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ORIGINAL ARTICLE

Cognitive and behavioral heterogeneity in genetic syndromes☆

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Abstract
Objective: this study aimed to investigate the cognitive and behavioral profiles, as well as the psychiatric symptoms and disorders in children with three different genetic syndromes with similar sociocultural and socioeconomic backgrounds.
Methods: thirty-four children aged 6 to 16 years, with Williams-Beuren syndrome (n = 10), Prader-Willi syndrome (n = 11), and Fragile X syndrome (n = 13) from the outpatient clinics of Child Psychiatry and Medical Genetics Department were cognitively assessed through the Wechsler Intelligence Scale for Children (WISC-III). Afterwards, a full-scale intelligence quotient (IQ), verbal IQ, performance IQ, standard subtest scores, as well as frequency of psychiatric symptoms and disorders were compared among the three syndromes.
Results: significant differences were found among the syndromes concerning verbal IQ and verbal and performance subtests. *Post-hoc* analysis demonstrated that vocabulary and comprehension subtest scores were significantly higher in Williams-Beuren syndrome in comparison with Prader-Willi and Fragile X syndromes, and block design and object assembly scores were significantly higher in Prader-Willi syndrome compared with Williams-Beuren and Fragile X syndromes. Additionally, there were significant differences between the syndromes concerning behavioral features and psychiatric symptoms. The Prader-Willi syndrome group presented a higher frequency of hyperphagia and self-injurious behaviors. The Fragile X syndrome group showed a higher frequency of social interaction deficits; such difference nearly reached statistical significance.
Conclusion: the three genetic syndromes exhibited distinctive cognitive, behavioral, and psychiatric patterns.

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PALAVRAS-CHAVE
Cognição;
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Síndrome de Williams-Beuren;
Síndrome de Prader-Willi;
Síndrome do X-Frágil

Heterogeneidade cognitiva e comportamental em síndromes genéticas

Resumo

Objetivo: investigar o perfil cognitivo e comportamental, sintomas e transtornos psiquiátricos em crianças com três diferentes síndromes genéticas, com antecedentes socioculturais e socioeconômicos semelhantes.

Métodos: trinta e quatro crianças, entre 6 e 16 anos, com as síndromes de Williams-Beuren (n = 10), de Prader-Willi (n = 11) e do X-Frágil (n = 13), dos ambulatórios de Psiquiatria Infantil e Genética Médica, foram avaliadas cognitivamente pela Escala Wechsler de Inteligência para Crianças (WISC-III). Posteriormente, o QI total, o QI Verbal, o QI de Execução, os escores ponderados dos subtestes e a frequência de sintomas e transtornos psiquiátricos foram comparados entre as síndromes.

Resultados: diferenças significativas foram encontradas entre as síndromes quanto ao QI Verbal e os subtestes verbais e de execução. A análise *Post-hoc* demonstrou que os escores dos subtestes vocabulário e compreensão foram significativamente superiores na síndrome de Williams-Beuren em relação às síndromes de Prader-Willi e do X-Frágil, e os escores dos subtestes cubos e armar objetos foram significativamente superiores na síndrome de Prader-Willi em relação às síndromes de Williams-Beuren e do X-Frágil. Além disso, houve diferença significativa entre as síndromes quanto às características comportamentais e os sintomas psiquiátricos. O grupo com síndrome de Prader-Willi apresentou maior frequência de hiperfagia e comportamentos autolesivos. Já o grupo com síndrome do X-Frágil apresentou maior frequência do déficit da interação social. Esta diferença quase alcançou a significância estatística.

Conclusão: as três síndromes genéticas apresentaram um padrão cognitivo, comportamental e psiquiátrico diferenciado quando foram comparadas entre si.

Introduction

Intellectual disability (ID), the current term for mental retardation, is one of the most commonly observed neuropsychiatric disorders that impairs social functioning and adaptive behavior of children and adolescents.[1] In underdeveloped countries, the prevalence of ID is almost two times higher than in developed countries.[2]

Common causes of ID are genetic diseases, problems during pregnancy or birth, birth defects that affect the brain, and problems during infancy, childhood, and adolescence, such as injuries, diseases, or brain abnormalities.[3] In underdeveloped and developing countries, malnutrition, socio-cultural deprivation, and poor healthcare are also factors frequently associated with ID.[4]

Patients with ID present higher risk for psychiatric disorders than the general population. The rate of psychiatric disorders in this population ranges from 30% to 50%.[4]

Despite the high prevalence of ID and strong association with psychiatric disorders, mental health professionals often fail to give proper attention to ID.[5,6] When caring for less prevalent conditions in mental healthcare, such as genetic syndromes with ID,[7] clinicians frequently ignore their specific cognitive, behavioral, and psychopathological characteristics.

Three genetic syndromes featuring ID have been receiving increasing attention by specialists in the care of children with genetic syndromes due to their diverse expression of cognitive and behavior characteristics: Williams-Beuren syndrome (WBS), Prader-Willi syndrome (PWS), and Fragile X syndrome (FXS).[8–10]

WBS, a rare neurodevelopmental disorder caused by a submicroscopic deletion on chromosome 7q11.23, is characterized by dysmorphic facial features, elastin arteriopathy, short stature, connective tissue abnormalities, infantile hypercalcemia, and ID.[11] Children with WBS usually display high sociability, excessive empathy (which may be inappropriate), anxiety, preoccupations and fears, impulsivity, inattention, sadness and depression, generalized anxiety disorder, phobias, and attention deficit hyperactivity disorder.[7,12] Relatively good language skills and verbal short-term memory, and a marked deficit in visuospatial skills have been described in WBS.[8,13]

PWS, a genetic disorder that results from abnormality or loss of a critical region of chromosome 15q11–13, is characterized by neonatal hypotonia, hyperphagia with eventual obesity, and ID.[7] Children with PWS usually have good performance in visuospatial construction tasks,[5,9] but present important deficits in mathematics[14] and expressive language.[15]

Individuals with PWS exhibit a distinctive behavioral phenotype, with temper tantrums, stubbornness, and excessive interest in food; as well as obsessive, compulsive, manipulative, oppositional, and defiant behaviors.[16] The psychiatric features commonly reported in PWS are obsessive-compulsive disorder, depression/mood disorder, psychosis, and self-injurious behaviors (skin picking).[7]

FXS, a disorder caused by an unusually large trinucleotide repeat (CGG) expansion in the long arm of the X chromosome, is the most common cause of inherited ID.[10] The cognitive profile in FXS includes deficits in executive control and in visuospatial abilities,[17] as well