Atypical visual evoked potentials in children with autism generated by both low and high spatial frequency gratings.

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Introduction

'Atypical visual perception' is a term which is increasingly being used to describe the observation that people with autistic spectrum disorders (ASD) perceive the world differently to typical observers. Researchers are only recently beginning to consider that due to deficits arising early in the visual processing stream, e.g. in the retino-thalamo-cortico pathway, the quality of visual inputs to the autistic brain may be compromised and that this may have significant knock-on effects for later perception, cognition and behaviour.

It is notoriously difficult to design visual tasks which can adequately target specific neuronal networks. At best the behavioural and psychophysical data presented to date provide an indirect measure of neuronal activity (Milne et al. 2002). In addition, traditional psychophysical and behavioural techniques to measure vision often involve presenting stimuli to threshold levels of detection in order to ascertain the sensitivity of particular parts of the visual system. The design of such tasks invariably involves the presentation of many trials in a repetitive format. Although researchers attempt to account for the effects of boredom and reduced motivation on performance, some researchers have suggested, and even modelled, that threshold data can be artificially obscured by reduced motivation and attention (McAnally, Stuart, & Castles, 2001; Roach, Edwards, & Hogben, 2004).

This is especially pertinent when testing children and clinical populations. Relying on behavioural data to infer psychophysical thresholds could therefore exaggerate the perceptual deficiencies in children with ASD. In contrast, the technique of EEG is comparatively freer of these concerns as the dependent variables of interest, amplitude and latency of evoked scalp potential, are outside of behavioural control. Scalp potentials can be measured without requiring the child to engage in demanding cognitive tasks so EEG data is not influenced by cognitive and motivational factors which can often present as confounding variables in behavioural measures of visual perception.

The aim of this study was to use simple visual stimuli to investigate whether children with ASD generate identifiable differences in their visual evoked potentials. Given the characteristic components detectable within the VEP this technique can be used to investigate whether specific components are atypical in children with autism. Based on the existing literature we predict that the VEP waveform will be different in children who have ASD compared to controls. However, depending on the nature of the abnormality we will be able to ascertain the level of abnormality. For example disruption of C1 will suggest early level abnormality, e.g. at V1 whereas disruption of P1 will suggest later abnormality, e.g. at extra striate areas. If differences are found, this will suggest abnormalities in the early stages of visual perception, however if there are no differences between the visual evoked potentials of children with autism and controls, this will suggest that early neuronal architecture is intact in ASD, and that another explanation must be found for experimental demonstrations of atypical perception in ASD. Using a range of spatial frequencies also allows us to test the prediction that low frequencies will be specifically atypical in autism and that high spatial frequencies may be intact.

Therefore we measured visual potentials in children with autism and typically developing controls evoked by simple sinusoidal gratings presented at 0.5cycle/°, 1 cycle/°, 4 cycle/° and 8 cycle/°.

Method

Participants

40 participants took part in this study; 20 children with autistic spectrum disorder (9 with a diagnosis of classic autism, 8 with a diagnosis of Asperger's syndrome and 3 with a diagnosis of autistic spectrum disorder) and 20 typically developing controls. 3 children with ASD had comorbid diagnoses; 2 had ADHD and 1 had Tourette's Syndrome. In addition, one child from the ASD sample was identified by clinicians as having 'slow motor skills'. The children with ASD were recruited via a local computer club for children with autism or via a local clinic where ASD diagnoses for the region takes place. All children who formed the experimental group had received a formal diagnosis of autism spectrum disorder from the child development team (which consists of a clinical psychologist, speech therapist and paediatrician) within this clinic. These formal assessments were based on standardise criteria using the DISCO (Wing, Leekam, Libby, Gould, & Larcombe, 2002). The typically developing

children were recruited from an e-mail list of volunteers. The parents or guardians of the children involved provided written informed consent prior to the start of the study. Two typically developing controls who were older than 16 provided their own informed consent. Each testing session lasted between 1 and 2 hours and participants were given a £10 book token as a gesture of thanks for their participation.

