GRM3和DTNBP1基因單一核?酸多態性與台灣精神分裂症之關聯性 = Correlations of single nucleotide polymorphisms in GRM3 and DT

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摘 要

精神分裂症（schizophrenia）是一種最嚴重的精神疾病，近期的研究顯示約64~81%的精神分裂症病患與基因遺傳有關。近年的研究指出麩胺酸神經傳導路徑與精神分裂症有關，因此我們挑選GRM3和DTNBP1基因來分析基因多態性與精神分裂症的關聯。GRM3產物是在神經突觸的麩胺酸G蛋白受體，對於麩胺酸的神經傳遞扮演重要的角色；DTNBP1是負責編碼dysbindin蛋白在人腦的多個區域表現，該蛋白參與建立和維持神經元和肌肉細胞的連繫，以正確完成大腦的指令，是麩胺酸和多巴胺神經傳導路徑的關鍵蛋白之一。 本研究針對藥物控制效果良好(第一型)和藥物控制效果不佳(第二型)的精神分裂症病患與正常人的GRM3和DTNBP1這兩基因的六組單一核?酸多態性（single nucleotide polymorphisms, SNPs）：rs2299225、rs1468412、rs7758659、rs760666、rs875462與rs3213207，分別設計引子來進行聚合?鏈鎖反應，擴增SNP附近序列。首先確認是否有插入或缺失突變，之後再進行序列分析，確認個別SNP是否有點突變和附近序列的正確性，並比較這些突變是否有統計意義，以了解DTNBP1和GRM3的個別SNP與精神分裂症是否有關聯。 精神分裂症發病年齡統計結果顯示，第一型與第二型精神分裂症病患在發病年齡上無顯著差異；在性別與發病年齡上，第一型與第二型精神分裂症病患皆無顯著差異。此外我們還發現41~50歲的病患人數百分比第一型精神分裂症小於第二型精神分裂症。由對偶基因頻率的關聯分析結果得知，GRM3基因的rs1468412和 DTNBP1基因的rs3213207與精神分裂症有關聯性（p=0.004和p=0.043），而其餘四組SNPs皆與精神分裂症無關聯性。在精神分裂症與性別在對偶基因頻率的關聯性分析結果發現，rs1468412達顯著水準（p=0.01）。在DTNBP1基因的rs875462鄰近位置NT_007592.15:g.15478430(A△)發現與精神分裂症具有關聯性（p=0.009）。 本研究結果證明GRM3和DTNBP1的基因多態性與台灣精神分裂症病患有關聯性，rs1468412和rs3213207這兩組SNPs變異，可能在我們台灣人族群是造成罹患精神分裂症的因子。

關鍵詞 : 精神分裂症、GRM3基因、DTNBP1基因、單一核?酸多態性

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