Research Report

Perceptual processing links autism and synesthesia: A co-twin control study

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Abstract

Synesthesia occurs more commonly in individuals fulfilling criteria for an autism spectrum diagnosis than in the general population. It is associated with autistic traits and autism-related perceptual processing characteristics, including a more detail-focused attentional style and altered sensory sensitivity. In addition, these characteristics correlate with the degree of grapheme-color synesthesia (consistency of grapheme-color associations) in non-synesthetes.

We investigated a predominantly non-synesthetic twin sample, including individuals fulfilling criteria for an autism spectrum diagnosis or other neurodevelopmental disorders (n = 65, 14–34 years, 60% female). We modelled linear relationships between the degree of grapheme-color synesthesia and autistic traits, sensory sensitivity, and visual perception, both within-twin pairs (22 pairs) where all factors shared by twins are implicitly controlled (including 50–100% genetics), and across the entire cohort.

We found that the degree of grapheme-color synesthesia was associated with autistic traits within the domain of Attention to Details and with sensory hyper-, but not hypo-sensitivity. These associations were stronger within-twin pairs than across the sample. Further, twins with a higher degree of grapheme-color synesthesia were better than their co-twins at identifying fragmented images (Fragmented Pictures Test).

This is the first twin study on the association between synesthesia and autism-related perceptual features and traits. The results suggest that investigating these associations within-twin pairs, implicitly adjusting for potential confounding factors shared by twins, is more sensitive than doing so in non-related individuals. Consistent with previous findings, the results suggest an association between the degree of grapheme-color synesthesia and autism-related perceptual features, while utilizing a different measure for sensory...
1. Introduction

Synesthesia is a non-pathological sensory condition where specific sensory inputs or concepts automatically trigger additional (often visual) sensations which can be more or less complex. For instance, a piano tone can trigger the sensation of an indigo blue sphere, moving in space, or the number seven might lead to the sensation of lime green (a type of indigo blue sphere, moving in space, or the number seven might lead to the sensation of lime green (a type of grapheme-color synesthesia)). Synesthesia is usually perceived consciously, occurs automatically, and is present from early childhood (Ward, 2013). Every synesthete has an individual pattern of associations which is remarkably consistent in adults, even over decades (Simner et al., 2005; Ward, 2013). Consistency is therefore one of the core criteria of synesthesia – which is usually assessed with a synesthesia consistency test (Baron-Cohen, Burt, Smith-Laittan, Harrison, & Bolton, 1996). In a typical consistency test, potential synesthetes are asked to indicate their synesthetic experiences (e.g., colors) for specific stimuli (e.g., letters and numbers) multiple times: synesthetes tend to choose the same (color) associations on each presentation of the same stimulus, allowing the test to discriminate between synesthetes and non-synesthetes. Research on the genetics of synesthesia is still in its infancy, but early results indicate that it is a hetero-genetic condition, involving genes associated with axonogenesis expressed during early childhood (Asher et al., 2009; Tilot et al., 2018; Tomson et al., 2011).

Whether synesthesia is better described as a continuous trait in the population or as a binary condition is currently still debated. Synesthesia consistency scores tend to vary substantially in the general population (Burghoorn, Dingemanse, van Lier, & van Leeuwen, 2020; Cuskley, Dingemanse, Kirby, & Van Leeuwen, 2019) which suggests a continuous distribution of the trait. These consistency scores in non-synesthetes are correlated with scores of structural (non-random) organization within vowel-color mappings (Cuskley et al., 2019), which are a form of cross-modal correspondence. This relation between synesthesia consistency scores and the way individuals combine information from different modalities provides evidence that synesthetic consistency in non-synesthetes does not simply reflect memory or perceptual abilities. On the other hand, it is argued that synesthetes are distinct from neuro-typical individuals (Ward, 2019). Both these views might be meaningful (Ward, 2019), in the sense that some features of synesthesia follow a continuum while others are specific to supra-threshold synesthetes, i.e., individuals who both score within the synesthetic range on a consistency test and additionally perceive synesthesia consciously. In this article, the ‘degree of grapheme-color synesthesia’ is defined as the extent to which someone experiences consistent color associations with graphemes, similar to the way in which synesthetes do, while a synesthete is defined as an individual with consciously experienced and highly consistent color associations. Using the degree of grapheme-color synesthesia as a proxy for synesthetic characteristics allows us to include non-synesthetes into our study instead of solely relying on (more difficult to recruit) verified synesthetes. This approach has been successfully deployed before in Burghoorn et al. (2020) and enables us to assess the associations between synesthesia and measures related to autism in a twin cohort that was originally recruited in order to study autism spectrum condition (ASC).

Both self-reported and objectively tested synesthesia are more common in individuals fulfilling diagnostic criteria for ASC (Baron-Cohen et al., 2013; Hughes, Simner, Baron-Cohen, Treffert, & Ward, 2017; Neufeld et al., 2013), from here referred to as ‘people on the autism spectrum’. ASC (defined as Autism Spectrum Disorder by the American Psychiatric Association (2013)) is a neurodevelopmental entity characterized by challenges in social communication and interaction, alongside restricted/repetitive patterns of behavior, interests, or activities and alterations in sensory perception. Synesthesia has also been suggested to play a key role for savant abilities, which occur in approximately 10% of people on the autism spectrum (Treffert, 2009). The co-occurrence between synesthesia and ASC seems to coincide with such talents (Baron-Cohen et al., 2007; Bouvet et al., 2014; Hughes et al., 2017), and single cases of savant synesthetes like Luria’s S. described their synesthetic sensations as crucial for remembering or differentiating inputs (Luria & Solotaroff, 1987). In addition, synesthetes seem to have an advantage in the acquisition of abilities resembling savant-talents (Hughes, Gruffydd, Simner, & Ward, 2019). Synesthesia is also associated with cognitive benefits in people without an autism spectrum diagnosis, including enhanced memory, creativity and mental imagery (Ward & Simner, 2020).

A link between synesthesia and ASC is further supported by studies showing that synesthetes have elevated autistic traits, and, similar to people on the autism spectrum (Ben-Sasson et al., 2009), an altered sensory processing style (Van Leeuwen, Neufeld, Hughes, & Ward, 2020; Van Leeuwen, van Petersen, Burghoorn, Dingemanse, & van Lier, 2019; Ward et al., 2017; Ward, Brown, Sherwood, & Simner, 2018). The latter includes both altered sensory sensitivity (hyper- or hypo-sensitivity) and an increased attention to details. More specifically, synesthetes consistently show sensory hyper-
sensory, based on both self-report (using the Glasgow Sensory Questionnaire; Robertson & Simmons, 2013) and on the Pattern Glare Test where grating patterns can evoke discomfort and sensory artefacts in more sensitive individuals (Van Leeuwen et al., 2019; Ward et al., 2017, 2018). Of these three studies, two also found higher levels of self-reported sensory hypo-sensitivity in synesthetes (Ward et al., 2017, 2018), but one did not (Van Leeuwen et al., 2019).

