P98

Impact of safinamide on central fatigue in Parkinson's disease: preliminary data

Caterina Pauletti, N. Locuratolo, D. Mannarelli, A. Maffucci, A. Petritis, F. Fattapposta

Department of Human Neuroscience, Sapienza University of Rome, Rome, Italy

Introduction: Central fatigue has been reported to be a common and disabling symptom in Parkinson's disease (PD), affecting up to 58% of PD patients [1-2]. Safinamide is an orally administered alfa-aminoamide derivative that selectively and reversibly inhibits MAOB and blocks/modulates voltage-dependent sodium and calcium channels, as well as glutamate release, targeting both dopaminergic and glutamatergic systems. Many studies demonstrated its effectiveness in improving motor functions and fluctuations, and also in reducing non-motor symptoms, such as mood fluctuations and chronic pain, in fluctuating PD [3].

Objective: The aim of the present study was to evaluate whether safinamide could represent an effective treatment to reduce central fatigue in PD patients, given safinamide's dual mechanism of action.

Methods: 28 non-demented mid- to late-stage fluctuating PD patients with central fatigue received safinamide 100 mg as add-on therapy to a stable antiparkinsonian treatment. Before and after 6 months of treatment, patients underwent an assessment of central fatigue, as well as secondary variables such as depression, quality of life, motor and non-motor symptoms, utilizing a battery of validated scales.

Results: Central fatigue significantly improved after 24 weeks of treatment (FSS p=0.04; PFS16 p=0.05). An improvement bordering on significance was observed also in the domain 3 (mood/cognition) of the NMSS (p=0.08). On the contrary no significant variation in UPDRS-III was found.

Conclusions: Our data seem to confirm that central fatigue is a symptom intrinsic to the pathological substrates associated with PD, rather than secondary to the motor impairment. Moreover safinamide seems to ameliorate central fatigue in fluctuating PD patients after 6 months of treatment. As for many non-motor symptoms, the pathophysiology of central fatigue appears to be complex and multifactorial and a dysfunction of both dopaminergic and non-dopaminergic systems may contribute to its development. Drugs that interact with several neurotransmission systems, such as safinamide, seem to be helpful in reducing this symptom in PD patients in later stages of the disease.

References

[1] A. Chaudhuri, P.O. Behan. Fatigue and basal ganglia. J Neurol Sci. 2000 Oct 1;179(S 1-2):34-42. doi: 10.1016/s0022-510x(00)00411-1. PMID: 11054483.

[2] J.H. Friedman, R.G. Brown, C. Comella, C.E. Garber, L.B. Krupp, J.S. Lou et al. Fatigue in Parkinson's disease: a review. Mov Disord 2007;22:297–308. https://doi.org/10.1002/mds.21240

[3] E. Peña, C. Borrué, M. Mata, J.C. Martínez-Castrillo, A. Alonso-Canovas, J.L.Chico, L. López-Manzanares, M. Llanero, J. Herreros-Rodríguez, A. Esquivel, T. Maycas-Cepeda, C. Ruíz-Huete. Impact of Safinamide on Depressive Symptoms in Parkinson's Disease Patients (SADness-PD Study): A Multicenter Retrospective Study. Brain Sci. 2021 Feb 13;11(2):232. doi: 10.3390/brainsci11020232.