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Neural correlates of texture and contour integration in children with autism spectrum disorders

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ABSTRACT

In this study, we have used an electrophysiological paradigm to investigate the neural correlates of the visual integration of local signals across space to generate global percepts in a group of low functioning autistic kids. We have analyzed the amplitude of key harmonics of the Visual Evoked Potentials (VEPs) recorded while participants observed orientation-based texture and contour stimuli, forming coherent global patterns, alternating with visual patterns in which the same number of local elements were randomly oriented in order to lose any globally organized feature. Comparing the results of the clinical sample with those obtained in an age-matched control group, we have observed that in the texture conditions the 1st and 3rd harmonics, containing signature of global form processing (Norcia, Pei, Bonneh, Hou, Sampath, & Pettet, 2005), were present in the control group, while in the experimental group only the 1st harmonic was present. In the Contour condition the 1st harmonic was not present for both groups while the 3rd harmonic was significantly present in the control group but absent in the group with autism. Moreover, the amount of organization required to elicit significant 1st harmonic response in the texture condition was higher in the clinical group. The present results bring additional support to the idea that texture and contour processing are supported by independent mechanisms in normal vision. Autistic vision would thus be characterized by a preserved, perhaps weaker texture mechanism, possibly mediated by feedback interactions between visual areas, and by a disfunction of the mechanism supporting contour processing, possibly mediated by long-range intra-cortical connections. Within this framework, the residual ability to detect contours shown in psychophysical studies could be due to the contribution of the texture mechanism to contour processing.

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1. Introduction

Autism Spectrum Disorder (ASD) is a developmental and behavioral condition affecting several behavioral and cognitive areas. Historically, ASD has been attributed to social and communicative impairments (Baron-Cohen, Leslie, & Frith, 1985; Bowler, 1992) or to high-level cognitive impairments (Leekam & Perner, 1991; Ozonoff, Pennington, & Rogers, 1991). Some of these skills are diagnosed as abnormal based on symptoms involving eye gaze or the ability to interpret facial expressions. Recently it has been considered that at least some of these high-level deficits could be explained in terms of lower level sensorial and perceptual abnormalities (Behrmann, Thomas, & Humphreys, 2006). Both eco-

logical observations and systematic studies of subjects with autism have found abnormalities of perceptual abilities, giving raise to general theories such as the Weak Central Coherence theory (Frith, 1989; Happe, 1994, 1999) and the Enhanced Perceptual Function theory (Mottron, Dawson, Soulières, Hubert, & Burack, 2006). In particular, three classes of perceptual abilities seem to exhibit atypical functioning in ASD: an inability to build up global forms based on the linking of local information, superior abilities of segregating local information in background noise and an impairment in visual motion, especially that of complex patterns (Dakin & Frith, 2005). The present study is a direct investigation of the neural correlates of the first two classes of visual phenomena, therefore the remainder of the introduction will focus on mechanisms allowing integration of local stimuli into global patterns and shapes and on the possibility that these middle vision mechanism were biased in observers with ASD.

Subjects with autism show improved performance in the Embedded Figure Test (Shah & Frith, 1993), as well as in

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reproducing block designs (Happé & Frith, 1996). It has also been shown a positive correlation between the impairment in face discrimination and more general perceptual global/local tasks with compound letters or more neutral geometric figures (Behrmann et al., 2006). Moreover, ASD observers seem to be resistant to context-based visual illusions such as the Poggendorf Illusion (Happé, 1996), even though Asperger patients do not exhibit the same pattern, being biased to illusions like normal observers (Ropar & Mitchell, 1999). In some visual search tasks ASD subjects show pop-out behavior for search targets defined by conjunctions of visual features, that typically yield significant set size effects in normal observers. Moreover, in a companion paper we show that high-functioning subjects show abnormal (i.e. superior) visual crowding responses (Baldassi et al., 2009). These results suggest a reduced effect of context in autistic 'middle-vision', i.e. the ability to isolate local elements without being 'distracted' by neighboring objects. While many of the tests directly probing the 'local bias' in autism show consistent results, the complimentary set of tests that were devised to probe the ability of structuring global patterns made out of a coherent arrangement of local elements are less consistent. In the classical Navon task, where a large letter is composed of many small, competing letters, the ability of autistic observers to attend to a target present only at the large scale was lower than in normals when attention was equally divided across the two spatial scales (Plaisted, Sweetenham, & Rees, 1999), although performance remains normal-like in different version of global–local tasks (e.g., Rondan & Deruelle, 2007). All these results, taken together suggest the possibility of a certain degree of inability to process global visual forms. However, a recent, comprehensive account of perceptual phenomena in ASD (Dakin & Frith, 2005) has concluded that the deficit of global form processing in autism is far from being understood, especially due to a lack of

studies using narrow-band stimuli (in the spatial frequency domain) to control for possible low-frequency cues supporting the identification of global structures. A few recent studies have used quantitative, psychophysical techniques in tasks requiring the observers to link several oriented lines arranged to form a coherent contour embedded in a background of randomly oriented lines. These studies have found that the psychophysical performance of observers with autism does not differ significantly from that of normal observer (Blake, Turner, Smoski, Pozdol, & Stone, 2003; Del Viva, Igliozzi, Tancredi, & Brizzolara, 2006; Kemner, Lamme, Kovacs, & van Engeland, 2007). One of these (Del Viva et al., 2006) has controlled the spatial frequency spectrum by building contours with appropriately arranged Gabor stimuli, local stimuli widely used in vision science for being limited both in space and in spatial frequency content. Even though the possibility of detecting similar 'dashed' contours (see Fig. 1 below for an example) based on low-frequency cues was widely reduced, the authors have found that the psychophysical performance of children with autism did not differ significantly from that of normal control observers. Essentially the same result was obtained using a card-based version of the same task (Kemner et al., 2007). Although they represented a significant advancement relative to the previous studies on global visual integration in autism, the use of psychophysical techniques in these studies have an intrinsic limit of implying cooperative observers involved in tasks based on precise instructions, hence being unsuited for low functioning ASD observers.

