

Migraine in Synesthetes and Nonsynesthetes: A Prevalence Study

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Abstract

Synesthesia 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 synesthesia links synesthesia to immune-related conditions such as migraine. More specifically, migraine with aura may be linked to grapheme-color synesthesia as both involve cortical hyperexcitability. In this study, 161 female synesthetes, and 92 female nonsynesthetes, completed an online questionnaire about synesthesia and migraine. We found no general link between migraine and synesthesia nor between migraine with aura and grapheme-color synesthesia. Exploratory analyses, however, showed that certain types of synesthetic inducer (non-linguistic visual experiences, scent, taste, emotion and personality) were associated with visual disturbances in headache among female participants, and touch as a concurrent was associated with migraine with aura. On the basis of our exploratory analyses, we hypothesize that specific subtypes of synesthesia are related to migraine. The relationship between these two conditions is likely to become clearer as research on the underlying causes of synesthesia and migraine progresses.

Keywords

headache, hyperexcitability, synesthesia

Introduction

Migraine is a neurological condition characterized 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% to 17% (Stewart, Shechter, & Rasmussen, 1994). The criteria for diagnosing migraine require at least five attacks of a lateralized, pulsating headache,

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lasting 4 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 5 to 20 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).

Synesthesia is also a neurological condition but is otherwise markedly different from migraine. Synesthesia is usually reported by synesthetes to be pleasant or neutral, rather than aversive, and is characterized 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 color; 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, synesthetes report that they have had their synesthesia for as long as they can remember.

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

The Immune Hypothesis of Synesthesia

Recently, Carmichael and Simner (2013) have suggested that the development of synesthesia 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 synesthesia, which have focused 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 the disinhibited feedback proposed to underlie synesthesia. Consequently, Carmichael and Simner hypothesize that synesthesia 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, 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 (Bockowski, Sobaniec, & Zelazowska-Rutowska, 2009; Bruno, Carpino, Carpino, & Zicari, 2007; Perini et al., 2005; Yilmaz et al., 2010). Carmichael and Simner (2013) also proposed that cytokines might play a role in synesthesia.

Cortical Hyperexcitability in Synesthesia and Migraine

An association between synesthesia 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 with 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-color synesthesia, 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 synesthesia, it is not known whether this effect is specific for grapheme-color synesthesia, or whether this is an example of a more widespread phenomenon.

Visual Processing in Migraine and Synesthesia

The immune hypothesis of synesthesia, and the hyperexcitation found in both grapheme-color synesthesia 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 synesthesia 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. (2011) proposed that hyperexcitability in grapheme-color synesthesia 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, Manahilov, Loffler, Gordon, & Dutton, 2010).

There are a number of reasons to suppose that the nature of hyperexcitability differs between migraine and synesthesia, 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 synesthesia, 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-color synesthesia is associated with enhanced ventral stream processing but impaired dorsal stream processing (Banissy, Tester et al., 2013; Barnett et al., 2008). Sensory processing in migraine is reduced in measures of contrast sensitivity, color, 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.

Are Migraine and Synesthesia Associated?

While cortical hyperexcitability is common to both grapheme-color synesthesia 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 synesthesia and migraine is limited. Visual-gustatory and auditory-visual synesthesia occurring specifically during migraine with aura have previously been reported in isolated case studies (Alstadhaug & Benjaminsen, 2010; Podoll & Robinson, 2002), and one synesthete has reported that synesthetic 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 synesthesia (Afra et al., 2012). More generally, migraine sufferers have been hypothesized 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 in migraine. These included transient visual illusions, hallucinations, and, of relevance to our study, synesthesia. They found an increased rate of synesthesia in migraine and particularly so with migraine with aura (Jürgens, Schulte, & May, 2014). However, since the study was used to assess the extent of sensory and neurological symptoms in general in migraine, they did not record the specific sensory or conceptual categories of inducers and concurrents in any detail. Also, the authors discussed the possibility that the use of a limited number of questions and recruitment of participants via a headache center, 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 synesthetes than in nonsynesthetes. However, they did not distinguish between migraine with and without aura nor between different types of synesthesia. The aim of our study was to break down these subgroups to analyze 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., 1994), while there is no difference in the prevalence of synesthesia across the sexes (Simner et al., 2006). While we would expect an association between migraine and synesthesia to be reflected in a greater rate of synesthesia 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 assume a rate of synesthesia in migraine that was, say, 3 times that in

