

# Acute brain attacks

**INSELSPITAL**  
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Neurologie  
Neurophysiologie  
Neurochirurgie  
Psychiatrie

**KINDERKLINIKEN**  
Bern

**F A S T**

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Medizinische Universitätskinderklinik

## Top 10 Symptoms and Signs Frequency in children with acute focal deficits

Symptoms/signs	Ranking?
Ataxia	
Visual disturbance	
Headache	
Facial paresis	
Loss of consciousness	
Hemiparesis	
Seizures	
Speech disturbance	
Altered mental state	
Vomiting	

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## Recognition tools for stroke: FAST For Paramedics

FAST	AIS total	Anterior circulation	Posterior circulation
Face	70%	76%	42%
Arm	61%	71%	33%
Speech	34%	38%	42%
At least 1	76%	88%	50%

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## Recognition tools for stroke: Rosier For Emergency Physicians

ROSIER		All	Anterior	Posterior
LOC / syncope	-	0	0	0
Seizure	-	17%	17%	17%
Asymm facial weakness	+	70%	82%	42%
Asymm arm weakness	+	61%	73%	33%
Asymm leg weakness	+	57%	67%	33%
Speech disturbance	+	34%	32%	33%
Visual defects	+	10%	6%	17%
Pos Rosier (≥1)		81%	85%	75%

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## ACT FAST ON THE FIRST SIGN OF STROKE

**F**: Make your child smile or cry (asymmetry)  
**A**: Let your child use both arms (asymmetry)  
**S**: Try to make your child talk (Unable or slurred)  
**T**: Lost time could be lost brain (Call an ambulance)

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What is your next step?

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## Magnetic resonance the first choice of imaging

First neuroimaging modality	AIS	HS
CT	43/65 (66%)	39/41 (95%)
MRI	28/28 (100%)	1/1 (100%)
USS	1/2 (50%)	

Age group	AIS	HS
<1 year	11.3 (2.4-24.5) (n=11)	1.0 (0.5-1.5) (n=3)
1-5 years	4.5 (2.7-22.5) (n=33)	1.7 (0.7-2.7) (n=6)
6-10 years	2.1 (1.1-4.3) (n=9)	1.4 (0.9-4.7) (n=12)
11-15 years	2.5 (0.7-73.5) (n=15)	1.1 (0.6-1.9) (n=13)
p Value	0.24	0.58

AIS, arterial ischaemic stroke; HS, haemorrhagic stroke.

First neuroimaging was diagnostic of stroke

By modality	AIS	HS
CT	43/65 (66%)	39/41 (95%)
MRI	28/28 (100%)	1/1 (100%)
USS	1/2 (50%)	

AIS, arterial ischaemic stroke; HS, haemorrhagic stroke; USS, cranial ultrasonography.

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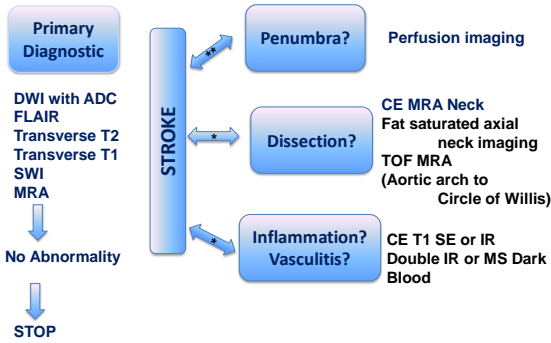
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## Fast imaging by magnetic resonance !!!!

