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Grey-matter thickness of the left but not the right primary visual area correlates with

autism traits in typically developing adults
We examined whether functional and structural variability in the primary visual area (V1) correlated with autism traits. Twenty-nine participants (16 males; $M_{\text{Age}} = 26.4$ years, $SD_{\text{Age}} = 4.0$ years) completed the autism-spectrum quotient (AQ) questionnaire prior to the magnetic resonance imaging session. The total AQ scores was used to assess the degree of self-reported autism traits. The average functional activation in V1 to visual stimulation and its average grey-matter thickness were calculated. There were no correlations between functional activation in V1 and autism traits. Conversely, grey-matter thickness of the left but not the right V1 correlated with autism traits. We conclude that structural changes in the left V1 could be a marker for the presence of autism traits.
Autism spectrum disorder (ASD) is a neurodevelopmental disorder that is traditionally characterised by impaired social communication, repetitive behaviours, and restricted interests (American Psychiatric Association 2013). In addition to these markers, atypical perceptual symptoms, including responses to auditory, tactile, and visual stimuli, have been widely documented in individuals with ASD and are now formally recognised as a clinical descriptor for the disorder (American Psychiatric Association 2013; Marco et al. 2011). Atypical perceptual experiences are considered critical to understanding ASD, yet little is known about the underlying neural substrates that are affected (Baum et al. 2015). Similar atypical perceptual experiences are also present in typically developing (TD) individuals with autism traits (Chouinard et al. 2016; Chouinard et al. 2018). The present investigation examined variations in autism traits in TD individuals as an approach to model and examine possible neural underpinnings of atypical visual experiences in ASD (Landry and Chouinard 2016).

Notably, atypical perceptual experiences in individuals with ASD encompass both perceptual improvements and deficits. Some studies found that individuals with ASD perform better than TD individuals in visual search (Kemner et al. 2008; O'Riordan 2004) and visual discrimination (Ashwin et al. 2009; O'Riordan 2004) tasks yet have more difficulties when asked to identify facial expressions (Loth et al. 2018; Macdonald et al. 1989) and the global direction of moving visual patterns (Robertson et al. 2014; Tsermentseli et al. 2008). Atypical integration of visual information in distributed brain regions may underpin these and other atypical perceptual experiences in individuals with ASD. There is preliminary evidence that one important node in this network could be the primary visual area (V1), which is the area of interest in the present investigation.

Earlier work has demonstrated that individuals with ASD perform better than TD individuals on tasks that require perceiving simple, non-social sensory stimuli yet have more difficulties on tasks that require perceiving more complex, social sensory stimuli (Bertone et
al. 2005; Vandenbroucke et al. 2008). The question arises as to why individuals with ASD process low-level features of a visual stimulus in a more veridical manner. The retinotopic organisation of the visual system allows one to investigate neural mechanisms underlying the perception of simple and complex stimuli. Namely, simple features of a visual stimulus could be processed at the earliest stages of the visual system while complex features of a visual stimulus require the involvement of later stages of the visual system for higher level information processing.

Bertone et al. (2005) tested whether low-level or high-level information processing differences are affected in individuals with ASD. In their study, participants performed an orientation discrimination task in which they judged the orientation of either simple or complex stimuli. The simple stimuli consisted of only luminance differences while the complex stimuli consisted of only textural information differences. Orientation-discrimination thresholds revealed that individuals with ASD performed better than TD individuals when they were asked to report the orientation of simple stimuli. In contrast, the TD group performed better than the ASD group when they were asked to report the orientation of complex stimuli. The authors speculated that the behavioural differences in individuals with ASD might be explained by atypical neural connections between early visual areas. They suggested that atypical neural connectivity in V1 enhances the extraction of orientation information for the simple stimuli while it hinders the integration of more complex information between early visual areas (from V1 to V2/V3).

Likewise, Vandenbroucke et al. (2008) provided further electrophysiological evidence for the involvement of early visual areas in the perceptual processing differences exhibited by individuals with ASD. They tested both ASD and TD individuals in a texture segregation task while recording electroencephalographic (EEG) activity. Their results revealed an atypical inhibition of horizontal connections in early visual areas in individuals with ASD. They further
reported a correlation between their electrophysiological results and behavioural performance on a low-level visual perceptual task.

Several studies revealed evidence that atypical visual experience in individuals with ASD are related to a general increase in neural activation (Keehn et al. 2008; Samson et al. 2012). For example, Keehn et al. (2008) demonstrated hypersensitive activation to visual stimulation in ASD compared to TD individuals using functional magnetic resonance imaging (fMRI). In their study, participants performed a visual search task in which they judged whether a target item was presented within an array of distractors. The difficulty of the task was manipulated by changing the number and composition of distractors. Their results showed that visual search efficiency was not affected by the composition of distractors in individuals with ASD. From differences in activation patterns, the authors could show how the degree of hypersensitivity in occipital and frontoparietal regions were associated with superior visual-spatial abilities in individuals with ASD.

