Abnormal cortical and thalamic development in children with Borderline Intellectual Functioning

Niels Bergsland[1,2], Francesca Baglio[1], Gisella Baglio[1], Raffaello Nemni[1,3], Mario Clerici[1,3], Michela Zanette[1], and Valeria Blasi[1]
[1]*Istituto IRCCS Santa Maria Nascente, Fondazione Don Gnocchi, Milan, Italy,* [2]*Dipartimento di Elettronica, Informatica e Bioingegneria, Politecnico di Milano, Milan, Italy,* [3]*Università degli Studi di Milano, Milan, Italy*

Target audience: This research is aimed at researchers and/or clinicians seeking to better understand gray matter alterations that are found in children that are classified with Borderline Intellectual Functioning.

Background/purpose: Borderline Intellectual Functioning (BIF) is a complex clinical entity that has received very little scientific investigation. According to the CONFIL consensus group BIF can be defined as a "health meta-condition characterized by various cognitive dysfunctions associated with an intellectual quotient (IQ) between 71 and 85 which determines a deficit in the individual's functioning both in the restriction of activities and in the limitation of social participation" [1]. BIF children present with cognitive, motor, social and adaptive limitations that result in learning disabilities and are more likely to develop psychiatric disorders later in life. Recent findings suggest that the level of performance in both motor and executive functioning, are highly correlated and that the development of the brain areas involved in both functions is closely interrelated[2]. Given to previous findings of our group[3], aim of our study was to investigate possible differences between BIF and typically developing (TD) children in their brain maturation in the sensory-motor circuitry (see Figure 1). To this purpose we used a surface- and volumetric segmentation-based MRI approach.

Methods: Forty four children with BIF (29 boys/15 girls, mean age of 9.5 years) and 16 TD children (9 boys/7 girls; mean age of 10.1 years) were enrolled. Children were diagnosed as BIF according to the American Psychiatric Association criteria (DSM-IV). IQ scores by means of the WISC-III ranged from 70 to 85. To avoid confounding effects and attempt to analyze a more homogenous sample, we focused on children with BIF without the presence of genetic syndromes and/or major neuropsychiatric problems, such as autism spectrum disorder or attention deficit hyperactivity disorder. The freely available FreeSurfer software package was used to obtain measures of cortical thickness and area from a high resolution 3D-T1 weighted MP-RAGE (1mm isotropic voxels) acquired using a1.5T MRI Siemens scanner. Specific parameters were TR/TE/TI=1900/3.37/1100 ms, flip angle=15°, 176 axial slices, 192x256 matrix, and FOV=250x250 mm^2. Region of interest analysis, based on the Desikan atlas[4], was used to estimate cortical thickness and area differences. Volumetric differences between BIF and TD groups of the basal ganglia (e.g. (caudate, putamen, pallidum), thalamus, and cerebellum were also investigated using FreeSurfer. A general linear model was used to compare cortical measures between groups using age and sex as covariates. Total intracranial volume was also included as a covariate for surface area and volumetric structure comparisons. In order to reduce the number of comparisons, left and right measures were combined into a single variable. Correlations between indices of intelligence and measures that were significantly different between the groups were subsequently evaluated using the Pearson correlation coefficient. An alpha level of .05 was used to assess significance.

Results: There were no significant demographic differences between the groups. The BIF group presented with a significantly increased superior frontal gyrus thickness (p =.046) whereas no significant differences were found for its area. For both the caudal middle frontal and precentral regions, neither thickness nor area measures significantly differed between the groups. The TD group had a significantly larger postcentral area (p = .004) whereas no significant differences in its thickness were found. Cerebellar WM was not significantly different although there was a trend for greater cortical matter (p=.055) in the TD group for this structure. The BIF group showed a significantly smaller thalamus (p = .020). The groups did not significantly differ in basal ganglia structure volumes. Thickness of the superior frontal gyrus thickness correlated with the Freedom from Distractibility Index (r=-.344, p=.022).

Discussion: Data herein demonstrate the presence of cortical deviations in BIF children in the sensory-motor circuitry. The close relationship between motor skills and IQ development has first been argued by Piaget, whose studies linked the development of thought with the emergence of skilled action and recently confirmed by recent literature demonstrating a strict relation between motor abilities and cognitive abilities[2]. The cortical deviations we observed consisted of increased thickness in superior frontal gyrus, reduced surface area in the post central gyrus, and reduced thalamic volume as well as a trend of reduced cerebellar cortex volume in BIF and can be due to altered or delayed brain development. In fact, the dynamic nature of brain development in childhood is characterized by regressive (pruning) and progressive changes (e.g. arborization, synaptogenesis) that are regionally specific. In dorsal frontal regions thinning mechanisms are predominant[5] while in the thalamus and cerebellum an increment in size is observed[6,7]). Interestingly, recent findings have demonstrated a crucial role of the thalamus in the morphologic development of neurons[8]. Furthermore, we observed that cortical thickness in the superior frontal gyrus was inversely related with the WISC III Freedom from Distractibility Index. This association is consistent with literature evidence showing that the superior frontal gyrus is crucial for motor and attentional processes involved in cognitive processing.

Conclusion: We demonstrated that BIF children show brain development delay in cortical areas as well as the thalamus, which are associated with motor and cognitive abilities crucial for intellectual functioning.

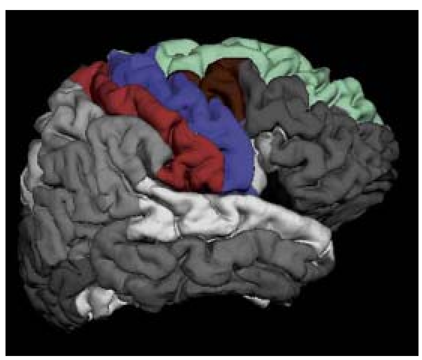

Figure 1: Representative cortical segmentation. Post central gyrus shown in red, pre central gyrus shown in blue, superior frontal gyrus shown in light green, and caudal middle frontal gyrus shown in brown.

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