Psychometric data

In addition to the EEG data, standardised psychometric data was collected. IQ was measured using the Wechsler Abbreviated Scales of Intelligence (Wechsler, 1999) which provides an index of verbal, performance and full scale IQ. Visual contrast sensitivity was measured using the CSV-1000 (VectorVision, 1991). This is a standardised test which measures contrast sensitivity at 3, 6, 12 & 18 cycle/°. The mean age, IQ and contrast sensitivity of the control and experimental groups is presented in table 1. In addition, the CARS behavioural observational schedule (Schopler, Reichler, & Renner, 1988) was used to measure autistic symptomatology during the testing session and parents were asked to complete the Social Communication Questionnaire (Berument, Rutter, Lord, Pickles, & Bailey, 1999) which is a 39 item questionnaire to assess autistic behaviour.

Electroencephalogram Recording

Stimuli and Apparatus

Sinusoidally modulated gratings were created using MATLAB® and the psychophysics toolbox (Brainard, 1997; Pelli, 1997). Images were presented on a 17 inch monitor, with a refresh rate of 75Hz. Stimuli were centrally presented on the grey background of the monitor which had an average luminance of 12.9 cd/m2. The space-average luminance of each grating was 16.3cd/m2, and the Michelson contrast (defined by L_max – L_min / L_max + L-Min) was 68%. At a viewing distance of 114cm, the gratings were presented at 0.5cycle/°, 1 cycle/°, 4 cycle/° and 8 cycle/°, and subtended 6.78° x 6.78°. An additional stimulus, a high-contrast grey-scaled image of a zebra was presented. This stimulus served as an attentional cue for the participants as they were instructed to press a button response every time they saw the zebra. The images used in the study are illustrated in figure 1.

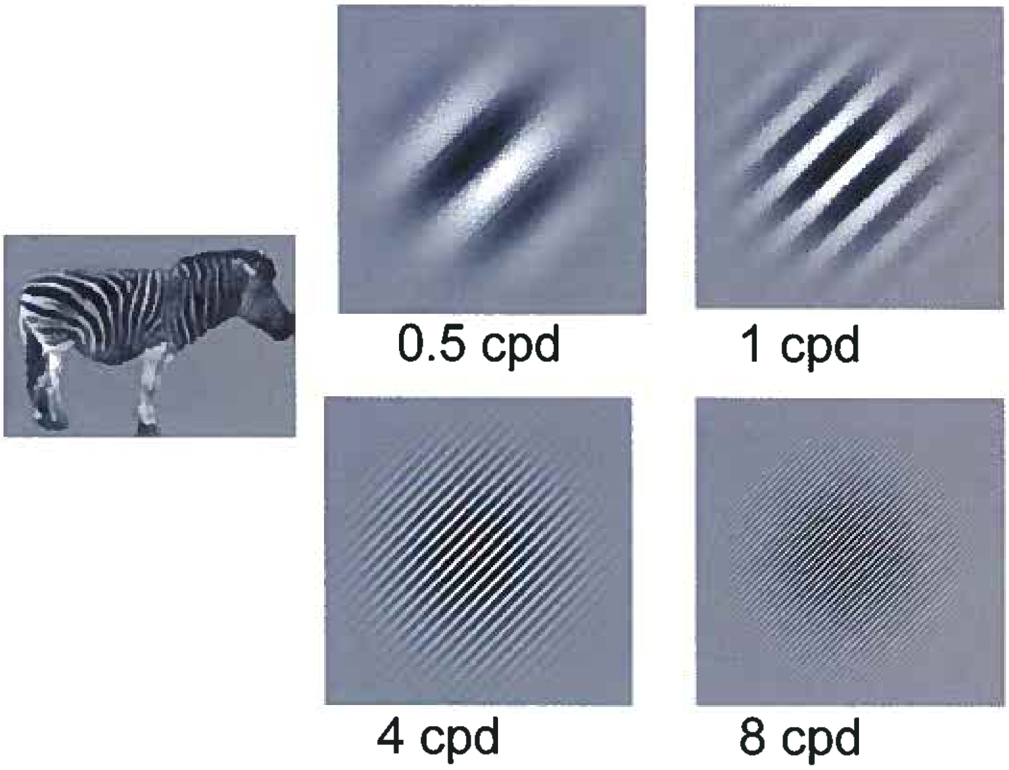


Figure 1 The stimuli presented in the experiment. For printing the images are to scale but not an accurate representation of spatial frequency.

