Title: Parvocellular pathway impairment in autism spectrum disorder: Evidence from visual evoked potentials

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Abstract

Visual information is processed via parallel channels: The parvocelular (P) pathway analyzes color and form perception whereas the magnocellular (M) stream plays an important role in motion analysis. Individuals with autism spectrum disorder (ASD) often show superior performance in processing of fine detail and inferior performance in processing of global structure and motion perception. To date, there have been no visual evoked potential (VEP) studies on the neural basis of these atypical characteristics of visual performance in ASD. VEPs were recorded with a 128-ch high density EEG system to elucidate how the P and M pathways are functionally altered in ASD. Chromatic (equiluminant red-green sinusoidal gratings) and achromatic (low contrast black-white sinusoidal gratings) stimuli were used to evaluate functions of P and M pathways within the primary visual cortex (V1), respectively. Unexpectedly, N1 component of VEPs to chromatic gratings were significantly prolonged in ASD. However, VEP responses to achromatic gratings did not differ significantly between the two groups. Chromatic stimulus preferentially stimulates the P-color but not P-form pathway, which suggest an impaired P-color pathway. Therefore, our study first demonstrates the electrophysiological evidence for the impaired P-color pathway with preserved M function at the V1 level in ASD.

Keywords: autism spectrum disorder (ASD), visual evoked potentials (VEPs), parallel visual pathways, parvocellular and magnocellular systems

1. Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social interaction and communication as well as restricted and repetitive behaviors and interests (Frith & Happé, 2005). Individuals with ASD exhibit superior performance on processing fine details (Happè, 1996; Happè & Frith, 2006; Ishida et al., in press; Jolliffe & Baron-Cohen, 1997), while those with high IQ are poor at processing global structure and motion perception (Bertone et al., 2003; Milne et al., 2002; Spencer et al., 2000). Two distinct hypotheses have been proposed on abnormal early processing of the visual system in ASD. Spencer *et al.* (2000) proposed the ñpathway-specificò hypothesis. This states that in ASD, dysfunctional M and preserved P pathway functions cause the elevated motion coherence threshold (the minimum number of coherently moving elements supporting direction discrimination at some criterion level of performance), and exhibit a preserved form coherence threshold (static analog of motion coherence threshold). Alternatively, Bertone *et al*. (2003) proposed the ñcomplexity-specificò hypothesis. They measured sensitivity to first-order (luminance-defined) and second-order (texture-defined) motion stimuli and found a decrease in performance for second-order motion only. They assumed that inefficient neuro-integrative functioning affects complex information analysis in autism, regardless of static or dynamic visual information. The authors also evaluated the function of sub-cortical visual processing by utilizing the flicker contrast sensitivity task, and concluded that sub-cortical visual processing was intact (Bertone et al., 2003, 2005; Bertone & Faubert, 2006).

Two major parallel visual pathways exist in humans, namely the parvocellular (P)

and magnocellular (M) pathways (Tobimatsu & Celesia, 2006). Both systems begin in the retina and project to the primary visual cortex (V1) via the lateral geniculate nucleus. The P pathway projects to area V4 via the P-blob (color) and P-inter blob (form) pathways of V1, and visual information is subsequently sent to the inferior temporal cortex. The P-color pathway is important for analyzing color information and the P-form pathway for processing detailed form information. In contrast, the M pathway projects to area V5/MT and terminates in the posterior parietal cortex. The M pathway plays an important role in detecting motion and processing of global structure (Livingstone & Hubel, 1988; Tobimatsu & Celesia, 2006). These distinct features depend on various physiological characteristics between the P and the M pathways. The former is characterized by high spatial resolution, color-sensitivity, low contrast sensitivity, and low temporal resolution, while the latter exhibits opposite characteristics of low spatial resolution, color insensitivity, high contrast sensitivity, and high temporal resolution (Livingstone & Hubel, 1988; Tobimatsu & Celesia, 2006). Based on the concept of parallel visual processing, atypical visual characteristics of superior processing of fine detail (local structure), inferior processing of global structure, and impaired motion perception in ASD might be related to superior function of the P pathway (particularly, the P-form pathway) and dysfunction of the M pathway.

Visual evoked potentials (VEPs) are a pertinent objective tool and have been useful in studies investigating physiology and pathophysiology of the human visual system, including visual pathways and the visual cortex (Regan, 1989; Tobimatsu & Celesia, 2006). VEPs detect abnormalities not only in patients with visual complaints, but also in patients with no visual symptoms upon examination (Tobimatsu & Celesia, 2006). VEPs exist in two formsð transient and steady-state (Tobimatsu & Celesia,

2006). Based on different stimulus selectivity between P and M pathways, our group previously evaluated the function of human parallel visual pathways in healthy subjects and patients with various neurological disorders through the use of VEPs with appropriate visual stimuli (Tobimatsu et al., 1995, 1999, 2004, 2006; Tobimatsu & Kato, 1998; Yamasaki et al., 2004; Nakashima et al., 2008). At lower-level (within V1) visual pathways, transient VEPs at low temporal frequency that use chromatic sinusoidal gratings with equal luminance and high spatial frequency are suitable for stimulating the P pathway within V1. This stimulus evokes a characteristic negative wave (Nl) with a peak latency around 120 msec. Conversely, steady-state VEPs at high temporal frequency that use achromatic sinusoidal gratings with low contrast and low spatial frequency are useful for evaluating the M pathway within V1. This stimulation induces a positive peak (P1) around 120 msec followed by steady-state responses (Gutschalk et al., 2002).

