Standardized psychological investigation of 59 patients with congenital hyperinsulinism

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Literature overview

Author /Journal	Patients (n)	Neurological outcome
Izumi et al (Japan) Acta Paediatr Jap 1997; 39: 10-17	5 (5/5 pancreatectomy)	4/5 epilepsy (4-22y.)
Cresto et al Arch dis Child 1998; 79(5): 440-4	26 (10/26 pancreatic resection)	11/26 neurological sequelae
Mahachoklertwattana et al (Thailand) J Pediatr Endocrinol Metab 2000; 13(1): 37-44	7/10 (neonate; Group 1 infantile; Group 2)	6/7 delayed development and subnormal IQ
Rother et al (USA) Ped. Diabetes 2001; 2(3): 115-22	8/15 (15/15 subtotal pancreatectomy 5/15 initially seizures 2/15 mental retardation)	8/8 attentional control impairment 4/8 subnormal intellectual functioning

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Menni et al (France) Pediatrics 2001; 107: 476-479.	90 (63 treated surgically 27 treated medically) Subsequent Normal Development; Group 1) Intermediate Disability; (Group 2) Severe Psychomotor Retardation; (Group 3)	n / Gr1 / Gr2 / Gr3 All patients 90 74% 18% 8% Neonates 54 68% 21% 11% Infants 36 82% 15% 3% Diffuse form 34 75% 14% 9% Focal form 29 68% 22% 10% Medical treatment 27 80% 16% 4%
Jack et al (Australia) Clin Endocrinol 2003; 58(3): 355-64	62 Group A: euglycemic < 35 days Group B: non-euglycemic > 35 days Neurological outcome (normal, mild deficit, severe deficit)	no different between Group A / B 44% with neurological deficits Group A: medical treatment 7/ 15 (4 mild; 3 severe deficit) Surgical treatment 2/ 18 (2 mild; 0 severe deficit)
Meissner et al (Germany) Eur J Endocrinol 2003; 149: 43-51	114 using standard questionaire	44% high degree of psychomotor or mental retardation 25% epilepsy

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Cherian et al Saudi Arabia J Pediatr Endocrinol Metab 2005; 18(12): 1441-8	10 (10/10 pancreatectomy 95 %)	1/10 sustained subarachnoid hemorrhage, cerebral edema, seizures in neonatal period 9/10 neurologically and developmentally normal
Mazor-Aronovitch et al (Israel) Eur J Endocrinol 2007; 157(4): 491-7	21 Ashkenazi CH medically treated (10/21 perinatal seizures of short duration 4/21 post-neonatal seizures, which remitted entirely) Telephone interview using standard questionaire	*Early childhood:* 4/21 hypotonia 8/21 fine motor problems 7/21 gross motor problems (clumsiness) 1/21 mild cerebral palsy 3/21 speech problems 8/21 required developmental therapy *School age:* 21/21 regular education 6/21 learning problems
Mercimek-Mahmutogly et al (Austria) J Pediatr Endocrinol Metab 2008; 21(6): 523-32	14 (7/14 pancreatectomy)	31% mental retardation 15% epilepsy

- Up to now only retrospective analysis (by reviewing hospital records or telephone interviews) of psychomotor development has been published
- motor and/ or intellectual disability in 138/257 children
- one prospective study in eight children (mean age 12.7 ±0.8)

- Drawback of retrospective studies:
  - very selective cohorts, e.g. after (95%) pancreatectomy
  - Inhomogeneity for etiology, e.g. syndromic or unknown cause
  - no standardized psychometry
  - missing values, e.g. duration of hypoglycemia

Prospective, standardized psychometric studies needed

INCLUSION CRITERIA

- ✓ clinical diagnosis of CHI
- ✓ mutation in KATP-channel genes
- ✓ metabolopathies: GCK, GLUD, others
- ✓ syndromic, chromosomal aberration
- ✓ no age limit

