

Reorganization of the cerebral functions in perinatal and early childhood stroke: a fMRI study

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Background

- **Stroke in adults** leads to severe cognitive and motor impairment
- **Brain damage after perinatal or childhood stroke** can have the comparably good functional outcome
- Due to brain plasticity compensatory reorganization of the language network occurs

Background

- The investigations of perinatal and childhood stroke are models to understand
 - the mechanisms of brain (re)organization
 - compensatory mechanisms due to cerebral plasticity after the brain damage

The neurocognitive development of infants with focal brain damage

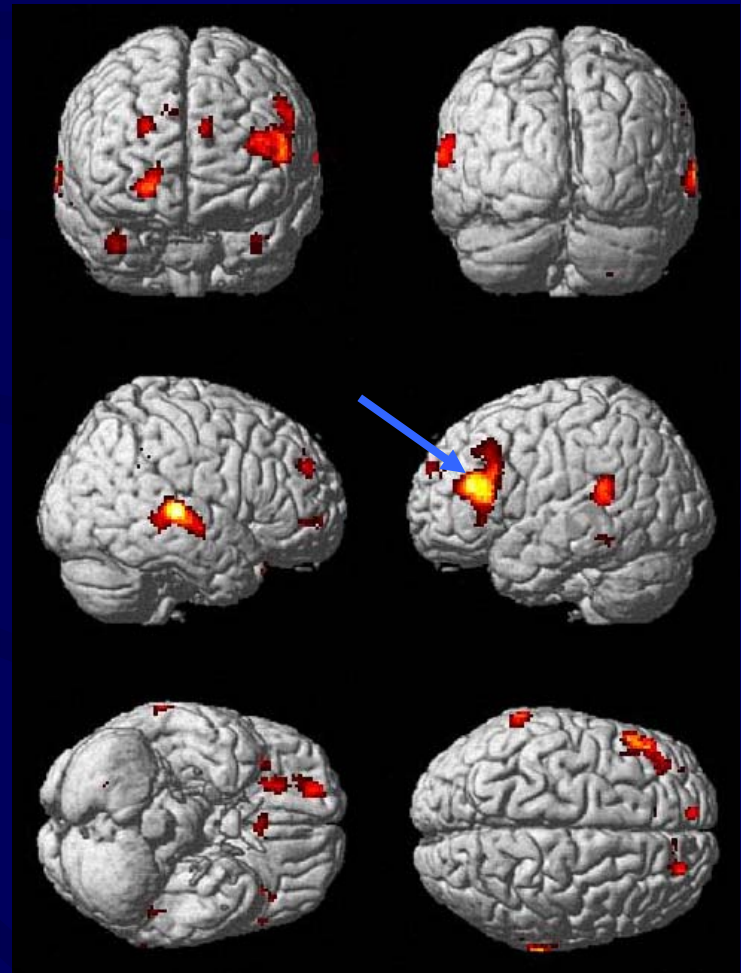
- is impaired compared to healthy children

Kolk A, et al., Brain and Development, 2001; 23: 88-96, Ricci D, et al., Stroke 2008; 39 403-10

- The impairment of different cognitive functions
 - in attention,
 - in language,
 - in visuospatial function,
 - in tactile functions,
 - in memory functions

Language control

- In most of right-handed persons
 - language is controlled by the left hemisphere,
 - the centers in both hemispheres take part in the language network



Normal development of language

- Healthy newborn infants
 - no differences between hemispheres in perception and expression of the language,
 - lateralization begins from the 3rd month
- (Ressel V, Brain Lang 2008)
- The lateralization of language is mostly complete by the age of 5 years
- The lateralization deepens by the age of 20

Everts et al., Child Neuropsychol 2008

The aim of the study

- to identify (re)organization of language function in children with perinatal and childhood stroke
- to correlate the findings with cognitive performance

Functional MRI study

- From Sept 2008 to May 2010 in Tartu University Hospital
- Infants from the epidemiological perinatal and childhood stroke cohort in Estonia

(Epidemiological study of Childhood Stroke in Estonia, cognitive disorders and individual neurorehabilitation programs in children with stroke, supervised by dr. Anneli Kolk)

Inclusion criteria

- Study group
 - Age range during fMRI investigations 6-14 years;
 - Left-side stroke > 1 year ago
 - Patients able to communicate and perform fMRI tests
- Control group
 - Healthy voluntary children without perinatal asphyxia
 - Normal neurodevelopmental and cognitive outcome
 - Age and sex matched with study group
(age range 9-14 years)

Methods I

NEPSY test to investigate the neuropsychological profile

Consisted of

- receptive language subtests
- productive language subtests
- visuo-spatial function tests
- sensomotor tests
- attention and executive function tests
- memory tests

