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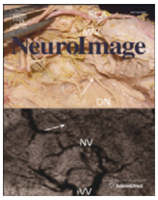

Spatial variability of functional brain networks in early-blind and sighted subjects

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ABSTRACT

To further the understanding how the human brain adapts to early-onset blindness, we searched in early-blind and normally-sighted subjects for functional brain networks showing the most and least spatial variabilities across subjects. We hypothesized that the functional networks compensating for early-onset blindness undergo cortical reorganization. To determine whether reorganization of functional networks affects spatial variability, we used functional magnetic resonance imaging to compare brain networks, derived by independent component analysis, of 7 early-blind and 7 sighted subjects while they rested or listened to an audio drama. In both conditions, the blind compared with sighted subjects showed more spatial variability in a bilateral parietal network (comprising the inferior parietal and angular gyri and precuneus) and in a bilateral auditory network (comprising the superior temporal gyri). In contrast, a vision-related left-hemisphere-lateralized occipital network (comprising the superior, middle and inferior occipital gyri, fusiform and lingual gyri, and the calcarine sulcus) was less variable in blind than sighted subjects. Another visual network and a tactile network were spatially more variable in the blind than sighted subjects in one condition. We contemplate whether our results on inter-subject spatial variability of brain networks are related to experience-dependent brain plasticity, and we suggest that auditory and parietal networks undergo a stronger experience-dependent reorganization in the early-blind than sighted subjects while the opposite is true for the vision-related occipital network.

Introduction

Congenital or early blindness affects the structure and function of the brain (Pascual-Leone et al., 2005). Although knowledge about the neural mechanisms underlying brain plasticity following early blindness is accumulating, a more thorough comprehension of experience-dependent brain plasticity is required and could aid e.g. in the development of sensory substitution devices for the blind. It is thus important to understand how the human brain adapts to missing sensory input. Recent methodological advances have provided new ways to study brain organization and plasticity. One rapidly growing field is the study of functionally-connected brain networks (Calhoun and Adali, 2012), such as the "resting-state networks". Commonly studied resting-state networks include (i) the default-mode network comprising areas within the posterior cingulate and precuneus, the parietal lobes bilaterally, and the medial prefrontal cortex (Raichle et al., 2001), (ii) the motor/sensory network comprising the pre- and postcentral gyri, and the premotor and supplementary motor areas (Biswal et al., 1995), (iii) the vision-related occipital network, and (iv) the superior temporal network covering auditory cortices (Damoiseaux et al., 2006). Topographies of these brain networks are rather similar both during rest and task performance (Smith et al., 2009), although hubs may shift during tasks, suggesting a more efficient information transmission (Di et al., 2013). As blind subjects cannot execute visual tasks, resting-state studies could be helpful in unraveling the functional connectivity of visual areas.

Early-blind subjects can have improved auditory and tactile abilities or maladjustments in senses other than vision. These two types of alterations are addressed by the compensatory-plasticity hypothesis and the general-loss hypothesis, respectively (Pascual-Leone et al., 2005). Early-blind subjects often perform better than sighted subjects in auditory (Gougoux et al., 2004, 2005) and tactile tasks (Goldreich and Kanics, 2003; Wan et al., 2010), which lends support to the compensatory-plasticity hypothesis. On the other hand, the general-loss hypothesis is supported by findings that blind subjects perform poorly in auditory localization tasks that seem to benefit from intact vision (Gori et al., 2014; Zwiers et al., 2001) and in tasks requiring auditory–tactile interaction in the peripersonal space (Collignon et al., 2009).

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Resting-state functional magnetic resonance imaging (fMRI) studies comparing early-blind with sighted subjects show reduced functional connectivity—in accordance with the general-loss hypothesis—within occipital areas and within a wide network extending from occipital to parietal somatosensory, frontal motor, and temporal multisensory areas (Yu et al., 2008). On the other hand, functional connectivity between visual and language areas is enhanced in anophthalmic (Watkins et al., 2012) and early-blind subjects, supporting the compensatory-plasticity hypothesis (Liu et al., 2007).

The structure and function of resting-state networks, such as the default-mode network and language-related networks, are in part genetically determined (Glahn et al., 2010; Jamadar et al., 2013). Environmental influences and experience, including practice (Jang et al., 2011) and disease (Greicius et al., 2004), however, induce changes in these networks. Accordingly, the investigation of variability in functional networks provides one approach to explore how experience, including early blindness, affects the brain (Lee et al., 2012; Liu et al., 2007; Mueller et al., 2013). Importantly, individual variability should not be considered noise, but rather as an essential feature helping to understand how the brain matures (Zilles and Amunts, 2013). Therefore, it is conceivable that sensory loss may affect brain structure and function in a variable manner and result in increased individual variability of functional brain networks.

