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Research Report

Adolescents with autism show typical fMRI repetition suppression, but atypical surprise response

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ABSTRACT

Recent theoretical frameworks have hypothesized that autism spectrum disorder (ASD) may be marked by an altered balance between sensory inputs and prior knowledge—the so-called hypoprior hypothesis. Yet evidence regarding such an altered balance is mixed. Here, we aimed to test this hypothesis within the domain of visual perception, by examining how neural activity in the visual system was modulated by stimulus repetition and stimulus expectation in healthy and ASD participants.

We presented 22 adolescents with ASD and 22 typically developing (TD) adolescents with pairs of object stimuli, while measuring brain activity using functional magnetic resonance imaging (fMRI). Stimulus pairs could be stimulus repetitions or not and could be expected or not. We examined neural activity in early (V1) and object-selective (LOC) visual cortex.

Both ASD and TD individuals showed robust and equal repetition suppression in LOC. By contrast, ASD and TD groups showed a different response to expected versus unexpected stimuli, specifically in V1. Thereby, our results suggest that while the more automatic modulation of activity by repetition is unaffected in ASD, there is some evidence that the balance between sensory evidence and prior knowledge may indeed be altered in early visual cortex of ASD.

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1. Introduction

Recently, it has been hypothesized that autism spectrum disorder (ASD) may be characterized by an altered balance between sensory input and prior beliefs. In particular, Pellicano and Burr (Pellicano, 2013; Pellicano & Burr, 2012) proposed the hypoprior hypothesis: they posit that in ASD, perception (and perhaps cognition) may be less biased by contextual factors, culminating in an underweighting of prior beliefs, compared to sensory evidence. As prior beliefs can often resolve the noisy and ambiguous information from the environment, this underweighting of priors may lead observers with ASD to often be in a state of surprise, in which they are overwhelmed by the sensory input.

Such an altered balance between top-down priors and bottom-up input would extend beyond the perceptual domain. Indeed, complex social interaction and communication require constant weighting of what we perceive others doing with what we know about their state of mind and context (Friston & Frith, 2015; Sinha et al., 2014). Thus, altering the balance between evidence and prior beliefs can profoundly alter our experience across many domains, and may contribute to a wide variety of behaviours associated with the autism spectrum.

Evidence for the hypoprior hypothesis, particularly at the level of the brain, is mixed. In one line of research, researchers examined the amount of adaptation in behaviour or brain response to repeated stimulation. Repeated stimulation usually results in a reduced sensory response (typically called repetition suppression, RS (Grill-Spector, Henson, & Martin, 2006)). This can be conceptualized as a modulation of the current sensory evidence by the prior, derived from recent history, given that the environment typically remains stable over short intervals (Kaliukhovich & Vogels, 2011; Summerfield, Trittschuh, Monti, Mesulam, & Egner, 2008). Ewbank and colleagues found that RS was inversely related to autistic personality traits in typically developing (TD) participants (Ewbank et al., 2014). Similarly, Ewbank observed less RS in the fusiform face area (FFA) for faces in ASD compared to TD adults. This difference did not extend to shapes in lateral occipital cortex (LOC) (Ewbank et al., 2017). In behavioural experiments, adaptation to sound loudness, stimulus numerosity, and eye-gaze have also been reported to be reduced in ASD individuals compared to TD participants (Lawson et al., 2015, 2017a; Turi et al., 2015).

However, phenomena such as RS may not directly probe the hypopriors hypothesis, because they do not necessarily target an integration of prior knowledge and sensory evidence. RS is likely to be (at least partly) implemented by passive, fatigue-like mechanisms (Auksztulewicz & Friston, 2016; Grotheer & Kovács, 2016; Henson, 2016). A potentially more direct approach to investigate how prior expectations modulate sensory processing could be to generate stimulus expectations (e.g., by statistical association or base rate manipulations). Using such manipulations, previous research has shown that expectation can modulate RS (Grotheer, Hermann, Vidnyánszky, & Kovács, 2014; Grotheer & Kovács, 2015; Summerfield et al., 2008), causing expected repetitions and alternations to evoke less brain activity than unexpected repetitions and alternations (Kremláček et al., 2016; Stefanics, Astikainen, & Czigler, 2014). More generally, expected perceptual events evoke less neural activity than unexpected perceptual events (Kok et al., 2012a, 2012b). Therefore, manipulating stimulus expectation may provide a window into the machinery with which we construct an understanding of our world.

