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Poster presentation

Molecular investigation of Angelman syndrome in Greece. Screening for UBE3A mutations: preliminary results

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Background

Angelman syndrome (AS) is a severe neurodevelopmental disorder characterized by mental retardation, absence of speech, ataxia, seizures and hyperactivity. Individuals with AS lack a normal active maternal copy of the UBE3A gene, encoding ubiquitin protein ligase (E6AP). In 80% of patients the clinical diagnosis is verified by molecular detection of one of the typical 15q11-q13 abnormalities, including chromosomal deletions (70%), paternal uniparental disomy (3- 5%) or imprinting centre mutations (7%). Heterozygous loss- of- function mutations of E6AP have been identified in approximately 8% of cases. UBE3A gene is imprinted in human brain, with the paternal allele being normally silenced. E6AP is a member of E3 ubiquitin ligase protein family which plays a role in defining substrate specificity of the ubiquitin- proteasome degradation system. The exact mechanism by which the defective E6-AP gene causes AS remains unknown. Clinical findings seem to be due to failure to degrade various proteins, accumulation of which may be harmful for an individual.

Materials and methods

30 patients referred for AS, with no other molecular defect identified, were screened for mutations in the UBE3A gene (exons 9, 12, 15 and 16). Direct automated sequencing together with ECMA assay were performed in order to identify mutations in this group of patients.

Results

No mutations were detected in any of the UBE3A exons studied.

Conclusions

Further screening of all exons of UBE3A, as well as other genes, related to AS- like phenotypes, such as MECP2 gene, will probably identify mutations, confirming the clinical diagnosis and providing information about the molecular mechanisms.