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Familial aggregation of synaesthesia with autism (but not schizophrenia)

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ABSTRACT
Introduction: This study determines whether there is a familial aggregation between synaesthesia and two neuropsychiatric conditions (autism and schizophrenia). METHOD We examined the prevalence of autism and schizophrenia among synaesthetes and non-synaesthetic controls, and among their first-degree relatives. Results: As predicted, autism occurred at elevated levels among synaesthetes and—we document for the first time—amongst their relatives. This was not found for schizophrenia, where a link may be expected, or in a control condition (type 1 diabetes) where we had no a priori reason to assume a link. Synaesthetes, compared to controls, were also more likely to have other synaesthetes in their family. People with three or more types of synaesthesia were more likely (compared to synaesthetes with fewer types) to have synaesthetic relatives and to report autism in themselves. People with two or more types of synaesthesia (compared to synaesthetes with only one type) were more likely to report familial autism. Conclusions: The results suggest a shared genetic predisposition between synaesthesia and autism, and more extreme synaesthetes may tend to hail from more neurodiverse families.

Synaesthesia is a condition in which sensory stimuli in a specific modality trigger additional sensations either in a different modality (e.g., the spoken word “Tottenham” triggering the taste of potato) or the same modality (e.g., the written letter “A” triggering the visual sensation of redness). This latter form, where letters or numbers induce the sensation of colours, is known as grapheme-colour synaesthesia (GCS), and is the most commonly studied type. Synaesthesia is thought to affect around 4% of the population (Simner et al., 2006). It has long been suspected that there exists a genetic predisposition for synaesthesia, with anecdotal evidence that synaesthesia runs in families from as far back as the nineteenth century (e.g., Galton, 1883). More recently, twin studies have confirmed its heritability (Bosley & Eagleman, 2015) and molecular genetic studies have identified specific chromosomal sites (Asher et al., 2009; Tilot et al., 2018; Tomson et al., 2011). Relatives of synaesthetes also display some traits associated with synaesthesia in
the absence of synaesthesia itself. Relatives of synaesthetes show similar tendencies to synaesthetes on cognitive and personality measures (Ward & Filiz, 2020) and structural and functional MRI (Colizoli et al., 2017). That is, there may be an endophenotype or intermediate phenotype linked to synaesthesia which has been called a “synaesthetic disposition” (Ward, 2019). As such, it is likely that there aren’t strictly any “genes for synaesthesia” but, instead, genes that convey susceptibility to synaesthesia have a more generic role in brain development. Hence, a genetic susceptibility to synaesthesia manifests itself not only as synaesthesia but also as other kinds of differences found both in synaesthetes and some of their relatives. These differences may include traits that are considered adaptive (e.g., enhanced cognitive ability in certain domains) and/or maladaptive, such as also conveying susceptibility to neuropsychiatric conditions (e.g., autism, schizophrenia).

Autism is a developmental condition characterised by deficits in social interaction and maintaining relationships, and repetitive patterns of behaviour (DSM-V, American Psychiatric Association, 2013). It is thought to occur in 1–2.6% of the population (Brugha et al., 2011; Lundström et al., 2015; Maenner et al., 2020). There is growing evidence that synaesthesia and autism may be linked. Notably, both conditions share several features. For example, synaesthetes have been found to score higher than expected on questionnaires measuring sensory sensitivity and attention to detail, both of which are recognised characteristics of autism (van Leeuwen et al., 2019; Ward et al., 2017; Ward et al., 2018). Beyond an overlap in characteristics, several studies have demonstrated a higher-than-typical prevalence of synaesthesia among autistic individuals (Baron-Cohen et al., 2013; Hughes et al., 2017; Neufeld et al., 2013). This may extend to families. Bouvet et al. (2019) reported the case of a single individual with synaesthesia and autistic savant abilities. Among his 39 family members, 15 self-reported synaesthesia and four had diagnosed autism (two of whom had both autism and synaesthesia). The co-occurrence of synaesthesia and autism both within individuals and within families raises the possibility that these are two different phenotypic outcomes of a similar neurodevelopmental process (van Leeuwen et al., 2020a). However, the evidence for a familial aggregation of synaesthesia and autism is presently anecdotal and the only molecular genetic study to explore this did not find evidence for a link (Tilot et al., 2019). (Note: the familial aggregation of synaesthesia (e.g., Barnett et al., 2008; Baron-Cohen et al., 1996) and the familial aggregation of autism (e.g., Bailey et al., 1995), as separate entities, is well-documented).

