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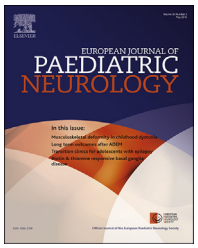

Original Article

The spectrum of long-term cognitive and functional outcome after hemispherectomy in childhood

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ABSTRACT

Purpose: To evaluate cognition, behavior, daily functioning and health-related quality of life (HrQoL) five years to more than a decade after hemispherectomy (HE) in childhood.
Methods: This countrywide Dutch cohort study of 31 patients, who underwent HE between 1994 and 2009, included a semi-structured interview with parents, an assessment of cognition, and screening of behavioral problems and HrQoL.
Results: Twenty-two school-age children and young adults [median age 13.8 years (0.5 at epilepsy onset, 5.3 at HE)] were assessed with age-appropriate cognitive tests. IQ ranged from 45 to 82 (median 61). Despite performing below mean norm scores, these participants could learn and remember, sustain attention, inhibit irrelevant responses, read and write. Nine more children [median age 9.7 years (0.25 at epilepsy onset, 1.4 at HE)] were so mentally retarded that age-appropriate testing was impossible. This group was almost totally dependent on others in daily activities, had the highest proportion of pre-existing contralateral MRI-abnormalities and after HE the highest rates of seizure recurrence and behavioral problems. Parents in both groups rated HrQoL surprisingly positively (mean VAS-score 72.5), with a scarce low rating (40). All parents reported problems with respect to their children's self-care, daily activities and mobility.
Conclusion: At least five years after HE, cognitive, behavioral and daily functioning encompasses a broad spectrum that varies from profound retardation and almost total dependence to low normal cognition and a reasonably independent existence. Pre-existing contralateral MRI abnormalities reflect a more generally affected brain with a limited ability to mediate development after HE.

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1. Introduction

The beneficial effect of pediatric hemispherectomy (HE)[d] on seizure control is an established fact.[1–4] Shorter duration of epilepsy and younger age at HE are associated with higher rates of seizure freedom.[5]

The ultimate goal of epilepsy surgery in children is not only seizure freedom and discontinuation of antiepileptic medication, but also opening a gate for (better) development.[6,7] Parents generally tell us that their child's functioning and general wellbeing improve after epilepsy surgery, also when the child does not become seizure free.[8] Yet, as far as HE is concerned, formal measures of cognition such as Intelligence Quotient (IQ) or Mental Developmental Index (MDI) scores do not often acknowledge the observations of parents. Significant cognitive improvement is uncommon and 61% of the children have no measurable change in IQ/MDI or Developmental Quotient (DQ) scores after HE (see review, Schooneveld & Braun, 2013).[9] Determining mental age (MA), however, unveils and quantifies change. Even children who had a very poor development with ongoing seizures, resume mental development after HE, as demonstrated by clear increases in mental age.[3]

Shorter duration of epilepsy prior to and seizure freedom following HE are independently related to better cognitive functioning,[1] as is withdrawal of anti-epileptic drugs (AEDs).[10] Contralateral MRI abnormalities, however, are significantly associated not only with seizure recurrence but also with severe mental delay and less chance of an IQ increase of 10 points.[11] These data pertain to rather short post-surgical intervals.

To the best of our knowledge, only two studies have reported long-term functioning after HE. Both were based on retrospective postal surveys, one completed during a telephone interview. Postoperative cognitive functioning largely reflected the pre-surgical capacities: late (beyond age 16 years) HE was associated with higher estimated intelligence and better psychosocial achievements.[12] Reading and spoken language were frequently impaired in the majority of ambulant patients, as described by Moosa et al. (2013)[13] who found seizure recurrence and contralateral MRI abnormalities to be the major predictors of poor skills.

We performed a comprehensive cognitive re-assessment of 31 children at least five years after HE; we also addressed behavior, everyday functioning and health-related quality of life (HrQoL) by questionnaires and semi-structured interviews.

2. Materials and methods

In The Netherlands, epilepsy surgery in children is performed solely in the University Medical Center Utrecht (UMCU).[14] Hence, we report on a countrywide cohort study. Inclusion criteria were 1) having undergone HE between 1994 and 2009, 2) age at HE younger than 18 years, and 3) neuropsychological evaluation shortly before HE, and re-evaluations two and more than five years thereafter. The medical ethical and research committee of the UMCU approved the study and concluded that the Dutch law on medical research involving subjects did not apply.

2.1. Participants

Of 47 HE patients, eight had not participated in the two-years' standardized neuropsychological follow-up. One of the 39 remaining children died. All attempts failed to establish contact with two families, and five families refused participation due to the emotional impact of seizure recurrence (n = 1), severe autistic problems (n = 1), or for no specified reason (n = 3). Finally, 31 (former) patients and their parents decided to participate in the long-term reassessment. With respect to gender, type of pathology, pre-surgical contralateral MRI abnormalities, age at onset of epilepsy and at HE, epilepsy duration, side of HE and seizure freedom two years after surgery, individuals who were not included in this long-term evaluation (n = 16) did not differ from those who participated. A subset of the study group has been described in papers on cognitive outcome at one to two years after surgery.[3,11]

2.2. Sources

2.2.1. Epilepsy status and daily activities

A semi-structured interview with parent(s) addressed epilepsy-related variables (seizure outcome, AEDs) as well as daily activities such as walking, talking, self-care, school career or employment, leisure activities and partner relationships.

2.2.2. Cognition

If possible, intelligence was assessed using Dutch versions of the Wechsler intelligence scales (Wechsler Preschool and Primary Scales of Intelligence III, Wechsler Intelligence Scales for Children III, Wechsler Adult Intelligence Scales III or IV). Full-scale IQ and its verbal (VIQ) and performance (PIQ) components (mean = 100, standard deviation = 15 in the general population) were determined. If age-appropriate intelligence testing was unfeasible, the Dutch version of the Bayley Scales of Infant Development was used. If testing the child was not possible, parents completed the Vineland Screener 0–6 years (three cases), and the raw scores were converted to the corresponding Mental Age (MA) as obtained from norm tables of the test manuals. We calculated mental developmental delay (MDD) by subtracting the child's MA from his/her chronological age. In addition, according to standard neuropsychological practice, cognitive domains[15] of memory, language (reading and writing were dichotomized as possible or not), calculation, processing speed, attention and executive functioning were assessed if possible (see Table 3 for tests and scores).

[d] The following abbreviations will be used more than once in this article: AED(s), antiepileptic drug(s); EQ Vas, EuroQol visual analog scale; EQ 5D, EuroQol 5 domains; HE, hemispherectomy; HrQoL, health related quality of life; IQ, intelligence quotient, MA, mental age; MDD, mental developmental delay; MRI, magnetic resonance imaging; PIQ, performance intelligence quotient; SDQ, strengths and difficulties questionnaire; TD, total difficulties; VIQ, verbal intelligence quotient.