people without migraine, we can calculate the predicted relative prevalence of synesthesia in men and women. These calculations are provided in Appendix A. However, given the very low prevalence of synesthesia, this would be unlikely to be detectable. For example, if the overall rate of grapheme-color synesthesia 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 synesthete and nonsynesthete populations.

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

Thus, we hypothesized that while there would not be a higher incidence of migraine among synesthetes, there would be a higher incidence of migraine with aura (but not other types of headaches) in grapheme-color synesthesia (but not other kinds of synesthesia). In addition to the strict criteria for the diagnosis of migraine with aura, we also hypothesized that grapheme-color synesthesia 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 synesthetes were associated with migraine, migraine with aura or visual disturbances in headaches, though we did not make any specific predictions about these possible associations.

Methods

Three hundred and nine participants¹ (mean age: 27.97 years; $SD = 12.20$, range = 18–82) were recruited via online communities of research volunteers and synesthetes, and from among the personal contacts of the researchers, to fill out an online questionnaire on synesthesia, personality characteristics (included as a check for response bias), and headache experiences (see Appendix B for full questionnaire). Participants were told that the questionnaire was about “personal experiences in synesthetes and nonsynesthetes” 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 Ethics Committee and is in accordance with the World Medical Association Helsinki Declaration (2008).

Of the participants, 56 were men and 253 were women. As we had so few male participants, and as there are known sex differences in self-reported rates of synesthesia (Simner et al., 2006), we report results for female participants only. Participants were classified on the basis of self-reported synesthesia (a subset of 23 had taken and passed the consistency test at www.synesthete.org—Eagleman, Kagan, Nelson, Sagaram, & Sarma, 2007—but this number was not sufficient to analyze consistency-verified and nonverified synesthetes 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, and 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, and 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 or cancel a social engagement, so severe you have to rest, and 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 to 72 h when it is left untreated (e.g., by pain medications)?* Possible answers: never, 1 to 2 times, 2 to 4 times, and 5 times or more. Never was categorized as *low frequency*, one 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, and 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, and 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 or migraine?* (Free response.)

Headache classification was determined as in Table 1. We summarize the number of female synesthetes and nonsynesthetes in each category in Table 2.

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 or no response
Migraine with aura	High	Bad	High	Yes	Yes	Any
Migraine without aura	High	Bad	High	No	Yes	Any
Tension ^a	Low or high	Not bad or bad	Low or high	No	No	Any
Other	Any other combination of symptoms					

^aTo 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 Synesthetes and Nonsynesthetes.

Headache classification	Synesthetes (N = 161)	Nonsynesthetes (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%)

Note. Percentages by column in parentheses.

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 synesthete 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.² We then summed the scores for all statements. If synesthetes were prone to agree with questions overall, they should have higher summed scores than the nonsynesthetes. However, this was not the case (Mann-Whitney $U(251) = 7065.00$; $Z = 0.61$, $p = .54$; synesthete median summed score = 155.0, nonsynesthete median summed score = 155.5).

Our second analysis was performed by recoding responses to reflect reverse-scoring and then performing Mann-Whitney tests on each personality characteristic. Compared with nonsynesthetes, synesthetes were significantly less extraverted (Mann-Whitney $U(251) = 6204.50$; $Z = -.215$, $p = .03$; synesthete median score = 24.0, nonsynesthete median score = 25.5) and significantly less agreeable (Mann-Whitney $U(251) = 6,272.00$; $Z = -2.03$, $p = .04$; synesthete median score = 34.0, nonsynesthete median score = 36.0). Synesthetes were also more open to new experiences than nonsynesthetes (Mann-Whitney $U(251) = 3738.50$; $Z = -6.59$, $p < .001$; synesthete median score = 42.0, nonsynesthete median score = 35.0). Synesthetes were nonsignificantly less conscientious (Mann-Whitney $U(251) = 6442.0$; $Z = -1.72$, $p = .09$; synesthete median score = 31.0, nonsynesthete median score = 33.0) and more neurotic (Mann-Whitney $U(251) = 6730.0$; $Z = -1.21$, $p = .23$; synesthete median score = 27.0, nonsynesthete median score = 25.0) than nonsynesthetes.

