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The time window for successful right-hemispheric language reorganization in children

Karen Lidzba [a,*], Hanna Küpper [a], Gerhard Kluger [b,c], Martin Staudt [a,b]

[a] Department of Pediatric Neurology and Developmental Medicine, University Children's Hospital, Hoppe-Seyler-Str. 1, 72076 Tübingen, Germany

[b] Clinic for Neuropediatrics and Neurorehabilitation, Epilepsy Center for Children and Adolescents, Schön Klinik, Krankenhausstraße 20, 83569 Vogtareuth, Germany

[c] Institute of Rehabilitation, Transition and Palliation of Children with Neurological Illnesses, Paracelsus Medical University, Strubergasse 21, 5020 Salzburg, Austria

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ABSTRACT

Aim: To identify, in a retrospective, observational study, the time window during which successful right-hemispheric language reorganization is possible after left-hemispheric brain damage.

Method: 25 patients (10 females; age 6–41 years; ≥12 months after insult; age at insult 0;3–15;11 years) with acute, language-relevant left-hemispheric insults acquired during childhood and adolescence completed questionnaires for self-assessment of language problems. 12 patients of those reporting no (n = 8) or only moderate (n = 4) language problems participated in language fMRI.

Results: Language outcome of lesions occurring before 5 years of age (n = 7) was always favorable, and language was right-lateralized (2 patients: age at lesion < 2 years) or bilateral (3 patients: age at lesion 2–5 years). Following lesions occurring after 5 years of age, language outcome was often unfavorable (11/18 patients: moderate or severe problems), and of the 7 patients without problems, none showed right-hemispheric reorganization (fMRI available in 4).

Interpretation: The combination of normal language outcome and right-hemispheric language reorganization after a left-hemispheric lesion sustained after the neonatal period is extremely rare. Functionally sufficient right-hemispheric language was documented in only two patients with lesions acquired before two years of age.

1. Introduction

The superior compensatory potential of the developing right hemisphere for language is one of the most prominent examples of early brain plasticity.[1] Extensive lesions to the left hemisphere, which result in severe and persisting language problems when acquired in adulthood, can often be compensated when the lesions occur perinatally by "shifting" language to the undamaged right hemisphere.[1] The relation of reorganization pattern and language outcome in children with perinatal stroke is not yet clearly determined. Atypical

* *Corresponding author*. University Children's Hospital, Department of Pediatric Neurology, Hoppe-Seyler-Str. 1, 72076 Tübingen, Germany.

E-mail address: Karen.lidzba@med.uni-tuebingen.de (K. Lidzba).

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language lateralization (i.e., right-hemispheric or bilateral) was associated with better language performance in one study,[2] but with worse performance in another.[3] Generally, perinatally acquired left-hemispheric lesions may cause delayed language acquisition,[4] but by school age, most children perform normally under naturalistic conditions.[5,6] Only when confronted with linguistically complex tasks do they show deficits, e.g., in grammar processing[7] and discourse.[8] Developmental functional brain imaging studies have demonstrated an initially strong right-hemispheric involvement in language development[9] with increasing left-lateralization during childhood and even adolescence.[10–12] Based on these data, one may assume that during this dynamic phase, right-hemispheric language reorganization after acute left-hemispheric lesions might be more successful than in adulthood. The time period when the right hemisphere loses the potential to successfully take over language function, however, has not been determined yet. After acute lesions occurring in the course of childhood and adolescence, right-hemispheric language dominance seems to be rare.[13] In those with documented aphasia, right-hemispheric language representation in the chronic phase is more frequent, however, mostly in those children still performing poorly on language tasks.[14] It seems, thus, that right-hemispheric language reorganization associated with satisfactory language outcome might be a phenomenon observed in the very immature brain only. The aim of our study was to define the age until which the right hemisphere is indeed able to satisfactorily take over language function after an acute left-hemispheric insult.

