Inverted event-related potentials response to illusory contour in boys with autism

Tatiana A. Stroganova[a], Elena V. Orekhova[d], Andrey O. Prokofyev[b], Irina N. Posikera[a], Alexey A. Morozov[c], Yuriy V. Obukhov[c] and Vladimir A. Morozov[c]

[a]Psychological Institute, Russian Academy of Education, [b]Moscow University of Psychology and Education, [c]Institute of Radio-Engineering and Electronics, Russian Academy of Sciences, Moscow, Russia and [d]Department of Clinical Neurophysiology, Sahlgrens University Hospital, Gothenburg, Sweden

Correspondence to Andrey Prokofyev, Faculty of Clinical and Abnormal Psychology, Moscow University of Psychology and Education, Sretenka, 29, 103051 Moscow, Russia
Tel: +7495 756 71 58; e-mail: vpf_child@mail.ru

Received 14 February 2007; accepted 16 February 2007

We examined the hypothesis of lower-level processing abnormalities related to perceptual grouping in boys with autism aged 3–6 years. We investigated event-related potentials response to visual elements that either formed perceptually coherent illusory contour or were arranged in a noncoherent way. The results showed that in healthy boys the illusory contour as compared with control stimulus elicited enhanced negativity of N1 peak (C effect), which has been previously found in adults. Autistic boys demonstrated the reliable *inverted* illusory contour effect, that is, more positive N1 amplitude to illusory contour. We hypothesized that boys with autism were sensitive to difference between illusory contour and control figures basing on collinearity processing mechanisms implemented in neural circuitry of primary visual cortex. *NeuroReport* 18:931–935 © 2007 Lippincott Williams & Wilkins.

Keywords: autism, children, event-related gestalt perception, Kanizsa square, occipital cortex, potentials

Introduction

Neuropsychological studies have highlighted atypical visuoperceptual processing in autism [1]. These perceptual abnormalities are usually interpreted in terms of the reduction in the contextual integration of information and a bias toward local rather than global processing [2]. The neural bases of decreased perceptual integration, however, are poorly understood. In particular, it is unclear whether specificity of visuoperceptual profile in autism arises from high-level cognitive processes or from lower-level processing of sensory information [3].

The lower-level perceptual processes related to perceptual completion in young children with autism can be studied using the illusory contour (IC) paradigm. The illusory Kanizsa square has been extensively used to explore neural mechanisms of 'intermediate' vision [4], which lead to effortless and automatic grouping of local elements in the visual field during perception of the IC. Neuroimaging studies revealed that the most common effect of illusory perception is additional activity in extrastriate cortical areas in response to the IC in comparison with a nonillusory figure [5–7]. Convergent evidence on the IC effect came from event-related potentials (ERPs) research in adults, which showed a higher amplitude of the N1 ERP component (a negative deflection at about 170 ms after stimulus onset) over posterior scalp areas for the illusory figure than for the non-IC [8–11]. The IC effect on ERP has been also reported in infants [12], a finding that is in line with behavioral evidence [13] and that point to the early developmental appearance of automatic perceptual completion processes. To date, there is no research on the developmental course of IC perception beyond infancy.

In this study we employed the ERP technique to investigate neural correlates of IC processing in young healthy and autistic boys aged 3–6 years, and to examine the hypothesis of early developmental disturbance of lower-level processing abnormalities related to perceptual grouping in autism. Given the results of previous studies, we predicted that the healthy children aged 3–6 years would show increased N1 amplitude in response to the Kanizsa square, and that the N1 amplitude in young children with autism would not discriminate ERP responses to IC and control stimuli.