To date, no studies have utilized VEPs to examine the neural basis of two distinct hypotheses, ñpathway-specificò and ñcomplexity-specificò hypotheses obtained by the psychophysical measurements. In addition, elemental chromatic and achromatic stimuli have not been previously used to study parallel visual pathways within V1. Therefore, we aimed at objectively evaluating the neural substrates of atypical visual performances in ASD. Special attention was paid to the lower level (within V1) of P and M pathways using appropriate visual stimuli.

2. Methods

2.1. Participants

Twelve ASD participants, comprising two adolescents and 10 adults with high-functioning ASD (8 males and 4 females, aged 17-38 years, mean age 28.1), and 12 healthy control participants, comprising one adolescent and 11 adults with similar chronological age and sex ratio (7 males and 5 females, aged 19-36 years, mean age 26.3), were enrolled in the study. The ASD group included six individuals with Aspergerôs disorder, three with autistic disorder, and three with pervasive developmental disorder not otherwise specified (PDD-NOS). A research team, including an experienced child psychiatrist (Y. K.), diagnosed the ASD participants according to DSM-IV criteria (APA, 1994) and based on clinical interviews with participants and/or parents using semi-structured interviews that were validated for Japanese PDD populations (PARS, Kamio et al., 2006). Diagnostic agreement among the team was obtained for all participants. Control participants were recruited from college students and faculties and, according to the interviews, were confirmed to have no developmental problems.

Intellectual function of ASD participants was evaluated using Japanese versions of WAIS-R. ASD participants with full scale IQ scores greater than 80 were recruited. All subjects exhibited normal or normal corrected visual acuity (>1.0), which was evaluated using the Landoltôs ring (Landolt, 1905). No subjects exhibited any color deficits, as determined by Ishihara color plates (Ishihara, 1997).

Informed consent was obtained after the nature of the experiment had been fully explained. The experimental procedures were approved by the ethics committee of the Graduate School of Medical Sciences, Kyushu University.

2.2. Visual stimuli

The stimuli were generated by ViSaGe (Cambridge Research Systems, Cambridge, U.K.) and were displayed on a gamma-corrected color monitor using a frame rate of 100 Hz (Electron22blue IV, LaCie, Tokyo, Japan). P and M pathways have distinct physiological characteristics (Livingstone and Hubel, 1988; Tobimatsu and Celesia, 2006). Therefore, appropriate stimuli were created to preferentially stimulate the lower level P and M pathways within V1 as described below.

The P pathway is characterized by high spatial resolution, color sensitivity, low contrast sensitivity, and low temporal resolution (Livingstone and Hubel, 1988; Tobimatsu and Celesia, 2006). Red/green chromatic sinusoidal gratings with equal luminance of red and green were used to evaluate the P pathway (Fig. 1a). Because this stimulus was very elemental, it could preferentially stimulate the P pathway, and more specifically, the P-color pathway within V1. The visual stimulus subtended 10 × 10 deg at a viewing distance of 114 cm. CIE coordinates (measured by a Chromameter CS 100, Konica Minolta, Tokyo, Japan) were x = 0.601, y = 0.365 (R); x = 0.267, y = 0.581 (G). Chromatic stimuli were surrounded by a homogeneous background containing a mixture of red and green (yellow). The luminance of red and green, as well as the homogeneous background, was 21 cd/m^2. The contrast level was 0% as defined by the Michelson contrast. The spatial frequency was set to 2 cycles/deg. Prior to experimentation, subjects viewed 15-Hz alternating red/green pattern stimuli to establish psychophysical isoluminance, and relative luminance was adjusted to minimize the perception of flicker (Yamasaki et al., 2008). A chromatic pattern appeared for 200 msec, and was subsequently replaced by a homogeneous stimulus background for 1000 msec. This stimulus elicits transient VEP responses (N1) (Tobimatsu et al., 1995). Subsequently, cartoon characters appeared for 1000 msec,

which were replaced by a homogeneous stimulus background for 1000 msec. Cartoon characters included 10 images, and these images were randomly presented in each session. An entire sequence was 3200 msec. A session included 30 sequences (about 1-2 min) and was repeated four times. Therefore, a total of 120 sequences were presented (about 6-7 min).

The M pathway is characterized by high temporal resolution, high contrast sensitivity, color insensitivity, and low spatial resolution (Livingstone & Hubel, 1988; Tobimatsu & Celesia, 2006). Achromatic (black/white) sinusoidal gratings were used to evaluate the M pathway (Fig. 1b). Because this stimulus was very elemental, it preferentially stimulated the M pathway prior to V1. The luminance of black was 17.5 cd/m^2, and that of white was 24.5 cd/m^2. A homogeneous background, containing a mixture of white and black (gray), surrounded the visual stimuli. The mean luminance of achromatic gratings and homogenous background was 21 cd/m^2, and the contrast level was 16.6%, as defined by the Michelson contrast. Spatial frequency was set to 1 cycle/deg. The stimulus pattern alternated in a square-wave fashion at a rate of 8 Hz (16 reversals/sec). Stimulation was presented for 2000 msec, and was subsequently replaced by a homogenous background for 1000 msec. This stimulus condition elicited a transient VEP response (P1), followed by steady-state responses (Gutschalk et al., 2002). Cartoon characters then appeared for 1000 msec and were subsequently replaced by a homogeneous stimulus background for 1000 msec. Cartoon characters included 10 images, and these images were randomly presented in each session. These cartoon characters were entirely different from those of chromatic condition. An entire sequence was 5000 msec. A single session included 30 sequences (about 2-3 min) and was repeated four times. Therefore, a total of 120 sequences were presented (about 10 min).

