Functional connectivity among resting state networks increases after constraint-induced movement therapy in children with brain injury

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Purpose. Constraint-induced movement therapy (CIMT), a combination of a restraint in the use of the unimpaired limb and intensive training of the affected one, is a strategy to improve upper limb function in pediatric patients with brain injury [1]. Aim of this study was to assess, using resting state (RS) functional magnetic resonance imaging (fMRI), changes of connectivity among functional networks in pediatric patients with chronic hemiplegia following CIMT.

Methods. From 14 children with acquired or congenital brain injury and 10 sex- and age-matched healthy controls, RS fMRI data were acquired before CIMT (baseline), at the end of CIMT (week 10) and after 6 months. Independent component analysis [2] was used to identify functionally relevant RS networks (RSN). The Functional network connectivity (FNC) toolbox [3] was used to assess significant interactions among RSNs at baseline, and changes of association between networks at the two follow-up evaluations. Correlations between network connectivity and clinical scores were also assessed.

Results. Patients had a significant improvement at clinical scales at the end of CIMT and a further amelioration 6 months after termination of therapy. At baseline, several connections among RSNs, which were significant in healthy controls, were not present in pediatric patients (Figure 1). Specifically, no connectivity was found between the sensorimotor and the visual networks, and between these networks and both the default mode (DM) and salience networks. No connectivity was also found between the auditory, executive control (ECN) and working memory networks.

At week 10, patients showed a significantly increased connectivity among several RSNs, which mainly involved the sensorimotor (p=range 0.001-0.01), visual (p=range 0.001-0.04) and DM (p=range 0.001-0.03) networks (Figure 2). These changes were significantly correlated with improvement at clinical scores following CIMT (r=range 0.58-0.80, p=0.002-0.04). This pattern of increased connectivity among RSNs persisted after 6 months.

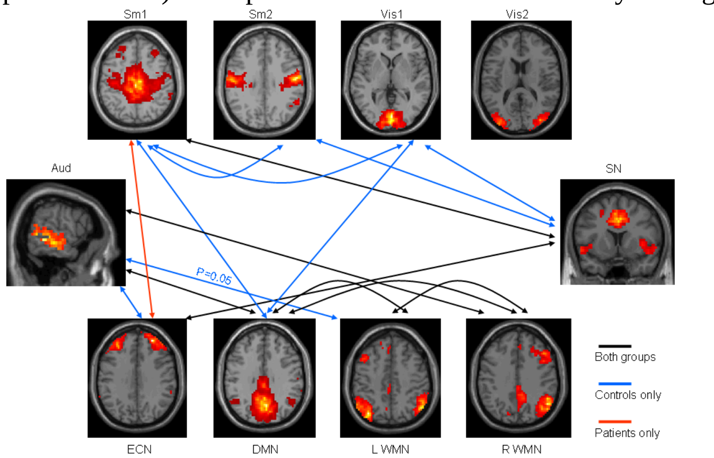

***Figure 1**. Diagram showing resting state networks having a significantly different pair-wise connectivity between controls and pediatric patients with chronic hemiplegia at baseline.*
Black arrows: connections present in both groups.
Blue arrows: connections present in healthy controls only.
Red arrows: connections present in pediatric patients only.

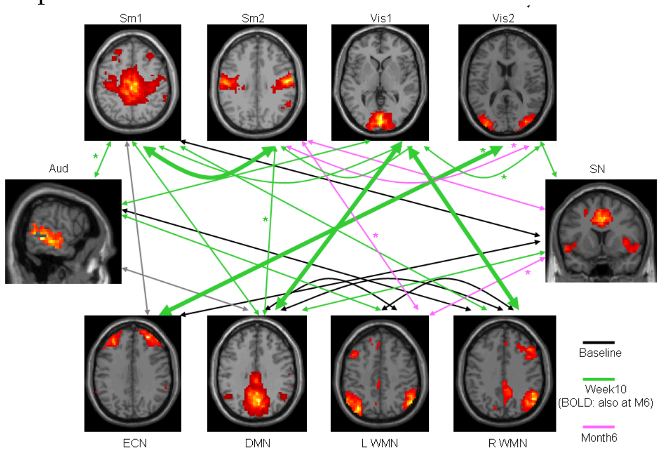

***Figure 2.** Diagram showing resting state networks having a significantly increasing pair-wise connectivity over time in patients with chronic hemiplegia following CIMT.*
Black arrows: connections present at baseline.
Green arrows: connections appearing at week 10
(bold arrows: connections persisting at month 6).
Pink arrows: connections appearing at month 6.

Conclusions. An increase of inter-network connectivity might contribute to explain clinical improvement in pediatric patients with chronic hemiplegia following CIMT.

References. [1] Taub E. Exerc Sport Sci Rev 1976;4:335-374. [2] Calhoun V, et al. Hum Brain Mapp 2001;14:140-151. [3] Jafri M, et al. Neuroimage 2008;39:1666-1681.