Hypofyse congres

Zeldzaam maar niet alleen

nederlandse hypofyse stichting

Paul van Trotsenburg &
Nitash Zwaveling-Soonawala

Kinderarts-endocrinologen

Workshop congenitaal hypopituïtarisme

Amsterdam UMC
Universitair Medische Centra

Interactieve Q&A

Congenitaal hypopituïtarisme (CHP)

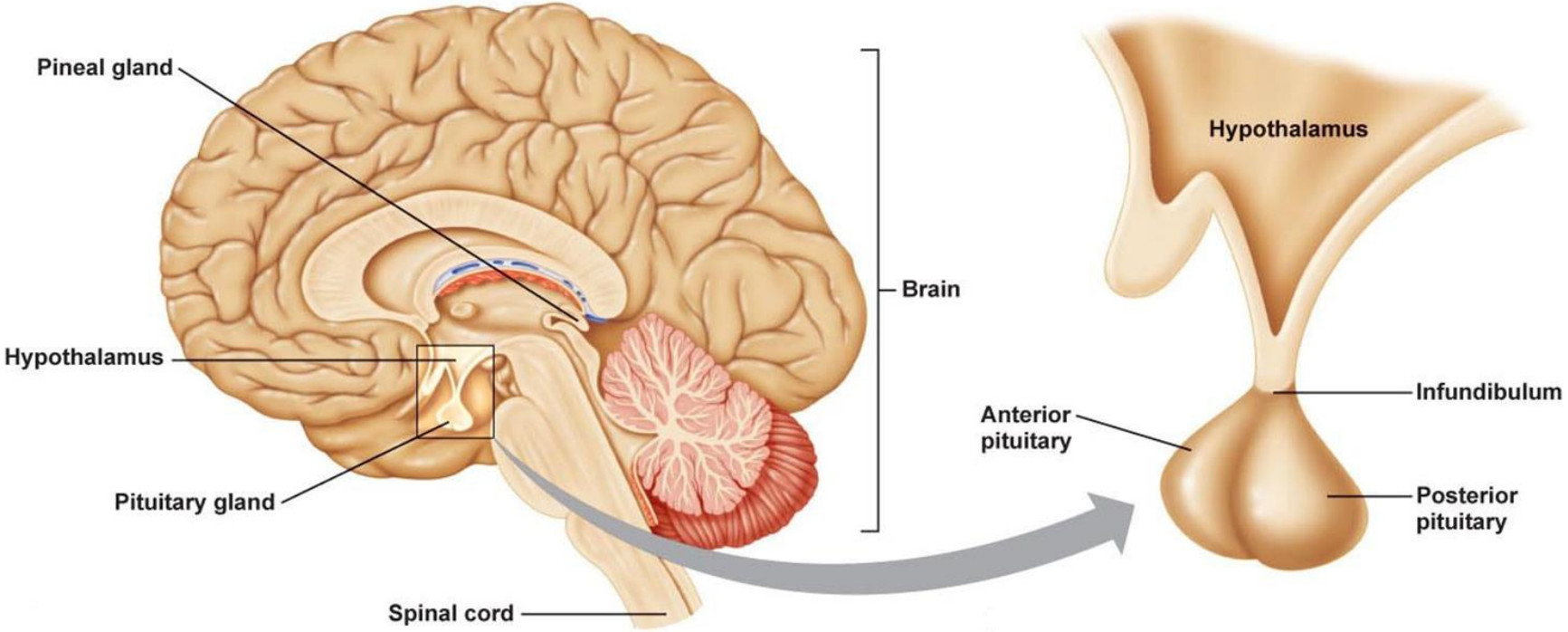
Aangeboren hypofyse insufficiëntie

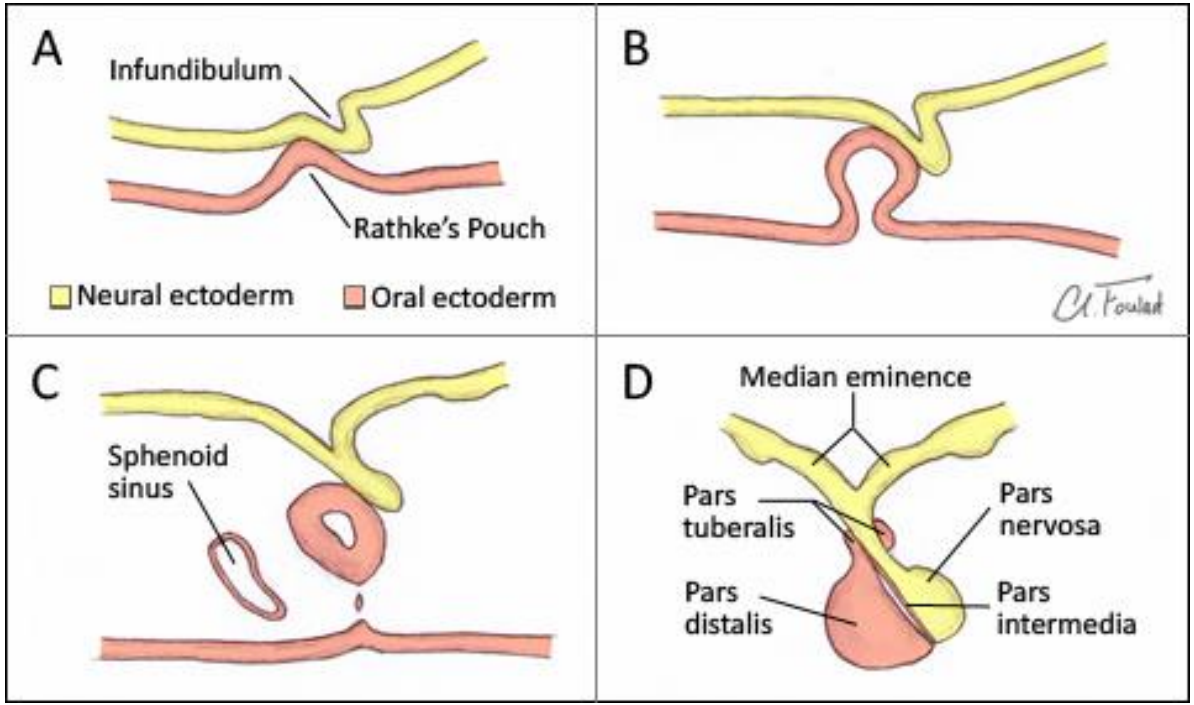
3 groepen:

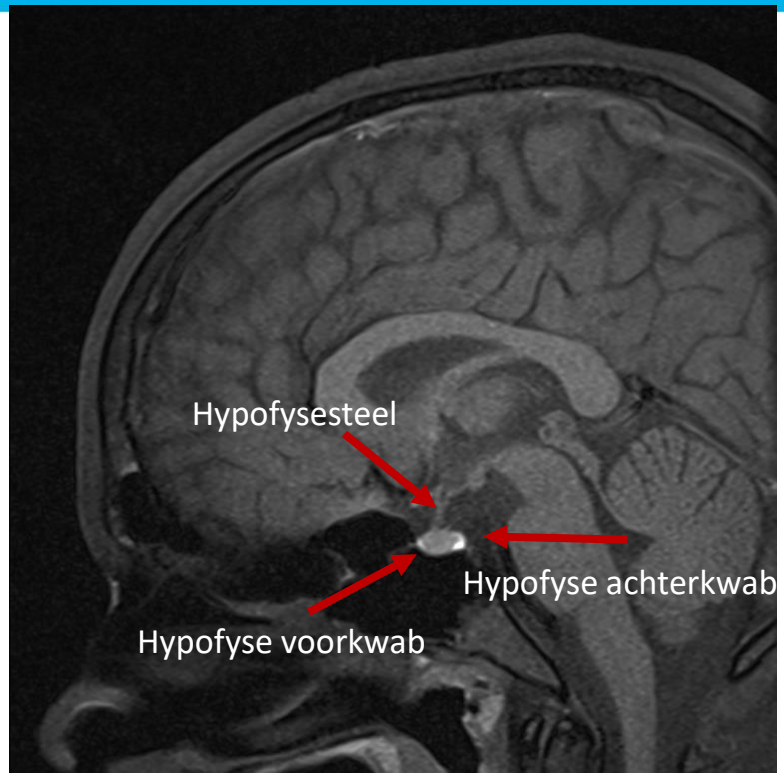
- Geïsoleerde aanlegstoornis: Pituitary stalk interruption syndrome; PSIS
= niet-syndromale CHP

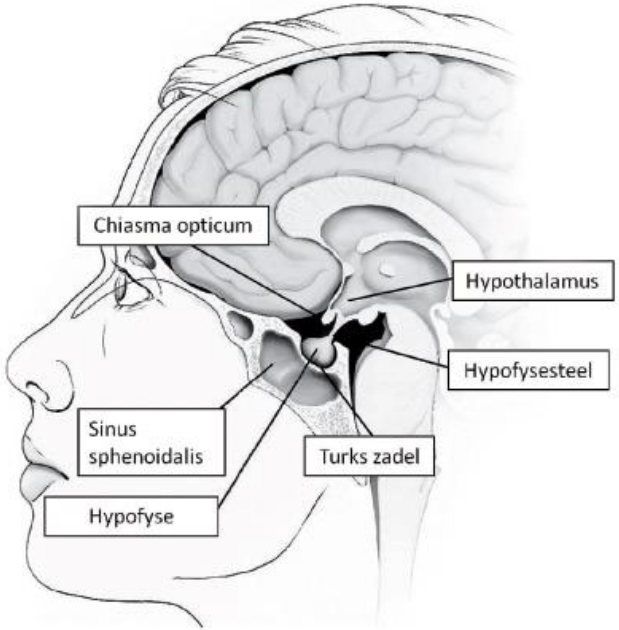
- Aanlegstoornis hypofyse met uitgebreidere hersenaanleg stoornis
= syndromale CHP

- Normaal aangelegde hypofyse met genetische afwijking waardoor hypofyse niet goed functioneert


Pineal gland
Hypothalamus
Pituitary gland
Spinal cord
Brain
Hypothalamus
Infundibulum
Anterior pituitary
Posterior pituitary