The phenomenological similarity between a synaesthetic experience and a hallucination might lead one to expect a closer relationship between synaesthesia and schizophrenia than with autism. Schizophrenia is a condition which is characterised by delusions and hallucinations, as well as impairment of cognition, motivation and emotional expression (American Psychiatric Association, 2013). It is thought to occur in 0.3%–0.75% of individuals (Moreno-Küstner et al., 2018; Saha et al., 2005). Carmichael et al. (2019) is the only known study to have looked at the prevalence of schizophrenia amongst people with synaesthesia but no significant association was documented (anxiety and autism were significant co-morbidities with synaesthesia, although autism did not survive correction for multiple comparisons). In terms of the subclinical trait of schizotypy, synaesthetes report elevated scores on the Unusual Experiences subscale of the O-LIFE (Oxford-Liverpool Inventory of Feelings and Experiences; Mason & Claridge, 2006) in two studies (Banissy et al., 2012; Janik McErlean & Banissy, 2016). Neither
study found differences for Introvertive Anhedonia or Impulsive Non-Conformity, and results for Cognitive Disorganisation were inconsistent. Tilot et al. (2019) found a significant but “very slight” association by applying polygenic risk scores relating to schizophrenia to the genomes of synaesthetes.

In summary, there is good evidence that autism and synaesthesia co-occur more than chance. This has not been documented for schizophrenia, although there is other suggestive evidence for a link. As such, we hypothesise that we will find an increased prevalence of autism in both synaesthetes and their relatives (the latter being documented systematically for the first time). The hypothesis that there will be increased prevalence of schizophrenia in synaesthetes and their relatives is more exploratory. It is possible that previous research has missed the link because synaesthetes with schizophrenia are less inclined to present themselves as research volunteers. By looking for schizophrenia in the relatives of synaesthetes we can avoid this potential recruitment bias (because the relatives themselves are not active research participants). A third health condition was included as a negative control because we were concerned that if positive associations were found to both autism and schizophrenia then the data could be interpreted as a non-specific effect (e.g., a reporting bias, or a tendency for synaesthesia to be linked to all kinds of medical conditions). Type 1 diabetes was included because it is not thought to have any links to synaesthesia and has a similar prevalence to autism and schizophrenia of around 0.3–1% (Atkinson et al., 2014; Prevention, 2020; Xu et al., 2018) Centre for Disease Control and Prevention.

A final hypothesis concerns heterogeneity amongst synaesthetes themselves. Specifically, we hypothesise that synaesthetes with a more extreme profile will come from more neurodiverse families. Some synaesthetes have only one or two types of synaesthesia and others possess many types. This variable predicts performance on measures of cognition and personality (Rouw & Scholte, 2016; Ward & Filiz, 2020) including questionnaire measures of autistic traits (van Leeuwen et al., 2019; Ward et al., 2018). Ward (2019) speculated that having many types of synaesthesia is an outcome of a more extreme underlying synaesthetic disposition (including both genetic and brain-based differences). Such individual differences may therefore be observable even in the relatives of these synaesthetes. Specifically, relatives of people with more extreme synaesthesia are hypothesised to be more likely to also have synaesthesia themselves and more likely to have schizophrenia and/or autism.

Methods

Participants

Participants were comprised of two separate groups. The synaesthesia group were 314 (f = 281, m = 32, other = 1) participants who had previously taken part in synaesthesia-related research and had expressed willingness to participate in further studies. Ages ranged from 20 to 80 (M = 40.04, SD = 15.11). The control group were 361 (f = 257, m = 102, other = 2) participants randomly selected through Testable Minds (testable.org). Ages ranged from 18 to 74 (M = 35.56, SD = 10.32). The survey was described as being related to “synaesthesia and family health” but with no advanced mention of the specific conditions being asked about. This was done in order to minimise self-selection.
Thirty-two responses in the synaesthesia group and 33 responses in the control group were removed because they were duplicate entries, were lacking essential information, or for failing a quality control check (discrepancy between the number of relatives reported across questions). In addition, 47 control respondents were removed because they thought they had synaesthesia (the control group was intended to be non-synaesthetes). This left 282 participants in the synaesthesia group and 281 in the control group.