2.3. VEP recordings

VEPs were recorded using a Geodesic EEG system, NetAmps 200 (Electrical Geodesics [EGI], Eugene, Oregon). A high-density, 128-channel, HydroCel Geodesic Sensor net (EGI) was applied over the scalp of the participant. This net held each electrode in place, and distributed electrodes from nasion to inion and from left to right mastoids at uniform intervals. Each electrode consisted of a silver chloride carbon fiber pellet, a lead wire, a gold-plated pin, and a potassium chloride-soaked sponge. This electrode configuration effectively blocked out electrochemical noise and minimized triboelectric noise. Signals were amplified via an AC-coupled, 128-channel, high-input impedance amplifier (NetAmps 200, EGI). The analog data were digitized at a sampling rate of 500 Hz/channel. Amplified analog voltages were hardware band-pass-filtered at 0.1-200 Hz. The experimenter individually adjusted all sensors until the impedance of each electrode was less than 80 kq (Ferree et al., 2001). Most of the electrode impedances were kept below 50 kq except for electrodes surrounding the ears and neck. The impedance levels were comparable between ASD (24.1 ± 3.6 kq (mean ± SD)) and control (32.1 ± 8.8 kq) groups. EEG data were collected using the vertex (Cz) electrode reference.

The participants were instructed to remain still and to fixate on a black dot fixation point at the center of the screen. The arousal level was carefully and visually monitored by the observer (T.F.) in the same room. The arousal level was also recorded by a video camera placed outside of the room and by EEG. If a participant became drowsy, he/she was alerted and provided a brief rest. To maintain stimuli attention, the participants were instructed to memorize the cartoon character names that were

presented between stimuli. Following VEP recording, all participants provided the cartoon character names. The order of chromatic and achromatic stimuli was counterbalanced among the subjects.

2.4. Offline data analyses

Epochs containing EEG deviations from the baseline, which were greater than 50 εV, were automatically rejected. Subsequently, epochs that contained blinks, horizontal or non-blank eye movements, A/D saturation, or obvious occipital Ŭ-activity were rejected. Electrodes surrounding the eyes were used to identify blink artifacts, as well as horizontal or non-blank eye movements. Then, epochs were re-referenced offline to an average of 99 channels that represented all channels except for channels surrounding the eyes, ears, and neck, because these channels were easily contaminated by muscle electric potential.

A total of 120 VEP samples with 400-ms epoch (from -100 to 300 ms) were averaged for chromatic stimuli using the software (Net Station, EGI). The required minimum number of viable trials for participation was defined as 80. VEPs, following a brief presentation of visual stimuli, provided the transient VEP responses. Initially, the scalp topography for the major component (N1) was created. Next, because the scalp topography of the N1 component exhibited maximal amplitude at Oz, and the Oz electrode reflected activity around V1, EEG data were analyzed at Oz.

A total of 120 VEP samples with 2000-ms epoch (from 0 to 2000 ms) were averaged for achromatic stimuli using the software (Net station, EGI). The required minimum number of viable trials for participation was defined as 80. Then, the scalp topography for the major component (P1) was created. Next, because the scalp

topography of the P1component exhibited maximal amplitude at Oz, and the Oz electrode reflected activity around V1, EEG data were analyzed at Oz.

Finally, scalp topography for the steady-state response (positive and negative phases) was created. Because the scalp topography of the steady-state response exhibited maximal amplitude at Oz, EEG data from Oz was used for further analysis. The average response was then subjected to fast Fourier transforms (FFTs), which yielded amplitude (square root of the power) and the phase for the major component (EMSE Suite, Source Signal Imaging, San Diego, CA, USA).

2.5. Statistical analyses

The mean number of viable trials between the two groups was analyzed using the unpaired *t*-test. With regard to N1 for chromatic stimuli and P1 for achromatic stimuli, peak amplitude and latency were measured from the pre-stimulus baseline in each subject. The latency difference between the two groups was analyzed using the unpaired *t*-test. The Mann-Whitney *U* test was used to assess amplitude differences. A level of $p < 0.05$ was considered to be statistically significant.

The steady-state VEP phase was analogous to the latency of transient VEPs, but phase data were distributed on a circular scale (from 0 to 360 degrees). Therefore, they were quantified using circular statistics, which was employed for evaluating phase data (Mardia, 1972; Zar, 1999). Three parameters were calculated: mean angle, phase coherence (r), and circular standard deviation (CSD) (Tobimatsu & Celesia, 2006). Both r and CSD were measures of dispersion in the phase data. The r-value varied from 0 when too much dispersion resulted in the lack of a definition for a mean angle; it varied to 1.0 when all data were concentrated in the same direction (Mardia, 1972; Zar,

1999). The reliability of r-values was quantified using the Rayleigh test for randomness (Batschelet, 1981). In the present study, a level of $P < 0.05$ was considered to be statistically significant. CSD was SD for phase measurements and appeared most similar to the linear SD (Mardia, 1972). The difference in VEP amplitude between the two groups was analyzed using the unpaired *t*-test. Because phase data were circularly distributed, the Mann-Whitney *U* test was used to assess phase data. A level of $P < 0.05$ was considered to be statistically significant.

3. Results

3.1. Intellectual function

The ASD participants exhibited normal IQ (verbal IQ, 111 ± 19.2 (mean ± SD); performance IQ, 110 ± 12.8; full scale IQ, 112 ± 13.8). No significant differences in chronological age (t-test) and sex ratio (χ^2 test) existed between the two groups.

