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Internal noise estimates correlate with autistic traits

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Abstract

Previous neuroimaging research has reported increased internal (neural) noise in sensory systems of autistic individuals. However, it is unclear if this difference has behavioural or perceptual consequences, as previous attempts at measuring internal noise in ASD psychophysically have been indirect. Here we use a 'gold standard' psychophysical double-pass paradigm to investigate the relationship between internal noise and autistic traits in the neurotypical population (n=43). We measured internal noise in three tasks (contrast perception, facial expression intensity perception and number summation) to estimate a global internal noise factor using principal components analysis. This global internal noise was positively correlated with autistic traits (r_s=0.32, p=0.035). This suggests that increased internal noise is associated with the ASD phenotype even in subclinical populations. The finding is discussed in relation to the neural and genetic basis of internal noise in ASD.

Keywords: internal noise, neural noise, double-pass, sensory, autism quotient, decision making

1 Introduction

Internal variability (noise) is an inherent property of neural systems and a limiting factor in neural signal transduction. Internal noise results from many sources at several processing scales from molecular and synaptic fluctuations (Faisal, Selen, & Wolpert, 2008; Schneeweis & Schnapf, 1999; Clifford et al., 2007) through to changes in internal states such as attention, arousal and top-down cognitive modulation (Fontanini & Katz, 2011). The collective internal noise resulting from these sources can be observed in electrophysiology and neuroimaging studies as signal variability (see Dinstein, Heeger, & Behrmann, 2015 for review) and behaviourally as varying responses to multiple presentations of a stimulus.

It has been proposed that internal noise is higher in Autism Spectrum Disorders (ASDs). This idea could account for a variety of abnormal sensory experiences associated with the condition (Horder, Wilson, Mendez, & Murphy, 2014; Robertson & Simmons, 2013; Simmons et al., 2009). Consistent with this theory, visual event-related potentials were found to be more variable in ASD individuals (Milne, 2011). Similarly, fMRI BOLD responses in the visual and auditory systems (Dinstein et al., 2012) are also more variable compared to neurotypical controls. Conversely, it has also been argued that internal noise may be unaltered (Butler, Molholm, Andrade & Foxe, 2017) or reduced (Davis & Plaisted-Grant, 2014) in ASD. In support of this latter idea, a study using a luminance increment paradigm targeting the magnocellular pathway found increased discrimination thresholds in individuals with high-functioning autism compared to neurotypical controls (Greenaway, Davis, & Plaisted-Grant, 2013). Greenaway et al. attribute this to stochastic resonance, a process by which low levels of internal noise would yield worse performance on the task, although evidence for this phenomenon is tenuous (Manning & Baker, 2015). Additionally, as Manning & Baker point out, increased discrimination thresholds are indicative of increased rather than decreased internal noise since higher neural variability degrades the neural signal during processing, impairing performance. As this should increase discrimination thresholds, the Greenaway et al study could be interpreted as evidence for increased internal noise in ASD.

Furthermore, mixed evidence for internal noise levels comes from motion coherence studies some of which show increased motion coherence thresholds indicating higher internal noise (Manning, Tibber, Charman, Dakin, & Pellicano, 2015; Milne et al., 2002; Pellicano, Gibson, Maybery, Durkin, & Badcock, 2005); and some show decreased thresholds suggesting lower noise (Manning et al., 2015). However, interpretation of motion studies is complicated by the possibility that participants might use different strategies, such as different sized pooling windows, in order to perform the task, and not all studies take this into account. So far, straightforward evidence for increased internal noise comes from EEG and fMRI research, however, it is unclear if and how increased variability in these measures affects perception and behaviour in ASD. It is therefore important to measure internal noise with a direct psychophysical paradigm.