Visual Evoked Potentials offer an alternative method for assessing visual function in autism that places minimal demands on the observer. Kemner et al. (2007), in addition to behavioral testing of contour integration also studied another mid-level function, texture segmentation. They recorded VEPs that are specific to the segmentation of a region based on a combination of cues arising from

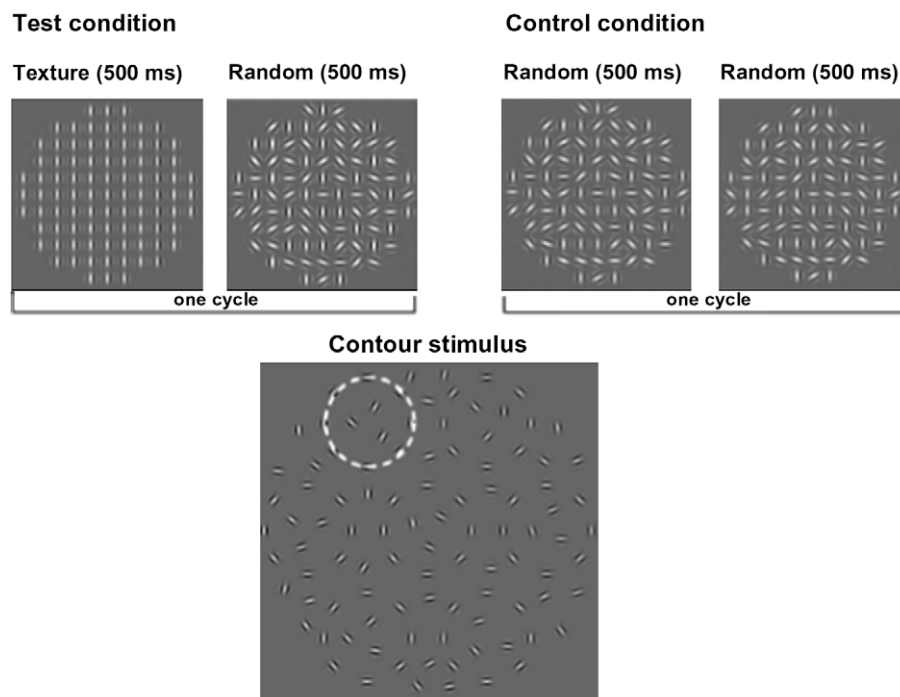


Fig. 1. Examples of the stimuli and of the experimental conditions. The test condition (*top left*) consisted in a periodic alternation of a texture display, whose local elements where coherently oriented, and a random display, identical to the texture except for the orientation of the local elements, each one being now independently tilted by a random amount. In the random condition (*top right*), two random configurations alternated at each cycle. The contour experiment had a temporal layout identical to the texture experiment except for the nature of the global configuration. In this case, a proportion of the local elements were arranged so that they formed seven circles each one made of eight Gabor elements (*bottom*). The average inter-element distance was the same in the texture and the contour stimulus to avoid possible density artifacts in comparing the results of the two conditions. Note that the layout of the figure was chosen to maximize comprehension of the different stimuli, thus the exact match between contours and textures is not preserved here only for graphical reasons.

local orientation discontinuities and orientation differences across regions. They found that their autistic group had normal peak latencies. From their results, they concluded that both horizontal connectivity within V1 as well as the feedback circuits feeding from higher cortical visual areas were preserved in ASD observers.

Two main types of stimuli are widely used to probe the middle vision processes: textures and contours (see Fig. 1 for an example). They have complementary roles in the visual integration process, in that they support the detection of contours and surfaces, respectively. More specifically, textures define surfaces as they are composed of shared image statistics across two spatial dimensions of an image; orientation-defined contours instead rely specifically on collinearity of local elements, along their axis of orientation, and may correspond to the outline of a visual shape. Both texture and contour are fundamental processes for figure-ground segmentation. The neuronal and computational processing mechanisms underlying these particular stimuli have been extensively investigated as they probe the fundamental intermediate step of vision lying between the low-level fragmentation occurring in the primary stages and the complete perceptual experience of shape and object recognition. Binding local elements into global patterns is plausibly based on the co-operative activity of networks of neurons representing the local elements and whose activity is modulated and partly dependent on the activity of other spatially separated receptive fields. Two distinct types of neural connectivity have been identified to support integration of information across space or along contours: vertical feed-back modulation from higher visual areas onto V1 neurons (Lamme, Rodriguez-Rodriguez, & Spekreijse, 1999; Lamme & Roelfsema, 2000; Salin & Bullier, 1995; Zipser, Lamme, & Schiller, 1996) and lateral, horizontal long-range connections correlating the activity of distant receptive fields within the primary visual cortex (Gilbert, Das, Ito, Kapadia, & Westheimer, 1996). Even though the stimuli used differ across the range of studies, most of the physiological and psychophysical studies in literature report results coherent with the idea that collinearity is extracted early on the base of facilitation occurring between relatively distant oriented channels lying along a relatively straight path (i.e. contour) along the preferred axis (Kapadia, Ito, Gilbert, & Westheimer, 1995). Moreover, side-by-side, iso-oriented elements would not yield facilitation (Levitt & Lund, 1997; Sillito, Grieve, Jones, Cudeiro, & Davis, 1995). The network activity generated on the base of intra-striate lateral connections are the base of the so-called 'association field' that has been called into play to explain contour detection (Field, Hayes, & Hess, 1993). A lower number of studies using orientation-defined textures seem to suggest that their processing is focused onto more associative areas, such as V4 and TEO (Kastner, De Weerd, & Ungerleider, 2000). Indeed, orientation-defined textures contain iso-oriented local elements all around the clock, and their extraction takes place when local items are bound both along their axis of preferred orientation, as it is for contours, than aside it. In fact, the measures of VEPs for textures arranged in different lattices shows that collinearity matters, but it is not needed for the extraction of a signal to the global orientation of a pattern of iso-oriented Gabor stimuli (Pei, Pettet, & Norcia, 2007). The extraction of textures, but not of contours, corresponds to the psychophysical concept of 2nd order 'collator unit' that would dilute linearly (i.e. average) information arising from several independent noisy channels (Baldassi & Burr, 2000; Dakin & Watt, 1997; Morgan, Ward, & Castet, 1998).

From a developmental point of view, textures and contours seem to mature at two different rates. The sensitivity to global orientation such as that of orientation-defined textures, seems to be achieved by the first four months of age (Atkinson & Braddick, 1992; Humphrey, Muir, Dodwell, & Humphrey, 1988), while detection of collinear elements forming contours is present in 3-years old (Pennefather, Chandna, Kovacs, Polat, & Norcia, 1999) observ-

ers but adult-like performance keeps improving until adolescence (Kovacs, Kozma, Feher, & Benedek, 1999). These results can be related to the observation that the development of long-range intracortical connections shows a long developmental pattern (Burkhalter, 1993; Singer, 1995). A recent psychophysiological study (Norcia et al., 2005) has measured steady-state Visual Evoked Potentials (VEPs) with Gabor-defined stimuli showing that the key harmonics for textures emerge between 2 and 5 months of age, while those for contours emerge later, between 6 and 13 months of age. Moreover, the extraction of textures defined by Gabor elements (i.e. sine-wave gratings windowed by a Gaussian envelope, sharply defined in both the space domain and the spatial frequency content) is contrast dependent, while that of Gabor-defined contours is not (Bonneh & Sagi, 1998; Bonneh & Sagi, 1999). These results suggest that contour and texture integration can be two separable, complementary aspects of middle-vision that support the higher level of integration of visual shapes and objects in complex visual scenes.