All three studies reported increased self-reported autistic traits, as assessed by the Autism Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001), in synesthetes. However, there was some inconsistency regarding which sub-domains where affected. The AQ was originally constructed to cover five domains of autistic traits (Communication, Social skills, Imagination, Attention Switching and Attention to Details), with sub-scales showing varying degrees of internal consistency (Cronbach’s alpha: .63-.77). However, factor analysis revealed a two-factor structure, with the Attention to Details domain being one factor and the remaining four sub-scales clustering together, referred to as AQ-Other here (Hoekstra, Bartels, Cath, & Boomsma, 2008). Ward et al. (2017 & 2018) found that both the Attention to Details domain and the AQ-Other domain were significantly elevated in synesthetes compared to controls, but only scores on the Attention to Details domain resembled those of people on the autism spectrum rather than the control sample’s scores and showed a dosage effect, i.e., an increase in Attention to Details score correlated with the amount of experienced synesthesia types. Van Leeuwen et al. (2019) found higher scores for synesthetes on the Social Skills sub-scale (within the AQ-Other domain) and the Attention to Details sub-scale, but a synesthesia dosage effect only with the Social Skills sub-scale. Finally, Burghoorn et al. (2020) found the degree of grapheme-color synesthesia in non-synesthetes, as indicated by synesthetic consistency scores, to correlate only with the total AQ score, but not the Attention to Details sub-scale (Burghoorn et al., 2020). Together, these findings illustrate that elevated self-reported autistic traits in synesthetes span across both social/communication and perceptual/sensory domains. While the perceptual and sensory nature of synesthesia provides an intuitive reason why autistic traits in synesthetes should be elevated in the perceptual/sensory domain, the relation in the social domain may point to a wider association with autism or similar developmental mechanisms in both conditions.

Synesthetes have further been found to perform more accurately than controls on the Embedded Figures Test (EFT) and the Change Blindness Task (Van Leeuwen et al., 2019; Ward et al., 2017). On the EFT, participants have to detect a smaller target shape that is embedded in a complex context image. On the Change Blindness Task, two images are alternated quickly and participants have to identify the difference between the two images, which is usually the absence/presence of a small object. Both these tasks require participants to suppress global information processing in order to detect smaller details, an ability that has been hypothesized and found to be enhanced in people on the autism spectrum (Mottron, Dawson, Soulieres, Hubert, & Burack, 2006; Shah & Frith, 1993). A recent meta-analysis nuances the idea of enhanced detail processing in ASC, rather suggesting a somewhat slower processing of global information (Van der Hallen, Evers, Brewaeyts, Van den Noortgate, & Wagemans, 2015). The degree of grapheme-color synesthesia in non-synesthetes did however not correlate with EFT performance (Burghoorn et al., 2020). Synesthetes have also been found to have a higher motion coherence threshold than controls (Banissy et al., 2013; Van Leeuwen et al., 2019), i.e., needing a higher proportion of dots to move synchronously vs randomly in order to identify the global direction of movement. This indicates that they might have a reduced integration of features into a whole, similarly as previously found in people on the autism spectrum (Milne et al., 2002; Fellicano, Gibson, Maybery, Durkin, & Badcock, 2005).

Whether the association between synesthesia and autism-like perception is driven by familial factors such as genetics and upbringing is currently unknown. Twin and family studies have the power to address this question. Apart from two case reports of individual twin pairs discordant for synesthesia (Smilek, Dixon, & Merkile, 2005; Smilek et al., 2002), the only synesthesia twin group study published so far assessed concordance rates of grapheme-color synesthesia in monozygotic (MZ) vs dizygotic (DZ) twins, yielding suggestive evidence of both genetic and environmental influence on synesthesia (Bosley & Eagleton, 2015). A higher concordance rate in MZ compared to DZ twins suggested heritability, in line with studies indicating that synesthesia runs in families (Barnett et al., 2008; Baron-Cohen et al., 1996). Familial factors comprise both genetic and environmental aspects shared by family members. Twins share many environmental factors, such as parental age and health, socioeconomic background and many other aspects of their upbringing. In addition, MZ twins share all their genes, while DZ twins share on average 50% of their genes. In order to model the influences of genetics, shared, and non-shared environment quantitatively, larger population-based twin or family samples are required. However, smaller, not randomly selected twin samples can be used in order to investigate associations within-twin pairs, which are not influenced by familial factors, given that these are shared between twins (McGue, Osler, & Christensen, 2010; Goldberg & Fischer, 2005; Neufeld et al., 2020). This approach therefore allows investigating associations more directly, since familial factors that influence either the dependent or the independent variable can also modulate their association (strengthen or weaken it). As an example, exposure to colored letter sets in childhood, which has been shown to influence synesthetic color associations (Witthoft & Winawer, 2006; Witthoft, Winawer, & Eagleton, 2015), is an environmental factor that is likely to be shared by twins (having a letter set toy at home or not). The current study is the first to investigate the link between synesthesia and autism-related characteristics in a twin sample, allowing to implicitly control for a wide range of familial confounding factors (including shared environment and 50–100% of genetics), and thereby investigating associations more directly and with a potentially higher sensitivity. In comparison, we also assess the same associations across a larger cohort that additionally includes singletons (twins whose co-twin was not assessed or excluded), while adjusting for twin clustering. The latter analysis is more similar to regression analyses in non-twin samples and allows, in comparison to the analysis within-twin pairs, some inferences about the influence of familial factors.
Our study complements the existing literature methodologically in several further ways. First, we investigated an opportunistic sample that was not conditioned on the presence of synesthesia, and included individuals on the autism spectrum and/or fulfilling diagnostic criteria for other neurodevelopmental disorders (NDDs). Second, we applied a twin design, allowing us to estimate associations free from familial factors. Third, we used a different measure to assess sensory sensitivity (Sensory Profile; Brown & Dunn, 2002), which has been used excessively within the autism literature (DuBois, Lymer, Gibson, Desarkar, & Nalder, 2017), but not yet in the context of synesthesia. Finally, in addition to the previously used Embedded Figures Test (EFT, Witkin, 1971), we also utilized the Fragmented Pictures Test (FPT, Kessler, Schaaf, & Mielke, 1993) as a test of detail- or globally oriented perception, which has not been used in previous synesthesia studies, assessing the ability to integrate fragments in order to construct a whole gestalt.

1.1. Hypotheses

We hypothesized that the degree of grapheme-color synesthesia (scoring more consistently, i.e., lower, on the synesthesia consistency test) would be associated with a) higher autistic traits b) increased sensory hyper- and hypo-sensitivity, and c) more detail-focused visual processing as indicated by faster disembedding in the EFT and the need for more visual information before being able to integrate fragments to a whole gestalt.

