

Luik III: follow-up study

Neurobehavioural and cognitive effects
of prenatal exposure to persistent
environmental toxicants
in three year old children (2002-2008):
Results

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- Selection of studygroup (N=206):
inclusion criteria

- Follow-up study: 0-36 maanden (N=130)

- Data:
 - Prenatal exposure: cord blood
 - Questionnaires: mother & child
 - Cognitive & behavioural tests
 - Covariates/confounders



Selected regions

Regions	participants
Non ferrous smelter	68
Harbor	80
Rural area	48
Household combustion incinerators	10
TOTAAL	206



Inclusion criteria

- Participant biomonitoring study in Flanders
- Pregnancy without complications
- born at term (>36 weeks)
- no major congenital abnormalities or diseases
- no twins
- no abnormal or asymmetrical reflexes during standard neurological screening during the first days
- Flemish as their mother-tongue
- Written informed consent



Exposure parameters

- **Prenatal** exposure in cord blood:
 - Cd
 - Pb
 - PCBs (PCB 118, 170 and 28, 52, 101, 138, 153, 180)
 - Dioxin-like compounds (CALUX-TEQ)
 - HCB
 - DDE

- **Postnatal** exposure: estimates from repetitive food intake questionnaire
 - First year: monthly
 - Second year: three-monthly



Covariates (1)

■ General information

- Gender
- Season of birth

■ Information family:

- family structure,
- parity, socio-economic state,
- Observation home environment (HOME-score)

■ General health of the child:

- weight,
- length,
- Apgar score,
- medical history,
- breastfeeding

Test procedures:

- Age of child at testing
- Test leader



Covariates (2)

■ Data on mother:

- age,
- highest education level,
- intelligence estimate,
- complications during pregnancy,
- medication during pregnancy and labour,
- STAI: anxiety mother,
- smoking, alcohol and drug use during pregnancy