In the current study, we investigated whether the interplay between prior information and sensory evidence differs between individuals with and without ASD, using fMRI. We presented our participants with a perceptual expectation paradigm that we previously developed (Utzerath, St. John-Saaltink, Buitelaar, & de Lange, 2017). In this paradigm, each trial consisted of a pair of stimuli. The pair could either be a stimulus repetition or not, and it could be an expected stimulus pair or not (where expectations were induced by consistently pairing particular stimuli). Thereby, this paradigm orthogonally manipulated stimulus repetition and stimulus expectation. We hypothesized that reduced integration of prior information and sensory evidence would result in a lessened modulation of the sensory response by stimulus repetition and/or expectation in the ASD group.

To preview, RS was robustly present in both the TD and ASD group and did not differ between groups. Yet the groups showed a subtly different modulation of activity in V1 when comparing expected with unexpected stimuli. This suggests that while the more automatic modulation of activity by repetition is unaffected in ASD, there may be a difference between TD and ASD in terms of how expected and surprising stimuli are processed by the early visual system.

2. Method

Data and code used for stimulus presentation and analysis are available online at the Donders Research Data Repository: http://hdl.handle.net/11633/di.dccn.DSC_3018026.01_044.

2.1. Participants

We included 44 participants (22 with and without ASD) as part of the project "Hypo-priors in autistic visual perception". Following guidelines from the local ethics committee, the sample was sized to be sensitive to group differences that had a large effect size (at least 80% power to detect differences with effect size of $d > .8$). ASD participants were recruited from referrals from Karakter Child and Adolescent Psychiatry University Centre, Nijmegen, The Netherlands. TD participants were recruited from local schools. All participants and their parents provided written, informed consent and understood that they could withdraw from the experiment at any time. They were compensated for their time with gift vouchers. The study protocol was approved by the local ethics committee (CCMO protocol NL45835.091.13) and was conducted within the approved procedures.

The sample was group-matched on gender (3 female, 19 male), age, and intellectual ability. Participants were included if they were between 12 and 18 years old, native Dutch speakers, had normal or corrected to normal vision, and had an IQ above 85. Any participant was excluded if there was a (comorbid) psychiatric or neurological disorder, history of brain surgery or brain trauma, current or recent alcohol or

drug addiction, use of antipsychotic or unstable medication, irremovable metal objects in the body (with the exception of dental wires), claustrophobia, or pregnancy.

To be considered for the ASD group, participants had to furthermore have a clinical diagnosis of Autism Spectrum Disorder according to criteria specific in the DSM-5 (Diagnostic and statistica, 2013), which was then confirmed by a structured interview [Autism Diagnostic Interview-Revised, ADI-R (Lord, Rutter, & Le Couteur, 1994)]. In order to be included in the TD group, participants had to have no history of neurological, developmental, or psychiatric disorders, which was controlled by scores on the screening questionnaires (see below).

2.2. General procedure

The procedure of the study is based on an earlier study (Utzerath et al., 2017). The study proceeded in three steps. After providing written, informed, consent, participants and their caregivers completed several tests and questionnaires to verify study eligibility and to match the groups. Then, participants would familiarize themselves with the perceptual expectations paradigm and MRI environment in a replica MRI scanner. Finally, participants would complete the MRI experiment. There were several opportunities for breaks and rest periods.

All participants completed four subtests of the Wechsler Intelligence Scale for Children/Adults [WISC-III/WAIS-III (Kort et al., 2002; Wechsler, 1991; Wechsler, 2000), based on their age at inclusion]. The four subtests used were picture completion, vocabulary, block design, and similarities. They completed the self-report Edinburgh Handedness Inventory (Oldfield, 1971) and the Adult-Adolescent Sensory Profile [AASP (Brown & Dunne, 2002)]. Parents filled out the Social Behaviour Questionnaire [CSBQ (Hartmann, Luteijn, Serra, & Minderaa, 2006)] about their child. Additionally, parents in the TD group completed the Child Behaviour Checklist [CBCL (Achenbach, 1991)] to control for the presence of psychopathology. Parents in the ASD group completed the Social Communication Questionnaire (Rutter & Bailey, 2003) and were administered the ADI-R (Lord et al., 1994).

Participants were then familiarized with the MRI environment with a replica MRI system. This served to alleviate possible anxiety in participants, ease participation, and afforded participants an informed choice on whether to enter the actual MRI scanner or not. Participants, parents, and experimenters documented the anxiety of the participant using the MR short anxiety screening tool (Durston et al., 2009). If either indicated anxiety levels of 8 or higher the experiment would be stopped; at levels between 6 and 8, the participant would be consulted. This ensured that all participants felt at ease during participation. At this point, participants also completed 134 practice trials of the fMRI task (see below).