Atypical patterns of brain activation are not the only difference observed between ASD and TD individuals. Neural structural differences have also been found in individuals with ASD compared to TD individuals (Bezgin et al. 2018; Hyde et al. 2010). Although these differences typically involve widespread increases in both grey-matter and white-matter volume, a previous report showed that grey-matter volume differences are more pronounced compared to white-matter volume differences (Lainhart and Lange 2011). Abnormal axonal pruning rates are thought to explain atypical grey-matter volumes. Both region-specific increases and region-specific decreases in grey-matter volume have been detected in individuals with ASD using voxel-based morphometry (Hyde et al. 2010). To date, as far as we know, no study has investigated grey-matter variability of V1 in TD individuals with varying degrees of autism traits. Yet, many have argued that atypical perceptual experiences related to autism could be
associated with structural differences in primary sensory areas (Lainhart 2015; Schwarzkopf et al. 2014).

So far, the literature has yielded mixed results in terms of functional and structural differences in individuals with ASD. The mixed results could have arisen from various nuisance factors. One possibility is that ASD is a heterogeneous disorder characterised by a wide range of symptoms varying in their presence and severity. It is unknown whether individuals with ASD in many earlier studies exhibited similar symptoms at comparable levels or not. Heterogeneity in cognitive abilities and the high prevalence of intellectual disabilities in ASD may also have had an impact on the results. In a review, Landry and Chouinard (2016) outlined the benefits of conducting experiments with individuals who exhibit subclinical, autistic-like features, as a model to study ASD indirectly rather than studying individuals with the diagnosed disorder. The authors suggested that examining the subclinical population makes it possible to (1) increase the number of participants, (2) avoid frequent comorbid disorders of ASD such as attention deficit-hyperactivity disorder, (3) test various traits in greater isolation, (4) use comparable age groups without considering mental age, and (5) conduct experiments that would otherwise make participants with ASD feel overwhelmed (Landry and Chouinard 2016). The latter is particularly relevant when presenting highly salient flickering visual stimuli, such as those used in the present investigation.

Recently, the broader autism phenotype has also been referred to the subclinical presentation of autism traits in the TD population irrespective of the presence of a relative with ASD (Landry and Chouinard 2016). Earlier studies on this phenotype only included close relatives of individuals with ASD who exhibited autism traits. This is because genetic liability for ASD has an influence on the risk of developing the disorder. However, it has also been demonstrated that almost 5% of the world-wide population share the same genetic liability for ASD and not all of these individuals have been diagnosed with ASD nor belong to the same
family pedigree (Bourgeron 2015). Therefore, it is possible to observe mild traits that are associated with ASD in the TD population and refer to this as a phenotype. In the present investigation, the autism spectrum quotient (AQ) questionnaire was used to measure ASD related traits in TD individuals (Baron-Cohen et al. 2001).

Our first aim was to test the relationship between functional activity in V1 and autism traits using MRI. We hypothesised that activation in V1 would correlate positively with autism traits, reflecting a possible underpinning to explain why individuals with ASD are more sensitive to visual stimulation compared to TD individuals. Our second aim of the study was to test the relationship between grey-matter thickness of V1 and autism traits. We hypothesised that grey-matter thickness of V1 would also change in individuals with higher degrees of autism traits, reflecting a possible underpinning to explain atypical visual experiences in individuals with ASD. We had no specific predictions regarding the direction of this change.

Method

Participants

Twenty-nine healthy volunteers took part in this study (16 males, 13 females; $M = 26.4$ years, $SD = 4.0$ years). All participants reported to have normal or corrected-to-normal vision, which as an inclusion criterion for this study. Exclusion criteria included a previous history of mental or neurological disorders. This included the exclusion of individuals with a diagnosis of ASD and a history of headaches/migraine, which could potentially be triggered by the highly salient flickering stimuli used in the present investigation. Standard MRI contraindications, such as
metal inside the body or pregnancy, were additional exclusion criteria (Sawyer-Glover and Shellock 2000). Written informed consent was obtained from each participant before the experiment. At the end of the experiment, all participants were provided with monetary reimbursement for their time and any inconveniences. The study was carried out in accordance with the Declaration of Helsinki and approved by the local human ethics committees.

Material and stimuli

Autism-spectrum quotient (AQ) questionnaire

The AQ was used to quantify autism traits (Baron-Cohen et al. 2001). Each participant’s social, communication, attention switching, attention to detail, and imagination skills were measured. Participants were asked to indicate their agreement on a four-point Likert scale ((1) Definitely agree, (2) Slightly agree, (3) Slightly disagree, (4) Definitely disagree). The AQ scale was scored in the standard manner as described by Baron-Cohen et al. (2001). Only the total AQ score was calculated in this study as it is the most robust outcome measure of the AQ questionnaire. High internal consistencies have been reported before for each trait group (Cronbach’s alphas between 0.63-0.67) (Baron-Cohen et al. 2001).