Visual Evoked Potentials offer an alternative method for assessing visual function in autism that places minimal demands on the observer. Kemner et al. (2007), in addition to behavioral testing of contour integration also studied another mid-level function, texture segmentation. They recorded VEPs that are specific to the segmentation of a regions based on a combination of cues arising from local orientation discontinuities and orientation differences across regions. They found that their autistic group had normal peak latencies. From their results, they concluded that both horizontal connectivity within V1 as well as the feedback circuits feeding from higher cortical visual areas were preserved in ASD observers. However, the scenario emerging in literature concerning visual integration deficits in ASD is fragmented, and the different studies are not easily comparable as they rely on different techniques, tasks and stimuli. In this study we tried to probe the integrity of the lateral and the vertical neural connectivities by studying the neural correlates of the integration of contours and textures in observers with ASD using comparable stimuli and measures in order to observe whether perceptual deficits at this level were due to the impairment of the mechanisms supporting contours and/or textures. To this aim, we have used Gabor-defined textures and contours (keeping under rigorous control the spatial frequency spectrum) and adapted the paradigm used by Norcia et al. (2005) to track the early development of the neural correlates of the extraction of orientation-defined contours and textures. The choice of this paradigm is motivated by the fact that patients with ASD, like infants, may have a limited behavioral repertoire and are unresponsive to task instruction, making behavioral and psychophysical tests particularly difficult to perform and noisy. Moreover, the results for contours and textures are strictly comparable as they use similar test and control stimuli and conditions, and share the same low-level features of the local component stimuli. In particular, one of the tasks probes integration mechanisms that are used to encode differences in the orientation statistics of different textures. These statistics must be gathered over large regions of the texture and thus probe integrative mechanisms possibly mediated by vertical communication and relying on higher associative areas. The other task probes the ability to integrate orientation information along contours in noise, a task that is assumed to be mediated by lateral interactions at the level of the primary visual cortex. The last experiment was executed to measure thresholds for orientation coherence in textures, in order to distinguish normal observers and ASD patients in a finer quantitative way. The results show relatively normal sensitivity for textures but not for contours in children with autism. Further analyses show that the amplitude of the key components of the Evoked Potential in textures could be used to predict the contour processing of our sample of autistic children, possibly pointing to the use of a sub-optimal mechanism for processing contours in autism, i.e. the neural mechanism for detecting and segregating textures.

2. Materials and methods

2.1. Subjects

We collected VEP data in a group of 26 autistic children from 4 and a half to 18 years old and in a control group of 18 age-matched children without any diagnosed neurodevelopmental or visual deficit. The clinical group met the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) clinical criteria and all subjects were assessed on the Autism Diagnostic Interview-Revised (ADI-R) (Lord, Rutter, & Le Couteur, 1994) and the Autistic Diagnostic Observation Schedule General (ADOS-G) (Lord et al., 2000). These two instruments, when combined together, yield a quantitative diagnostic algorithm, which discriminates autistic from non-autistic subjects.

Individuals with chromosomal abnormalities associated with autistic-like behavior, such as fragile X syndrome, tuberous sclerosis complex, Prader-Willi Syndrome or Angelman Syndrome, were excluded from our sample by means of genetic tests. Patients with brain malformations, blindness, deafness and other sensory conditions that could impair typical social and behavioral development, were also excluded from the study.

Each patient underwent a child psychiatric evaluation including developmental history, clinical examination (ADI-R and ADOS-G) and cognitive assessment by tests to measure performance IQ (PIQ): Leiter-R and Performance Scale of Griffiths and Wechsler Intelligence Scales-Revised, depending on the age of the subject. We found that our sample was composed by 13 high-functioning (PIQ 70) and eight low-functioning patients; for three subjects we did not conclude cognitive evaluation because the families were not available.

The control group was matched by age rather than by cognitive or by performance scores for two main reasons: (1) the specific paradigm used here has been successfully used in previous studies with newborns and infants (Norcia et al., 2005; Pei et al., 2007) and measures low-level neural mechanisms whose development can be considered independent of any high-order cognitive skill and is mainly dependent on age and on factors other than experience, (2) our focus on low-functioning observers would have required control group of much younger normal observers if we matched by IQ, making the two groups incomparable in terms of age. It is important to notice that while there are studies showing a correlation between some EEG and IQ (Jolij et al., 2007), our criteria turned out to be correct *a posteriori* as the experimental measures of the present studies are completely uncorrelated with the IQ.

Observers of this group were free of any possible diagnosis of neurological or psychiatric disorder. Control group was well matched to patients for educational background and type of school, since our patients were inserted in regular classes, according to the Italian school system.

All the subjects of both groups have normal or corrected to normal vision.

The study was approved by the Ethical Committee of the Stella Maris Scientific Institute and was therefore performed in accordance with the ethical standards of the 1964 Declaration of Helsinki. Informed consent for participation was obtained from parents of all children.

Because of the priorities we set across experimental conditions (1. Texture, 2. Contours, 3. Random, 4. Texture Sweep) and the fact that we interrupted the session whenever an observer became significantly stressed by the test (i.e. she/he did not watch at the screen, looked tired or sleepy, etc.), only a fraction of the entire clinical sample of the 26 subjects finished all four conditions we planned. Specifically, all the subjects yielded data for the texture and the Contour conditions, 18 of them for the random condition, but only 16 of them were tested for the swept texture condition.

2.2. Experimental procedure

We asked the subjects to look at the center of the screen and to maintain fixation for the duration of the trial (10 s, see below). An experimenter standing behind the display monitored fixation by observing from the back of the monitor whether the corneal reflex of the monitor was centered in the subject's pupils. For some of the subjects we had to use a small toy suspended over the center of the screen to control fixation and as an accommodative cue for the plane of the monitor. Data collection was paused when the subject broke fixation and recording resumed after fixation was regained. The stimulus value of the sweep was decremented to the previous value before resuming the trial in order to minimize startup transients. We collected 5–12 trials for each condition depending of the subject's level of cooperation and the signal-to-noise ratio (SNR) of the VEP – the lower the SNR the more the trials needed. The average number of trials did not differ between groups or conditions. Signal and noise stimuli alternated every 500 ms (1 Hz). Individual trials lasted 12 s, with the first and last second being discarded; therefore, the data of each of the following experiments will be based on 50–120 presentations of signal and noise displays (see Section 2.3 and following for details).