Synesthetes are known to be less agreeable and more open to new experiences than nonsynesthetes (Banissy et al., 2013) as we found here. In the remaining three characteristics, synesthetes all report less socially desirable characteristics (significantly less extraversion, nonsignificantly less conscientiousness, and more neuroticism) than nonsynesthetes, 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 synesthesia at the start of the questionnaire (see Appendix B) and were asked to rate how well they understood the nature of synesthesia 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 synesthesia (synesthetes) and those who reported no types of synesthesia (nonsynesthetes). Both groups reported a good understanding of synesthesia, though synesthetes rated their understanding as better (median = 9) than nonsynesthetes (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 synesthetes' subjective knowledge of the experience of synesthesia.

We first assessed whether any particular headache classification was associated with synesthesia *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-color synesthesia would be particularly associated with migraine with aura. Given that it is not clear whether grapheme-color synesthesia is the only type of synesthesia associated with cortical hyperexcitability, we excluded synesthetes without grapheme-color synesthesia from this analysis but retained synesthetes who reported

other types of synesthesia alongside grapheme-color. We collapsed our headache classifications into those with migraine with aura and those without migraine with aura and our grapheme-color synesthesia classifications into those who self-reported letter-color and number-color synesthesia and those who reported no synesthesia (Table 3). Tests on the data in Table 3 found no significant result ($\chi^2(1) = 0.72, p = .40, \phi = -.06$).

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 ($\chi^2(1) = 1.50, p = .22, \phi = -.09$).

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

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

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

Table 3. Frequency of Migraine with Aura in Headache Among Female Grapheme-Color Synesthetes and Nonsynesthetes.

Migraine with aura?	Grapheme-color synesthetes (N = 95)	Nonsynesthetes (N = 92)
Yes	16 (17%)	20 (22%)
No	79 (83%)	72 (78%)

Note. Percentages by column in parentheses.

Table 4. Frequency of Visual Disturbances in Headache Among Female Grapheme-Color Synesthetes and Nonsynesthetes.

Visual disturbances?	Grapheme-color synesthetes (N = 95)	Nonsynesthetes (N = 92)
Yes	33 (35%)	40 (43%)
No	62 (65%)	52 (57%)

Note. Percentages by column in parentheses.

Table 5. Frequency of Migraine With Aura in Headache Among Female Grapheme-Color, Day-Color, and Month-Color Synesthetes and Nonsynesthetes.

Migraine with aura?	Synesthetes (N = 110)	Nonsynesthetes (N = 92)
Yes	17 (15%)	20 (22%)
No	93 (85%)	72 (78%)

Note. Percentages by column in parentheses.

where p_s is the probability of migraine with aura in the synesthesia group, and p_n is the probability of migraine with aura in the nonsynesthesia group. In our case, the odds ratio represents the strength with which migraine with aura is associated with synesthesia. A ratio greater than one indicates a positive association. We calculated 1,000,000 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 synesthetes with nonsynesthetes. 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).

Exploratory Analyses in the Synesthete Group

For these analyses, we split synesthete participants only into groups by reported inducer and concurrent,³ analyzing 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 to 10. As we have conducted multiple tests on the same data, we corrected the α -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.⁴ 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.

Although 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., nonlinguistic) visual experiences, scent, taste, emotion, and personality. Further, touch as a concurrent is associated with migraine with aura.

