A distinct electrophysiological signature for synaesthesia that is independent of individual differences in sensory sensitivity

Article (Accepted Version)

Ward, Jamie, Baykova, Reny, Dyson, Ben, Chew, Jowinn, Schreiter, Marie Luise, Beste, Christian and Sherman, Maxine (2021) A distinct electrophysiological signature for synaesthesia that is independent of individual differences in sensory sensitivity. Cortex. ISSN 0010-9452

This version is available from Sussex Research Online: http://sro.sussex.ac.uk/id/eprint/97548/

This document is made available in accordance with publisher policies and may differ from the published version or from the version of record. If you wish to cite this item you are advised to consult the publisher’s version. Please see the URL above for details on accessing the published version.

Copyright and reuse:
Sussex Research Online is a digital repository of the research output of the University.

Copyright and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable, the material made available in SRO has been checked for eligibility before being made available.

Copies of full text items generally can be reproduced, displayed or performed and given to third parties in any format or medium for personal research or study, educational, or not-for-profit purposes without prior permission or charge, provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.

http://sro.sussex.ac.uk
A Distinct Electrophysiological Signature for Synaesthesia that is Independent of Individual Differences in Sensory Sensitivity

Jamie Ward¹,², Reny Baykova¹,², Ben Dyson¹, Jowinn Chew¹, Marie Luise Schreiter³, Christian Beste³, & Maxine Sherman¹,²

¹ School of Psychology, University of Sussex, Falmer, Brighton, BN1 9QH, U.K.
² Sackler Centre for Consciousness Science, University of Sussex, Falmer, Brighton, BN1 9QH, U.K.
³ Cognitive Neurophysiology, Department of Child and Adolescent Psychiatry, Faculty of Medicine, TU Dresden, Germany

Manuscript Submitted to: Cortex

Running head: Sensory sensitivity
Address correspondence to :-
Prof. Jamie Ward,
School of Psychology,
University of Sussex,
Falmer, Brighton,
BN1 9QH, U.K.
Tel. : +44 (0)1273 876598
Fax. : +44 (0)1273 678058
E-mail : jamiew@sussex.ac.uk

Abstract
People with synaesthesia have been reported to show atypical electrophysiological responses to certain simple sensory stimuli, even if these stimuli are not inducers of synaesthesia. However, it is unclear whether this constitutes a neural marker that is relatively specific to synaesthesia or whether it reflects some other trait that co-occurs with synaesthesia, but is not specific to it. One candidate is atypical sensory sensitivity (e.g. strong aversion to certain lights and sounds, ‘sensory overload’) which is a feature of both synaesthesia and autism and that varies greatly in the neurotypical population. Using visual evoked-potentials (to stimuli varying in spatial frequency) and auditory-evoked potentials (to stimuli varying in auditory frequency), we found that synaesthetes had a modulated visual evoked-potential around P1/N1 (emanating from fusiform cortex), a greater auditory N1, as well as differences in the time-frequency domain (increased alpha and beta induced power for visual stimuli). This was distinct from that found in non-synaesthetes. By contrast, no significant electrophysiological differences were found that were linked to neurotypical variation in sensory sensitivity.
**Introduction**

People with synaesthesia have anomalous perceptual experiences such as letters and numbers eliciting colours (grapheme-colour synaesthesia), sequences such as the months of the year being visualised in spatial patterns (sequence-space synaesthesia), or music triggering visual experiences. It emerges early in life (Simner & Bain, 2013) and runs in families (Baron-Cohen, Burt, Smith-Laitanan, Harrison, & Bolton, 1996). However, surprisingly little is known about the causal mechanisms that give rise to synaesthesia in certain individuals and not others. One possibility is that people with synaesthesia have an essentially ‘normal’ neurocognitive profile outside of their synaesthetic experiences themselves. For instance, synaesthesia may reflect normal mechanisms of associative learning during childhood that differ only in their propensity to survive into adulthood (Witthoft & Winawer, 2013; Yon & Press, 2014). In this view, the neurocognitive differences between synaesthetes and non-synaesthetes would be minimal to non-existent, with some researchers claiming that “Rather than being a neurological condition (i.e., a structural or functional brain anomaly), synaesthesia could be reconsidered as a special kind of childhood memory, whose signature in the brain may be out of reach with present brain imaging techniques.” (p.1, Hupe & Dojat, 2015). The alternative viewpoint, is that synaesthesia is a neurological condition linked to structural and functional brain differences (e.g. Hubbard, Brang, & Ramachandran, 2011). A related but more subtle version of this account is to say that synaesthesia is a product of a particular set of structural and functional brain differences that predispose towards these kinds of atypical experiences emerging (Ward, 2019b). In this view, synaesthesia is but one feature of a larger constellation of neurocognitive differences relating to, for instance, memory, imagery and perception (and the brain mechanisms that support them). This research is concerned with individual differences in perception as revealed through electrophysiological markers.

The primary motivation for the present study comes from a previous EEG study of visual-evoked potentials (VEPs) in grapheme-colour synaesthetes (Barnett et al., 2008). Barnett et al. (2008) presented participants with: striped patterns (Gabor patches) of different spatial frequencies; checked patterns varying in contrast; and red-green chromatic patterns (equated for luminance). Synaesthetes showed enhanced amplitude of VEPs in several early components (< 200 msec) that was particularly apparent for visual stimuli that load highly on the parvocellular system (specialised for high spatial frequency, high contrast, colour). The fact that these differences were found for stimuli that do not elicit synaesthesia is important because it points to wider functional differences in the synaesthetically brain (i.e. the differences are hard to explain by the atypical retention of childhood grapheme-colour associations per se). It suggests, instead, that there are differences in the early sensory processing of visual stimuli in synaesthesia and Barnett et al. (2008) speculated that these may predate the emergence of synaesthesia itself (because the visual cortex becomes tuned to spatial frequency differences prior to literacy acquisition). Other studies using visually-evoked potentials have also shown larger amplitude early (< 200 msec) VEPs in synaesthetes when processing non-inducing stimuli such as line drawings (Sinke et al., 2014) or coloured squares (Goller, Otten, & Ward, 2009), as well as when processing synaesthesia-inducing stimuli (graphemes) themselves (Brang, Kanai, Ramachandran, & Coulson, 2011; Schreiter, Chmielewski, Ward, & Beste, 2019).

However, more recent research has made us question whether these kinds of electrophysiological differences are a specific neural marker of synaesthesia or whether they reflect the presence of some other trait that is co-morbid with synaesthesia (i.e. that acts as a potential confound). Specifically, autism and synaesthesia tend to be co-morbid (Baron-Cohen et al., 2013; Neufeld et al., 2013) and, even where a formal diagnosis of autism is not met there is evidence that synaesthetes have elevated levels of autism-related traits (Ward et
Autism is linked to differences in visual-evoked potentials, such as amplitude increases to high spatial frequency visual gratings (Vlamings, Jonkman, van Daalen, van der Gaag, & Kemner, 2010), that resemble those reported by Barnett et al. (2008). Moreover, the trait of heightened subjective sensory sensitivity is a shared feature of both autism and synaesthesia, more so than other symptoms such as socio-communicative impairments (Ward et al., 2017). High sensory sensitivity includes symptoms such as finding certain lights and sounds to be unusually intense and aversive (Ward, 2019a). In these behavioural studies, sensory sensitivity was measured using a self-report scale (Glasgow Sensory Questionnaire, GSQ; Robertson & Simmons, 2013) that includes items from different sensory modalities. Synaesthetes, similarly to people with a diagnosis of autism, show increased scores across all these types of items (Ward et al., 2017). In particular, it is not the case the people with grapheme-colour synaesthesia trivially have heightened visual sensory sensitivity because of their ‘extra’ sensations in the visual modality. Instead, atypical sensory sensitivity is pervasive across sensory modalities and extends across multiple kinds of synaesthesia (Ward, Brown, Sherwood, & Simner, 2018).