Stimuli used for the retinotopic mapping of V1
Visual stimuli were presented on a monitor driven by MATLAB (MathWorks, Natick, MA, USA) Psychophysics Toolbox, Version 3 (Brainard 2011; Pelli 1997). Contrast reversing (4 Hz) checkerboard stimuli were displayed over a grey background. The stimuli had a 100% contrast. For polar angle mapping, a semicircle checkerboard subtending 20 degrees of visual angle in diameter (i.e. along its base) rotated either clockwise or counter-clockwise around a fixation point (Fig. 1, left panel). The checkerboard semicircle that rotated clockwise and the one that rotated counter-clockwise were presented in separate runs. For eccentricity mapping, a checkerboard ring that either expanded outward or contracted inwards around the fixation point was used (Fig. 1, right panel). The maximal width of the ring was 5 degrees of visual angle. The checkerboard ring that expanded and the one that contracted were presented in separate runs. These stimuli allowed us to activate approximately half of the ganglion cells within a concentric visual field extending 20 degrees of visual angle. Each stimulus completed a cycle 12 times in each run and each cycle of rotation or expansion/contraction took 24 seconds.

Procedure

Participants completed the AQ questionnaire prior to the MRI session. The questionnaire was completed online through a survey on Qualtrics (Qualtrics, Provo, UT, USA) in the participant’s own time. On the day of the MRI session, participants first underwent a brief familiarisation phase in which they saw the various types of visual stimulation that they would later see during the fMRI procedures. The stimuli were presented on a BOLDScreen 24" LCD
(Cambridge Research Systems Ltd., Rochester, UK) fMRI compatible monitor driven by MATLAB Psychophysics Toolbox, Version 3. The monitor had a 60 Hz refresh rate and a 1920 x 1080 display resolution. The participants’ heads were secured by means of foam pads to minimise head movements. The participants viewed the stimuli on the screen situated at the back of the bore of the scanner via angled mirrors mounted on the head coil. The viewing distance was 78 centimetres. In total, four functional runs were completed. Both the checkerboard semicircle and the checkerboard ring were presented once in each direction.

FMRI data acquisition

The anatomical and functional data were acquired on 3 Tesla Siemens TIM Trio MR Scanner (Siemens AG, Munich, Germany). Two anatomical T1 scans were performed at the start and at the end of the scanning session using a 32-channel head coil. Acquisition consisted of 1.0 × 1.0 × 1.0 mm slices with a TE of 2.52 ms, a TR of 1,900 ms and a flip angle of 90 degrees. The matrix size of the anatomical images was 350 × 263 in the horizontal direction. For the functional runs, only the posterior portion of the 32-channel head coil (20 channels) was used to allow the participant to see the stimuli through the mirror without any occlusion of vision. The blood oxygen level-dependent (BOLD) signal was measured using a T2* weighted echo-planar imaging sequence (Ogawa et al. 1992). All functional runs were performed by acquiring 2.0 × 2.0 × 2.0 mm slices with a TE of 30.0 ms, a TR of 1,000 ms, and a flip angle of 45 degrees. The matrix size of the functional images was 96 × 96 in the coronal direction. The field of view was 192 mm in both dimensions and covered the posterior half of the brain. A total of 288 volumes were acquired for each functional run.
The pre-processing of the data were carried out using a combination of in-house software scripts written in MATLAB, as well as the Statistical Parametric Mapping (SPM 12) (Wellcome Trust Centre for Neuroimaging, London, UK), Freesurfer (Martinos Center for Biomedical Imaging, Harvard University, Cambridge, MA, USA), and FMRIB Software Library (FSL) (Analysis Group, FMRIB, Oxford, UK) software packages. For each participant, a mean anatomical image was calculated by averaging the two anatomical T1 scans. Each participant’s functional data were motion corrected to spatially match the mean of all the functional data. The spatially realigned functional MRI data were then upscaled to a 1-mm isotropic resolution and co-registered to the mean structural MRI data. A 3-mm Gaussian spatial smoothing was then applied to the functional data to help improve signal-to-noise. Afterwards, the functional data were concatenated as four-dimensional volumes, each concatenation corresponding to a run. Within a run, the functional data were detrended and converted as a percent signal change with the overall mean representing the baseline.

Fourier analyses were carried out on the pre-processed fMRI images using procedures similar to those first described by Sereno et al. (1995) for the purposes of retinotopic mapping. The analyses informed us about the amplitude and the phase of the harmonic corresponding to the stimulus being presented at a point in the visual field at a cyclical rate of 0.042 Hz. The correlation between the harmonic and the time series was computed by dividing the amplitude of the harmonic component to the power of square root of the time series. The rotating semi-circle provided a topographic phase map for polar angle and the expanding/contracting ring provided a topographic phase map for eccentricity. The average of the anatomical images
obtained from the two anatomical T1 scans was used to generate an inflated cortex for each participant using Freesurfer’s automated procedures.