For all the three experiments the viewing distance was 70 cm, the contrast 80% and the mean luminance was 85 cd/m².

All the stimuli were presented on a Power Macintosh G3 computer using conventional raster graphics methods (800 × 600 pixels at a 72 Hz refresh-rate) on a CRT monitor (Mitsubishi Diamond Pro 19").

2.3. Experiment 1: fixed-parameter textures

For the first condition, we compared the responses of autistic and normal observers to texture stimuli that alternated their state of global organization every 500 ms. The stimuli alternated between a globally ordered state consisting of a single orientation and a globally random state (see Fig. 1). The overall orientation of the ordered state was randomized on successive presentations. Textures were composed by high-contrast Gabor patches (sine-wave gratings windowed by a Gaussian envelope) with 2 cpd carrier and the envelope allowing approximately 2 cycles to be visible. Individual Gabor stimuli were placed in the intersection a parallel grid and the center-to-center separation between each Gabor in the nearest case was 3λ ($1\lambda = 1$ full cycle of the carrier grating). The textures were presented in a circular field (15.6° diameter) surrounded by a rectangular mean luminance background.

2.4. Experiment 2: contour stimuli

In the contour experiment, some of the Gabor patches were arranged along invisible circular paths and were embedded in a noise field made up of other Gabor patches. Approximately the same total number of patches were used in the texture and Contour conditions. Each contour contained eight Gabor patches and a total of seven was displayed within a circular field (15.6° diameter) surrounded by a rectangular mean luminance background like the one used for Experiment 1. The patches alternated every 500 ms between a "circle" configuration in which some of the patches were tangent to the invisible spline of the contours and a random state in which each patch was randomly arranged (see Fig. 1), giving a configuration identical to the one used for the random texture transition. The Gabor patch spacing along the contours was equal to 3λ and matched the average spacing of the noise interval to ensure that contours could not be detected on the basis of density elements. We compared this condition with the random condition (see next paragraph).

2.5. Random condition

The neural signal measured in the two main experimental conditions was compared with that obtained in a control condition where two independent random configurations, identical to the noise stimulus of the main experiments, alternated every 500 ms (see Fig. 1). The orientation of each individual patch was randomly changed at each alternation.

2.6. Experiment 3: swept parameter textures

The stimulus alternated between an organized texture and a random one at 1 Hz (i.e. 500 ms organized, 500 ms random). During a trial, the coherence of the organized texture was swept from 30% to 100% in ten steps each lasting one second. Texture coherence was defined as the percentage of patches that were all of the same orientation in the organized state of the alteration. Sweep VEP responses recorded from each trial were partitioned into ten one-second bins corresponding to each step of coherence in the stimulus sweep. In this way we measured responses as a function of the degree of global organization by varying the fraction of patches that were plotted at random orientations.

2.7. Eeg recording

Brain electrical activity was recorded with Grass gold-cup electrodes placed on the scalp with a conductive gel (10–20, D.O. Weaver). A row of 3 electrodes, each referenced to C_z included Oz and O1 and O2 (eg. 3 cm to the left and right of Oz). Electrode impedance was between 3 and 10 k Ω . The EEG was amplified by a factor of 50,000 times. We used a Grass Model 12 amplifiers with analog filter settings of 0.3–100 Hz, measured at –6 dB points. The EEG was digitized to 16 bits accuracy at a sampling rate of 432 Hz.

2.8. VEP signal analysis

For the fixed parameter recordings (experiments 1 and 2), time-locked average waveforms were computed for each subject and grand averages were computed across subjects (Fig. 2). The time-averages were digitally filtered using an inverse Discrete Fourier Transform that computed a synthesis of the first 53 harmonics of the stimulus frequency.

The analysis of the VEP in the frequency domain is better suited to that in the time domain for the following reasons. First the difference between the signal recorded for the globally organized patterns and the globally random patterns in the test conditions is nearly sinusoidal, as already shown in the developmental study by Norcia et al. (2005). Second, due to the periodical nature of the stimulus all the stimulus-related activities are forced to occur at exact integer multiples of the stimulus frequency used. All the activities that differ for the two transitions of the stimuli will project onto the odd harmonics (1, 3, 5, 7 Hz, etc.), whereas all activity that is common to the two transitions will project onto the even harmonics (2, 4, 6, 8 Hz, etc.). Therefore the spectrum analysis of periodic responses provides a substantial improvement in the signal-to-noise ratio of the relevant response components compared with that available from time-averages, as any point in the temporal waveform is affected by noise over the entire frequency range, while that of each harmonic is restricted to a limited bandwidth centered on any given harmonic. The spectral analyses for single observer data were performed using an adaptive filter (Tang & Norcia, 1995). We then focused on the 1st and 3rd harmonic (1 Hz and 3 Hz), since odd harmonics at the lowest frequencies show good signal-to-noise ratios and were shown to be specific markers to reveal configural-specific activity (Norcia et al., 2005). Note that by configural activity we refer to the neural activity that is evoked

by the transition between a globally organized and a globally random pattern in the absence of local cues indicating any possible difference between the local items.

In the fixed trials, the amplitude and phase for each 10 s record was averaged coherently, that is the real and imaginary components for each trial were first averaged separately before computing the amplitude and phase for a given stimulus condition. Group averages were computed in a similar way – each observer's complex amplitudes were averaged coherently. Error statistics for the group averages were computed using the T^2 circ statistic (Victor & Mast, 1991). The T^2 circ statistic is related to Hotelling's T^2 statistic, that assumes equal variance and covariance between the real and the imaginary spectral coefficients equal to zero. The presence of a statistically significant response at a given harmonic indicated when the value of the T^2 circ statistic (an F -ratio) did not include zero. Error bars in the figures are vector standard errors, some of which cross zero when the vector mean amplitude is small. Vector mean amplitude goes to zero in the limit for EEG noise.

2.9. Threshold and gain estimation from the swept response functions

For the swept stimulus condition, response thresholds were estimated by linear regression of amplitudes from the bins of the average response function using the region of the function in which the response decreased linearly to the point of stimulus invisibility. The range of bins eligible for regression depended on the statistical significance and phase-consistency of the response according to previously published algorithm (Norcia et al., 2005). The regression range was limited to those bins where the following criteria were met: (1) response p -value in each bin was at most 0.16; (2) the difference in response phase for each pair of consecutive bins was between 80° and -100° , where phase increases with response latency; (3) at least one pair of consecutive bins had response p -values of 0.077 or less; and (4) to exclude spike artifacts, the amplitude of the bin immediately before and the bin immediately after any given bin in the range could not both be less than 0.3 times the amplitude of that given bin. Once the regression range was established, the threshold stimulus value was determined by extrapolating the regression line to zero response amplitude (for more details on the methods, see Pei et al., 2007).

