Cerebral laterality for phonemic and prosodic cue decoding in children with autism

Yasuyo Minagawa-Kawai[a,c], Nozomi Naoi[b,c], Naoko Kikuchi[b], Jun-ichi Yamamoto[b,c], Katsuki Nakamura[c,d] and Shozo Kojima[b,c]

This study examined the cerebral functional lateralization, from a phonological perspective, in children with autism spectrum disorder (ASD) and typically developing children (TDC). With near infrared spectroscopy, we measured auditory evoked-responses in the temporal areas to phonemic and prosodic contrasts in word contexts. The results of TDC showed stronger left-dominant and right-dominant responses to phonemic and prosodic differences, respectively. Furthermore, although ASD children displayed similar tendencies, the functional asymmetry for phonemic changes was relatively weak, suggesting less-specialized left-brain functions. The typical asymmetry for the prosodic condition was further discussed in terms of acoustic-physical perceptual ability of ASD children. The study revealed differential neural recruitment in decoding phonetic cues between ASD children and TDC and verified the applicability of near infrared spectroscopy as a suitable neuroimaging method for children with developmental disorders. *NeuroReport* 20:1219–1224 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.

NeuroReport 2009, **20**:1219–1224

Keywords: auditory area, cerebral lateralization, children with autism, near infrared spectroscopy, phoneme, prosody, speech perception

[a]Graduate School of Human Relations, [b]Department of Psychology, Keio University, Mita, Minato-ku, Tokyo [c]Japan Agency of Science and Technology, Saitama, Japan and [d]Primate Research Institute, Kyoto University, Aichi, Japan

Correspondence to Dr Yasuyo Minagawa-Kawai, PhD, 2-15-45 Mita, Minato-ku, Tokyo 108-8345, Japan
Tel: +81 3 5427 1156; fax: +81 3 5427 1209; e-mail: myasuyo@bea.hi-ho.ne.jp

Received 11 June 2009 **accepted** 14 June 2009

Introduction

Developmental language disorders – including language-specific impairment, dyslexia, and autism – are often discussed in relation to immature or atypical brain structures and networks with multiple genes involved [1–3]. In particular, atypical hemisphere specialization in speech processing has been one of the key issues that is not yet fully understood [1–3]. This study focuses on hemispheric specialization at the phonological level of speech processing in children with autism spectrum disorder (ASD).

The characteristics of the language problem in children with ASD vary considerably across children; of these children, some are unable to acquire speech. Even in children with verbal ability, language difficulties are often characterized by the atypical use of pragmatics [4]. However, some populations with ASD display phonological problems exemplified by impaired phonemic perception or difficulties in understanding prosody [5–7]. Deficits in this type of auditory perception have often been discussed in the context of the hemispheric specialization of the auditory cortex in processing temporal and spectral acoustic characteristics – that is, a specialized role of the left auditory cortex in processing rapidly changing stimuli (i.e., temporal variable) as in phonemes and that of the right cortex in tonal pitch perception (i.e., spectral variable) as in prosody [8–10]. In healthy participants, the neural recruitment of the temporal areas is determined by such acoustic factors as well as linguistic factors including semantics and phonology. As these two types of factors influence the brain activations differently depending on the task and stimulus patterns such as phonological category, context, and presentation, previous studies have found brain lateralization to sometimes be inconsistent [10–13]. However, it is at least clear that children with developmental disorders tend to show an atypical lateralization pattern in speech processing. In fact, previous near infrared spectroscopy (NIRS) studies [14,15] with phoneme and pitch contrasts have shown an abnormal cerebral lateralization pattern in children and adults who stutter. In ASD, atypical hemispheric specialization has been suggested as a possible cause of language disorder, as shown by a reduced right-ear advantage in dichotic listening tests [3] and atypical patterns of evoked responses to vowel or tone stimuli [1,2,8,16]. Despite this, however, only a few imaging studies have examined functional brain asymmetries in ASD by contrasting two types of stimuli that differ in acoustic properties.