Methods II

- MRI investigation (the size and location of the damage)
- The functional MRI
 - with Siemens „Magnetom Symphony” 1.5T
 - Mathematical analysis with software SPM8 running in Matlab (Mathworks, Natick, MA, USA) performed by physicists

Functional MRI tasks

I Noun-verb generation task

- To activate the productive language area in the left frontal lobe
- Upon hearing a noun, subject was asked to silently generate "verb that goes with the noun"
- Fingertapping with nonparetic hand as control block

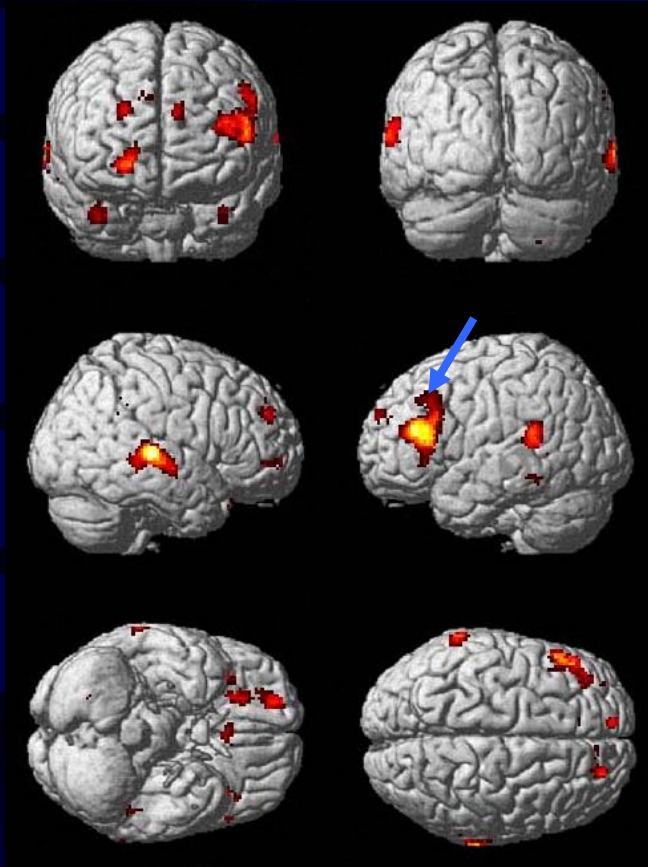
II Sentence comprehension task

- To activate receptive language area in temporal lobe
- Upon hearing a sentence, subject was asked to silently decide if it is right or wrong: ("The bird is singing vs the bird is barking").
- Fingertapping with nonparetic hand between the blocks

fMRI analysis

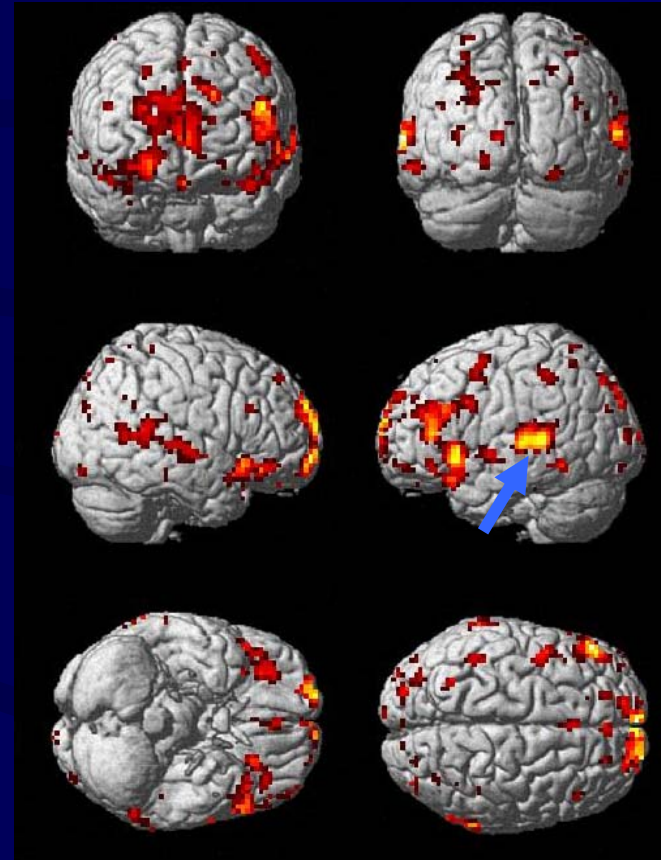
- The resulting t-maps for each subject were analyzed within
 - Brodmann areas (BA) 44+45 (frontal lobe)
 - Brodmann areas 22 (temporal lobe), defined by MRIcro templates.
- The highest Z-scores of signal intensity change were identified
- the weighted mean laterality indices (wLI) were found

