Head circumferences of patients with Dravet syndrome show growth slowdown

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Abstract

The measurement of head circumference (HC) represents a useful and reliable tool to monitor brain growth. Many genetic conditions are associated with an abnormal pattern of head growth, but no specific pattern has been described in Dravet Syndrome (DS). To investigate the head growth trajectories in a pediatric population with DS, a retrospective analysis of medical records of patients with DS was performed in 2 epilepsy centers. Quantitative data were compared with z-score growth curve of standard population, and an independent samples t-test was performed using 6-month ranges. A total of 137 subjects aged less than 18 years were included, with a total of 529 HC values and a mean of 3.9 measures per patient. From birth until 24 months of life, HC values were almost equally distributed around the mean trajectory of the reference population from each side of the curve. This trend line deflects from the mean curve after 24 months showing a head growth slowdown reaching a statistical significance (p < .05) from 48 months for males and 60 for females. Future prospective studies are needed to assess factors that can impact head growth and explore possible phenotype–genotype correlation with HC.

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Keywords:
Dravet Syndrome
Head circumference
Developmental and epileptic encephalopathy

1. Introduction

The measurement of head circumference (HC) is a major step of the clinical examination and represents a useful and reliable tool to monitor brain growth in childhood since it correlates with brain volume and weight. Many genetic conditions with epilepsy are associated with an abnormal pattern of head growth, but no specific pattern has been described in Dravet Syndrome (DS).

Dravet Syndrome is a developmental and epileptic encephalopathy (DEE) occurring in the first year of life in previously healthy infants, characterized by the onset of recurrent febrile and afebrile seizures often evolving to status epilepticus. Epilepsy is drug-resistant and associated with a slowing of cognitive development and psychiatric, behavioral, motor, and sleep disorders with a high rate of Sudden Unexpected Death in Epilepsy (SUDEP) [1]. In a small series of adults with DS (n = 14), HC was reported in normal range without reporting HC measurements [2]. However, signs of mild and diffuse cerebral or cerebellar atrophy were occasionally reported in patients with DS [3]. Furthermore, in some patients, brain atrophy appeared during follow-up [3,4].

We aimed in this pilot study to investigate head growth trajectories in pediatric patients with DS.

2. Material and methods

We performed a retrospective analysis of HC from medical records of patients with DS in 2 pediatric epilepsy centers in Paris, France and Verona, Italy. We included data from all patients with definite diagnosis of DS and who had at least 2 HC measures reported in the medical file. A total of 137 subjects aged less than 18 years were included (76 males and 61 females) with a total of 529 HC values (298 for males, 231 for females) and a mean of 3.9 measures per patient (2–17).

Quantitative data were compared with z-score growth curve of standard French population [5] similar to the World Health Organization (WHO) chart available until the age of 5 years. An independent samples t-test was performed to assess statistically significant differences between average values of our cohort and general population, using 6-month ranges. This study had the approval of both institutions ethics committees.

3. Results

From birth until 24 months of life, HC values are normally distributed around the mean trajectory of the reference population from each side of the curve (−2SD, +2SD). This trend line deflects from
This slowing that initiates after the age of 2 years and is usually present earlier in boys than in girls. This difference may be due to the lower number of measures for female sample (298 for males, 231 for females); however, a different course related to gender cannot be excluded. 

This study has some limitation. Although involving 2 centers and a large number of patients with DS, it was retrospective with multiple providers, which might increase the variability of HC measure.

5. Conclusions

We found a head growth deflation starting from the second year of life in a large population of patients with DS. This finding seems to confirm the previous suppositions about a brain volume reduction documented in small series of patients with DS. Future prospective studies might help to establish a correlation between HC development, patient phenotype, and gender and mutation type.

Ethical publication statement

We confirm that we have read the journal’s position on issues involved in ethical publication and affirm that this report is consistent with these guidelines.

Financial disclosures

Tommaso Lo Barco, MD – Reports no disclosures.
Nicole Chemaly, MD, PhD – Reports no disclosures.
Theo Teng, MS – Reports no disclosures.
Francesca Darra, MD – Reports no disclosures.
Rima Nabbout, MD, PhD – Reports no disclosures.

Declaration of competing interest

Authors declare no COI.

Acknowledgments

This work was supported by a state funding from the Agence Nationale de la Recherche under “investissements d’avenir” program (ANR-10-IAHU-01) and the “Fondation Bettencourt Schueller”. Authors thank Dravet Italia Onlus who supported the statistical analysis.

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