The number of types of synaesthesia a person has was based on the analysis of Ward and Simner (2022) which considered ten clusters of types of synaesthesia: Language-colour (including grapheme-colour); Language-taste; Language-touch; Visualised Sensations; Smell/Taste concurrents; Sequence-space; Personification; Hearing-motion; Tickertape; and Mirror-touch. The mean number (out of 10) in that study was reported as 3.5. Therefore, we took three or less as a “few” category (N = 175 synaesthetes) and four or more as a “many” category (N = 107 synaesthetes) in the current analyses. In the present study the mean was 3.10 (S.D. = 1.59). Alternative cuts of the data are reported as exploratory. The synaesthetes minimally had either grapheme-colour or sequence-space because these were the types of synaesthesia that had been verified by previous research (using the methods of Rothen et al., 2013; Ward et al., 2018). In brief, these tests involve presenting a set of graphemes (10 digits, 26 letters) or a set of sequential concepts (7 days, 12 months, 10 digits) and asking participants to choose a corresponding colour (for grapheme-colour synaesthesia) or location on the screen (for sequence-space synaesthesia). Each item is repeated three times so that within-item consistency can be calculated (measures of distance within RGB colour space or distance on the screen). More consistent responding is linked to lower scores, with a score below the published threshold being considered diagnostic of synaesthesia.

The families of the synaesthetes consisted of 169 brothers, 194 sisters, 89 daughters and 98 sons. The families of controls consisted of 230 brothers, 170 sisters, 90 daughters and 78 sons. Including the parents, we obtained information about 1114 first-degree relatives of synaesthetes and 1130 of controls (excluding the probands themselves), with the number of male and female relatives not differing between the groups: $X^2 (1, N = 2244) = 1.81, p = .178$. A power analysis is reported below.

This study was deemed low risk and was granted ethical approval from the Sciences & Technology Cross-Schools Research Ethics Committee (C-REC) at the University of Sussex.

**Materials and procedure**

Participants completed the questionnaire online using Qualtrics (Provo, UT), taking around 10 minutes.

The questionnaire contained four groupings of questions. The first grouping related to basic demographic and personal information to connect the synaesthetes with previous data (on their consistency and number of subtypes).

The second grouping included four questions under the heading: “How many people do you have in your immediate family?”. The respondent entered numerical values for how many brothers, sisters, sons and daughters they had. They were asked to exclude half-brothers and half-sisters, and step family. They were then told “If you add up these four numbers and then add two more people (for your mother and father) this
gives you the total number of your first-degree relatives. A first-degree relative means that you share half of your genes with each of them.

The third grouping contained a brief description of what synaesthesia is: “Synaesthesia comes in many different forms, some of which are shown in the figure. Synaesthetes may have colours for numbers, tastes for words, habitually visualise their own mental calendar, have personalities or genders for letters, or hear sounds when they see silent objects move. Examples of synaesthesia: (see Figure 1)” Note that the image on the left is taken from (Skelton et al., 2009).

They were then asked the following questions “Considering these people (brothers, sisters, sons, daughters, mother, father) ...”

(1) How many members of your family can you CONFIDENTLY say [also] have synaesthesia? (i.e., you have asked them about synaesthesia and they report having some of these kinds of experiences)
(2) How many members of your family can you CONFIDENTLY say do NOT have synaesthesia? (i.e., you have asked them about synaesthesia and they deny having these kinds of experiences)
(3) How many members of your family are you UNSURE about whether they have synaesthesia or not?

Controls were also asked whether they thought that they themselves had synaesthesia, with the options of “I am sure I do not have it”, “unsure” and “I am sure I do have it”. This was followed by the statement “If there is anything else you would like to add to clarify this then you may do so here” and a freeform response box.

In the fourth and final group of questions, they were then asked to consider “these people (brothers, sisters, sons, daughters, mother, father)” to answer the following questions by clicking checkboxes or a “prefer not to say” option:

(1) How many members of your family have received a diagnosis of autism spectrum condition?
(2) How many members of your family have received a diagnosis of schizophrenia?
(3) How many members of your family have received a diagnosis of type 1 diabetes?
(4) Have you ever been diagnosed with any of these conditions? (tick as many as apply) [autism; schizophrenia; type 1 diabetes; prefer not to say]

Figure 1. Example types of synaesthesia used to explain the concept.
Analyses

**Inferential statistics and power calculations**

Degree of association was assessed via a chi-square test when possible, with Fisher’s exact test used when not possible (small N, expected values in a cell below 5). Effect sizes are reported in terms of odds ratios (OR) and the small, medium, and large categories of Chen et al. (2010), respectively OR = 1.68, 3.47, and 6.71.

Power calculations were performed using G*Power and were based on an assumed control prevalence of 1.00% across the three conditions and one-tailed predictions (i.e., more prevalent in synaesthetes). Based on our samples of N = 1130 and 1114, the study was able to detect a minimum prevalence amongst the relatives of synaesthetes of 2.35% (OR = 2.38) at a power of 0.80 and alpha = 0.05. Amongst probands, based on N = 281 and 282, we were able to detect a minimum prevalence amongst synaesthetes of 4.5% (OR = 4.56) at a power of 0.8 and alpha = 0.05. For comparison, Carmichael et al. (2019) reported OR = 4.9 for a diagnosis of autism amongst synaesthetes compared to controls.