Control patient: 9y old right-handed girl



Noun-verb task

Left F activation in BA 44-45 in
productive language area



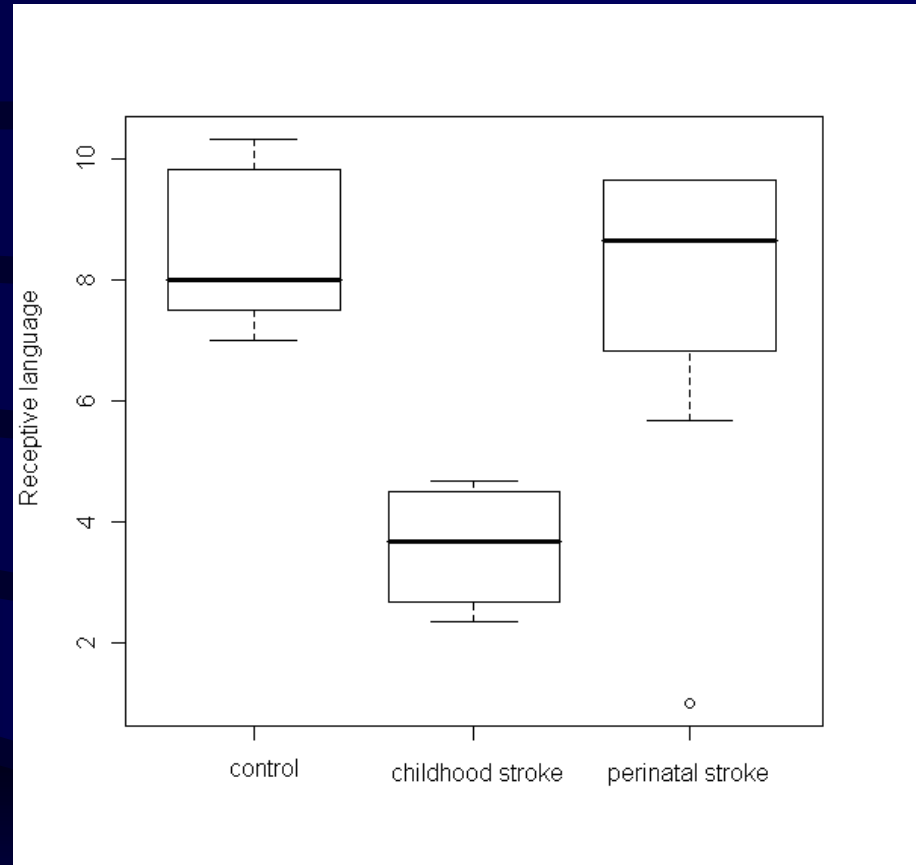
Sentence comprehension task

Left T activation in BA 22
in receptive language area

Patients

	Control group N=11	Study group N=13
Boys/girls	5/6	7/6
Mean age (min-max)	11.1 years (9-14 y)	10.5 years (6-14y)
N of perinatal stroke	0	8
N of childhood stroke	0	5