Methods

Participants

Two groups of children participated in this study: 19 boys with autism (BWA) aged 3–6 years (mean age=60.4 months, SD=13.9) and 19 age-matched typically developing boys (TDB; mean age=61.4 months, SD=14.7). BWA were recruited from local departments of developmental disabilities and from psychiatry clinics. The control group comprised boys attending regular schools or day-care centers. The diagnosis of autism was made by an experienced clinician on the basis of *Diagnostic and Statistical Manual of Mental Disorder-IV-TR* criteria and confirmed by a clinical psychologist using the Childhood Autism Rating Scale [14]. Developmental quotients in BWA were evaluated by mental-age-appropriate tests. The Psychoeducational

profile [15] was used in 10 boys (young and/or without speech). The Kaufman Assessment Battery for Children [16] was used for the remaining nine BWA. Given that different tests were used to assess IQ and mental age, we recalculated the relative developmental delay on the basis of psycho-educational profile mental age or mental age derived from IQ measurement according to the formula: %delay= 100−(Mental Age × 100/Chronological Age). In the BWA group, the mean developmental delay was 26.4% (SD=18.6, range 0–60.3).

Informed consent was obtained from the parents of all children.

Stimuli

All stimuli were presented with Presentation software (Neurobehavioral Systems Inc., Albany, California, USA) on a 17-inch computer screen 50 cm in front of the participant. Two experimental stimuli were composed of four symmetrical black inducer disks. Each disk had one missing 90° segment with the length of inducing edges equal to the radius. These disks were arranged to produce the illusory percept of a Kanizsa square (134 trials), or not to yield the illusory percept (134 trials) (Fig. 1). No instruction was given to the children, and to maintain their attention to the computer screen, the test stimuli were interspersed with 67 short (3–6 s) animation movies. The same set of movies was presented to each participant. All stimuli were presented pseudorandomly on the white background of a PC monitor. Each trial started by presenting a fixation cross in the center of the screen, and then one of the stimuli appeared. Stimulus duration was 500 ms and interstimulus intervals varied randomly between 500 and 1000 ms. The whole stimulus subtended 8.94° × 8.94° of visual angle.

Procedure

Electroencephalograms (EEG) were recorded using 32-channel SynAmps system (Neuroscan, El Paso, Texas, USA) with a linked ears reference and 0.5–100 Hz band-pass filter at a sample rate of 500 Hz. Four electrooculogram channels were used to record eye movements. Electrode impedance was kept below 10 kΩ for all channels. The data were stored on a hard disk synchronously with the video record. The behavior of the participants was coded offline to identify epochs when they were not attending the stimuli. The trials in which a participant did not fixate on the picture and EEG epochs with movement artefacts and extreme signal amplitudes (≥100 mV) were excluded from the further analysis. All participants achieved ≥29 valid epochs for each stimulus type (mean 64.8±5.4 epochs). Electro-oculogram artefact correction was performed using regression approach implemented in SCAN 4.2 software (Scan 4.2 System, El Paso, Texas, USA). No difference was found between BWA and TDB with respect to the number of artefact-free EEG epochs sampled for Kanizsa [F(1,36)=3.93, ns] or control [F(1,36)=3.88, ns] trials. Recorded continuous EEG was epoched offline with 500 ms prestimulus and 1000 ms poststimulus onset duration.

Analysis was performed for six posterior scalp regions of interest (ROI): O1, O2, P3, P4, Oz, Pz. The epoched EEG data were baseline corrected, averaged, and then low-pass filtered at 30 Hz. For each EEG channel, the amplitude and latency values of the N1 component were measured at the maximum of negativity in the poststimulus time window