Following on from this evidence, one possibility is that electrophysiological differences to simple sensory stimuli in synaesthetes reflect group differences in sensory sensitivity rather than the presence of synaesthesia per se. The aim of the present study is to test this hypothesis. If electrophysiological differences in synaesthetes are due to the confounding variable of high sensory sensitivity, then we predict that any group differences in VEPs between synaesthetes and neurotypical people will disappear when sensory sensitivity is controlled for. Given that subjective sensory sensitivity in synaesthesia extends to non-visual stimuli too, we predict the same pattern of results for auditory-evoked potentials (AEPs). However, if synaesthesia is linked to a distinctive set of functional brain differences then electrophysiological differences related to synaesthesia should remain after differences in sensory sensitivity are controlled for. As there are no previous studies that have explored electrophysiological correlates of individual differences in sensory sensitivity, at least as measured by the GSQ, this was the aim of Study 1. In Study 1 we contrasted different levels of sensory sensitivity (high v. low GSQ scores) within a neurotypical sample in a between-subjects design. In Study 2, we used the same EEG procedure on a group of synaesthetes and compared this to the neurotypical sample from Study 1 who were matched to the synaesthetes in terms of GSQ and autism-spectrum quotient (AQ) scores. In addition to collecting EEG data, at the end of the session we collect behavioural ratings of subjective discomfort for the auditory and visual stimuli and a measure of perceptual distortions (such as gratings eliciting movement or bending do lines, and sounds eliciting pain or hairs on end). These are generally taken as indicative features of high sensory sensitivity (e.g., Baguley & Hoare, 2018; Conlon, Lovegrove, Chekaluk, & Pattison, 1999).

**STUDY 1: Electrophysiological Differences linked to Subjective Sensory Sensitivity**

Study 1 contrasts a high sensory sensitivity group against a low sensory sensitivity group (all non-synaesthetes) presenting them with simple visual stimuli (gratings differing in spatial frequency) and simple auditory stimuli. The hypothesis was that the high sensory sensitivity group would have a larger electrophysiological response, particularly to stimuli rated as uncomfortable. By using EEG we can determine whether these differences are likely to reflect early sensory processing or post-perceptual differences. It remains to be determined whether these differences manifest themselves in the amplitude of ERP components (i.e. high sensory sensitivity is reflected in the magnitude of the neural response) or in the time-frequency domain (i.e. high sensory sensitivity is reflected in periodic fluctuations in neural
excitability) or both. No part of the study procedures or analyses were pre-registered prior to the research being conducted

Method
Participants
A total of 168 participants completed the online questionnaires which were used to select to participants for the EEG study (the mean GSQ score was 54.5. S.D.=17.9, from which the upper third, GSQ>=60, were classified as ‘high’, although subsidiary analyses with GSQ treated as a continuous variable are reported). A total of 63 participants took part in the EEG study (average age = 23.00 years, S.D. = 5.54; range=18-49; 47 females, 15 males, 1 undeclared). The high sensory sensitivity group comprised 25 participants (mean age = 22.68; 6 males) and the complementary low sensory sensitivity group comprised 38 participants (mean age = 23.21; 9 males, 1 undeclared). Although the two groups differed significantly on GSQ scores (high: mean=75.00, S.D.=12.66; low=41.42, S.D.=9.87; t(61)=11.80, p<.001) they did not differ significantly on overall AQ (high: mean=19.40, S.D.=8.00; low=16.39, S.D.=6.66; t(61)=1.617, p=.111), and they were matched by age (t(61)=0.369, p=.713). The difference in subjective sensory sensitivity was large (Cohen’s d = 3.0), and the sample sizes are sufficient for detecting effect sizes in EEG signatures of sensory sensitivity of d > 0.7 (power=0.8, alpha=0.05). All participants had normal or corrected-to-normal vision and none reported synaesthesia (see Study 2). Participants received course credit for completing the questionnaire (if they were first and second year undergraduates at University of Sussex), and all participants were offered either £16 or course credits for completing the EEG study.

The research was approved by the Science and Technology Cross-Schools Research Ethics Committee at the University of Sussex.

Stimuli and materials
The questionnaire materials consisted of the GSQ and AQ. The GSQ is a 42-item questionnaire that assesses hyper- and hypo-sensitivities across seven sensory modalities: visual, auditory, gustatory, olfactory, tactile, vestibular, and proprioception (Robertson & Simmons, 2013). Example items included “Do bright lights ever hurt your eyes/cause a headache?” and “Do you dislike loud noises?”. Items were answered using the five-point scale: “Never – Rarely – Sometimes – Often – Always”, with responses coded on a scale from 0 (Never) to 4 (Always), providing possible scores from 0-168. The AQ is a 50-item questionnaire assessing autistic traits across five domains: social skills, attention switching, attention to detail, communication, imagination (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). Example items included “I find it very easy to play games with children that involve pretending” and “I find social situations easy”, and are answered on a four-point scale (Definitely Agree, Slightly Agree, Slightly Disagree, Definitely Disagree). Approximately half the questions are reverse coded and all items were scored by one point given for each “slightly” or “definitely” response to an autistic-like behaviour. Consequently, responses were coded as 0 or 1, allowing scores ranging from 0 to 50.

The EEG experiment and behavioural rating study used six visual and six auditory stimuli. The visual stimuli were horizontally oriented line gratings with different spatial frequencies: 0.328, 0.748, 1.745, 2.618, 3.491, and 5.236 cycles per degree (cpd) with a visual angle of 18 degrees. The line gratings varied sinusoidally in contrast between black and white (standard deviation of the Gaussian envelope, sigma, of 10 pixels) with the wavelength of the sinusoid (lambda) varying according to spatial frequency (between 5 and 80 pixel units). The auditory stimuli consisted of notched noise sounds covering six non-overlapping frequency intervals: 500-1000Hz, 1500-2500Hz, 2500-3000Hz, 3500-4000Hz,
4500-5000Hz, and 5500-6000Hz. The gratings were created in Matlab, and the white noise stimuli were created in Audacity.

**Procedure**

The study consisted of two sessions. The first session consisted of the two questionnaires (GSQ and AQ), which were completed online and remotely using Qualtrics software and took around 15 minutes. Participants were then invited to take part in the EEG study, with selection being based on the GSQ sensory sensitivity score to try to obtain approximately equal numbers of the rarer sample of participants with a high sensitivity (GSQ>=60) and a low-to-mid sensitivity group (GSQ<60 with most having scores less than 50).