Results of receptive language subtests with NEPSY

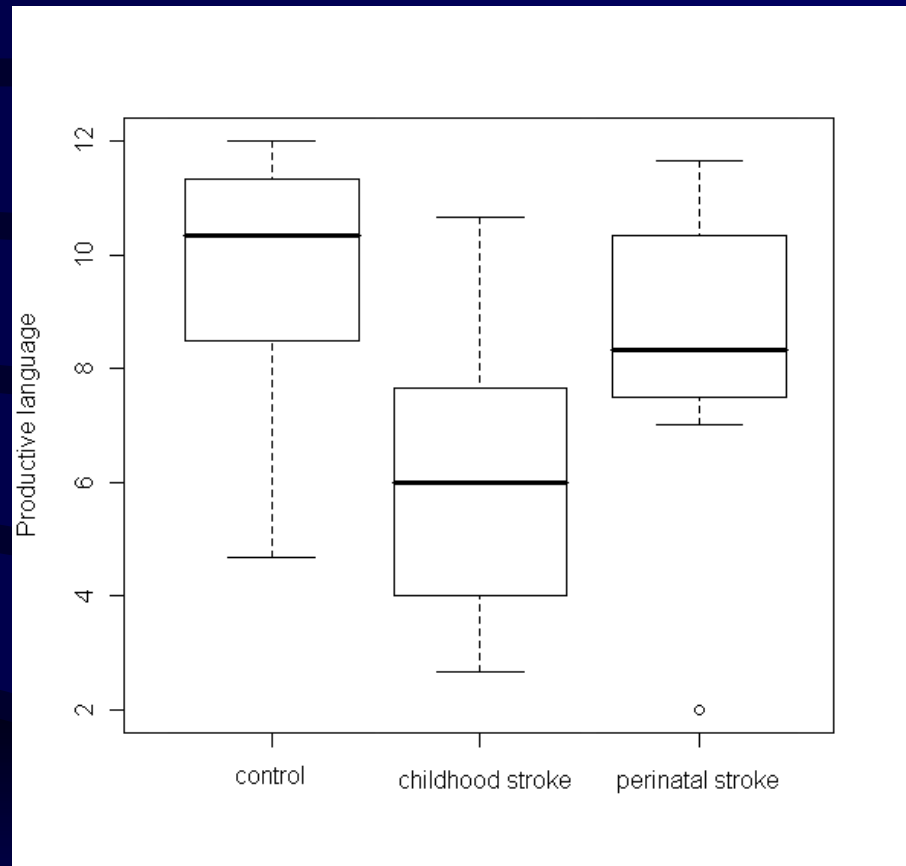


$p=0.008$ controls vs childhood stroke

$p<0.05$ childhood stroke vs perinatal stroke

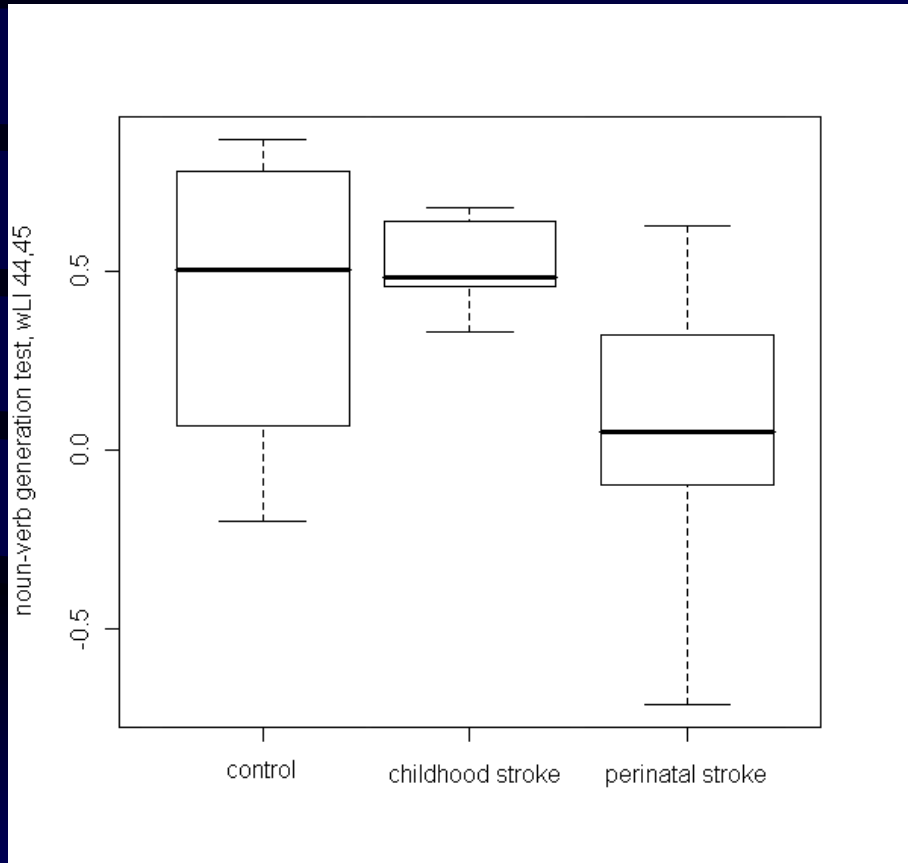
(Wilcoxon Two-Sample Test)

Results of productive language subtests with NEPSY



$p=0.05$ controls vs childhood stroke
(Wilcoxon Two-Sample Test)

