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Language-related cerebral oscillatory changes are influenced equally by genetic and environmental factors

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ABSTRACT

Twin studies have suggested that there are genetic influences on inter-individual variation in terms of verbal abilities, and candidate genes have been identified by genome-wide association studies. However, the brain activities under genetic influence during linguistic processing remain unclear. In this study, we investigated neuromagnetic activities during a language task in a group of 28 monozygotic (MZ) and 12 dizygotic (DZ) adult twin pairs. We examined the spatio-temporal distribution of the event-related desynchronizations (ERDs) in the low gamma band (25–50 Hz) using beamformer analyses and time–frequency analyses. Heritability was evaluated by comparing the respective MZ and DZ correlations. The genetic and environmental contributions were then estimated by structural equation modeling (SEM). We found that the peaks of the low gamma ERDs were localized to the left frontal area. The power of low gamma ERDs in this area exhibited higher similarity between MZ twins than that between DZ twins. SEM estimated the genetic contribution as approximately 50%. In addition, these powers were negatively correlated with the behavioral verbal scores. These results improve our understanding of how genetic and environmental factors influence cerebral activities during linguistic processes.

Introduction

Language functions are affected by not only environmental but also genetic influences. Children learn their native languages within a few years, without the aid of analytical thinking and without explicit grammar instruction as generally taught in schools. Thus, genetic influences play an important role in language functions. Previously, a large-scale twin study based on a verbal battery test showed that genetic effects accounted for approximately 65% of the verbal ability (Plomin and Craig, 1997). Recently, several genes with prominent roles in language development and ability have been identified by the advances in genetic and genomic analyses of speech and language disorders (Szalontai and

Abbreviations: AIC, Akaike's information criterion; BA, Brodmann area; CNTNAP2, contactin-associated protein-like 2 gene; DZ, dizygotic; ERD, event-related desynchronization; ERSP, event-related spectral perturbation; ERS, event-related synchronizations; fMRI, functional magnetic resonance imaging; ICC, intra-class correlation; MEG, magnetoencephalography; MZ, monozygotic; MNI, Montreal Neurological Institute; SEM, structural equation modeling; SPM8, Statistical Parametric Mapping 8; WMS-R, Wechsler Memory Scale-Revised.

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Csiszar, 2013; Konopka and Roberts, 2016; Mozzi et al., 2016). Therefore, language-related cerebral activities are also considered to be affected by genetic influences.

Many neuroimaging studies have demonstrated that several cortical regions contribute to the processing of language function, such as the lateral prefrontal area and dorsal temporal area (Koechlin and Jubault, 2006; Warburton et al., 1996). Recently, using magnetoencephalography (MEG), the frequency-dependent spatio-temporal modulations of the cerebral oscillation, e.g., attenuation of its power, which are referred to as event-related desynchronizations (ERDs), were associated with language functions (Cornelissen et al., 2009; Goto et al., 2011; Shinshi et al., 2015). In particular, Hirata et al. (2010) showed that the lateralization of beta (13–25 Hz) or low gamma (25–50 Hz) ERDs in the lateral prefrontal area corresponded well with language dominance and localization. However, some individual differences exist in the spatio-temporal patterns of language-related ERDs (Hirata et al., 2004), and little is known about the factors responsible for individual differences in these ERDs. Moreover, it is unclear how language-related ERDs are related to verbal ability.

In this study, we hypothesized that language-related ERDs are affected by genetic and environmental influences based on an assumption that genetically identical brains function differently following long-term exposure to different environments, thereby reflecting brain plasticity.

To estimate the genetic and environmental influences on the language-related ERDs, we conducted a twin study. Twin studies based on comparisons of monozygotic (MZ) and dizygotic (DZ) twins are useful for investigating genetic and environmental effects, assuming that MZ twins share 100% of their genes, whereas DZ twins only share half of their segregating genes on average. Many studies have compared the similarities in brain activity between MZ twins and DZ twins using electroencephalography (Begleiter and Porjesz, 2006; Smit et al., 2005), MEG (Ahveninen et al., 2006; Van't Ent et al., 2010), and functional magnetic resonance imaging (fMRI) (Moodie et al., 2014; Pinel and Dehaene, 2013). For example, in terms of visual function, an MEG study showed that the peak frequency of the gamma-band synchronization in the visual cortex was highly correlated in MZ twins, but not in DZ twins or genetically unrelated subjects, and the heritability of the gamma-band frequency was approximately 90% (van Pelt et al., 2012). However, no functional neuroimaging or neurophysiological studies have demonstrated genetic and environmental effects on language processing.

