438     | -.06   |
|                  | No              | 33 (34)              | 65 (66) |          |          |        |

## 4. Discussion

To summarise, we replicated Rich et al.'s (2005) finding of no overall association between migraine and synaesthesia. Furthermore, we did not find the predicted increased incidence of migraine with aura/visual disturbances in grapheme colour synaesthesia. However, we did find associations of certain synaesthetic inducer categories and visual disturbances in headache in our participants: scent, emotion, personality (as in, for

example, personality-colour synaesthesia), non-linguistic visual experiences, and taste, all fell into this category. Among concurrents, touch was associated with migraine with aura, but no other associations were found. However, these results must be taken with a pinch of salt since false positives are possible even with our FDR correction for multiple comparisons.

From the lack of association between grapheme-colour synaesthesia and migraine with aura we can conclude that the cortical hyperexcitability seen in each group is likely to have two separate causes. It is important here to appreciate that hyperexcitability is but one of a number of visual processing differences that are associated with migraine. Poorer performance in measures of sensitivity to contrast, orientation, colour, and global form and motion, have all been found in migraine (De Marinis et al., 2007; McKendrick et al., 2006; McKendrick & Sampson, 2009). While grapheme-colour synaesthesia is similarly associated with poorer global motion perception, it is also associated with *improved* sensitivity to colour (Banissy et al., 2013). These differences suggest that the underlying sensory processing differences in migraine and synaesthesia are not completely overlapping, and that the root cause in the two cases are not the same. As discussed earlier, it is possible that hyperexcitability is the cause of increased neural noise in synaesthesia, but a compensation for increased noise in migraine.

It is also difficult to conclude from our findings whether the immune hypothesis of synaesthesia (Carmichael & Simner, 2013) is correct, since we did not find that synaesthesia is in general associated with migraine, but specific inducers appear to be associated with visual disturbances in headache (a hallmark of migraine with aura) and touch as a concurrent is associated with migraine with aura. This interpretation of the data also explains the asymmetry between the increased incidence of synaesthesia found among migraine sufferers (Jürgens et al., 2014) and our own null result: the association with

synaesthesia can be attributed specifically to an increased incidence of those who experience touch as a concurrent in the migraine with aura group. Indeed, in Jürgens et al., the highest proportion of migraine patients (and migraine patients split into those with and without aura) is seen among auditory-sensory synaesthetes (Jürgens et al., Table e-2). These synaesthetes have tactile concurrents (May, personal communication), in line with our findings. However, it should be noted that this group's auditory inducers are not in line with our findings. Again, we note that our results should be interpreted with caution.

There are also possible relationships between synaesthesia and migraine that the current data do not allow us to rule out. First, aura without headache is possible, but is uncommon, especially in the young, and is a diagnosis of exclusion (Kunkell, 2005). It is possible that this group *does* have an increased incidence of synaesthesia compared to the general population but we have simply been unable to detect it. Furthermore, since aura sometimes manifests as temporary synaesthesia (Alstadhaug & Benjaminsen, 2010; Podoll & Robinson, 2002), it is also possible that some people with aura without headache are misreporting their aura as synaesthesia. We believe this latter possibility is unlikely, though, since synaesthesia occurring during aura is probably rare (because there are case studies, indicating that it can happen, but no prevalence study, indicating that it is probably not common enough to warrant one).

We end our discussion with two caveats. First, the data in this study are based on self-reports of both synaesthesia and migraine. However, we believe that people are likely to be accurately reporting their own experiences since they did not know that the questionnaire related to headaches prior to taking part, and we encouraged both synaesthetes and non-synaesthetes to take part. Self-disclosure is more common among women than among men, and this sex difference appears to be a function of a male

tendency not to disclose rather than a female tendency to confabulate (Dindia & Allen, 1992), so the inclusion of female participants only should mean that self-reports in this study are accurate. Further, of the 24 participants who reported synaesthesia and completed a consistency test, only one failed the test. This test may be failed for a variety of reasons, only one of which is confabulation about synaesthesia; for example, some synaesthetes have reported informally to the experimenters that the way in which the consistency test works is not immediately obvious. Nonetheless, this one participant suggests a maximum confabulation rate of 1/24, which scales to 8 of the 188 synaesthetes who took part – a number small enough to be unlikely to influence the results.

Second, many more women than men volunteered to take part in our study, which is likely due to the biased sex distribution in some of the groups we approached (psychology students, online communities of self-identified synaesthetes). Consequently, it is possible that synaesthesia and migraine are qualitatively different in men and women and so the conclusions drawn in this study (based on female participants' answers) may not be generalisable to men.