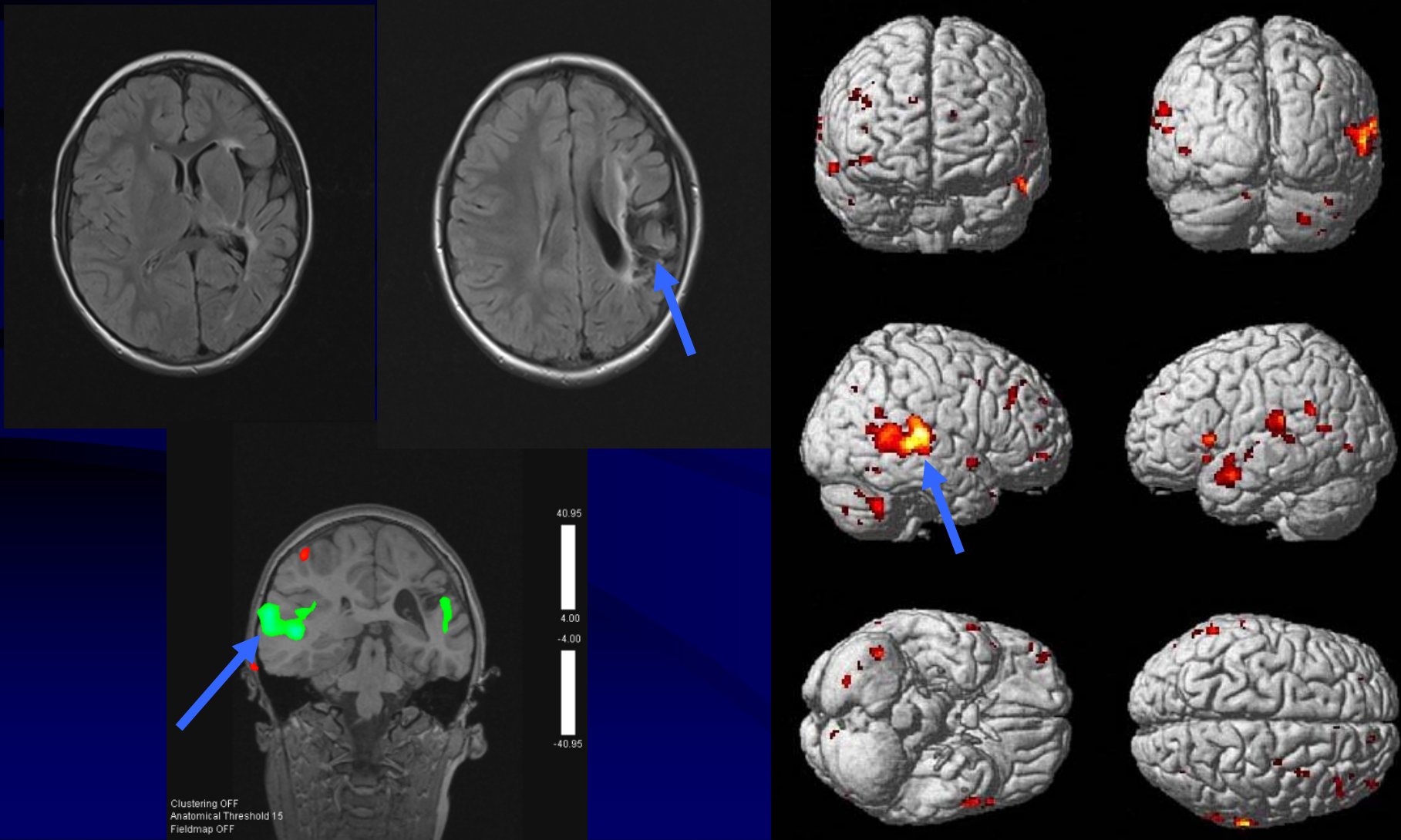
wLI after noun verb task during fMRI in productive language area in BA 44/45 in frontal lobe



- Atypical lateralization of language in patients with perinatal stroke in the left hemisphere (due to brain plasticity)

$p=0.05$ perinatal vs childhood stroke
(Wilcoxon Two-Sample Test)

Perinatal stroke: 9y girl, with large focal damage in the left hemisphere
with right-side hemiparesis without significant language problems
Sentence comprehension task: bilateral T activation with dominance
atypically in the right T lobe BA 22

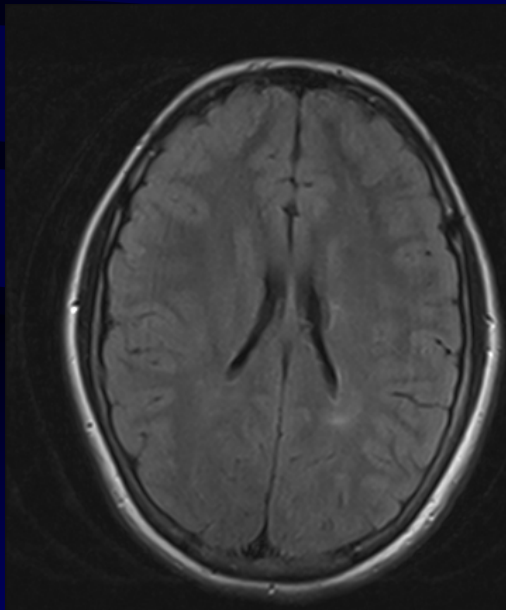


Childhood stroke: 13 y old boy with stroke at the age of 2y 8m presented with right side hemiparesis and aphasia