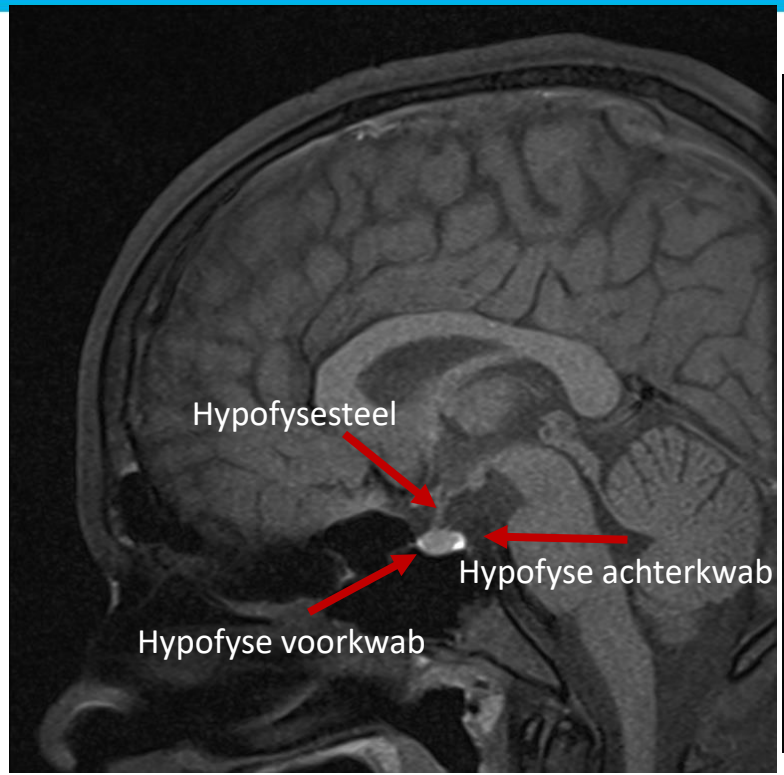

A
Infundibulum
Rathke's Pouch
Neural ectoderm
Oral ectoderm
B
C
Sphenoid sinus
D
Median eminence
Pars tuberalis
Pars nervosa
Pars distalis
Pars intermedia

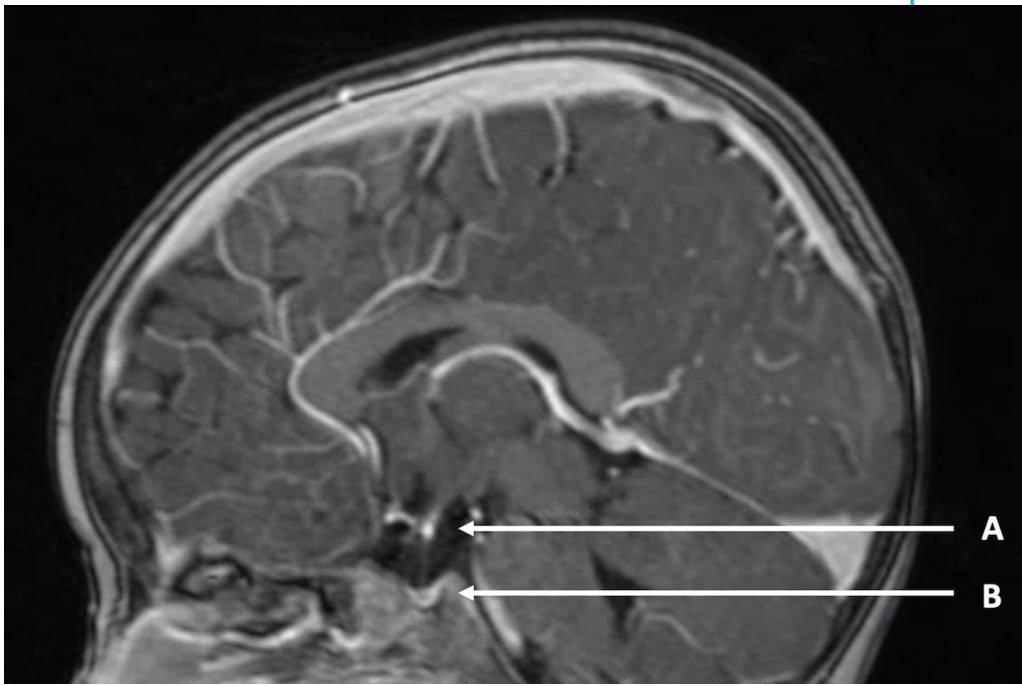

Hypofysesteel
Hypofyse achterkwab
Hypofyse voorkwab


Chiasma opticum
Hypothalamus
Hypofysesteel
Sinus sphenoidalis
Turks zadel
Hypofyse

Pituitary stalk interruption syndrome (PSIS)

