

SCIENTIFIC REPORTS



OPEN

Lateral prefrontal activity as a compensatory strategy for deficits of cortical processing in Attention Deficit Hyperactivity Disorder

Francisco Zamorano^{1,2}, Pablo Billeke¹, Leonie Kausel³, Josefina Larrain¹, Ximena Stecher^{2,8}, Jose M. Hurtado¹, Vladimir López^{3,4}, Ximena Carrasco^{6,7} & Francisco Aboitiz^{3,5}

Attention Deficit Hyperactivity Disorder (ADHD) is the most common neuropsychiatric disorder in childhood and is characterized by a delay of cortical maturation in frontal regions. In order to investigate interference control, which is a key function of frontal areas, a functional MRI study was conducted on 17 ADHD boys and 17 typically developing (TD) boys, while solving the multi source interference task (MSIT). This task consists of two conditions, a “congruent condition” and an “incongruent condition”. The latter requires to inhibit information that interferes with task-relevant stimuli. Behavioral results showed that ADHD subjects committed more errors than TD children. In addition, TD children presented a larger MSIT effect - a greater difference in reaction times between the incongruent and the congruent conditions - than ADHD children. Associated to the MSIT effect, neuroimaging results showed a significant enhancement in the activation of the right lateral prefrontal cortex (rLPFC) in ADHD than in TD subjects. Finally, ADHD subjects presented greater functional connectivity between rLPFC and bilateral orbitofrontal cortex than the TD group. This difference in connectivity correlated with worse performance in both groups. Our results could reflect a compensatory strategy of ADHD children resulting from their effort to maintain an adequate performance during MSIT.

Attention Deficit Hyperactivity Disorder (ADHD) is the most common neuropsychiatric disorder in childhood¹, affecting between 5%² and 15%³ of the school-aged population. While the incidence of this condition is greater among children in pre-school and school age, the disorder can persist into adolescence and adulthood in 30% to 60% of the cases⁴. During childhood, one of the main consequences of the syndrome is that children show poor school performance. During adolescence and adulthood, problems such as decreased self-esteem, social isolation, increased risk of accidents and psychiatric comorbidity become manifest, which are important in the context of public health⁵⁻⁷. Currently, it is posited that a good therapeutic outcome depends largely on early and appropriate treatment⁸, but also on a correct diagnosis and management of comorbidities that are usually associated with ADHD and that are often much more disruptive than ADHD itself^{7,9-11}. Mainly due to the complexity of the clinical and biological features of this disorder, its diagnosis remains controversial¹². In this context, it is increasingly necessary to study more closely the neurobiological mechanisms underlying ADHD.

In the last years, structural MRI studies have shown that ADHD children present a delay in their cortical maturation¹³. Brain areas such as the insula and striatum are affected^{14,15}, even though the alterations in the prefrontal cortex might be the most prominent ones^{16,17}. It has also been shown that the degree of maturation delay in the

¹División de Neurociencia, Centro de Investigación en Complejidad Social (neuroCICS), Facultad de Gobierno, Universidad del Desarrollo, Santiago, Chile. ²Unidad de Imágenes Cuantitativas Avanzadas, Departamento de Imágenes, Clínica Alemana de Santiago, Santiago, Chile. ³Centro Interdisciplinario de Neurociencias, Pontificia Universidad Católica de Chile, Santiago, Chile. ⁴Escuela de Psicología, Pontificia Universidad Católica de Chile, Santiago, Chile. ⁵Departamento de Psiquiatría, Escuela de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile. ⁶Servicio de Neurología, Facultad de Medicina, Clínica Alemana Universidad del Desarrollo, Santiago, Chile. ⁷Servicio de Neurología y Psiquiatría, Hospital Luis Calvo Mackenna, Facultad de Medicina, Universidad de Chile, Santiago, Chile. ⁸Departamento de Imágenes, Facultad de Medicina, Clínica Alemana Universidad del Desarrollo, Santiago, Chile. Correspondence and requests for materials should be addressed to F.Z. (email: fzamorano@udd.cl)

Received: 19 September 2016

Accepted: 27 June 2017

Published online: 3 August 2017