This study examines functional lateralization (FL) from the perspective of phonological processing in children with ASD and typically developing children (TDC). Evoked responses to phonemic and prosodic contrasts were measured using NIRS. These phonemic and

0959-4965 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins DOI: 10.1097/WNR.0b013e32832fa65f

prosodic contrasts differed in terms of spectral and temporal acoustic properties at the speech level. This study has two purposes. Our principal aim is to examine cerebral lateralization associated with phonetic cue-decoding in children with autism. Second, we examine the practical use of NIRS to assess children with autism. NIRS is a noninvasive technique that can be used in natural experimental settings that do not require the participant's head to be fixated. To our knowledge, this study is the first in the literature to report an attempt to apply NIRS to children with autism.

Methods

Thirteen children with ASD and nine TDC participated in the NIRS recording. Data from nine children with ASD were analyzed as the final dataset, as some data were discarded due to motion artifacts. The mean age of the ASD group (seven boys and two girls) was 9.2 years (6–11 years, $SD = 1.8$). TDC (seven boys and two girls) had a mean age of 7.3 years (5–9 years, $SD = 1.7$). Handedness of TDC and the ASD group was assessed by using the Edinburgh Handedness Inventory [17]; the averaged laterality quotients (LQs) were 98.8 ($SD = 4$) for TDC and 96.6 ($SD = 6$) for ASD group with no significant difference between them ($t = 1.75$, $P = 0.27$). The quotients ranged from 88.2 to 100, showing all the participants are right handed.

All the participants in the ASD group met the criteria for autistic spectrum disorders [5] on the Autism Screening Questionnaire. The Vineland Adaptive Scale [18] and Weschler's Intelligence Scale for Children - third edition or the Kyoto Scale of Psychological Development were used to test their social and cognitive functions. Subgroups of high-functioning and low-functioning ASD were determined on the basis of a cut-off criterion of a complete intelligence quotient/developmental quotient score of 70 obtained in either Weschler's Intelligence Scale for children-third edition or The Kyoto Scale of Psychological Development. The ASD group included four low-functioning and five high-functioning children. Children with Asperger syndrome were not included in this group. Our experimental protocol was approved by the Ethic Committee of Keio University (No. 04001), and written informed consent in accordance with the protocol was obtained from the children's guardians before the experiment.

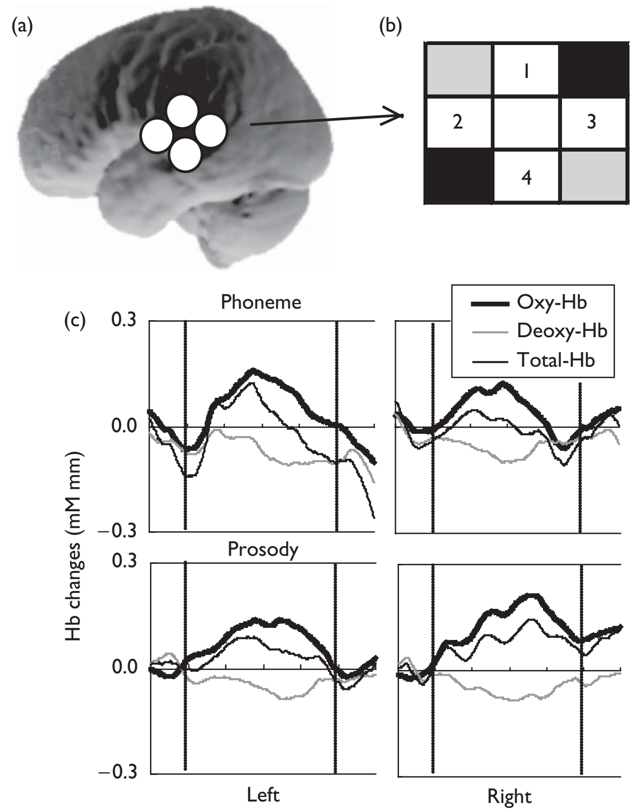
Three different forms of the Japanese verb /iku/ (go) were used as the stimuli: an affirmative form /itta/ (he/she has gone), an imperative form /itte/ (go away), and a interrogative form /itta?/ (has he/she gone?) [19]. The stimuli were produced using an analysis by the synthesis system (ASL, Kay Elemetrics Corporation, New Jersey, USA) based on a speech signal produced by a male adult. These three stimuli have identical first syllables and differ only in the final syllables. The phonemic contrasting pair /iita/ versus /itte/ has a different final vowel due to the manipulation of formants 1 and 2 but has identical falling pitches. The prosodic contrasting pair /iita/ versus /itta?/ is only different in pitch contours.