3.2. Parvocellular function

All participants correctly named the cartoon character names following VEP recording, which confirmed good performance. The numbers of trials rejected for Ŭ-activity were less than five in both groups. There was no significant difference in the mean number of viable trials between the groups (control group, 104.5 ± 10.3; ASD group, 100.7 ± 13.1, p = 0.43). These results suggested that arousal and attentional levels did not affect VEP responses.

Grand-average VEP waveforms, in response to chromatic stimuli at Oz, are shown in Fig. 2. In both groups, the negative component at approximately 100 msec

(N1) was elicited as a major component. In the scalp topography, N1 was located at the occipital area (maximum at Oz), and there was no obvious difference in N1 distribution between the two groups (Fig. 3). The mean N1 latency in the ASD group (108.6 ± 7.7 msec) was significantly longer than the control group (102.8 ± 5.3 msec) ($p = 0.04$). In contrast, there was no significant difference in mean N1 amplitude between control (15.5 ± 7.2 εV) and ASD groups (13.0 ± 6.3 εV) ($p = 0.47$).

Six ASD participants (50%) exhibited N1 latency within normal range (102.8 ± 5.3 msec). Thus, additional analyses (unpaired t-test) were performed to examine the characterization/phenotypic difference between the subgroups within or out of the normal range. However, there was no significant difference between the two subgroups.

3.3. Magnocellular function

All participants correctly named the cartoon character names following VEP recording, which confirmed good performance. The number of trials rejected for Ŭ-activity was less than 15 in both groups. The mean number of viable trials in the ASD group was not different from the control group (control group, 105.3 ± 14.9; ASD group, 101.8 ± 11.8, $p = 0.53$). These results suggested that arousal and attention levels did not affect the VEP responses.

In both groups, VEPs, in response to achromatic stimuli at Oz, exhibited a positive component (P1) at around 120 ms, as well as quasi-sinusoidal waveforms that corresponded to the reversal frequency (16 Hz) (Fig. 4a). Scalp topography revealed that P1 and steady-state responses in the positive and negative phases were predominantly distributed at the occipital area (maximum at Oz). There was no obvious difference in distribution of P1 and steady-state responses between the two groups (Fig.

5).

There was no significant difference in mean P1 latency between the control group (129.5 ± 5.3 msec) and the ASD group (132.0 ± 7.2 msec) ($p = 0.38$). In addition, no significant difference in mean P1 amplitude between the control (9.01 ± 3.34 εV) and ASD groups (7.73 ± 2.47 εV) was found ($p = 0.43$). For steady-state responses in FFTs, the second harmonic (2F) component was evident as a major component in both groups (Fig. 4b). Therefore, phase and amplitude of this component were analyzed. In the control group, mean 2F amplitudes and phases were 0.57 ± 0.33 εV and 142.3 ± 62.9 (CSD) deg, respectively. r-value was 0.548 ($p < 0.05$). In the ASD groups, mean 2F amplitudes and phases were 0.51 ± 0.22 εV and 128.2 ± 53.6 (CSD) deg, respectively. The measure of r was 0.646 ($p < 0.05$), suggesting the narrow angle dispersion. Statistically, there was no significant difference in mean 2F amplitudes and phases between the groups (amplitude, $p = 0.55$; phase, $p = 0.63$).

4. Discussion

4.1. Dysfunction of the parvocellular-color pathway in ASD

Chromatic stimuli with equal luminance do not stimulate M neurons. In response to chromatic stimuli, the mean N1 latency in high-functioning adults with ASD was significantly longer than the control group. The chromatic stimuli used in this study preferentially activated the color pathway but not the form pathway, because higher spatial frequency with high-contrast gratings was preferable to stimulate the form pathway (Tobimatsu & Celesia, 2006). Accordingly, these results indicated a dysfunctional P-color pathway at a lower level.

Although anecdotal evidence suggests that differences in color perception exist in children with autism and typically developing children, few studies have directly addressed this. To the best of our knowledge, only one psychophysical study investigated color perception in ASD, revealing that color perception abnormalities (color memory, color search, and chromatic discrimination) in children with ASD existed without color deficits in Ishihara color plates (Franklin et al., 2008). The authors concluded that abnormal color perception in ASD was due to differences in anatomical and functional organization of the brain, in particular to disruption to one or more of the visual pathways. Therefore, the present neurophysiological results were consistent with these previously described psychological findings in demonstrating a dysfunctional visual pathway that is responsible for analyzing color information in ASD. The present study is the first study to elucidate an impaired function within the P-color pathway.

The P-color pathway anatomically interacts with the P-form pathway (Yabuta & Callaway, 1998). Although the P-form function itself was not assessed in the present study, the possibility that P-color dysfunction (color perception) and P-form biased function (detailed form perception) can be speculated based on abundant evidence of strength in fine form perception in ASD (Dakin & Frith, 2005). To test this hypothesis, further VEP studies are needed to evaluate P-form pathway functions using appropriate visual stimuli, such as high-contrast achromatic gratings with high spatial frequency in children, as well as adults with ASD.

4.2. Normal function of the magnocellular pathway within V1 in ASD

P neurons respond poorly to achromatic low-contrast patterns with high temporal frequency (Tobimatsu & Celesia, 2006). In the present study, there was no

significant difference in VEP responses to achromatic stimuli between the groups. This indicated that M pathway functions are preserved at a lower level in ASD adults.