2.3. Stimuli

We presented image outlines (a lion, a turtle, a bike, a car), following designs by Rossion and Pourtoise (Rossion & Pourtois, 2004) that were matched in terms of mean spatial frequencies and mean luminance using the SHINE toolbox (Willenbockel et al., 2010). We also generated Fourier scrambles of these images for use in the localizer scan, by randomly scrambling the phase of the images' spatial frequencies. These, too, were matched again using the same SHINE procedure. Stimuli subtended a visual angle of approximately 7.5° by 5°. The tasks were programmed using MATLAB R2012b (The MathWorks, Natick, MA, USA) in combination with PsychToolbox (Brainard, 1997).

2.4. Practice and fMRI task

The perceptual expectation paradigm used in this study was previously tested in adult student volunteers (Utzerath et al., 2017). On each trial, we presented the participants with two consecutive stimuli (a pair). Pairs consisted of either the repetition of a single stimulus, or an alternation between two stimuli. Importantly, when participants practiced the task in the replica MRI scanner, the pairings were fixed, creating perceptual expectations. In the subsequent fMRI task, two stimuli had a 75% probability of repeating, and two had a 75% probability of alternating. This resulted in four possible outcomes: expected and unexpected repetitions, as well as expected and unexpected alternations (Fig. 1a). Which stimuli would repeat was counter-balanced between participants. Trials were presented in randomized order.

During practice, participants were instructed to report with a button press whether the second image in every trial depicted a vehicle or an animal. During the fMRI experiment, participants mainly watched stimuli passively. Occasionally a stimulus was presented at 60% of its original size (the target). Participants had to press a button whenever they detected a target. Of all trials, 17.4% contained a target, and the presentation of a target was equally spread across conditions.

Crucially, target trials were not considered for the main fMRI analysis, meaning that the behavioural response did not influence the brain response of interest. It is further important that the transitions learned during practice were irrelevant for performing the fMRI task. This means that the stimulus transitions were unattended, ruling out attentional confounds in the sensory response.

All trials started with the sequential presentation of one of the stimulus pairs. Each stimulus was shown for 250 msec, separated by an inter-stimulus interval of 500 msec. Trials ended with an inter-trial interval of 4.5 sec, to which up to 2 sec of jitter were added (Fig. 1b). During fMRI, participants engaged in two runs of the perceptual expectations task, for a total of 184 trials during approximately 18 min scanning time. Lastly, we performed a localizer scan to identify object-sensitive brain regions. The localizer task lasted 9 min and consisted of blocks of 10 sec, during which one stimulus or scrambled image was shown at a time, flashing on and off at 2 Hz. Participants' task was to detect whenever a stimulus was presented slightly off-centre for about 300 msec, which occurred on average twice per block.

2.5. Image acquisition and pre-processing

Images were acquired on a 3 T Siemens Prisma MRI system (Siemens, Erlangen, Germany). A high-resolution structural image was created using a T1-weighted sequence

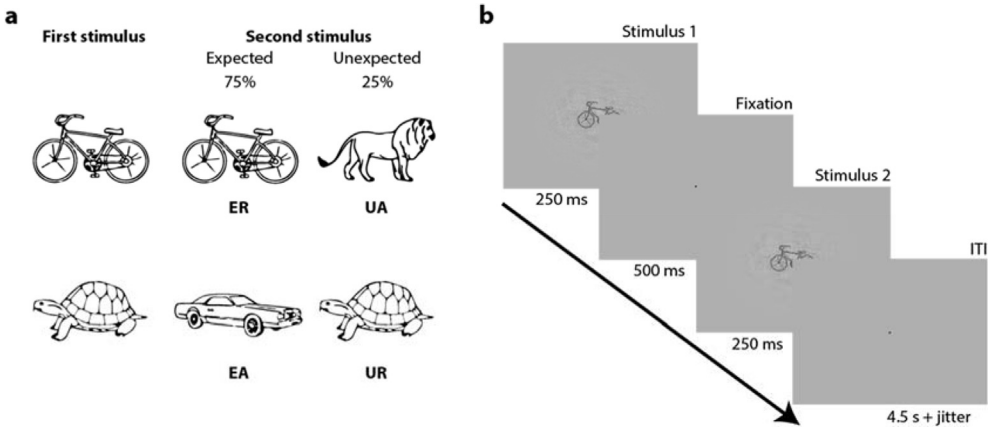

Fig. 1 – Perceptual expectations paradigm. (a) Examples of fixed stimulus pairings. During a practice task, participants implicitly learned that some stimuli are most likely to repeat, whereas others are most likely to alternate, thus creating expected repetitions (ER) and expected alternations (EA), as well as unexpected repetitions (UR) and unexpected alternations (UA). (b) Stimulus display, here showing an expected repetition (ER) trial. In the behavioural discrimination task, participants responded to the category of the second stimulus (vehicle or animal) during the inter-trial interval (ITI). During the fMRI task, participants responded to occasional targets (17.4% of trials) in which the stimulus was shown at 60% of its normal size.

