Department of Occupational
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Mercury – Health - Food

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Greenland
Iceland
Norwegian Sea
FAROE ISLANDS
Sápmi
Finland
Norway
Åland Islands
Shetland Islands
Sweden
North Atlantic Ocean
Orkney Is.
Western Isles (Hebrides)
Est.
Latvia
Scotland
North Sea
Baltic Sea
Lith.
Denmark
N. Ireland
Russia
Man
Ireland
Poland
Wales
England
Netherlands
Germany
Belgium
France
Lux.
Czech Rep.

- Homogeneous, western culture
- Scandinavian-type health care and social security
- Traditional food includes pilot whale meat (MeHg) and blubber (POPs)
- Individual reliance on traditional foods varies, depends on seasonal availability, and is weakly associated with confounders

Cohort studies in the Faroes

- 1986/87: 1023 children
- 1994: 182 children
- 1998/99: 650 children
- 2000/01: 150 mothers
- 2007/09: 500 children

Total mercury in umbilical cord blood in Faroese cohorts in µg/l

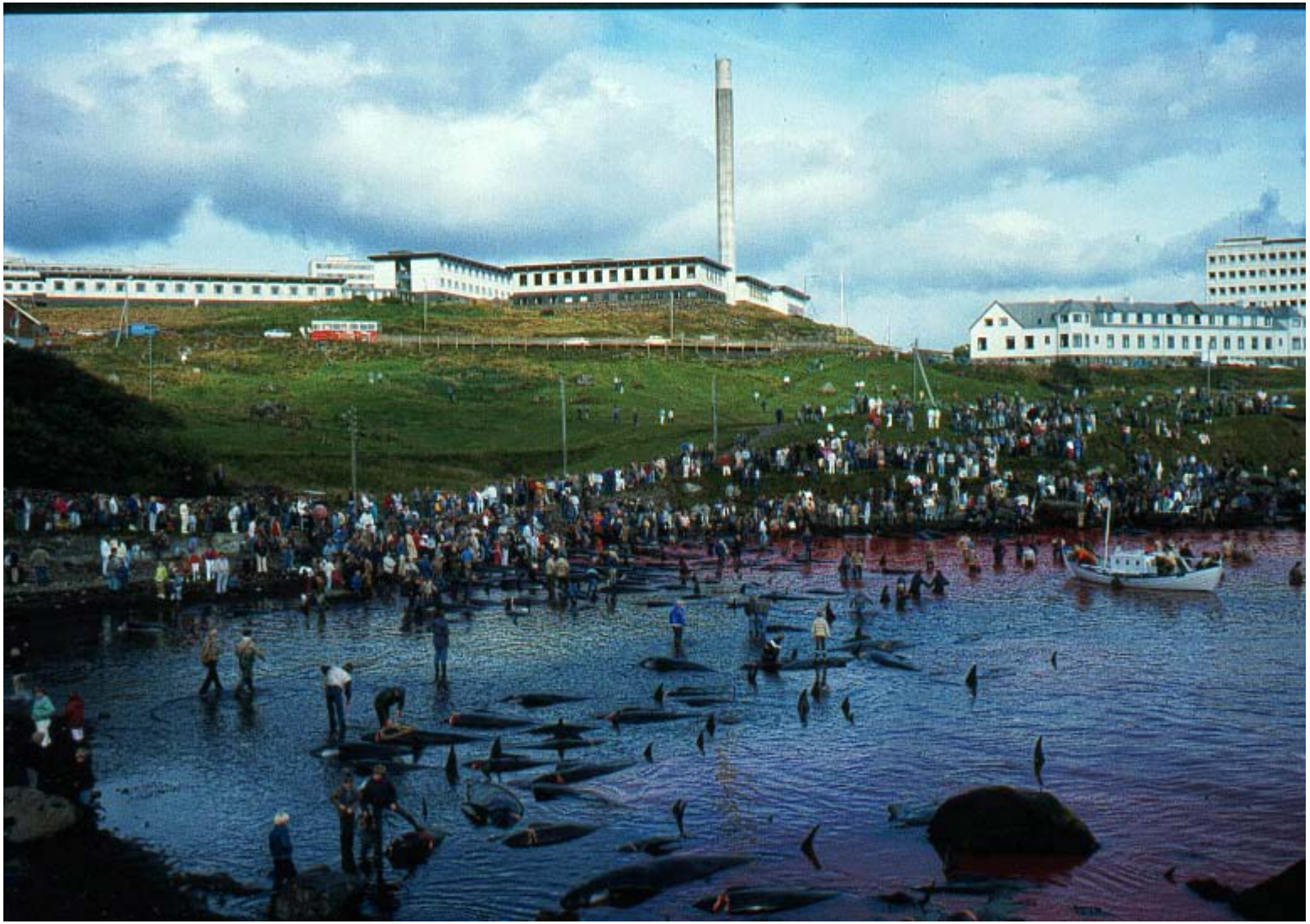
Cohort	Year	N	Geometric mean	Min.	Max.
Cohort 1	1986-87	894	22.9	0.90	351
Cohort 2	1994	163	20.9	1.90	102
Cohort 3	1998 -2000	603	12.3	1.60	193
Cohort 4 (mother-serum)	2000-2001	148	1,86	.001	7.50
Cohort 5	2007-2009	490	3.01	0.25	37.6