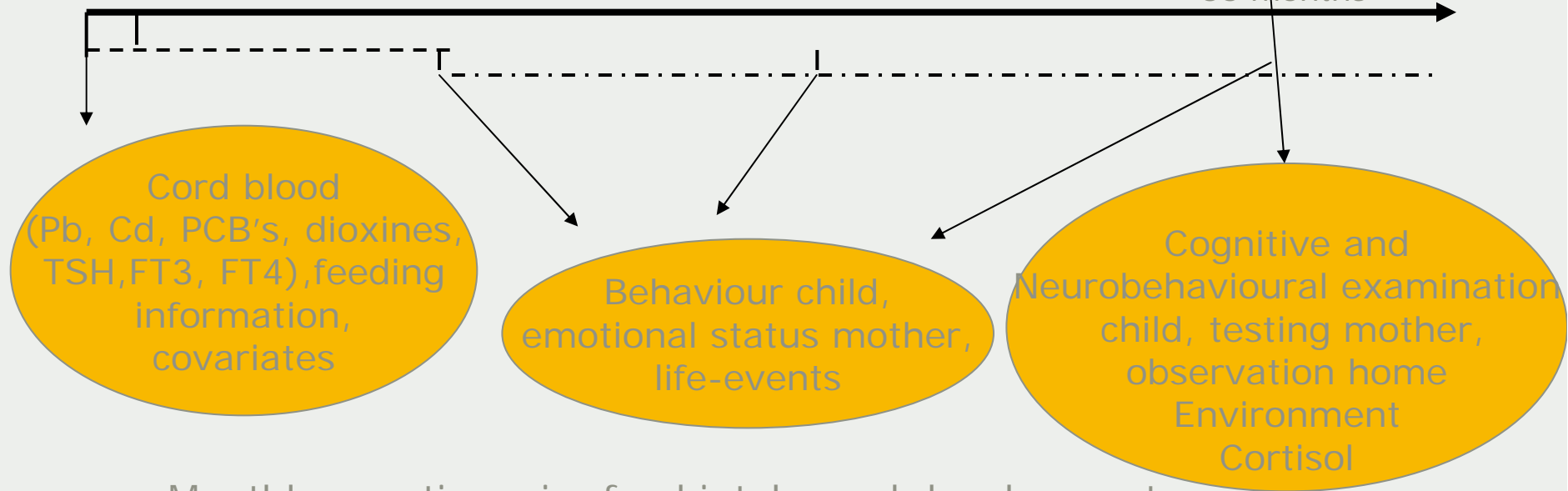
Overview measurements and examinations



Information pregnancy,
Postnatal depression



0 months 1 month 12 months 24 months 36 months



----- Monthly questionnaire food intake and development

..... Three-monthly questionnaire food intake and development



Tests and questionnaires concerning children

Test	Measurement type	Time of assessment
Snijders-Oomen non-verbal intelligence test (SON-R 2.5-7)	Intelligence: reasoning and visuo-spatial abilities	36 months
Bayley Scales of Infant Development (BSID-II-NL)	cognitive development: results in mental and motor indices	36 months
Reynell Language Developmental Scale (RTOS)	receptive language development level measured by oral instructions to carry out small tasks while playing with toys	36 months
Questionnaires/observation	Measurement type	Time of assessment
Milestones	Skills and abilities	0-36 months
Infant behaviour Questionnaire (IBQ)	Temperament as observed by the mother	12 months and 24 months
Child behaviour Checklist (CBCL) & Caregiver-Teacher's Report Form (C-TRF)	Functioning of the children as perceived by the mother and the teacher/kindergarten.	24 and 36 months
Observation of toy preference	7 min. lasting observation of masculine/feminine play behaviour	36 months



Test and questionnaires concerning mother

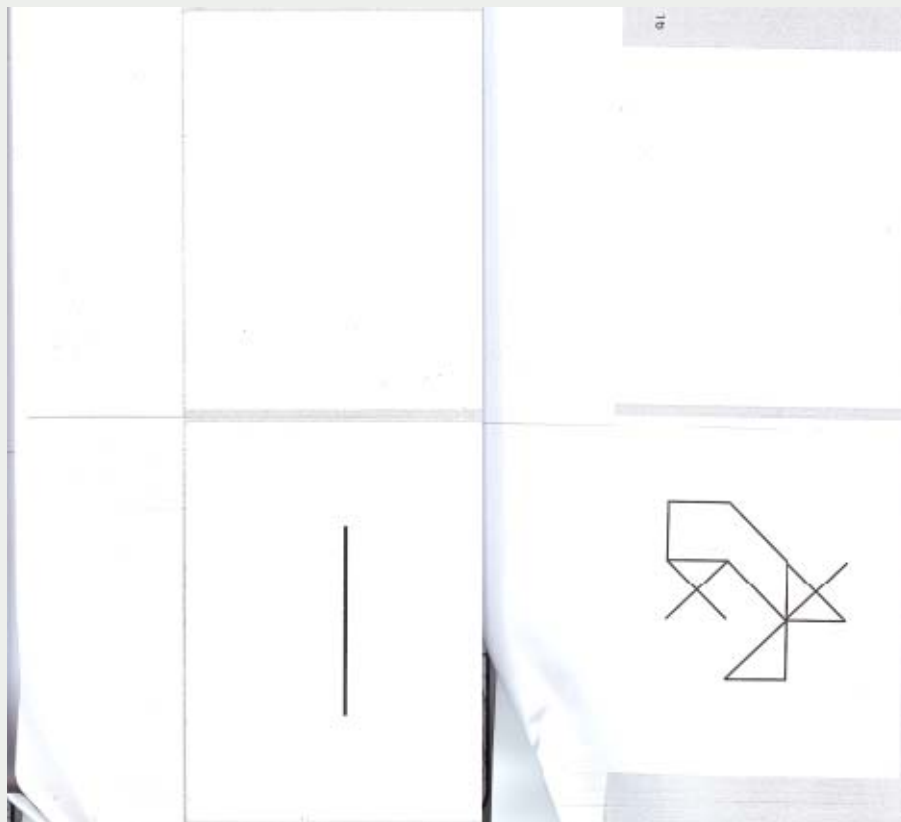
Test	Goal	Time of assessment
WASI	Intelligence estimate (verbal & performal)	36 months
State Trait Anxiety Inventory (STAI)	Anxiety: neuroticism, depression	12, 24 & 36 months
Perceived Stress Scale	Stress-measurement	12, 24 & 36 months
Life-events	important events in last year	12, 24 & 36 months
NEO-PI-R	Personality	36 months