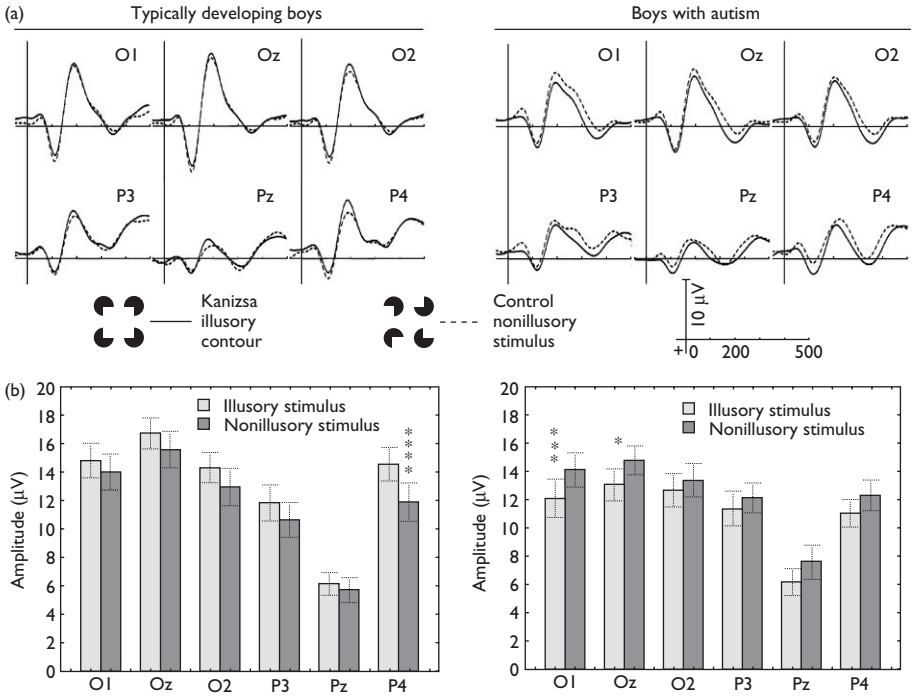

Fig. 1 Event-related potentials (ERPs) elicited by illusory contour and nonillusory stimuli in typically developing boys and boys with autism groups. (a) Grand average ERP waveforms at three occipital [two lateral (O1–O2) and one midline (Oz)] and three parietal [two lateral (P3–P4) and one midline (Pz)] electrodes. (b) N1 component amplitudes from each stimulus condition. Asterisks indicate statistically significant difference (Bonferroni test) between the Kanizsa and control stimuli: *$P < 0.05$; ***$P < 0.005$; ****$P < 0.001$.

between 150 and 300 ms. The N1 peaks were visually identified in six ROI for all participants.

Statistical analysis was performed using repeated-measures analysis of variance (ANOVA), with Stimulus (Kanizsa, control), Area (occipital, parietal), and Location (left, midline, right) as the within-participants factors and Group (autistic, healthy) as a between-subject factor. Participant's age was taken as a covariate. Post-hoc comparisons were performed using Bonferroni test and Sign test with Bonferroni correction. Only effects including Stimulus and Group factors will be considered further. The application of ANOVA to ERP data is not well justified owing to violation of the normality assumption for ERP amplitude distribution [17]. Therefore, we used the non-parametric step-wise subtraction technique [18] supplementary to the ANOVA to evaluate the statistical significance of multiway interactions. In short, the application of this method to the analysis of Group × Stimulus × Area × Hemisphere in this study was performed via the step-by-step subtractions. At the first step, the difference in N1 amplitude between Kanizsa and control trials (Δ_1) was calculated for each of four ROI separately and the resulting 152 Δ_1 values (4 ROI × 38 participants) entered into the second step. In the second step, the difference in Δ_1 between left and right locations of the same areas (Δ_2) was computed and yielded 76 Δ_2 (2 area × 38 participants). In the third step, the difference between occipital and parietal areas in the Δ_2 was computed and gave 38 values of Δ_3, one for each participant. Finally, we formed 19 autism-healthy age-matched pairs, and to estimate the significance of the four-way interaction effect compared the Δ_3 values of each boy with autism with his partner by means of a one-tailed Wilcoxon signed-ranks test. When testing more simple interactions, that is, two-way Group × Stimulus interactions, one must exclude the influence of topographical dimensions of Area and Location on the dependent measure. To reduce the dimensionality of the data, we introduced the principal component analysis and computed the factor scores of each data item (each participants in Kanizsa or control trials) on the first principal component explaining the maximum of data variance. Then, we computed the difference in these factor scores between Kanizsa and control stimuli for each participant (Δ_1), formed 19 autism-healthy pairs and submitted the resulting values to a one-tailed Wilcoxon signed-ranks test.

Results

The grand-average visual ERPs to Kanizsa and control stimuli in both TDB and BWA groups were characterized by a prominent N1 component (Fig. 1). Peak latencies of N1 determined from the grand-average waveforms varied between 180 and 228 ms at different electrode locations.

N1 amplitude

An ANOVA for the N1 peak amplitudes did not reveal the main effect of Group [$F(1,35)=0.25$, NS], suggesting that there was no difference between BWA and TDB in N1 amplitude when responses to both stimuli were collapsed.