We used a deterministic as opposed to a probabilistic approach to define V1 given that its location in standardised space, as well as its location relative to structural landmarks, can vary across individuals (Wandell and Winawer 2011; Dumoulin et al. 2003). To take this variance into consideration, we used the information from each participant’s phase-encoded retinotopic maps to define their V1 without considering probabilistic maps from the general population. Namely, each participant’s V1 was defined by their polar angle and eccentricity phase maps superimposed over their inflated cortex, as described below and in more detail elsewhere (Engel et al. 1997; Wandell and Winawer 2011). Unlike a probabilistic mapping approach, our manual retinotopic mapping at the individual level allowed us to define regions of interest (ROIs) corresponding to the left and right V1 for each participant with certainty. Therefore, we can confidently say that V1 ROIs corresponded to V1 in every individual, enabling us to obtain more power with fewer participants than a probabilistic approach would require to make up for noise arising from anatomical inter-subject variability in standardised space and inter-subject variability in V1 activation relative to structural landmarks.

Fig. 2a provides an illustrative example of how V1 was defined in a representative participant using information obtained from these maps. The upper (shown in yellow, Fig. 2a) and lower (shown in blue, Fig. 2a) meridians were defined as the first reversals in the direction of change in polar angle retinotopy ventrally and dorsally to the calcarine sulcus, respectively. For the purposes of defining V1, the anterior border was defined where both the polar angle and eccentricity phase maps were no longer discernible, corresponding to the part of V1 where the visual stimulation reached its limits in the periphery.
After labelling the left and right V1 on the inflated cortex, we converted the labels to three-dimensional volumes using Freesurfer’s command mri_label2vol, which flagged all voxels between the pial surface and the grey-white matter border. After this was done, we verified by visual inspection that these labels corresponded to sulcal grey matter in volumetric space. **Fig. 2b** provides an illustrative example of V1 ROIs in volumetric space that were defined in the same representative participant as in **Fig. 2a**. As exemplified by **Fig. 2b**, these visual inspections consistently demonstrated good correspondence between grey matter and the V1 ROIs defined in all participants. From these ROIs, we extracted both the average functional amplitude obtained from the Fourier analysis using FSL’s command fslstats and the average grey-matter thickness using Freesurfer’s command mris_anatomical_stats. We further extracted the average grey-matter thickness from the entire left and right hemispheres using Freesurfer. This was done so that we could determine whether any effects obtained for V1 were specific to this area or not.

**Statistical analyses**

Three dependent variables were analysed: functional activation in V1, grey-matter thickness in V1, and grey-matter thickness across the entire hemisphere. For each V1 ROI in each participant, functional activation was calculated as the average amplitude to the retinotopic visual stimulation across functional runs while grey-matter thickness was calculated as the average grey-matter thickness between the pial surface and the grey-white matter border. Similar to the latter, hemispheric grey-matter thickness was calculated as the average grey-
matter thickness between the pial surface and the grey-white matter border but this time across the entire hemisphere. We performed separate analyses of variance (ANOVA) for each dependent variable with Hemisphere ((1) left, (2) right) as a within-subjects factor and Gender ((1) female, (2) male) as a between-subjects factor. Gender was included in the ANOVA to gain insight as to whether the females might be grossly representative of the males, which is arguably an important consideration for this type of research. However, larger sample sizes would be required to detect more subtle gender effects, if they exist. Partial eta squares ($\eta_p^2$) are reported.

We also performed Pearson correlation coefficients ($r$) to determine if our three dependent variables predicted autism traits, as measured by the overall scores on the AQ. Both fMRI activation and grey-matter thickness are known to change with age (Sowell et al. 2003; Kennedy et al. 2015). To control for this, partial correlations were also performed to verify whether any resulting relationship between autism traits and our different measurements still survived when age was entered as a nuisance variable. Effects of gender are also considered in Supplementary Material. The Bonferroni method was used to correct for multiple correlations. Namely, corrected $p$ values ($p_{corr}$) were obtained by multiplying the observed $p$ values ($p_{uncorr}$) by the number of correlations performed for each dependent variable that was correlated with autism traits (i.e., $p_{corr} = p_{uncorr} \times 6$).

In addition to null hypothesis statistical testing (NHST), we calculated Bayes factors (BF10) denoting the plausibility of the observed data under the alternative (i.e., the presence of an effect) relative to the null (i.e., the absence of an effect) hypothesis using the JASP software package version 0.8.6 (University of Amsterdam, Amsterdam, Netherlands). Unlike NHST, Bayesian statistics allowed us to make inferences about null results. We considered BF10 values greater than 3 as indicating substantial support for the alternative hypothesis and BF10 values of less than 0.33 as indicating substantial support for the null hypothesis (Jeffreys
1961). We used the defaults prior settings in JASP (ANOVA: the r scales were set at 0.5 and 1.0 for fixed and random effects, respectively; correlations: the stretched beta prior width was set at 1).

**Results**

Table 1 provides descriptive statistics for the amplitude measurements obtained from the Fourier analyses, the mean grey-matter thickness in the left and right V1, the mean grey-mean thickness in the left and right hemispheres, and the overall AQ scores. The AQ scores ranged between 1 and 35 ($M = 14.379$, $SD = 7.528$). The mean AQ was slightly below the typical mean of the non-clinical population identified in a meta-analysis carried out by Ruzich et al. (2015) (i.e. $M = 16.940$). The AQ range in the present investigation seems comparable to the one reported in this meta-analysis. An independent samples t-test revealed that there were no differences between females and males in AQ scores ($t (27) = 1.249$, $p = .222$, Cohen’s $d = 0.466$, 95% HDI [-1.058, 0.290], BF10 = 0.626).