One consequence of internal noise is that responses to the same stimulus over multiple repetitions will be inconsistent. This can be measured quantitatively using the 'double-pass' method, that was originally developed in auditory psychophysics (Green, 1964) and has subsequently been used to estimate noise in the visual system (Burgess & Colborne, 1988a; Lu & Dosher, 2008), as well as in higher level cognitive tasks (Hasan, Joosten, & Neri, 2012). The double-pass method has mostly been used in contrast perception research using white pixel noise to inject variability (Burgess & Colborne, 1988a). However, white pixel noise confounds adding external noise with increased cross-channel suppression (Baker & Meese, 2012), and so poses limitations on the accuracy of internal noise estimation (Baldwin, Baker, & Hess, 2016) and is not applicable outside of low-level visual properties. An alternative way to render a stimulus 'noisy' (and so able to induce variability into the detecting neural system) is to jitter the intensity of the stimulus along a continuum (Baker & Meese, 2012, 2013), such as contrast, tone, frequency, facial expression intensity, etc.

The double-pass paradigm measures internal noise by repeating noisy stimuli twice (two passes) and calculating the consistency of responses between the passes (Burgess & Colborne, 1988; see *Figure 1*). In a two-alternative forced-choice design two stimulus samples are drawn for each trial from a continuous normal distribution of stimulus intensities (e.g. contrast, tone frequency, etc.). The participant is asked to choose the more intense stimulus every time (first pass). This same procedure is then repeated again (second pass) with the exact same stimuli in each trial, and the consistency of responses across the first and second passes is calculated. The lower the consistency between passes, the higher the internal noise of the participant, because strong internal noise results in more highly variable responses.

Given the complexity and range of symptoms in ASD, the novel method (Baker & Meese, 2012, 2013) of introducing noise into the stimuli paired with the double-pass method can be applied to many perceptual and cognitive tasks in which internal noise may be implicated. To date, very little is known about internal noise throughout the brains of ASD individuals as research has been limited to low level visual properties. It is also not known how internal noise relates to autistic traits in subclinical populations. The current study investigates three tasks in which ASD individuals' performance has been reported to be differential from neurotypical individuals: contrast perception (CP; Bertone, Mottron, Jelenic, & Faubert, 2003, 2005; Greenaway et al., 2013), facial expression intensity (FE; see Harms, Martin, & Wallace, 2010 for review) and mathematical number summation (NS; Iuculano et al., 2015). The study aimed to investigate the relationship between autistic traits as measured with the Autism Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) and internal noise in three neural systems. We hypothesised that if internal noise is a general factor associated with autistic traits, there would be a relationship between AQ and a global estimate of internal noise all three tasks.

2 Methods

2.1. Participants

Forty-five neurotypical participants (aged 18-39, 16 males) with normal or corrected-to-normal vision were recruited for the study. Two of the participants were not included in the analysis because of missing data in one or more of the tasks.

2.2. Materials

Stimuli for all tasks were presented on a gamma corrected Iiyama VisionMaster Pro 510 CRT monitor running at 100Hz, with a mean luminance of 32 cd/m^2. To enable accurate rendering of low contrast stimuli in the CD experiment, we used a ViSaGe device (Cambridge Research Systems Ltd., Kent, UK) running in 14- bit mode. Participants used a computer mouse to make their responses. The AQ questionnaire was delivered and scored automatically by computer.

2.3. Stimuli and paradigm

Examples of the stimuli are displayed in *Figure 1*. Stimuli were presented in pairs in each trial and the participants were asked to pick the more intense stimulus. CD stimuli were horizontal sine-wave gratings with a spatial frequency of 0.5c/deg in cosine phase. Stimuli flickered between 0 and their maximum intensity (on/off flicker) at 7Hz for 429ms (3 cycles). The stimulus intensity for CD was the contrast level of the stimulus. There were two conditions, target present and target absent. In the target absent condition, the stimuli in the two intervals of each trial had random contrast levels drawn from a Gaussian distribution centred around 0% Michelson contrast (defined as $C_{\%}=100*(\frac{L_{max}-L_{min}}{L_{max}+L_{min}})$, where L_{max} and L_{min} are the maximum and minimum luminances of the grating), with a standard deviation of 4%. Negative values reversed the polarity of the grating so that it became dark in the centre. In the