Our prediction of abnormal brain response in BWA to IC was supported by a highly significant Group × Stimulus interaction [$F(1,35)=11.16$, $P<0.002$], indicating differences between BWA an TDB in the differential N1 response to Kanizsa and control stimuli (Fig. 1a and b). The nonparametric analysis of this interaction confirmed the effect (signed-ranks test: $P<0.002$). Post-hoc comparisons found a significantly *higher* (more negative) N1 component to Kanizsa than to control stimuli in the TDB group (Bonferroni test: $P<0.06$; signed-ranks test: $P<0.03$). Surprisingly, experimental manipulations in the BWA group yielded just the opposite effect: N1 amplitude was *lower* (more positive) in response to Kanizsa compared with control stimuli (Bonferroni test: $P<0.05$; signed-ranks test: $P<0.02$). The between-group difference in N1 amplitude was marginally significant for Kanizsa only: this stimulus elicited a more positive N1 amplitude in BWA than in their healthy peers (Bonferroni test: $P<0.28$; signed-ranks test: $P<0.03$). The N1 amplitude to the control stimulus did not differ between two groups (Bonferroni test: $P>0.6$; signed-ranks test: $P>0.38$).

An ANOVA also yielded a significant four-way interaction Group × Stimulus × Area × Location [$F(2,70)=3.83$, $\varepsilon=0.9$, $P<0.035$], implying that the between-group difference in IC effect was mostly pronounced at the particular areas of the scalp. Post-hoc comparisons (Fig. 1b) revealed that in TDB the Kanizsa being compared with the control stimulus elicited significantly more negative N1 amplitude (Bonferroni test: $P<0.001$) at the parietal scalp area of the right hemisphere (P4). No significant difference was found for any of the pair-wise comparisons at other electrode locations (Bonferroni test: all NS). In BWA, the significant Kanizsa–control difference in N1 amplitude was focused on two occipital locations – midline (Oz) (Bonferroni test: $P<0.04$) and left occipital (O1) (Bonferroni test: $P<0.005$) – where the N1 amplitudes were more positive in response to the Kanizsa than to the control stimulus. None of the between-stimulus comparisons for other electrode locations, being tested separately, reach the accepted significance level (Bonferroni test: all NS). To confirm the validity of this *a priori* nonpredicted interaction effect, the N1 amplitude at O1, O2, P3, and P4 electrode locations in BWA and TDB were subjected to nonparametric analysis. Owing to the limitation of the methodology (only main effects and interactions of the factors with even number of levels may be analyzed), we omitted the midline electrodes Oz and Pz in this particular case. The nonparametric assessment confirmed the previous ANOVA four-way interaction effect (signed-ranks test: $P<0.01$), and post-hoc nonparametric comparisons (N1 amplitude to Kanizsa vs control at P4 in TDB: signed-ranks test: $P<0.002$; Kanizsa vs control at O1 and Oz in BWA: signed-ranks test: $P<0.008$ and $P<0.008$, respectively) were also consistent with the results of post-hoc Bonferroni test.

N1 latency

No significant interaction effects including both Group and Stimulus factors were found for N1 latency.

Discussion

This study revealed that (i) in healthy preschool boys the visual N1 component in response to Kanizsa stimulus was significantly larger than that evoked by the control stimulus (the IC effect), and (ii) BWA of the same age demonstrated an *inverted* IC effect, that is, a larger N1 amplitude to a nonillusory control figure compared with IC.

The effect of the IC on N1 amplitude in healthy boys was similar to that found in adults. This effect is linked to the

completion of IC and/or perceptual grouping *per se* rather than to influence of other higher- or lower-order processes, for example, selective attention or the presence of collinear line segments in IC [9,10]. The IC effect on N1 amplitude in children was most pronounced at parietal areas of the right hemisphere. Likewise, right-hemispheric localization of the IC effect on ERP amplitudes over parieto-occipital sites was described previously in 8-month-old infants [12].