For functional activation in V1, ANOVA did not reveal a main effect of Hemisphere ($F (1, 27) = 0.001$, $p = .973$, $\eta^2_p < 0.001$, BF10 = 0.260), a main effect of Gender ($F (1, 27) = 0.162$, $p =$
.691, \( \eta_p^2 = 0.006, \text{BF10} = 0.620 \), or an interaction between these two factors (\( F(1, 27) = 0.246, p = .624, \eta_p^2 = 0.009, \text{BF10} = 0.367 \)). Pearson correlation coefficients \( r \) assessed whether functional activity in V1 was associated with autism traits. The correlations between functional activity and autism traits were not significant in the left V1, \( r(27) = -0.047, p_{\text{corr}} > .999 \) (Fig. 3a), or the right V1, \( r(27) = 0.053, p_{\text{corr}} > .999 \) (Fig. 3b). Bayes factors indicated substantial evidence for the null hypothesis for both the left V1, 95\% HDI [-0.388, 0.310], BF10 = 0.237, and the right V1, 95\% HDI [-0.304, 0.393], BF10 = 0.239. Partial correlations controlling for age demonstrated similar results (left V1: \( r(26) = -0.039, p_{\text{corr}} > .999 \); right V1: \( r(26) = 0.073, p_{\text{corr}} > .999 \)). The same analyses performed separately in females and males seemed to yield consistent findings (see Supplementary Material). Thus, fMRI responses in V1 did not correlate with autism traits.

[Insert Fig. 3 about here]

V1 grey-matter thickness

For V1 grey-matter thickness, ANOVA did not reveal a main effect of Hemisphere (\( F(1, 27) = 4.122, p = .052, \eta_p^2 = 0.132, \text{BF10} = 1.177 \)), a main effect of Gender (\( F(1, 27) = 0.321, p = .576, \eta_p^2 = 0.012, \text{BF10} = 0.442 \)), or an interaction between these two factors (\( F(1, 27) = 0.898, p = .352, \eta_p^2 = 0.032, \text{BF10} = 0.465 \)). Pearson correlation coefficients \( r \) assessed whether grey-matter thickness of V1 predicted autism traits. The correlations were significant in the left V1, \( r(27) = 0.532, p_{\text{corr}} = .018 \) (Fig. 4a), but not in the right V1, \( r(27) = 0.037, p_{\text{corr}} > .999 \) (Fig. 4b). Bayes factors provided substantial evidence for the alternative hypothesis in the left V1,
95% HDI [0.188, 0.735], BF10 = 15.342, and substantial evidence for the null hypothesis in the right V1, 95% HDI [-0.318, 0.380], BF10 = 0.235. Partial correlations controlling for age demonstrated similar results (left V1: $r(26) = 0.544, p_{corr} = .018$; right V1: $r(26) = 0.042, p_{corr} > .999$). The same analyses performed separately in females and males seemed to yield consistent findings (see Supplementary Material). Thus, grey-matter thickness in the left but not the right V1 correlated with autism traits.

Hemispheric grey-matter thickness

For hemispheric grey-matter thickness, ANOVA did not reveal a main effect of Hemisphere ($F(1, 27) = 2.085, p = .160, \eta_p^2 = 0.072, BF10 = 0.695$), a main effect of Gender ($F(1, 27) = 0.035, p = .852, \eta_p^2 = 0.001, BF10 = 0.774$), or an interaction between these two factors ($F(1, 27) = 0.332, p = .569, \eta_p^2 = 0.012, BF10 = 0.423$). Pearson correlation coefficients $r$ assessed whether hemispheric grey-matter thickness was associated with autism traits. Correlations were not significant in the left hemisphere, $r(27) = 0.286, p_{corr} = .795$ (Fig. 5a) and the right hemisphere, $r(27) = 0.228, p_{corr} > .999$ (Fig. 5b). In terms of Bayesian analyses, correlations between grey-matter thickness and autism traits were inconclusive in the left hemisphere, 95% HDI [-0.088, 0.569], BF10 = 0.679 and the right hemisphere, 95% HDI [-0.146, 0.527], BF10 = 0.452. Partial correlations controlling for age demonstrated similar results (left hemisphere: $r(26) = 0.345, p_{corr} = .432$; right hemisphere: $r(26) = 0.301, p_{corr} = .714$). The same analyses performed separately in females and males seemed to yield consistent findings (see...
Supplementary Material). Thus, hemispheric grey-matter thickness did not correlate with autism traits.