SON-R: performale schaal

Vb1. patronen:

makkelijk item moeilijk item

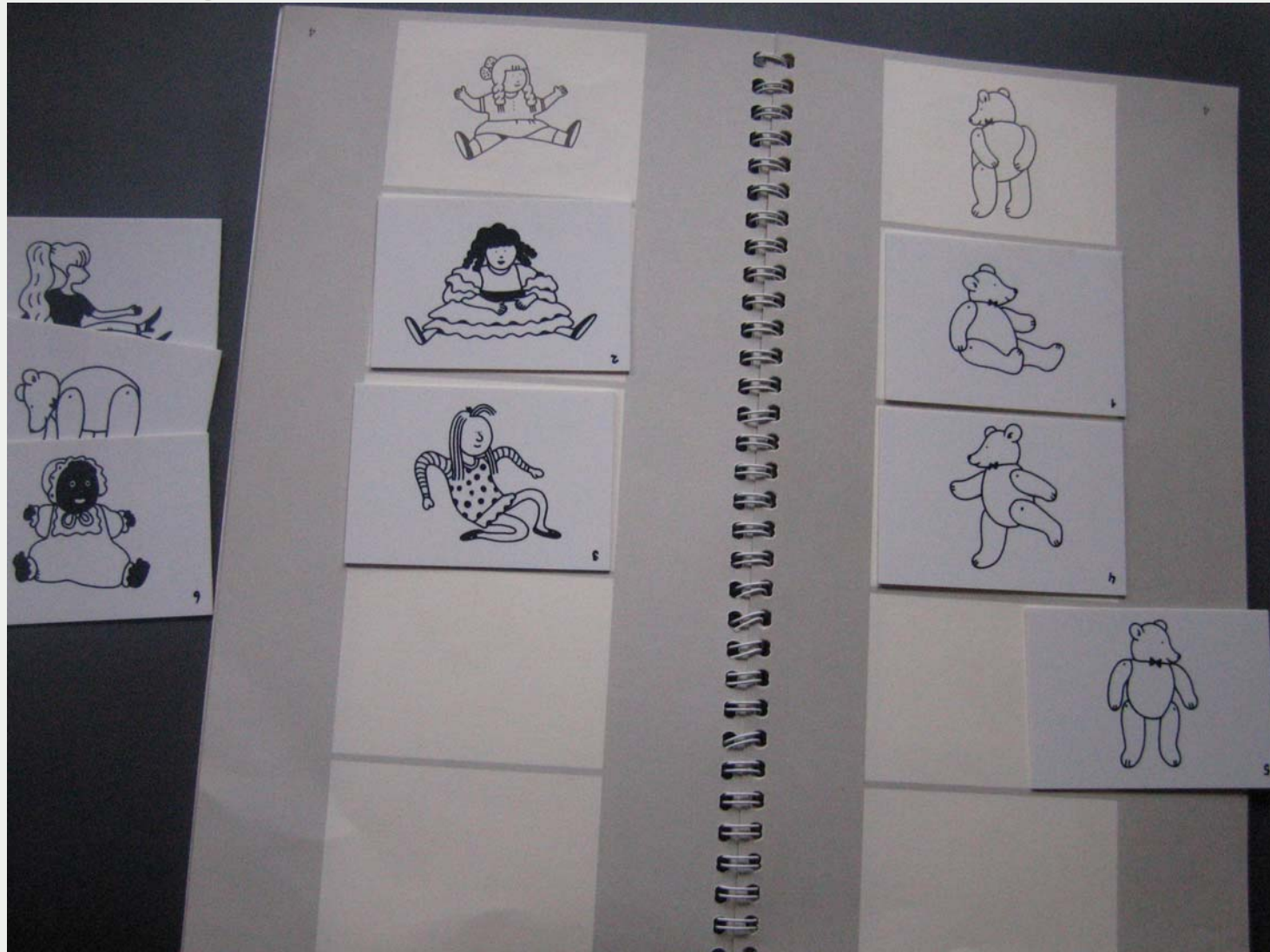


vb2. Puzzels:



SON-R: redeneerschaal

Vb. categorieën:



BSID: mentale schaal



RTOS: taalbegrip



- Structured observation of play behaviour:
3 types of plays:
 - Masculine (%): auto's, lorry, revolver, Duplo (Lego)
 - Feminine(%): hairdresser doll, baby doll with flask, tea service, 2 barbie dolls
 - Neutral (%): puzzel, booklet

- %, number of changes



Spelobservatie

OPZ *Geel*

Openbaar Psychiatrisch Zorgcentrum



Infant behaviour Questionnaire (IBQ)

- Filed by mother
- Temperament very young children
- Attention, reaction on stimuli,...
- Measurements on 12 and 24 months



Milestones

- 0-36 months
- Milestones in development:
Certain skills that children acquire at a certain age: laughing, crawling, first steps, use of a pot,...
- Expressed in months



Results

- All analyses were done in SPSS 12.0
- Distribution outcome variables: no transformations needed
- No test leader effects (ANCOVA, $p > 0,100$)
- Stepwise linear regression



Effecten Pb (1)

COGNITIE/INTELLIGENTIE

- SON-R: Reasoning IQ (reasoning) ↓
 $\beta = -0,194$; $P = 0.018$ min-max: **14,2 IQ-punten**
Significant covariates: **gender, home, BMI child**
- BSID: Mental Scale (intelligence) girls ↓
 $\beta = -0,273$; $P = 0.031$ min-max: **23,6 IQ-punten**
Significant covariates: **IQ mother, breastfeeding**



Effecten Pb (2)

GEDRAG

1. Milestones:

- Rolling over ↑ $\beta=0,255; P=0.015$
- *Pulling oneself up* ↑ $\beta=0,185; P=0.062$

2. IBQ 12 months: attention & reaction to stimuli: Activity↑

$\beta=0,221; P=0.029$

(more pronounced in boys)



Effecten Pb (3)

3. CBCL/TRF: gedragsvragenlijsten

- 12 months
 - Activity level ↑ $\beta=0,221; P=0.029$
 - Activity level (Boys) ↑ : $\beta=0,203; P=0.007$
- 24 months:
 - withdrawn ↑ $\beta=0,351; P=0.004$
- 36 months:
 - withdrawn ↑ $\beta=0,214; P=0.048$
 - Attention problems ↑ $\beta=0,306; P=0.005$
 - Affective problems ↑ $\beta=0,260; P=0.017$
 - Other problems ↑ $\beta=0,232; P=0.018$
 - Total problems ↑ $\beta=0,209; P=0.047$

4. Gender related play behaviour in girls:

- Feminine ↓ $\beta=-0,426; P=0.002$
- Masculine ↑ $\beta=-0,364; P=0.009$



Cognition/Intelligence

- RTOS: language comprehension (Σ PCB) $\downarrow \beta = -0,200; P = 0.047$
- RTOS: language comprehension (PCB170) $\downarrow \beta = -0,243; P = 0.016$

Behaviour (Σ PCB)

- Milestones: steps alone \uparrow (require more time) $\beta = 0,338; P = 0.020$
- CBCL/TRF 36 months:
 - Somatic complaints \downarrow $\beta = -0,257; P = 0.031$
 - Emotionally reactive \downarrow $\beta = -0,231; P = 0.076$
 - Other problems \downarrow $\beta = -0,264; P = 0.035$



Play Behaviour - gender

■ Boys

- PCB 180: 'switches' ↓ $\beta = -0,432; P = 0.007$
- \sum PCB : 'switches' ↓ $\beta = -0,367; P = 0.025$
- PCB118: neutral ↑ $\beta = 0,490; P = 0.004$