In the phonemic condition, the stimulus /itta/ was repeated at every 1 s for 20 s as a baseline block followed by another 20 s of a target block where /itte/ and /itta/ were presented in a pseudorandom order at every 1 s. These two blocks were repeated at least five times. In the prosodic condition, similar procedures were performed by using the prosodic contrasting stimuli /itta?/. The presentation order of these two conditions was counterbalanced.

Bilateral auditory areas were measured using NIRS (ETG 7000, Hitachi Medical Corporation, Tokyo, Japan). Using this instrument, changes in the concentration and oxygenation of hemoglobin (Hb) accompanying regional brain activities can be noninvasively measured by emitting and detecting continuous near-infrared lasers with two wave lengths. Two studies on adults used either NIRS or magnetoencephalography [14,19] and revealed auditory-evoked responses to the present stimuli in the auditory cortices. Therefore, in this study, the number of NIRS probes was limited to only cover the bilateral auditory areas. Accordingly, two incidents and two detection probes, each of which was separated by a 3-cm square lattice, were placed in each temporal area (Fig. 1). To make the probe positioning uniform for all the participants, the detector probe D was set to the T3 position and the located probe C-D line to approximately fit to the T4-Fp1-Fp2-T3 line in the international 10-20 system. The same procedure was undertaken for the right hemisphere. According to the estimation of the responses in the brain areas by using the NIRS channels through the spatial registration procedure of functional NIRS [20] and the findings of the previous studies [14,19], the auditory area including Wernicke's area were roughly covered in CH 1, CH 2 and CH 3.

The NIRS recording was performed in a sound-attenuated room, and stimuli were generated from an audio interface (Firewire 410; M-Audio, Irwindale, California, USA) and presented through a loud speaker (65 dB sound pressure level). During the stimulus presentation, the children were made to listen to the stimuli with one experimenter who tried to reduce their body movements by entertaining them with toys. All the experiments were DVD-recorded to monitor the children's body movement. After each session, the children were asked three questions to measure their phonetic and phonological perception of the presented stimuli: (i) did you hear only one type of sound or word? (correct answer: no), (ii) how many sounds did you hear? (correct answer: two), (iii) can

Fig. 1



(a) Approximate near infrared spectroscopy (NIRS) channel locations in the left hemisphere. The channel positions in the right side are symmetrical to this. (b) The optode and channel grids placed onto the participant's head. The detector below channels 3 was placed in the T3 position of the head. (c) The averaged NIRS responses [oxygenated hemoglobin (oxy-Hb), deoxygenated-Hb (deoxy-Hb), and total-Hb] to phonemic and prosodic conditions in the left and right hemispheres for children with autism. Moving average of 3 s was applied in this figure. Two vertical lines indicate the target block which has 20 s of duration.

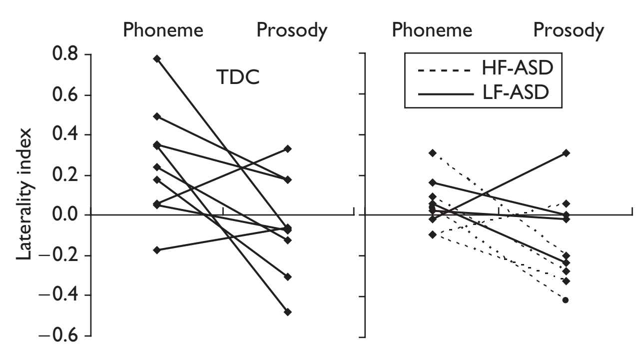
you tell me what those sounds are like? (correct answer: /itta/ and /itte/ or /itta/ and /itta?/). Each correct answer was counted as 1 point, adding up to a full score of 4 points in each condition. Although we asked the participants to listen to the stimuli carefully to answer the questions before the session, complete behavioral data from four ASD children were not successfully obtained due to the difficulty in getting clear answers.