The aim of this study was to determine the relative contributions of genetic and environmental effects to language-related brain activity by comparing the power of ERDs in the low gamma band during a verb generation task using adult MZ twins and DZ twins. We also examined the correlations between the individual powers of ERDs and behavioral verbal scores with respect to language to determine the relationship between language-related ERDs and verbal ability.

Materials and methods

Subjects

Japanese twins were recruited by the Osaka University Center for Twin Research. The eligibility criteria required that the twins were over 20 years of age and both twins were capable of attending the research center at the same time. We assessed 28 pairs of MZ twins (mean age $\pm$ SD $=$ 57.8 $\pm$ 12.5 years) and 12 pairs of DZ twins (mean age $\pm$ SD $=$ 60.4 $\pm$ 16.9 years). The MZ group comprised nine male and 19 female twin pairs, and the DZ group comprised six male and six female twin pairs. All of the subjects were native Japanese speakers who were determined as right-handed based on their scores in the Edinburgh Handedness Inventory (Oldfield, 1971). All subjects had no history of neurological or psychiatric episodes. Written informed consent was obtained from all subjects after explaining the purpose and possible consequences of the study. This study was approved by the ethics committee of Osaka University Graduate School of Medicine (No. 10190).

The zygosity of the pairs was confirmed using 15 short tandem repeat markers derived from the blood, which have been demonstrated as both accurate and reliable by previous studies (Krenke et al., 2002; Yang et al., 2006). Twin pairs that agreed completely for these short tandem repeat markers were designated as monozygotic, whereas all of the other pairs were designated as dizygotic.

MEG task

A verb generation task was performed during MEG measurements for each subject. Japanese semantic words comprising three Japanese hiragana or katakana characters were used as visual stimuli. Each word was one monomorphemic and monosyllabic three-mora Japanese word (e.g., あひる: duck, メロン: melon, etc.) selected from the standard reference of lexical properties of Japanese (Amano et al., 2007; Amano and Kondo, 2000). A word was presented visually for 3 s after the presentation of a control stimulus for 3 s. As the control stimulus, the randomized dot patterns of the corresponding word were randomized spatially. In addition, an eye-fixation point was presented at the center of the display. In total, 100 words were presented in series. Subjects were instructed to silently read each presented word only one time immediately after word presentation, before silently generating a verb associated with the word without moving their mouths.

MEG measurements

Neuromagnetic activities were recorded in a magnetically-shielded room using a 160-channel whole-head MEG system equipped with coaxial type gradiometers (MEG Vision NEO; Yokogawa Electric Corporation, Japan). Subjects lay in a supine position on the bed with their head centered. Visual stimuli were displayed on a projection screen, 325 mm from the subject's eyes, using a visual presentation system (Presentation; Neurobehavioral Systems, USA) and a liquid-crystal projector (LVP-HC6800; Mitsubishi Electric Corporation, Japan).

Anatomical magnetic resonance imaging (MRI) data were obtained using a 3.0-T magnetic resonance scanner with an 8-channel whole-head coil (Signa Excite HDxt 3.0T; GE Healthcare, USA). In order to align the MEG data with individual MRI data, we scanned the three-dimensional facial surface of each subject (FastSCAN Cobra; Aranz Scanning Ltd., New Zealand). Five head marker coils were attached to the scalp before recording MEG, which provided the approximate position and orientation of the MEG sensors relative to the head. The three-dimensional facial surface data were superimposed onto the anatomical facial surface obtained from the MRI data.

The MEG data were sampled at a rate of 1000 Hz with an online low-pass filter at 200 Hz. To reduce contamination from muscle activities and eye movements, we instructed the subjects to avoid body movements and to watch the center of the display without moving their eyes. After data acquisition, a 60-Hz notch filter was employed to eliminate the AC line noise and eye blink artifacts were rejected by applying the signal-space projection, which is one of the approaches included in the Brainstorm program (http://neuroimage.usc.edu/brainstorm) to reject external disturbances (Tadel et al., 2011).

Beamformer and group statistical analyses

The MEG data were analyzed using a beamformer method, which is a narrow-band adaptive spatial filtering method (Dalal et al., 2008). Estimates of differences in the source power between the control period and the period of interest for selected frequency bands and time windows were computed as pseudo-T values (Hirata et al., 2004). The distribution of the pseudo-T values was then superimposed onto the individual anatomical MRIs coregistered to the MEG data. Positive and negative values indicated event-related synchronization (ERS) and ERD, respectively.

The beamformer analyses created a volume that covered the whole brain of each individual with a voxel size of $5 \times 5 \times 5$ mm. The control