■ Girls

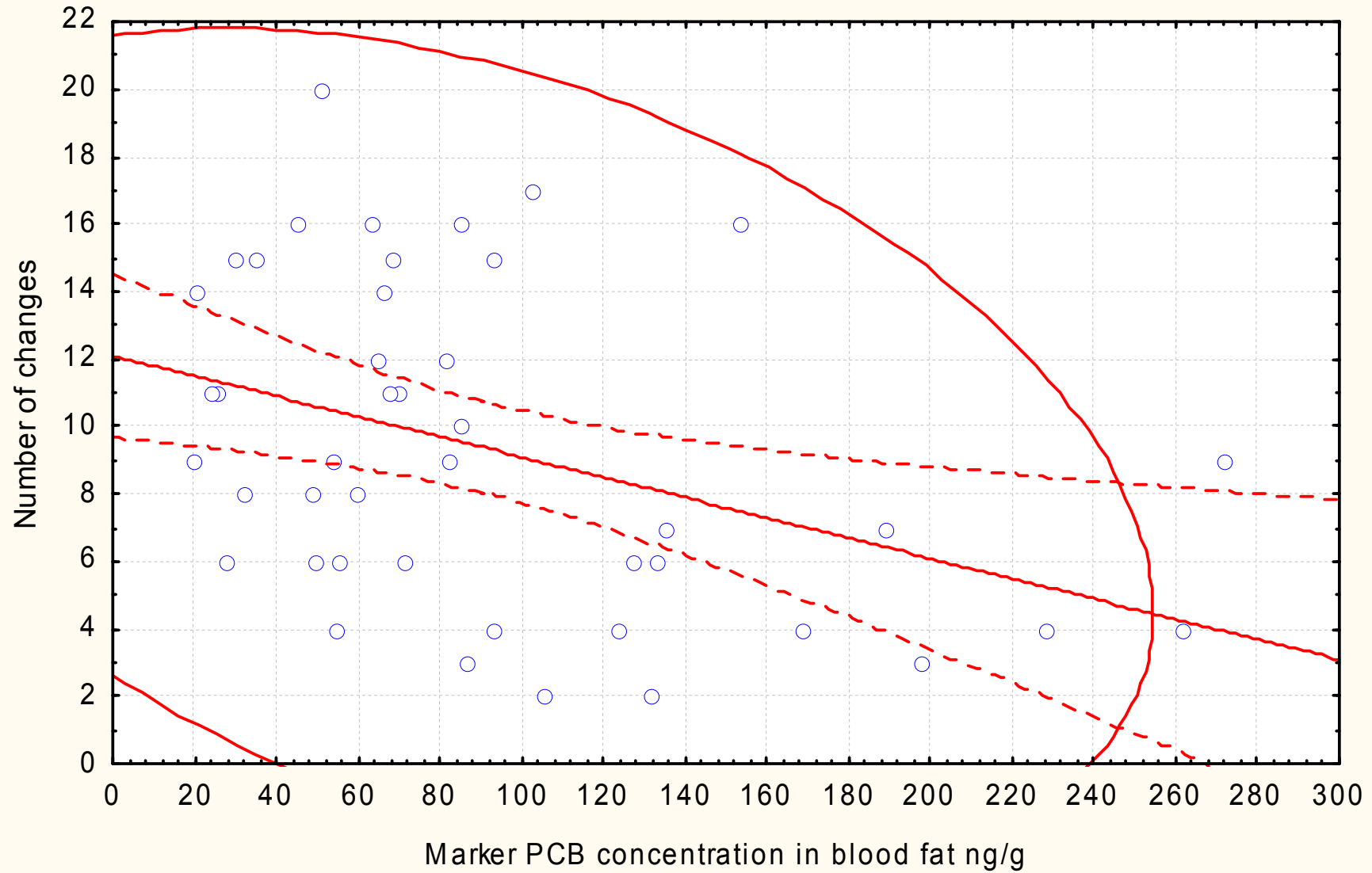
- *PCB 118: masculine* ↓ $\beta = -0,318; P = 0.029$
- \sum PCB: neutral ↑ $\beta = 0,317; P = 0.041$
- PCB170: neutral ↑ $\beta = 0,314; P = 0.032$