(TR = 2.3 sec, TE = 3.03 msec, 1 mm isometric in-plane resolution). Functional images were acquired using a 3D Multiband sequence (acceleration factor 8, TR = .68 sec, TE = 39 msec, 2.4 mm isometric resolution, 64 sagittal slices). Data were pre-processed using SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK). We discarded the first four volumes of every run to allow for initial equilibrium. Functional images were first spatially realigned to the mean functional. The mean functional image was brought in register with the T1. The T1 was furthermore segmented using SPM12's segment function, which yielded normalization parameters into MNI space. Finally, functional images were normalized into MNI space, and smoothed (6x6x6 mm FWHM).

2.6. Construction of individual regions of interest (ROIs)

Using the same procedures as described in our previous study (Utzerath et al., 2017), we created individual regions of interest for each participant. These ROIs covered V1 and LOC.

LOC was individually identified based on each participant's LOC localizer. We identified the 100 voxels per hemisphere that responded most strongly to objects in comparison to scrambled objects during the localizer session, based on the corresponding contrast image. To ensure a consistent overall anatomical location between subjects, only voxels were considered that were also part of a significant cluster for objects > scrambles at the group level, using an auxiliary threshold of $p < .05$, corrected for family-wise error (Fig. 2a). Voxels that fell within the boundary of V1 (see below) were excluded.

In order to identify every participant's V1, we used Freesurfer's automatic anatomical reconstruction algorithm to parcellate every participant's T1 in native space (surfer.nmr.mgh.harvard.edu/) (Benson et al., 2012). We used an automated method to predict V1 based on cortical folds. This method can be used to predict the retinotopic organization of striate cortex for an individual with accuracy equivalent to 10–25 min of functional mapping (Benson et al., 2012; Hinds et al., 2008) (Fig. 2b; Figure S1). The reconstructed surface was brought in register with the functional scans and the labels corresponding to the predicted sites of V1 were converted into volume space. Using SPM12, this ROI was transformed into MNI space. As V1 typically responds more strongly to scrambles compared to objects (Lerner, Hendler, Ben-Bashat, Harel, & Malach, 2001), we chose voxels that positively responded to the contrast objects > baseline instead of objects > scrambles, thus highlighting voxels that were activated by the object stimuli. As with LOC, we furthermore only allowed voxels that fell into an activated cluster of that same contrast at the group level, using a threshold of $p < .05$, corrected for family-wise error. For data analysis, we then selected a subset of the 100 most responsive voxels to the contrast objects > baseline in V1. Both ROIs were characterized by consistent response patterns over different voxel selections, indicating their robustness (Figure S2). This method ensured that these voxels were responsive to the stimuli and located at anatomically plausible sites. Finally, any voxels that, based on this selection procedure, came into consideration for both V1 and LOC were discarded entirely. This ensured that there was no overlap between the ROIs.

2.7. Statistical analysis

Response times and percentage correct during the fMRI task were compared between groups using independent samples *t*-tests.

Our ROI analysis was based on a General Linear Model (GLM) that was performed in SPM12. We used a 128 sec high-pass filter to remove scanner drifts. For the main experiment, we modelled separate regressors for expected repetitions, unexpected repetitions, expected alternations,

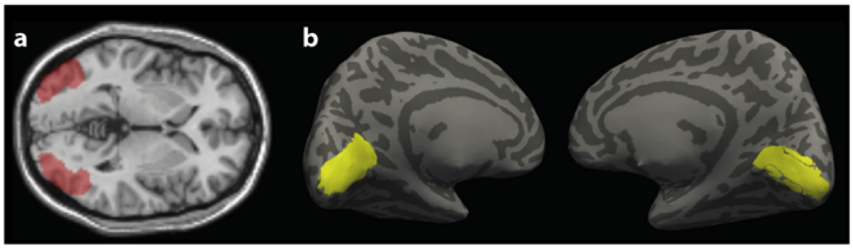

Fig. 2 – Construction of the ROIs. (a) LOC was created individually on the basis of a localizer session. Each individual's LOC mask fell within the group LOC mask that characterized the group's response to objects *vs* scrambles, shown in red. (b) V1 was created individually by reconstructing each participant's anatomy in Freesurfer, here shown in yellow (see section 2.6).

unexpected alternations, targets, and null events. For the localizer, we modelled null events, object and scramble presentations. These regressors were then convolved with SPM12's canonical hemodynamic response function. We furthermore included the motion parameters obtained during realignment, as well as their first and squared first derivatives as nuisance regressors. We then extracted the resulting beta parameter estimates within LOC and V1 and calculated each participant's mean parameter estimate per ROI, hemisphere, and condition.

Per ROI, our data were finally subjected to a 2 (expected versus unexpected) x 2 (repetition versus alternation) within-subjects repeated measure analysis of variance (ANOVA) with Diagnosis (ASD, TD) as between-subjects factor.