Why whales concentrate pollutants

Long-lived and large, but accumulation of pollutants depends on food:

1) Baleen whales: feed on plankton and fish low in the food chains – less pollution

2) Toothed whales: feed on larger fish and squid higher up in the food chains - more pollution



Faroe Islands: Pilot whales are taken for food, but cause exposures to methylmercury, PCB, etc.

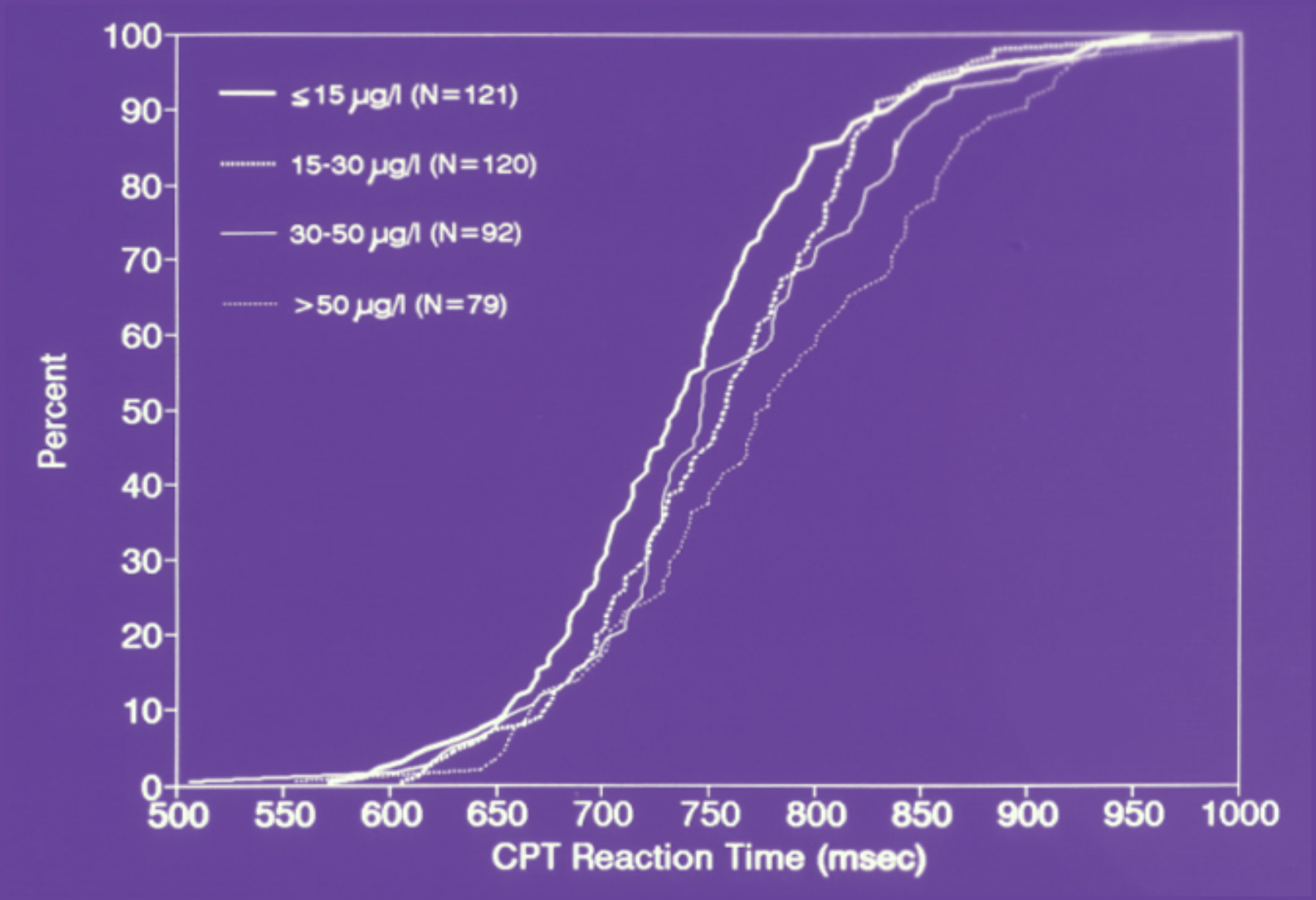
Summary of follow-up at age 11 years in the Nunavik Child Study