2. Material and methods

2.1. Participants

Participants for this study were recruited from the Roots of Autism and ADHD Twin Study in Sweden (RATSS, Bölte et al., 2014). Within RATSS, individuals (twins) already completed a battery of different cognitive tests and questionnaires and were assessed diagnostically at an initial assessment. For the current study, all RATSS participants who were 12 years or older at the time of the synesthesia assessment were invited to participate, either directly during their visit or up to eight years after the initial assessment within RATSS. Those who completed the online synesthesia assessment from home after their initial visit responded to an invitation letter sent to them after their initial study participation. In total, 149 participants agreed to take part in the synesthesia assessment. This included a synesthesia consistency test and a questionnaire about different synesthesia types. Of the individuals who completed the synesthesia assessment, we excluded 66 individuals who did not complete the adult self-report version of the AQ (because they were below 16 years of age at the time of initial assessment) from all analyses. This because we wanted to assess all associations within the same cohort and because associations between measures assessed at different time points are more likely to be compromised in individuals who went through puberty between assessments. Of the remaining 83 individuals, 18 individuals did not have valid synesthesia consistency test scores due to a failure to follow task instructions (see section “Consistency test”) so they were excluded from analyses (exclusion at step 2). The final included sample (n = 65) comprised 22 complete twin pairs and 21 singletons (twins whose co-twins either did not choose to take part in the online synesthesia assessment or were excluded due to an invalid consistency score). Most of these included participants (59 out of 65) completed the synesthesia assessment after the initial RATSS assessment. Sample characteristics for both the entire included sample and the 22 complete twin pairs are summarized in Table 1. Zygosity was determined based on a DNA test (Hannelius et al., 2007) for 18 of the complete twin pairs and a 4-item zygosity questionnaire for the four remaining twin pairs. Of the 22 complete twin pairs, 13 were monozygotic (MZ) and nine dizygotic (DZ).

Twins in RATSS are predominantly recruited from a population twin sample (Anckarsäter et al., 2011), and selected if one or both twins show increased levels of autistic or ADHD traits, based on a parent interview. Consequently, the current sample included individuals diagnosed with ASC and/or NDDs. The final sample investigated in this study included 12 people with an NDD diagnosis (see Table 1). Five of the individuals fulfilling criteria for an NDD diagnosis were people on the autism spectrum, of which two also fulfilled criteria for ADHD. Three participants fulfilled diagnostic criteria for ADHD but not ASC. Further three individuals fulfilled diagnostic criteria for tic disorders and one individual was diagnosed with a specific learning disorder. The sample included also 20 individuals fulfilling diagnostic criteria for one of more psychiatric conditions (anxiety disorders = 13 individuals, depression or dysthymia = seven individuals, obsessive-compulsive disorder = three individuals, insomnia = three individuals and depersonalization/derealization disorder = one individual).

Written informed consent was obtained from all participants and/or their caregivers for participating in the RATSS study as a whole, and electronic informed consent was additionally collected online from all participants who also

Table 1 – Sample characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Full included sample</th>
<th>Complete twin pairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (female)</td>
<td>65 (39)</td>
<td>44 (29)</td>
</tr>
<tr>
<td>N NDD diagnosis (ASC)</td>
<td>12 (5)</td>
<td>8 (3)</td>
</tr>
<tr>
<td>MZ/DZ</td>
<td>39/26</td>
<td>26/18</td>
</tr>
<tr>
<td>Mean age (SD) at synesthesia assessment</td>
<td>26.7 (4.6)</td>
<td>26.8 (4.8)</td>
</tr>
<tr>
<td>Age range at synesthesia assessment</td>
<td>17–34</td>
<td>17–34</td>
</tr>
<tr>
<td>Mean age (SD) at first assessment</td>
<td>23.2 (5.4)</td>
<td>23.9 (5.4)</td>
</tr>
<tr>
<td>Age range at first assessment</td>
<td>14−32</td>
<td>16−32</td>
</tr>
<tr>
<td>Mean time passed between assessments in years (SD)</td>
<td>3.4 (2.2)</td>
<td>2.8 (2.1)</td>
</tr>
<tr>
<td>Range time passed between assessments in years</td>
<td>0–8</td>
<td>0–8</td>
</tr>
</tbody>
</table>

Note. ASC = fulfilling criteria for an ASC diagnosis; NDD = fulfilling criteria for a neurodevelopmental disorder; MZ = monozygotic; DZ = dizygotic.

* One individual completed the adolescent/adult AQ version (which is usually used form 16 years of age) despite being only 14 (almost 15) years old.
completed the synesthesia assessment. For completing the synesthesia online assessment, participants received a small compensation (worth 100 Swedish crowns; equivalent of ~10 U.S. dollars) in the form of a voucher that can be used in a wide range of shops.

2.2. Synesthesia online assessment

2.2.1. Screening questionnaire
Participants received a short description of what synesthesia is and then completed 15 multiple choice questions in which they were asked to rate to what extent they experienced different types of synesthesia (for the questionnaire, see the Supplementary Material section Appendix 1, p. 13–14). The questions contained examples of possible synesthetic experiences. An example question, translated from Swedish, is: “Do you associate numbers with colors (Example: Do you usually see or think of a certain color when you see the number ’3’)?” Answer possibilities were: “yes”, “yes, to some extent”, “no” and “I don’t know”. In addition, an open question concerning potential synesthesia types that had not been addressed was included. The first two multiple-choice questions concerned letter-color, and digit-color synesthesia, and the answers to these questions, in combination with the consistency score, were used to identify grapheme-color synesthetes. Synesthe-
tias were calculated from the 16 items of the question-
naire, where types that cluster together were counted as single type (Novich, Cheng, & Eagleman, 2011).

2.2.2. Consistency test
Participants completed a Swedish version of an online grapheme-color consistency test, which had been used previously as a Dutch version (Van Leeuwen et al., 2019; Cuskley et al., 2019). This test was similar to an online test (Eagleman, 2011) that differentiates between synesthetes and non-synesthetes with a high (90% and 94%) sensitivity and specificity when applying the same calculation method used here (Rothen, Seth, Witzel, & Ward, 2013). Stimuli were the 26 letters of the Latin alphabet plus the three Swedish umlauts (Å, Ä and Ö) and digits 0–9, pre-
sented three times each in one of four pseudorandom orders (avoiding an item to occur twice in a row), assigned randomly to participants. Participants were presented with one stimulus at a time and asked to choose the color that fit the stimulus best by clicking in a color matrix (see Supplementary Figure S1). Synesthetes tend to choose the exact same color on each presentation of the same stimulus, allowing the test to discriminate between synesthetes and non-synesthetes, who choose color associations less consistently. For each participant, we calculated a consistency score using Euclidean distances in CIELUV color space between participant responses for the three different trials per item (Rothen et al., 2013), with lower consistency scores indicating higher levels of synesthetic color consistency (similar colors chosen). Only items where colors were chosen for all three trials were included. The consistency scores of 18 participants were deemed invalid because they had less than five valid items or only chose one or two different colors across all items (see Supplementary Material, section 1.1 “Consistency test scoring” for details).

2.2.3. Identification of synesthetes
Participants were categorized in grapheme-color synes-
thes and non-synesthetes based on their consistency test results and their answers on the synesthesia questionnaire. Participants having a valid consistency score and scoring below a cut-off value of 135.30 for digits, letters, or both categories were classified as synesthetes if they in addition also reported experiencing grapheme-color synesthesia for the relevant category in the questionnaire (answering “yes” or “yes, to some extent” to one or both of the first two questions). Participants were included in the analyses regardless whether they qualified as synesthetes or not. For details on self-reported versus verified synesthetes, please see Supplementary Material, section 1.2 “Correspondence between self-reported and objectively tested grapheme-color synesthesia”.

2.3. Measures acquired during the initial assessment

In their initial assessment within the RATSS study, twins were assessed diagnostically and completed a large battery of questionnaires and tests during a 2.5 days lab visit. Details are described below.