All statistical testing was performed in JASP (Love et al., 2017) within a frequentist framework. Additionally, for reference, we estimated the relative likelihood of the alternative compared to the null hypothesis and reported the corresponding Bayes Factors (BF_{10}) for post-hoc t-tests. Bayes Factors larger than three and ten are typically considered as moderate and strong evidence for the alternative hypothesis, respectively. Conversely, BFs smaller than 1/3 and 1/10 are typically considered as moderate and strong evidence for the null hypothesis, respectively (Jeffreys, 1961; Rouder, Speckman, Sun, & Morey, 2009; Wetzels, Wetzels, Raaijmakers, Jakab, & Wagenmakers, 2009).

3. Results

3.1. Sample characteristics

Sample characteristics are detailed in supplementary table ST1. On average, our participants were 15 years and 0 months of age. The groups did not differ significantly in age ($p = .41$, $BF_{10} = .394$), gender, or intellectual ability (Table ST1; all $p > .2$, all $BF < .6$).

Across all scales of the CSBQ, ASD participants scored significantly higher than TD participants (all $p < .001$; all $BF_{10} > 200$; Table ST1). On the AASP, ASD participants reported elevated scores with regards to Low Registration and Sensory Avoiding (both $p < .01$; both $BF_{10} > 6$; Table ST1). On the CBCL, the TD participants scored within normal range (Table ST1). The ASD group scored within the lower clinical range on the SCQ (Table ST1) and their diagnoses were replicated on the ADI-R (Table ST2).

There were no reliable differences between groups in terms of the amount of movement during the task in the scanner, as revealed by a comparison of motion parameters for head translation and rotation (all $p > .28$, all $BF_{10} \leq .48$).

3.2. Behavioural performance

Mean percentage correct during the fMRI task was high (98.1%) and did not significantly differ between groups ($p = .12$, $BF_{10} = .8$), indicating that both groups attended the task. ASD participants had slightly longer response times than TD participants [622 msec *vs* 561 msec; $t(42) = -2.24$, $p = .03$, $BF_{10} = 2.12$] when responding to the targets. Note that these trials with targets were not of interest for the fMRI analysis, which focused on the non-target trials that formed the majority of trials.

3.3. Neural effects of stimulus expectation and repetition

The response of LOC and V1 is shown in Fig. 3. Mean evoked activity did not differ between groups in LOC ($p = .88$, $BF_{10} = .3$), whereas it trended towards being slightly lower in the ASD compared to the TD group in V1 ($p = .076$, $BF_{10} = 1.1$).

Across groups, alternations robustly evoked more activity than repetitions in LOC, indicating repetition suppression [RS; $F(1,42) = 12.8$, $p < .001$, $BF_{10} = 36.35$]. In V1, there was a weak, non-significant trend towards RS ($p = .095$, $BF_{10} = .64$). Importantly, RS did not differ between the ASD and TD groups, neither in LOC ($p = .987$, $BF_{10} = .163$) nor in V1 ($p = .67$, $BF_{10} = .32$).

There was a tendency for LOC activity to increase in response to unexpected stimuli in the TD group, but decrease in the ASD group, resulting in a Expectation*Diagnosis interaction that trended towards significance ($p = .096$, $BF_{10} = .94$). The same pattern was visible in V1, where the corresponding Expectation*Diagnosis interaction was significant [$F(1,42) = 4.26$, $p = .045$, $BF_{10} = 1.6$]. Further examining this interaction, the reduction of the visual response in the TD group was not significant [$t(21) = 1.202$, $p = .243$, $BF_{10} = .422$]; neither was the increase of activity in the ASD group [$t(21) = -1.702$, $p = .103$, $BF_{10} = .769$].

Generally, there was no interaction between stimulus expectation and repetition in either LOC or V1 (LOC: $p = .99$, $BF_{10} = .16$; V1: $p = .87$, $BF_{10} = .17$), and this lack of interaction did not differ between groups (LOC: $BF_{10} = .39$; V1 = $BF_{10} = .33$).

To examine the possible influence of development on these results, we included the participants' age as covariate. This did not explain a significant amount of variance in any of our analyses (all $p > .16$, $BF < .67$).