[Insert Fig. 5 about here]

**Discussion**

The present study investigated whether functional activity in V1 and grey-matter thickness of V1 correlated with individual differences in autism traits quantified by the AQ in a TD population. We hypothesised that functional activity in V1 and the grey-matter thickness of this brain area would change in TD individuals with higher degrees of self-reported autism traits. To test the relationship between neural activity and autism traits, we calculated the average amplitude to retinotopic visual stimulation in V1 ROIs defined at the individual level. We did not find any correlations between fMRI responses in V1 and autism traits. To test the relationship between grey-matter thickness of V1 and autism traits, we calculated the average grey-matter thickness in these same ROIs. We revealed that the grey-matter thickness of the left but not the right V1 correlated with autism traits. As we will discuss, these findings suggest that structural changes in the left V1 could be a marker for the presence of autism traits. Because V1 is an important node in the processing of visual information in a network of distributed brain regions, we speculate that the structural changes in the left V1 may explain some of the atypical visual experiences associated with autism traits. Future work can examine this possibility more directly.

Several studies have proposed that functional and structural variations that correlate with autism traits in TD participants could be used as a biomarker for ASD (Billeci et al. 2016). A number of studies have reported atypical patterns of brain activation in TD individuals who
Many individuals with ASD are hypersensitive to visual stimulation (Keehn et al. 2008; Manjaly et al. 2007). Previously, Sperandio et al. (2017) reported that TD individuals who exhibit more autism traits are also hypersensitive to visual stimulation. They tested hypersensitivity by measuring the duration of afterimages. Their results showed that individuals who exhibited more autism traits experienced longer afterimages. Given that the magnitude and duration of functional activation in V1 changes as a function of afterimage duration (Sperandio et al. 2012), the authors speculated that this hypersensitivity might also be observed in V1 activity in TD participants with more autism traits. In line with this, we hypothesised that functional activation in V1 might correlate positively with autism traits. However, our results showed that functional activity in V1 was not related to autism traits. Perhaps TD individuals who exhibit more autism traits may not exhibit changes in functional activity in the same way as individuals with ASD. Another possible explanation is that changes in V1 activation may vary as a function of autism traits but only when top-down processes, such as attention or prior knowledge about the upcoming stimuli, are involved (Pellicano and Burr 2012). Thus, TD individuals with more autism traits may exhibit similar changes in
functional activity as individuals with ASD but only if the task requires the involvement of top-
down processes.

Other studies have also failed to show a relationship between autism traits and V1
activation (Hadjikhani et al. 2004; Koh et al. 2010; Schwarzkopf et al. 2014). Hadjikhani et al.
(2004) performed fMRI retinotopy in high-functioning individuals with ASD and a control
group of TD individuals. Their results did not reveal any group differences in V1 activation,
nor did they indicate group differences in the retinotopic organisation of the visual system.
Instead, Hadjikhani et al. (2004) proposed that atypical visual experiences in individuals with
ASD may arise from attentional mechanisms rather than problems in the circuitry of early
visual areas. In line with Hadjikhani et al.’s findings, Koh et al. (2010) could not find any
differences between ASD and TD individuals in contrast sensitivity functions, which are reliant
on processing in early visual areas.

Similar to the present investigation, other studies have examined variations in brain
structure that correlate with autism traits in TD participants (Barnea-Goraly et al. 2010; E.
Peterson et al. 2006; Gebauer et al. 2015). Barnea-Goraly et al. (2010) found similarities in the
white-matter structure of TD individuals who exhibit more autism traits and individuals with
ASD in brain regions that are associated with social cognition and face processing. Gebauer et
al. (2015) showed that grey-matter structure correlates with autism traits in the orbitofrontal
gyrus, lingual gyrus, and central sulcus. E. Peterson et al. (2006) reported larger grey-matter
volume in the occipital lobe in individuals who exhibit more autism traits, which is in line with
our results demonstrating a correlation between grey-matter volume and AQ. Together, these
findings demonstrate that structural changes in brain regions that are associated with visual
processing are observable in individuals who exhibit more autism traits.
Contrary to our approach, these studies quantified structural changes in standardised space and defined their regions using probabilistic brain maps (Barnea-Goraly et al. 2010; E. Peterson et al. 2006; Gebauer et al. 2015). This approach suffers from noise arising from inter-subject differences in sulcal locations in standardised space and inter-subject functional activation relative to structural landmarks (Saxe et al. 2006). For example, the location of the calcarine sulcus between two individuals in Talairach space could be as far apart as by a few centimetres (Amunts et al. 2000). This creates a problem for correlating anatomy with the AQ using sample sizes like those we used.

In contrast, our deterministic approach allowed us to investigate the relationship between grey-matter thickness and autism traits in a functionally defined brain area. We can confidently say that V1 ROIs corresponded to V1 in every individual. Studies that use probabilistic approaches cannot say the same thing and require larger sample sizes to achieve similar results. Using our more sensitive approach, we demonstrated how structural variations in the left but not the right V1 correlated with the presence of autism traits in a TD group. These results are in line with the “left hemispheric dysfunction theory” of ASD (Dawson et al. 1982; Hier et al. 1979) and a recent diffusion tensor imaging (DTI) study revealing white matter abnormalities in individuals with ASD that are mostly lateralised to the left hemisphere (D. Peterson et al. 2015). The authors of the latter study postulated that deficits in left lateralized functions, such as language, could be a consequence of left lateralised white matter abnormalities. Similarly, Zinkstok (2010) showed a left lateralised decrease in the white matter of the occipital lobe.

