Research Project Proposal
Academic year 2021-2022
Máster en Investigación Biomédica

Project Nº 04 ASIGNADO

Title: *Brain Metabolic signatures in primary progressive aphasia variants.*

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Summary *Primary progressive aphasia (PPA) captures a group of neurodegenerative syndromes in which progressive language impairment is the initial and predominant deficit. Three clinical variants have been described: nonfluent/agrammatic variant (agPPA), semantic variant (svPPA), and logopenic variant (lvPPA). Diagnostic criteria for these clinical variants are well stablished. However, 10-40% of patients with PPA are not classifiable as one of the previous mentioned variants, which are designated as unclassifiable PPA.*

The objective of this study is to characterize a cohort of patients with a clinical diagnosis of PPA, and to stablish and validate the metabolic abnormalities assessed by FDG-PET related to each clinical variant.

We will retrospectively include patients with a clinical diagnosis of PPA followed in the Memory Unit at Department of Neurology (CUN). All patients should have undergone a thorough neurological and neuropsychological examination, and a multimodal neuroimaging study (brain MRI, FDG-PET and amyloid PET).

Regarding FDG-PET imaging data, we will use two different methods to analyse the glucose metabolic abnormalities associated to the variants of PPA. On the one hand, we will perform a univariate analysis using the Statistical Parametring Mapping version 12 (SPM12) implemented on Matlab®. A factorial ANOVA will be used to identify the differences in regional metabolism between the groups (agPPA vs healthy controls -HC-, svPPA vs HC, lvPPA vs HC, agPPA vs svPPA, agPPA vs lvPPA and svPPA vs lvPPA), including sex, age and PET procedures as fixed factors. SPM t-maps will be created considering clusters with a size of >50 voxels at a defined threshold of $p<0.05$, with a multiple comparison correction by family-wise error. We will also perform conjunction analyses to assess the common metabolic abnormal regions between variants of PPA.

On the other hand, we will perform a multivariate analysis (scaled subprofile modeling/principal component analysis, SSM/PCA) to identify a PPA related pattern within each variant among the FDG-PET data from the identification populations (svPPARP, agPPARP and lvPPARP). The identification populations will encompass each variant of PPA and HCs. We will apply an automated algorithm based on the method described by Spetsieris and Eidelberg. This analysis can be used to calculate subject scores not only in the identification subjects, but also in new subjects. The diagnostic accuracy of the three patterns will be validated onto an independent population that will include different variants of PPA and unclassifiable PPA. We will use Receiver Operating Characteristic curves analyses to assess the diagnostic accuracy of the expression of each pattern. To compare the individual expression of each pattern between groups we will use a one-way ANOVA with a correction for multiple comparisons (Bonferroni method).

Finally, we will correlate specific linguistic features of each PPA variant with brain metabolism abnormalities.

yes	
no	**X**

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?