Multimodal neuroimaging and behavioral assessment of alpha-synuclein polymorphism rs356219 in older adults

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Introduction

The single-nucleotide polymorphism rs356219 in the a-synuclein (SNCA) gene has been shown to significantly contribute to an earlier age at onset of Parkinson's disease (PD), and regulates SNCA expression in PD brain regions, blood, and plasma. In the present study, we use an approach that combines multimodal magnetic resonance imaging (MRI) and genetics to determine if healthy older adults who carry a risk genotype for SNCA rs356219 have imaging markers in the brain that mimic those of people with a diagnosis of PD. This approach is an important first step toward understanding the role of SNCA in brain function in health and disease.

Experimental

Here, we used multimodal magnetic resonance imaging (MRI) to study healthy adults with and without the rs356219 risk genotype. Motor and cognitive tests were administered, and all participants underwent functional and structural MRI. Imaging analyses included (1) task-based functional MRI; (2) task-based functional connectivity; (3) free-water diffusion MRI of the substantia nigra; (4) voxel-based morphometry; and (5) surface-based morphometry.

Results and Discussion

There were no differences between the 2 groups in motor and cognitive performance, or brain structure.
However, carrying a PD risk variant was associated with reduced functional activity in the posterior putamen and primary motor cortex. Moreover, the posterior putamen had reduced functional connectivity with the motor cortex during motor control in those with a risk genotype compared to those without.

Conclusions

These findings point to functional abnormalities in the striatocortical circuit of rs356219 risk genotype carriers.

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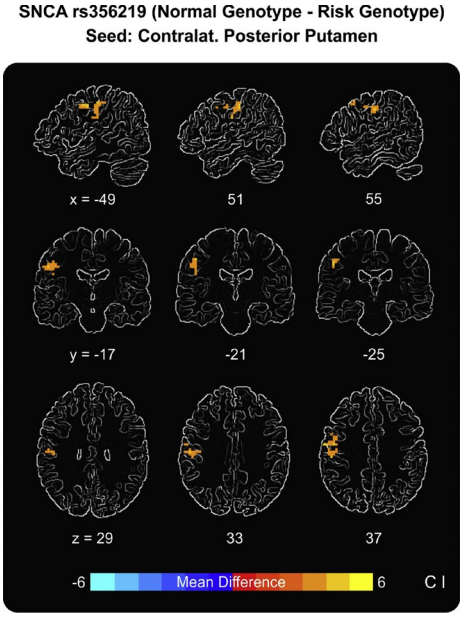

Figure 1. Task-based functional connectivity results using the contralateral posterior putamen as a seed. Results show reduced functional connectivity during grip force between the contralateral posterior putamen and a cluster in the contralateral cortical motor areas (peak in M1) in the risk genotype group compared to the normal genotype group. Abbreviation: C, contralateral; M1, primary motor cortex; I, ipsilateral.