We predicted that perceptual grouping abnormalities in autism will be reflected by decreased differential N1 response to the IC stimuli. Contrary to the expectations, the N1 component in BWA did differentiate between IC and control stimuli, but the scalp topography and polarity of the IC effect was different in BWA and TDB. Specifically, in BWA the Kanizsa square evoked a less negative N1 component than the control stimulus, whereas the opposite effect was observed in TDB. Moreover, in BWA, differences in processing of Kanizsa and control figures were focused at midline occipital electrode sites extending into the occipital scalp area of the left hemisphere, whereas in TDB it was located in the right parietal region.

The inverted IC effect in BWA clearly points to qualitatively different neural mechanisms of IC processing in this disorder. The decreased occipital N1 amplitude (greater positivity) in response to Kanizsa square in BWA closely resembles the collinearity-dependent ERP effect that has been recently described in normal adults [19]. This effect characterized differential ERP responses to two simple visual stimuli with and without collinear lines. The authors reported that processing of collinearity was associated with greater *occipital positivity* in the time window spanning the N1 component and the earlier ERP components starting from 80 s poststimulus.

It is noteworthy that in our study the collinear lines were presented in the Kanizsa square but not in the control figure, thus constituting the additional dimension discerning both stimuli beyond the presence or absence of IC. The greater *positivity* of the occipital N1 component in response to a Kanizsa square than to a control figure in BWA may, therefore, reflect an abnormally enhanced collinearity effect. The collinearity processing takes place in the network of local, long-range, horizontal connections between cortical pyramidal cells with similar orientation preferences in early cortical visual areas [20]. This network is especially sensitive to elements with a similar orientation configuration in a collinear arrangement, and seems to extract information about contour edges at the early stage of visual cortical processing [21]. A likely explanation of the difference in the IC effect on ERP in TDB and BWA is that whereas perception of IC in TDB involved higher-order perceptual grouping processing, BWA were sensitive to differences between Kanizsa square and control figures based predominantly on collinearity processing mechanisms implemented in the neural circuitry of the primary visual cortex (V1). In autism, enhanced local lateral connections in V1 [22] in combination with long-range between-area underconnectivity [23], may lead to the imbalance in lower- and higher-order visual processing of the Kanizsa square that favors stimulus processing in lower-order cortical areas. Although this interpretation remains speculative in the absence of more direct data on the source localization of the revealed inverted IC effect, it is compatible with current views on altered, low-level perceptual information processing in autism [1,24].

The choice of typically developing children as a control group in this study limits our ability to assess the specificity of observed IC-processing abnormalities to autism. Potentially, an inverted IC effect might reflect the aberrant perceptual integration that is common in a number of developmental disorders, which are, like autism, characterized by decreased cognitive capacities. A recent ERP study of IC perception, however, in individuals with Williams syndrome who similarly to autistic individuals have mental retardation in combination with difficulties in integrating perceptual features, did not demonstrate any difference between N1 amplitude elicited by the Kanizsa square and the control figure [25]. It is likely, therefore, that the observed inverted IC effect represents the unique electrophysiological endophenotype of autism.

Conclusion

Current findings on the inverted IC effect on ERP in young boys with autism point to aberrant neural mechanisms of IC processing in this disorder. The suggested explanation of its neural underpinnings is consistent with the hypothesis of overfunctioning of processing mechanisms in lower-order visual areas in autism [24].

Acknowledgements

We are grateful to Natalia Rimashevskaya for helping with collection of the autistic sample. This study was partly supported by BIAL foundation (Grant 87/04.5.465) and the Russian foundation for basic research (RFBR grant 06-07-89302).