Changes in the concentrations of oxygenated Hb, deoxygenated Hb, and total Hb [14] were calculated from the attenuation data of the 780 and 830 nm laser beams sampled at 10 Hz. After the removal of inappropriately fitted channels and blocks including motion artifact, all the data were averaged synchronously to the onset of the target blocks and smoothed with a 5 s moving average. After normalizing the target block data with a 10-s baseline period just before the target block, the response peaks of the averaged target block were evaluated. For further statistical analysis, by averaging the data of two conditions in each channel, one of the auditory channels on each side that showed maximal changes were chosen. Although the total Hb data was indicated, statistics was applied exclusively to values of the laterality index. This is to avoid the contamination of differential path length factors in Hb values as there had been two groups of participants who differed in age and, thus, in thickness of scalp and skull.

Results

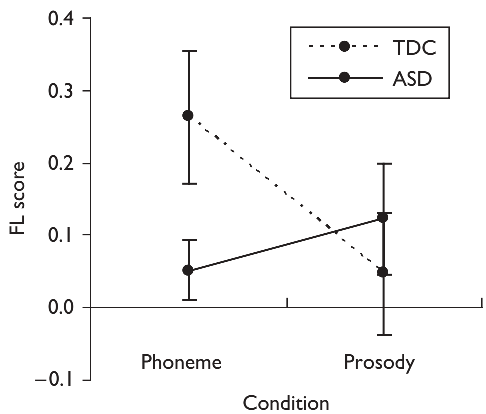
For both the TDC and ASD groups, consistent hemodynamic responses – peaking at 6–12 s after the stimulus onset – to the stimulus changes were observed in the auditory areas (Fig. 1). The averaged values of response peaks in mM mm on the left and right sides for the ASD group are: phoneme condition, left, 0.178 (SE 0.02); right, 0.171 (SE 0.02); prosody condition, left, 0.135 (SE 0.03); right, 0.174 (SE 0.04). Those for TDC are: phoneme condition, left, 0.173 (SE 0.02); right, 0.103 (SE 0.03); prosody condition, left, 0.126 (SE 0.01); right, 0.143 (SE 0.02). To examine the cerebral lateralization depending on the stimulus characteristic, a LQ was calculated using the formula $(L-R)/(L+R)$, where L and R are the maximum total Hb responses on the left and right side, respectively (Fig. 2). Overall, TDC displayed positive values for the phonemic condition against negative values for the prosodic condition. A similar tendency was observed in the ASD group; however, the differences between the two conditions are relatively small in comparison to the TDC group. The FL score was calculated by inverting the signs of the LQ values for the prosodic condition. The FL scores indicate the amplitude of hemispheric functional specialization; the higher the FL score, the stronger the leftward dominance for phonemic processing and the stronger the rightward dominance for prosodic processing. As seen in the strong FL in normal adults [14], the typicality of FL

Fig. 2



The laterality quotients for the phoneme and prosodic contrasts of typically developing children (TDC) and autism spectrum disorder (ASD) children. ASD has subgroups of low-function (LF)-ASD and high-function (HF)-ASD.

Fig. 3



Functional lateralization (FL) scores for typically developing children (TDC) and autism spectrum disorder (ASD) children in different conditions.

is also reflected in the FL score (Fig. 3). An analysis of variance with participant group and stimulus condition as factors was applied to the FL scores. As the interaction between the participant group and the stimulus condition was statistically marginal [$F(1,35) = 3.82$, $P = 0.065$], post-hoc tests were performed in addition. The results revealed a significant difference between the two groups exclusively in the phonemic condition ($P < 0.05$, $t = 2.13$), which indicates weaker lateralization for the ASD only in the phonemic condition.