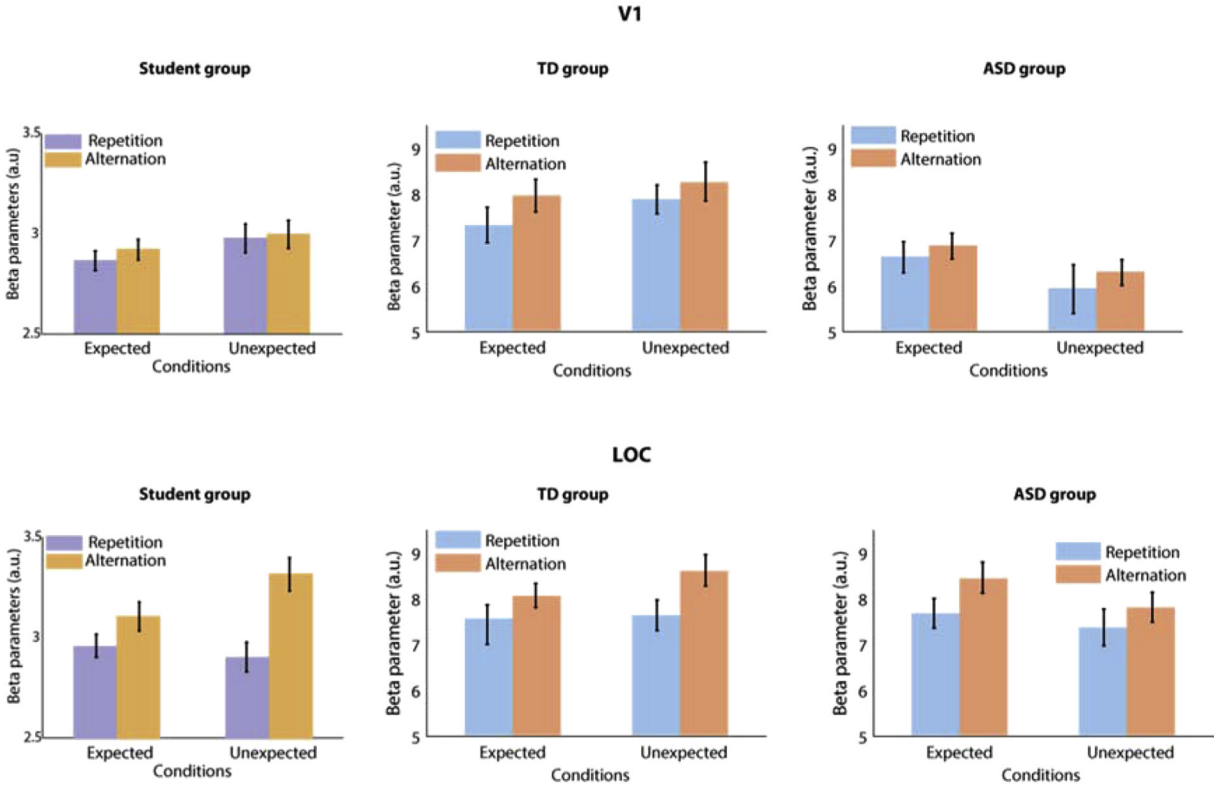

Fig. 3 – ROI beta parameters per group and ROI. The first row shows responses in V1. The second row shows responses in LOC. The first column reproduces the data from an earlier study in healthy student volunteers (Utzerath et al., 2017) for comparison. The second and third column represent the TD and ASD group from the present experiment, respectively. Error bars reflect SEM. See Figure S3 for a comparison of the main effects.

3.4. *Whole-brain fMRI results*

We carried out an exploratory whole-brain analysis, examining the neural consequences of stimulus repetition and expectation. This analysis indicated significant RS in bilateral LOC (see Fig. 4), but there were no other brain regions showing an effect of repetition or expectation, nor group differences of these measures. We furthermore compared the *task > baseline* contrast between groups to examine whether there were any general activity differences between groups. There were no group differences in any region for this comparison.

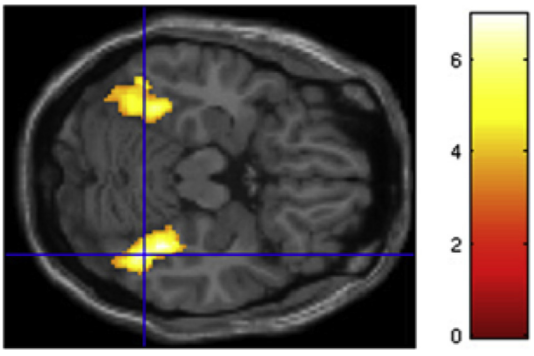

Fig. 4 – Repetition suppression in LOC (Right hemisphere: $MNI_{XYZ} = [38\ -42\ -18]$, $t = 6.96$, $k = 1372$, $p_{FWE} < .001$; left hemisphere: $MNI_{XYZ} = [-38\ -58\ -14]$, $t = 6.74$, $k = 1738$, $p_{FWE} < .001$). Figure represents slice at $z = -18$.

