How does the body representation system develop in the human brain?

Aurelie Fontan [a,b], Fabien Cignetti [a,b], Bruno Nazarian [c], Jean-Luc Anton [c], Marianne Vaugoyeau [a,b], Christine Assaiante [a,b,*]

[a] Aix Marseille Univ, CNRS, LNC, Laboratoire de Neurosciences Cognitives, Marseille, France
[b] Aix Marseille Univ, CNRS, Fédération 3C, Marseille, France
[c] Aix-Marseille Université, CNRS, INT UMR 7289, Centre IRM, France

ARTICLE INFO

ABSTRACT

Exploration of the body representation system (BRS) from kinaesthetic illusions in fMRI has revealed a complex network composed of sensorimotor and frontoparietal components. Here, we evaluated the degree of maturity of this network in children aged 7–11 years, and the extent to which structural factors account for network differences with adults. Brain activation following tendon vibration at 100 Hz ('illusion') and 30 Hz ('no illusion') were analysed using the two-stage random effects model, with or without white and grey matter covariates. The BRS was already well established in children as revealed by the contrast 'illusion' vs 'no illusion', although still immature in some aspects. This included a lower level of activation in primary somatosensory and posterior parietal regions, and the exclusive activation of the frontopolar cortex (FPC) in children compared to adults. The former differences were related to structure, while the latter difference reflected a functional strategy where the FPC may serve as the 'top' in top-down modulation of the activity of the other BRS regions to facilitate the establishment of body representations. Hence, the development of the BRS not only relies on structural maturation, but also involves the disengagement of an executive region not classically involved in body processing.
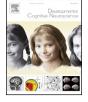
1. Introduction

Neural representations of the body formed within the human brain, known as the body representation system (BRS), is central to the understanding of motor functions (Ehrsson et al., 2003; Longo and Haggard 2010). The BRS is constantly updated using sensory information, especially proprioception that encompasses the perception of positional changes and movements of body parts (Proske and Gandevia, 2012). Using vibration-evoked proprioceptive illusions, neuroimaging studies suggested that two networks constitute the cerebral basis of the BRS (Naito et al., 1999, 2002, 2016; Naito and Ehrsson, 2006): (i) a sensorimotor control network – i.e. motor and somatosensory cortical regions, basal ganglia, thalamus, cerebellum – that contributes to the formation of the body representations, and is involved in on-line control (fast corrections) of movement, and (ii) a fronto-parietal network extending from the inferior frontal gyrus to the posterior parietal cortex (e.g. inferior parietal lobule) that integrates environmental information together with bodily information into a single percept, thereby providing a corporeal representation adjusted to the environmental context. Furthermore, the fronto-parietal network in the right hemisphere has also been found to be involved in corporeal self-awareness (Cignetti et al., 2014; Naito et al., 2005). Although it is obvious that the BRS must be updated during development due to many factors such as morphological changes, acquisition of motor skills, and cognitive practice, age-related changes in its cerebral correlates have never been investigated directly.

Indirect information on the developmental trajectory of the BRS comes from resting state functional magnetic resonance imaging (fMRI) studies. The sensorimotor control network is already topologically adult-like by the age of two while higher-order networks including the fronto-parietal network are topologically incomplete, presenting a less specialized architecture compared to adults (Gao et al., 2015). Further studies reported that within-network connectivity changes stop in late childhood (~10 years old) for the sensorimotor network and that they continue until adulthood for the frontal and parietal networks (Jolles et al., 2011; Kelly et al., 2009). Therefore, the fronto-parietal network supporting the BRS presents an extended development compared to the sensorimotor network. A recent fMRI study using tendon vibration also demonstrated that the proprioceptive brain network still

* Corresponding author at: Aix Marseille Univ, CNRS, LNC, Laboratoire de Neurosciences Cognitives, Marseille, France.
E-mail address: christine.assaiante@univ-amu.fr (C. Assaiante).

undergoes refinements during and beyond adolescence, mostly the fronto-striatal connections that exhibit functional pruning leading to a more restricted topology (Cignetti et al., 2016a). Therefore, although the sensorimotor network is likely earlier to mature compared to the fronto-parietal network, it may not yet be mature by late childhood.

Outcomes from structural MRI studies would support this view. Studies on cortical grey matter development from childhood to adulthood reported a maturational sequence from sensorimotor to higher-order association regions, specifically from the precentral gyrus to the prefrontal cortex in the frontal lobe and from the postcentral gyrus to the angular/supramarginal gyri in the parietal lobe (e.g. Gogtay et al., 2004; Shaw et al., 2008). Likewise, a study by Zielinski et al. (2010) showed that grey matter networks establishing sensory and motor regions were already well-developed in early childhood, although not yet adult-like. In contrast, higher-level cognitive networks were undeveloped in early childhood and showed an important amount of change during adolescence. However, regional variations in the grey matter maturation pattern of the sensorimotor network appear to exist, especially in the subcortical regions that demonstrate important age-related changes in grey matter density during adolescence (Sowell et al., 1999).