2.3.1. Diagnostic assessment
Twins were assessed by a team of experienced clinicians. Diagnosis for ASC and other NDDs such as ADHD, tic disor-
ders, specific learning disorders and intellectual disability (ID), as well as psychiatric disorders such as depression and anxiety were determined based on a multitude of information sources. These included medical history, parent interviews and gold standard diagnostic tools (First & Gibbon, 2004; Kaufman et al., 1997; Kooij, 2010; Lord et al., 2012; Lord, Rutter, & Le Couteur, 1994).

2.3.2. Autistic traits
Autistic traits were measured by the Swedish adult self-report version of the Autism Spectrum Quotient, AQ (Baron-Cohen et al., 2003). Sub-scores were calculated for the two sub-domains “Attention to Details” and “AQ-Other” according to previous factor analyses (Hoekstra et al., 2008) and in accordance with previous studies on the association between synesthesia and autistic traits (Ward et al., 2017, 2018; Van Leeuwen et al., 2019). These sub-scales have been found to have acceptable internal consistency (Cronbach’s α of Attention to Details = .68 and of AQ-Other = .77) in the general population (Hoekstra et al., 2008). In our sample, internal consistency was somewhat lower for Attention to Details (Cronbach’s α = .59) and higher for the AQ-Other domain (Cronbach’s α = .88).

2.3.3. Sensory processing
Variation in sensory processing was assessed with the self-report adolescent/adult Sensory Profile (AASP), a question-
naire that comprises 60 questions dividing into four quad-
rants (15 questions each), related to sensory hyper- or hypo-responsiveness across different sensory modalities (Brown & Dunn, 2002). The Sensory Profile is the most commonly used measure of sensory hyper- and hypo-responsiveness in studies involving clinical samples such
as adults and adolescents on the autism spectrum (DuBois et al., 2017), but has so far not been used in synesthesia studies. The quadrants Sensory Sensitivity and Low Registration represent higher or lower sensory thresholds (hyper- and hypo-sensitivity). The remaining two AASP quadrants, Sensation Seeking and Sensation Avoiding, represent actions undertaken to limit or increase sensory input. We only included the quadrants representing high vs low sensory thresholds in our analyses (Sensory Sensitivity and Low Registration), because we believe that they represent purer measures of hyper- and hypo-sensitiveness (with less impact of other factors such as self-regulation abilities) and because we wanted to avoid including several correlated predictor variables within the same model (correlation between the different AASP quadrants in our sample was \( r = -.34 \) to .68).

### 2.3.4. Perceptual tasks
Two tasks (pen and paper versions) were used to assess the participants’ style of global vs local visual information processing (links to example images can be found in the Supplementary Material, section 1.3). The Embedded Figures Task (EFT; adult version) requires dis-embedding different smaller targets from 12 larger distracting contexts (one target per context) within 180 s (Witkin, 1971). For each of the 12 contexts, the amount of errors (pointing to the wrong area) and the time until correct response were noted. The maximum time of 180 s was noted if the participant was unable to correctly identify the target within the time limit (overall maximum time = 2160 s). Mean reaction time until correct response and the amount of errors were used as the outcome measures of this task.

The Fragmented Pictures Task (FFT) assesses the ability to integrate visual fragments into a meaningful whole (Kessler et al., 1993). Participants browsed with a steady pace through 10 sets of fragmented drawings of objects, animals or persons that were gradually completed in 10 sequential steps, and were asked to identify each drawing verbally as soon as possible. The latter requires both bottom-up visual feature integrations, and a top-down matching between image and internal shape representations from memory (Van Eylen, Boets, Steyaert, Wagemans, & Noens, 2015). The number of images (corresponding to state of completeness) needed in order to correctly identify each drawing was summed up across the 10 trials as the total FFT score.

Of the 65 included participants, four were lacking FFT test results of which one was additionally lacking FFT results, leading to a total of 61 participants (20 complete twin pairs) included in the analyses.

### 2.3.5. Intellectual ability
The Wechsler Intelligence Scales for Children (if below 18 years of age) or Adults, fourth editions (WISC-IV/WAIS-IV) were used to assess intellectual ability (Wechsler, 2003; 2008). The General Ability Index (GAI) was calculated as measure of IQ, based on three verbal comprehension and three perceptual reasoning subtests.

### 2.4. Statistical analyses

#### 2.4.1. General performance assessment
We reported all the mean scores and values obtained from the whole sample included in this study, and we assessed whether these scores and values were extremely different compared to previously published scores and values from typically developing participants (TD). We performed this check in order to evaluate the representativeness of our cohort compared to studies including only TD participants and in order to verify that questionnaires and tasks were completed according to instructions. Furthermore, we explored the data set by comparing the group means of dependent and independent variables between individuals that were included in the study and those that were excluded at step 2 because they did not reach a valid consistency score, individuals included in this study and those included in the entire RATSS sample, and between individuals with and without any NDD diagnoses. Finally, we compared autistic traits between included participants who reported any synesthesia type to those not reporting to have any synesthesia type.

#### 2.4.2. Main modeling analyses
Three conditional linear regression analyses were conducted in R within the Generalized Estimating Equations (gee) framework with doubly robust standard errors (degree package) (Zetterqvist & Sjölander, 2015), in order to investigate within pair associations between synesthesia and autistic traits, sensory sensitivity and perceptual task performance. More specifically, each of the 22 twin pairs (or in case of the visual tests 20 pairs) formed a cluster and the synesthetic consistency score was the dependent variable in all three models while either autistic traits (AQ-Attention to Details and AQ-Other), sensory sensitivity (Sensory Sensitivity and Low Registration) or visual task performance (EFT reaction time and error rate, and the total FFT score) were the main independent variables.

In a second step, three linear regressions with the same variables were conducted across the full cohort, were each participant was treated as individual but cluster-robust standard errors were estimated in order to account for the non-independence of twins. This second analysis resembles therefore a conventional linear regression and is hence more comparable with previous studies on non-twin samples.

Standardized scores (mean-centered values divided by the standard deviation) of all measures were used, leading to standardized model estimates which can be interpreted as effect size estimates. Across the cohort, we controlled for age when completing the synesthesia consistency test, since our sample had a wide age range. We also included general intellectual ability (GAI, at the time of the initial assessment in RATSS), to control for IQ differences and increase sensitivity, both within-twin pairs and across the cohort. We speculated that synesthesia consistency scores might be affected by IQ, e.g., because individuals with higher IQ might remember more often which colors they chose for previous items, or be better at finding strategies to remember the colors. However, this latter hypothesis has not been tested previously, to the best of
our knowledge. We did not include sex as a covariate because sex differences in synesthesia have only been reported in studies relying on self-report rather than objective tests (Simner et al., 2006; Simner & Carmichael, 2015), and there were no significant sex differences in the consistency test score in our sample (females M = 234.1, males M = 253.4; t = −.828, df = 47.923, p-value = .412). Further, all but one of the twin pairs were of same sex, meaning that sex effects can be largely ruled out for our within-pair analyses.

2.4.3. Verification analyses
We performed several additional analyses to verify that our results are robust against different analysis choices. More specifically, we re-run all three models while A) excluding the four verified synesthetes and while B) additionally including NDD diagnosis as binary co-variates. Further, we re-run the model with autistic traits as main predictor C) with the total AQ score and D) with alternative AQ-sub-scales, based on a 3-factor model (Russel-Smith et al., 2011).

3. Results

3.1. General performance assessment

For an overview of means and standard deviations of all included variables across the whole group and for complete twin pairs, please see Table 2.