Discussion

To summarize, we replicated Rich et al.'s (2005) finding of no overall association between migraine and synesthesia. Furthermore, we did not find the predicted increased incidence of migraine with aura or visual disturbances in grapheme-color synesthesia. However, we did find associations of certain synesthetic inducer categories and visual disturbances in headache in our participants: scent, emotion, personality (as in, for example, personality-color synesthesia), nonlinguistic 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.

Table 6. Frequency of Visual Disturbances in Headache Among Female Grapheme-Color, Day-Color, and Month-Color Synesthetes and Nonsynesthetes.

Visual disturbances?	Synesthetes ($N = 110$)	Nonsynesthetes ($N = 92$)
Yes	36 (33%)	40 (43%)
No	74 (67%)	52 (57%)

Note. Percentages by column in parentheses.

Table 7. Migraine (With and Without Aura) Among Female Synesthetes ($N = 161$), Split by Inducer Types.

Inducer type	Has inducer	Migraine?		χ^2	p	φ
		Yes (%)	No (%)			
Linguistic sequences^a	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)			

Note. In all tables 7–12 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.

^aNumbers, letters, days, or months.

Table 8. Migraine With Aura Among Female Synesthetes ($N = 161$), Split by Inducer Types.

Inducer type	Has inducer?	Migraine with aura?		χ^2	p	φ
		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

(continued)

Table 8. Continued.

Inducer type	Has inducer?	Migraine with aura?		χ^2	<i>p</i>	ϕ
		Yes (%)	No (%)			
Taste	No	16 (15)	88 (85)	0.62	.430	-.06
	Yes	11 (21)	42 (79)			
Touch	No	17 (16)	84 (91)	0.65	.422	-.06
	Yes	9 (21)	33 (79)			
Pain	No	19 (16)	100 (84)	3.74	.053	-.15
	Yes	13 (26)	37 (74)			
Emotion	No	15 (14)	96 (86)	0.82	.364	-.07
	Yes	12 (21)	45 (79)			
Personality	No	16 (15)	88 (85)	0.34	.558	-.05
	Yes	10 (20)	40 (80)			
	No	18 (16)	93 (84)			

Note. In all tables 7–12 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.

Table 9. Visual Disturbances Among Female Synesthetes (*N* = 161), Split by Inducer Types.

Inducer type	Has inducer?	Visual disturbances?		χ^2	<i>p</i>	ϕ
		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)			

Note. In all tables 7–12 highlighted cells indicate largest unstandardized 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.

Table 10. Migraine (With and Without Aura) Among Female Synesthetes ($N = 161$), Split by Concurrent Types.

Concurrent type	Has concurrent?	Migraine?		χ^2	p	φ
		Yes (%)	No (%)			
Color	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)			

Note. In all tables 7–12 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.

Table 11. Migraine With Aura Among Female Synesthetes ($N = 161$), Split by Concurrent Types.

Concurrent type	Has concurrent?	Migraine with aura?		χ^2	p	φ
		Yes (%)	No (%)			
Color	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)			

(continued)

Table 11. Continued.

Concurrent type	Has concurrent?	Migraine with aura?		χ^2	<i>p</i>	ϕ
		Yes (%)	No (%)			
Touch	Yes	12 (34) ^{*+}	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)			

Note. In all tables 7–12 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.

Table 12. Visual Disturbances Among Female Synesthetes (*N* = 161), Split by Concurrent Types.

Concurrent type	Has concurrent?	Visual disturbances?		χ^2	<i>p</i>	ϕ
		Yes (%)	No (%)			
Color	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)			

Note. In all tables 7–12 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.

From the lack of association between grapheme-color synesthesia 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, color, 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-color synesthesia is similarly associated with poorer global motion perception, it is also associated with *improved* sensitivity to color (Banissy et al., 2013). These differences suggest that the underlying sensory processing differences in migraine and synesthesia are not completely overlapping, and that the root causes in the two cases are not the same. As discussed earlier, it is possible that hyperexcitability is the cause of increased neural noise in synesthesia, but a compensation for increased noise in migraine.