3. Results

3.1. VEP response in the time domain

The response waveform averaged across trials and observers for the most representative channel (OZ), the two groups (Control and ASD) and the three stimulus conditions (textures, contours and random) are reported in Fig. 2. In order to emphasize the difference between the response to the organized configurations and the random configurations we have overlapped the waveforms for the first and the second half of the response for each individual condition (Fig. 2, left column). The difference potential between the first and the second half of the response is plotted in the right column of graphs. The thick lines of the difference potential indicate significant difference based on a t test.

The entire set of data show a qualitative match with similar conditions of Norcia et al. (2005). In their Figure 2 and 3 they compare the response of the organized conditions over an entire trial (1st and 2nd half consecutively) with the response to the random condition. Here, we overlap the two halves as it allows a more direct comparison with previous studies measuring the EEG response to global configurations in autism (Kemner et al., 2007; Vandenbroucke, Scholte, van Engeland, Lamme, & Kemner, 2008).

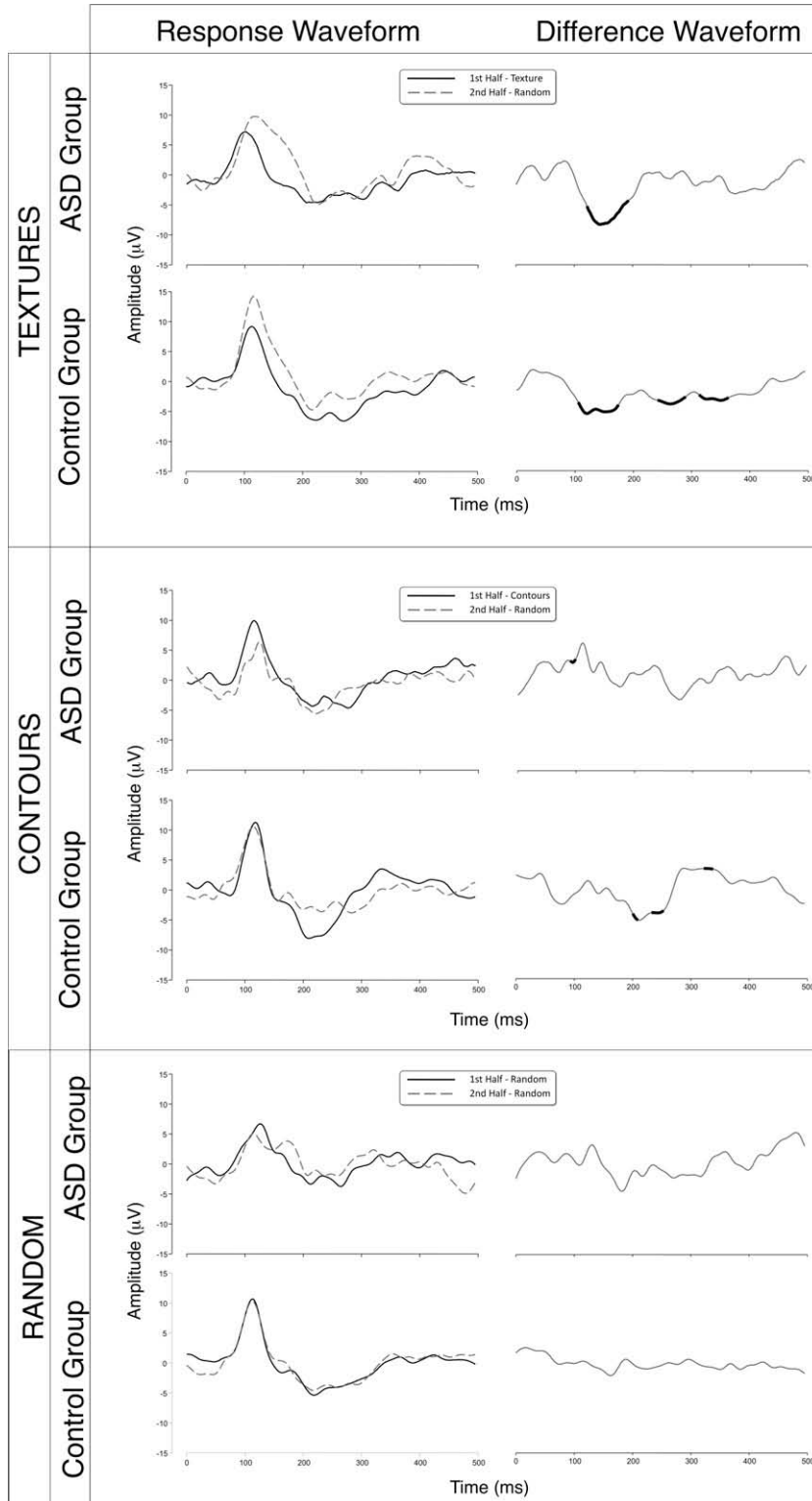


Fig. 2. Response waveforms for each of the two alternating stimuli, a globally organized (*black continuous lines*) and a globally random pattern (*gray dashed lines*). The column of graphs to the left shows the difference waveform (response to 1st minus response to 2nd half) for each group and condition with significant points evidenced by thick black lines. The block of graphs to the top shows waveforms for the texture condition for the two groups of observers, ASD (*top*) and control (*bottom*). The central block shows the same layout for the contour condition while the block on the bottom of the figure reports waveform for the condition in which two globally random patterns alternated every 500 ms.

The most basic and fundamental result is that the random condition, in which each half of the response is evoked by a globally random pattern, does not reveal any difference in either groups, with random fluctuations of the difference potential around zero.

However, the ASD group shows a broader variability of such fluctuations. This is coherent with the evidence of higher neural noise in subject with autism reported in literature (Dinstein et al., 2008; Markram, Rinaldi, & Markram, 2007; Rubenstein & Merzenich,

2003). In the texture and contour condition instead, the two halves describe the neural responses to a globally organized pattern (Fig. 2, black continuous lines) and to a globally random pattern (Fig. 2, gray dashed lines) alternating every 500 ms. Here the EEG shows a trend which is specific to the global stimulus used. In all cases a sharp peak is evidenced after about 100 ms from the transition between the two configurations. The righthand side of this lobe is wider for the 2nd half in both groups, as evidenced by a significant difference in between 100 and 200 ms. Then, the texture condition shows a long negative wave that is significantly deeper in the 1st half of the response of the control group. Overall, the two groups show a qualitatively good match of the responses for the texture condition. As for the contour condition, the initial peak at 100 ms does not differentiate the two conditions; rather, the difference between the response to organized vs. random global patterns seems to lie in a negative peak between 200 and 250 ms, which shows significant differences only in the control group. On the other hand, the Contour response of the ASD group seems generally similar to the activity recorded in the random condition.