CLINICAL DIAGNOSIS OF CHI

- ✓ glucose demand > 8 mg/kg/min
- ✓ glucagon response (30mg/kg s.c. or i.m.)
- ✓ simultaneous:
  - ✓ Glucose < 2.6 mmol/l
  - ✓ Insulin > 3 mU/l
- ✓ FFA < 600 mmol/l, ketones (BOHB) <0.1mmol/l

OBJECTIVES

Primary objectives:

- intellectual and physical development and motor function of patients with congenital hyperinsulinism

Secondary objectives:

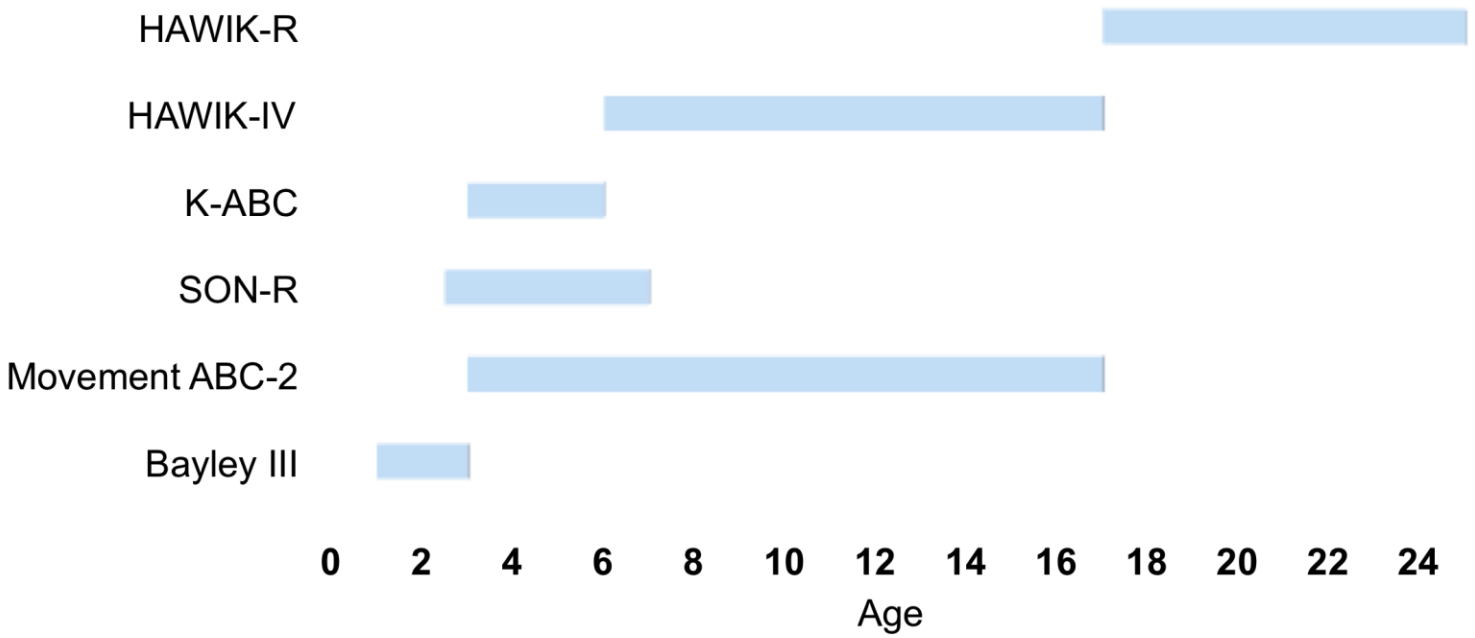
- noticeable behaviour problems
- disturbance in quality of life (descriptive analysis)
- influence of hypoglycaemia based on nutrition

Parental Home Magdeburg

PATIENTS and METHODS

- 59 patients (male=35; age: 3 months up to 57 years)
- Genetic defects: ABCC8 (n=16), KCNJ11 (n=4), Glucokinase (n=3), GDH (n=2)
- Application of **standardized psychological procedures** to acquire data of cognitive, speech and social-emotional development in patients with hyperinsulinism