Another consideration is that our sample had almost as many females ($n = 13$) as it did males ($n = 16$). One could make the argument that it would have been preferable for us to have had disproportionately more males than females to better reflect the gender composition of ASD. We disagree with this reasoning given that we examined the influence of the broader
autism phenotype in the TD population, which consists of almost as many males as females, to model ASD. Our sample would not be representative of the TD population had we imposed a gender sampling bias. For this reason, previous research correlating various facets of cognitive abilities with AQ typically have a balanced composition between genders. Furthermore, our ANOVA did not reveal any evidence for gross gender differences. However, a greater sample would be required to determine more appropriately whether our female participants were truly representative of our male participants.

In closing, the present investigation provides evidence for increased grey-matter thickness in the left V1 and autism traits. It is attempting to infer that variations in visual processing that correlate with autism traits in the TD population could be explained by these structural variations. Future research can investigate this further by correlating performance on visual tasks and grey-matter thickness in the left V1. It is also attempting to infer that people with as ASD diagnosis may also demonstrate increased grey-matter thickness in the left V1. Future research can investigate if this is in fact the case.
Figure 1. Stimuli used for retinotopic mapping. The left panel illustrates the half circle that rotated clockwise or counter-clockwise to map polar angle. The right panel illustrates the ring that expanded outwards or contracted inwards around the fixation point to map eccentricity.
**Figure 2.** The figure provides an illustrative example of how V1 was defined in a representative participant using information obtained from the polar angle map. (a) The top portion of the figures shows a polar angle map superimposed over the inflated cortex of the participant. The upper meridian is represented in yellow. The ventral border of V1 was defined as the first reversal in the direction of change in polar angle retinotopy ventral to the calcarine sulcus. The lower meridian is represented in blue. The dorsal border of V1 was defined as the first reversal in the direction of change in polar angle retinotopy dorsal to the calcarine sulcus. (b) The bottom portion of the figure shows the resulting ROIs for this individual. The left and right V1 ROIs are shown in blue and yellow, respectively.
Figure 3. The relationship between overall AQ scores and functional activity in the left (a) and right (b) V1. Functional activity in V1 is reported as the mean amplitude measurement obtained from the Fourier analysis across the four different types of retinotopic runs. Statistical values presented in the figure consist of Pearson correlation coefficients (r), Bonferroni-corrected p values (p_{corr}), and Bayes Factors (BF10).
Figure 4. The relationship between total AQ scores and grey-matter (denoted as GM in the figure) thickness in the left (a) and right (b) V1. Grey-matter thickness represents the average grey-matter thickness of V1 within the boundaries of the pial surface and the grey-white matter border. Statistical values presented in the figure consist of Pearson correlation coefficient ($r$), the Bonferroni-corrected $p$ values ($p_{corr}$), and the Bayes Factors (BF10).
Figure 5. The relationship between total AQ scores and grey-matter (denoted as GM in the figure) thickness in the left (a) and right (b) hemispheres. Grey-matter thickness represents the average grey-matter thickness of entire hemisphere within the boundaries of the pial surface and the grey-white matter border. Statistical values presented in the figure consist of Pearson correlation coefficient \( r \), the Bonferroni-corrected \( p \) values \( (p_{\text{corr}}) \), and the Bayes Factors (BF10).
<table>
<thead>
<tr>
<th>Functional activity in left V1 (amplitude)</th>
<th>Functional activity in right V1 (amplitude)</th>
<th>Grey-matter thickness in left V1 (mm)</th>
<th>Grey-matter thickness in right V1 (mm)</th>
<th>Grey-matter thickness in left hemisphere (mm)</th>
<th>Grey-matter thickness in right hemisphere (mm)</th>
<th>AQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>M</td>
<td>A</td>
<td>F</td>
<td>M</td>
<td>A</td>
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</tr>
<tr>
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<td>Mean</td>
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<tr>
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<tr>
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<tr>
<td>Max</td>
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<td>2.454</td>
<td>3.91</td>
<td>3.227</td>
<td>2.373</td>
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</tr>
</tbody>
</table>

Table 1. Descriptive statistics for functional activity within V1, grey-matter thickness within V1, grey-matter thickness across the entire hemisphere, and overall autism-spectrum quotient (AQ) scores for female (F), male (M), and all (A) participants. Functional activity in V1 is reported as the mean amplitude measurement obtained from the Fourier analyses across the four different types of retinotopic runs. Grey-matter thickness is reported as the average grey-matter thickness between the pial surface and the grey-white matter border.
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We performed Pearson correlation coefficients ($r$) to determine if three different measurements (functional activation in V1, grey-matter thickness in V1, and grey-matter thickness across the entire hemisphere) predicted autism traits, as measured by the overall scores on the AQ. To control for the effects of age differences, partial correlations were also performed to verify whether any resulting relationship between autism traits and our different measurements still survived when age was entered as a nuisance variable. Correlations were performed on all participants for the main paper and separately for females and males in the following Supplementary Material. Note that the sample sizes below are low. For this reason, these correlations should be interpreted with caution.