■ Total group

- \sum PCB: 'switches' ↓ $\beta = -0,236; P = 0.030$
- \sum PCB: neutral ↑ $\beta = 0,242; P = 0.037$
- PCB170: neutral ↑ $\beta = 0,246; P = 0.024$
- \sum PCB: masculine ↓ $\beta = -0,174; P = 0.057$
- PCB 118: mannelijk ↓ $\beta = -0,242; P = 0.008$



Linear regression
Boys
Number of changes of toy



Effects dioxin-like substances

CBCL/TRF: Behaviour questionnaires

□ 36 months:

- withdrawn ↓ $\beta = -0,290$; $P = 0.016$
- Emotionally Reactive ↓ $\beta = -0,329$; $P = 0.009$
- Total problems ↓ $\beta = -0,179$; $P = 0.087$

Language development:

- Vocabulary ↓ $\beta = -0,252$; $P = 0.041$



Effects of Hexachlorobenzene

IBQ & CBCL/TRF: Behaviour questionnaires

□ IBQ 24 months:

- Smiling & laughter ↑ $\beta=0,316; P=0.010$
- Distress to limitations ↓ $\beta=-0,271; P=0.034$

□ 36 months:

- Internal scale (CBCL) ↓ $\beta=-0,229; P=0.043$
- Emotionally reactive (TRF) ↓ $\beta=-0,293; P=0.023$
- Aggressive behaviour (TRF) ↓ $\beta=-0,268; P=0.038$
- Other problems (TRF) ↓ $\beta=-0,271; P=0.030$
- Total problems (TRF) ↓ $\beta=-0,258; P=0.047$
- Total problems (CBCL) ↓ $\beta=-0,221; P=0.041$

Milestones

- First steps alone: requires more time $\beta=0,330; P=0.023$

Reynell Language Developmental scales

- Language Comprehension ↓ $\beta=-0,262; P=0.010$



Effects of DDE

CBCL/TRF: gedragsvragenlijsten

□ 24 months:

- Other Problems (TRF) ↓ $\beta = -0,399; P = 0.005$
- Total problems (TRF) ↓ $\beta = -0,356; P = 0.020$

Gender related play behaviour in boys:

- Masculine ↓ $\beta = -0,326; P = 0.037$



Effects of interactions

□ sumPCB*HCB:

- RTOS Language comprehension ↓ $\beta = -0,327; P = 0.001$

□ SumPCB*DDE:

- First steps alone (required more time) $\beta = 0,343; P = 0.018$



Cord blood - Relationship pollutants & THs

(preliminary results, in collaboration with
Johan Maervoet, UIA)

Pollutant ($\mu\text{g/L}$)	Log ft_4 (ng/dl)		Log ft_3 (pg/ml)		Log TSH (mIU/L)	
	β	p	β	p	β	p
PCB 118	-0.318	< 0.0001	-0.192	0.010	-0.087	0.261
PCB 138	-0.392	< 0.00001	-0.235	0.004	-0.158	0.063
PCB 153	-0.176	0.041	-0.083	0.327	-0.050	0.567
PCB 170	-0.346	< 0.0001	-0.192	0.022	-0.101	0.242
PCB 180	-0.332	< 0.001	-0.248	0.004	-0.058	0.522
Calux TEQ	-0.165	0.038	-0.154	0.043	-0.018	0.830
HCB	-0.270	< 0.001	-0.151	0.052	-0.108	0.179
p,p'-DDE	-0.169	0.018	-0.104	0.137	-0.042	0.569
Zn	+0.277	0.0001	+0.185	0.008	+0.005	0.940

Multiple linear regression - Adjusted for total lipids, age mother, sex, gestational age, and alcohol consumption ($n \geq 182$)



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