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WCN17-2572

SHIFT 1 - MOVEMENT DISORDERS

The efficacy and safety of unilateral deep brain stimulation for patients with Parkinson's disease

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Background: Deep brain stimulation (DBS) has been utilized successfully for patients with Parkinson's disease (PD). Simultaneous bilateral subthalamic nucleus- DBS is commonly performed for PD patients. However, there are few data investigating the effect of unilateral DBS.

Objective: The aim of this study is to investigate the efficacy and safety of unilateral globus pallidus interna (GPi)-DBS.

Patients and Methods/Material and Methods: Medication refractory PD patients undergoing unilateral or staged bilateral GPi-DBS were included. Unified Parkinson's Disease rating Scale (UPDRS) motor score was used to record at baseline and six months. Postoperative scores were recorded with DBS turned OFF and ON.

Results: Consecutive 12 patients underwent unilateral GPi-DBS were enrolled in this study. UPDRS motor score was significantly improved when baseline off scores were compared to scores with the medication off and the DBS ON (49.4 vs. 37.6, $p < 0.001$). The improvements were noted not only contralateral side (16.2 vs. 8.4, $p = 0.003$) but also ipsilateral side (15.1 vs. 13.6, $p = 0.045$). There were no neurological or neuropsychological worsening associated with DBS.

Conclusion: In this study, unilateral GPi-DBS in advanced PD patients demonstrates moderate benefit and safety. It is important to note that improvement was seen in not only contralateral side but also ipsilateral side of GPi-DBS. This study suggested unilateral GPi-DBS and subsequent staged bilateral GPi-DBS might become patient-tailored option. Symptom specific approach considering neuropsychological functions and the laterality of symptoms will be proposed to optimize outcome of the DBS. Further studies were needed with a large sample size and longer clinical follow up.

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SHIFT 1 - MOVEMENT DISORDERS

Increased interleukin 1RA and VCAM 1 in Parkinson patients with fatigue

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Background: The pathological processes causing Parkinson's disease (PD) related fatigue remains unknown. Inflammation may contribute to the development of both motor and non-motor symptoms and altered immune activation is one of the hypotheses behind fatigue in several diseases, including PD.

Objective: Serum concentrations of a panel of inflammatory markers (IL-8, TNFalpha, MCP1, MIP-1B, IL-6, IL-6R, p-selectin, Eselectin-1, ICAM, VCAM, CCL5, IL-1ra, TNFR1) were measured using ELISA technology in PD patients with and without fatigue to assess potential relationships with clinical measures.

Patients and Methods/Material and Methods: We included 49 drug naïve, newly diagnosed PD patients with low (≤3.0) or high (>5.0) fatigue levels evaluated by the Fatigue Severity Scale (FSS). Strict diagnostic criteria were applied for inclusion. Patients with possible confounding causes for fatigue were excluded.

Results: Fatigued PD patients had significantly higher levels of the IL-1 receptor antagonist (IL-1ra) (1790 pg/ml (SD1007) vs. 1262 pg/ml (SD379) and of the adhesion molecule VCAM 1, (1071 ng/ml (SD276) vs 895 ng/ml (SD229) than nonfatigued patients.
A binary logistic regression model, including high or low FSS score as the dependent variable and UPDRS motor score, MADRS, MMSE, ESS and IL-1ra as independent variable showed a significant effect only for IL-1ra and VCAM 1.

Conclusion: Higher serum levels of inflammatory molecules were associated with higher fatigue levels in patients with newly-diagnosed, drug naïve PD. These findings highlight altered immune response as a potential contributor to PD-related fatigue from the earliest clinical stages of the disease.

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SHIFT 1 - MOVEMENT DISORDERS

Clomiphene hydrochloride induces autophagy by inhibition of mTORC1 with partial lysosomal neutralization effects especially under starvation

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Background: Because conditional loss of autophagy in the central nervous system causes neurodegeneration with neuronal inclusions, autophagy enhancement is expected for novel therapeutic strategy against neurodegenerative disease.

Objective: In this context, we performed a screening with clinically approved library consisting of 800 medicines in Japan for autophagy enhancer detection for neurodegeneration therapy.

Patients and Methods/Material and Methods: A chemical library containing clinically approved medicines in Japan is established by Prof. Hideyuki Saya. HeLa cells stably expressing GFP-LC3 treated with 10 mM each chemical from the library for 24 hours were analyzed with a fluorescence microscope according to the method previously reported.

Results: Herein we show that clomiphene increased the levels of LC3-II in a dose-dependent manner as well as a time-dependent manner. Autophagic flux assessed by clomiphene treatment associated with/witout lysosomal proteinases inhibitors was enhanced. Likewise, the number of abnormally elongated huntingtin aggregates, a well-established autophagy substrate, was decreased by clomiphene treatment. Levels of phosphorylated proteins in the downstream of mTORC1, p70 ribosomal protein S6 kinase (Thr 389), S6 ribosomal protein (Ser235/236) were significantly suppressed by clomiphene treatment, whilst that of phosphorylated Akt (Ser473) was not changed. U0126, an inhibitor of mitogen-activated protein kinase kinase 1/2, did not suppress the clomiphene-induced autophagy.

Conclusion: Although mild lysosomal neutralization presenting with reduced autophagic flux of clomiphene in starvation condition was