Modulation of resting-state brain networks in newborns by heel prick

Lara Lordier[1], Frédéric Grouiller[2], Dimitri Van de Ville[2,3], Ana Sancho Rossignol[4], Maria Isabel Cordero[4], François Lazeyras[2], François Ansermet[4], and Petra S. Hüppi[1]

[1]Division of Development and Growth, Department of Pediatrics, University of Geneva, Geneva, Geneva, Switzerland, [2]Department of Radiology and Medical Informatics, Geneva University Hospital, Geneva, Switzerland, [3]Institute of Bioengineering, Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland, [4]Division of Child and Adolescent Psychiatry, Department of Pediatrics, University of Geneva, Geneva, Switzerland

Target Audience : Neuroscientists, Pediatricians, Neonatologists, Engineers

Purpose :

Using resting-state functional magnetic resonance imaging (RS-fMRI), it is possible to establish resting-state networks (RSNs) that show temporally coherent (typically low-frequency) BOLD signal fluctuations. Very similar resting state networks than those found in adults have been found in newborns [1].

However, little is known about the development and role of those RSNs in newborns. Furthermore, previous studies in adults reported that spontaneous brain activity can be modulated by learning, training, but also by behavioral states, which is supporting the idea that low-frequency BOLD signal fluctuations are modulated by recent experience [2,3]. The aim of this study is to map RSNs in newborns and to investigate if these low-frequency BOLD signal fluctuations could be modified after a painful event.

Methods :

Acquisition: Nine healthy full-term newborns (mean gestational age: $39^{1/7}$ weeks) were scanned at 3-4 days of life on a Siemens 3T MRI using 8-channel neohead coil. Two runs of 8 minutes of RS-fMRI were acquired with EPI (TR=1600 ms, TE=30 ms, 30 slices, voxel size=2.5x2.5x3.0mm^3) during natural sleep or while resting quietly in the scanner without any sedation. Between these two runs, each newborn underwent a "Guthrie test", which is a heel prick to get a few drops of blood for metabolic screening.

Preprossessing: RS-fMRI data, acquired immediately before and after this painful event, were realigned; normalized to a neonatal template; and spatially smoothed (6 mm FWHM). All volumes with an absolute displacement from frame-to-frame higher than 0.5mm were removed (mean: 37 images removed) and remaining images have been concatenated. If more than 25% of the volumes had motion, children's data were not included in the analyses.

Analyses: Data have been analysed in a group independent component analysis (ICA) using GIFT package. A mask, based on newborns template segmentation, has been used to remove cerebrospinal fluid and eyes. ICA was repeated 20 times using ICASSO to ensure stability of the 20 components (fixed number of components).

For each pair of components, we calculated the correlation between their time-course resulting in a connectivity matrix. Paired t-test and Wilcoxon signed rank test were performed to assess correlation for each pair.

Results:

We observed RSNs commonly found in adults including cerebellum, visual, medial prefrontal cortex, sensorimotor, superior frontal, precuneus, orbitofrontal, auditory and basal ganglia networks (Fig.1).

Functional connectivity between the orbitofrontal component and the basal ganglia component is significantly increased after the heel-prick (paired t-test, p=0.0247; Wilcoxon signed-rank test, p=0.0039) (Fig.2).

Fig1 :

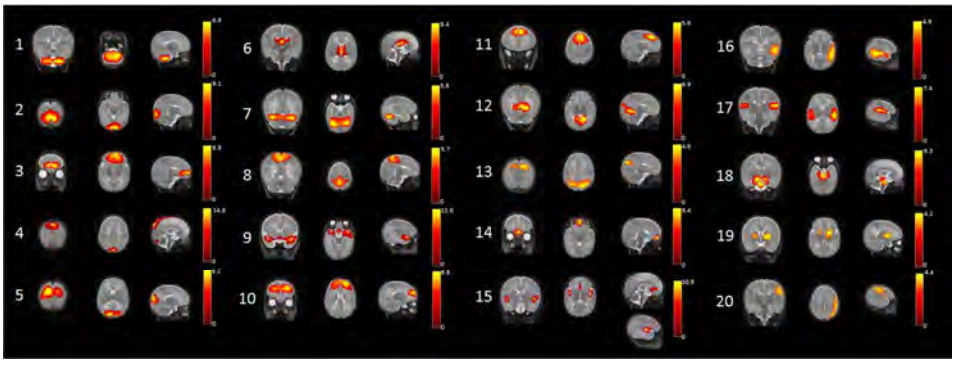

Fig2 :

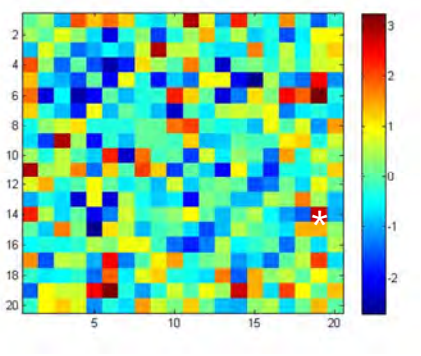

Fig1. Each row shows components thresholded at Z-score > 3 superimposed on a T2-weighted MR infant brain template. The color-bars shows the corresponding Z-score.

Fig2. Matrix showing the t-statistics (t-values) for differences of connectivity (before and after heel prick) in each pair of components. Connectivity modulation between components 14 and 19 was significant (*) using a Wilcoxon signed rank test: p<0.005.

Discussion and conclusions:

Networks located in cerebellum (1), visual (2), sensorimotor (8), superior frontal (11), precuneus (13), auditory (17), and basal ganglia (19) are consistent with those previously described in infants [1] and most of them have been found in adults.

Basal ganglia are involved in the integration of information between cortical and thalamic regions through "cortico-basal ganglia-thalamic loops". These loops have an important role in pain processing and pain regulation [4]. An increased connectivity between basal ganglia and orbitofrontal components reflects the integration and modulation of the pain experience, i.e. the heel prick, that babies just experienced.

The project also ultimately aims at identifying the effects of mother's antenatal distress on fetal brain development, RSNs, fetal reactivity and early child physiological and behavioral reactivity in pain and stress processing.

References:

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