Different basal concentration and different response of BDNF to prolonged release methylphenidate between ADHD subtypes

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Statement of the problem: Brain-derived neurotrophic factor (BDNF), a member of the family of neurotrophic receptors, appears to intervene in the pathogenesis and treatment response in Attention deficit hyperactivity disorder (ADHD), hypothesis based on the conceptualization of ADHD as a neurodevelopmental disorder and the importance of the BDNF for normal neural development. In addition, in experimental models, psychostimulants and antidepressants increase the brain concentration of BDNF. Genetic polymorphisms related with the activity of the BDNF seem to correlate with the incidence, clinical manifestations, endophenotypes or the treatment response in ADHD. We aim to define if the response to prolonged release methylphenidate treatment is different in the main ADHD subtypes, in an open, quasi-experimental and controlled study.

Methods: A total of 148 (115 males, 33 females) patients, of 9.77 (2.56) years old, were subdivided in two group. (1) Control group (n=37; 27 males, 10 females); healthy siblings of the ADHD patients. (2) ADHD group (n=111; 88 males, 23 females), without epilepsy and with a normal value in an abbreviated intelligence test (KBIT). In all subjects, after written informed consent, we performed identical clinical, psychometric and biochemical study, before and after (only ADHD group) treatment. ADHD group were diagnosed according Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria and sub-classified in the primary ADHD subtypes by EDAH scale (). Measurement: BDNF by ELISA (IBL International, ref. RB59041), in serum samples obtained at 09:00 and 20:00 h, before and after 4.63 (2.3) months of the daily morning ingestion of PRMPH.

Statistic: factorial analyses using statistical package STATA 12.0.

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Results: In the control group serum BDNF concentration in the morning (36.36±11.62 ng/ml) was very similar to the value seen in the predominantly inattentive subgroup of ADHD children, although evening concentration was higher (31.78±11.92 ng/ml). The treatment with prolonged release methyphenidate do not modify the daily fluctuation of BDNF in the children with hyperactive/impulsive/conduct disorder children, whereas in children with predominantly inattentive disorder PRMPH induces a significant decrease ($\chi2=6.62$, $p=0.010$). Serum BDNF (ng/ml) in ADHD children Pre-MPH Post-MPH ADHD subtype Day Night Day Night PHI/CD 30.76±12.34 29.09±12.82 30.29±12.5 27.25±12.93 PDA 35.31±12.85 26.41±11.55 26.97±10.3 25.05±10.21 PDA: Day vs. Night, pre: $\chi2=11.63$, $p=0.0019$. ADHD pre- vs. post-treatment, day: $\chi2=6.62$, $p=0.010$. All statistical values for comparisons not shown were non-significant.Our results show both similar morning concentrations and daily fluctuation of BDNF, between predominantly inattentive ADHD children and healthy sibling controls. The PRMPH treatment does not modify the reduced BDNF concentration (vs. controls) in hyperactive/conduct disorder children, nor the absence of daily fluctuation; but contrary to expectation reduces the concentration in the predominantly inattentive patients to values similar to that observed at night, disappearing the highly significant basal day/night fluctuation also noted in the control group.

Conclusion: Besides our data in hyperactive/conduct disorder children has been reported that the major depression is also associated with a decrease in BDNF concentration. As serum BDNF seem parallel with intra-cerebral concentration, especially in messencephalic areas, this neurotrophin could be the link between ADHD and major depression, and provide a new pathway for the development of drugs for ADHD.