Procedure

Prior to electroencephalogram recording each participant underwent a training session (of 36 trials) in which they were instructed to press a button on a response pad when they saw a zebra on the screen. The task was presented as a game of "find the real zebra" and participants were instructed to press the keypad as quickly as possible after they saw the zebra, but not to press when the zebra did not appear. This practice session was intended to ensure that each participant was familiar with the behavioural aspect of the task, no ERP data was collected.

Following the practice session, the electrode net was applied to the head of each participant. Each of the four grating stimuli were shown 72 times, and the zebra stimuli was shown 36 times, giving a total of 324 stimulus presentations. The order of stimulus presentation was randomised. Each stimulus remained on screen for 38 refresh cycles (507 msec), with an additional variable inter-stimulus interval of either 23 (307 msec), 38 (500 msec) or 53 (700 msec) refresh cycles. A white fixation cross measuring 0.2° by 0.2° remained in the centre of the screen for the duration of the task.

EEG recording

The electroencephalogram (EEG) was continuously recorded using a high-density array of 128 Ag /AgCl electrodes (Electrical Geodesics Inc, Tucker, 1993). The signal was amplified (x1000) and filtered on line with a band-pass of 0.01 – 80Hz. It was digitised online with a sampling rate of 1000Hz. Impedance was kept below 50 KΩ. Electrooculogram (EOG) was recorded from electrodes located at the outer canthi and above and below the left and right eyes. Data were referenced to the vertex electrode.

ERP data reduction

Following the EEG recording, the signal was segmented into epochs based on the 5 different types of stimuli presented (grating of 0.5, 1, 4, or 8 cycle/° or the zebra). Each epoch encompassed 607 msec which included 100 msec pre-stimulus baseline. Any trials containing blink artefacts, defined as signal greater than 300 μV, were deleted. ERPs from each participant were averaged as a function of spatial frequency of grating and then corrected to the 100 msec pre-stimulus baseline. All signals were digitally filtered with a band pass filter of 0.1Hz to 40 Hz.

ERP data extraction

Spatial frequency gratings.

As C1 and P1 deflections are known to have different neuronal generators, they were detected from different electrodes. C1 occurs over posterior midline sites so was analysed by averaging the signal from channels 76 and 82 which corresponds to Oz according to the 10-20 system. P1 occurs over anterior occipital regions so was extracted from channels 65 & 66 which correspond to O1 and 70 & 71 which correspond to O2.

Results

Data attrition

The number of segments marked bad for each condition for participant was recorded. Data from two children with autism (and with co-morbid diagnoses of ADHD) and from two typically developing children were discarded on the basis of too few artefact free trials. Data are reported for the remaining group of children with ASD ($N = 18$) and typically developing children ($N = 18$). After removing these children from further analysis no significant differences between the groups in terms of chronological age, full scale IQ, performance IQ or verbal IQ were present.