The phonological behavioral scores for the phonemic condition were significantly lower in the ASD group (mean = 45.0%, SD = 20.9) than in TDC (mean = 80.5%, SD = 16.6) ($t = 3.50$, $P < 0.004$). The scores in the prosodic condition were also significantly lower in the ASD group (mean = 65.0%, SD = 28.5) than in TDC (mean = 91.6%, SD = 17.6) ($t = 2.18$, $P < 0.049$). The correlation coefficients between LQ and other measures including age, the handedness score, and the phonemic and prosodic behavioral scores did not reach significance. For the ASD group, only a moderate correlation was observed between age and the phonemic LQ ($R = 0.62$, $P = 0.09$), and an inverse correlation between LQ and prosodic behavioral score ($R = 0.80$, $P = 0.09$).

Discussion

This study tested a group of children with ASD for their FL in speech processing and some behavioral measures (Fig. 3). We then compared their LQ to phonemic and prosodic stimuli to the LQ of TDC. Although TDC clearly exhibited asymmetrical LQ in the phonemic and prosodic conditions, the ASD group showed a similar LQ pattern only in the prosodic condition, suggesting a weaker or differential cerebral lateralization with speech processing in children with ASD. In accordance with NIRS data, the ASD group exhibited lower scores for behavioral perception tests, although these behavioral data should be considered with a caution as different levels of intelligence and cognitive abilities may have lowered the score of the ASD group.

Although interhemispheric specialization in the temporal area may be chiefly driven by acoustic-physical factors of stimuli (temporal vs. spectral) [10–12], it is now apparent that linguistic factors play a crucial role in cerebral specialization in healthy adults [13]. For example, segmental features tend to induce left-dominant activations, whereas vowels are less likely to evoke left-dominance than consonant vowel syllables due to their acoustic nature [11,21]. However, linguistic information such as whether the vowel contrast is phonemically distinctive in the native language and whether it appears in the word context, seems to enhance the leftward lateralization [13,14,19,22–24]. In fact, as our stimuli occur in the context of words in which case changes in vowels switch the word meaning, left-dominant activation may be evoked in healthy adults [14]. In contrast, speech prosody is mediated primarily by the right hemisphere. However, there are far more complex factors that explain the laterality: although emotional prosody is basically processed in the right hemisphere, results from patients and imaging studies on linguistic prosody report both right-ward and left-ward dominance [14,24–26]. This divergence derives from the task or stimulus-dependent neural activation mechanism of linguistic prosody. The present investigation tested children with ASD using two types of stimuli that typically activate different hemispheres [14,19] without the need to perform any task. We revealed differential hemispheric asymmetries for two conditions in ASD children as compared with the case in TDC. The analysis of variance results showed an interaction between the participant group and stimulus condition. These were resulted from atypical FL for the left temporal area in response to phonemic changes in ASD children, in contrast to a typical pattern in prosodic processing. According to previous studies employing a similar task to ours on the left-hemispheric specialization in vowels [22,23], weak left dominance may be a cause of language disorders. A lack of left dominance suggests less-specialized brain functions and less-efficient cerebral networking for phonemic processing. This may impair phonemic or other higher processing such as morphology or semantics processing. The other possible interpretation of this data is that it is not the left temporal area but the right side that aggravates the function. Specifically, the hyperactivities in the right hemisphere in ASD children [27] may have affected the neural recruitment of the phonemic processing and lowered the LQ values. The total Hb values in the right auditory area, in fact, yielded larger values for the ASD than for TDC groups. However, due to the possible difference in the light path length of NIRS for different age groups, we cannot directly compare the Hb values for our participants in this study. Therefore, this interpretation of right-hyperactivity remains speculative.

