Reviewer's report

Title: Test-Retest Variability of High Resolution Positron Emission Tomography (PET) Imaging of Cortical Serotonin (5HT2A) Receptors in Older, Healthy Adults

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Reviewer: W G Frankle

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Review

This manuscript addresses an important issue in receptor imaging studies; namely ‘what is the effect of age on the ability to reliably measure receptor parameter with PET’. The authors attempt to address this question by examining the test-retest for the radiotracer [18F]setoperone, a 5-HT2A receptor specific tracer, in 6 healthy controls > 60 years old. They examined the intraclass correlation coefficient, the repeatability coefficient and the between scan variability for the BPnd values derived via SRTM in the frontal, temporal, anterior cingulate and insular cortices. They report high reliability (ICC > .90) and low between scan variability in the frontal, temporal and insula regions with less robust parameters in the anterior cingulate.

Overall all this is a well done study by a group with extensive experience in performing receptor imaging analysis. I would recommend acceptance with a few modifications.

- In the introductions the authors state that radiolabeled metabolites of [11C]MDL enter the brain, however, a recent study (Hinz et al, JCBF 2007) addressed this issue did not find any evidence that these metabolites enter the brain.

- The time between scans ranged from 5 – 16 weeks. This seems to be quite a large range. Since this is a small study of 6 subjects, it would be helpful and possible to state the exact time between scans for each subject, this would allow the reader a better idea of the distribution in the time between scans and provide a breakdown of how many subject feel into the ‘shorter’ and ‘longer’ categories used in the statistical test.

- The [18F]setoperone BPnd values obtained in this population are quite low, ranging from .22 to .60. The authors highlight this point in the discussion around the low values obtained in the anterior cingulate and state that a partial volume
correction may be necessary for between group comparisons. If available, it would enhance the manuscript if a partial volume correction was applied to these data. This would allow the authors to provide evidence for the utility of such a correction in the study of elderly individuals with [18F]setoperone.

- In the discussion it would be interesting if the authors provided a comparison of the BPnd values from the literature in elderly individuals obtained with the other radiotracers for the 5HT2A receptor. If possible, a conclusion/recommendation by the authors of which radiotracer provides the best signal-to-noise ratio (i.e. BPnd) and therefore should be used in future studies in this population.