**MR >>> CT**

- CT might be negative
- Radiation by CT/ CTA
- MRA perfusion, Dark blood, enhanced TOF, fat suppression

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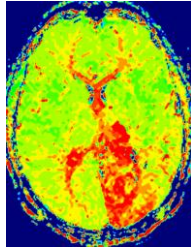
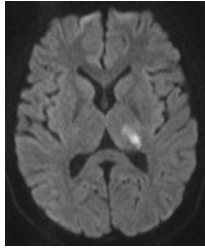
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### Diffusion – Perfusion Mismatch



Important for decisions on endovascular interventions

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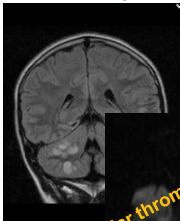
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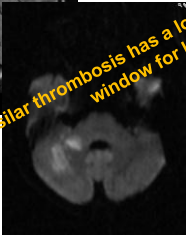
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### Careful for posterior circulation stroke!



Basilar thrombosis has a longer therapeutic window for lyses



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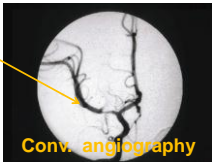
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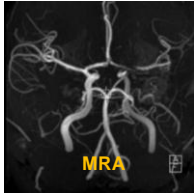
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### Suspicion of an inflammatory process



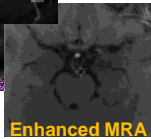
Conv. angiography



MRA



T1 dark blood



Enhanced MRA

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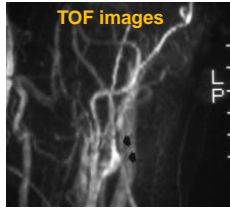
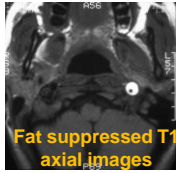
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### Search for dissection




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The top 10 aetiologies for acute focal deficits in in children please rank their frequency

	Children	Adults
Bell's palsy		
CNS infection		
Seizures/epilpsy		
Psychiatric		
Cerebellitis		
Encephalopathy		
CNS demyelination		
Stroke		
peripheral NS		
Migraine		

and in adults?

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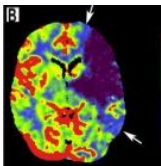
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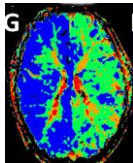
### Differential diagnosis stroke versus migraine



Sudden onset  
Staggering sy  
Motor>Sensory  
Neglect for sy



Family/personal hx  
Jacksonian march  
Sensory sy starting  
Visual Plus sy  
Freightedened by sy




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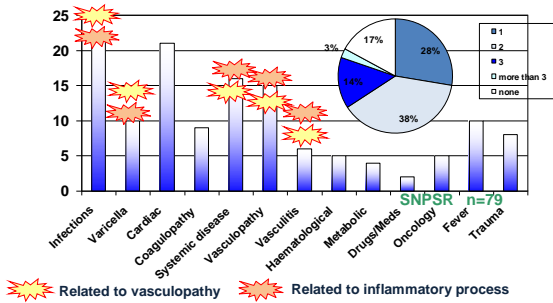
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### Risk factors SNPSR




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### Suggested investigations



	Results as an emergency	To do at diagnosis	To do at appropriate time
Blood	BC, SR, CRP, electrolytes, glucose, liver and renal function, coagulation, lactate	Viral serology ( as Varicella/Herpes simplex/ Mycoplasma/Enterovirus) Borreliosis Vasculitis ? ( ESR, ACLA, ANA, LA)	Lipid profile, Homocystein Alipoprotein Prothrombotic studies (Factor V , Prothrombin and MTHRF mut., Protein S and C) Specific investigations
Urine		Organic Amino acids* if suspected metabolic!	
CSF	Opening pressure cells, protein, glucose, lactate	PCR varicella other PCR / serologies	

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### Treatment in First Hours

- Body temperature 36.5-37 °Celsius
  - Avoid Hypo- und Hyperglycemia (rare in children!)
  - Monitoring of level of consciousness
  - Blood pressure monitoring
  - Treat seizures (in about on 20%!)
- Symptoms of increased cranial pressure**

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## Thrombolyses and Thrombectomy in children Why considering it?

### Pro

- Outcome  
50% with hemiparesis  
66% with cognitive problems
- Children not less affected than young adults<sup>5, 24</sup>
- Younger children have higher risk for problems

### Contra

- Different aetiologies
- Different Penumbra course?  
n= 31
- Different time course of vessel occlusion?