The current lack of information on this plastic time-window becomes critical when it comes to the treatment of children with a potentially progressive epileptic disease of the left hemisphere (e.g., Rasmussen's encephalitis). While the epilepsy may respond to pharmacological intervention for a long time, surgical intervention might later become necessary. And how can we know if the "plastic window" enabling interhemispheric language reorganization will, then, still be open, protecting the child from persistent aphasia? With better data on the time-course of neural plasticity, it would be easier to decide how long to "wait and see".

Many previous publications on successful right-hemispheric language reorganization after lesions acquired during childhood report on patients with therapy-refractory epilepsies who underwent fMRI or Wada testing during their pre-surgical work-up, or who received left hemispherectomies.[1,15,16] In most of these patients, however, the age at onset of the underlying disorder (e.g., Rasmussen's encephalitis) and, therefore, the age at onset of the reorganizational process, cannot precisely be determined. For the current study, we recruited a highly selective sample of patients with acute left-hemispheric insults, a history of aphasia or, in preverbal children, MRI evidence for lesions in language relevant areas, and without any evidence for pre-existing brain pathologies, so that the age at insult could safely be taken for the onset of reorganization. We excluded patients with pre-, peri- or neonatal lesion onset (although much more easily available) since for these, satisfactory language outcome of right-hemispheric reorganization has already been demonstrated.[5,6]

2. Method

2.1. *Participants*

For this retrospective study, the clinical databases of two large neuropediatric centers (Schön Klinik Vogtareuth and University Children's Hospital Tübingen) were searched for patients with left-hemispheric brain lesions, acquired $\geq$ 12 months before the study, at an age between 4 weeks and 18 years, without evidence for pre-existing brain anomalies or epilepsy, and aphasia >4 weeks post insult as documented by a speech/language pathologist, or, if younger than 24 months at time of insult, MRI evidence of a structural lesion in clearly language-relevant brain regions, i.e., in inferior frontal and/or superior temporal cortex.[17] Database searches covered the period from 1984 to the time of recruitment (2013). Approval of the local ethics review board (65/2013BO1) and written informed consent of the patients or their caregivers were obtained prior to the investigations.

2.2. *Language outcome*

All patients or their families (in case of minors) were sent questionnaires on persisting language problems. The following questions were rated (*yes, very much/yes, a little/no*): "Do you/Does your child have difficulties … " (1) "*… to talk?*"; (2) "*… to understand what is said?*"; (3) "*… to read?*"; (4) "*… to write?*". Ratings of persisting language problems were then categorized in "none" ($\leq$1 answer *yes, a little*), "moderate" ($\geq$2 answers *yes, a little*, and no answer *yes, very much*) and "severe" ($\geq$1 answer *yes, very much*). In addition, we asked if the patient currently attends speech/language therapy.

2.3. *Language lateralization*

Patients reporting "no" or only "moderate" persisting language problems were invited for fMRI, and residual aphasia was excluded by the *Aachener Aphasie Test* (AAT), short version,[18] or by neuropsychological assessment (including WISC-IV Verbal IQ). The AAT is a standardized German test for the detection and classification of aphasia, not for the quantification of linguistic abilities in general. The short version consists of the Token Test (a well-established test for language comprehension) and an assessment of written language (assembly or writing of words and sentences by dictation). Language fMRI was conducted according to a standardized protocol using two well-established language production tasks in block design.[19] In the active condition of the vowel-identification task (VIT), pictures of concrete objects are presented, with the task to silently generate the name of the object and to decide by pressing a button if the name contains the phoneme/i:/. In the control condition, a small and a large abstract picture (fractals) are presented, with the task to decide by pressing a button whether the small picture was part of the large picture (like in a puzzle). The contrast between conditions usually elicits activation in inferior frontal and posterior temporal brain regions, correspondent to the processes of silent word generation and phonological analysis. In the active condition of the synonyms task (SYN), two printed words are presented