In sum, this prevalence study has confirmed that there is no general association between synaesthesia and migraine, but that particular types of synaesthesia may be associated with migraine with aura and more generally with visual disturbances in headache. These selective associations generate new hypotheses about the nature and causes of certain types of headache.

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## Appendix 1: Probability calculations for the prevalence in migraine and synaesthesia

Migraine is three times more prevalent in women than in men. Here, we consider the implications for prevalence of synaesthesia, if there were a link between the two conditions. We assume equal numbers of men and women in the population:

$$p(\text{♀})=0.5$$

$$p(\text{♂})=0.5$$

but different rates of migraine:

$$p(M \mid \text{♀}) = 0.15$$

$$p(M \mid \text{♂})=0.05$$

where  $p(M \mid \text{♀})$ , for example, represents the probability that someone experiences migraine, given that she is female. We also assume that the rate of synaesthesia  $p(S)$ , over the whole population, is 1%:

$$p(S)=0.01$$

This overall rate of synaesthesia depends on both the ratio of men and women in the population, and the rate of synaesthesia in each group:

$$p(S) = p(S|\text{♀})p(\text{♀}) + p(S|\text{♂})p(\text{♂})$$

$$p(S) = 0.5(p(S|\text{♀}) + p(S|\text{♂}))$$

We now assume that the rate of synaesthesia is different in migraine, but otherwise does not differ between men and women:

$$p(S | M, \text{♀}) = ka$$

$$p(S | \sim M, \text{♀}) = a$$

$$p(S | M, \text{♂}) = ka$$

$$p(S | \sim M, \text{♂}) = a$$

where  $k$  and  $a$  are constants and  $k$  is the degree to which rates of synaesthesia is increased in migraine. We have unequal rates of migraine in men and women, and unequal rates of synaesthesia in people with and without migraine. We can now calculate the probability of synaesthesia separately for men and women:

$$\begin{aligned} p(S | \text{♀}) &= p(S | M, \text{♀}) \cdot p(M | \text{♀}) + p(S | \sim M, \text{♀}) \cdot p(\sim M | \text{♀}) \\ &= 0.15ka + 0.85a \end{aligned}$$

$$\begin{aligned}
 p(S \mid \sigma) &= p(S \mid M, \sigma).p(M \mid \sigma) + p(S \mid \sim M, \sigma).p(\sim M \mid \sigma) \\
 &= 0.05ka + 0.95a
 \end{aligned}$$

Since the rate of synaesthesia in the total population is 1%,

$$0.5(0.15ka + 0.85a) + 0.5(0.05ka + 0.95a) = 0.01$$

$$(0.85 + 0.95)a + (0.15 + 0.05)ka = 0.02$$

If we assume a large difference in the rate of synaesthesia in migraine, such that  $k=3$ , this gives:

$$\begin{aligned}
 p(S \mid \text{♀}) &= 0.15ka + 0.85a \\
 &= 0.15 \cdot 3 \cdot 0.0083 + 0.85 \cdot 0.0083 \\
 &= 1.07\%
 \end{aligned}$$

and

$$\begin{aligned}
 p(S \mid \sigma) &= 0.05ka + 0.95a \\
 &= 0.05 \cdot 3 \cdot 0.0083 + 0.95 \cdot 0.0083 \\
 &= 0.91\%
 \end{aligned}$$

In other words, the rate of synaesthesia for both men and women is predicted to be close to 1%. We can also calculate  $p(M \mid S, \text{♀})$  and  $p(M \mid S, \sigma)$ :

$$p(M|S, \text{♀}) = p(S|M, \text{♀})p(M, \text{♀})/p(S|\text{♀})=0.35$$

$$p(M|\sim S, \text{♀}) = p(\sim S|M, \text{♀})p(M, \text{♀})/p(\sim S|\text{♀})=0.15$$

In other words, if there is a greater rate of synaesthesia in migraine we should indeed see a greater rate of migraine in synaesthesia. We can also perform the same calculations for male participants, in order to compare the rate of migraine in synaesthetes across the two sexes:

$$p(M|S, \text{♂}) = p(S|M, \text{♂})p(M, \text{♂})/p(S|\text{♂})=0.14$$

$$p(M|\sim S, \text{♀}) = p(\sim S|M, \text{♀})p(M, \text{♀})/p(\sim S|\text{♀})=0.05$$

This means that we predict the rate of migraine should be higher in women than men, for both synaesthetes and non-synaesthetes.

## Appendix 1: Questionnaire

### *Personal experiences in synaesthetes and non-synaesthetes.*

#### Demographic information

How old are you? (Possible answer range: 18-100)

What is your gender?