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## Thrombolyses and Thrombectomy in children

	Considering in case of	Caveats
Thrombolysis Intravenous / - arterial	Vessel occlusion <b>and</b> DW/perfusion mismatch pedNIH >>4; within 4.5 hour time window	Evidence limited to uncontrolled case reports, often not conforming to adult guidelines
<b>Thrombectomy</b>	Large vessel occlusion <b>and</b> diffusion/perfusion mismatch pedNIH >>4; within recommended adult time win.	Evidence limited to uncontrolled case reports

Steinlin and Mackay, in press, Ellis et al 2014, Fransen et al 2015

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## Aspirin versus Heparin

	Indications	Caveats
Aspirin	Baseline treatment 5mg/kg BW <b>Positive studies for adults</b>	r/o first dissection and cardiac problem
Heparinoids*	Extracranial dissection Cardioembolic stroke <b>Negative study for kids</b>	Caution required with large hemispheric or posterior fossa infarction

Steinlin and Mackay, in press, Berge et al 2002, Monagle et al 2011

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## The Role of Steroids?

	Considering in.....	Caveats
Steroids	Focal (transient) arteriopathy	No evidence
	Medium to large vessel vasculitis	
Immuno-suppression	Small vessel vasculitis	

Steinlin and Mackay, in press; Benseler 2014

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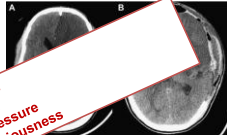
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## Decompressive craniotomy in children

### Malignant media infarction

21 children malignant media infarction  
aged 1 5/12 – 18y  
Glasgow coma scale 4-9;  
13/13 dilated pupil;  
Craniotomy < 48h in 13 (22%)



**Surveillance in ICU**  
First symptoms:  
Increase of blood pressure  
Change of level of consciousness

**Posterior circulation stroke**  
11% craniotomy  
all within 72hours

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### Prenotify Stroke Team

Emergency  
Neuropaediatrician  
Stroke team  
Neuroradiology  
Anaesthesia



Imaging

Emergency

Intervention




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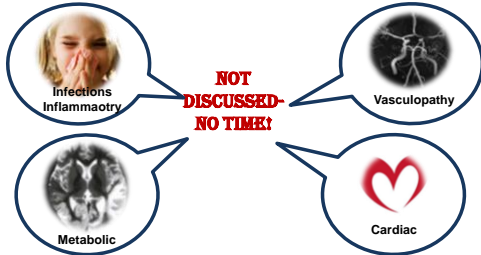
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# RISK FACTORS




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Vasculopathy: in about 50% of children with stroke

PCS	Swiss (Bürki et al)	British (Wraige et al)	Arteriopathy n=277	
Sickle cell	0	16 (12%)	FCA	69 (25%)
Cardioembolic	16 (20%)	10 (7% <sup>9</sup> )	Moyamoya	61 (22%)
Moyamoya	5 (6%)	18 (13%)	Art. dissection	56 (20%)
Art. dissection	2 (3%)	18 (13%)	Vasculitis	33 (12%)
Stenoocclusive	25 (31%)	42 (31%)	Sickle cell arteriop.	21 (8%)
Other determined	16 (20%)	15 (11%)	Postvarizella	19 (7%)
Multiple probable/possible	8 (10%)	5 (5%)	Other	10 (4%)
Undetermined	4 (5%)	15 (11%)	Unspecified	9 (3)
Not classifiable	3 (5%)			

DMCN: 2010, Bürki et al; 2005 Wraige et al

Circulation, Amlic-Lefond 2009

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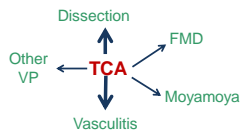
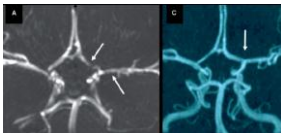
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## Transient focal arteriopathy