The EEG study lasted approximately 90 minutes including electrode cap fitting (45 minutes), the EEG recording task (35 minutes), and post-task subjective ratings of the stimuli (10 minutes). Participants were seated in a darkened booth with Faraday cage. Stimuli were presented on a 21-inch CRT Dell monitor with a resolution of 1024 X 768 pixels and a refresh rate of 100Hz. They were sat 60cm away from the screen. The sounds were delivered through over-ear headphones at a fixed volume (75% of the maximum). A small number of participants requested a reduction in volume to 60% and this was approximately evenly distributed across groups (3 high sensitivity, 6 low sensitivity).

The EEG task was carried out in Presentation, and consisted of randomly ordered auditory and visual stimuli (each 500 msec in duration). The inter-trial interval was jittered between 600 msec and 1100 msec as shown in Figure 1. A blue fixation point was presented in the middle of the screen during the entire duration of a block, and participants were instructed to maintain central fixation. The participants’ task was to monitor for an infrequent (oddball) target consisting of change in colour of the central fixation dot from blue to red. This task was performed during both auditory and visual trials, and was included to ensure that participants remained attentive and fixated. According to current theories of perception and attention (e.g. Lavie, 2005), having an easy or ‘low load’ perceptual task should ensure that the task-irrelevant stimuli (sounds and gratings) are processed efficiently even if they are from another modality (e.g. Macdonald & Lavie, 2011). Target trials in which the dot changed colour were excluded from the analyses. Participants completed a set of practice trials followed by 10 experimental blocks. In each block they were presented with 11 repetitions of each auditory and visual stimulus (132 trials per block in total), with a blue-to-red target appearing once for each stimulus (i.e. 120 non-target trials and 12 target trials per block).
After completing the EEG experiment, participants rated each of the stimuli. The ratings were collected with PsychoPy software. Each stimulus was presented twice, in separate auditory and visual blocks, with the 12 trials in each block randomly ordered. Each stimulus was played/displayed for 3000 msec after which participants made two judgments. Firstly, participants were asked to indicate how comfortable it was to look at or listen to the stimulus on Visual Analogue Scale a ranging from “Very uncomfortable” (coded as -10) to “Very comfortable” (coded as +10). Secondly, participants were asked to note if the stimulus induced any additional experiences. For visual stimuli, they clicked as many or as few from the following list: colours, blending of lines, blurring of lines, shimmer / flicker, fading, shadowy shapes, other/specify (these are taken from Wilkins & Evans, 2010). For auditory stimuli, we created a novel list of the following nine items: pain, shivers, hairs on end, muscle tension, goose-bumps, tingling, increased heart rate, perspiration and other/specify.

**EEG recording and pre-processing**

The EEG data were recorded using an ANT system with 1000 Hz sampling rate, no online filtering, and 64 Ag/AgCl electrodes arranged following the 10/20 system. Electrode impedances were kept below 10 kΩ. EEG recordings were referenced online to a ground electrode placed on the forehead.

The EEG data were pre-processed and analysed in MATLAB using the toolboxes EEGLAB and ERPLAB. The data were downsampled to 256 Hz, then high-pass (0.1Hz) and low-pass (50Hz) filtered using finite impulse response (FIR) filters with cut-off frequencies of -6dB. (Five participants were tested at the lower 256 Hz sampling rate in error, so downsampling was not necessary). Excessively noisy channels, identified through ERPLAB (kurtosis z-score threshold of 5), were interpolated with their neighbouring channels (using spherical interpolation), and the data were referenced to the average signal. The continuous EEG was then divided epochs starting from -200ms to 700ms relative to stimulus onset, and the epoched data was corrected to baseline (-200ms to 0ms relative to stimulus onset). Trials on which the fixation point changed colour or participants incorrectly reported it had were excluded. Finally, artefact rejection was performed on the epoched data using the ‘moving
window peak to peak’ procedure with 50msec steps (from -50 to 500 msec) and 50μV threshold followed by visual inspection of deleted artefacts.

**ERP analysis**

Analysis was conducted on the C1, P1, N1, and P2 components of the VEP, and the P1, N1, and P2 components of the AEP (Table 1). Electrode clusters were selected on the basis of showing the largest deflections with reference to the previous literature (e.g. Barnett et al., 2008; Brandwein et al., 2015) and from visual inspection of the group-level data (i.e. the grand mean, collapsing across group and stimulus). For each individual and each stimulus, the timings of the peaks for each component were extracted using the peak detection function in EEGLab searching in a time window informed by the group average peaks detailed in Table 1 (visual C1: 30-100 ms negative-going peak; visual P1: 80-120 ms positive-going peak; visual N1: 120-180 negative-going peak; visual P2: 180-240, positive-going peak; auditory P1: 45-100 positive-going peak; auditory N1: 110-170 ms negative-going peak; auditory P2: 190-260 ms positive-going peak). From this, the average amplitude around the peak was extracted from a 20 msec window centered on the subject-specific peak latency for that stimulus.

**Table 1: A summary of the electrode clusters used to define each component and the average peak latency for visual-evoked potentials and auditory-evoked potentials as a function of stimulus type (spatial frequency in vision, mean frequency in audition).**

<table>
<thead>
<tr>
<th>Visual (stimulus)</th>
<th>Electrode Cluster</th>
<th>VEP Average Peak Latency (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cycles per degree, cpd</td>
<td>0.33 0.78 1.75 2.62 3.49 5.24</td>
</tr>
<tr>
<td>Visual C1</td>
<td>Oz, POz, O2, O1</td>
<td>48 50 57 70 72 79</td>
</tr>
<tr>
<td>Visual P1</td>
<td>Oz, POz, O2, O1</td>
<td>103 101 100 94 101 104</td>
</tr>
<tr>
<td>Visual N1</td>
<td>PO7, PO5, P7, P5, PO6, PO8, P8, P6</td>
<td>159 159 154 153 152 152</td>
</tr>
<tr>
<td>Visual P2</td>
<td>Oz, POz, O2, PO4, O1, PO3</td>
<td>219 218 211 206 207 206</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Auditory (stimulus)</th>
<th>Electrode Cluster</th>
<th>AEP Average Peak Latency (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hz</td>
<td>500-1000</td>
</tr>
<tr>
<td>Auditory P1</td>
<td>FCz, Fz, Cz, FC2, FC1</td>
<td>72 73 73 70 64 64</td>
</tr>
<tr>
<td>Auditory N1</td>
<td>FCz, Fz, Cz, FC2, FC1</td>
<td>134 135 134 134 135 135</td>
</tr>
<tr>
<td>Auditory P2</td>
<td>Cz, CPz, FCz, C2, C1</td>
<td>226 226 223 228 226 224</td>
</tr>
</tbody>
</table>