It is also difficult to conclude from our findings whether the immune hypothesis of synesthesia (Carmichael & Simner, 2013) is correct, since we did not find that synesthesia 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 synesthesia found among migraine sufferers (Jürgens et al., 2014) and our own null result: The association with synesthesia 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 synesthetes (Jürgens et al., 2014, Table e-2). These synesthetes have tactile concurrents (A, May, personal communication, 10th December, 2014) 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 synesthesia 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 (Kunkel, 2005). It is possible that this group *does* have an increased incidence of synesthesia compared with the general population, but we have simply been unable to detect it. Furthermore, since aura sometimes manifests as temporary synesthesia (Alstadhaug & Benjaminsen, 2010; Podoll & Robinson, 2002), it is also possible that some people with aura without headache are misreporting their aura as synesthesia. We believe this latter possibility is unlikely, though, since synesthesia 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 synesthesia 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 synesthetes and nonsynesthetes 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 synesthesia 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 synesthesia; for example, some synesthetes 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 synesthetes 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 synesthetes). Consequently, it is possible that synesthesia 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 generalizable to men.

In sum, this prevalence study has confirmed that there is no general association between synesthesia and migraine but that particular type of synesthesia 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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Conflict of interest

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Notes

1. 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 categorized 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 categorize the type of headaches they experienced. Finally, one participant was removed because they claimed to be a synesthete but did not pass the consistency test.
2. Because this test was about agreement with statements, *not* about the extent to which a participant felt, they had a certain personality characteristic.
3. Not including types of synesthesia 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 synesthesia), 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 synesthetes (Burrack, Knoch, & Brugger, 2006).