3.2. Signature activity at the odd harmonics

Fig. 3 shows histograms of the vector average amplitudes of the 1st and 3rd harmonics, respectively measured in the control group for the three main conditions of our study (texture, contours and random condition) and for the three occipital electrodes we have used (O1, Oz and O2). The key comparison is between the amplitude of the harmonics of the two 'globally coherent' conditions (texture and contours) and that of the 'globally random' condition. Because the two phases of the globally random stimulus each contain no global structure, we do not expect any odd harmonic responses. The amplitudes measured thus provide an estimate of the background EEG level from a stimulus that is matched for local contrast and motion transients. In the control group the activity at the 1st harmonic for the Contour condition is not different from that measured in the random condition, although there is a trend, consistent over channels, of an increased activity relative to the baseline. The amplitude of texture condition on the other hand is

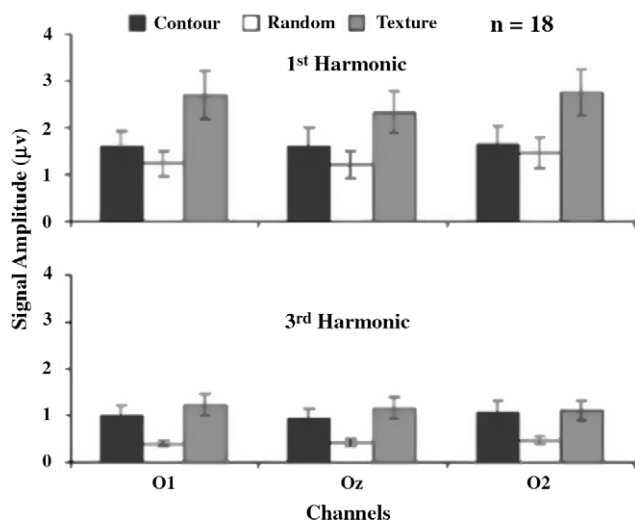


Fig. 3. Amplitude of the 1st and 3rd harmonics (top and bottom panels, respectively) of the Control group measured at the three Occipital electrodes O1 (left, black bar), Oz (middle, white bar) and O2 (right, gray bar). The average amplitude of normal observers was higher at the 1st harmonic only for textures, whereas both contours and textures alternating with noise showed an amplitude of the 3rd harmonic that was more than twice stronger than that produced by the alternation of two globally random configurations.

about twice as large as the Control condition. The 3rd harmonic of the control group in both the texture and contour conditions, is consistently larger than the random condition. Configural activity thus manifests itself at the 1st and 3rd harmonics for the texture condition but only at the third harmonic for the Contour condition. The relative lack of a 1st harmonics in the Contour condition suggests that these responses are more transient than the texture response.

Fig. 4 shows data from the experimental group of low functioning autistic children in the same format as used for Fig. 3. The top histograms plot the amplitudes of the 1st harmonic for the three stimulus conditions and the channels measured. In this case the relative distribution of amplitudes across conditions is similar to that obtained in the control group, with the texture condition showing an amplitude that is about twice as large as that of the other conditions. The bottom histogram plots the amplitudes at the 3rd harmonic for the autistic group. Here, in contrast to the control group, the responses in the texture and contour conditions do not differ from those of the random condition. This indicates a specific deficit of configural processing for both stimulus types. All the histograms shown here collapse the entire sample throughout the entire age range, as there was no difference whatsoever when two age groups were formed, both by equating the sample size in the groups (the 13 youngest vs. the 13 oldest) and by equating the range size (4–11 years old vs. 12–18 years old). Note also that the absolute scale does not change substantially across the two groups

3.3. Sweep threshold for textures

Fig. 5 plots the amplitudes of the 1st harmonic at the 10 different coherence values over which the texture stimulus was swept. Each function represents the group average for the group of children with autism (left) or the age-matched control group (right) for the individual electrodes (gray functions) or for the average across recording sites (filled black circles and squares, respectively for the two groups). Percent coherence refers to the percent of coherently oriented Gabor patches relative to the entire set of stimuli displayed. In both groups, the functions show relatively steady amplitudes for low levels of coherence then, presumably at the time the signature neural signal for global processing begins to dominate over the neural noise, amplitudes begin a linear rise with increasing coherence, with similar patterns across electrodes. As highlighted in the methods section, thresholds correspond to the coherence value where the regression drawn through the significant bins meets an amplitude of zero. In both groups of observers, the first set of bins at lower coherence did not meet the criteria for inclusion in the pool of bins used for determining the threshold, with an amplitude of the 1st harmonic ranging around 3 µV. Then, the amplitude relative to the following bins began to rise steeply with increasing coherence. The lowest coherence value included in the regression differed in the two groups and were equal to 58% and 67% respectively for the experimental and the control group. Most importantly, the threshold value differed between groups, with the experimental group showing thresholds that were in the region of 30% coherence, that is about twice as large as those recorded in the control group. This difference is stable across the different electrodes and is confirmed by the total average, that lies at 16% for the control group and 29% for the group of children with autism.

Therefore, even though the clinical sample of observers show significant neural response for textures at the 1st harmonic, it takes more coherence to elicit such a response relative to the normal observers. We should acknowledge here that this paradigm (Norcia et al., 2005) has allowed a quantitative measure that is not possible to perform with any previously adopted measure of

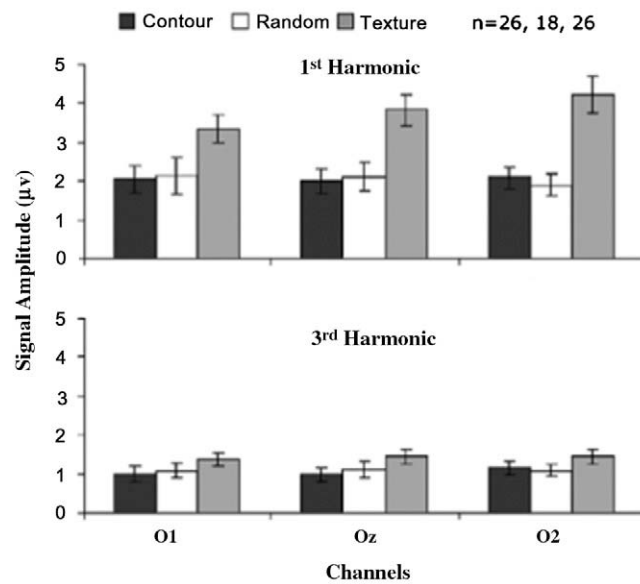


Fig. 4. Amplitude of the 1st and 3rd harmonics for the experimental group of observers with autism. The representation of the histogram is identical to that of Fig. 2. This group shows normal-like activity at the 1st harmonic, where texture yield significantly stronger amplitudes, but the configural activity exhibited by normal observers at the 3rd harmonic for both contours and textures was completely absent in the clinical group.