- Stenosis pref. M1 and A1, unilateral  
Irregularities 32% Collaterals 5% +/-Vessel enhancement
- Worsening in acute phase:  
FU Normalisation (23%) improvement /stabilisation (45/32%)
- Recurrence in first year: 18%? No recurrence on longterm

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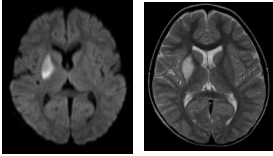
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## Transient focal arteriopathy



Previously healthy child  
 Stuttering onset of symptoms  
 hemiparesis  
 with dystonic involvement  
 Varicella preceded in 44%  
 (Braun et al, 2009)

Typical location of infarction: Basalganglia  
 Sometimes involving caudate, adjacent grey/white matter  
 Sparing of internal capsule

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## Medium to large vessel vasculitis

Non progressive  
 Transient focal  
 arteriopathy?  
 Stroke



Progressive  
 Persistent headache/  
 Cognitive problems  
 Stroke

focal unilateral stenosis  
 medial and anterior CA  
 vessel wall thickening

T1 dark blood

multifocal, > 1 vessel bed  
 unilateral seldom bilateral  
 vessel wall thickening

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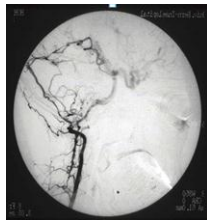
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## Moyamoya

chronic progressive stenosing vasculopathy  
 with typical collaterals

- Typically terminal internal carotid/  
 posterior circulation in about 30%
- Frequently warnings:  
 TIA, minor strokes
- Children more likely to have  
 ischaemic problems
- Fluctuand symptoms,  
 increasing neuropsychological problems




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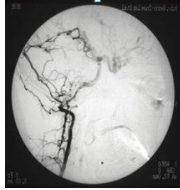
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### Moyamoya a spectrum!

- Associated with:
  - Sickl cells
  - Neurofibromatosis
  - Downs syndrom
  - Radiation
- RNF213 polymorphism in Japanese
- Coriskfactors for ischaemic events:
  - Infection, art. Hypertension
  - Coagulopathy, homocystinemie




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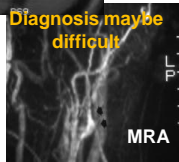
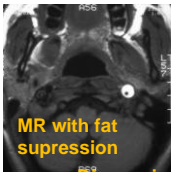
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### Dissection: cervical and intracranial



- Infection (31%)  
(Guillon, 2003)
- Trauma (minimal)
- Cervical bone abnormalities  
(Cushing 2001, Ganesan; Hasan 2002)
- Homocystinemia  
(Ganesan 2002, Pezzini 2002)
- Vasculopathy
- Migraine  
(Tzourio 2002)

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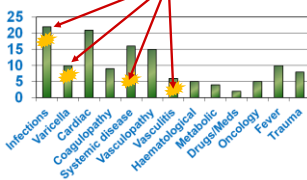
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### Infections are frequent!

**Infection /inflammation in 1/3 of paediatric stroke a risk factor!**



- Known germs:
- Varicella (Sébire et al 1999, Askalan et al 2001)
  - Mycoplasma
  - Enterovirus
  - Parvovirus
  - Borreliosis

- Focal vasculopathy
- Dissection
- Medium to large vessel vasculitis

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### Infections in childhood stroke IPSS



- 310 cases compared to 289 controls (35 centres)
- Infection ≤1week prior to stroke: 6.5-fold risk of AIS  
OR 4.7, 95% CI 3.1-13.5, p<0.0001
- Cases were under-vaccinated compared to controls  
Some/few/no routine vaccinations: risk of AIS risk ↑ OR 6.7,  
(95% CI 2.3-19.6) p<0.0001
- Protective: Having received an  
MMR, polio, or pneumococcus vaccine

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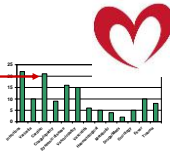
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### Cardiac problems: children Second on the hit list