**Time-Frequency analyses**

The pre-processed EEG data was decomposed into the time-frequency domain. Morlet wavelet decomposition with constant window length of two oscillatory cycles generated coefficients for 183 linearly spaced time points, from -118 to 518 ms inclusive, and 35 linearly spaced frequencies from 6 to 50 Hz inclusive. This was performed separately for each participant, condition (i.e. stimulus modality and type), and electrode. The time-frequency data was then converted into induced power (the squared magnitude of the
complex wavelet coefficients), in decibels, relative to baseline (0-100ms, i.e. the entire pre-stimulus period remaining after wavelet decomposition). For the analysis, the electrodes were grouped into 4 clusters – Occipital, Parietal, Fronto-central and Central – corresponding to those also used in the ERP analysis (respectively for visual C1/P1, visual N1, auditory N1/P1, and auditory P2). For each participant, electrode cluster, modality and time-frequency point the evoked power for each visual/auditory stimulus was considered. To determine whether there were statistically significant differences between high and low sensory sensitivity groups (study 1) or synaesthetes and non-synaesthetes (study 2), participant-wise power maps were fed to the Fieldtrip toolbox and cluster-based significance was determined on summed t-statistics via Monte-Carlo approximation with 5,000 draws. The interaction between group and stimulus was computed in the same way, using a two-tailed independent t-test (high versus low sensory sensitivity) on the high – low spatial frequency maps. False discovery rate (FDR), using the Benjamini and Hochberg (1995) correction was used to correct for two-tailed multiple comparisons over the four electrode clusters, two modalities (auditory and visual), and the two comparisons (main effect and interaction) with p<.05, two-tailed.

RESULTS

Three participants were excluded entirely due to a high number of artefacts (>50% or trials, 1 high and 1 low sensory sensitivity participant) or technical problems in recording triggers (1 high sensory sensitivity participant). These criteria were established prior to data collection.

Behavioral Data

In terms of their engagement with the central task during the EEG study (detecting a colour change), the mean hit rate was 98.8% (SD=1.96%) and the mean false alarm rate was 0.89% (SD=3.50%).

Two participants did not complete the post-EEG stimulus ratings. The results for the remaining participants are summarised in Figure 2. Overall, the high sensitivity group tended to rate the stimuli as more uncomfortable and more likely to induce additional experiences.

For the visual comfort ratings, these were entered into a 6x2 ANOVA contrasting stimulus (6 levels) and group (high, low sensitivity). There was a main effect of stimulus (F(5,280)=2.451, p=.034, $\eta_p^2=.042$), a main effect of group (F(1,56)=6.118, p=.016, $\eta_p^2=.681$), and a significant interaction (F(5,280)=2.535, p=.029, $\eta_p^2=.043$). The high sensory sensitivity group tended to find the stimuli more uncomfortable and this was more pronounced for higher spatial frequencies (the greatest difference being 3.491 cpd). The overall number of induced experiences tended to be low and, hence, were collapsed across stimuli. The difference between the overall number of induced experiences reported across groups was not significant for either high spatial frequency / HSF (t(56)=1.536, p=.130; Cohen’s d=0.407) or low spatial frequency / LSF (t(56)=0.646, p=.521; Cohen’s d=0.174), grouping across the 3 highest and lowest stimuli (such that HSF is 2.6, 3.5, and 5.2 cpd, and LSF is 0.3, 0.7, and 1.7 cpd).

For the auditory comfort ratings, no effects were significant (main effect of stimulus: F(5,280)=1.839, p=.105, $\eta_p^2=.032$; interaction: F(5,280)=.616, p=.699, $\eta_p^2=.011$; F(1,56)=3.151, p=.081, $\eta_p^2=.053$). The difference between the overall number of induced experiences reported across groups was not significant (t(56)=1.876, p=.066; Cohen’s d=0.246).

INSERT FIGURE 2 ABOUT HERE
Figure 2. Top row: ratings of comfort and discomfort for six visual stimuli varying in spatial frequency (cycles per degree) and auditory notched noise varying in mean frequency (Hz). Bottom row: the mean number of induced experiences for each stimulus. Error bars show +/- 1 SEM.

Event-Related Potentials

Visual stimuli

The results for visual evoked potentials are summarised in Figure 3. The results were analysed as a 6 x 2 ANOVA contrasting stimulus against group for each VEP component separately (C1, P1, N1 and P2), and averaging over electrodes within the 20 msec time window.
Figure 3: Left: grand-average visual-evoked potentials in microvolts (grey bars show +/- 1 SEM). Right: the peak amplitudes for each component by group and stimulus. Error bars show +/- 1 SEM.

There were no main effects of group on any of the four VEP components: C1 ($F(1,58)=.403, p=.528, \eta^2_p=.007$); P1 ($F(1,58)=.633, p=.429, \eta^2_p=.011$); N1 ($F(1,58)=.014, p=.908, \eta^2_p=.014$); or P2 ($F(1,58)=.522, p=.473, \eta^2_p=.009$). Similarly, there were no group X stimulus interactions for any component: C1 ($F(5,290)=1.235, p=.293, \eta^2_p=.021$); P1 ($F(5,290)=.982, p=.429, \eta^2_p=.017$); N1 ($F(5,290)=.611, p=.691, \eta^2_p=.010$); or P2 ($F(5,290)=1.528, p=.181, \eta^2_p=.181$). In sum, there was no evidence that subjective sensory sensitivity has a significant impact on visual-evoked potentials. A consideration of effect sizes (Cohen’s d) showed that all of the simple group comparisons across stimuli or components (i.e. out of 24) showed small or negligible effects (see Supplementary data).

All four components were influenced by the spatial frequency of the stimulus (i.e. main effects of stimulus). Namely, high spatial frequencies are associated with larger and more negative-going C1 amplitudes ($F(5,290)=34.219, p<.001, \eta^2_p=.371$), and lower spatial frequencies were associated with larger and more positive-going P1 amplitudes ($F(5,290)=28.501, p<.001, \eta^2_p=.329$). Both the visual N1 ($F(5,290)=4.526, p=.001, \eta^2_p=.072$) and visual P2 ($F(5,290)=34.154, p<.001, \eta^2_p=.371$) showed larger negative and positive going peaks, respectively, with mid-range spatial frequencies.

**Auditory stimuli**

The results for auditory evoked potentials are summarised in Figure 4. The results were analysed as a 6 x 2 ANOVA contrasting stimulus against group for each AEP component separately (P1, N1 and P2).
Figure 4: Left: Grand-average auditory-evoked potentials in microvolts (grey bars show +/- 1 SEM). Right: peak amplitudes by group and stimulus for each component (P1, N1 and P2). Error bars show +/- 1 SEM.

For all three auditory components there were no main effects of group: P1 (F(1,58)=.033, p=.857, \( \eta^2_p = .001 \)); N1 (F(1,58)=.048, p=.828, \( \eta^2_p = .001 \)); or P2 (F(1,58)=1.271, p=.264, \( \eta^2_p = .021 \)). Similarly, there was no group X stimulus interaction for either P1 (F(5,290)=1.168, p=.325, \( \eta^2_p = .020 \)), N1 (F(5,290)=1.253, p=.289, \( \eta^2_p = .021 \)), or P2 (F(5,290)=1.212, p=.303, \( \eta^2_p = .020 \)). In sum, there was no evidence that subjective sensory sensitivity has a significant impact on auditory-evoked potentials. A consideration of effect sizes (Cohen’s d) showed that all of the simple group comparisons across stimuli or components (i.e. out of 18) showed small or negligible effects (see Supplementary data).