Previous reports demonstrated an elevated motion coherence threshold in ASD (Spencer et al., 2000; Milne et al., 2002). An additional psychophysical study (Bertone et al., 2003) revealed that motion sensitivity in ASD was similar to control groups for first-order (luminance-defined) motion stimuli related to V1 function. However, second-order (texture-defined) motion stimuli related to V2/3 resulted in significantly decreased motion sensitivity in ASD patients, when compared to control groups. Moreover, relative to typical developing children (Pellicano et al., 2005), children with ASD displayed an elevated global motion threshold, in addition to equivalent flicker contrast sensitivity. These findings suggested abnormal functions in the higher-level M pathway in ASD patients, but an intact lower level in the M pathway, which further supported the present electrophysiological findings (normal functioning, lower-level M pathway).

The human visual system can detect a small percentage of coherently moving dots against incoherently moving dots (Baker et al., 1991). This ability depends on V5/MT integration of local motion signals from V1 into global motion (Snowden et al., 1991). Therefore, coherent motion stimuli are considered to be more useful than second-order motion to investigate a higher level of the M pathway. Accordingly, replication is necessary for children with ASD, and further VEP studies using coherent motion stimuli are needed to confirm whether the higher M pathway is functionally impaired in children, as well as adults, with ASD.

4.3. Methodological reservations

Although special care was taken when creating the appropriate visual stimuli for P-and M pathways, our sample size was relatively small. Clinical diagnoses were performed based on extensive clinical interviews, and standard interview tools, such as ADI-R or ADOS-G, were not used. Instead, a widely-used scale (PARS) was used to distinguish individuals with PDD of all ages with high sensitivity and high specificity in Japanese populations (Kamio et al., 2006). Intellectual functions were not assessed in the control participants but they were recruited from college students and faculties without developmental problems.

4.5. Conclusion

High-functioning adolescents and adults with ASD displayed a dysfunctional P pathway and a preserved M pathway, within the visual pathway of V1. These neurophysiological findings partly support the ñcomplexity-specificò hypothesis, rather than the ñpathway-specificò hypothesis. Furthermore, our results suggested color-processing abnormalities in high-functioning ASD. The P-form pathway within V1 as well as higher-level P and M pathway functions, however, should be fully investigated to determine the various visual pathway functions in ASD from a developmental perspective.

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Figure legends

Fig. 1 Visual chromatic (a) and achromatic (b) stimuli used in this study. (a) The equal luminance red/green chromatic sinusoidal gratings (visual angle, 10×10 deg; mean luminance, 21 cd/m^2; spatial frequency, 2 cycles/deg). Visual stimulus is surrounded by a homogeneous background, with a mixture of red and green colors (mean luminance, 21 cd/m^2). This pattern stimulus appears for 200 msec and is replaced by a homogeneous stimulus background for 1 sec. (b) The achromatic (black/white) sinusoidal gratings (visual angle, 10×10 deg; mean luminance, 21 cd/m^2; spatial frequency, 1 cycles/deg). Visual stimulus is surrounded by a homogeneous background, with a mixture of black and white colors (mean luminance, 21 cd/m^2; contrast, 16.6%). This stimulus is rapidly alternated in a square-wave fashion at 8 Hz (16 reversals/s) and appears for 2000 msec, followed by a homogenous background for 1 sec.

Fig. 2 Grand average waveforms of VEPs in response to chromatic stimuli at the Oz electrode in control (a) and ASD (b) groups. In both groups, a negative component around 100 msec (N1) is elicited, which is regarded as a major component.

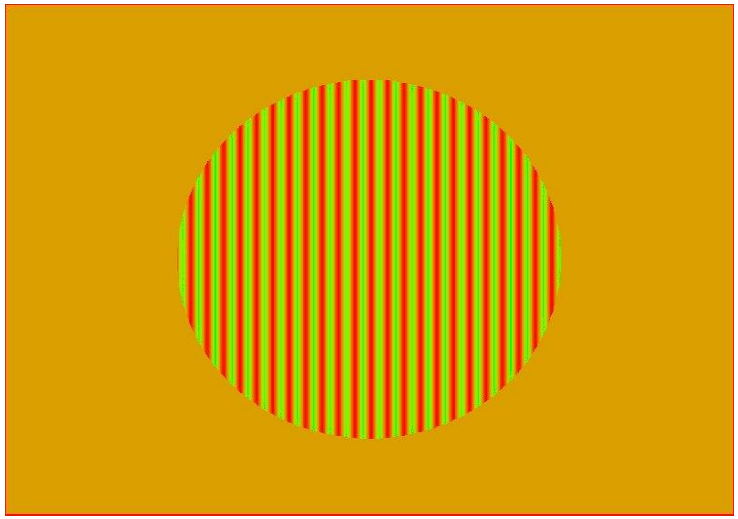
Fig. 3 Grand-averaged scalp topography of the N1 component in control (at 102 ms) (a) and ASD groups (at 108 ms) (b). In both groups, the N1 component is predominantly distributed at occipital areas (maximum at Oz). There is no obvious difference in N1 distribution between the two groups. L: left, R: right, A: anterior, P: posterior in this and Fig. 5.

Fig. 4 Representative waveforms of VEPs (a) and Fourier spectra (FFTs, b) in response to achromatic stimuli at the Oz electrode in control (left) and ASD (right) subjects. In both subjects, a positive component around 120 msec (P1) and quasi-sinusoidal waveforms correspond to the reversal frequency (16 Hz) (a). FFTs show that the second harmonic (2F) component is a major component in both groups (b).