3.5. *Brain-behaviour correlations*

To investigate whether the effects of stimulus expectation and repetition were related to inter-individual variation in traits among autistic participants, we calculated Pearson correlations between the main effects of Expectation and Repetition and the scores on the AASP as well as the total score of the CSBQ. The main effects of Expectation and Repetition here were defined as the difference between alternations and repetitions, as well as expected and unexpected trials, in LOC and V1.

Total CSBQ was not reliably correlated with any activity differences in LOC or V1 (all $r < .23$, $p > .13$). Similarly, there was no significant correlation between the AASP and main effects of Expectation or Repetition (all $r < 031$, $p > .052$).

4. Discussion

We investigated whether the integration of sensory evidence and prior information differs between individuals with and without ASD. Participants viewed pairs of stimuli comprising either the same image presented twice (repetition) or two different objects (alternation). Additionally, both repetitions and alternations could be either expected or unexpected. We hypothesized that effects of stimulus repetition and expectation may be diminished in the ASD group, if this group is marked by a reduced integration of prior and sensory

evidence. The data showed that repetition suppression was robustly present in both groups, did not differ between the groups, and furthermore did not correlate with measures of sensory processing and social-communicative problems. In contrast, we found a difference in how expected *vs.* unexpected stimuli were processed in V1, where ASD and TD observers had differing responses to expectation-confirming relative to expectation-violating events.

4.1. *Repetition suppression intact in both groups*

Individuals with and without ASD did not significantly differ in the magnitude of RS, neither in LOC nor V1. Indeed, the associated Bayes Factors were <1/3 in both V1 and LOC, providing moderate support for the null hypothesis (no difference) over the alternative hypothesis (difference between groups). This stands in contrast to some previous studies that found that autism or related personality traits and diagnosis exhibits altered adaptation (e.g., (Ewbank et al., 2014; Ewbank et al., 2017; Jiang et al., 2013; Kleinhans, Richards, Greenson, Dawson, & Aylward, 2016; Lawson et al., 2015; Lawson et al., 2017a; Swartz, Lee Wiggins, Carrasco, Lord, & Monk, 2013),). There are several factors that can explain this divergence in findings.

The first factor is to distinguish here between measures of brain and behaviour. In particular, Lawson and colleagues (Lawson et al., 2015, 2017a) used behavioural measures to index adaptation in auditory and visual paradigms. Our study on the other hand investigates adaptation of sensory regions in a behaviour-free context.

The second factor is the sampled populations. While we sampled adolescents with a clinical ASD and TD individuals, several other studies recruited TD individuals who varied on personality traits related to ASD (Ewbank et al., 2014; Lawson et al., 2017a). For instance, the autism quotient that is used to quantify personality traits related to ASD may emphasize different aspects of the spectrum compared to the clinical diagnosis we used.

A third factor to take into consideration is the stimulus. Many experiments that probed stimulus adaptation used face stimuli. Notably, Jiang and colleagues (Jiang et al., 2013) showed that relative to a control dataset, individuals with autism showed decreased adaptation, which was linked to decreased discriminability of faces in the FFA response and predicted poorer face discrimination performance. Weaker adaptation might then be a result of a more heterogeneous underlying brain response processing those faces. Therefore, experiments using faces as stimuli may not be ideally suited to study RS in ASD, as a generally atypical response to faces might confound observable differences in RS between individuals with and without ASD.

In line with this view, Ewbank did not find differing RS between individuals with and without ASD when the experimenters presented shapes instead of faces (Ewbank et al., 2017). Likewise, in our pilot study where TD adults performed the perceptual expectation task on objects, variation in ASD-related personality traits did not predict RS either (Utzerath et al., 2017). Thus, the converging evidence hints at the possibility that not RS itself is atypical in ASD, but rather that atypical face processing may manifest itself as reduced adaptation.

4.2. *TD and ASD groups show opposing brain responses to surprise*

The hypopriors hypothesis predicts that the difference between unexpected and expected stimuli should be diminished in the ASD group, compared to TD group. In our experiment, participants with and without ASD showed opposing responses when contrasting expectation-confirming and expectation-violating stimuli in V1. Specifically, in TD observers, the presentation of expected stimuli tended to decrease brain activity, whereas it tended to be increased in the ASD group. It should be noted though that while the interaction between groups was statistically significant, post-hoc tests garnered no statistical support for either a reduction of expected stimuli in the TD group, nor an increase in the ASD group. Given the small sample size and associated statistical uncertainty, these findings should be interpreted with caution.

Qualitatively though, the TD group showed the same patterns of effects as we obtained in TD adults in the previous study (Utzerath et al., 2017) (Fig. 3, left and middle column). One could therefore interpret the results as indicating that the TD group showed expectation suppression, similar to an earlier dataset, while this was not the case for the ASD group.