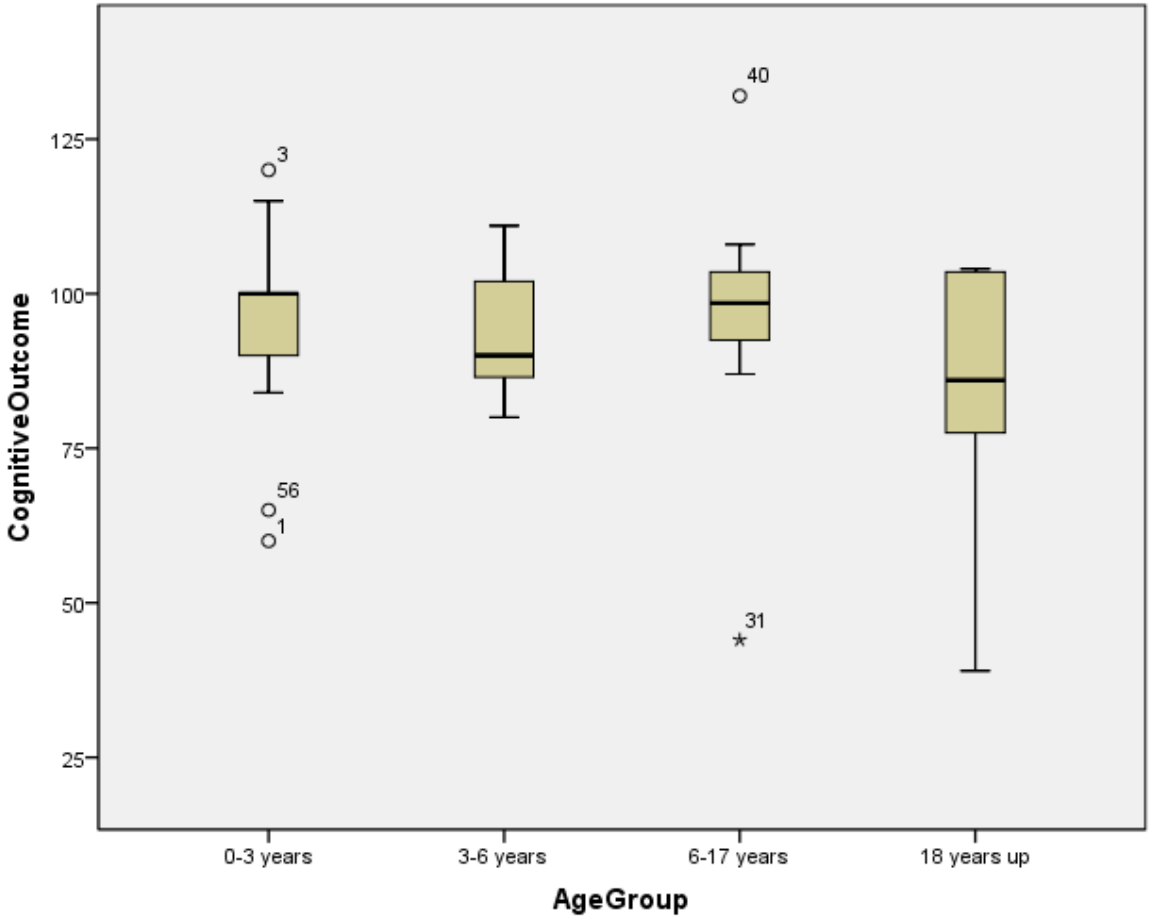
Standardized psychometric tests



RESULTS

	0-3 years	3-6 years	6-17 years	adults
cognitive impairment	7%	21%	9%	42%
speech delay	22%	-	-	-
motor delay	35%	20%	42%	-
social-emotional delay/ behaviour	4%	no	36%	no

Cognitive Development (M=100; SD=15)



CONCLUSION

- 26 of 59 patients show developmental delay
- A connection with the basis defect could not be detected (up to now)
- Motor delays dominate (one out of three)
- An early integration of patients in therapeutic treatments (e. g. occupational therapy) is essential to prevent further delay