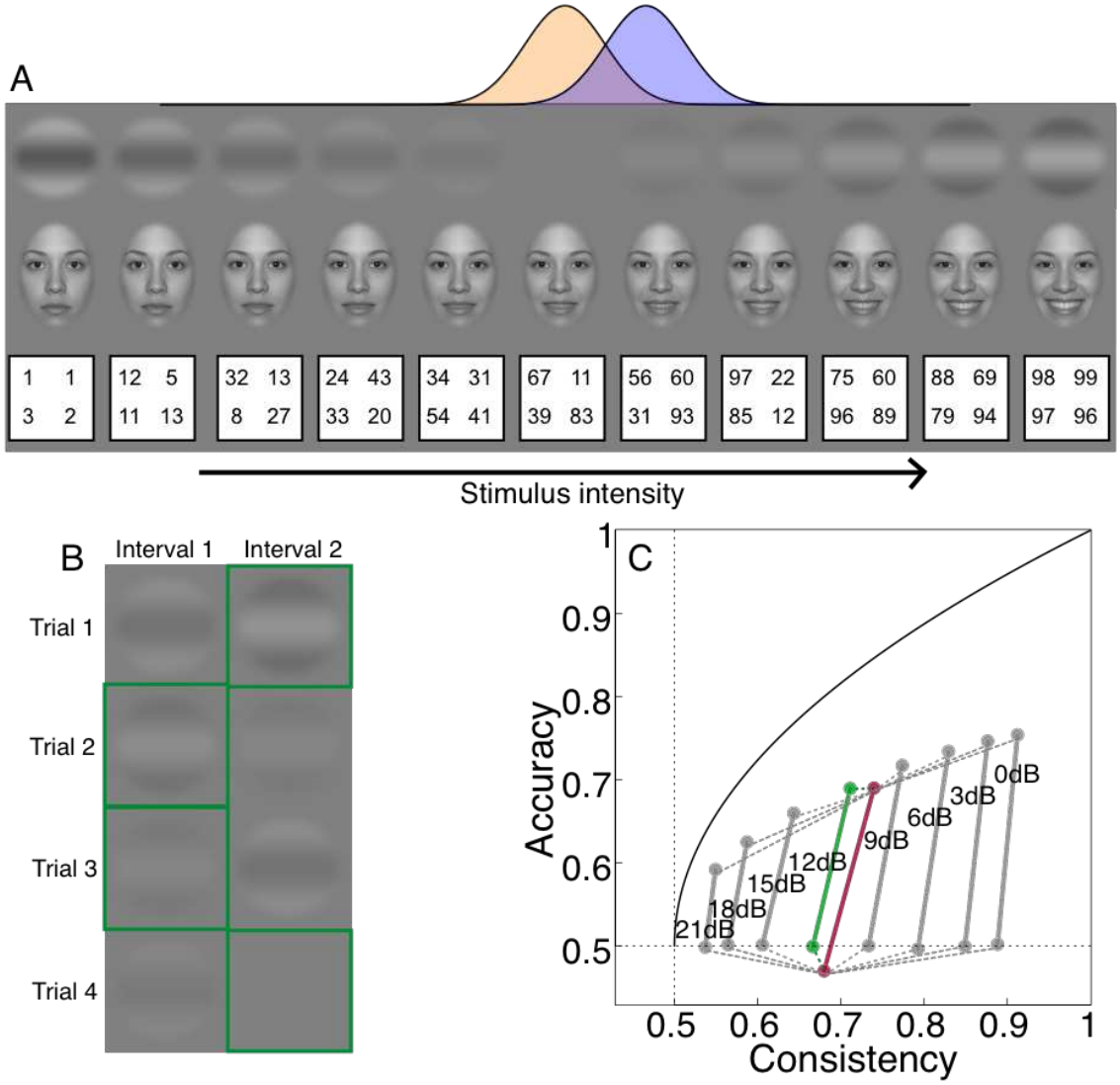

Figure 1. Panel A. Stimuli used for the double-pass 2AFC discrimination tasks: contrast (top row), facial expression intensity (middle row) and number summation (bottom row). In 50% of trials (no target condition) a stimulus was drawn for each of the two intervals from a stimulus intensity distribution (orange) centered around 0% contrast, 50% facial expression morph and 200 sum for the numbers task. In the other 50% of trials (target present condition) one of the intervals was drawn from a higher stimulus intensity distribution (e.g. 4% contrast), shown in purple. Panel B. Examples of the two intervals in four hypothetical trials of the CP task with correct choices indicated by green borders. The same trials are repeated in a double pass experiment, with interval order randomized. Panel C. Estimation of internal noise by model simulations. The red dots and connecting line shows accuracy and consistency scores from an example participant for the two conditions (target present condition at the top). The green and grey dots and solid lines show simulated curves (see text for details) for an example range of internal noise levels (expressed in dB). Errors between participant scores for each condition were calculated (shown as dotted lines) and the internal noise level which produced the smallest error (averaged over conditions) was assigned to the participant (in this case green, 12dB). In the main analysis, we used a finer sampling of internal noise levels (0.1dB steps) than depicted here. The solid black line represents the expected performance in the absence of external noise (Klein & Levi, 2009) and the dashed lines show chance levels.

target present condition, a positive contrast increment of 4% was added to one of the intervals in each trial, so that the distribution in that interval had a mean and standard deviation of 4%.

Similarly to CD, facial expression intensity was drawn from a Gaussian distribution of a continuous morph between a neutral and an expressive face (Figure 1), with a mean of 32% and a standard deviation of 16%. In the target absent condition both intervals within a trial were selected from the same Gaussian distribution whereas in target present an expression increment of 16% was added to one of the intervals (we imposed a floor of 0% so that expressions could not become negative). Six emotional expressions (anger, sadness, happiness, fear, surprise and