Fig. 5 Grand-averaged scalp topography of steady-state responses (positive (a) and negative (b) phases) in control (left) and ASD (right) groups. In control group, scalp topography of positive phase at 787 ms (left, a) and negative phase at 755 ms (left, b) are mapped, while that of positive phase at 634 ms (right, a) and negative phase at 660 ms (right, b) are depicted in ASD group. In both groups, steady-state responses are predominantly distributed at occipital areas (maximum at Oz). There is no obvious difference in distribution of steady-state responses between the two groups.

Fig. 1

a) Chromatic gratings



b) Achromatic gratings

Fig. 2

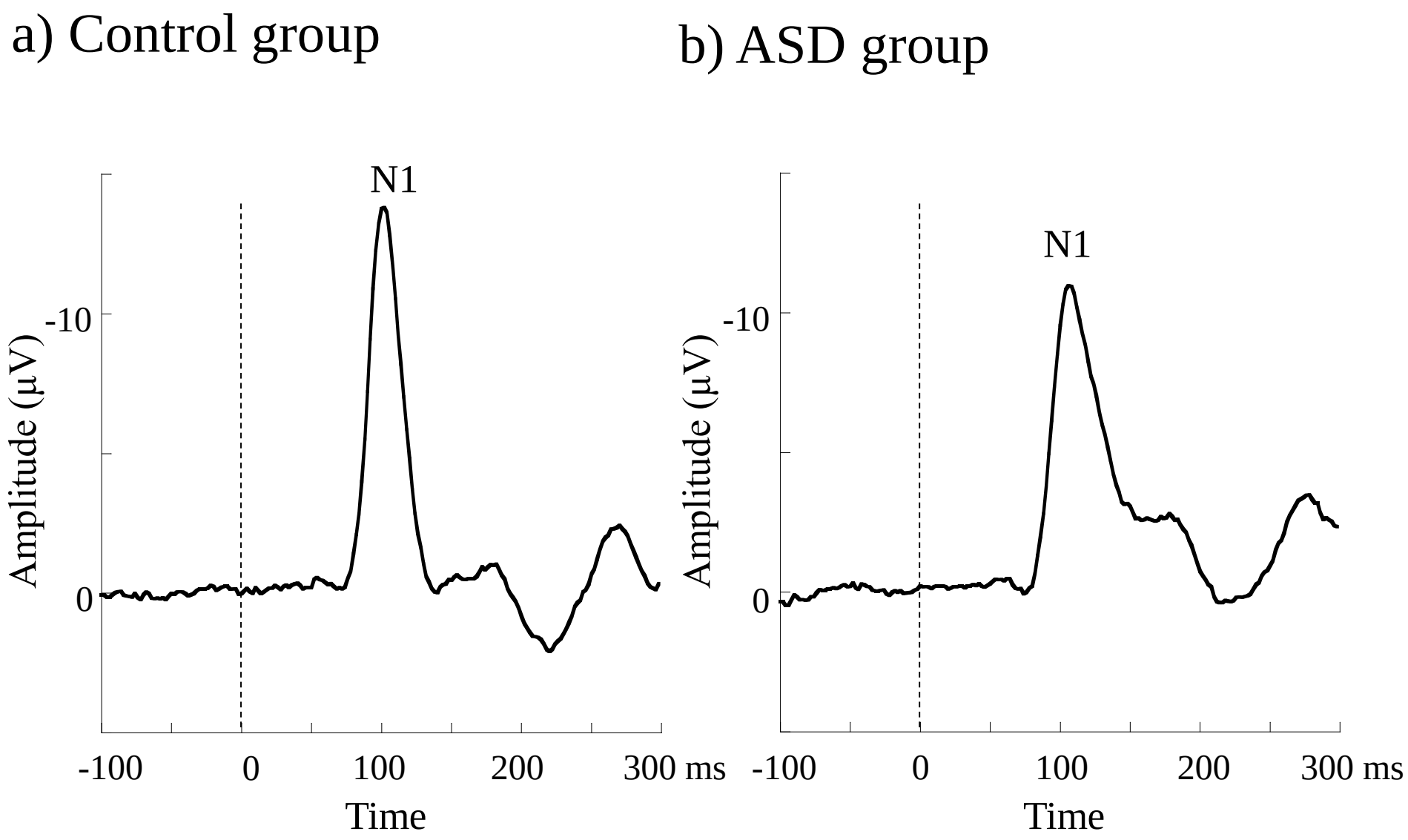

a) Control group
b) ASD group
N1
N1
-10
-10
0
0
Amplitude (μV)
Amplitude (μV)
-100
0
100
200
300 ms
-100
0
100
200
300 ms
Time
Time