**Coding of freeform text**

Responses in the freeform text essentially took two forms: clarifications and further information about suspected but undiagnosed conditions, some of which were relevant (notably around autism) and some of which were not relevant to the present study (e.g., information about more distant relatives, other conditions).

The clarifications lead to some recoding of data. For the question asking whether respondents had autism, schizophrenia or type 1 diabetes, N = 29 control respondents selected “prefer not to say”. However, eight of these respondents indicated in the subsequent freeform response box that they had selected “prefer not to say” because there was no option to indicate that they had none of these conditions (they should in fact have left the question blank). For example, freeform comments included “Prefer not to say = I don’t have any of those three conditions” and “I have not been diagnosed with any of them”. These eight “prefer not to say” responses were thus recoded as negative responses for these conditions. Other respondents indicated that they did not include information about synaesthesia for relatives who had died and these were recoded into the “unsure” category.

There were a significant number of comments on suspected but undiagnosed autism. These were coded as separate variables labelled as “probable” and “possible” autism (where probable indicates more likely than not). The coding procedure is described below and the raw data and codings are available for inspection in the supplementary material. A primary coder created a set of example codings to be shared with a secondary
coder with responses divided into probable/possible and whether the comment referred to proband versus relative. Examples with their coding included the following:

“Am currently waiting to be evaluated by a psychologist, as I may have autism spectrum disorder. My father may as well too, however he has not been diagnosed” [possible – proband, and, possible - 1 relative]

“I believe I have autism but have never gone to ask for diagnosis”. [probable – proband]

“I have one diagnosed daughter and 2 sons who are without [doubt] on the autistic spectrum but I won’t be having them screened as the process is too arduous”. [1 diagnosed relative; 2 probable relatives]

The freeform text was blind coded with respect to synaesthesia/control status. The codings of the primary coder were retained and used for analysis, whereas the codings of the secondary coder were used to assess inter-rater reliability.

For cases of “probable autism” among respondents (where each freeform response was given a binary outcome of “probable case” or “not probable case”), Cohen’s Kappa was calculated: $K = 0.8$. This is an excellent level of inter-rater agreement. For cases of “possible autism” among respondents, Cohen’s Kappa was also calculated: $K = 0.63$. This is a good level of inter-rater agreement, suggesting good reliability of the scale. For cases of “probable autism” among first-degree relatives (where each freeform response had a different range of coding outcomes, ranging from 0 to that respondent’s number of first-degree relatives), percentage agreement between raters was calculated: percentage agreement = 94.78%. For cases of “possible autism” among first-degree relatives, percentage agreement was also calculated: percentage agreement = 95.65%.

**Results**

**Association between synaesthesia and autism**

The results are summarised in Figure 2.

*Probands.* In the synaesthesia group (n = 282), 11 respondents had diagnosed autism, 10 had probable autism and six had possible autism. Two participants chose “prefer not to say” but one of these was recoded based on freeform response as a possible case, and the other was excluded from analysis. In the control group (n = 281), one respondent had diagnosed autism, one had probable autism and five had possible autism. Twenty-one participants chose “prefer not to say” of which one was recoded as a probable case, one as a possible case, and the remaining 19 were excluded from analysis. In all three cases, autism was more common in synaesthetes (3.93% respondents diagnosed autistic, 3.57% probable autistic, 2.14% possible autistic) than controls (0.38% diagnosed autistic, 0.38% probable autistic, 1.91% possible autistic). This compares to typical population prevalence for diagnosed autism of 1–2.6% (Baio et al., 2018; Brugha et al., 2011; Lundström et al., 2015), albeit with a lower prevalence in women (0.20% in Lundström et al., 2015; and 0.69% in Maenner et al., 2020). Three Fisher’s Exact tests of independence were conducted to examine the distribution of autism among synaesthetes and controls depending on the strictness of the evidence: diagnosed only; diagnosed and probable only; or diagnosed, probable and possible. All three were significant ($p = .006$, $p < .001$, and $p = .001$ respectively). Odds ratios for the occurrence of autism, comparing the
synaesthesia group to the control group, were also calculated. For diagnosed autism, OR = 10.63, 95% CI (1.36, 82.94), \( p = .024 \). For diagnosed and probable autism, OR = 10.5, 95% CI (2.44, 45.24), \( p = .002 \). For diagnosed, probable and possible autism, OR = 3.87, 95% CI (1.66, 9.05), \( p = .002 \). These indicate a large effect of having synaesthesia on the likelihood of also having autism (particularly diagnosed and diagnosed + probable autism).