disgust) were used and data were collapsed over expressions. The RMS contrast of each expression was equated before morphing, ensuring that all stimuli had equal contrast. Facial stimuli were within-gender averages of from the NIMSTIM face database (Ekman & Friesen, 1971), with 23 male models and 19 female models (Adams, Gray, Garner, & Graf, 2010). Face gender was randomly determined on each trial, but was constant for both intervals of each trial. The faces were windowed by an oval raised cosine envelope, and spanned 10x16 degrees of visual angle. Face stimuli were presented for 100 ms.

In the NS task, two boxes, each containing four double-digit numbers were presented. In the target absent condition the four numbers in each box on each trial were selected from a distribution centred around 50, with a standard deviation of 10 (and an average sum of 200). In the target present condition one of the boxes had a mean of 50 and the other had a mean of 60.

For all tasks, each trial was repeated twice (pass one and pass two), preserving the exact samples of stimulus intensity, once in each half of the experiment.

2.4. Procedure

The method of constant stimuli was used. There were 100 trials in each target condition in each pass (400 trials in total per participant in each experiment). All experiments were carried out in a dark room at 57cm distance from the computer monitor using a chin-rest. Participants had breaks between sessions and the entire experiment took approximately two hours in total per participant.

2.5. Estimating noise from model

Accuracy and consistency scores were used to obtain accurate estimates of internal noise for each participant. In order to obtain a single measure of internal noise that averages out measurement error, double-pass accuracy and consistency scores were simulated for different levels of internal noise using a noisy linear model. We then determined the level of internal noise that best described the data for each observer. Simulated responses to the target and the null intervals within a trial were given by:

$$resp_{target} = \sigma_{int} + \sigma_{ext} + C_{mean} + C_{target}$$

$$resp_{null} = \sigma_{int} + \sigma_{ext} + C_{mean}$$

where $resp_{target}$ and $resp_{null}$ are the responses in the target and null intervals respectively, σ_{int} and σ_{ext} represent internal and external noise, C_{mean} is the mean intensity of the stimulus and C_{target} is the target intensity added in the target interval. The noise variables (σ_{int} and σ_{ext}) were drawn on each simulated trial from Gaussian distributions with a mean of zero, and the appropriate standard deviation for each experiment. The interval with the larger response was selected. This was repeated twice with identical values of σ_{ext}, but different values of σ_{int}, in order to simulate both accuracy and consistency scores. There were 100000 simulated trials for each internal noise level and this was done for 801 noise levels (ranging from -40dB to 40dB in steps of 0.1dB). The errors between the model simulations and empirical data points in each condition (in the accuracy-consistency space) were calculated for each participant. The internal noise level that produced the smallest absolute error (averaged over conditions) was then assigned to that participant. This was repeated for each of the three experiments.

3 Results

Mean accuracy in the target present condition was 0.67 (SD=0.06) for CP, 0.67 (SD=0.05) for FE and 0.68 (SD=0.06) for NS, indicating participants were performing above chance. The consistency scores were also above chance for CP (mean=0.81, SD=0.10), FE (mean=0.70, SD=0.08) and NS (mean=0.69, SD=0.06) tasks. We used these values along with the modelling approach described above to derive an estimate of internal noise for each participant in each experiment. The noise estimates from the CP and FE tasks were not normally distributed when tested with the Shapiro-Wilk test of normality (p<0.001 and p=0.009 respectively) therefore two-tailed Spearman signed rank correlations were used throughout the analysis.

Internal noise was significantly correlated with AQ in the CP (r_S=0.34, p=0.028) and NS (R=0.31, p=0.042) but not the FE task (r_S=0.26, p=0.091). There were strong significant positive correlations between noise estimates across all three tasks (r_S≥0.60, see *Figure 2* for r_S and p values). Since this suggested the presence of a single underlying factor, we performed principal component analysis (PCA) on the model estimates of internal noise. PCA is a dimension-reduction technique that attempts to condense a multivariate dataset of correlated variables into a smaller number of uncorrelated factors. Internal noise estimates from the CP, FE and NS tasks loaded onto a single factor, 'global internal noise', which was extracted by Keiser's criterion (eigenvalue of 2.30) explaining 76.81% of the variance. Factor loadings were extracted for participants and the inverse values were taken as a global measure of noise (such that small values indicate low noise).

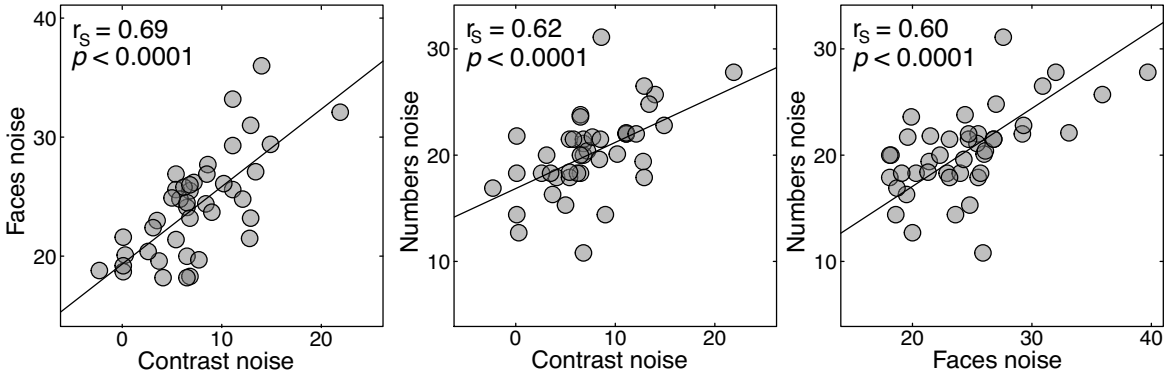

Figure 2. Scatterplots showing correlations between the estimated noise levels in all three tasks, expressed in logarithmic (dB) units. Black lines represent best-fit Deming regression lines.