In this section, it is important to discuss why the ASD group showed a typical LQ pattern only in the prosodic condition, regardless of their lower behavioral scores. This can be explained by two levels of neural processing: acoustic-sensory and linguistic levels. Unlike the left-dominant network for phonemic or semantic processing, the extent to which pure linguistic factors are related to the right temporal network for speech prosody [28] is unclear. It is possible that speech prosody is chiefly processed in the right hemisphere – not because of this hemisphere's distinct network solely dedicated to linguistic prosody but because of its shared networks that process the acoustic properties of long-term spectral changes [26], as in music. It is well known that musicians perform better in extracting prosodic information than do nonmusicians [29]. Given this, it is possible that in ASD, right-dominant responses to prosodic changes reflect perceptual processing at the acoustic-physical level and indicate normal or considerably enhanced sensory processing at this early level. However, ASD may exhibit a problem at a later stage when a prosodic contour is combined with semantic or syntactic factors. This inference is supported by the fact that children with autism show normal or over-specialized music and pitch perceptions [30]. Recent behavioral studies have reported that children with ASD are superior in perceptually processing speech contours but inferior in semantically judging contour meaning [6]. Further study using speech and nonspeech stimuli, perhaps considering additional NIRS channels, is required to elucidate whether the right dominance in the ASD group is attributable to the acoustic-perceptual level or linguistic aspects of prosody. Furthermore, the prefrontal region may also be another factor contributing to impaired prosodic processing in relation to attention deficits [31]. It is possible that such attentional deficits may have reduced the behavioral scores in the ASD group.

Conclusion

This study shows that the use of NIRS for functional imaging is particularly suitable for children with disabilities who are often resistant to staying still. Although almost all the previous imaging studies on ASD tested high-functioning children with ASD, our NIRS study successfully measured low-functioning children with ASD. Above all, by using temporally and spectrally different speech stimuli in linguistic contexts, this study reveals a dissociated pattern of functional cerebral lateralization in phonemic and prosodic changes in children with ASD.

Acknowledgements

The authors thank R. Tsuchiya for help with recruiting children, S. Minagawa for help with the experiment, T. Imaizumi for providing us with the sound stimuli, F. Ramus for comments on the first draft, and S. Harcourt-Brown for assistance with English in the first draft. This work was supported by Japan Agency of Science and Technology and the Global COE (Center of Excellence) program Keio University.

References

1 Flagg EJ, Cardy JE, Roberts W, Roberts TP. Language lateralization development in children with autism: insights from the late field magnetoencephalogram. *Neurosci Lett* 2005; **386**:82–87.
2 Oram Cardy JE, Flagg EJ, Roberts W, Roberts TP. Delayed mismatch field for speech and non-speech sounds in children with autism. *Neuroreport* 2005; **16**:521–525.
3 Prior MR, Bradshaw JL. Hemisphere functioning in autistic children. *Cortex* 1979; **15**:73–81.
4 Martin I, McDonald S. Weak coherence, no theory of mind, or executive dysfunction? Solving the puzzle of pragmatic language disorders. *Brain Lang* 2003; **85**:451–466.
5 American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders. Text revision.* 4th ed. Washington, DC: American Psychiatric Association; 2000.
6 Järvinen-Pasley A, Wallace GL, Ramus F, Happé F, Heaton P. Enhanced perceptual processing of speech in autism. *Dev Sci* 2008; **11**:109–121.
7 Kujala T, Lepisto T, Nieminen-von Wendt T, Näätänen P, Näätänen R. Neurophysiological evidence for cortical discrimination impairment of prosody in Asperger syndrome. *Neurosci Lett* 2005; **383**:260–265.
8 Gage NM, Siegel B, Callen M, Roberts TPL. Cortical sound processing in children with autism disorder: an MEG investigation. *Neuroreport* 2003; **14**:2047–2051.
9 Samson F, Mottron L, Jemel B, Belin P, Ciocca V. Can spectro-temporal complexity explain the autistic pattern of performance on auditory tasks? *J Autism Dev Disord* 2006; **36**:65–76.
10 Zatorre RJ, Belin P. Spectral and temporal processing in human auditory cortex. *Cereb Cortex* 2001; **11**:946–953.
11 Jäncke L, Wüstenberg T, Scheich H, Heinze HJ. Phonetic perception and the temporal cortex. *Neuroimage* 2002; **15**:733–746.
12 Zaehle T, Jancke L, Meyer M. Electrical brain imaging evidences left auditory cortex involvement in speech and non-speech discrimination based on temporal features. *Behav Brain Funct* 2007; **3**:63.
13 Zatorre RJ, Gandour JT. Neural specializations for speech and pitch: moving beyond the dichotomies. *Philos Trans R Soc Lond B Biol Sci* 2008; **363**:1087–1104.
14 Furuya I, Mori K. Cerebral lateralization in spoken language processing measured by multi-channel near-infrared spectroscopy NIRS. *Brain Nerve* 2003; **55**:226–231.
15 Sato Y, Mori K, Koizumi T, Minagawa-Kawai Y, Tanaka A, Ozawa E. Functional lateralization in stutterers during spoken word: processing, measured by near-infrared spectroscopy. *Jpn J Logoped Phoniatr* 2004; **45**:181–186.
16 Gage NM, Siegel B, Roberts TP. Cortical auditory system maturational abnormalities in children with autism disorder: an MEG investigation. *Brain Res Dev Brain Res* 2003; **1442**:201–209.
17 Oldfield R. The assessment and analysis of handedness: the Edinburgh Inventory. *Neuropsychologia* 1971; **9**:97–113.
18 Sparrow SS, Balla DA, Cicchetti DV. *The Vineland Adaptive Behavior scales.* Circle Pines, Minnesota: American Guidance Service; 1984.
19 Imaizumi S, Mori K, Kiritani S, Hosoi H, Tonoike M. Task-dependent laterality for cue decoding during spoken language processing. *Neuroreport* 1998; **9**:899–903.
20 Okamoto M, Dan H, Sakamoto K, Takeo K, Shimizu K, Kohno S, *et al.* Three-dimensional probabilistic anatomical cranio-cerebral correlation via the international 10–20 system oriented for transcranial functional brain mapping. *Neuroimage* 2004; **21**:99–111.
21 Shankweiler D, Studdert-Kennedy M. Identification of consonants and vowels presented to left and right ears. *Q J Exp Psychol* 1967; **19**:59–63.