4. Where i = the rank of the p value, α = the threshold p value (i.e., .05) and m = the total number of p values.

References

- Afra, P., Anderson, J., Funke, M., Johnson, M., Matsuo, F., Constantino, T., . . . Warner, J. (2012). Neurophysiological investigation of idiopathic acquired auditory–visual synesthesia. *Neurocase*, *18*, 323–329. doi:10.1080/13554794.2011.608363
- Alstadhaug, K. B., & Benjaminsen, E. (2010). Synesthesia and migraine: case report. *BMC Neurology*, *10*, 121. doi:10.1186/1471-2377-10-121
- Aurora, S. K., & Wilkinson, F. (2007). The brain is hyperexcitable in migraine. *Cephalalgia*, *27*, 1442–1453. doi:10.1111/j.1468-2982.2007.01502.x
- Banissy, M. J., Holle, H., Cassell, J., Annett, L., Tsakanikos, E., Walsh, V., . . . Ward, J. (2013). Personality traits in people with synaesthesia: Do synaesthetes have an atypical personality profile? *Personality and Individual Differences*, *54*, 828–831. doi:10.1016/j.paid.2012.12.018
- Banissy, M. J., Tester, V., Muggleton, N. G., Janik, A. B., Davenport, A., Franklin, A., . . . Ward, J. (2013). Synesthesia for color is linked to improved color perception but reduced motion perception. *Psychological Science*, *24*, 2390–2397. doi:10.1177/0956797613492424
- Banissy, M. J., Walsh, V., & Ward, J. (2009). Enhanced sensory perception in synaesthesia. *Experimental Brain Research*, *196*, 565–571. doi:10.1007/s00221-009-1888-0
- Bargary, G., & Mitchell, K. J. (2008). Synaesthesia and cortical connectivity. *Trends in Neurosciences*, *31*, 335–342. doi:10.1016/j.tins.2008.03.007
- Barnett, K. J., Finucane, C., Asher, J. E., Bargary, G., Corvin, A. P., Newell, F. N., . . . Mitchell, K. J. (2008). Familial patterns and the origins of individual differences in synaesthesia. *Cognition*, *106*, 871–893. doi:10.1016/j.cognition.2007.05.003
- Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society. Series B (Methodological)*, *57*, 289–300.
- Bockowski, L., Sobaniec, W., & Zelazowska-Rutkowska, B. (2009). Proinflammatory plasma cytokines in children with migraine. *Pediatric Neurology*, *41*, 17–21. doi:10.1016/j.pediatrneurol.2009.02.001
- Brigo, F., Storti, M., Nardone, R., Fiaschi, A., Bongiovanni, L. G., Tezzon, F., . . . Manganotti, P. (2012). Transcranial magnetic stimulation of visual cortex in migraine patients: a systematic review with meta-analysis. *The Journal of Headache and Pain*, *13*, 339–349. doi:10.1007/s10194-012-0445-6
- Bruno, P. P., Carpino, F., Carpino, G., & Zicari, A. (2007). An overview on immune system and migraine. *European Review for Medical and Pharmacological Sciences*, *11*, 245–248.
- Burrack, A., Knoch, D., & Brugger, P. (2006). Mitempfindung in synaesthetes: Co-incidence or meaningful association? *Cortex*, *42*, 151–154. doi:10.1016/S0010-9452(08)70339-3
- Carmichael, D. A., & Simner, J. (2013). The immune hypothesis of synesthesia. *Frontiers in Human Neuroscience*, *7*, 563. doi:10.3389/fnhum.2013.00563
- De Marinis, M., Rinalduzzi, S., & Accornero, N. (2007). Impairment in color perception in migraine with and without aura. *Headache*, *47*, 895–904. doi:10.1111/j.1526-4610.2007.00774.x
- Dindia, K., & Allen, M. (1992). Sex differences in self-disclosure: A meta-analysis. *Psychological Bulletin*, *112*, 106–124. doi:10.1037/0033-2909.112.1.106
- Eagleman, D. M., Kagan, A. D., Nelson, S. S., Sagaram, D., & Sarma, A. K. (2007). A standardized test battery for the study of synesthesia. *Journal of Neuroscience Methods*, *159*, 139–145. doi:10.1016/j.jneumeth.2006.07.012
- Goadsby, P. J., Lipton, R. B., & Ferrari, M. D. (2002). Migraine—current understanding and treatment. *New England Journal of Medicine*, *346*, 257–270. doi:10.1056/NEJMra010917
- Headache Classification Subcommittee of the International Headache Society. (2004). The International Classification of Headache Disorders: 2nd Edition. *Cephalalgia*, *24*(Suppl. 1): 9–160. doi:10.1111/j.1468-2982.2003.00824.x
- Jäncke, L., Beeli, G., Eulig, C., & Hänggi, J. (2009). The neuroanatomy of grapheme–color synesthesia. *European Journal of Neuroscience*, *29*, 1287–1293. doi:10.1111/j.1460-9568.2009.06673.x