www.hypofyse.nl



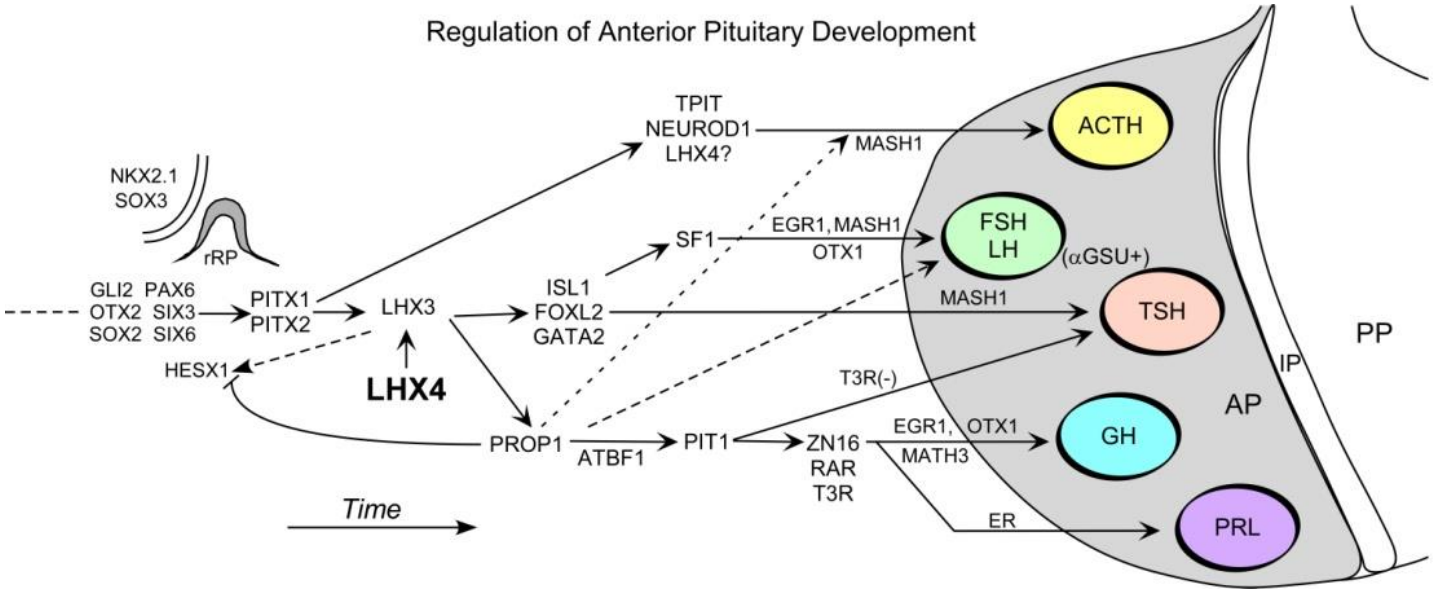


Gevolgen van PSIS

Hypofyse voorkwab werkt niet goed

Hypofyse achterkwab werkt wel

Niet erfelijk



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Combined pituitary hormone deficiency

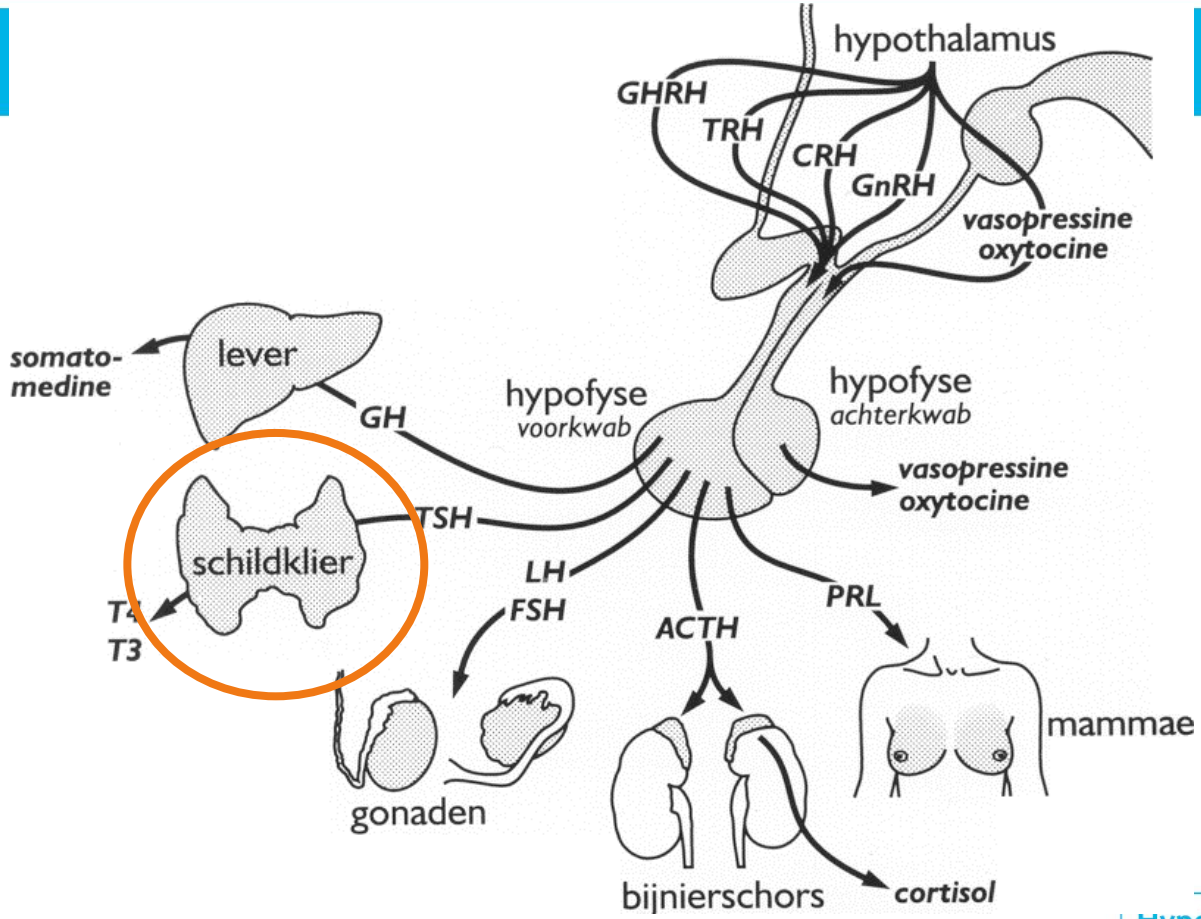
POU1F1	GH, TSH and prolactin deficiencies
PROP1	GH, TSH, LH, FSH, PRL and evolving ACTH deficiencies

