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GENETIC “METABOLIC” EVALUATION OF INTELLECTUAL DISABILITY: INVESTIGATING INBORN ERRORS OF METABOLISM AS CAUSE OF MENTAL RETARDATION

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Introduction: Inborn errors of metabolism (IEMs) comprise a subgroup of genetic disorders characterized, in most cases, by a dysfunction of an enzymatic pathway involved in cellular metabolism. With around 350 different diseases identified to date, IEMs represent about one-third of genetic diseases; nevertheless they are overlooked as a cause of mental retardation in studies of groups with mental impairment. Furthermore, although rare, the collective incidence of IEMs is 1 in 1,500 persons, which justifies the creation of a specific protocol to investigate the incidence of IEMs in patients with mental retardation/global developmental delay.

Aims: The aim of this study was to evaluate patients of APAE (Associação dos Pais e Amigos dos Excepcionais), special school for children and adults with mental impairment, located at Limeira, Sao Paulo State, southeast Brazil.

Material and methods: We surveyed 300 patients through a standard protocol for investigation of intellectual disability (clinical evaluation, cytogenetical studies, PKU and hypothyroidism screening in Guthrie card, FRAXA and FRAXE PCR molecular screening); 102 out of 300 patients were selected for “metabolic screening” with a metabolic panel (GAGs analyses, organic acids and aminoacids chromatography, creatin studies, T3/T4/RT3 blood studies, ammonia, lactate, CK, glycemia, acid uric and homocystein dosage, SAICAR analysis and fibroblasts studies, when indicated).

Results: 13 patients were diagnosed with an IEM. MCAD deficiency, folate remethylation defects, creatin transport deficiency, Hunter syndrome, urea cycle disorders, Niemann-Pick type C disease, holocarboxylase synthetase deficiency were some of the IEMs identified.

Conclusion: A diagnosis of an IEM offers not only the opportunity to discuss treatment, prognosis, and genetic recurrence risk for the families but also the possibility of a specific therapeutic approach since many metabolic hereditary disorders are amenable to treatment.