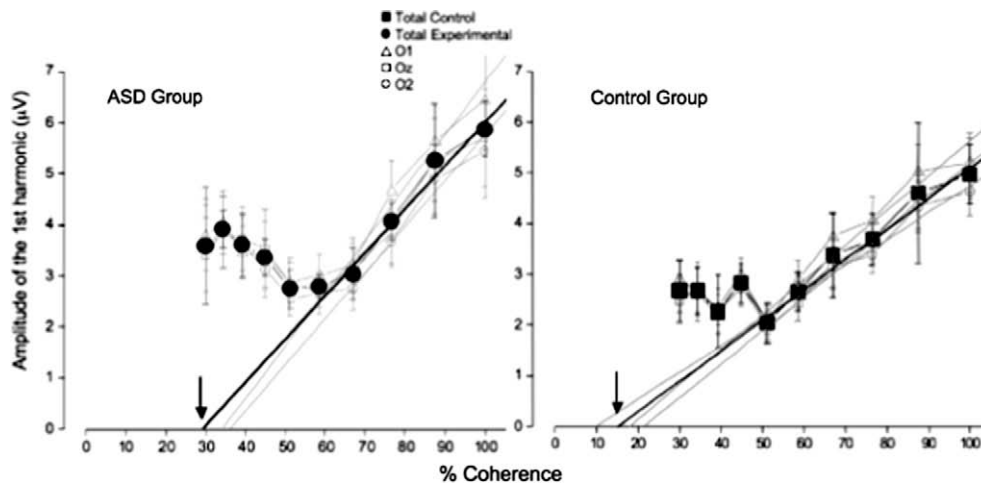


Fig. 5. Amplitudes of the 1st harmonic at the 10 different coherence of the texture Sweep experiment for the group of observers with autism (left) and the control group (right). Each function represents the group average for the individual electrodes (gray functions) or for the average across registration sites (filled black circles and squares, respectively for the two groups). The lines are linear fits of the cluster of coherence levels showing increase of activity relative to baseline (see text for details). The point where the fit meets 0 on the abscissae, indicated by a downward pointing arrow, represents the coherence threshold, that is of 29% for the experimental group and 16% for the control group.

global perceptual integration in autistic populations. The possible implications of these results are pondered later in the discussion.

3.4. Texture and contours: same or different mechanisms

Observers with autism show a dissociation with normal observers at the 3rd harmonic both for the texture and the contour condition. Thus we can speculate that the 1st harmonic, present just in the texture, reflects the activity of a mechanism located at a different level than the one generating the 3rd harmonic. To support this idea, in Fig. 6 we have replotted our data at the two key harmonics in a scattergram relating individual responses to textures, on the

abscissa, with responses to contours, in the ordinate, as expressed by the ratio texture/random and contour/random, what we call here ‘Coherence Index’. The simplest, straightforward hypothesis is that if the two global stimuli relied on independent neural circuits, then there should be no correlation between the two ratios, while if the two stimuli were seen by overlapping mechanisms one response could be predictive of the other.

As the scattergram illustrates clearly, subjects with autism exhibit in both harmonics a positive, significant correlation of the ratios of amplitudes calculated against the same random condition in both the texture and the contour condition. The control group instead shows no significant correlation between the two measures.

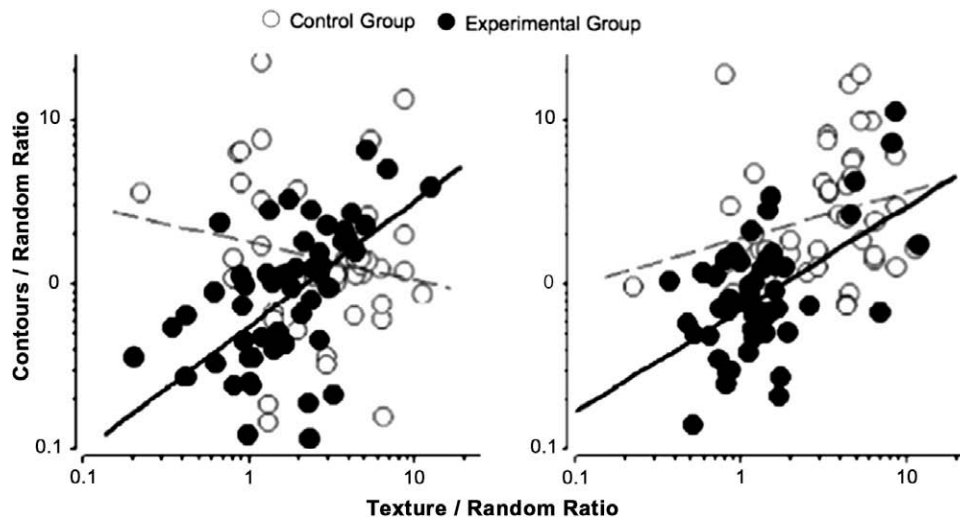


Fig. 6. Scattergram of the coherence index for contours (*Y*-axis) and textures (*X*-axis) for individual observers of the control group (*empty symbols*) and of the experimental group (*filled symbols*) at the 1st harmonic (*left panel*) and the 3rd harmonic (*right panel*). The black straight and the dashed gray lines are linear fit on log co-ordinates. The fit of the autistic group is for both harmonics positive and significant (1st H: $R^2 0.58 \pm 0.05$, $p < 0.0001$; 3rd H: $R^2 0.58 \pm 0.04$, $p < 0.0001$), while for the control group is not significant (1st H: $R^2 -0.17 \pm 0.07$, $p = 0.025$; 3rd H: $R^2 0.26 \pm 0.06$, $p = 0.08$). Note that the *N* are matched in the two groups as we had only 18 observers from the experimental group with measure of the random condition.

Even though this pattern can have several different implications, we can pose the speculation that it may be a sign that while the two stimuli rely on independent neural mechanisms in the observers of the control group, they are processed by the same mechanism in the group of autistic observers, and possibly this is the mechanism that in normal observers support texture processing and has residual abilities to link contours. In turn, this can imply that the preserved skills of detecting contours in noise shown by autistic subjects in psychophysical tasks is supported by these residual abilities of the texture hardware.