For the auditory P2, there was a significant main effect of stimulus (F(5,290)=19.845, p<.001, \( \eta^2_p = .255 \)), with low auditory frequencies eliciting larger positive responses. There were no main effects of stimulus for P1 (F(5,290)=.328, p=.896, \( \eta^2_p = .006 \)) or N1 (F(5,290)=.985, p=.427, \( \eta^2_p = .017 \)).

Treating sensory sensitivity as a continuous measure

The analyses above divided sensory sensitivity into two groups, but the overall (null) pattern of results is retained if sensory sensitivity is treated as a continuous measure. Correlating GSQ scores against peak amplitude for different components and stimuli revealed no significant effects and no correlation coefficient above r=.20. The average effect sizes for C1, P1, N1 and P2 (across stimuli) were r=-.01, +.11, +.06, and -.14 respectively. By contrast, some differences relating to the AQ were noted. Specifically, the AQ was correlated with the amplitude of the P1 (r=.39, p=.002; with a similar trend across all visual
stimuli), as noted previously by Vlamings et al. (2010) when contrasting autistic against typically developing children.

No significant effects or medium effect sizes were observed for the auditory evoked potentials and either the GSQ (as a continuous measure) or AQ.

The Supplementary Material contains a full table to correlations between the various EEG measures, trait measures (AQ, GSQ) and behavioural measures (mean level of comfort, number of induced experiences) in addition to a figure showing the significant relationship between AQ and visual P1.

**Time-Frequency Analysis**

Next we compared induced oscillatory power between the high and low sensory sensitivity groups, separately for visual stimuli and auditory stimuli, and separately for each electrode cluster. We found no significant time-frequency clusters. We also tested the Group x Stimulus interaction in each electrode cluster. This was done by comparing the effect of stimulus (high minus low spatial frequency or auditory frequency) across the two sensory sensitivity groups. Again, no significant clusters were found for any electrode set or for any stimulus modality. In summary, we did not identify neural correlates of sensory sensitivity in oscillatory power. Results are depicted in Figure 5 and statistics are presented in Table 2.

**Visual Stimuli**

![Image of time-frequency z-score maps for visual stimuli](image)

**Auditory Stimuli**

![Image of time-frequency z-score maps for auditory stimuli](image)

Figure 5. Time-frequency z-score maps for Study 1, separately for visual (top) and auditory (bottom) stimuli. Strong red (or blue) colours represent clusters with large positive (or negative) z-scores.
Table 2. Experiment One time-frequency results

<table>
<thead>
<tr>
<th>Visual stimuli</th>
<th>Group x Stimulus</th>
<th>T_{sum}</th>
<th>p_{uncorrected}</th>
<th>p_{corrected}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occipital High - Low</td>
<td></td>
<td>71.633</td>
<td>0.537</td>
<td>0.716</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>405.739</td>
<td>0.113</td>
<td>0.541</td>
</tr>
<tr>
<td>Parietal High - Low</td>
<td></td>
<td>316.598</td>
<td>0.166</td>
<td>0.541</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>No clusters found</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central High - Low</td>
<td></td>
<td>98.194</td>
<td>0.497</td>
<td>0.716</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>456.599</td>
<td>0.081</td>
<td>0.541</td>
</tr>
<tr>
<td>Fronto-Central High</td>
<td></td>
<td>108.209</td>
<td>0.453</td>
<td>0.716</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>505.584</td>
<td>0.063</td>
<td>0.541</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Auditory stimuli</th>
<th>Group x Stimulus</th>
<th>T_{sum}</th>
<th>p_{uncorrected}</th>
<th>p_{corrected}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occipital High - Low</td>
<td></td>
<td>-63.554</td>
<td>0.696</td>
<td>0.759</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>-73.455</td>
<td>0.659</td>
<td>0.759</td>
</tr>
<tr>
<td>Parietal High - Low</td>
<td></td>
<td>-60.570</td>
<td>0.712</td>
<td>0.759</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>-156.572</td>
<td>0.382</td>
<td>0.716</td>
</tr>
<tr>
<td>Central High - Low</td>
<td></td>
<td>-286.919</td>
<td>0.198</td>
<td>0.541</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>121.594</td>
<td>0.497</td>
<td>0.716</td>
</tr>
<tr>
<td>Fronto-Central High</td>
<td></td>
<td>202.091</td>
<td>0.332</td>
<td>0.716</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>-246.242</td>
<td>0.203</td>
<td>0.541</td>
</tr>
</tbody>
</table>

Summary
The present study did not find reliable differences in VEPs or AEPs related to self-reported subjective sensory sensitivity (derived from a commonly used questionnaire measure).

STUDY 2: Is there a Distinct Electrophysiological Profile Linked to Synaesthesia?

Study 2 contrasts the neurotypical participants from the previous study (combined sample), against a sample of synaesthetes (predominantly grapheme-colour). Synaesthetes have been shown to have VEP differences to viewing simple achromatic stimuli (Barnett et al., 2008) and to report high sensory sensitivity (Ward, Brown, et al., 2018; Ward et al., 2017). As such, our initial reasoning was that the electrophysiological differences in synaesthetes may reflect their high sensitivity trait, rather than synaesthesia per se. Here we demonstrate, however, that synaesthetes have a distinctive electrophysiological profile that cannot be account for by this.

Method
Participants
A further 24 participants with synaesthesia were also tested as part of this study. There were 18 females and 6 males, with an average age of 32.38 years (S.D. = 14.63, range=19-63). The synaesthetes were contrasted against the N=60 (after exclusions) non-synaesthetes reported previously. This has sufficient power to detect group difference effect sizes of Cohen’s d > 0.7 (power=.80, alpha=.05), noting that the previous study of Barnett et al. (2008) found effects in this range (e.g. a group difference of d=0.91 for high-spatial frequency Gabor patterns). The synaesthetes did not differ from non-synaesthetes in terms of the GSQ (synaesthetes=52.04, S.D.=22.57; t(82)=.440, p=.661) or the AQ (synaesthetes=20.63, S.D.=8.81; t(82)=1.497, p=.138), but they were on, average, significantly older (with Levene’s correction, t(25.8)=3.032, p=.005). However, both groups were young adults (means ages of 23 and 32 years) whereas age-related differences in VEP/AEP tend to be found in elderly groups (Amenedo & Diaz, 1998; Wright, Williams, Drasdo, & Harding, 1985). Although previous research has shown that synaesthetes tend to
score higher on AQ and GSQ, it is to be noted that the sample recruited for Study 1 deliberately targeted high scorers on these measures (i.e. it was not an opportunistic sample).

Two synaesthetes were excluded due to a high number of EEG artefacts (>50% trials). Of the remaining sample, most synaesthetes (N=20/22) reported grapheme-colour synaesthesia, amongst other kinds, and this was verified using consistency scoring with all participants scoring <1.43 indicating high consistency over time (Rothen, Seth, Witzel, & Ward, 2013). There were 10 synaesthetes reporting sequence-space synaesthesia: 8 of whom also had grapheme-colour, and 2 of which reported this as their main kind (and was verified using the method of Ward, Ipser, et al., 2018). It was also important to consider the presence of auditory-induced synaesthesias: 8 participants reported sound-to-vision synaesthesia (including colour experiences) and 2 participants reported tickertape synaesthesia (speech elicits mental images of the spellings of words).

