

Identifying Brain Areas with Significant rCBF Differences between Parkinson's Disease and Normal Control Subjects

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INTRODUCTION: Despite extensive studies in Parkinson's disease (PD) in recent decades, the neural mechanisms of this common neurodegenerative disease remain incompletely understood. Functional brain imaging technique such as single photon emission computerized tomography (SPECT) has emerged as a tool to help us understand the disease pathophysiology by assessing regional cerebral blood flow (rCBF) changes. This study applies Independent Component Analysis (ICA) to assess the difference in rCBF between PD patients and healthy controls to identify brain regions involving in PD.

METHOD: Twenty PD patients (7 with Hoehn-Yahr stage I and 13 with stage III PD) and forty eight normal-control volunteers participated in this study. Patients were imaged after at least 1 month of stable anti-parkinsonian therapy with optimal clinical benefit. Prior to scanning, subjects were injected with 740MBq (20 mCi) of [99mTc] HMPAO 30 minutes using the Dual-head Gamma Camera VariCam (GE, USA) with high resolution collimator. For each subject, the brain images were re-oriented and spatially normalized to the standard MNI (Montreal National Institute) template in SPM99. The normalized images were then analyzed by Independent Component Analysis to extract spatial independent brain areas that either account for the differences of rCBF between (normal vs PD) groups or subject variability in anatomy or rCBF. After the ICA training converged, we applied a simple statistic analysis (t-test) to the columns of unmixing matrix to identify components that account for group rCBF differences.

RESULT: The brain areas, identified by ICA accounting for group rCBF differences, including many regions in the basal ganglia, the brainstem, the cerebellum and the cerebral cortex, are consistent with pathophysiological reports in PD. Most prominently, ICA finds many significant rCBF changes in the cerebral cortex that has been largely overlooked by the previous studies using region-of-interest approaches, yet the results are consistent with pathophysiological reports. We also found decreased rCBF in the substantia nigra in PD patients. According to basal ganglia circuitry model, the neuronal loss in this region is the cause of clinical motor features of PD. However, until now, only the neuropathological study has demonstrated the involvement (i.e. neuronal loss) of this region in PD. Our result may be the first direct evidence to the well-anticipated decreased rCBF in this pathogenic region in PD.

CONCLUSION: The use of ICA can complement hypothesis-driven methods for analyzing SPECT data because: (1) ICA does not rely on a priori knowledge of the involvement of brain regions in PD. (2) ICA can be used to separate the component processes accounting for disease-related metabolic responses, non-disease related physiological phenomena and subject anatomical variability. ICA thus might be able to reveal additional connections, interactions or associations between different brain areas in PD, which might have been overlooked by some hypothesis-driven methods. Furthermore, this ICA-based data-driven approach may help or suggest neurologists to consider alternative disease and brain circuitry model in PD or other neurodegenerative diseases with a broader and more comprehensive aspect.