P44

Quantitative dopamine transporter imaging assessment in Parkinson's disease (PD) patients carrying GBA gene mutations compared with Idiopathic PD patients: a case-control study

Sara Grisanti[1], F. Cavallieri[2], A. Fraternali[3], V. Fioravanti[2], M. Casali[3], G. Toschi[2], L. Ferri[2,4], R. Sabadini[2], A. Scaglioni[5], V. Ferrari[2], M. Scarano[6], G. Biagini[7], A. Versari[3], F. Valzania[2]

[1]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy.
[2]Neurology Unit, Neuromotor and Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy.
[3]Nuclear Medicine Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy.
[4]Department of Neuroscience, Imaging and Clinical Sciences, "G. D'Annunzio" University of Chieti-Pescara, Chieti, Italy.
[5]Centro S. Maria ai Servi, Fondazione Don Gnocchi, Parma, Italy.
[6]Dipartimento di Cure Primarie, Azienda Unità Sanitaria Locale (AUSL) Modena, Modena, Italy.
[7]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy.

Background: Mutations in the glucocerebrosidase (GBA) gene are the single largest risk factor for development of Parkinson's Disease (PD) [1]. Compared to idiopathic PD (I-PD), GBA-PD is characterized by earlier onset, worse motor impairment, higher risk of cognitive decline and depression, more rapid progression, and decreased survival [2]. However, even if clinical differences have been found, data about possible differences of dopaminergic imaging studies is still lacking.

Objectives: To compare single photon emission computed tomography (SPECT) with Ioflupane I123 injection quantitative parameters from two homogenous cohorts of GBA-PD and I-PD patients and to correlate them with clinical variables.

Methods: This case-control study included two homogenous cohorts of GBA-PD and I-PD patients. All patients have been previously screened for the presence of pathogenic LRKK2, GBA, SNCA and PARKIN genes mutations. Each GBA-PD patient has been matched with a 1:1 pairing method with an I-PD subject according to sex, age, age at disease onset, and comorbidities. For each patient the following clinical variables have been collected: Charlson Comorbidity Index (CCI), Levodopa Equivalent Daily Dose (LEDD), motor phenotype (Postural Instability and Gait Disorders [PIGD] or tremor phenotype), Hoehn and Yahr (H&Y) staging, most affected side, disease duration. All patients previously underwent single photon emission computed tomography (SPECT) with Ioflupane I123 injection at the time of PD diagnosis. Quantitative volumetric data were extrapolated from [123I]-FP-CIT using the DatQuant software. The following quantitative measures were calculated: bilateral specific binding ratio (SBR) for Striatum, Caudate, Putamen (anterior, posterior, and global); putamen and caudate asymmetries; putamen/caudate ratios and SBR in the most affected and least affected putamen and caudate nuclei. Mann Whitney test was performed to compare the two groups while Spearman rank correlation test was performed in each group to find correlations between clinical and DatQuant variables. Significant p-value has been considered at 0.05.

Results: 50 PD patients were included in the analysis (30 males, mean age: 65.18 years; mean disease duration: 6.92 years; mean H&Y: 2.33; mean LEDD: 688.06 mg; mean CCI: 2.78) including 25 GBA-PD that were matched with 25 I-PD. The two cohorts (GBA PD and I-PD) were superimposable in terms of sex, age at disease onset, disease duration, CCI, motor phenotype, H&Y stage and side of disease onset. In terms of comparison between the two groups, we have identified a significant

statistical difference in terms of SBR of the most affected anterior putamen (P=0.028) and SBR of the left caudate (P=0.043). Regarding the GBA-PD cohort, we found a negative correlation between the SBR of the most affected posterior putamen and H&Y stage (C=-0.568, P=0.003) meaning that patients whit a lower uptake in this region at diagnosis showed a higher disease severity after a mean six-year follow-up. Concerning the I-PD cohort we found a negative correlation between the SBR of the most affected caudate and LEDD (C=-0.460, P=0.021) meaning that patients whit a lower uptake in this region at diagnosis showed a higher total dosage of dopaminergic medications after a mean six-year follow-up.

Conclusions: This comparison analysis has underlined subtle significant differences in quantitative DaTquant parameters between two homogeneous cohort of GBA-PD and I-PD at PD diagnosis suggesting that the nigrostriatal system denervation may differ in GBA-PD especially in the anterior putamen. Furthermore, in the GBA-PD cohort the SBR of the posterior putamen at time of diagnosis has been confirmed as a potential indicator for evaluating the severity of the disease [3].

References:

[1] O'Regan G, deSouza RM, Balestrino R, Schapira AH. Glucocerebrosidase Mutations in Parkinson Disease. J Parkinsons Dis. 2017;7(3):411-422.

[2] Petrucci S, Ginevrino M, Trezzi I, Monfrini E, Ricciardi L, Albanese A, Avenali M, Barone P, Bentivoglio AR, Bonifati V, Bove F, Bonanni L, Brusa L, Cereda C, Cossu G, Criscuolo C, Dati G, De Rosa A, Eleopra R, Fabbrini G, Fadda L, Garbellini M, Minafra B, Onofrj M, Pacchetti C, Palmieri I, Pellecchia MT, Petracca M, Picillo M, Pisani A, Vallelunga A, Zangaglia R, Di Fonzo AB, Morgante F, Valente EM; ITA-GENE-PD Study Group. GBA-Related Parkinson's Disease: Dissection of Genotype-Phenotype Correlates in a Large Italian Cohort. Mov Disord. 2020 Nov;35(11):2106-2111. doi: 10.1002/mds.28195.

[3] Wang J, Zuo CT, Jiang YP, Guan YH, Chen ZP, Xiang JD, Yang LQ, Ding ZT, Wu JJ, Su HL. 18F-FP-CIT PET imaging and SPM analysis of dopamine transporters in Parkinson's disease in various Hoehn & Yahr stages. J Neurol. 2007 Feb;254(2):185-90.