The global internal noise factor was positively correlated with AQ scores (r_S=0.32 p=0.035) suggesting that higher internal noise is related to higher levels of autistic traits. As raw double-pass consistency scores are sometimes used as a measure of internal noise (low consistency means high internal noise), the PCA was repeated on mean consistency scores (averaged over the two target conditions). The internal noise factor extracted in this way explained 77.13% of variance and was also significantly correlated with AQ (r_S=0.33, p=0.032). This suggests higher levels of autistic traits are related to higher internal noise (see *Figure 3*). However, as the accuracy scores in the NS task were significantly correlated with AQ (R=-0.43, p=0.004), the modelled estimates of internal noise which take into account both the accuracy and consistency are preferred. AQ was not significantly correlated with accuracy in CP (R=-0.14, p=0.384) or in FC (R=-0.14, p=0.364).

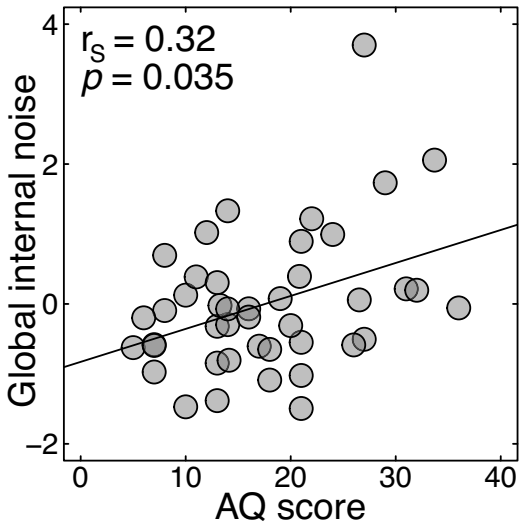

Figure 3. Scatterplot showing the significant positive correlation between AQ scores and internal noise. The black line represents a Deming regression line.

4 Discussion

The current study reports the first direct psychophysical estimate of internal noise in relation to autistic traits. Using the double-pass method in three different tasks we found a positive relationship between autistic traits in the neurotypical population and overall levels of internal noise. Individual differences in internal noise in the CP, FE and NS tasks were largely accounted for (76.81% of the variance) by a single internal noise factor suggesting a common noise source. This factor was positively correlated with autism spectrum quotient (AQ) scores. We suggest that this factor is either global internal noise affecting perception and behaviour regardless of task complexity or neural mechanism involved, or it is late decision making noise.

4.1. Neural basis of internal noise in ASD

The current finding of increased internal noise being associated with more autistic traits supports previous electrophysiological and neuroimaging studies that found more variable responses to sensory stimuli in clinical ASD populations (Dinstein et al., 2010, 2012; Milne, 2011). Increased internal noise can also manifest as decreased coherence in natural neural oscillations such as γ-band activity. Rojas, Maharajh, Teale, & Rogers (2008) found reduced phase-locking in γ-band oscillations, indicative of increased neural noise, in adults with ASD and also in neurotypical parents of ASD children compared to controls. Increased neural variability in neurotypical first-order relatives of ASD individuals suggests a genetic influence of an ASD genotype on the level of internal noise in the brain. This is not surprising as ASD has a complex but strong genetic basis (see Miles, 2011 for review) which may, at least in part, be mediated by neural noise factors. The finding of

the present study, as well as Rojas et al (2008), suggest that internal noise is intrinsic to the ASD phenotype and extends beyond clinical ASD populations. As others have proposed, noisier sensory processing throughout development could plausibly lead to several of the social difficulties (i.e. facial expression perception) typically associated with ASD (Simmons et al, 2009).