- John, O. P., & Srivastava, S. (1999). The Big Five trait taxonomy: History, measurement, and theoretical perspectives. In L. A. Pervin, & O. P. John (Eds), *Handbook of personality: Theory and research* (2nd ed. pp. 102–138). New York, NY: The Guilford Press.
- Jürgens, T. P., Schulte, L. H., & May, A. (2014). Migraine trait symptoms in migraine with and without aura. *Neurology*, *82*, 1416–1424. doi:10.1212/WNL.0000000000000337
- Kemper, R. H. A., Meijler, W. H., Korf, G., & Ter Horst, G. J. (2001). Migraine and function of the immune system: A meta-analysis of clinical literature published between 1966 and 1999. *Cephalgia*, *21*, 549–557. doi:10.1046/j.1468-2982.2001.00196.x
- Köhler, T., Eisentraut, R., & Graeber, E. (1995). Headache classification based on questionnaire data: Which symptoms are especially suitable? *Journal of Clinical Epidemiology*, *48*, 797–803. doi:10.1016/0895-4356(94)00182-P
- Kunkel, R. S. (2005). Migraine aura without headache: Benign, but a diagnosis of exclusion. *Cleveland Clinic Journal of Medicine*, *72*, 529–534. doi:10.3949/ccjm.72.6.529
- McKendrick, A. M., Badcock, D. R., & Gurgone, M. (2006). Vernier acuity is normal in migraine, whereas global form and global motion perception are not. *Investigative Ophthalmology & Visual Science*, *47*, 3213–3219. doi:10.1167/jovs.05-1549
- McKendrick, A. M., & Sampson, G. P. (2009). Low spatial frequency contrast sensitivity deficits in migraine are not visual pathway selective. *Cephalgia*, *29*, 539–549. doi:10.1111/j.1468-2982.2008.01817.x
- Novich, S., Cheng, S., & Eagleman, D. M. (2011). Is synaesthesia one condition or many? A large-scale analysis reveals subgroups. *Journal of Neuropsychology*, *5*, 353–371. doi:10.1111/j.1748-6653.2011.02015.x
- Palmer, J. E., Chronicle, E. P., Rolan, P., & Mulleners, W. M. (2000). Cortical hyperexcitability is cortical under-inhibition: Evidence from a novel functional test of migraine patients. *Cephalgia*, *20*, 525–532.
- Perini, F., D'Andrea, G., Galloni, E., Pignatelli, F., Billo, G., Alba, S., . . . Toso, V. (2005). Plasma cytokine levels in migraineurs and controls. *Headache*, *45*, 926–931. doi:10.1111/j.1526-4610.2005.05135.x
- Podoll, K., & Robinson, D. (2002). Auditory-visual synaesthesia in a patient with basilar migraine. *Journal of Neurology*, *249*, 476–477. doi:10.1007/s004150200042
- Rich, A. N., Bradshaw, J. L., & Mattingley, J. B. (2005). A systematic, large-scale study of synaesthesia: Implications for the role of early experience in lexical-colour associations. *Cognition*, *98*, 53–84. doi:10.1016/j.cognition.2004.11.003
- Schürks, M., Buring, J. E., & Kurth, T. (2010). Migraine, migraine features, and cardiovascular disease. *Headache*, *50*, 1031–1040. doi:10.1111/j.1526-4610.2009.01609.x
- Schwedt, T. J. (2013). Multisensory integration in migraine. *Current Opinion in Neurology*, *26*, 248. doi:10.1097/WCO.0b013e3283360edb1
- Simner, J., & Haywood, S. L. (2009). Tasty non-words and neighbours: The cognitive roots of lexical-gustatory synaesthesia. *Cognition*, *110*, 171–181. doi:10.1016/j.cognition.2008.11.008
- Simner, J., Mulvenna, C., Sagiv, N., Tsakanikos, E., Witherby, S. A., Fraser, C., . . . Ward, J. (2006). Synaesthesia: The prevalence of atypical cross-modal experiences. *Perception*, *35*, 1024. doi:10.1068/p5469
- Steiner, T. J., Scher, A. I., Stewart, W. F., Kolodner, K., Liberman, J., & Lipton, R. B. (2003). The prevalence and disability burden of adult migraine in England and their relationships to age, gender and ethnicity. *Cephalgia*, *23*, 519–527. doi:10.1046/j.1468-2982.2003.00568.x
- Stewart, W. F., Shechter, A., & Rasmussen, B. K. (1994). Migraine prevalence. A review of population-based studies. *Neurology*, *44*(6 Suppl. 4): S17–S23.
- Terhune, D. B., Tai, S., Cowey, A., Popescu, T., & Cohen, K. R. (2011). Enhanced cortical excitability in grapheme-color synesthesia and its modulation. *Current Biology*, *21*, 2006–2009. doi:10.1016/j.cub.2011.10.032
- Tibber, M. S., Kelly, M., Jansari, A., Dakin, S. C., & Shepherd, A. J. (2014). An inability to exclude visual noise in migraine. *Investigative Ophthalmology and Visual Science*, *55*, 2539–2546.