- Female
- Male
- Other
- Prefer not to say

#### About your synaesthesia

Please read the following paragraph carefully.

*What is synaesthesia?*

In our everyday lives we are constantly combining information that is received from the senses. For example, when we smell grass which has just been cut we expect this sense to be complemented by the sight of grass cuttings on the ground. At a more abstract level we may make metaphorical associations between concepts such as a 'tree of knowledge' or a 'melting pot of ideas'.

A small proportion of the population consistently makes strong associations between different senses or aspects of the same sense. This phenomenon is called 'synaesthesia'. People who experience synaesthesia find that a percept in one of the senses automatically triggers another sensory experience. One of the most common forms of synaesthesia is called 'grapheme- colour' synaesthesia' in which seeing a black number or letter triggers a perception of colour. Other types of synaesthesia include associating musical notes with colours, combining words with tastes and seeing numbers in unusual spatial configurations. There are approximately 61 recorded types of synaesthesia and this number is growing as study in this field continues.

Having read the above paragraph, how well would you say you understand what synaesthesia is on a scale of 0 to 10, where 0 is *I have no understanding of synaesthesia* and 10 is *I understand exactly what synaesthesia is, even if I do not experience it myself?* \_\_\_\_

Do you think you have any type of synaesthesia?

- Yes
- No
- Not sure

If you have answered *yes* or *not sure*, please fill out the table below. If you have answered *no*, please skip to the next section (**About your personality**).

Please check the kinds of synaesthesia you have in the table below. The left-hand column lists things that might cause synaesthesia, and the top row lists things that can be experienced as a result of synaesthesia, so if you experience colours when you see letters, you should check the top left hand box.

|   | Colours | Shapes | Spatial | Sounds | Scents | Tastes | Touch | Pain | Emotion | Gender | Personality | Other (please state) |
|---|---------|--------|---------|--------|--------|--------|-------|------|---------|--------|-------------|----------------------|
| Letters                                       |         |        |         |        |        |        |       |      |         |        |             |                      |
| Numbers                                       |         |        |         |        |        |        |       |      |         |        |             |                      |
| Days of the week                              |         |        |         |        |        |        |       |      |         |        |             |                      |
| Months of the year                            |         |        |         |        |        |        |       |      |         |        |             |                      |
| Words (spoken)                                |         |        |         |        |        |        |       |      |         |        |             |                      |
| Words (written)                               |         |        |         |        |        |        |       |      |         |        |             |                      |
| Other visual experiences (please state below) |         |        |         |        |        |        |       |      |         |        |             |                      |
| Sounds  |         |        |         |        |        |        |       |      |         |        |             |                      |
| Scents  |         |        |         |        |        |        |       |      |         |        |             |                      |
| Tastes  |         |        |         |        |        |        |       |      |         |        |             |                      |
| Touch   |         |        |         |        |        |        |       |      |         |        |             |                      |
| Pain  |         |        |         |        |        |        |       |      |         |        |             |                      |
| Emotion                                       |         |        |         |        |        |        |       |      |         |        |             |                      |
| Personality                                   |         |        |         |        |        |        |       |      |         |        |             |                      |
| Other (please state below)                    |         |        |         |        |        |        |       |      |         |        |             |                      |

If you have any other synaesthetic experiences that do not fit in this table, please state them below.

|  |
|--|
|  |
|--|

If you have completed the Synaesthesia Battery at [www.synesthete.org](http://www.synesthete.org), please share your results with us. You can do this by logging in, selecting 'Go To My Battery' from the toolbar, then on 'Click here to give a researcher access to your data'. When it prompts you for an email address, please enter [c.n.jonas@uel.ac.uk](mailto:c.n.jonas@uel.ac.uk). Please note the email address you used to register with the Synaesthesia Battery here so that we can link your results on the battery with your answers to this questionnaire:

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### About your personality

| I see myself as someone who...             | Disagree strongly | Disagree a little | Neither agree nor disagree | Agree a little | Agree strongly |
|--|-------------------|-------------------|----------------------------|----------------|----------------|
| 1. Is talkative                            |                   |                   |                            |                |                |
| 2. Tends to find fault with others         |                   |                   |                            |                |                |
| 3. Does a thorough job                     |                   |                   |                            |                |                |
| 4. Is depressed, blue                      |                   |                   |                            |                |                |
| 5. Is original, comes up with new ideas    |                   |                   |                            |                |                |
| 6. Is reserved                             |                   |                   |                            |                |                |
| 7. Is helpful and unselfish with others    |                   |                   |                            |                |                |
| 8. Can be somewhat careless                |                   |                   |                            |                |                |
| 9. Is relaxed, handles stress well         |                   |                   |                            |                |                |
| 10. Is curious about many different things |                   |                   |                            |                |                |
| 11. Is full of energy                      |                   |                   |                            |                |                |
| 12. Starts quarrels with others            |                   |                   |                            |                |                |
| 13. Is a reliable worker                   |                   |                   |                            |                |                |
| 14. Can be tense                           |                   |                   |                            |                |                |
| 15. Is ingenious, a deep thinker           |                   |                   |                            |                |                |
| 16. Generates a lot of enthusiasm          |                   |                   |                            |                |                |
| 17. Has a forgiving nature                 |                   |                   |                            |                |                |
| 18. Tends to be disorganized               |                   |                   |                            |                |                |
| 19. Worries a lot                          |                   |                   |                            |                |                |
| 20. Has an active imagination              |                   |                   |                            |                |                |

|   |  |  |  |  |  |
|---|--|--|--|--|--|
| 21. Tends to be quiet                             |  |  |  |  |  |
| 22. Is generally trusting                         |  |  |  |  |  |
| 23. Tends to be lazy                              |  |  |  |  |  |
| 24. Is emotionally stable, not easily upset       |  |  |  |  |  |
| 25. Is inventive                                  |  |  |  |  |  |
| 26. Has an assertive personality                  |  |  |  |  |  |
| 27. Can be cold and aloof                         |  |  |  |  |  |
| 28. Perseveres until the task is finished         |  |  |  |  |  |
| 29. Can be moody                                  |  |  |  |  |  |
| 30. Values artistic, aesthetic experiences        |  |  |  |  |  |
| 31. Is sometimes shy, inhibited                   |  |  |  |  |  |
| 32. Is considerate and kind to almost everyone    |  |  |  |  |  |
| 33. Does things efficiently                       |  |  |  |  |  |
| 34. Remains calm in tense situations              |  |  |  |  |  |
| 35. Prefers work that is routine                  |  |  |  |  |  |
| 36. Is outgoing, sociable                         |  |  |  |  |  |
| 37. Is sometimes rude to others                   |  |  |  |  |  |
| 38. Makes plans and follows through with them     |  |  |  |  |  |
| 39. Gets nervous easily                           |  |  |  |  |  |
| 40. Likes to reflect, play with ideas             |  |  |  |  |  |
| 41. Has few artistic interests                    |  |  |  |  |  |
| 42. Likes to cooperate with others                |  |  |  |  |  |
| 43. Is easily distracted                          |  |  |  |  |  |
| 44. Is sophisticated in art, music, or literature |  |  |  |  |  |

## About your health

How often do you have a headache?

- All the time
- About once a day
- Several times a week
- Several times a month
- Once a month or less frequent
- Once a year or less frequent

How bad are your worst headaches?

- Noticeable but not distracting
- Fairly distracting
- Bad enough to take time off work/cancel a social engagement
- So severe you have to rest
- Almost unbearable

Either before your headache starts or during it, do you notice any of the following?

Change in your vision?

- Never
- Sometimes
- Usually
- Always
- Don't know

If you do notice a change in your vision, is it:

- Always on the left
- Usually on the left
- Sometimes left, sometimes right
- Always on the right
- Usually on the right
- Always on both sides
- Usually on both sides
- No changes in vision

If you do notice a change in your vision, please describe briefly what happens in the box below. (Free response)

|  |
|--|
|  |
|--|

Mistakes in your speech or difficulty in finding your words?

- Never
- Sometimes
- Usually
- Always
- Don't know

Numbness or tingling or some other strange feeling in any part of your body?

- Never
- Sometimes
- Usually
- Always
- Don't know

If you do notice a feeling of this kind, is it:

- Always on the left
- Usually on the left
- Sometimes left, sometimes right
- Always on the right

- Usually on the right
- Always on both sides
- Usually on both sides
- No changes in feeling

Weakness in any part of your body?

- Never
- Sometimes
- Usually
- Always
- Don't know

If you do notice a feeling of this kind, is it:

- Always on the left
- Usually on the left
- Sometimes left, sometimes right
- Always on the right
- Usually on the right
- Always on both sides
- Usually on both sides
- No changes in feeling

During your headache, but not before, do you: (Please tick your answers)

|                          | Never | Sometimes | Usually | Always | Don't know |
|--------------------------|-------|-----------|---------|--------|------------|
| Lose your appetite       |       |           |         |        |            |
| Feel sick in the stomach |       |           |         |        |            |
| Vomit                    |       |           |         |        |            |
| Feel light-headed        |       |           |         |        |            |

5. Have you ever seen a doctor about headaches and/or migraine? (Free response)