**Relatives.** Among first-degree relatives of synaesthetes (\( n = 1114 \)), 33 had diagnosed autism, 12 had probable autism and eight had possible autism. Two respondents, with eight first degree relatives, chose “prefer not to say”. One of these relatives was recoded as

![Figure 2](image-url)
a possible case, and the remaining seven were excluded from analysis. Among first-degree relatives of controls (n = 1130), 19 had diagnosed autism, two had probable autism and eight had possible autism. In all three cases, autism was more common in first degree relatives of synaesthetes (2.98% respondents diagnosed autistic, 1.08% probable autistic, 0.72% possible autistic) than first degree relatives of non-synaesthetes (1.68% diagnosed autistic, 0.18% probable autistic, 0.71% possible autistic). This compares to typical population prevalence for diagnosed autism of 1–2.6% (Baio et al., 2018; Brugha et al., 2011; CDC, 2020b; Lundström et al., 2015). Three chi square tests of independence were conducted to examine the distribution of autism among first-degree relatives of synaesthetes and controls. The first looked solely at diagnosed autism, and was significant, X² (1, N = 2237) = 4.16, p = .041. The second looked at a combined category of diagnosed and probable autism, and was significant, X² (1, N = 2237) = 9.51, p = .002. The third looked at a combined category of diagnosed, probable and possible autism, and was significant, X² (1, N = 2237) = 7.81, p = .005. The odds ratio for diagnosed autism was OR = 1.8, 95% CI (1.02, 3.18), p = .044. For diagnosed and probable autism, OR = 2.24, 95% CI (1.32, 3.78), p = .003. For diagnosed, probable and possible autism, OR = 1.91, 95% CI (1.21, 3.03), p = .006. These indicate a moderate effect of having synaesthesia on the likelihood of first-degree relatives having autism.

**Association between synaesthesia and schizophrenia**

**Probands.** In the synaesthesia group (n = 282), one respondent had schizophrenia (0.36%). Two chose “prefer not to say”. In the control group (n = 281), 0 respondents had schizophrenia. Twenty-one chose “prefer not to say”. Statistical analyses were not conducted due to the low number of self-reported cases.

**Relatives.** Among first-degree relatives of synaesthetes (n = 1114), 10 had schizophrenia (0.9%). One respondent, with five first-degree relatives, chose “prefer not to say”, and these relatives were excluded from analysis. Among first-degree relatives of controls (n = 1130), 15 had schizophrenia (1.33%). This compares to a typical population prevalence of 0.3%–0.75% (Moreno-Küstner et al., 2018; Saha et al., 2005). A chi square test of independence was conducted to examine the distribution of schizophrenia among first-degree relatives of synaesthetes and controls. This was non-significant, X² (1, N = 2239) = 0.92, p = .338, indicating that schizophrenia does not occur more commonly in first-degree relatives of non-synaesthetes than synaesthetes. The odds ratio for the occurrence of schizophrenia, comparing first-degree relatives of synaesthetes and first-degree relatives of controls, was: OR = 0.68, 95% CI (0.3, 1.51), p = .341.

**Association between synaesthesia and type 1 diabetes (control condition)**

**Probands.** In the synaesthesia group (n = 282), no respondents had type 1 diabetes. Two chose “prefer not to say”. In the control group (n = 281), seven respondents had type 1 diabetes (2.7%). Twenty-one chose “prefer not to say”. This compares to typical population prevalence of 0.3–1% (Atkinson et al., 2014; CDC, 2020a; Xu et al., 2018). A Fisher’s exact test of independence was significant (p = .006).

**Relatives.** Among first-degree relatives of synaesthetes (n = 1114), 22 had type 1 diabetes (1.9%). One respondent chose “prefer not to say”. Among first-degree relatives of controls (n = 1130), 34 had type 1 diabetes (3.01%). A chi square test of independence
indicates that type 1 diabetes did not occur significantly more commonly in first-degree relatives of non-synaesthetes than first-degree relatives of synaesthetes in this sample: \(X^2(1, N = 2239) = 2.41, p = .120\). The odds ratio for the occurrence of type 1 diabetes, comparing first-degree relatives of synaesthetes and first-degree relatives of controls, was: \(OR = 0.65, 95\% CI (0.38, 1.12), p = .120\).