AQ scores were within the expected range for a sample of individuals with autism spectrum, reaching a mean total AQ score of 14.0 (SD = 8.9) which is within the reported range for non-clinical populations (range: 11.9 − 17.6, CI = 13.0 − 17.1, Table 2 from a meta-analysis by Ruzich et al., 2015). Sensory Profile scores in the current sample were comparable to scores from earlier representative studies using the Adult Sensory Profile in the general population (Brown, Cromwell, Filion, Dunn, & Tollefson, 2003; Kamath et al., 2020). For Sensory Sensitivity, the mean score of 32.1 (SD = 9.9) is similar to the mean score in Kamath et al., 2020 (30.77 ± SD = 6.29) and slightly below one SD from the mean score (38.0 ± SD = 5.4) in Brown et al. (2003). For Low Registration, the mean score of 27.7 (SD = 8.4) is comparable to the scores from both earlier studies (28.14 ± SD = 4.48, Kamath et al., 2020; 31.1 ± SD = 4.9, Brown et al., 2003).

The performance on the visual tests in this sample was within the expected range. On the FPT, participants identified the images between step 6 and 7 on average (total score across 10 trials of 64.5, SD = 5.6), similar to comparable fragmented pictures studies reporting identification at around 60% visibility levels (e.g., Doniger et al., 2001; Snodgrass & Corwin, 1988). EFT performance (RT 46.2 sec, SD = 22.7) in our sample was similar to the reaction times of normative individuals (51.5 ± SD = 12.6, Table 3 from Bölte, Holtmann, Poustka, Scheurich, & Schmidt, 2007).

Intellectual ability in the included sample was slightly higher (mean = 105.9, SD = 14.2) than average in the general population.

For additional descriptive statistics of data from included participants vs those excluded at step 2, differences between the included study sample and entire RATSS sample, participants with and without an NDD diagnosis, and autistic traits in participants who did or did not self-report any form of synesthesia please see the Supplementary Material (Supplementary Section 2. “Additional descriptive analyses” and Supplementary Tables S1, S2 and S3).

3.2. Regression outcomes

Regression analyses findings with the degree of grapheme-color synesthesia as dependent variable are described below per model, each calculated both within-twin pairs and across individuals, and all models’ results are summarized in Table 3.

3.2.1. Degree of grapheme-color synesthesia and autistic traits

Within-twin pairs, only Attention to Details, but not the AQ-Other subscale of the AQ, predicted higher synesthetic consistency for graphemes (= lower consistency scores) within-twin pairs, (β = −.65, 95% CI = −1.19, −.12, p = .017). This means that twins with a one standard deviation higher Attention to Details score would score about half a standard deviation lower, i.e., more consistent, in the consistency test compared to their co-twins. Across individuals, an effect in the same direction was not significant (β = −.25, 95% CI = −.54, .03, p = .089).

3.2.2. Degree of grapheme-color synesthesia and sensory sensitivity

Hyper-, but not hyposensitivity, predicted stronger synesthetic consistency, in line with our hypothesis, both within pairs (β = −.59, 95% CI = −1.14, −.04, p = .036) and across individuals (β = −.35, 95% CI = −.68, −.01, p = .044).

Table 2 – Descriptive results.

<table>
<thead>
<tr>
<th></th>
<th>Full included sample</th>
<th>Complete twin pairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) consistency score</td>
<td>241.8 (89.0)</td>
<td>240.94 (82.01)</td>
</tr>
<tr>
<td>N verified synesthetes</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Mean number of self-reported synesthesia types (SD)</td>
<td>1.6 (1.4)</td>
<td>1.4 (1.4)</td>
</tr>
<tr>
<td>Mean (SD) IQ</td>
<td>105.9 (14.2)</td>
<td>106.6 (14.5)</td>
</tr>
<tr>
<td>Mean (SD) AQ total</td>
<td>14.0 (8.9)</td>
<td>13.0 (7.9)</td>
</tr>
<tr>
<td>Mean (SD) AQ-Attention to Details</td>
<td>3.8 (2.1)</td>
<td>3.9 (2.1)</td>
</tr>
<tr>
<td>Mean (SD) AQ-Other</td>
<td>10.0 (7.6)</td>
<td>9.3 (6.7)</td>
</tr>
<tr>
<td>Mean (SD) Sensory Sensitivity</td>
<td>32.1 (9.9)</td>
<td>31.3 (8.6)</td>
</tr>
<tr>
<td>Mean (SD) Low Registration</td>
<td>27.7 (8.4)</td>
<td>27.0 (7.7)</td>
</tr>
<tr>
<td>Mean (SD) EFT RT (s)</td>
<td>46.2 (22.7)</td>
<td>46.2 (21.9)</td>
</tr>
<tr>
<td>Mean (SD) EFT errors</td>
<td>4.5 (3.6)</td>
<td>4.7 (3.8)</td>
</tr>
<tr>
<td>Mean (SD) FPT total score</td>
<td>64.5 (5.6)</td>
<td>64.2 (5.1)</td>
</tr>
</tbody>
</table>

Note. IQ = intelligence quotient based on the general ability index of the Wechsler intelligence scale of children or adults, 4th version; AQ = Autism Spectrum Quotient; EFT = Embedded Figures Test; RT = reaction time; FPT = Fragmented Pictures Test.

a The mean number of synesthesia types was calculated from the 16 items of the questionnaire, where types that cluster together according to Novich et al. (2011) were only counted as one, hence the maximal number of self-reported synesthesia types was six.
**Table 3 – Regression results.**

<table>
<thead>
<tr>
<th></th>
<th>Within-twin pairs (n = 44)</th>
<th>Across individuals (n = 65)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β (95% CI)</td>
<td>SE</td>
</tr>
<tr>
<td><strong>Model 1: Autistic traits</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attention to Details</td>
<td>−.65 (−1.19, −.12)</td>
<td>.27</td>
</tr>
<tr>
<td>AQ-Other</td>
<td>.02 (−.42, .46)</td>
<td>.22</td>
</tr>
<tr>
<td>IQ (scaled score)</td>
<td>−.40 (−.87, .06)</td>
<td>.24</td>
</tr>
<tr>
<td>Age</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td><strong>Model 2: Sensory Profile</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensory Sensitivity</td>
<td>−.59 (−1.14, −.04)</td>
<td>.28</td>
</tr>
<tr>
<td>Low Registration</td>
<td>−.43 (−1.14, .27)</td>
<td>.36</td>
</tr>
<tr>
<td>IQ (scaled score)</td>
<td>−.29 (−.76, .19)</td>
<td>.24</td>
</tr>
<tr>
<td>Age</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td><strong>Model 3: Perceptual task performance</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EFT (accuracy)</td>
<td>−.24 (−.74, .25)</td>
<td>.25</td>
</tr>
<tr>
<td>EFT (RT)</td>
<td>.21 (−.49, .90)</td>
<td>.35</td>
</tr>
<tr>
<td>FPT score</td>
<td>.42 (0.06, .78)</td>
<td>.18</td>
</tr>
<tr>
<td>IQ (scaled score)</td>
<td>−.13 (−.86, .60)</td>
<td>.37</td>
</tr>
<tr>
<td>Age</td>
<td>−</td>
<td>−</td>
</tr>
</tbody>
</table>

Note. Regression outcomes (with 2-sided p-values) from conditional linear regressions within-twin pairs (left column) and linear regressions across individuals with standard errors adjusted for twin clustering (right column) with synesthesia consistency score as the dependent variable. AQ = Autism Spectrum Quotient; IQ = Intelligence Quotient assessed as General Ability Index from the 4th version of the Wechsler Intelligence Scale for children or adults, EFT = Embedded Figures Test, FPT = Fragmented Picture Test, β = standardized regression coefficient, CI = confidence interval, SE = standard error.