References

1. Caron M-J, Mottron L, Berthiaume C, Dawson M. Cognitive mechanisms, specificity and neural underpinnings of visuospatial peaks in autism. *Brain* 2006; **129**:1789–1802.
2. Happe F, Frith U. The weak coherence account: detail-focused cognitive style in autism spectrum disorders. *J Autism Dev Disord* 2006; **36**:5–25.
3. Behrmann M, Thomas C, Humphreys K. Seeing it differently: visual processing in autism. *Trends Cogn Sci* 2006; **10**:258–264.
4. Humphreys GW, Riddoch MJ, Donnelly N, Freeman T, Boucart M, Muller H. Intermediate visual processing and visual agnosia. *The Neuropsychology of High-Level Vision: Collected Tutorial Essays* 1994:63–101.
5. ffytche DH, Zeki S. Brain activity related to the perception of illusory contours. *Neuroimage* 1996; **3**:104–108.
6. Hirsch J, DeLaPaz RL, Relkin NR, Victor J, Kim K, Li T, *et al*. Illusory contours activate specific regions in human visual cortex: evidence from functional magnetic resonance imaging. *Proc Natl Acad Sci U S A* 1995; **92**:6469–6473.
7. Ritzl A, Marshall JC, Weiss PH, Zafiris O, Shah NJ, Zilles K, *et al*. Functional anatomy and differential time courses of neural processing for explicit, inferred, and illusory contours. An event-related fMRI study. *Neuroimage* 2003; **19**:1567–1577.
8. Brodeur M, Lepore F, Debruille JB. The effect of interpolation and perceptual difficulty on the visual potentials evoked by illusory figures. *Brain Res* 2006; **1068**:143–150.
9. Herrmann CS, Bosch V. Gestalt perception modulates early visual processing. *NeuroReport* 2001; **12**:901–904.
10. Murray MM, Imber ML, Javitt DC, Foxe JJ. Boundary completion is automatic and dissociable from shape discrimination. *J Neurosci* 2006; **26**:12043–12054.
11. Proverbio AM, Zani A. Electrophysiological indexes of illusory contours perception in humans. *Neuropsychologia* 2002; **40**:479–491.
12. Csibra G, Davis G, Spratling MW, Johnson MH. Gamma oscillations and object processing in the infant brain. *Science* 2000; **290**:1582–1585.
13. Otsuka Y, Kanazawa S, Yamaguchi MK. The effect of support ratio on infants' perception of illusory contours. *Perception* 2004; **33**:807–816.

14. Schopler E, Reichler R, Remler BR. The childhood autism rating scale (CARS) for diagnostic screening and classification of autism. 1986.
15. Schopler E, Reichler R, Bashford A, Lansing M, Marcus L. *Psychoeducational profile (rev.)*. Austin, TX: Pro-Ed; 1990.
16. Kaufman AC, Kaufman NL. *Kaufman assessment battery for children: administration and scoring manual*. Circle Pines, MN: American Guidance Service; 1983.
17. Bertrand O, Tallon-Baudry C. Oscillatory gamma activity in humans: a possible role for object representation. *Int J Psychophysiol* 2000; **38**: 211–223.
18. Morozov AA, Morozov VA, Obukhov YV, Stroganova TA. Non-parametric multi-way analysis of human EEG. *Artif Intell* 2006; **3**: 603–612.
19. Khoe W, Freeman E, Woldorff MG, Mangun GR. Electrophysiological correlates of lateral interactions in human visual cortex. *Vis Res* 2004; **44**:1659–1673.
20. Schmidt KE, Goebel R, Lowel S, Singer W. The perceptual grouping criterion of colinearity is reflected by anisotropies of connections in the primary visual cortex. *Eur J Neurosci* 1997; **9**:1083–1089.
21. Hess RF, Hayes A, Field DJ. Contour integration and cortical processing. *J Physiol Paris* 2003; **97**:105–119.
22. Casanova MF, Buxhoeveden DP, Switala AE, Roy E. Minicolumnar pathology in autism. *Neurology* 2002; **58**:428–432.
23. Barnea-Goraly N, Kwon H, Menon V, Eliez S, Lotspeich L, Reiss AL. White matter structure in autism: preliminary evidence from diffusion tensor imaging. *Biol Psychiatry* 2004; **55**:323–326.
24. Bertone A, Mottron L, Jelenic P, Faubert J. Enhanced and diminished visuo-spatial information processing in autism depends on stimulus complexity. *Brain* 2005; **128**:2430–2441.
25. Grice SJ, Haan MD, Halit H, Johnson MH, Csibra G, Grant J, *et al*. ERP abnormalities of illusory contour perception in Williams syndrome. *NeuroReport* 2003; **14**:1773–1777.