Fig. 3

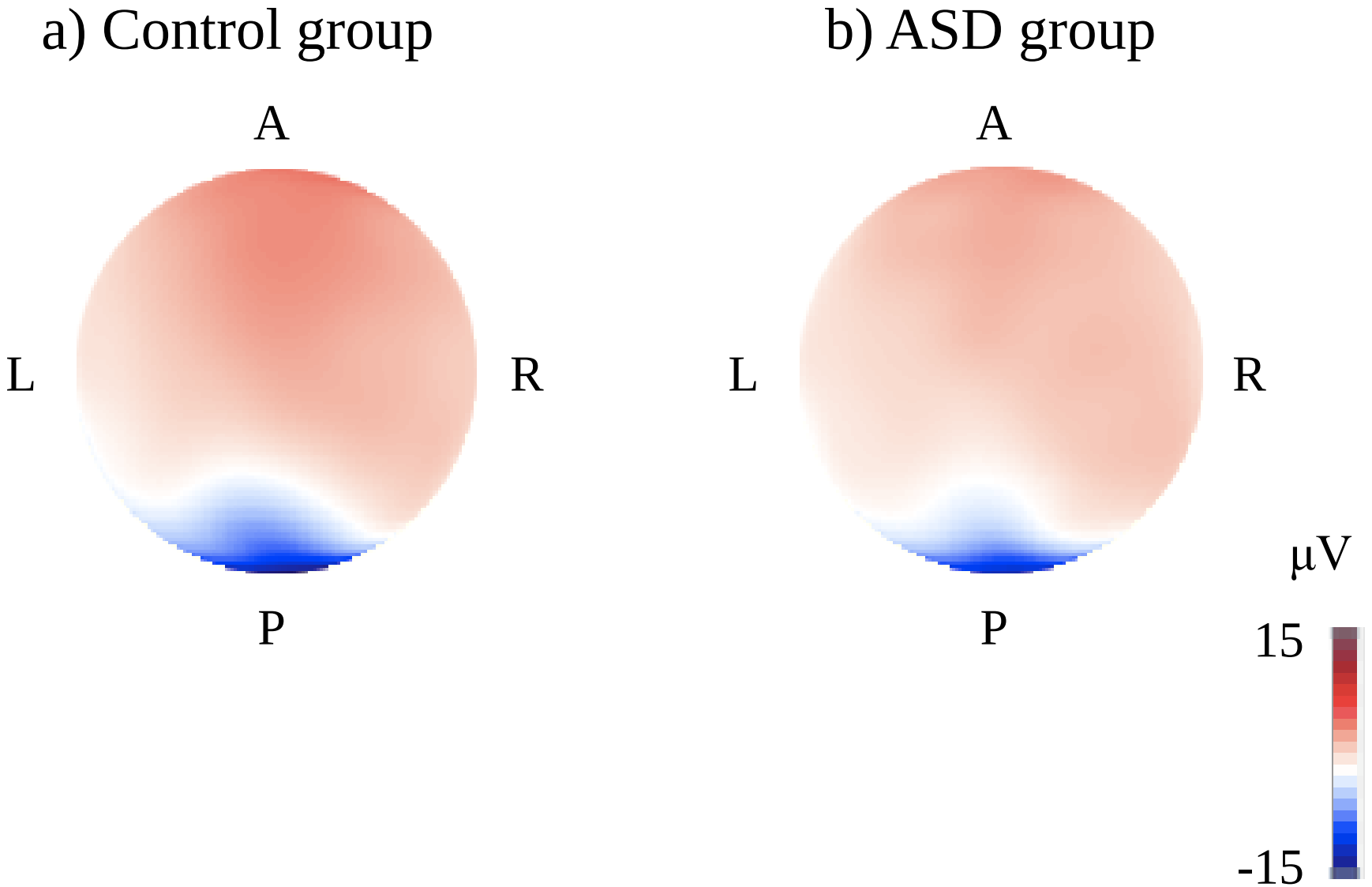


Fig. 4

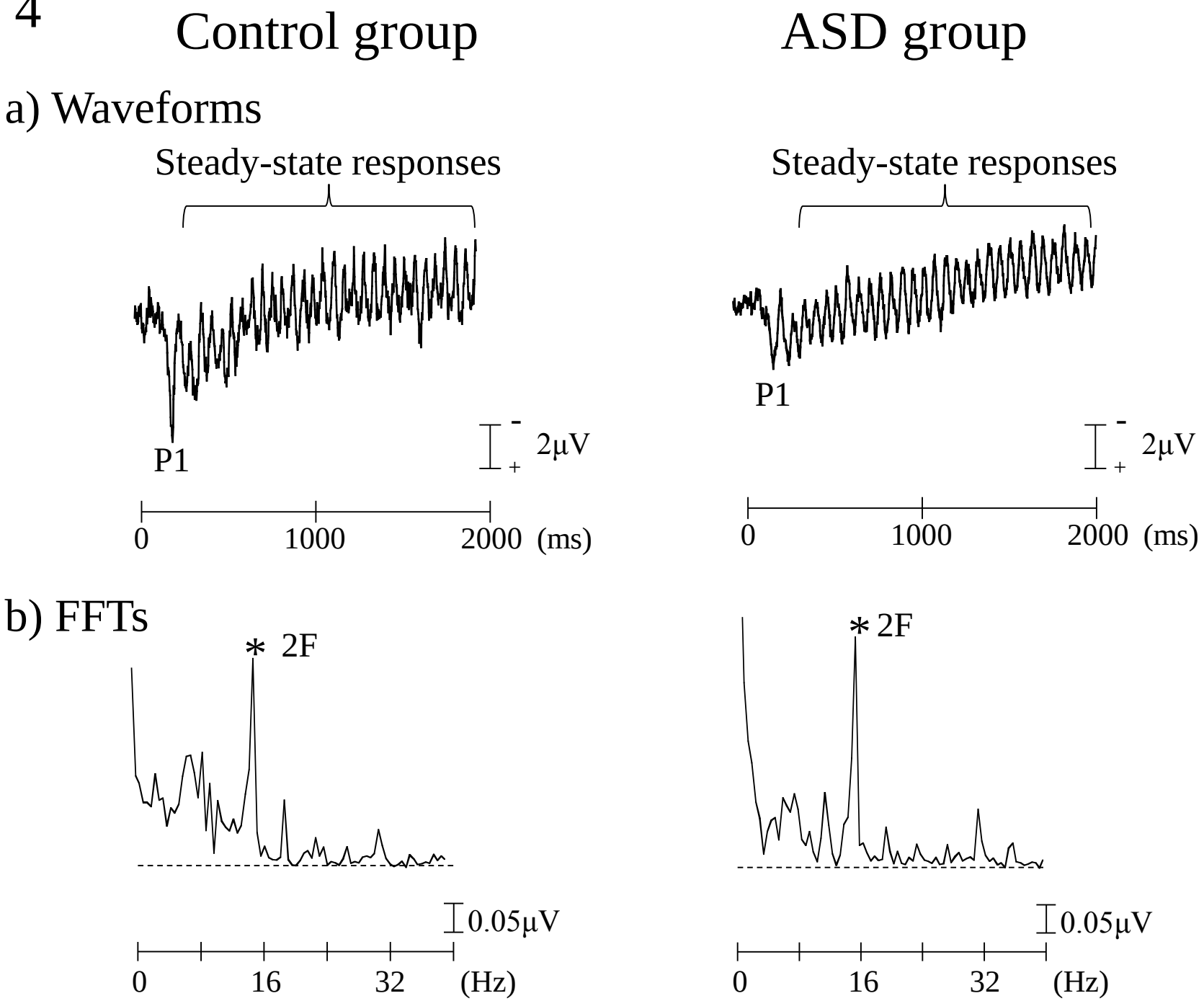
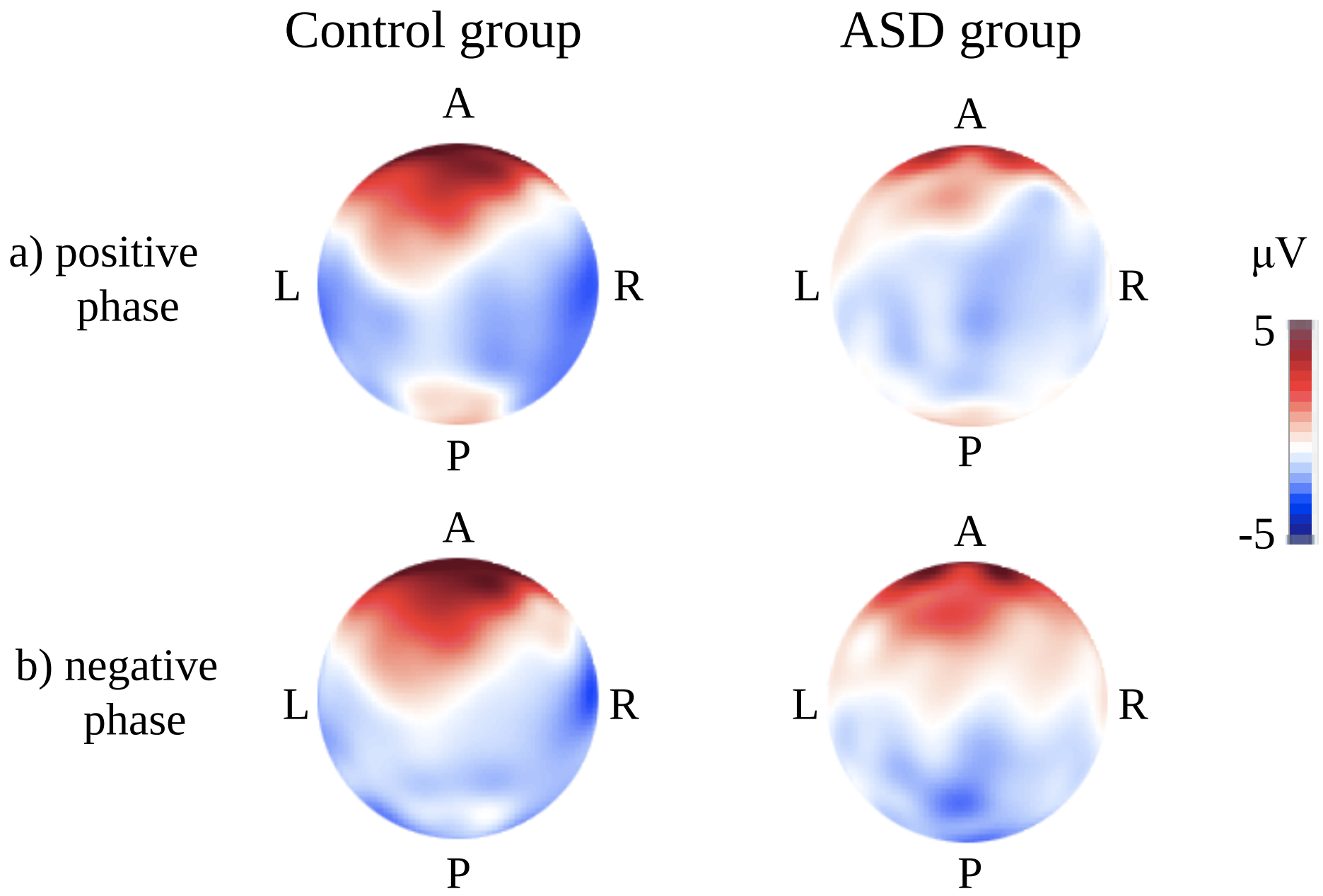

Control group
ASD group
a) Waveforms
Steady-state responses
Steady-state responses
P1
P1
2μV
2μV
0
1000
2000
(ms)
0
1000
2000
(ms)
b) FFTs
* 2F
* 2F
0.05μV
0.05μV
0
16
32
(Hz)
0
16
32
(Hz)

Fig. 5


Control group
ASD group
a) positive phase
b) negative phase
A
L
R
P
μV
5
-5