3.2.3. Degree of grapheme-color synesthesia and perceptual task performance

Dis-embedding ability, as assessed with the EFT (reaction times and number of errors), was not associated with the degree of grapheme-color synesthesia, neither within-twin pairs (RT: β = .21, 95% CI = −.49, .90, p = .546; accuracy: β = −.24, 95% CI = −.74, .25, p = .337), nor across individuals (RT: β = −.11, 95% CI = −.23, .46, p = .511; accuracy: β = −.03, 95% CI = −.41, .35, p = .883). We found no evidence for our hypothesis that people who perform worse on the FPT would score more like a synesthete on the consistency test. Instead, better performance (i.e., a reduced need of visual information for correct object identification) in the FPT predicted higher synesthetic consistency within-twin pairs (β = .42, 95% CI = .06, .78, p = .022; the regression coefficient was positive since both, higher consistency and better FPT performance are reflected by lower scores). No association was observed across individuals (β = .16, 95% CI = −.15, .47, p = .305).

3.2.4. Effects of controlling variables

Intellectual ability was not associated with the degree of synesthesia within-twin pairs in any model (β-range: −.40 to −.13, p-range: .090 to .727). Across individuals, higher IQ consistently predicted higher synesthetic consistency, as strongest included predictor, even though only at trend level in the model with perceptual task performance as main predictors (β-range: −.27 to −.42, p-range: .051 to <.001). Age was not associated with synesthetic consistency in this sample (please see Table 3 for details).

3.2.5. Verification analyses

A) Excluding synesthetes. We verified that our main results were similar after exclusion of the four verified synesthetes or twin pairs where at least one twin was identified as a synesthete, respectively. In this analysis (see Supplementary Table S4), the main regression results were similar, holding for the associations with the AQ-Attention to Details sub-scale and the FPT.

B) NDD diagnosis as covariate. Since fulfilling criteria for an NDD diagnosis (e.g., ADHD) might have affected individuals’ ability to conduct the synesthesia consistency test correctly, thereby potentially influencing the consistency score, we reran the models including NDD diagnosis as binary covariate (see Supplementary Table S5). This did not change the results for autistic traits, sensory sensitivity or visual task performance; only the association with IQ across the cohort was significant instead of a strong trend in the third model with visual tasks as main independent variables.

C) Total AQ score. Additionally, for comparison to the results of Burghoorn et al. (2020), we performed a regression analysis with AQ-Total instead of AQ-Attention to Details and AQ-Other. The regression analysis with the total AQ score revealed no significant associations (see Supplementary Material Section 3.1).

D) Alternative AQ sub-scales. According to an alternative 3-factor model of AQ scores (Russel-Smith et al., 2011), the AQ scores were divided into the factors Social skills (13 items), Details/Patterns (7 items) and Communication/Mindreading (8 items). When performing the analysis using this 3-factor model, the results were similar as before in the sense that only the Details/Patterns sub-scale showed a negative association with the degree of grapheme-color synesthesia (see Supplementary Table S6). However, this association was below the significance threshold (p = .062).

4. Discussion

In this study, we investigated the relationships between the degree of grapheme-color synesthesia (synesthetic
consistency) and autistic traits, sensory sensitivity and detail focus in visual perception in a twin sample. We controlled for general intellectual ability and across individuals also for age (which is implicitly controlled for within-twin pairs). Importantly, shared environmental factors, such as family background, and 50–100% of genetic effects are additionally implicitly controlled for within-twin pairs, and hence the within-pair associations are not influenced by these familial factors. Four main findings emerged. First, only Attention to Details, but not the other domain of autistic traits (including sub-scales related to social skills), predicted higher synesthetic consistency within-twin pairs. Second, sensory hyper-sensitivity but not hypo-sensitivity predicted higher synesthetic consistency. Third, these within-twin pair associations pointed in the same direction as associations across all individuals, but were stronger within pairs, indicating that the within-pair analysis was more sensitive in order to detect these effects. Finally, the need for visual information in the FPT (but not dis-embedding ability in the EFT) was associated with synesthetic consistency within-twin pairs. Twins who needed less visual information than their co-twins in order to construct a meaningful whole from a fragmented image scored more like a synesthete on the consistency task. The latter finding was contrary to our hypothesis that individuals who are more consistent in the synesthesia test would integrate visual fragments less automatically into a whole gestalt because of a more detail-focused attentional style.

4.1. Autistic traits and the degree of grapheme-color synesthesia

Similar to previous studies and in line with our hypothesis, we found a positive association between the degree of synesthesia and autistic traits. We found this association to be specific to the area of Attention to Details. This association was significant within-twin pairs but only a trend in the same direction across all individuals. Our results are consistent with prior work that found increased autistic traits in synesthetes compared to non-synesthetes, with a stronger increase within the Attention to Details compared to the AQ-Other domain (Ward et al., 2017, 2018). That work also found the amount of different synesthesia types in synesthetes to correlate with Attention to Detail but not with the AQ-Other sub-domain. In Van Leeuwen et al. (2019), synesthetes similarly showed an increase in Attention to Detail compared to non-synesthetes, although this was also the case for one of the AQ-Other sub-scales, namely Social Skills.

In contrast to the previously mentioned studies, we did not compare synesthetes with non-synesthetes but instead used the degree of grapheme-color synesthesia as assessed as continuous synesthetic consistency score in an opportunistic sample. Using the same approach, Burghoorn et al. (2020) found a correlation between degree of grapheme-color synesthesia and autistic traits, but only for the total AQ score and not the Attention to Details sub-domain. In contrast to Burghoorn et al. (2020), we investigated a twin sample where 18% had an NDD diagnosis, and adjusted for IQ and age. Further, Burghoorn et al. (2020) used the total AQ score and the original AQ sub-division into five sub-scales (validated in a British sample). These differences can possibly explain the discrepancy in the results – checking in our data, a regression analysis with the total AQ score revealed no significant associations (Supplementary Material Section 3.1). However, our results confirm the finding of Burghoorn et al. (2020) that an association between the degree of grapheme-color synesthesia and autistic traits (here within a sub-domain) is also apparent in a non-synesthete sample (our main regression results are similar after exclusion of verified synesthetes, Supplementary Table S4).

In line with some previous evidence (Ward et al., 2017, 2018), but in contrast to the findings by Burghoorn et al. (2020), our findings support the notion that Attention to Details is more consistently associated with synesthesia than autistic traits that are more closely related to social functioning. This is consistent with the idea that the link between synesthesia and autism is not a general one, but specifically at the level of perceptual and attentional processes. It is, however, worth noting that synesthesia tends to co-occur with a broader range of mental conditions rather than being specifically linked to autism, e.g., schizotypy, post-traumatic stress disorder, obsessive-compulsive disorder, or anxiety disorders (Carmichael, Smees, Shillcock, & Simner, 2019; Hoffman et al., 2019; Titot et al., 2019; Wendler & Schubert, 2019). Interestingly, altered sensory processing has been reported in several of these conditions, including obsessive-compulsive disorder or anxiety disorders, but received less attention than in autism (Houghton, Stein, & Cortese, 2020).