- 5.4 stroke per 1000 children operated  
risk increased: older age at operation  
cardiopulmonary bypass  
reoperation
- Co risk factors hereditary coagulopathy  
infection

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### Cardiac problems: neonates



- Perinterventionally silent!  
**Missed !!?**
- Preoperative stroke in 39% -  
significantly higher risk after balloon atrial septostomy
- Postoperative: injury of white matter in 35%  
especially: single ventricles and aortic arch obstructions  
after cp bypass, low intraoperative Hb,  
low mean blood pressure during first day postop

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### Metabolic problems: rare but....

Metabolic infarction

Vasculopathy

Cardiac problems

Coagulopathy



Menkes  
Fabry disease

Hyperlipidemia

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## OUTCOME

OUTCOME



Motor



Quality of life



Cognitive

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## Mortality



• Top 10 causes of death in children in US

Haemorrhagic stroke > SVT > arterial ischaemic stroke

• Mortality arterial ischaemic stroke

California	(Fullerton et al)	5%
Canada	(de Veber et al)	10%
London area	(Gandesan/Kirkham et al)	6%
Sweden	(Christerson 2010)	8%
Denmark (first 30 days)	(Tuckuviene 2011)	4%
CH	(SNPSR 2000-2008)	7%; 1/3 due to stroke
Melbourne	(Mackay)	

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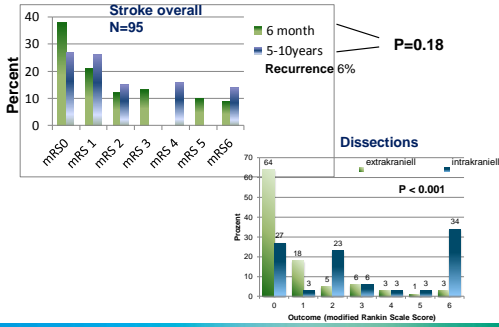
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### Outcome over years / different subpopulations




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### Stroke in children and young adults



	Children n=128	Adults n=199	P value
pedNIH/ NIH scores	5	6	0.102
Mod Ranking score 0-1	59%	60%	0.907
Mortality	4%	6%	0.436

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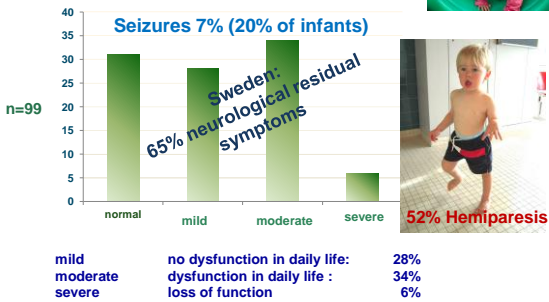
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### Outcome after 2 years

SNPSR




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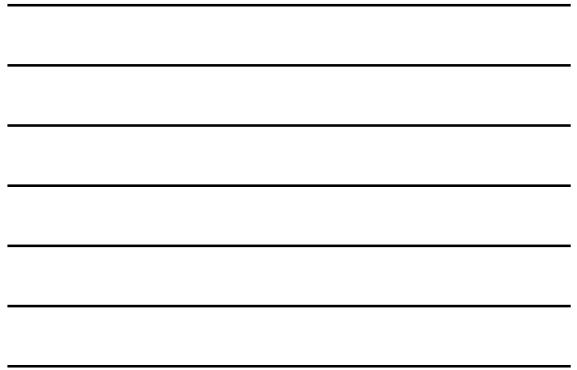
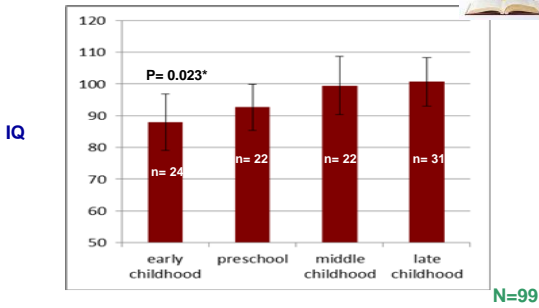
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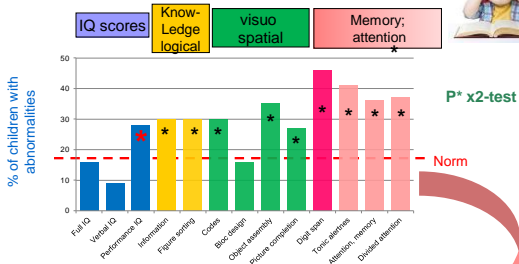
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## Cognitive outcome and age at stroke



