**Meeting Abstract**

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**Effects of ADHD medications on brain metabolism: a microPET imaging study in rats**

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**Introduction:** Attention-deficit hyperactivity disorder (ADHD) is a developmental disorder including inattention, hyperactivity and/or impulsivity. Psychostimulants such as methylphenidate (MPH) are the gold standard treatments for this disorder and mainly target the dopamine neurotransmission. In this study, we used positron emission tomography (PET) to better understand the impact on brain metabolism of an injection of MPH (i) in naive Wistar rats at 28 days of postnatal life (P28) and (ii) in the same rats at 70 days of postnatal life (P70) after a daily treatment that started at P28. The effects of MPH were compared to those of another psychostimulant, i.e. lisdex-amphetamine (LDX), which targets the dopamine and noradrenergic neurotransmissions, and to those of a non-psychostimulant ADHD medication, i.e. guanfacine (GFC), which acts on the noradrenergic system.

**Methods:** Wistar rats were treated with MPH (2 mg/kg, i.p.), LDX (0.3 mg/kg, i.p.), GFC (0.3 mg/kg, i.p.) or saline from P28 to P70. The impact of such treatments on brain metabolism were evaluated using [¹⁸F]2-fluoro-2-desoxy-D-glucose ([¹⁸F]DG) on freely moving Wistar rats performed after the first (P28) and last (P70) injection of each compound.

**Results:** An acute MPH injection at P28 increased [¹⁸F]DG uptake in the orbitofrontal cortex, thalamus and dorsal hippocampus, and decreased [¹⁸F]DG uptake in the dorsal striatum, amygdala, and ventral hippocampus. In contrast, LDX and GFC increased [¹⁸F]DG uptake in the ventral striatum, globus pallidus and amygdala, and decreased [¹⁸F]DG uptake in thalamus and dorsal hippocampus. At P70, MPH, LDX and GFC injections increased [¹⁸F]DG uptake in the ventral striatum. MPH and GFC also increased [¹⁸F]DG uptake in the orbitofrontal cortex and thalamus. Conversely, LDX induced decreases in [¹⁸F]DG uptake in the cingular, orbitofrontal and parietal cortices and also in the thalamus.

**Discussion:** We showed distinct effects of acute MPH vs. LDX and GFC injections at P28, while modifications in brain metabolism observed at P70 were more similar. Overall, these data suggest a crucial role for the ventral striatum in the effects of LDX and GFC injections at P28, and MPH, LDX and GFC injections at P70. The similar effects of GFC and MPH treatments at P70 despite their distinct actions on the dopamine neurotransmissions are highly interesting. These results may help to better understand how dopamine and non-dopamine medications improve ADHD patients care and follow-up.

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