4.2. Sensory sensitivity and degree of grapheme-color synesthesia

Partially confirming our hypothesis, we found an association between sensory hyper-sensitivity (assessed with the Sensory Sensitivity subscale of the AASP) and degree of grapheme-color synesthesia. This association was robust both within- twin pairs and across the entire sample. Increased sensory sensitivity predicted a higher degree of synesthesia (lower consistency scores). In contrast, contrary to our hypothesis, we did not find such an association with hypo-sensitivity (assessed with the Low Registration sub-scale of the AASP). These results correspond to findings by Van Leeuwen et al. (2019) that synesthetes score higher than controls on sensory hyper-sensitivity, but not hypo-sensitivity, on the Glasgow Sensory Questionnaire (GSQ). However, Ward et al., 2017, 2018 found elevated scores in both hyper- and hypo-sensitivity GSQ domains. In one of these studies, hyper-sensitivity in synesthetes was additionally indicated by more self-reported discomfort evoked by Gabor patterns in the Pattern glare test (Ward et al., 2017).

There is a possibility that the discrepancy between our results (a significant association of the degree of grapheme-color synesthesia with specifically hyper- but not hypo-sensitivity) and previous findings is due to the different questionnaire that we used. The Low Registration AASP subscale contains items that are likely influenced by inattention, clumsiness, and being slow in thinking. This is quite different from the GSQ hypo-sensitivity subscales used in previous studies, which focuses on reduced sensitivity to sensory stimuli, i.e., asking questions about reactions to stimuli such as strong smells, loud sounds, pain, cold, etc. Further, the estimate of the association
between the Low Registration AASP sub-scale and the degree of grapheme-color synesthesia was quite similar to the association of the Sensory Sensitivity AASP sub-scale, yet with a wider confidence interval. In a larger twin sample (see ‘Strength and limitations’ section for details on power), we might have found this association to be significant.

Taken together, the association between synesthesia and hypo-sensitivity remains controversial, while the association between synesthesia and hyper-sensitivity occurred more consistently across several studies. Our study adds to this evidence by using a different self-report measure that is widely used in the autism literature (AASP instead of the GSQ).

4.3. Visual perception and degree of grapheme-color synesthesia

Previous studies found that synesthetes performed more accurately in different versions of the EFT (Van Leeuwen et al., 2019; Ward et al., 2017, 2018), in line with a more detail-oriented visual performance style resembling the perceptual style commonly found in people on the autism spectrum (Ben-Sasson et al., 2009; Shah & Frith, 1993). Contrary to these studies and our hypothesis, we did not find an association between the degree of grapheme-color synesthesia and dis-embedding ability while using a different version of the task. While we used the original on-paper version of the EFT (Witkin et al., 1971), the two previous studies used online computer versions of the task. The on-paper version of the test has the advantage that we can be more confident of participants’ attentional engagement, and the disadvantage that the interaction with the test administrator adds a social component, which could affect the performance in some individuals more than in others. Van Leeuwen et al. (2019) used a more recent version of the task (Leuven Embedded Figures Test; L-EFT, De-Wit et al., 2017) that allows differentiating different degrees of dis-embedding difficulty. They only found convincing group differences between synesthete and non-synesthete participants in the most difficult condition. Unfortunately, the test version we used does not allow differentiating different degrees of difficulty: however, given the maximum time for completion of one trial (180 sec) we assume our version is quite hard to complete (RTs in Van Leeuwen et al., 2019 in the most difficult condition were 8 sec on average). Further, accuracy is measured differently in our version of the EFT, where several errors could be made per trial, compared to the L-EFT, where each trial is counted as either correct or incorrect, hence we cannot compare error rates. Further, performance in the EFT in people on the autism spectrum is usually modulated by general intellectual ability (Muth, Hönekopp, & Falter, 2014) and, after checking, was also correlated with IQ in our study (r = .34 for accuracy and r = .38 for reaction time), which might have impacted the results. On the other hand, Burghoorn et al. (2020) also did not find an association between L-EFT performance and degree of grapheme-color synesthesia, which is in line with our study. They concluded that better L-EFT performance might be specific to supra-threshold synesthesia, which might also explain our null result.

In contrast to our prediction, we found that twins who needed less visual information than their co-twins in the FPT scored more synesthetically. We had predicted the opposite because a more detail-focused attentional style has been hypothesized to not only be associated with advantages in detecting details, but also a reduced drive to integrate details into a more global picture (Shah & Frith, 1993). Further, previous studies found reduced feature integration in synesthetes, as indicated by the need for more dots to move in the same direction in order to detect coherent motion (Banissy et al., 2013; Van Leeuwen et al., 2019). However, Burghoorn et al. (2020) did not find an association between motion coherence thresholds and the degree of grapheme-color synesthesia. While both the FPT and the motion coherence task require the integration of visual features, the tasks differ in many ways. As an example, FPT performance is partly dependent on matching the image with representations from memory. Since synesthetes have previously been shown to outperform non-synesthetes in a wide range of memory tasks (Ward, Field, & Chin, 2019), a better FPT performance in more synesthetic individuals might be driven by memory effects. Further, synesthetes seem to have more vivid visual mental imagery (Ward & Simner, 2020), which likely is also required in the FPT matching process. It remains to be investigated how FPT performance relates to supra-threshold synesthesia.

Finally, studies in individuals with autism found evidence for more locally biased attention to be more consistent if the task leaves it to participants to attend either the global picture or smaller details (Van der Hallen et al., 2015) but not when explicitly instructed to focus on global features (Mottron, Burack, Iarocci, Belleville, & Enns, 2003). In a similar way, synesthetes might overcome their more detail-oriented default attentional style in order to solve the task.

4.4. Covariate effects

Intellectual ability was also associated with higher synesthetic consistency across individuals. The latter might either indicate that higher IQ increases the likelihood of achieving more consistent scores, or that more synesthetic individuals tend to have a higher IQ. Future studies should investigate this question in a larger typically developed sample with IQ as main predictor. Further, it seems that individuals with NDD diagnoses or lower IQ were less likely to take part in this study and complete the online test correctly (please see Supplementary Material section 2.2 and Supplementary Table S1 and S2). Future studies should investigate the degree of grapheme-color synesthesia and its prevalence in larger NDD samples and in a wider range of psychiatric trait measures, with special attention to the altered sensory processing that seems to be a common thread, across diagnostic boundaries.

4.5. Twin design specific implications

Within-twin pairs, all factors shared by twins are implicitly adjusted for. An environmental factor that might influence an individual’s synesthetic consistency and which is more likely to be shared by twins compared to unrelated individuals is the exposure to colored letter sets in childhood, which influences synesthetic color associations (Witthoft et al., 2015; Witthoft & Winawer, 2006). In addition, factors that might have added noise to the model across individuals might be shared by twins, hence potentially weakening the across sample
associations but not the within pair effects. Stronger associations within-twin pairs compared to across the sample in this study suggest an increased sensitivity within pairs. In this study, one such factor might have been the time that had passed between initial and online assessment, which was the same for twins of a pair. Interestingly, the association between cognitive ability and synesthetic consistency was only significant across individuals, but lost within pairs. This association was strong across the sample despite the time gap between assessments, but might be driven by shared familial factors, for instance genetics.

