

(Claron Technology Inc., Canada) positioned on either side of the PET scanner (Kyme et al, 2011) while the animal moves freely within the chamber. Pose data are used to smoothly adjust the position of the chamber within the PET FoV (Zhou et al., 2013) and to correct coincidence events for motion within a list mode MLEM reconstruction algorithm (Rahmim et al., 2008).

Two adult male Sprague-Dawley rats were administered 45MBq (<1 nmol) [¹¹C]raclopride via an indwelling jugular vein catheter and imaged in the Open Field system for 50min. One animal was administered 2 mg.kg⁻¹ of unlabelled raclopride (D2 antagonist) and the other animal I $mg.kg^{-1}$ of sumanirole (full D2 agonist) 20 minutes after tracer injection. Dynamic PET data were analysed by least squares fitting striatal and cerebellar time-activity curves with the lp-ntPET ligand displacement model (Normandin et al., 2012). The posterior probability distributions of displacement parameters were further analysed using an Automated Bayesian Computation rejection algorithm (Marin et al., 2011). Behavioral data were analysed by measuring absolute head displacement as a proxy for locomotor activity before and after drug injection and compared with the timing and magnitude of [¹¹C]raclopride displacement.

Results:

Both drugs caused a measurable displacement of $[{}^{11}C]$ raclopride which corresponded to their injection times, i.e. approximately 20min (figure 1). In the case of sumanirole the displacement also correlated with increased locomotor activity (492%), consistent with agonist effects on the indirect thalamo-striatal dopaminergic pathway. The displacement was similar in magnitude ($k_{2a}(t) = 1.5$ -2x baseline) for the two studies but more prolonged in the case of raclopride than sumanirole.

Conclusions:

The Open Field PET technique thus allows simultaneous measurements of PET derived changes in regional receptor binding and behavioral responses due to controlled stimuli in conscious unrestrained animals.

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BrainPET Oral Session: Preclinical Imaging

UNCOUPLING BETWEEN STRIATAL DOPAMINE TRANSPORTER AND GLUCOSE METABOLISM IN DIET INDUCED OBESITY

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Abstract

Introduction: Dopamine receptor was down regulated in obese animals and humans brain (Nummennmaa et al, 2012). Data are conflicting about the density of dopamine transporter in obese striatum. Furthermore, while striatal D2R availability is negatively associated with frontocortical glucose metabolism in obese patient (Volkow et al, 2004), the impact of obesity on striatal metabolism is unknown. Methods: Fourteen adults mini-pigs were imaged for dopamine transporter and glucose metabolism in lean and obese conditions. Obesity was induced by high fat, high glucose diet supplied at 200% metabolic requirement (measured by indirect calorimetry) during 3 months. Brain glucose metabolism was obtained using PET imaging (HR+ Siemens) after the IV injection of 250 MBq FDG (IBA). The density of dopamine transporter was evaluated



using SPECT imaging (Millenium, GE) after the IV injection of 180 MBq DatScan (GE). Sinograms were corrected for attenuation using STIR software. FDG images were coregistered against a PET template (n=20 animals) obtained using the same machine and identical pig breed in our laboratory. DATScan images were also coregistered using a DATscan template (n=10 animals). Both templates were within the same tridimensionnal reference i.e. a pig brain atlas consisting in 70 paired structures and 30 unpaired ones (Saikali et al, 2010). Coregistration was achieved using FNIRT from FSL software. The amount of radioactivity in specific areas was obtained using Pmod software adapted to our pig brain atlas with SVC applied. Data afte normalisation were also analysed without apriori using SPM8 software.

Results: The animals almost doubled their weight during the three months high calorie, high fat/glucose diet (87 \pm 4.4 versus 36 \pm 3.9 Kg). Striatal dopamine transporter density expressed as the ratio between striatum vs occipital cortex was significantly less in the obese than in lean situation (1.8 \pm 0.04 vs 1.6 \pm 0.02, p<0.01). Inversely, the striatal glucose metabolism expressed as the ratio between striatum vs cerebellum was significantly greater in the obese than in the lean condition (1.4 \pm 0.02 vs 2.3 \pm 0.02, p<0.01). Identical figures were obtained with statistical parameter mapping analyses.

Conclusions: Our results demonstrated clearly a reduced density of striatal dopamine transporter in morbid obese animal. This was associated with an increased striatal metabolism that might compensate for changes in synaptic dopamine availability. This uncoupling might a critical mechanism to explain overeating in obesity.

Figure I - Statistical image showing the decreased dopamine transporter density in obese compared to lean condition (shades of blues mean that the radioactivty is less in obese than in lean condition whereas shades of red mean that the radioactivity is more in obese than in lean condition) at the striatal level. The striatum is highlighted in white underlined with orange line for comprehension. It is visible arround the most intense blue spot

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BrainPET Oral Session: Preclinical Imaging

TSPO AVAILABILITY IS A ROBUST MEASURE OF SEVERITY IN A RAT MODEL OF MULTIPLE SCLEROSIS

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Abstract

Objectives

Increased expression of 18kDa translocator protein (TSPO) by activated glia in the CNS has been reported in various neuroinflammatory conditions^{1,2}. Positron emission tomography (PET) with the new generation TSPO radioligands may provide a sensitive and non-invasive approach for quantifying inflammatory processes *in vivo*. Myelin oligodendrocyte glycoprotein (MOG)-induced experimental autoimmume encephalomyelitis (EAE) is an established preclinical model of multiple sclerosis. We investigated whether the change in TSPO availability induced in the EAE model can be detected *in vivo* using the TSPO ligand [¹¹C]PBR28.

Methods

All procedures were carried out in accordance with the UK Home Office Animal (Scientific Procedures) Acts 1986. Recombinant MOG corresponding to the N-terminal extracellular domain of mouse (rmMOG,1–116a.a.)