V1 functional activation
Pearson correlation coefficients $r$ assessed whether functional activity in V1 was associated with autism traits. Results revealed that fMRI responses in V1 did not correlate with autism traits in either females or males.

**Females**

The correlations between functional activity and autism traits were not significant in the left V1, $r (11) = 0.009$, $p_{uncorr} = .976$, or the right V1, $r (11) = 0.061$, $p_{uncorr} = .842$. In terms of Bayesian analyses, correlations were inconclusive in the left V1, 95% HDI [-0.491, 0.503], BF10 = 0.341, and the right V1, 95% HDI [-0.456, 0.537], BF10 = 0.347. Partial correlations controlling for age demonstrated similar results (left V1: $r (10) = 0.024$, $p_{uncorr} = .940$; right V1: $r (10) = 0.081$, $p_{uncorr} = .802$).

**Males**

The correlations between functional activity and autism traits were not significant in the left V1, $r (14) = -0.092$, $p_{uncorr} = .735$, or the right V1, $r (14) = 0.077$, $p_{uncorr} = .777$. Bayes factors indicated substantial evidence for the null hypothesis for both the left V1, 95% HDI [-0.519, 0.388], BF10 = 0.325, and the right V1, 95% HDI [-0.399, 0.509], BF10 = 0.320. Partial correlations controlling for age demonstrated similar results (left V1: $r (13) = -0.126$, $p_{uncorr} = .655$; right V1: $r (13) = 0.048$, $p_{uncorr} = .865$).

**V1 grey-matter thickness**

Pearson correlation coefficients $r$ assessed whether grey-matter thickness of V1 predicted autism traits. Results revealed that grey-matter thickness in the left but not the right V1 correlated with autism traits in both females and males.

**Females**
The correlations were significant in the left V1, \( r (11) = 0.591, p_{\text{uncorr}} = .033 \), but not in the right V1, \( r (11) = 0.121, p_{\text{uncorr}} = .694 \). In terms of Bayesian analyses, correlations were inconclusive in the left V1, 95% HDI [0.029, 0.830], BF10 = 2.644, and the right V1, 95% HDI [-0.414, 0.574], BF10 = 0.366. Partial correlations controlling for age demonstrated similar results (left V1: \( r (10) = 0.587, p_{\text{uncorr}} = .045 \); right V1: \( r (10) = 0.100, p_{\text{uncorr}} = .756 \)).

Males

The correlations were significant in the left V1, \( r (14) = 0.511, p_{\text{uncorr}} = .043 \), but not in the right V1, \( r (14) = 0.050, p_{\text{uncorr}} = .854 \). Bayes factor was inconclusive in the left V1, 95% HDI [0.004, 0.772], BF10 = 2.034, while it provided substantial evidence for the null hypothesis in the right V1, 95% HDI [-0.419, 0.491], BF10 = 0.313. Partial correlations controlling for age demonstrated similar results (left V1: \( r (13) = 0.534, p_{\text{uncorr}} = .040 \); right V1: \( r (13) = 0.027, p_{\text{uncorr}} = .924 \)).

Hemispheric grey-matter thickness

Pearson correlation coefficients \( r \) assessed whether hemispheric grey-matter thickness was associated with autism traits. Results revealed that hemispheric grey-matter thickness did not correlate with autism traits in either females or males.

Females

Correlations were not significant in the left hemisphere, \( r (11) = 0.374, p_{\text{uncorr}} = .208 \), or the right hemisphere, \( r (11) = 0.294, p_{\text{uncorr}} = .329 \). In terms of Bayesian analyses, correlations between grey-matter thickness and autism traits were inconclusive in the left hemisphere, 95% HDI [-0.206, 0.719], BF10 = 0.701, and the right hemisphere, 95% HDI [-0.154, 0.748], BF10
Partial correlations controlling for age demonstrated similar results (left hemisphere: $r(10) = 0.434, p_{uncorr} = .159$; right hemisphere: $r(10) = 0.384, p_{uncorr} = .218$).

**Males**

Correlations were not significant in the left hemisphere, $r(14) = 0.221, p_{uncorr} = .410$, or the right hemisphere, $r(14) = 0.177, p_{uncorr} = .511$. In terms of Bayesian analyses, correlations between grey-matter thickness and autism traits were inconclusive in the left hemisphere, 95% HDI [-0.283, 0.603], BF10 = 0.422, and the right hemisphere, 95% HDI [-0.320, 0.576], BF10 = 0.377. Partial correlations controlling for age demonstrated similar results (left hemisphere: $r(13) = 0.233, p_{uncorr} = .403$; right hemisphere: $r(13) = 0.184, p_{uncorr} = .511$).