Sex-Differences In Amphetamine-Induced Dopamine Release Studied With [^{11}C]RAC/PET: Does Partial Volume Correction Make a Difference?

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I. Introduction

Compared to women, men are 2 to 3 times more likely to develop drug addiction. The neurobiology underlying the differential vulnerability has not been determined, but may relate to sex differences in striatal dopamine response to drug exposure. There are, however, conflicting reports regarding the existence of sex differences in "dopamine release" following an amphetamine (AMP) challenge.

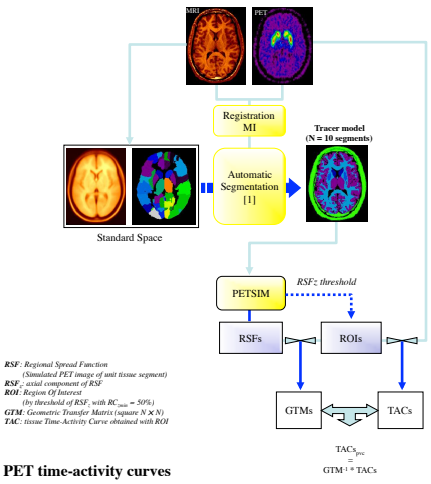
II. Objective

To assess whether differences in brain size between men and women could confound the greater dopamine release observed in the male striatum [1].

III. Methods

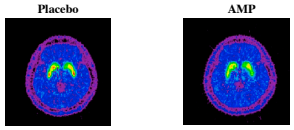
Overview

- population: 38 normal volunteers (18-46 y/o, 18 F 20 M)
- PET scanner: GE-Advance (35 slices, ≈ 6x6x6 mm resolution)
- tracer: D2/D3 benzamide antagonist [^{11}C]raclopride bolus injection ≈ 18 mCi
- PET scans: 5 min after placebo (1) & AMP (2) administration (.3 mg/kg) for 90 min.
- MR scanner: GE Signa 1.5T, SPGR sequence
- MR segmentation: ANIMAL + INSECT [2]
- MR-PET registration: Mutual Information (MI)
- PVC method: Geometric Transfer Matrix (GTM-PVC) [3]
- Tracer model (N = 10): left/right (L/R) Caudate (CN) and Putamina (PU), Cerebellum, other Grey, White Matter, Brainstem, Scalp, other non-brain.
- data generation /extraction: automated, RC_{zmin} criterion-based ROI [4]
- physiological modeling: SRT approach [5] (Cerebellum)
- outcome: dopamine release DArel = $[BP_{ND}(1) - BP_{ND}(2)] / BP_{ND}(1)$

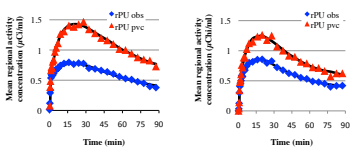


PET time-activity curves

Typical time-activity curves observed in the striatum



(e.g., right Putamen rPU)

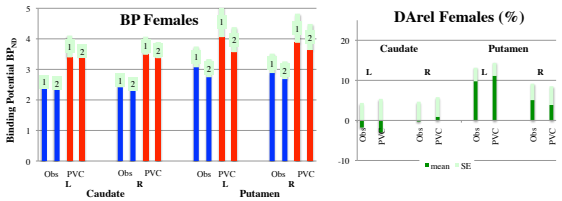


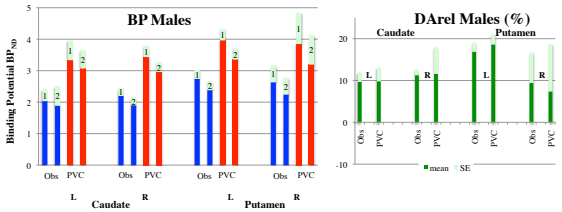
IV. Results

BP_{ND} were significantly increased in both caudate and putamen of both female and male brains after PVC ($p < 0.01$).

The observed (obs) DArel of 10% in caudate of male brains was not significantly altered after PVC, whereas caudate of female brains showed no dopamine release either before or after PVC. Female showed a 10% DArel in left putamen and 5% in right putamen, while males showed close to 20% DArel in left Putamen and close to 10% in right Putamen (no significant lateral differences).

Males showed significantly higher DArel in caudate whether before ($p = 0.03$) or after PVC ($p = 0.05$). Observed DArel were significantly higher in right putamen of males compared to females before ($p < 0.03$) and after PVC ($p < 0.02$) while DArel in left Putamen was found significantly higher in males than in females only after PVC ($p = 0.04$)





V. Discussion & Conclusions

Our application of PVC to the striatum induced a significant increase in BP_{ND} of [^{11}C]raclopride in both caudate and putamen, but the greater dopamine release seen in males was preserved after partial volume correction, indicating that striatal regions are surrounded by background of non-specific activity not affected by the amphetamine challenge.

It is however expected that regions such as striatal subdivisions that are adjacent to each other will be differentially affected by the amphetamine challenge, and would therefore benefit from PVC to achieve an even greater level of accuracy and discrimination in dopamine release estimates in the human brain.

V. References

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VI. Acknowledgements

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