P 14 PECULIAR RESPONSE TO METHYLPHENIDATE IN ADOLESCENT COMPARED TO ADULT RATS: A PH-MRI STUDY

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Adolescent rats and mice differ markedly from adults in several neuro-behavioral parameters. In addition, behavioral response to psychostimulant drugs may be dampened and "paradoxical" effects are often reported. Methylphenidate (MPH) is a psychostimulant elective drug therapy for the Attention Deficit Hyperactivity Disorder (ADHD). We aimed to investigate brain function peculiarities in the response of adolescent rats to MPH, using pharmacological imaging (Ph-MRI).

Adolescent (PND 34 to 43) and adult (PND>60) Sprague-Dawley rats were anaesthetised with isoflurane and examined by a 4.7 T Varian Inova MRI system (USA). After anatomical MRI, axial gradient echo images were collected continuously. After baseline recording (30 min), animals received MPH (4 mg/kg) or saline (SAL) and were recorded for further 30 min. The image sequences were realigned, restored through a Bayesian MCMC approach and detrended. Firstly, for each animal, blood-oxigenation level dependent (BOLD) data were collected from specific ROIs (Prefrontal Cortex, PFC; Nucleus Accumbens, NAcc; Hippocampus, Hip) and analysed with three-way ANOVA (age x drug x time design). Secondly, images were coregistered to one brain template for each group. A parametric Random Effect Analysis was performed on the averaged BOLD signal of the templates.

Region-specific changes in the BOLD signal were evident as a function of age. As expected, among adults MPH induced an increase of BOLD signal in nucleus NAcc and prefrontal PFC, with no effects in the Hip. Notably, among adolescents, MPH induced a marked and generalized decrease of BOLD signal which occurred earlier in NAcc and PFC. Any bias in the BOLD responses was excluded by the measurement of physiological parameters.

Present findings highlight the utility of Ph-MRI to detect brain functional changes following psychoactive agents in animal models. The peculiar negative BOLD effect found in adolescent rats may be suggestive of a reduced cerebro-vascular feedback and/or an increased MPH-induced neuronal activation. Data seem in agreement with age-related rearrangement in the function of central nervous system, and are relevant for a better understanding of brain/behavioral regulations during adolescence.

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