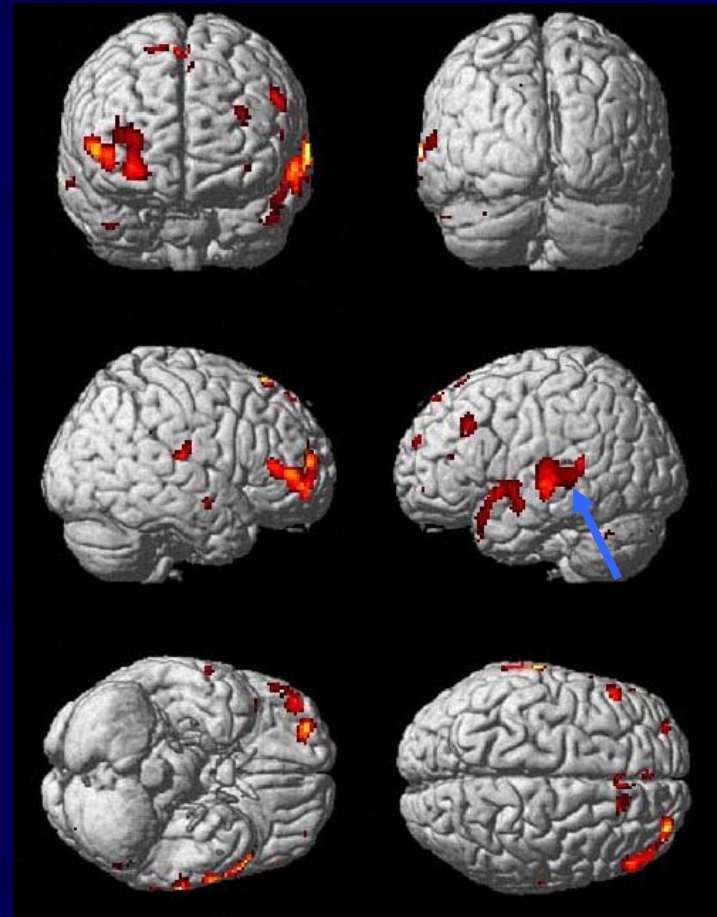
Moderate impairment in receptive and productive language.

Severe attention deficit.