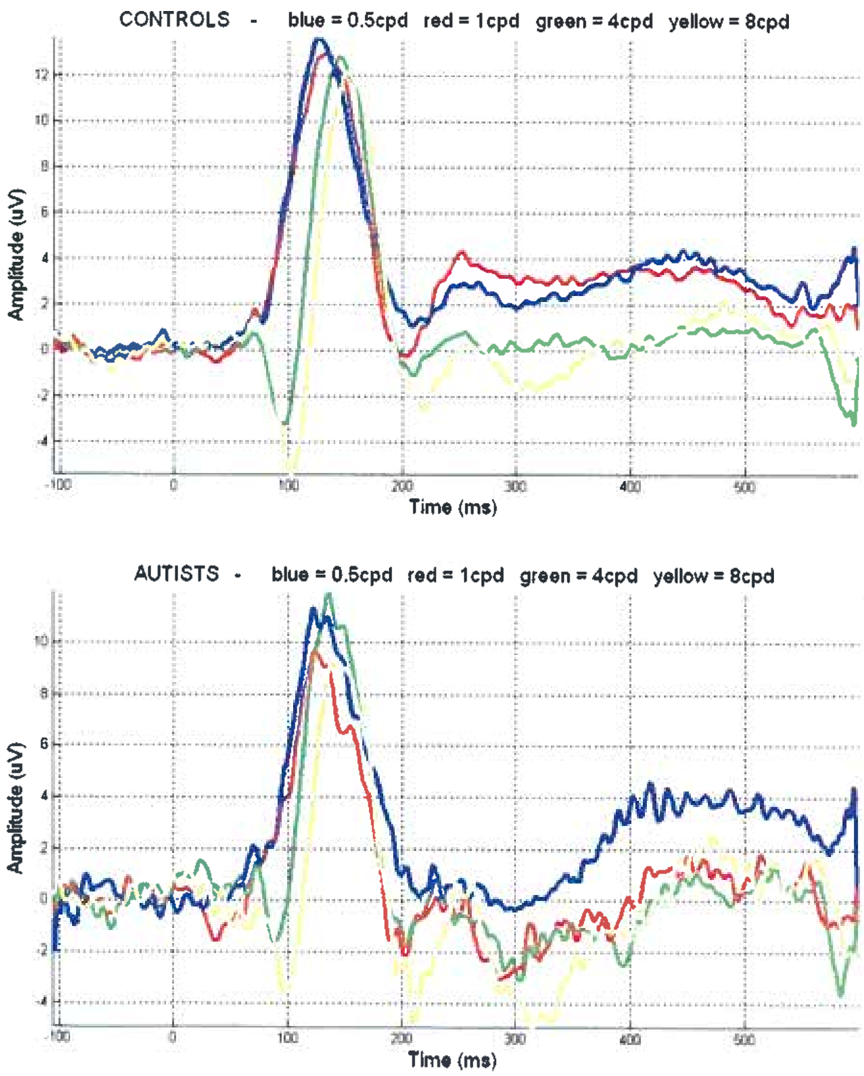
Behavioural Data

There were no significant group differences for any of the behavioural variables. The mean number of targets (zebras) detected by the control and ASD groups was 32.6 and 33.1 respectively ($F<1$, $p > .1$). The number of commission errors made by each group was .9 and 1.8 respectively ($F = 2.2$, $p > .1$) and the mean response time was 410 ms and 403.8 ms respectively ($F<1$, $p > .1$).

Electrophysiological data

Visual inspection of the data revealed an expected pattern of results in the typically developing children. C1 peaked at around 100 ms and was measurable only in response to the higher spatial frequencies (4 & 8 cycle/°). P1 peaked at around 130 ms and was visible in response to all the spatial frequencies. In order to extract variables of interest, the peak of C1 was defined as the minimum amplitude that occurred within a time window of 70 – 120 msec after stimulus onset. P1 was defined as the maximum amplitude that occurred within a time window of 100 – 170 msec after stimulus onset. Visual inspection of the data from each participant confirmed that these time windows allowed for detection of the peak deflection of both components. To investigate if group differences in the morphology of the waveform were present (see figure 2), several analyses were carried out. Initially we measured the amplitude and the latency of the peak of the waveform within circumscribed time windows at Oz for C1 and O1 & O2 for P1. The latency and amplitude values extracted for each participant were then entered into repeated measures ANOVA. As the low spatial frequencies did not elicit a C1 component in either group, only signals elicited by 4 or 8 cycle/° were analysed for this component. Values for C1 were entered into a 2 (group) x 2 (spatial frequency) ANOVA. Values for P1 were entered into a 2 (group) x 2 (hemisphere) x 4 (spatial frequency) ANOVA. We then measured the amplitude and the latency of the peak waveform at the site where the signal was largest amongst all occipital electrodes, and repeated the analyses as above. Finally we also measured C1 by calculating the area under the curve rather than the peak amplitude of the deflection. This was because peak measurements can be significantly distorted by the averaging process, specifically, peaks can appear reduced if the individual trials are subject to variation in latency. These data were entered into a 2 (group) x 2 (spatial frequency) ANOVA.