4.6. **Strengths and limitations**

Strengths of our approach are the more sensitive twin design and the inclusion of individuals fulfilling diagnostic criteria for one or more NDD diagnosis. We also used novel ways of assessing sensory sensitivity (the Sensory Profile) and perceptual processing (the Fragmented Pictures Test) compared to earlier synesthesia studies, allowing us to confirm as well as expand on previous findings. Limitations of our design are the limited sample size for regression analyses (n = 65), although the sample size is still larger than in the earlier paper by Burghoorn et al. (2020). Especially the sample of complete twin pairs was small (22 pairs = 44 individuals) and likely only sufficient to detect larger sized effects (assuming an effective sample size of >30, >80% power for multiple linear regressions with three predictors is only given for effect sizes of Cohen's f² >/.25; G*Power3.1.9.2). Hence, we might have overlooked smaller effects. Further, this prevented us from comparing estimates of MZ and DZ sub-cohorts, which would have enabled differentiating genetic and environmental contributions. Since the sample included both MZ and DZ twin pairs, the amount of genetics controlled for could lie anywhere between 50 and 100% and differed from pair to pair.

Also, our sample did not consist solely of complete twin pairs but also included singletons in analyses across individuals, and hence, the samples were not entirely identical within-twin pairs and across the sample. When interpreting the findings related to the degree of grapheme-color synesthesia in non-synesthetes, we acknowledge the possibility that synesthetic consistency in non-synesthetes may not reflect sub-threshold synesthesia, but instead could reflect other cognitive traits such as enhanced memory or greater color discrimination abilities. At the same time, there is evidence that synesthetic consistency is related to non-randomness of cross-modal correspondences (Cuskley et al., 2019), suggesting a relationship of the consistency score to integration across the senses (see also 2. Introduction, p. 2). It should further be mentioned that it is unclear whether the associations found in relation to the degree to grapheme-color synesthesia are generalizable to other synesthesia types, which were not tested in this study. In previous studies, cohorts of different types of synesthetes were included (e.g., Ward et al., 2017, 2018; Van Leeuwen et al., 2019), for instance comprising individuals with sequence-space synesthesia or multiple synesthesia types, possibly affecting the nature of the relationship with autistic traits. Although a subgroup analysis in Van Leeuwen et al. (2019) did not reveal any differences in AQ scores across different types of synesthetes, it cannot be ruled out that effects are stronger or weaker across different synesthesia types. While we used the same AQ sub-scores as previous studies on the association between synesthesia and autistic traits, the internal consistency of the Attention to Details domain was relatively low. Using an alternative 3-factor sub-division of the AQ (according to Russell-Smith, Maybery, & Bayliss, 2011), results pointed into the same direction but fell below significance (see Supplementary Table S6). Reasons why the association between Details/Patterns and the degree of synesthesia was not significant could be the reduction in power, induced by testing three instead of two sub-scales and due to fewer AQ items being included in this sub-scale than in the Attention to Details sub-scale suggested by Hoekstra et al. (2008) (for a comparison between this 3-factor solution and the 2-factor sub-division used in the main analysis, please see Supplementary Material, section 4 “Alternative AQ sub-scales”). However, future studies on the association between synesthesia and autistic traits should also consider this alternative sub-division.

Finally, an additional limitation is the time gap between the initial assessment in RATSS (perceptual tests, questionnaires) and the synesthesia experiment, which could be as long as 8 years (~3 years on average). While it is rather unlikely that the time gap has introduced associations that otherwise would not have been found, it is quite likely that it introduced some noise, which might have weakened the associations. Since the sample included in this study had a lower proportion of individuals diagnosed with an NDD and an on average higher IQ compared to the total RATSS cohort (see Supplementary material section 2.2), it is possible that individuals with more cognitive difficulties found it less feasible to complete the synesthesia test, maybe especially online by themselves. Since most of the included participants completed the synesthesia assessment after the initial participation in RATSS, they had to respond actively to an invitation letter, which might have been an additional hindrance to participate, especially for people with an NDD diagnosis.

5. **Conclusions**

The current study complements previous evidence for a link between synesthesia and autistic traits (in the perceptual domain) and sensory hyper-sensitivity, using several novel questionnaires and tests compared to previous research, and a twin sample where 18% fulfilled diagnostic criteria for an NDD diagnosis. The findings are in line with the idea that the link between autism and synesthesia is strongest at the level of perceptual and attentional processes. Importantly, all associations were more pronounced within-twin pairs, where they are more direct because a large amount of familial factors are implicitly controlled. Results from visual tests were less consistent with the literature and demand to be investigated in larger samples including more supra-threshold synesthetes.

**Data availability statement**

The conditions of our ethics approval do not permit public archiving of anonymised study data. Readers seeking access
to the data should contact the corresponding author. Access will be granted to named individuals in accordance with ethical procedures governing the reuse of sensitive data, including completion of a formal data sharing agreement. The synesthesia questionnaire (in Swedish) is available in the Supplementary Material (Appendix 1, p.13-15) and the Autism Spectrum Quotient is available for download at the Autism Research Centre (https://www.autismresearchcentre.com/tests/). The synesthesia test used here is available for download at https://github.com/BSTN/syntest-sweden and an easy to implement open source version of a very similar application is available at https://github.com/mdingemanse/colouredvowels/blob/master/SenseTest/README.md. The R package used to calculate the consistency scores is freely available at https://github.com/AnonZebra/synrats. In addition, an updated R package with additional functions can be downloaded at https://github.com/datalowe/synr and a detailed description of the package can be found at https://datalowe.github.io/synr/.

Legal copyright restrictions prevent public archiving of the AASP (https://www.pearsonassessments.com/store/usassessments/en/Store/Professional-Assessments/Motor-Sensory/Adolescent-Adult-Sensory-Profile/p/100000434.html), Embedded Figures Task (Consulting Psychologists Press), and Fragmented Pictures Test (Hogrefe, https://www.ub.uni-bielefeld.de/testothek/4098937), which can be obtained from the copyright holders - please see also the cited references.

Pre-registration and sample size statement

No part of the study procedures or analyses was pre-registered prior to the research being conducted. We report how we determined our sample size, all data exclusions, all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study.

Credit author statement

Tessa van Leeuwen: contribution to design and drafting, Lowe Wilsson: contribution to setup and analyses, Hjalmar Nobel Norrmann: contribution to literature search, Mark Dingemanse: contribution to setup and commenting on draft, Sven Böhle: access to twin sample and commenting on draft, Janina Neufeld: conceptualization, received funding, analyses, and contribution to drafting.

Declaration of competing interest

S. Böhle discloses that he has in the last three years acted as an author, consultant or lecturer for Shire, Medice, Roche, Eli Lilly, Prima Psychiatry, GLGroup, System Analytic, Kompetento, Expo Medica, Prophaze, and receives royalties for text books or diagnostic instruments from Huber/Hogrefe, Kohlhammer and UTB. The remaining authors declare that they have no conflicts of interest.

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Supplementary data

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References