Difficulties in visual memory

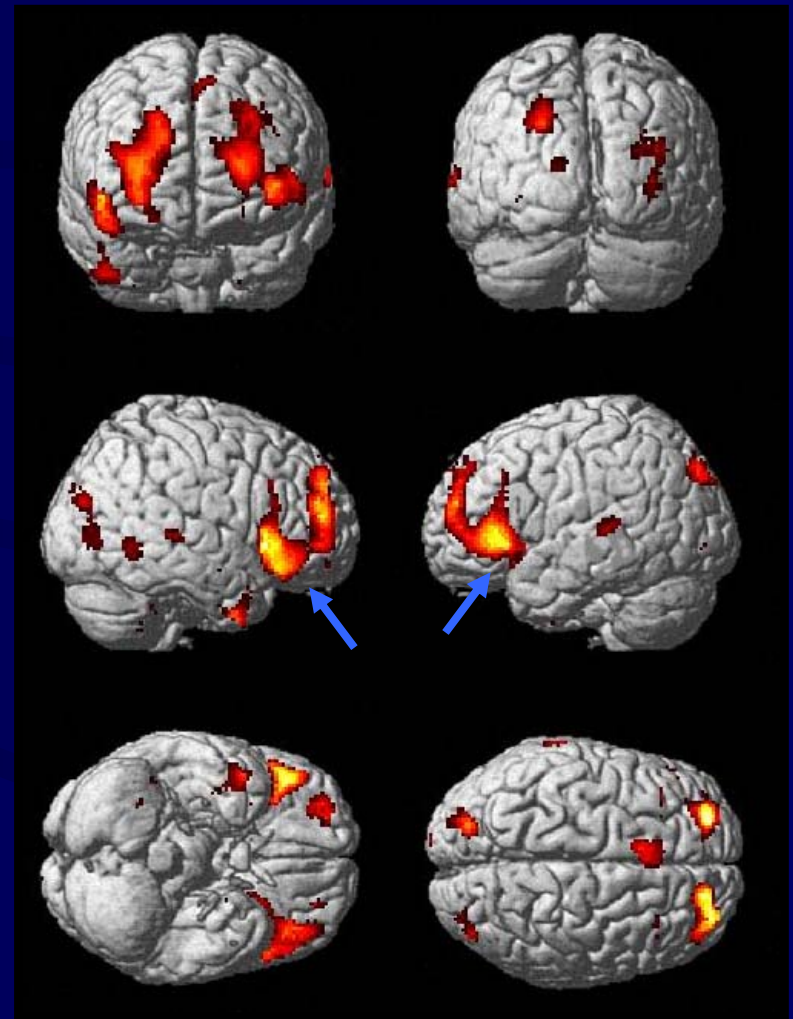
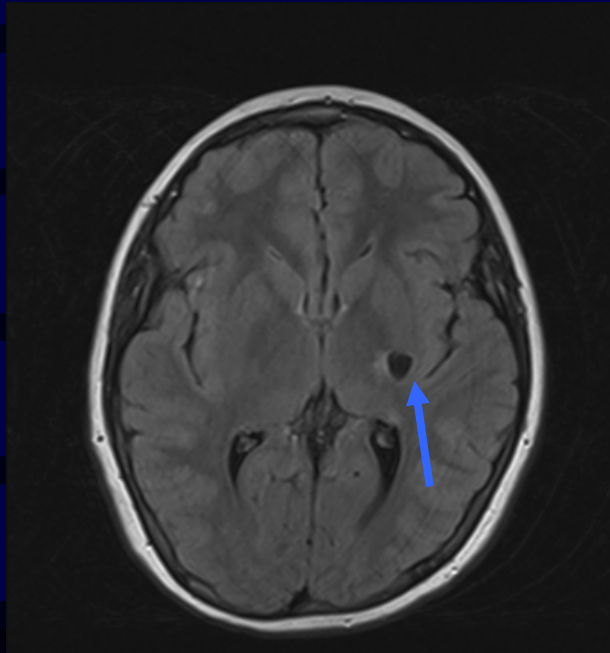


Left side paraventricular damage



Sentence comprehension task activation in the left T lobe

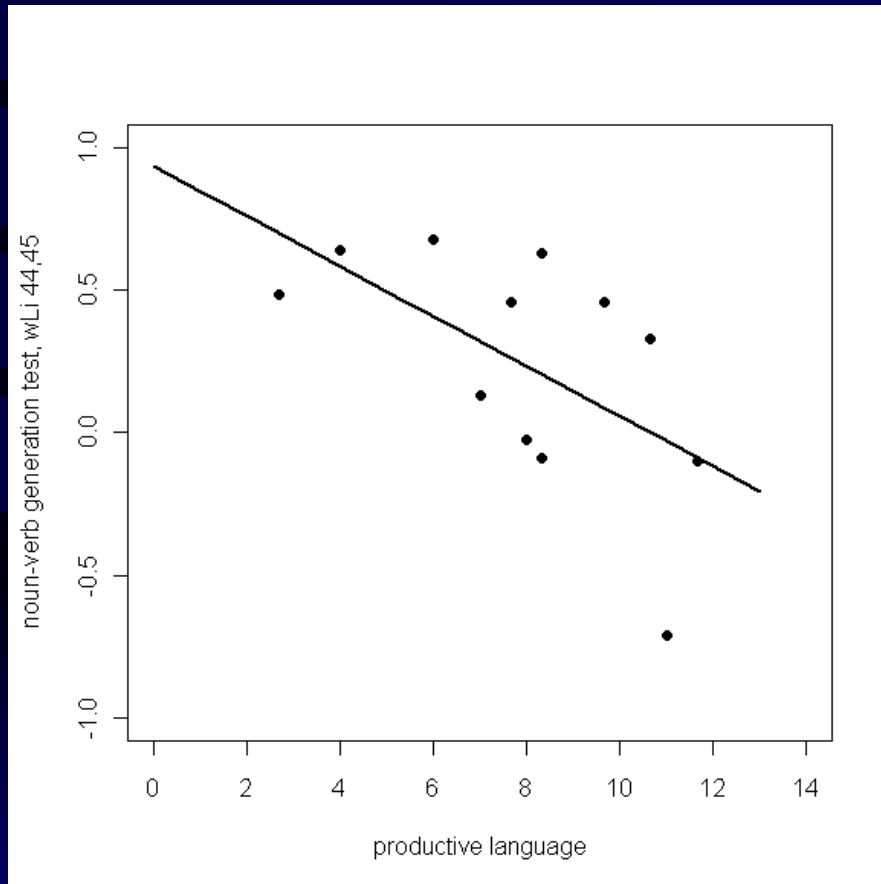
Childhood stroke: 10 y old boy with stroke at age 2 y presented with hemiparesis and dysarthria, normal cognitive profile



