ALS AND FTLD: COGNITIVE CHANGES AND GENETIC MARKERS

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BACKGROUND

Amyotrophic lateral sclerosis (ALS) may be accompanied by cognitive impairment; when present, it is mainly in the form of frontotemporal impairment. Frontotemporal lobar degeneration (FTLD) is a focal, non-Alzheimer form of dementia, clinically characterized as either behavioral or aphasic variants (1). The overlap between dementia and ALS is demonstrated by the presence of cognitive, behavioural, executive dysfunction and change of personality in up to 50% of ALS patients (2). Behavioural features are mostly due to changes in serotoninergic and catecholaminergic system (3).

OBJECTIVE

To identify genetic correlates of cognitive changes with the emphasis on executive function in ALS patients.

MATERIALS AND METHODS

In a prospective study, two tests of executive functions (Controlled oral word association – FAS test; Tower of London (TOL)), were applied on 16 ALS patients (10 male, 60.5 ± 5.8 years), as defined by El Escorial Criteria. All subjects also completed the Dementia Rating Scale II (DRS-II). 1021 C/T polymorphism of DBH gene, 102 C/T polymorphism of 5-HT2A receptor gene, val66met polymorphism of COMT gene and val 158/108met polymorphism of BDNF gene were correlated with a cognitive tests.

RESULTS

ALS patients carrying GG, GA and AA genotype of the BDNF gene polymorphism were 73%, 20% and 7%, respectively. The frequency of GG, GA, AA genotype for COMT gene polymorphism was 33%, 53% and 14%, respectively. The DBH gene polymorphism distribution was 47%, 47% and 6% for CC, CT and TT genotype, respectively. The frequency of CC, CT, TT genotype for 5-HT2A gene polymorphism was 30%, 60% and 10%, respectively. 57% of patients showed deficient word generation capability. 21% of patients were impaired on TOL Total move score and 33% of patients on TOL Total rules violation score. 40% of patients were impaired at DRS II Conceptualization subtest and 20% of patients on DRS-II Memory subtest. No significant ($p>0.05$) relationship between genes polymorphism and variables of executive functional tests was found (4).

CONCLUSIONS

The preliminary findings reveal a tendency for executive deficit in ALS. There is a potential genotype-specific influence in ALS for executive functions. Further studies on a larger sample, however, are needed in order to confirm it.

References:

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