**Familial aggregation of synaesthesia**

Among first-degree relatives of synaesthetes (n = 1114), 140 had synaesthesia, 543 did not, and 426 were deemed as “unsure”. Two respondents, with five first-degree relatives in total, did not answer questions about numbers of relatives with synaesthesia, and these relatives were excluded from analysis. Among first-degree relatives of controls (n = 1130), 43 had synaesthesia, 473 did not, and 614 were deemed as “unsure”. Synaesthesia was more common among first-degree relatives of synaesthetes (12.62%) than first-degree relatives of controls (3.81%). This compares to typical population prevalence of around 4% (Simner et al., 2006). The difference was significant, excluding “unsure” responses, \(X^2 (1, N = 1199) = 33.63, p < .001\). The odds ratio for occurrence of synaesthesia, comparing first-degree relatives of synaesthetes and first-degree relatives of controls, indicates a small-to-moderate effect of having synaesthesia on the likelihood of first-degree relatives also having synaesthesia: \(OR = 2.83, 95\% CI (1.97, 4.08), p < .001\).

**Do extreme synaesthetes come from more neurodiverse families?**

Figures 3 and 4 shows the summary of this analysis considering only differences amongst synaesthetes themselves rather than differences between synaesthetes and controls. Our pre-planned analysis divided synaesthetes into those with “few” (1–3 types) versus “many” (4+) types reflecting the midpoint of the distribution (binning is helpful because the number of positive cases is small even though this is a continuous measure). None of the findings were significant. For diagnosed autism: \(X^2 (1, N = 1114) = 0.001, p = .982\). For diagnosed and probable autism: \(X^2 (1, N = 1114) = 0.052, p = .819\). For diagnosed, probable and possible autism: \(X^2 (1, N = 1114) = 1.42, p = .233\). For schizophrenia, Fisher’s exact \(p = .344\). For synaesthesia: \(X^2 (1, N = 1114) = 1.913, p = .167\).

Exploratory analyses were conducted for other cuts of the data, which are reported in full in the Supplementary Material. (They are exploratory in the sense of not being pre-planned and would not survive correction for multiple comparisons, so would require replication). A significant difference was found between having a single type versus multiple (2+) types of synaesthesia on familial prevalence of autism (diagnosed and probable autism: \(X^2(1) = 4.63, p = .031, OR = 3.40 [1.04–11.08]\); diagnosed, probable and possible autism: \(X^2(1) = 9.31, p = .002, OR = 5.14 [1.60–16.54]\)). We also find a significant difference between having two or less versus three or more kinds of synaesthesia on the familial prevalence of synaesthesia \(X^2(1) = 5.81, p = .016, OR = 1.58 [1.09–2.29]\), and for rates of autism amongst the probands themselves (diagnosed and probable autism: \(X^2(1) = 6.44, p = .011, OR = 4.44 [1.28–15.44]\); diagnosed, probable and possible autism: \(X^2(1) = 8.13, p = .004, OR = 4.36 [1.47–12.98]\)). That is, we find evidence of heterogeneity amongst synaesthetes and their families but only when we divide them with a low cut (1 or 2 types against 3–10 types).
Discussion

Previous research has shown that autism and synaesthesia are more likely to occur in the same individual. Our research replicates this finding and extends it in an important way by showing that autism and synaesthesia are more likely to occur within the same family such that one family member may have synaesthesia and a different family member has autism (for previous anecdotal evidence from a single large family see Bouvet et al., 2019). We provide illustrative examples from a number of our families:

- Synaesthete EQ does not report autism in herself. She has three sons and three daughters: one daughter has a confirmed diagnosis of autism and two sons have suspected autism (“I won’t be having them screened as the process is too arduous”). None of her first-degree relatives have synaesthesia.
- Synesthete CC reports that she also has possible autism. Her father has possible autism but not synaesthesia. Her brother and mother have synaesthesia but not autism. Thus, all of her first-degree relatives have either autism or synaesthesia (with CC reporting both).
- Synesthete KM does not report autism in herself, but she has a son with a confirmed diagnosis of autism and a daughter with synaesthesia.
The familial aggregation of synaesthesia and autism appears to be relatively specific insofar as we failed to observe this for schizophrenia (where a link has been speculated) and a control condition of Type 1 diabetes (where we had no reason to expect a link). This is consistent with prior research which asked about a large range of mental/physical health conditions amongst synaesthetes and found few associations (Carmichael et al., 2019). The current research deliberately focused on a small number of conditions of interest to maximise our statistical power. As such, we cannot rule out associations to other conditions such as PTSD (Hoffman et al., 2019) or anxiety (Carmichael et al., 2019) which have been previously linked to synaesthesia.