Noun-verb task, bilateral F and preF activation in productive language area

Negative correlation was found

between the mean score of productive language tests
and wLI within productive language area in BA 44+45
($p < 0.05$)



Patients with high mean
language tests scores
have low wLI with
atypical lateralization of
language due to brain
plasticity

Conclusions

The (re)organization of the language functions can depend on the time of the damage in the left hemisphere

- In perinatal stroke the atypical right hemisphere language dominance or asymmetric bilateral activation occurs
- In childhood stroke the language centers activate in the left hemisphere or asymmetric bilateral activation occurs

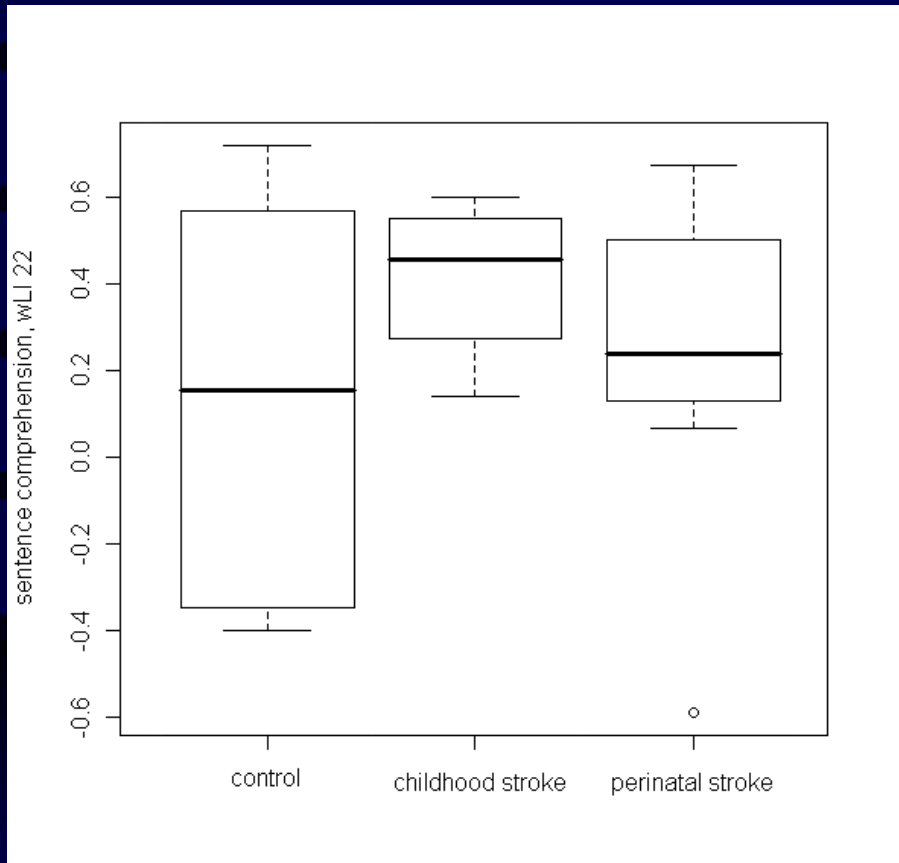
Conclusions

- Reorganization of language function correlates with cognitive performance
 - relatively good recovery with atypical lateralization of the language center in the right hemisphere after left-side perinatal stroke
 - Relatively poor outcome with language center in the left hemisphere after childhood stroke
- Older children have lower plasticity after the damage of the brain

fMRI team of the University of Tartu

- Dr. Tiiu Tomberg- radiologist
- Dr. Anneli Kolk: child neurologist
- Dr. Rael Laugessaar: child neurologist
- Prof. Tiina Talvik: child neurologist
- Kalle Kepler: physicist
- Joosep Kepler: physicist
- Andrus Aavik: physicist
- René Randver : psychologist
- Mari-Liis Kaldoja: psychologist
- Consultants
 - Dr. Martin Staudt: The University of Tübingen
 - Paul Morgan The University of Nottingham
 - Dr. Christine Ojango The University of Nottingham

wLI after sentence comprehension task in receptive language center in BA 22 in temporal lobe



Atypical lateralization of language in patients with perinatal stroke in the left hemisphere compared to childhood stroke patients

$p=0.05$ perinatal vs childhood stroke
(Wilcoxon Two-Sample Test)