4.2. Early versus late noise

It is unclear from the current study whether the internal noise we measured affects the neural signal early or late in processing. Noise in early sensory regions will be passed forward to decision making processes and so produce variable responses. As we find that internal noise is common across our three tasks, this type of noise would need to span multiple regions of the brain to account for our data. Autistic traits may be related to early sensory noise as previous research suggests increased neural variability in several sensory regions of the brain (Dinstein et al., 2012). Alternatively, the internal noise we measured may be a late decision-making noise that influences behaviour at the level of executive processing. This possibility is consistent with research showing poorer executive function (Hughes, Russell, & Robbins, 1994; Kenworthy, Black, Harrison, della Rosa, & Wallace, 2009) and abnormal connectivity of white matter in frontal lobes (Sundaram et al., 2008) in clinical ASD populations. In either case, internal noise may pose a limitation on brain function for individuals high on the autistic spectrum.

4.3. Innovation in noise measurement

This study benefits from a novel implementation of the double-pass paradigm for measuring internal noise. The application of intensity jitter rather than traditional white pixel noise (as often used in contrast detection experiments; Burgess & Colborne, 1988) extends the viability of double-pass methods to other sensory and cognitive modalities. We have also developed accurate model-based estimates of internal noise that take into account any sensitivity differences between individuals. Previous studies (Burgess & Colborne, 1988) used raw consistency scores as a measure of internal noise. However, we observed a high correlation between accuracy and consistency scores in our data ($r_S \geq 0.41$, $p \leq 0.006$). This is not surprising since it follows that higher performance on a task would yield more consistent responses (in the limiting case of perfect performance, consistency is necessarily 100%). The modelled estimates of noise take into account both accuracy and consistency scores and so are not biased by individual differences in sensitivity.

The current methodology measures noise more directly than previous psychophysical studies (Greenaway et al., 2013; Manning et al., 2015). The equivalent noise approach used in other work (Manning et al., 2015; Manning, Charman, & Pellicano, 2013; Milne et al., 2002; Pellicano et al., 2005), relies on a specific (usually linear) model of the underlying mechanism that may not accurately reflect how stimuli are processed, and cannot disambiguate differences in noise from differences in sensitivity (see Baldwin, Baker & Hess, 2016). Double-pass techniques avoid these problems, and additionally have high internal reliability and produce internal noise estimates consistent with those from another psychophysical paradigm (Vilidaite & Baker, 2017). As this study investigated the relationship between internal noise and autistic traits in neurotypical individuals, it would be of great interest to use the double-pass method to measure internal noise in clinical ASD. Considering current findings and previous studies we would expect higher internal noise in ASD individuals when compared to controls.

4.4. Summary and conclusions

Neurotypical individuals exhibiting higher levels of autistic traits had higher internal noise, measured using three psychophysical tasks. This finding supports previous studies that found higher internal noise in ASD populations using neuroimaging methods. Increased internal noise seems to be a fundamental feature associated with ASD in clinical and subclinical populations, and may explain some of the symptoms and traits of ASD (Simmons et al., 2009). We suggest that a genetic link between the autistic phenotype and internal noise could account for the current findings.

5 Ethics, consent and permissions

The study was approved by the University of York Ethics Committee and informed consent was obtained from all participants.

6 Acknowledgements

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7 Competing Interests

There were no competing interests.

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9 Lay abstract

Previous research has shown that autistic individuals show more variable brain responses (measured with electroencephalography and magnetic resonance imaging) than neurotypical individuals. Such increased variability (or internal noise) means that when an individual is presented with an identical stimulus or task multiple times, their responses (or choices) vary more between presentations than a neurotypical participant's. Recent theories suggest that internal noise may impact on sensory symptoms in autism and can account for inconsistent findings in previous literature in autism research. In this study we used three simple tasks (visual contrast; facial expression; and number summation) to measure internal noise in the brain from choice variability in 43 neurotypical individuals. The participants also completed the Autism Quotient questionnaire to measure their levels of autistic traits. We found a positive correlation between the internal noise, measured behaviourally, and number of autistic traits reported. This is in accordance with previous neuroimaging studies in autistic individuals and suggests that the autistic phenotype has observable impact on the brain even in non-clinical populations. Our measure of internal noise can also be applied to other task performance in autistic and other clinical populations.