In this discussion, we first focus on the limitations of the study. We then consider the possible links between synaesthesia and autism / schizophrenia. Finally, we consider synaesthesia itself, including individual differences amongst synaesthetes.

**Limitations**

Before discussing the implications of our findings it is important to acknowledge the limitations. The most significant limitation is that we cannot verify the truthfulness of
responding. A related concern is that the control group may be less inclined to disclose health issues. Notably, they give more “prefer not to say” responses which may be masking positive cases. However, we note that the reported prevalences amongst controls and their relatives are similar to published norms for those conditions. The decision to code freetext responses could be questioned, although we note that our results do not hinge on this; the effect sizes are comparable when we limit the analysis to diagnosed cases. Even assuming truthful responding, there is undoubtedly variability in diagnosis-seeking behaviour, and variability in diagnosis-attainment (access to professionals, imperfect diagnostic criteria). It is possible that synaesthetes are more proactive in seeking and obtaining an autism diagnosis, and their family members are too. But converging evidence shows that high autism levels are found in synaesthesia even without a formal diagnosis (van Leeuwen et al., 2019; Ward et al., 2017; Ward et al., 2018).

In the case of the null result between synaesthesia and schizophrenia, the power analysis is necessarily post-hoc (i.e., based on the actual sample size obtained rather than the sample size needed) because the expected effect size is unknown. Similarly, to prove the null (e.g., using Bayes factors) one would need a suitable estimate of an expected effect size. As such, we do not claim to have proven the absence of a link between synaesthesia and schizophrenia. But we do argue that this is one of the most rigorous attempts to find a link to date.

Another possible limitation is that our synaesthetes may not be typical of the wider synaesthetic population recruited by screening the general population (Simner, 2019). It may indeed be the case that autism is found primarily in people with multiple forms of synaesthesia, and so the observed degree of association between autism and synaesthesia is dependent on sample characteristics (which itself depends on sampling method). Finally, the accuracy of reporting of familial cases of synaesthesia is likely to be noisy, particularly amongst non-synaesthetes where it is less likely to have been discussed. We included an “unsure” category to try to capture this. However, the inclusion of this question was also motivated by an interest in comparing synaesthetes with few versus many types where it is more reasonable to assume that knowledge of synaesthesia amongst family members is better matched.

**Synaesthesia and autism**

If you are a synaesthete then the odds ratio that a given first-degree relative has autism is similar to the odds ratio that a given first-degree relative will have synaesthesia—both are medium effects (i.e., OR in the range 1.63–3.47 defined by Chen et al., 2010). The fact that synaesthesia and autism co-occur amongst different individuals within the same families speaks against the simple view that synaesthesia causes autism or vice versa. Instead the evidence is consistent with a heritable latent variable that biases the brain to develop one or other conditions (or both). van Leeuwen et al. (2019) outline various scenarios that are consistent with this, including a similar brain connectivity profile, but further research that directly compares these conditions on the same metric is needed.

Autism is a heterogeneous condition and one possibility is that a link to synaesthesia (within individuals, within families) helps to explain that heterogeneity in terms of symptom profile, severity, or different genetic risks in different individuals. Is synaesthesia a phenotypic outcome of having “mild autism”? Although that idea is intriguing, the
evidence from our study speaks against this by demonstrating that synaesthetes are more likely to reach a diagnostic threshold (of course many more may lie below that threshold too). The possibility that synaesthetes have a different autistic symptom profile is possible based on current evidence. For example, synaesthesia has been linked to savant skills in autism (Hughes et al., 2017; Mottron et al., 2013) and, on formal tests and questionnaires, they have heightened abilities on attention-to-detail measures (Ward et al., 2017). Other conditions linked to shifts up the autism spectrum, such as anorexia nervosa, show a different profile of characteristics (Westwood et al., 2016). This suggests qualitative differences in the autism profile (relative degree of sensory and social features), and recent molecular genetic evidence also supports this division (Warrier et al., 2019). One obvious difference between autism and synaesthesia is that autism is more prevalent in males at least in diagnosed cases (Brugha et al., 2011; Lundström et al., 2015; Maenner et al., 2020), but no sex differences are found in synaesthesia when opportunistic screening is carried out (Simner et al., 2006; Simner & Carmichael, 2015). (Self-referred samples of synaesthetes, such as in the present study, tend to be predominantly female as is generally the case when relying on this sampling method.) Women with autism may engage in social camouflaging—deliberate attempts to mask or compensate for their difficulties (Hull et al., 2020); and there are diagnostic biases that act against autistic women (Gould & Ashton-Smith, 2011). Nevertheless, a recent consensus paper argues that there remains at least a 2:1–3:1 male:female autistic prevalence difference even accounting for such factors (Halladay et al., 2015). As such, one important future line of research is whether autism is equally prevalent in male and female synaesthetes (as found in the present sample, see Supplementary Material for a more detailed breakdown by sex/gender). This would present a clear departure from the pattern in the general population where males outnumber females. The diagnosed prevalence in our predominantly female samples were 0.38% (controls) and 3.93% (synaesthetes) compared to published prevalence rates in females of 0.20% (Lundström et al., 2015) and 0.69% (Maenner et al., 2020).