**Procedure**

The procedure was identical to that described in Study 1.

**EEG analyses**

The EEG pre-processing and analyses were identical to Study 1, with the exception of an additional source localization analysis for one of the EEG components which showed a different between-group scalp topography.

Source localization was conducted using standardized low resolution brain electromagnetic tomography (sLORETA) (Pascual-Marqui, 2002). SLORETA reveals high convergence with fMRI and validity of the sources estimated using sLORETA has also been confirmed in neuro-navigated EEG/TMS studies (Dippel & Beste, 2015; Sekihara, Sahani, & Nagarajan, 2005). Furthermore, it has been mathematically shown that this method provides reliable results without a localization bias (Pascual-Marqui, 2002). Thus, sLORETA gives a single linear solution to the inverse problem, based on extra-cranial measurements without a localization bias (Pascual-Marqui, 2002). For sLORETA, the intracerebral volume is partitioned into 6239 voxels at 5 mm spatial resolution. The standardized current density at each voxel is calculated in a realistic head model using the MNI152 template (Mazziotta et al., 2001). In this study, the voxel-based sLORETA images of synaesthetes were compared to controls using the sLORETA-built-in voxel-wise randomization tests with 2000 permutations, based on statistical nonparametric mapping (SnPM). Voxels with significant differences (p < 0.01, corrected for multiple comparisons) between contrasted conditions (visual N1) were located in the MNI-brain (www.unizh.ch/keyinst/NewLORETA/sLORETA/sLORETA.htm).

**Results**

**Behavioural Results**

The results are summarised in Figure 6. For the visual comfort ratings, these were entered into a 6x2 ANOVA contrasting stimulus (6 levels) and group (syn v. non-syn). Unlike in Study 1, here there was no main effect of stimulus (F(5,385)=0.598, p=.702, $\eta^2_p=.008$), no main effect of group (F(1,77)=.233, p=.631, $\eta^2_p=.003$), and no significant interaction (F(5,385)=0.313, p=.905, $\eta^2_p=.004$).

As for Study 1, for the auditory comfort ratings there was no main effect of stimulus (F(5,385)=0.407, p=.844, $\eta^2_p=.005$), no main effect of group (F(1,77)=.934, p=.337, $\eta^2_p=.012$), and no significant interaction (F(5,385)=0.769, p=.510, $\eta^2_p=.010$). In terms of number of induced experiences, there were no significant differences for visual stimuli (F(1,77)=0.693, p=.408, $\eta^2_p=.009$) or auditory stimuli (F(1,77)=3.071, p=.084, $\eta^2_p=.038$).

As such, synaesthetes were behaviourally indistinguishable from non-synaesthetes in
their behavioural ratings. Nevertheless, they differ substantially in their electrophysiological correlates.

**Figure 6:** Top row: ratings of comfort and discomfort for six visual stimuli varying in spatial frequency (cycles per degree) and auditory notched noise varying in mean frequency (Hz). Bottom row: the mean number of induced experiences for each stimulus. Error bars show +/- 1 SEM.

**Event-Related Potentials**

The VEPs for synaesthetes versus non-synaesthetes are shown in Figure 7. The visual components (C1, P1, N1, and P2) were analysed as separate 6x2 ANOVAs. For three of these components (C1, P1, P2) there were no group effects, and no group by stimulus interactions (all p’s>.1) and the main effects of stimulus were the same as those reported previously. There was, however, a significant group difference around the Visual N1 (F(1,80)=14.554, p<.001, ηp²=.154) and a group X stimulus interaction (F(5,400)=2.283, p=.046, ηp²=.028). Stimulus had no main effect on the amplitude of the N1 (F(5,400)=1.594, p=.161, ηp²=.020). All visual stimuli elicited a significantly larger negative peak in synaesthetes (t’s >2.4, p’s<.05). The N1 result is summarised in Figure 7 and a closer inspection of the scalp topographies suggests that groups start to diverge somewhat earlier (from ~100 msec during the P1 peak) with a distinct electrophysiological profile over a wide range of posterior and central electrodes. The sLORETA analysis revealed that this differential effect in N1 amplitudes between controls and synaesthetes, at the 140 ms peak, was associated with a single source within left the fusiform gyrus (BA19; peak MNI coordinate of x=-43,y=-72,z=-18), shown in Figure 8. This region is, in other contexts, commonly referred to as the Visual Word Form Area (VWFA) because, in fMRI, it is activated by written words more than other kinds of visual stimuli (based on the neurosynth
database maximal posterior probability; Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011). As a point of reference, the coordinates of V4 taken from the meta-analysis of Bartels and Zeki (2000) are centered at x=-28, y=-74, z=-13 (with an SD of ~5 in either direction). As such, our results point to atypical stimulus responsivity in this region in synaesthetes: the region responds more to line gratings in synaesthetes than it does in controls and this reveals itself as an enhanced visual N1 in EEG. We return to this in the discussion.

If one fractionates the synaesthetes into sub-groups according to the presence/absence of sequence-space synaesthesia or the presence/absence of auditory-induced visual experiences then the amplitude of the visual N1 (averaged across all stimuli) does not differ significantly across the sub-groups (+/- SSS: t(18)=-.651, p=.523; +/- auditory-inducers: t(18)=-.893, p=.384). Hence, the effect is generally found amongst the synaesthetes tested here rather than driven by one sub-group.

![Figure 7](image_url). Grand-average visual evoked potentials for synaesthetes and controls over different electrode clusters, grey regions represent +/- 1 SEM (left) and peak amplitudes for these components broken down by group and stimulus (right). Error bars show +/- 1 SEM.
Figure 8. The scalp distribution from 100-160 ms for synaesthetes and controls for visual stimuli (top) and auditory stimuli (bottom). sLORETA for visual stimuli at 140 ms (top right) shows a different neural source in synaesthetes that contributes to the N1-P1 complex (shown in cyan). For comparison, the white and yellow stars indicate the approximate locations of the visual word-form area \( (x=-42, y=-57, z=-15; \text{McCandliss, Cohen, & Dehaene, 2003}) \) and the occipital word-form area respectively \( (x=-38, y=-80, z=-10; \text{Strother, Coros, & Vilis, 2016}) \).

The analysis of the auditory components also revealed a significant group difference: synaesthetes have a larger auditory N1 component \( (F(1,80)=6.644, p=.012, \eta_P^2=.077) \). The scalp distribution is shown in Figure 8 (bottom) and the AEPs are shown in Figure 9. There were no significant group by stimulus interactions, and the main effects of stimulus were as reported previously. If one fractionates the synaesthetes into sub-groups according to the presence/absence of auditory-induced visual experiences then the amplitude of the auditory N1 (averaged across all stimuli) did not differ significantly across the sub-groups \( t(18)=-.893, p=.384 \). As such, these electrophysiological differences seem to reflect the presence of synaesthesia per se rather than whether sounds act as an inducer or not.
Figure 9. Grand-average auditory evoked potentials for synaesthetes and controls over different electrode clusters, grey regions represent +/- 1 SEM (left) and peak amplitudes for these components broken down by group and stimulus (right). Error bars show +/- 1 SEM.

