Apomorphine-induced BOLD activations correlate with motor deficits and basal ganglia dysfunction in hemiparkinsonian rhesus macaques

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Abstracts will be considered for both poster and platform presentations

Movement disorders

OBJECTIVE: Identification of Parkinson's disease at the earliest possible stage of the disease may provide the best opportunity for the use of disease modifying treatments. However, diagnosing the disease during the pre-symptomatic period remains an unmet goal. Our study is to assess whether pharmacological MRI (phMRI) can be used as a diagnostic tool in the early diagnosis of Parkinson's disease.

METHODS: We used phMRI to assess the function of the cortico-basal ganglia circuit in a non-human primate model of dopamine deficiency to determine the possible relationships between phMRI signals with behavioral, neurochemical, and histological measurements.

RESULTS: Animals with unilateral treatments with MPTP that expressed stable, long-term hemiparkinsonism showed improved parkinsonian features and structure-specific phMRI blood oxygen level-dependent (BOLD) activation responses upon treatment with the dopaminergic receptor agonist apomorphine. Greater phMRI activations in the basal ganglia and cortex were associated with slower movement speed, decreased daytime activity, or more pronounced parkinsonian features. In addition, these animals showed decreased stimulus-evoked dopamine release in the putamen and substantia nigra pars compacta coupled with lower basal glutamate levels in the motor cortex on the MPTP-lesioned hemisphere compared to the contralateral hemisphere. The altered neurochemistry was significantly correlated with phMRI signals in the motor cortex and putamen. Finally, greater phMRI activations in the caudate nucleus correlated with fewer tyrosine hydroxylase-positive (TH+) nigral cells and decreased TH+ fiber density in the putamen.

CONCLUSION: Our data provide support of the possible utility of phMRI as a diagnostic tool in the early diagnosis and clinical progression of Parkinson's disease.