This study thereby provides tentative evidence that the balance between prior knowledge and sensory evidence may be altered in ASD, at the level of the brain. Further work should be devoted to precisely understand the nature of this alteration. The original proposal of the hypoprior did not make predictions about the underlying neural implementations (Pellicano, 2013; Pellicano & Burr, 2012). However, several hypotheses have been put forward regarding the neuro-computational basis of a hypoprior in the context of predictive coding (Friston, 2005; Rao & Ballard, 1999). Lawson & Friston (Lawson, Rees, Friston; Lawson, Rees, & Friston, 2014) argue that a hypoprior corresponds to a weakening of the precision of the prediction. That is, the prediction signal that is fed back to sensory cortex may convey the correct mean, but have a large variance. Therefore, when this prediction is compared to the incoming stimulus, sensory cortex will emit a large error signal. In line with this view, Lawson and colleagues (Lawson et al., 2017b) found that individuals with ASD overestimate the volatility of their sensory environment. As a result, their behavioural and pupillometric responses showed a lessened response to surprising events. Instead of focusing on the prediction signal, Van de Cruys and colleagues (Van de Cruys et al., 2013, 2014) posit that a hypoprior affects the generation of the prediction error. Specifically, the precision of the prediction error should be inflexibly exaggerated. This means that regardless of the correctness of the prediction, sensory cortex would always feed forward a relatively large error signal. Thus, both proposals predict that individuals with ASD would experience constant sensory surprise. However, the cause of the surprise is thought to be different.

It is not possible to test these two rivalling hypotheses with the present data. Both predict that the BOLD response in surprising and unsurprising contexts should be similar. A promising approach would be to dissociate the sensory prediction from the prediction error. This would require a

paradigm and technique with which the feedforward and feedback signals in the cortex can be distinguished from one another. Techniques with high temporal resolution, such as electro- or magnetoencephalography may be able to achieve this, as they would allow to isolate and compare brain activity directly preceding and following the presentation of a stimulus.

At first glance it may appear that the perceptual expectation paradigm we used showed a different response pattern than earlier experiments on expectation effects on RS (Kovács et al., 2012, 2013; Larsson & Smith, 2012; Summerfield et al., 2008), possibly complicating an interpretation of the current work in the context of these earlier studies. Namely, earlier studies are often described as showing larger RS for expected relative to unexpected repetitions. However, this apparent divergence arises from the way in which data are presented in event-related and blocked designs. In blocked studies, RS is measured in different contexts: in blocks where repetitions are frequent and therefore expected, and blocks where repetitions are infrequent and therefore unexpected. Thus, when determining RS during repetition blocks, one is comparing frequent (expected) repetitions to infrequent (unexpected) alternations. Similarly, in alternation blocks, one is comparing infrequent (unexpected) repetitions to frequent (expected) alternations. When taking this into account, our previous (Utzerath et al., 2017) and current results are in good agreement with earlier studies using a blocked manipulation of expectation.

In sum, our data provide tentative support for the notion that the integration of prior beliefs and sensory evidence may differ between observers with and without ASD in V1. It is unlikely that attentional differences confounded this finding. Yet further work is needed to verify and understand this phenomenon.

4.3. *The role of attention in the present study*

One might wonder to which extent potential differences in attention between groups may play a role in explaining the obtained pattern of results. First, it is conceivable that individuals with ASD might prefer regular (i.e., expected) events, devoting stronger attention to this event type. Of note, it has been found that attending expected stimuli as opposed to not attending them can reverse the activity-suppression by stimulus expectation into an enhancement (Kok et al., 2012a). This might result in larger activity for expected as opposed to unexpected stimuli. Yet at the whole-brain level, we found no group difference in the effect of expectation that would suggest that the ASD group devoted more attention to expected events.

Second, given that attending expected stimuli might reverse expectation suppression into expectation enhancement (Kok et al., 2012a), one might wonder if this experiment had yielded different expectation effects had the stimuli been task-relevant. The hypopriors framework itself is agnostic to the sign of top-down modulations: both enhancing and suppressive top-down modulations should have lessened effects on the sensory response in ASD (Pellicano, 2013; Pellicano & Burr, 2012). Therefore, had the stimuli been made task-relevant, we might expect an inverted effect of attention. Yet relative to the TD group, this effect should still be lessened in the ASD group.

5. Conclusion

We found robustly present and unaltered repetition suppression in LOC of individuals with ASD, suggesting intact sensory adaptation in object-selective visual cortex. By contrast, ASD and TD groups showed a different response to expected versus unexpected stimuli in V1. Thereby, our results provide some preliminary support to the notion that the balance between sensory evidence and prior knowledge may be altered in early visual cortex of ASD. Further work with increased statistical power should verify and shed more light on the precise nature of this alteration.

Declarations of interest

None.

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Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.cortex.2018.08.019.

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