Specific syndrome

HESX1	Septo-optic dysplasia
LHX3	GH, TSH, LH, FSH, PRL deficiencies, limited neck rotation
LHX4	GH, TSH, ACTH deficiencies with cerebellar abnormalities
SOX3	Hypopituitarism and mental retardation
GLI2	Holoprosencephaly and multiple midline defects
SOX2	Anophthalmia, hypopituitarism, learning difficulties, esophageal atresia
GLI3	Pallister–Hall syndrome
PITX2	Rieger syndrome

Hoe wordt de diagnose gesteld

- Neonatale hielprik: schildklierhormoon tekort “centrale hypothyreoïdie”
- Lage bloedsuikers na de geboorte
- Afbuigende lengtegroei
- Niet starten van de puberteit



Hypofyse congres
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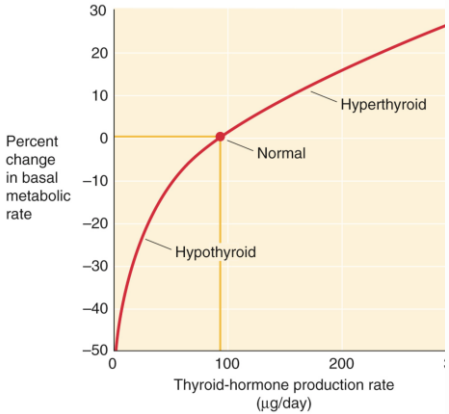
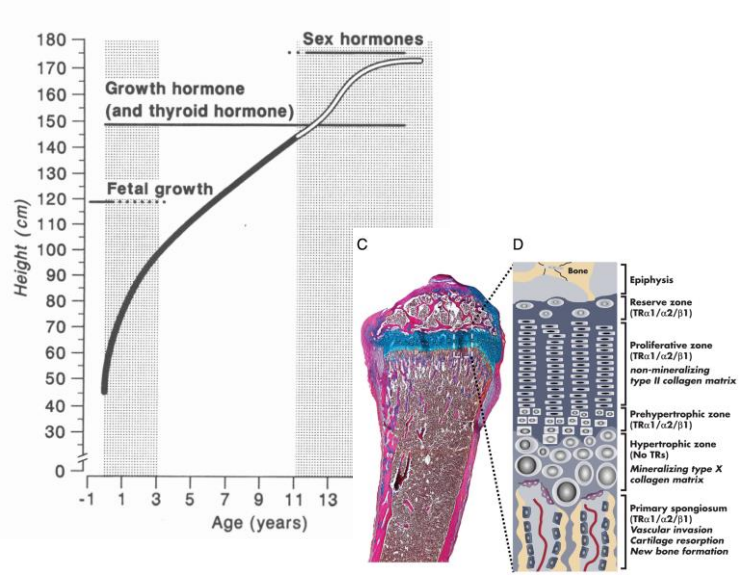
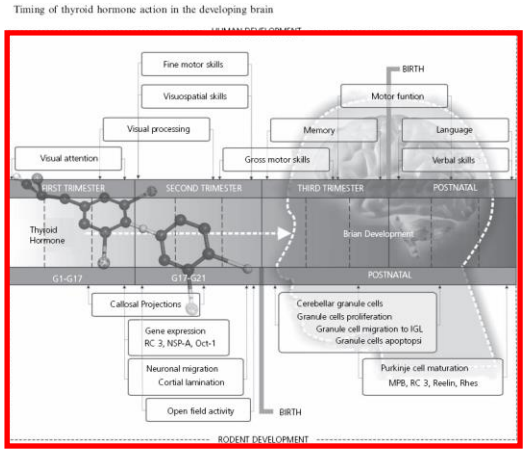
Effecten van schildklierhormoon



Stofwisseling



Groei



Hersengroei en -ont

Hypofyse congres
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Prognose congenitale hypothyreoïdie sinds start neonatale screening

PREVALENCE OF CONGENITAL HYPOTHYROIDISM AND DEVELOPMENTAL OUTCOME OF AFFECTED PATIENTS BEFORE AND AFTER SCREENING

	Before screening	Since screening
Prevalence	One in 6,700	One in 2,500
Mean IQ	86	95–105[a]
% with IQ < 70	8%–27%	None

[a] Other benefits: ↓ in neurologic dysfunctions and learning difficulties.
Adapted from: Grosse SD, Van Vliet G. Prevention of intellectual disability through screening for congenital hypothyroidism: how much and at what level? *Arch Dis Child* 2011;96(4):374–379; Deladoëy J, Ruel J, Giguère Y, et al. Is the incidence of congenital hypothyroidism really increasing? A 20-year retrospective population-based study in Québec. *J Clin Endocrinol Metab* 2011;96(8):2422–2429.

