variantes com maior probabilidade de ser funcionais, foram aplicadas as ferramentas: RegulomeDB, que prediz SNPs com funções regulatórias; SIFT, Polyphen2, CADD e CONDEL para selecionar aqueles com efeitos deletérios; e o MirSNP para identificar os que estão em sítios de ligação a miRNA. Entre os 254 SNPs selecionados pelo RegulomeDB, 14 atingiram um escore igual a um, (máximo). Responsáveis por afetar a função de 181 diferentes miRNAs, foram identificados 58 SNPs distribuídos em 24 genes. Cinco variantes foram preditas como potencialmente deletérias, quatro delas (rs641351, rs2279574, rs4833837 e rs3764002) apontadas por todas as ferramentas e uma (rs602662) por pelo menos três delas. Assim, 317 variantes no total foram priorizadas por apresentarem um maior potencial de serem causais. Esse trabalho continua em andamento e os próximos passos são refinar a priorização dessas variantes selecionadas utilizando bancos de dados de transcriptômica e metiloma, bem como testar esse conjunto final de variantes para os diferentes desfechos clínicos do TDAH numa amostra de pacientes diagnosticados no Programa de Déficit de Atenção e Hiperatividade (PRODAH) do Hospital de Clínicas de Porto Alegre.

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MAY LYSOSOMAL-RELATED GENES BE LINKED TO ATYPICAL PARKINSONISM?

CATEGORIA DO TRABALHO: PESQUISA

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Introduction: Atypical parkinsonism (AP) refers to a group of diseases that presents clinical manifestations of a parkinsonian syndrome. AP consists of the following diseases: progressive supranuclear palsy (PSP), multiple system atrophy (MSA), corticobasal degeneration (CBD) and Lewy body dementia (LBD). Some genes have been implicated as being potentially involved in the pathophysiology of AP forms. It is already known that patients with Gaucher disease (GD) who have pathogenic variants in both alleles of the GBA1 gene and their relatives showed signs of parkinsonism more often than expected. In addition, other genes related to lysosomal diseases distinct that GD seems to be related to parkinsonism. Aim: The aim of this study was to verify the existence of variants in genes associated with lysosomal diseases in patients with AP. Methods: Thirteen patients with regular care at the Hospital de Clínicas de Porto Alegre (HCPA) with the diagnostic criteria for PSP, MSA, LBD and CBD were recruited, and six patients were previously analyzed. Peripheral blood was collected for DNA extraction. A customized research panel, already developed and validated, was used to sequence all exons and their boundaries regions of GBA1, SMPD1, LIPA, NPC1, NPC2 and PSAP genes. The sequencing was carried out using the Ion S5 System platform. Ethics Committee Approval: CAAE 286171831001532. Results: Out of 6 patients, only one presented a suspect variant located in a coding region. This patient had a previous diagnosis of PSP and the identified variant p.Asn222Ser (c.665A>G) is located in the NPC1 gene. Forty-five control samples were also analyzed, and none presented this variant. Using four different in silico tools for pathogenicity prediction (Mutation Taster, Polyphen, SIFT and M-CAP), results for p.Asn222Ser were conflicting. This variant was classified as variant of uncertain significance according to the ACMG criteria. However, the p.Asn222Ser variant has already been associated with PD and CBD patients in other studies. In the rest of the patients, none possibly pathogenic variants were found. Conclusions: Although our results are preliminary, we highlight that the p.Asn222Ser may be involved in AP. Further studies with a bigger number of AP patients are needed to better understand this association.

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DOENÇA DE PARKINSON DE CAUSA MONOGÊNICA: RELATO DE UM NOVO CASO COM MUTAÇÃO NO PARK7

CATEGORIA DO TRABALHO: RELATO DE CASO ÚNICO

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