Considering white matter maturation, it is less clear whether the sensorimotor network reaches maturity before the fronto-parietal network. Diffusion tensor imaging (DTI) studies showed that the microstructural characteristics of association fibres, and especially the superior longitudinal fasciculus that connects the parietal cortex to the frontal gyrus, become adult-like by late adolescence (Asato et al., 2010; Lebel et al., 2008, 2012; Lebel and Beaulieu, 2011; Simmonds et al., 2014). This supports an extended development of the fronto-parietal network. However, late to mature in adolescence are also projection fibres, such as the corona radiatia connecting the basal ganglia to the cortex, as well as cerebellar connections (Asato et al., 2010; Lebel et al., 2008; Simmonds et al., 2014). Moreover, connections at terminal grey matter sites in basal ganglia were found to mature even in later adulthood (Lebel et al., 2008; Simmonds et al., 2014). Therefore, a set of white matter fibres involved in the sensorimotor network continue to mature during and beyond adolescence, suggesting once again that this network is not completely mature by late childhood.

Using a protocol of kinaesthetic illusions in children (7–11 years) and adults (25–40 years) in fMRI, the aim of the present study was to evaluate the degree of maturation of the sensorimotor and fronto-parietal networks subtending the BRS by late childhood. We expected to find larger differences in activation levels between children and adults in fronto-parietal regions, i.e. a more immature fronto-parietal network by late childhood. A secondary objective was to examine the extent to which structural brain maturation influences the functional development of the networks that implement the BRS. To this end, we investigated group differences in fMRI results while statistically controlling for differences in grey and white matter between children and adults.

2. Methods

2.1. Participants

Forty seven healthy right-handed individuals including fifteen adults (mean age $\pm$ SD: 32.4 ± 4.5; 9 females) and thirty two children (from seven to eleven years old) took part in the experiment. Data from 9 of the adult participants were previously reported by Cignetti et al. (2014) and six additional adult participants were recruited to complete the adult group. The children sample was finally restricted to twenty-two individuals (mean age $\pm$ SD: 9.0 ± 1.4; 15 females) due to the exclusion from the analysis of

10 children with excessive head movements during fMRI scanning (cf. Section 2.5.1 fMRI data analysis). Sex distribution did not differ between the two age groups (χ^2 (4, n = 37) = 0.3; p = 0.6). Adult participants, parents of minors, and children gave written informed consent. The study was approved by the research ethics committee CPP Sud-Méditerranée 1.

2.2. Paradigm

The cerebral correlates of the BRS were examined using a tendon vibration paradigm, which consisted in vibrating the tendons of the right and left tibialis anterior muscles to excite the muscle spindle primary endings (e.g. Cignetti et al., 2014, 2016a). To this end, custom-made pneumatic vibration devices, driven by constant air pressure, were placed perpendicularly to the anterior right and left ankles using elastic straps (contact area = $\sim 6\,cm^2$). Frequencies were delivered at 30 Hz and at 100 Hz with a 0.5 mm amplitude, leading to four vibration conditions: right and left tendon vibration at 30 Hz (R30 and L30; the control 'no illusion' condition) and at 100 Hz (R100 and L100; the 'illusion' condition). These stimulation parameters were selected based on the fact that (i) 20–40 Hz frequencies drive weak discharges of the primary endings, which are not likely to elicit kinaesthetic illusions, and (ii) ∼100 Hz frequency optimally activates primary endings, generally providing consistent illusory movements (i.e. plantar-flexion) (Cignetti et al., 2014, 2016a; Naito et al., 1999; Radovanovic et al., 2002; Roll and Vedel, 1982; Roll et al., 1989).

2.3. Pre-scanning session

In the present study, participants first experienced a pre-scanning session lying supine outside the scanner with the eyes closed, during which they were presented with the four vibratory stimulations (12-s long R30, L30, R100, and L100 vibrations; each stimulation presented twice). The vibration conditions were presented in a random order and each vibration was followed by a rest period during which the participants were questioned as to whether the stimulation generated illusory movements, and were then requested to verbally describe them. The six additional adults reported illusory movement at 100 Hz but not at 30 Hz stimulation. Finer-grained evaluation was conducted in children to increase confidence in self-reports on illusions. After the 12 seconds period of vibration, the children had to report about what they felt and were asked to reproduce (if any) the illusory percept by moving their foot. In the 100 Hz condition, all children felt their foot 'going down' and produced a plantar-flexion. In the 30 Hz condition, 6 children reported plantar-flexion illusion while the other 16 children reported a 'vibrating' sensation. Children were also asked to (i) score the vividness defined as how realistic the illusion was, between 0 and 4, a score of 0 corresponding to the absence of illusion and a score of 4 to a plantar-flexion illusion similar to an actual movement (Naito et al., 1999), and (ii) to report the amplitude of the illusory movement, using an angle measurement scale. The angle measurement scale corresponded to a lying individual with a degree of freedom about the ankle. The experimenter rotated the foot until the estimated position was reached, as indicated by the children. An angle of $0°$ corresponded to the absence of illusory plantar-flexion and a positive value to a plantar-flexion, the larger the value the more important the plantar-flexion. In sum, none of the adults reported experience of illusory movement in the 30 Hz conditions while all of them experienced illusory plantar-flexion in the 100 Hz conditions. Six children out of twenty-two reported illusory movements in both the 30 Hz and the 100 Hz conditions, with a tendency for less vivid and important illusions in the former conditions (vividness R30: 1.5 ± 1.4; vividness L30: 1.3 ± 1.2; angle R30: $17.5 \pm 10.3°$; angle L30: $19.2 \pm 9.3°$) com-