Primaire CH -> vroege opsporing en behandeling helpt!

Grosse SD, Van Vliet G. Arch Dis Child. 2011 Apr;96(4):374-9

Clinical and genetic characteristics of Dutch children with central congenital hypothyroidism, early detected by neonatal screening

J C Naafs[1,2], **P H Verkerk**[3], **E Fliers**[2], **A S P van Trotsenburg**[1] and **N Zwaveling-Soonawala**[1]

Correspondence

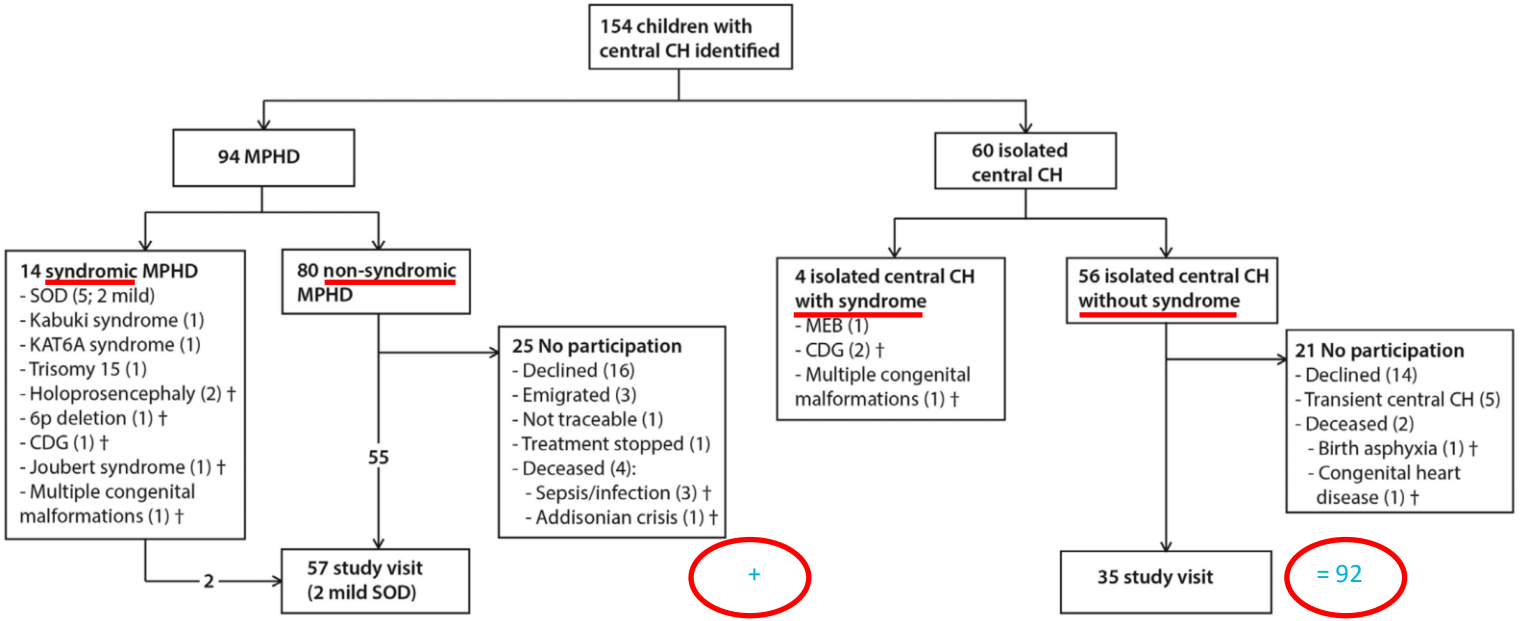
European Journal of Endocrinology, December 2020

2005-2015

- 154 kinderen met centrale hypothyreoïdie
- 1 op de 25.000 levend geborenen
- 94 multipele hypofysehormoon uitval (MPHD)
- 60 geïsoleerde centrale hypothyreoïdie

Clinical and genetic characteristics

of dutch children with central CH, early detected by neonatal screening



congres alleen nederlandse hypofyse stichting

- 20 jaar cohort
  - 2/3 MPHD, 1/3 geïsoleerde centrale CH
- MPHD: voornamelijk PSIS
- Geïsoleerde centrale CH bijna allen genetisch bevestigd
- Meerderheid opgenomen in eerste levensweek maar zelden klinische diagnose

Lange termijn uitkomsten

Clinical Study | J C Naafs and others | Cognition in congenital central hypothyroidism | **182**:3 | **351**–361

Cognitive outcome in congenital central hypothyroidism: a systematic review with meta-analysis of individual patient data

J C Naafs[1], L M Vendrig[1], J Limpens[2], H J van der Lee[3], R G Duijnhoven[4], J P Marchal[5], A S van Trotsenburg[1] and **N Zwaveling-Soonawala[1]**