Time-Frequency Analysis
In line with the ERP results, on trials where visual stimuli were presented synaesthetes exhibited sustained increases in low-to-mid frequency induced oscillatory power over all electrode sets (corrected $p_{\text{occipital}} = .016, p_{\text{parietal}} = .016, p_{\text{central}} = .032, p_{\text{fronto-central}} = .016$). As shown in Figure 10, this effect of synaesthesia started at approximately 20ms post-stimulus, and continued to the end of the epoch (500ms). These sustained differences are found in the 6-20Hz range, but also extend up to 33Hz at around 100 msec. This effect of synaesthesia did not depend upon grating spatial frequency, as no significant clusters for the Group x Stimulus interaction were found.

For auditory stimuli, no time-frequency clusters for the main effect of synaesthesia or for the Group x Stimulus interaction survived correction for multiple comparisons. Full results are presented in Table 3.
Figure 10. Time-frequency $z$-score maps for Experiment Two, separately for visual (top) and auditory (bottom) stimuli. Strong red (or blue) colours represent clusters with large positive (or negative) $z$-scores. White outlines depict significant clusters prior to correction for multiple comparisons.

Table 3. Experiment Two time-frequency results

<table>
<thead>
<tr>
<th>Region</th>
<th>Condition</th>
<th>$T_{\text{sum}}$</th>
<th>$P_{\text{uncorrected}}$</th>
<th>$P_{\text{corrected}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual stimuli</td>
<td>Occipital Synaesthete - Control</td>
<td>4967.025</td>
<td>0.003</td>
<td>0.016</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>216.450</td>
<td>0.269</td>
<td>0.305</td>
</tr>
<tr>
<td></td>
<td>Parietal Synaesthete - Control</td>
<td>4832.747</td>
<td>0.003</td>
<td>0.016</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>-498.141</td>
<td>0.070</td>
<td>0.120</td>
</tr>
<tr>
<td></td>
<td>Central Synaesthete - Control</td>
<td>2039.628</td>
<td>0.008</td>
<td>0.032</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>320.464</td>
<td>0.155</td>
<td>0.207</td>
</tr>
<tr>
<td></td>
<td>Fronto-Central Synaesthete - Control</td>
<td>4274.745</td>
<td>0.001</td>
<td>0.016</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>456.742</td>
<td>0.075</td>
<td>0.120</td>
</tr>
<tr>
<td>Auditory stimuli</td>
<td>Occipital Synaesthete - Control</td>
<td>-574.322</td>
<td>0.066</td>
<td>0.120</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>-385.380</td>
<td>0.093</td>
<td>0.135</td>
</tr>
<tr>
<td></td>
<td>Parietal Synaesthete - Control</td>
<td>-1117.058</td>
<td>0.023</td>
<td>0.061</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>-198.849</td>
<td>0.267</td>
<td>0.305</td>
</tr>
<tr>
<td></td>
<td>Central Synaesthete - Control</td>
<td>210.809</td>
<td>0.305</td>
<td>0.305</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>-739.479</td>
<td>0.033</td>
<td>0.075</td>
</tr>
<tr>
<td></td>
<td>Fronto-Central Synaesthete - Control</td>
<td>212.557</td>
<td>0.300</td>
<td>0.305</td>
</tr>
<tr>
<td></td>
<td>Group x Stimulus</td>
<td>-1005.724</td>
<td>0.016</td>
<td>0.051</td>
</tr>
</tbody>
</table>
Summary
Synaesthetes show a distinctive electrophysiological profile to simple auditory and visual stimuli. This is observed in terms of larger amplitude components (visual N1, auditory N1), which reflect group-related regional differences in activity underpinning the visual N1, and differences in the time-frequency domain (synaesthetes show persistent increases in induced power across the duration of visual stimulus presentation). These cannot be reduced to differences in sensory sensitivity because the groups were matched on this trait (Study 2) and because high v. low sensory sensitivity individuals does not show the same pattern (Study 1). Nor can they be due to synaesthesia per se: the visual stimuli did not induce synaesthesia, and the same pattern of AEPs is found irrespective of whether sounds do or do not induce synaesthesia. It suggests instead that this is part of a broader phenotype of the synaesthetic brain.

General Discussion
The aim of this study was to document electrophysiological markers linked to increased sensory sensitivity and synaesthesia. Increased sensory sensitivity is a symptom of a number of clinical conditions - most notably autism - that is characterised by a broad range of sensory aversions and behaviours (e.g. repetitive action or “stimming”) across multiple senses (Ward, 2019a). In particular, we wanted to test the hypothesis that previously documented electrophysiological differences previously linked to autism and synaesthesia - two conditions where sensory sensitivity is known to be higher – might be due to differences in sensory sensitivity (rather than the presence of these conditions per se). In contrast to these original aims, we found no reliable electrophysiological markers related to our measure of sensory sensitivity (Glasgow Sensory Questionnaire, GSQ). However, we did observe that neurotypical variation in other autistic traits (the Autism Quotient, AQ) was related to the visual P1 amplitude (Study 1), consistent with previous research (Vlamings et al., 2010). Moreover, we found that synaesthesia (Study 2) was linked to differences in the visual N1 and the auditory N1, as well post-stimulus changes in induced oscillatory power. Overall, it suggests that there are differences in visual and auditory processing linked to synaesthesia that cannot be reduced to differences in sensory sensitivity (or indeed to other traits linked to autism).

In the more detailed discussion below, we first consider the implications for synaesthesia and secondly the implications for our understanding of individual differences in sensory sensitivity.

Implications for Synaesthesia
The current study was strongly motivated by the similar previous study of Barnett et al. (2008) which reported larger VEPs to simple achromatic stimuli (checkerboards and gratings) in grapheme-colour synaesthetes. Although we too found larger VEPs, the results do not agree in terms of specific details. Barnett et al. (2008) found differences in the earlier C1/P1 components and found a group X stimulus interaction (larger effects for high spatial frequency). In contrast, we found a larger visual N1 in synaesthetes that was common to all stimuli. This difference could reflect minor changes in the experimental design (e.g., our study interleaved auditory and visual trials), or difference in participant characteristics (e.g., we show that a larger P1 is linked to higher autistic traits which often co-occur with synaesthesia but were matched in the present study). It is also to be noted that although our group difference was significant for the visual N1 component it may reflect earlier emerging differences in the P1-N1 time window. Our result does resemble other findings in the literature. Sinke et al. (2014) presented participants with line drawings alongside three
different conditions (congruent sound, incongruent sound, no sound) and found that synaesthetes had a larger visual N1 irrespective of the accompanying stimulus or task. Other research has found enhanced N1 components in response to viewing graphemes in synaesthetes (Brang et al., 2011; Schreiter et al., 2019). Whilst these results could be explained by the induction of synaesthesia per se, our findings point to a different conclusion. Namely, that there are generic differences in the processing of visual information by synaesthetes across many/most visual stimuli that may not be related to the presence of anomalous experiences per se. Instead, our speculative conclusion is that it may act as an electrophysiological marker of brain differences that led to the emergence of synaesthesia in the first place. Others have argued that the brains of synaesthesia differ only from non-synaesthetes by virtue of storing a special kind of childhood memory (Hupe & Dojat, 2015). Our findings speak against that claim.