Figure 2: Control and Austistic group – Grand averages across participants



Components at Oz

C1

Analysis of C1 amplitude revealed a main effect of spatial frequency; $F(1,34) = 21$, $p < .001$, partial $\eta^2 = .40$, which reflected the fact that the negative deflection elicited by 8 cycle/° was greater than the negative deflection elicited by 4 cycle/°. There was a marginally significant effect of group; $F(1, 34) = 3$, $p = .089$, $\eta^2 = .08$, the amplitude of the deflection was greater in the typically developing children than the children with ASD. This was the case for the deflection elicited by 8 cycle/°; $F(1, 34) = 4.1$, $p = .05$, $\eta^2 = .11$, but not for the deflection elicited by 4 cycle/° $F(1, 34) = 1.0$, $p > .1$, $\eta^2 = .03$. Analysis of C1 latency revealed a main effect of group; $F(1,34) = 5.1$, $p < .05$, $\eta^2 = .13$, reflecting the fact that the latency to peak was faster in the children with ASD than the typically developing children. No other main effects or interactions were significant.

P1

Analysis of P1 amplitude revealed a main effect of hemisphere; $F(1, 34) = 18.1$, $p < .001$, $\eta^2 = .35$, which reflected the fact that the amplitude of the deflections in the right hemisphere were larger than the amplitude of deflections in the right hemisphere. No other main effects or interactions were significant. Analysis of P1 latency revealed a main effect of spatial frequency; $F(3, 102) = 27.6$, $\eta^2 = .45$ which reflected the fact that as spatial frequency increased, the peak to latency increased. There was also a main effect of group; $F(1, 34) = 19.9$, $p < .001$, $\eta^2 = .37$, which reflected the fact that latency to peak was faster in the group with ASD than the control group. No other main effects or interactions were significant.

These analyses suggests that, although the amplitude of the P1 component of the VEP did not differ in children with ASD compared to controls, the amplitude of the C1 component is reduced. However, it is possible that the C1 deflection occurs over a different part of the scalp in children with ASD. Therefore, we inspected each participant's data individually and identified the channel, within the occipital region (electrodes 64 - 96) which showed the largest deflection in response to each spatial frequency. For deflections elicited by gratings of 8cycle/° 16 children within the control group had maximum peak deflections within the central occipital region, 1 had maximum peak deflections in electrodes on the right and the other had maximum peak deflections on the left, and within the ASD group 10 had maximum deflection in the central area, 5 had maximum deflection on the left and 3 had maximum deflection on the right. For deflection elicited by gratings of 4 cycle/° 12 children from the control group had maximum deflections from electrodes within the central occipital region, 3 had maximum deflection on the right and 3 had maximum deflection on the left. Within the ASD group, 7 had maximum deflection in the central occipital region, 6 had maximum deflection on the left and 5 had maximum deflection on the right. To establish whether the children with ASD showed reduced amplitude of C1 elicited by gratings of 8cycle/° even when the value is measured from the electrode which shows the largest peak, the peak amplitude and latency to peak at the maximum electrode was extracted and entered into repeated measures ANOVA. Given that only one location was sampled P1 was no analysed with a 2 (group) x 4 (spatial frequency) ANOVA. The pattern of results remained the same as when values were measured from Oz.

Summary and Conclusion

The latency of both the C1 and the P1 evoked by a range of spatial frequencies is reduced in children with ASD. The magnitude of the C1 evoked by high spatial frequency is reduced in ASD. The finding reported here reflects the fact that 61.2% of the participants with autism did not have a negative component in their waveforms. This lack of C1 in some participants does not appear to correlate with age, IQ, severity of symptoms (as measured by the ASQ & CARS) or behavioural performance. It is now crucial to determine if such impairment influences the development of social cognitive functions such as face processing. Faces represent a crucial category of stimulus input providing an early channel of communication prior to the onset of linguistic communication between infant and carer. Impairment or abnormalities in the visual system may affect the way faces are processed or remembered and may interfere with a the development of a normal social life.

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