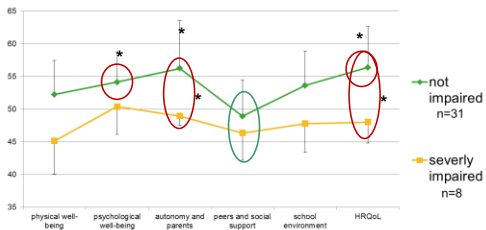
## Follow Up: Neuropsychology n=37/31



**Conners RS:** Global Index 43% 0.043\*  
 Attention 57% 0.001\*\*

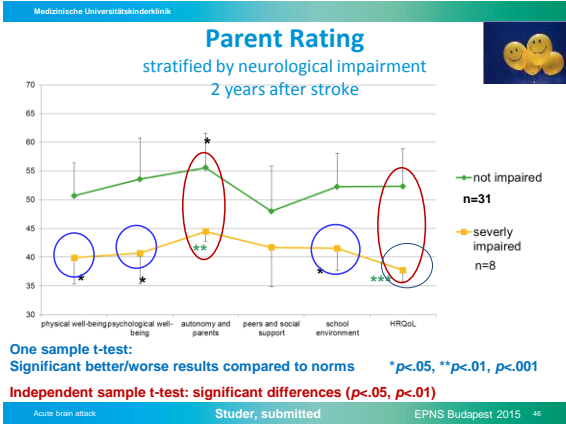


## Children Rating stratified by neurological impairment 2 years after stroke



**One sample t-test:** Significant better results compared to norms.  
 \*p<.05, \*\*p<.01  
**Independent t-test:** Significant difference in one scale






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**Helpful literature**

- Mackay MT, et al. «Arterial ischemic stroke risk factors: The international pediatric stroke study.» *Ann Neurol*, 1 2011: 130-40.
- Steinlin M. A Clinical approach to arterial ischemic childhood stroke: increasing knowledge over the last decade. *Neuropediatrics*. 2012;43: 1-9. Review
- Monagle P et al «Antithrombotic therapy in neonates and children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.» *Chest*. 2012 Feb;141(2 Suppl):e7375-801S, Feb 2012: e7375-801S
- Roach ES, et al «Management of stroke in infants and children: a scientific statement from a Special Writing Group of the American Heart Association Stroke Council and the Council on Cardiovascular Disease in the young.» *Stroke*, 2008: 2644-91.

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Medizinische Universitätskinderklinik

**Helpful literature**

- Mallick AA et al „Diagnostic delays in paediatric stroke.“ *J Neurol Neurosurg Psychiatry*. 2014 Oct 23. pii: jnnp-2014-309188 epub ahead of print, 2014
- Mackay MT et al „Stroke and nonstroke brain attacks in children.“ *Neurology*, Bd. 82, pp. 1434-40, April 2014
- Yock-Corrales A et al „Can the FAST and ROSIER adult stroke recognition tools be applied to confirmed childhood arterial ischemic stroke?“ *BMC Pediatr*, Bd. 11, p. 93, 21 October 2011
- Ellis MJ et al „Endovascular therapy in children with acute ischemic stroke: review and recommendations.“ *Neurology*, Bd. 79, pp. 158-64, 25 September 2012

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