The synesthetes uniquely elicited an additional neural response in the left fusiform gyrus, which resulted in the change in waveform morphology (around visual P1-N1), as recorded on the scalp. The functional role of this region is not clear but it is in the vicinity of the visual-word form area and the colour-sensitive region V4. In neither case would we expect this region to respond strongly to achromatic gratings. The ‘textbook’ model of visual processing, stemming from Hubel and Wiesel, is that of a hierarchy of stimulus features of increasing complexity (Ward, 2020). Thus, early visual regions (e.g. V1) rare specialised for line orientations and spatial frequency whereas later regions along the ventral stream (including fusiform) respond to combinations of those features such as junctions (e.g. as in the letter ‘T’). One possibility is that, in synaesthetes, this tuning is aberrant such that visual regions that are normally later in the hierarchy have an unusually high responsiveness to simple visual features. The net effect is greater propagation of activity throughout the ventral visual stream resulting in changes to VEP components such as the visual N1. Similar results have been reported for resting state fMRI in which a seed region in visual ventral stream (V4, in this study) had far more widespread connectivity in synaesthetes within the visual ventral stream and beyond (Dovern et al., 2012). Our findings from EEG time-frequency analysis are also consistent with greater visual event-related synchronisation (primarily within the alpha and beta range) across a distributed brain network. The visual-evoked differences between synaesthetes and controls are unlikely to reflect the colored fixation dot (as opposed to the gratings) because the fixation dot was also present on auditory trials (where a different pattern was found) and during the baseline period of all stimuli.

Comparatively less is known about auditory processing differences in synaesthetes either behaviourally or in terms of neural correlates. In the present study we find that synaesthetes have an enhanced auditory N1 to notched noise stimuli (across different frequencies) with a similar scalp topography to that observed in non-synaesthetes (although this was not explored in detail). This was found irrespective of whether synaesthetes reported that sounds act as an inducer or not. That is, as with the VEP findings they appear to be a general feature of being a synaesthete that is not tied strongly to the induction of synaesthesia by the experiment itself. In terms of comparability with previous research, one previous study specifically tested sound-colour synaesthetes and found lower auditory evoked potentials over several components, including N1 (Goller et al., 2009) – i.e. the opposite to that reported here – and another study used speech sounds and reported no group difference in amplitudes (Beeli, Esslen, & Jancke, 2008). As such, the findings in the literature with regards to auditory evoked potential are contradictory and may reflect experimental differences (e.g. in stimuli such as differences in aversiveness), different participant characteristics, or genuine failures of replication (i.e. one or more false positive results).

**Implications for Individual Differences in Sensory Sensitivity**
It is unclear why Study 1 failed to reveal any electrophysiological markers relating to individual differences in sensory sensitivity, but caution is needed in interpreting this because we did not prove the null. The GSQ measure is being widely adopted (we know of translations in at least 4 other languages: Kuiper, Verhoeven, & Geurts, 2019; Sapey-Triomphe, Moulin, Sonie, & Schmitz, 2018; Takayama et al., 2014; Ward, Ren, & Qiu, submitted) and the differences between our high and low sensitivity group on this measure was large (Cohen’s d = 3.0). But how these real-world self-reported sensory differences translate into lab-based differences with simple stimuli isn’t known. Our results show that people with high GSQ score are more likely to report visual discomfort for high spatial frequency stimuli which accords well with other research relating to visual stress (Juricevic, Land, Wilkins, & Webster, 2010; Wilkins et al., 1984). Effects for auditory stimuli were weaker but showed a trend in the same direction. Whilst other EEG studies have examined the relationship between the spatial frequency of visual stimuli and overall levels of stimulus-induced discomfort (O’Hare, 2017; O’Hare, Clarke, & Pollux, 2015), these studies did not explore trait-level differences in sensory sensitivity.

It is possible that larger samples would be needed to detect EEG correlates of these individual differences and it is to be noted that all of our analyses point to small effect sizes. However, there are more interesting theoretical reasons as to why we might not have observed significant results. It may be that brain regions that don’t directly contribute to scalp EEG, such as the thalamus, are relevant to these differences. However, even in this case, we would expect, based on previous results (Green, Hernandez, Bookheimer, & Dapretto, 2017), that thalamic inputs would modulate cortical sensory regions (which do contribute to the EEG signal). Other accounts link heightened sensory sensitivity with increased neural noise (e.g. Rubenstein & Merzenich, 2003; Simmons et al., 2009), although there are multiple ways in which that could be instantiated. Increased spontaneous, non-synchronised, neural activity would be averaged out by standard EEG analyses, although this could potentially reveal itself in measures such as trial-by-trial variability (Dinstein et al., 2012). Other possibilities are that neural noise reflects a coordinated propagation of activity to other brain regions; as appears to be the case in synaesthesia. Here, we would expect to observe differences.

Another possibility is that individual differences in sensory sensitivity are context dependent – reflecting, for instance, particular stimulus or task properties that were not considered here. A recent study reported a link between sensory sensitivity (using a different questionnaire measure) and visual-evoked gamma suppression (~70Hz) to moving circular gratings in MEG (magnetoencephalography) but the relationship was only apparent at the highest velocity (Orehkova et al., 2019). Temporal factors, such as adaptation, might also be relevant to individual differences in sensory sensitivity but were not modelled in our study. For instance, people of low-to-normal sensitivity may be better able to adapt to repeated presentations of aversive or irrelevant stimuli, whereas people with high sensory sensitivity may not be able to attenuate their response. Failures of adaptation have been reported in a number of conditions linked to high sensory sensitivity including migraine (Brighina, Palermo, & Fierro, 2009) and autism (Pellicano, Jeffer, Burr, & Rhodes, 2007). In our study, each stimulus was presented one hundred times (and with discomfort ratings taken only at the end of the session). Future research could model how evoked responses change across repetitions (our data is open access to facilitate a reanalysis of this). Future research should also take behavioural ratings at different time points (to determine if discomfort itself changes).

To summarise, this study demonstrated the existence of electrophysiological markers linked to synaesthesia that suggest heightened perceptual processing of auditory and visual
stimuli (whether they elicit synaesthesia or not) that cannot be accounted for by differences in trait-level subjective sensory sensitivity. Note that individual differences in sensory sensitivity can manifest in multiple ways (Ward, 2019): as differences in subjective sensory sensitivity (e.g., finding sounds and vision aversive, as measured by the GSQ); behavioural sensory sensitivity (e.g., ability to discriminate/detect sensory stimuli); and neural sensory sensitivity (increased neural/neurophysiological responsiveness to sensory stimuli). Neural correlates of these individual differences in subjective sensory sensitivity remain elusive, but the present study suggests concrete new directions in which to explore this and also suggests that neural sensory sensitivity (in synaesthetes) is not necessarily linked to subjective sensory sensitivity.

Online Data

Raw and summarised data is available via DOI 10.17605/OSF.IO/BEJ72
References