22 Minagawa-Kawai Y, Mori K, Naoi N, Kojima S. Neural attunement processes in infants during the acquisition of a language-specific phonemic contrast. *J Neurosci* 2007; **26**:315–321.

23 Näätänen R, Lehtokoski A, Lennes M, Cheour M, Huotilainen M, Iivonen A, *et al*. Language-specific phoneme representations revealed by electric and magnetic brain responses. *Nature* 1997; **385**:432–434.

24 Shtyrov Y, Pihko E, Pulvermuller F. Determinants of dominance: is language laterality explained by physical or linguistic features of speech? *Neuroimage* 2008; **27**:37–47.

25 Bradvik B, Dravins C, Holtas S, Rosen I, Ryding E, Ingvar D. Disturbances of speech prosody following right hemisphere infarcts. *Acta Neurol Scand* 1991; **84**:114–126.

26 Wildgruber D, Ackermann H, Kreifelts B, Ethofer T. Cerebral processing of linguistic and emotional prosody: fMRI studies. *Prog Brain Res* 2006; **156**:249–268.

27 Mason RA, Williams DL, Kana RK, Minshew N, Just MA. Theory of Mind disruption and recruitment of the right hemisphere during narrative comprehension in autism. *Neuropsychologia* 2008; **46**:269–280.

28 Emmorey K. The neurological substrates for prosodic aspects of speech. *Brain Lang* 1987; **30**:305–320.

29 Marques C, Moreno S, Castro S L, Besson M. Musicians detect pitch violation in a foreign language better than nonmusicians: behavioral and electrophysiological evidence. *J Cogn Neurosci* 2007; **19**:1453–1463.

30 Mottron L, Peretz I, Ménard E. Local and global processing of music in high-functioning persons with autism: beyond central coherence? *J Child Psychol Psychiatry* 2000; **41**:1057–1065.

31 Čeponiené R, Lepisto T, Shestakova A, Vanhala R, Alku P, Näätänen R, *et al*. Speech-sound selective auditory impairment in children with autism: they can perceive but do not attend. *Proc Natl Acad Sci* 2003; **100**:5567–5572.