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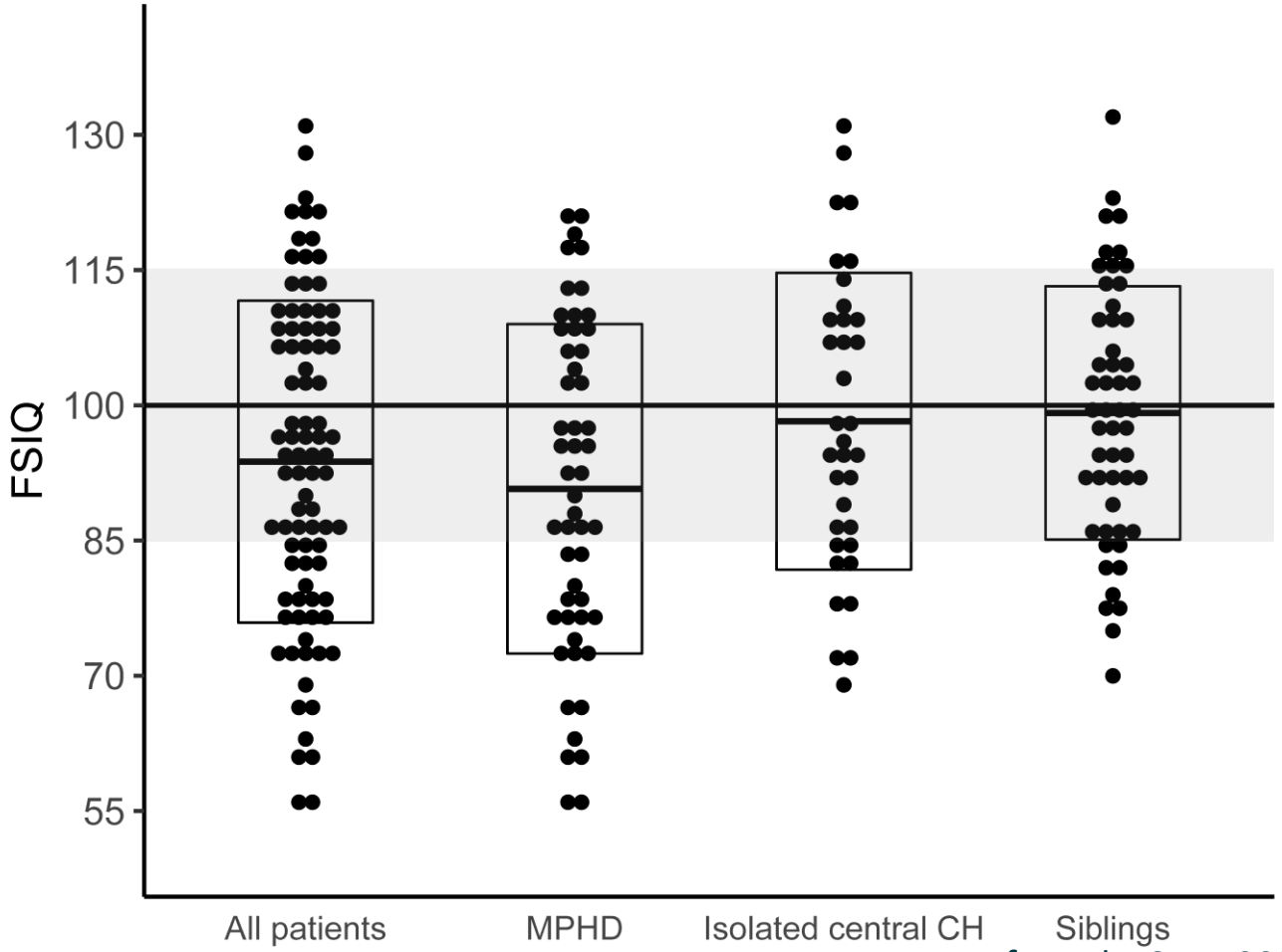
Correspondence should be addressed to N Zwaveling-Soonawala
Email n.zwaveling@amsterdamumc.nl



Naafs et al. *JCEM*. 2021

	Estimated marginal means (95% CI)			
Outcome	**MPHD patients (*n* = 52)**	**Isolated central CH patients (*n* = 35)**	**Siblings (*n* = 52)**	***p*-value**
Mean FSIQ	90.7 (86.4–95.0)	98.2 (93.0–103.5)	98.6 (94.5–102.8)	0.002
Processing speed	91.2 (86.9–95.6)	91.4 (86.1–96.7)	101.7 (97.4–106.0)	<0.001
WPPSI/WISC: Verbal IQ*	97.2 (91.9–102.5)	102.9 (97.0–108.9)	96.3 (91.6–101.0)	0.11
WPPSI/WISC: Performance IQ*	89.1 (84.2–94.0)	96.1 (90.6–101.6)	99.9 (95.6–104.2)	<0.001
WAIS: Verbal comprehension*	94.4 (87.9–101.0)	101.4 (91.0–111.9)	104.0 (95.4–112.6)	0.07
WAIS: Perceptual reasoning*	91.0 (82.2–99.7)	98.0 (84.4–111.7)	103.5 (93.2–113.9)	0.02
WAIS: Working memory*	94.9 (87.1–102.8)	95.6 (83.1–108.1)	104.5 (93.6–115.3)	0.21
Milestone: sitting independently (months)*	8.9 (8.2–9.7)	8.5 (7.6–9.4)	8.3 (7.5–9.0)	0.29
Milestone: standing (months)*	11.7 (11.0–12.5)	11.0 (10.0–11.9)	10.6 (9.8–11.4)	0.07
Milestone: walking independently (months)*	15.9 (15.0–16.7)	14.9 (13.9–16.0)	14.3 (13.4–15.2)	0.02