**Synaesthesia and schizophrenia**

Our results failed to find any link between synaesthesia and schizophrenia at an individual or familial level. No previous research has documented a link in terms of co-morbidity, although two studies have found elevated scores on the Unusual Experiences scale of a schizotypy measure (Banissy et al., 2012; Janik McErlean & Banissy, 2016) and synaesthetes show a significant, albeit very slight, association to polygenic risk scores for schizophrenia (Tilot et al., 2019).

It is noteworthy that whilst respondents chose to enter freeform text about sub-clinical autism, they did not do so for schizophrenia. Although the notion of schizophrenia being on a spectrum is debated by academics (Guloksuz & van Os, 2018; Lawrie et al., 2010), this has not permeated lay culture in the same way as the commonly agreed notion of an autism spectrum. Linscott and van Os (2013) argue that psychotic experiences, such as hallucinations, may be as common as 7.2% but to transition into psychosis would require other risks such as delusional interpretations or affective disorder. It is conceivable that synaesthetes occupy that initial state but are unlikely to possess the triggers for a transition into psychosis.

Theoretically it has been argued that both hallucinations in schizophrenia (Sterzer et al., 2018) and synaesthetic experiences (Seth, 2014) may be explained by strong or inflexible
priors within a predictive processing framework of perception. That is, such individuals may be more inclined to generate (or distort) sensory evidence to fit their internal models of the world, rather than to change their internal models in light of conflicting sensory evidence. These would constitute mid-level priors that are separate to higher-order beliefs (Seth, 2014). In the case of synaesthesia, they are aware of the “false” nature of their experiences (i.e., at the higher belief level they are not delusional) but such awareness does not attenuate the experience itself. Future research should directly compare synaesthetes and people with schizophrenia (with and without hallucinations) on experimental tasks that manipulate perceptual priors (e.g., see van Leeuwen et al., 2020b, for an example). It remains conceivable that there are mechanistic similarities between the two groups which, if borne out, would mean that synaesthesia could be an important test case for why unusual experiences do not necessarily lead to psychosis.

**Implications for synaesthesia**

Finally, the results have implications for synaesthesia itself. The study provides further evidence on the heritability of synaesthesia. Synaesthesia itself is heterogeneous with a broad range of types, and a wider phenotype of cognitive and behavioural differences (Ward & Filiz, 2020). Some of these are linked to autism (e.g., attention-to-detail) whereas others are not (e.g., vividness of mental imagery). There is evidence that people with more types of synaesthesia have a more distinctive (and more extreme) cognitive profile on these measures (Ward & Filiz, 2020). One explanation for this is in terms of a latent continuously varying “synaesthetic disposition” that makes synaesthesia likely to emerge in some people but not others, and also makes synaesthesia emerge multiple times in the same individual (Ward, 2019). This is assumed to include a genetic predisposition to synaesthesia leading to the prediction that people with many kinds of synaesthesia may themselves hail from families that are more neurodiverse. However, there is no agreement as to how to define “many kinds of synaesthesia”. Whilst we can think of the number of kinds of synaesthesia as a continuous dimension, it is unclear how that translates to brain and behaviour (e.g., it may be that differences in brain and behaviour plateau at some point). Here we divided our synaesthetes according to the midpoint of the distribution of number of types (1–3 versus 4+). There were no significant differences when the sample of synaesthetes were divided in this way. However, inspection of the data and further analyses show that people with only one or two types of synaesthesia were less likely to report autism in themselves and less likely to report synaesthesia or autism in their family members (compared to other synaesthetes).

As such, whilst the link between specific manifestations of synaesthesia and autism requires further investigation, a more general association between synaesthesia and autism appears to be robust and has important implications for understanding the causal mechanisms and wider phenotypic profile of these conditions.

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Availability of data and material
The anonymized data is deposited in https://osf.io/wrhdk/.

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