4. Discussion

In this study, we have measured configuration-specific VEPs to two stimuli that require the integration of orientation information across space in both typically developing and autistic children. The analysis in the temporal frequency domain has allowed to highlight selective differences between normal observers and observers with ASD in the neural responses to textures and contours. Comparing the amplitude of configural response components (1st and 3rd harmonics) we have found a specific deficit in the neural signature of global visual processing between autistic and normal observers. Children with autism lack a measurable 3rd harmonic component of their response to both contour and texture stimuli. This deficit is not a general one because their 1st harmonic response to the texture stimuli is normal.

Moreover, in the effort to perform more quantitative assessment of the relative maturity of visual global processing in the two groups, we have used a 'sweep' version of the texture paradigm that allows the measure of thresholds, that is the minimum level of coherence needed to elicit significant activity at the key harmonics, and have found that children with autism required a higher proportion of coherently oriented patches in order to exhibit the same neural activity for global stimuli shown by normal age-matched observers. Note that while sweep contours were not measured for practical reasons, *a posteriori* they turned out to be useless as we did not find configural response for contours even at 100% coherence.

Our data, in light of the current knowledge of the mechanisms supporting global integration of textures and contours discussed

in the introduction, may suggest that patients with ASD bind global forms by relying on intact feedforward and feedback connections between striate and extrastriate cortex but without relying on the complementary mechanism that connects distant striate receptive fields. This interpretation is consistent with that provided in a recent study to explain detection of object boundaries in ASD observers (Vandenbroucke et al., 2008).

However, a number of recent studies in autism have investigated the integration of local stimuli into global shapes or patterns using quantitative measures and comparable orientation-defined stimuli and found results that do not follow strictly the predictions of our finding. The results of these studies are summarized in Table 1.

The studies in Table 1 are comparable to our present investigation in that they all involve middle level processing of global integration and/or segregation. Each of these studies has found positive evidence for at least some level of global processing in observers with autism. Thus these studies are not consistent with other studies that have argued for a general deficit of global integration in autism (Frith, 1989; Happe, 1994a; Happe, 1999; Mottron et al., 2006). We find positive evidence for at least some level of global integration in observers with autism in the form of a normal 1st harmonic to the texture stimuli. However, the 3rd harmonic is missing from the response of ASD observers to textures. We were unable to detect contour specific activity in the clinical sample at either the 1st or 3rd harmonics. Normal children lack the first harmonic and thus this component cannot be used as a reference for the 3rd harmonic. Therefore, our study suggests a greater degree of abnormality for texture stimuli than it has been reported with a task involving texture *segregation* (not texture *integration* as in our case) by Kemner et al. (2007), and also a greater abnormality of contour integration than the psychophysical studies reported in Table 1 that have previously used comparable stimuli in ASD observers (Blake et al., 2003; Del Viva et al., 2006; Kemner et al., 2007). Using our stimuli and response measure, we were unable to detect the presence of the neural correlate of contour integration in autism. Each of the previous studies of contour integration in autism used a behavioral task and static stimuli and found contour integration to be normal. There are a number of possible reasons for the discrepancy between our result and those shown in these

Table 1

Synoptic view of the recent studies investigating texture and/or contour integration in ASD observers. The table summarizes the stimuli used, the type of measure (psychophysical vs. electrophysiological) and the relevant results.

Reference	Contours			Textures		
	Stimuli	Measures	Results	Stimuli	Measures	Results
Blake et al. (2003)	Contours of line segments in noise	Psychophysical thresholds	Normal-like thresholds			
Del Viva et al. (2006)	Contours of Gabor patches in noise	Psychophysical thresholds	Normal-like thresholds			
Kemner et al. (2007)	Contours of Gabor patches in noise	Psychophysical thresholds	Normal-like thresholds	Texture segregation of orientation contrasted lines	Time domain ERPs	Normal-like activity
Pei et al. (in press)	Contours of Gabor patches in noise	Frequency domain VEPs	Lack of signal at the 3rd harmonic	Texture integration of Gabor patches	Frequency domain VEP and Texture Sweep Thresholds	Normal-like 1st harmonic. Sweep threshold twice as high as controls

studies. First, a simple differences in the severity of autism might be an explanation for the differences across studies highlighted in Table 1. Also, it is possible that the dynamic nature of our stimuli is the critical factor or it may be that we are tapping different mechanisms by recording the VEP.

However, because we used similar stimulus elements across tasks and a common response measure, we can be more confident of the specificity of the loss of contour sensitivity. Even though both textures and contours require the activation of integration stages beyond the scope of individual cortical neurons of the striate cortex, they seem to rely on different mechanisms. The VEP response to texture stimuli becomes adult-like much earlier, in normal development, than the response to contour stimuli (Norcia et al., 2005). The dissociation we see here in autism converges with the suggestion that the two tasks are tapping different mechanisms.

In Fig. 6 we have observed that the neural response to the two classes of stimuli is strongly correlated in the clinical sample, while it is independent in normal observers, possibly implying that textures and contours are mediated by two different neural mechanisms. In the sample of autistic observers, the mechanism linking elements to form a texture would be preserved while the one binding element to form contours would be impaired. Alternatively, the mechanism supporting contour integration would emerge later in the development, as previously shown and the relevant activity might emerge in samples of older autistic observers. This will be one of the objects of further investigations from our group.

As far as these paradigms can directly demonstrate, we cannot go beyond indirect speculations on the exact circuitry supporting visual integration of local pieces into a global, coherent image that is intact or impaired in these Pervasive Developmental Disorders. However, our present study has used a robust methodology to show, possibly for the first time, that there is some weak or missing link in the cascade of events that build up a coherent percept out of an initial fragmentation performed by the specialized filters at the level of the primary visual cortex. Since these visual processing depends on network activities among neurons at the same cortical stage or across different stages, through feed-back modulation, it is plausible to speculate that it may be connected with a recent finding that one of the genetic correlates of autism involves the gene *DOCK4* that is directly involved in controlling dendritic growth (Maestrini et al., 2009).

Given the observations of the present study, we have recently worked on a prediction that has several large scale behavioral implications (such as, for example, in reading): the idea that if implicit binding of contours is impaired, then observers with autism should be resistant to visual crowding, i.e. the compulsory, detrimental influence on identification of peripheral visual items by closely surrounding elements. The data have supported our prediction and are part of a companion paper (Baldassi et al., 2009).

5. Conclusions

Many recent studies have investigated low-level properties of the visual functions in autism spectrum disorders, reinforcing the idea that high-level symptoms (i.e. face processing) might be secondary to specific impairments of basic processing at an earlier stage in the input–output hierarchy of stages underlying normal visual perception. The present study is one of the first reports showing the neural correlates of highly specific deficits in the middle vision of low functioning children with autism. The abnormalities that we have found here are coherent with several visually-driven behaviors of these patients, such as face avoidance or reading abnormalities. Future studies will have to understand how strictly the specific functions we have investigated here are related to these general visually-driven behavior.

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