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ORIGINAL ARTICLE

Concordance between a head circumference growth function and intellectual disability in relation with the cause of microcephaly☆,☆☆

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Microcephaly;
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Abstract
Introduction: Our aim was to investigate the correlations between patterns of head growth and intellectual disability among distinct aetiological presentations of microcephaly.
Patients and methods: 3269 head circumference (HC) charts of patients from a tertiary neuropaediatric unit were reviewed and 136 microcephalic participants selected. Using the *Z*-scores of registered HC measurements we defined the variables: HC Minimum, HC Drop and HC Catch-up. We classified patients according to the presence or absence of intellectual disability (IQ below 71) and according to the cause of microcephaly (idiopathic, familial, syndromic, symptomatic and mixed).
Results: Using discriminant analysis a *C*-function was defined as *C* = HC Minimum + HC Drop with a cut-off level of *C* = −4.32 *Z*-score. In our sample 95% of patients scoring below this level, severe microcephaly, were classified in the disabled group while the overall concordance was 66%. In the symptomatic-mixed group the concordance between HC function and outcome reached 82% in contrast to only 54% in the idiopathic-syndromic group (*P*-value = 0.0002).
Conclusions: We defined a HC growth function which discriminates intellectual disability of microcephalic patients better than isolated HC measurements, especially for those with secondary and mixed aetiologies.

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Concordancia entre una funcion de crecimiento del perimetro cefalico y la discapacidad intelectual en relacion con la etiologia de la microcefalia

Resumen
Introducción: Nuestro objetivo fue investigar la correlación entre patrones de crecimiento cefálico y discapacidad intelectual entre distintas presentaciones etiológicas de microcefalia.
Pacientes y métodos: 3.269 gráficas de perímetro cefálico (PC) de una unidad de neuropediatría terciaria fueron revisadas y 136 participantes con microcefalia seleccionados. Utilizando las puntuaciones Z de las medidas de PC registradas definimos las variables: PC Mínimo, Caída de PC y Recuperación de PC. Los pacientes se clasificaron según la existencia o no discapacidad intelectual (CI inferior a 71) y según la causa de la microcefalia (idiopática, familiar, sindrómica, sintomática y mixta).
Resultados: Mediante el uso del Análisis Discriminante se definió una función C como C = PC mínimo + Caída de PC con un nivel de corte de puntuación Z de C = −4.32. En nuestra muestra, el 95% de pacientes con resultados por debajo de este nivel, microcefalia severa, presentaban discapacidad intelectual. La concordancia global entre la función de PC y la presencia de discapacidad intelectual fue del 66%. En el grupo de sintomáticas y mixtas esta concordancia alcanzó el 82%, en contraste con sólo el 54% del grupo de idiopáticas y sindrómicas (P = 0,0002).
Conclusiones: La utilización de una función de crecimiento del PC discrimina la discapacidad intelectual en pacientes con microcefalia mejor que mediciones aisladas de PC, especialmente en etiologías secundarias y mixtas.

Introduction

Head circumference (HC) measurement is an easy method to assess brain growth. Microcephaly, defined as a statistically abnormally low HC, has a relationship with mental retardation which is well known since the 19th century.[1] This relationship was extensively studied during the second half of the 20th century[2–10] and for a general population it was established that a HC below −2 standard deviations (SD) for age and sex is associated with an IQ below 70 in 10% of the children, and in 51% for those with a HC below −3 SD.[9]

Head growth patterns have been proposed as an important tool in the assessment of microcephaly.[11,12] However, they have been defined using the shape of the HC curves on the charts rather than on mathematical models. It is clear that the lower the HC the child has the greater the likelihood of neurological impairment is.[9] But it is not known for all aetiologies of microcephaly which level of low velocity in HC growth is associated with a comparable outcome.

There are many different neurological conditions causing microcephaly or slow HC growth and some of them have already been object of research. In hypoxic–ischaemic encephalopathy slight decelerations imply neurological impairment even before the microcephalic range is attained[13] and the patterns of lesions found in magnetic resonance imaging (MRI) correlate with HC growth and neurological status.[14] Research on congenital rubella[15] has shown normal intelligence in the presence of microcephaly when children with hearing and vision losses were excluded. Conversely, microcephaly was the most specific early predictor of mental retardation in congenital CMV infection[16] while neurologic disorders do not develop in the majority of congenitally infected infants.[17] In very low weight birth infants Hack and cols[18] found that HC at 8 months of age was the best growth predictor of intelligence quotient at 3 years of age. In another study the presence of HC catch-up growth before the age of 6 months was associated with fewer motor abnormalities at 12 months.[19] A normal HC at 12 months in pre-term infants with intracranial haemorrhage was associated with a better outcome.[20] Regev and cols[21] found that slow head growth after intra-cranial haemorrhage correlated with a poor neurodevelopmental outcome. Ionizing radiation exposure,[22] malnutrition,[23] medication during pregnancy[24] and genetic or primary microcephaly[25,26] are other known causes of small head and mental retardation. Microcephaly is also a clinical feature of hundreds of multiple malformation syndromes.

In a hospital based retrospective study of 58 microcephalic patients, neuroimaging was concluded to be the best study in order to establish aetiology[27] and in another study MRI was abnormal in 80% of 55 microcephalic paediatric patients.[28]

In our study we aimed to investigate the concordance of a HC growth function with intellectual disability among different aetiological clinical presentations in a sample of microcephalic infants and children.

Patients and methods

We retrospectively studied patients from a tertiary hospital neuropaediatric unit in Spain which serves as a referral area for three million people. Since 1982 a follow-up HC Nellhaus Chart[11] according to patient's sex was routinely placed in every medical record during the first visit regardless of