Program#/Poster#: 97.13/OO56

Title: Brain region morphological and volumetric quantitative assessment using the 17.6T MRI in rats chronically exposed to methylphenidate (MP)

Location: Georgia World Congress Center: Halls B3-B5

Presentation Start/End Time: Saturday, Oct 14, 2006, 1:00 PM - 2:00 PM

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MP is the most common pharmacotherapeutic treatment of ADHD. Previous studies have shown that MP regulates gene expression in multiple regions of the immature rat brain (Chase et al 2005). Other studies have shown global and regional gray matter reductions in ADHD children (Carmona et al 2005) and also a reduction of the total brain size at the following areas: prefrontal, caudate putamen and cerebellum. However it is not clear if these results were the result of chronic MP treatment or a consequence of ADHD.
In the present study we examined the morphological and volumetric differences of brain regions after an 8 month treatment with oral MP (1 & 2 mg/kg) or water in 4 week old SD rats. Following treatment, rats were perfused intracardially and their brains harvested and imaged with a 17.6 Tesla MRI. Brain scans generated two types of images: i) high resolution (50x50x50 µm isotropic) and ii) lower resolution (62x64.4x250 µm). Images were segmented for the following regions of the rat brain: cerebellum, caudate putamen, hippocampus & fibria, external capsule and neocortex. After segmentation, volumetric analysis was performed using the Active Shape Model (ASM) method (Metaxas et al 2004). ASM is a statistical deformable shape modeling technique that creates an initial model guess based on training data which is deformed to fit the image. These deformations were chosen such that they minimize a certain energy (cost) function and are consistent with the a priori knowledge concerning the shape of the target object to be segmented. Results will allow us to determine the impact of chronic oral MP treatment in rats on the morphology and volume of intact brain regions without the use of stereological histology techniques that have been shown to cause various deformations (Buckmaster et al 2005). It will also allow us to validate the ASM technique as it relates to the study of the brain.

Disclosures: **V. Boronikolas**, None; **M. Michaelides**, None; **G. Wang**, None; **S. Blackband**, None; **S.C. Grant**, None; **D.N. Metaxas**, None; **J. Zhou**, None; **N.D. Volkow**, None; **P.K. Thanos**, None.

Support: NIDA, NIDA

NIAAA, (Intramural Research Program, LNI), NIAAA, (Intramural Research Program, LNI)

The U.S. Department of Energy under contract DEAC02-98CH10886, The U.S. Department of Energy under contract DEAC02-98CH10886

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