- Tyler, C. W. (2005). Varieties of synesthetic experience. In L. C. Robertson, & N. Sagiv (Eds), *Synesthesia: Perspectives from cognitive neuroscience* (pp. 34–46). New York, NY: Oxford University Press.
- Wagner, D. (2011). *The investigation of visual function in migraine* (PhD thesis). Glasgow Caledonian University, UK.
- Wagner, D., Manahilov, V., Loffler, G., Gordon, G. E., & Dutton, G. N. (2010). Visual noise selectivity degrades vision in migraine. *Investigative Ophthalmology & Visual Science*, *51*, 2294–2299. doi:10.1167/iops.09-4318
- Yang, W., Chu, B., Yang, J., Yu, Y., Wu, J., & Yu, S. (2014). Elevated audiovisual temporal interaction in patients with migraine without aura. *The Journal of Headache and Pain*, *15*, 1–10. doi:10.1186/1129-2377-15-44
- Yilmaz, I. A., Ozge, A., Erdal, M. E., Edgunlu, T. G., Cakmak, S. E., & Yalin, O. O. (2010). Cytokine polymorphism in patients with migraine: Some suggestive clues of migraine and inflammation. *Pain Medicine*, *11*, 492–497. doi:10.1111/j.1526-4637.2009.00791.x.

Appendix A: Probability Calculations for the Prevalence in Migraine and Synesthesia

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

$$p(\text{♀}) = .5$$

$$p(\text{♂}) = .5$$

but different rates of migraine:

$$p(\text{M}|\text{♀}) = .15$$

$$p(\text{M}|\text{♂}) = .05$$

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

$$p(\text{S}) = .01$$

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

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

$$p(\text{S}) = .5(p(\text{S}|\text{♀}) + p(\text{S}|\text{♂}))$$

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

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

$$p(S|\sim M, \text{♀}) = a$$

$$p(S|M, \text{♂}) = ka$$

$$p(S|M, \text{♀}) = a$$

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

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

$$p(S|\text{♂}) = p(S|M, \text{♂}) \cdot p(M|\text{♂}) + p(S|\sim M, \text{♂}) \cdot p(\sim M|\text{♂}) = 0.05ka + 0.95a$$

Since the rate of synesthesia 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 synesthesia in migraine, such that $k=3$, this gives:

$$p(S|\text{♀}) = 0.15ka + 0.85a = 0.15 \times 3 \times 0.0083 + 0.85 \times 0.0083 = 1.07\%$$

and

$$p(S|\text{♂}) = 0.05ka + 0.95a = 0.05 \times 3 \times 0.0083 + 0.95 \times 0.0083 = 0.91\%$$

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

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

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

In other words, if there is a greater rate of synesthesia in migraine we should indeed see a greater rate of migraine in synesthesia. We can also perform the same calculations for male participants, in order to compare the rate of migraine in synesthetes 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 synesthetes and nonsynesthetes.

Appendix B: Questionnaire

Personal Experiences in Synesthetes and Nonsynesthetes

Demographic information. How old are you? (Possible answer range: 18–100)

What is your gender?

- Female
- Male
- Other
- Prefer not to say

About your synesthesia. Please read the following paragraph carefully.

What is synesthesia?

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 “synesthesia.” People who experience synesthesia find that a percept in one of the senses automatically triggers another sensory experience. One of the most common forms of synesthesia is called “grapheme-color synesthesia” in which seeing a black number or letter triggers a perception of color. Other types of synesthesia include associating musical notes with colors, combining words with tastes and seeing numbers in unusual spatial configurations. There are approximately 61 recorded types of synesthesia and this number is growing as study in this field continues.

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

Do you think you have any type of synesthesia?

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

	Spatial	Other (please state)
	Colors Shapes locations	Sounds Scents Tastes Touch Pain Emotion Gender Personality
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 synesthetic experiences that do not fit in this table, please state them below.

If you have completed the Synesthesia Battery at 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. Please note the email address you used to register with the Synesthesia Battery here, so that we can link your results on the battery with your answers to this questionnaire:

About your personality.

	Disagree strongly	Disagree a little	Neither agree nor disagree	Agree a little	Agree strongly
I see myself as someone who . . .					
1. Is talkative					
2. Tends to find fault with others					
3. Does a thorough job					

(continued)

Continued.

	Disagree strongly	Disagree a little	Neither agree nor disagree	Agree a little	Agree strongly
I see myself as someone who . . .					
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 or 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 or migraine? (Free response)