We hypothesized that experience-dependent brain plasticity is reflected in inter-subject spatial variability of functional networks. In line with this hypothesis, the brain regions of children communicate locally with other regions, but with increasing age communication becomes more distributed as a result of experience-dependent processes (Fair et al., 2009; Satterthwaite et al., 2013). We explored whether the networks compensating for early-onset visual deprivation would exhibit more inter-subject spatial variability in the early-blind than sighted subjects. We also investigated whether some of the networks that are little used after early-onset visual deprivation, e.g. occipital networks devoid of visual input, would exhibit less inter-subject spatial variability in the blind than the sighted subjects. We estimated functional networks with independent component analysis (ICA) that, in contrast to seed-based correlation analysis, requires no anatomical seed regions and can reliably reveal comparable intrinsic and task-related connectivity patterns (Smith et al., 2009), despite coactivation of distinct networks during tasks (Joel et al., 2011). Thus ICA allowed us to compare the functional networks found in the data collected during rest and audio-drama listening. We also searched for possible between-group differences in functional network connectivity (Jafri et al., 2008) in the networks displaying large spatial variability between the blind and sighted subjects.

We analyzed both resting-state data and data collected while the subjects listened to an audio drama. In line with our hypothesis, the functional networks showing more variability in the blind than the sighted subjects encompassed auditory, parietal, and sensorimotor areas, i.e. regions that are modulated by altered sensory experience due to early-onset blindness. One network that encompassed visual occipital areas was less variable in the blind than sighted subjects.

Methods

Subjects

Seven early-blind subjects (4 females, 3 males; age range 19–43 years, mean age 34 years; 6 right-handed and one ambidextrous by report; see Table 1 for the causes and durations of the blindness) and 16 normally-sighted subjects (7 females, 9 males; age range 19–37 years; mean age 24 years, all right-handed by report) with no recorded history of neurological or psychiatric problems participated in the experiment; the data of 13 normally-sighted subjects were obtained from our previous study (Boldt et al., 2013). All blind subjects read Braille (mean ± SD 4.9 ± 2.6 h/week; range 2–8). For the main analysis, an age- and gender-matched control group (4 females, 3 males; age range 19–37 years, mean age 27 years) was formed of the sighted subjects; the data of the remaining 9 normally-sighted subjects were only used for creating a reference distribution (see Creating a reference distribution section). The subjects were native Finns and fluent in Finnish although one blind and one sighted subject included in the main analysis were Swedish-speaking bilinguals. The subjects participated after informed consent, and the study was approved by the ethics committee of the Helsinki and Uusimaa Hospital District.

Data acquisition and preprocessing

MRI data were obtained with a Signa VH/i 3.0 T MRI scanner (General Electric, Milwaukee, WI, USA). First, a structural image of 178 axial slices was acquired using a T1-weighted 3D-MPRAGE-sequence, TR = 10 ms, TE = 30 ms, preparation time = 300 ms, flip angle = 15°, FOV = 25.6 cm, matrix = 256 × 256, and voxel size = $1 \times 1 \times 1$ mm^3. Next, functional images were acquired using a gradient echo-planar-imaging sequence with the following parameters: TR = 2.5 s, TE = 30 ms, flip angle = 75°, FOV = 22.0 cm, matrix = 64 × 64, slice thickness = 3.5 mm, voxel size = $3.4 \times 3.4 \times 3.5$ mm^3 and number of oblique axial slices = 43. Slices were obtained using interleaved acquisition. Altogether 246 functional volumes were collected, but the first 6 dummy volumes were automatically discarded. The resting-state scan lasted about 10 min. Subjects were instructed to lie still with their eyes closed, not to fall asleep and not to think of anything in particular. After the resting-state scan, an audio drama was presented (Boldt et al., 2013). The functional images during the audio drama were acquired using the same parameters as in the resting-state scan, but the scan lasted about 19 min resulting in 456 functional volumes. We refer to this set of data as the audio-drama data.

As described in detail in our previous study of normally-sighted subjects (Boldt et al., 2013), the audio drama comprised sequences from a Finnish movie "Postia Pappi Jaakobille" ("Letters to Father Jaakob", director Klaus Härö, Production company: Kinotar Oy, Finland, 2009), in which a woman arrives at a run-down parsonage to help an old blind priest. The stimulus included sounds from the original movie, and a narration for blind people. The audio drama was presented binaurally with UNIDES ADU2a audio system (Unides Design, Helsinki, Finland) from a

Table 1
Characteristics of the early-blind subjects.

Gender	Age (years)	Age when blind	Cause of blindness
M	36	Since birth	Norrie's disease, no other neurological deficits
F	36	Since 3 years of age	Cataract, aniridia
F	19	Since birth	Leber's congenital amaurosis
F	40	Since birth	Leber optic atrophy
F	39	Since 6 months of age	Retinopathy of prematurity
M	43	Shadows and light until the age of 3 years	Retinopathy of prematurity
M	27	Since birth	Retinopathy of prematurity

F = female, M = male.