ORIGINAL ARTICLES
www.jpeds.com • The Journal of Pediatrics

Newborn Screening Results in Children with Central Hypothyroidism

Todd D. Nebesio, MD, Michael P. McKenna, MD, Zeina M. Nabhan, MD, MSc, and Erica A. Eugster, MD

Newborn Screening Results in Children with Central Hypothyroidism

Table. Comparison of children with central hypothyroidism on the basis of newborn screening results

Variable	Abnormal results (n = 8)	Normal results (n = 34)	*P* value
Sex	6 male (75%)	16 male (47%)	.157
Initial T4 on newborn screening	3.7 ± 0.6	9.8 ± 3.4	<.001
Growth hormone deficiency	7/8 (87%)	25/34 (73%)	.405
Corticotropin deficiency	6/8 (75%)	28/34 (82%)	.63
Diabetes insipidus	1/8 (12%)	8/34 (23%)	.49
Abnormal CNS imaging (CT or MRI)	8/8 (100%)	31/34 (91%)	.076
Prolonged neonatal hospitalization	8/8 (100%)	26/34 (76%)	.087
Developmental delay	2/8 (25%)	19/34 (56%)	.115
Time to endocrine consult (months)	4.6 ± 5.0	16.9 ± 26.7	.037

CT, Computed tomography.

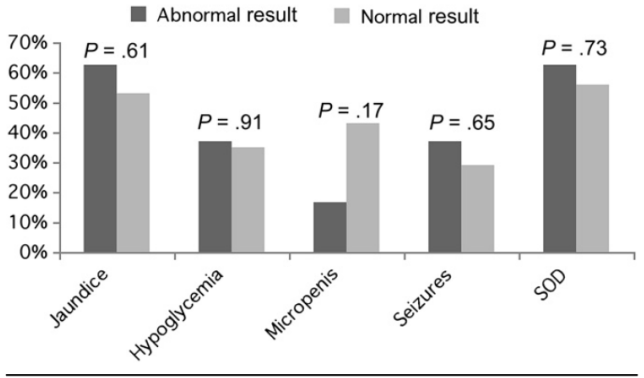


Figure. Associated features of hypopituitarism in children with central hypothyroidism. There was no statistically significant difference ($P < .05$) between those children with abnormal newborn screening results and children with normal newborn screening results. SOD, septo-optic-dysplasia.

Ontwikkelingsachterstand: 21/42 = 50%

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Nebesio TD et al, 2010

Samenvattend

IQ geïsoleerde centrale CH	komt overeen met broertjes/zusjes
IQ MPHD	8 punten lager
Processing speed beide patiënten groepen	10 punten lager

Motorische problemen
meer prevalent in beide patiënten groepen

The Journal of Clinical Endocrinology & Metabolism, 2021, Vol. XX, No. XX, 1–11
doi:10.1210/clinem/dgab209
Clinical Research Article

ENDOCRINE SOCIETY

OXFORD

Clinical Research Article

Health-Related Quality of Life in Patients With Early-Detected Central Congenital Hypothyroidism

Self-report scores (62 patients; 36 siblings)				
	Estimated marginal means (95% CI)			
PedsQL domain	**MPHD (*n* = 33)**	**Isolated central CH (*n* = 29)**	**Siblings (*n* = 36)**	***p*-value LMM**
Total score	79.8 (75.6–84.0)	82.7 (78.2–87.3)	84.4 (80.3–88.4)	0.25
Physical functioning	86.5 (82.4–90.7)	87.5 (83.0–92.0)	89.0 (85.0–93.0)	0.63
Emotional functioning	76.5 (70.4–82.6)	79.0 (72.4–85.5)	79.4 (73.6–85.3)	0.76
Social functioning	80.6 (75.2–85.9)	90.8 (85.0–96.6)	87.9 (82.9–93.0)	0.02
Role functioning	71.7 (65.8–77.5)	70.9 (64.6–77.3)	78.5 (72.9–84.1)	0.06
Parent(proxy-)report scores (73 patients; 42 siblings)				
	Estimated marginal means (95% CI)			
PedsQL domain	**MPHD (*n* = 41)**	**Isolated central CH (*n* = 32)**	**Siblings (*n* = 42)**	***p*-value LMM**
Total score	77.0 (72.9–81.2)	83.7 (78.9–88.4)	87.2 (83.2–91.2)	<0.001
Physical functioning	83.9 (79.2–88.6)	88.1 (82.7–93.5)	93.2 (88.6–97.8)	<0.01
Emotional functioning	71.3 (65.7–76.8)	77.0 (70.7–83.4)	78.3 (72.9–83.6)	0.10
Social functioning	75.3 (69.8–80.9)	88.8 (82.4–95.2)	90.4 (85.0–95.8)	<0.001
Role functioning	74.1 (68.1–80.1)	78.3 (71.4–85.2)	82.3 (76.4–88.2)	0.08

Samenvattend

- Kinderen zelf geven hoge score voor kwaliteit van leven
- Ouders geven opvallend lagere score
- Verklaring?