
Cognitive ability characterization of rat model with mutated alpha-synuclein overexpression

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Résumé

Objective: The present study aims to assess cognitive function in a rat model of mutated alpha-synuclein overexpression in order to determine whether this model can be relevant to study early cognitive alterations in Parkinson's disease (PD).

Background: One third of PD patients suffer from cognitive impairments, sometimes preceding the classical motor symptoms, which has consequences for the patient's quality of life. A recent model of AAV-mediated overexpression of mutated alpha-synuclein in midbrain showed a progressive dopaminergic neurodegeneration associated with PD motor symptoms (Bourdenx et al, 2015). This progressive model can be interesting to study early cognitive alterations in PD.

Method: Twenty-four male adult Sprague Dawley rats were included in the cognitive function test (French ethical committee authorization). AAV2/9 vectors carrying the human mutant p.A53T alpha-synuclein were injected into both substantia nigra of fourteen rats and AAV-GFP marker in ten rats (as controls). A comprehensive behavioral battery of tests was performed every 4 weeks for motor skills, anxiety, working memory and object recognition for 4 months. In parallel, touchscreen based operant tasks were performed for visual discrimination (Pictures discrimination task) and attention processes (5-choices serial reaction time).

Results: Behavioral parameters analysis revealed that AAV-h α -syn injections did not induce global locomotor alteration but affected sensorimotor skills within the first month. The spontaneous alternation and the novel object recognition tests remained in the normal range suggesting no early and major working or recognition memories alteration; however anxious behavior was detected within the first 2 months on the elevated plus maze and the open-field tests. Analysis of touchscreen based operant conditioning tasks revealed that AAV-h α -syn injected rats presented attentional deficits and visuo-spatial discrimination alterations. Response on the tactile screen and food collection latencies were delayed as compared to control rats but trial number performed and sucrose appetite for the liquid reward were not affected.

Conclusion: The early anxiety, attention and visuospatial alteration observed in this nigral

*Intervenant

hm- p.A53T alpha-synuclein rat model provide a relevant opportunity to explore underlying physiopathological mechanisms and propose potential therapeutic target to improve PD patient's quality of life.

References: Bourdenx M, Dovero S, Engeln M, Bido S, Bastide MF, Dutheil N, Vollenweider I, Baud L, Piron C, Grouthier V, Boraud T, Porras G, Li Q, Baekelandt V, Scheller D, Michel A, Fernagut PO, Georges F, Courtine G, Bezard E, Dehay B. Lack of additive role of ageing in nigrostriatal neurodegeneration triggered by α -synuclein overexpression. *Acta Neuropathol Commun.* 2015 Jul 25;3:46.

Mots-Clés: Cognition, synucléine, rat