	Mercury (Hg)	Lead (Pb)	Polychlorinated biphenyls (PCBs)
Prenatal exposure			
	Poorer early processing of visual information Alteration of attentional mechanisms modulating processing of sensory information Lower estimated IQ Poorer comprehension and perceptual reasoning Poorer immediate memory and recollection of information stored into memory Increased risk of attention problems and ADHD behavior	Smaller height Poorer early processing of visual information Lower estimated IQ Poorer working memory	Poorer information processing when the information is being consciously evaluated
Childhood exposure			
	Decreased heart rate variability	Increased risk of ADHD behavior, especially the hyperactive-impulsive type Deficit in response inhibition	Reduced physical growth (height, weight, head circumference, BMI) Non-optimal cognitive processes associated with error monitoring, which result in reduced efficiency during cognitive tasks Poorer immediate memory

How we have measured neurodevelopment in the Faroes

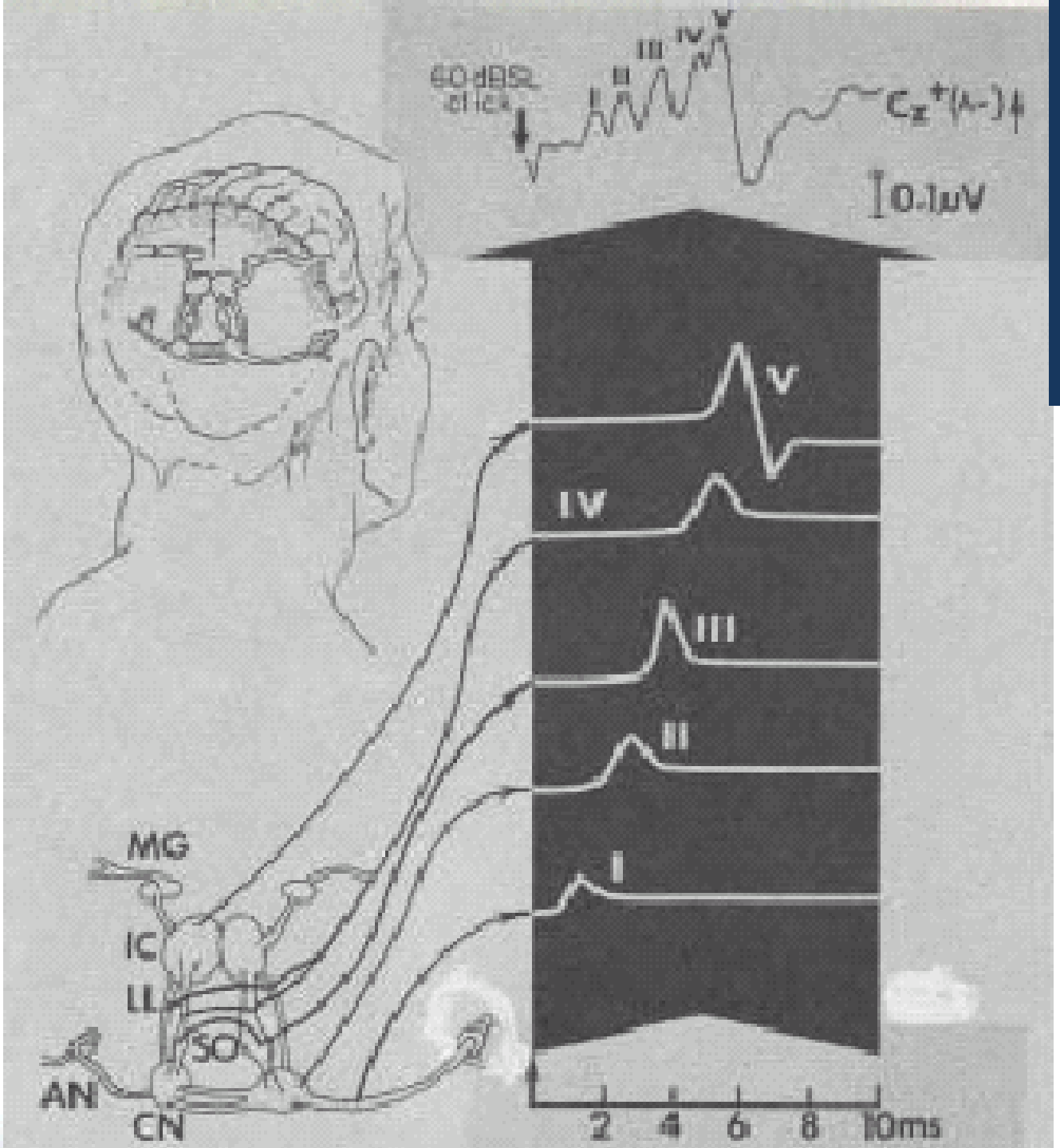
- Neuropsyhological methods
- Neurophysiological methods
- Neuropediatric methods
- Neuroradiographic methods

NES – Reaction Time, Age 7



EP- visual

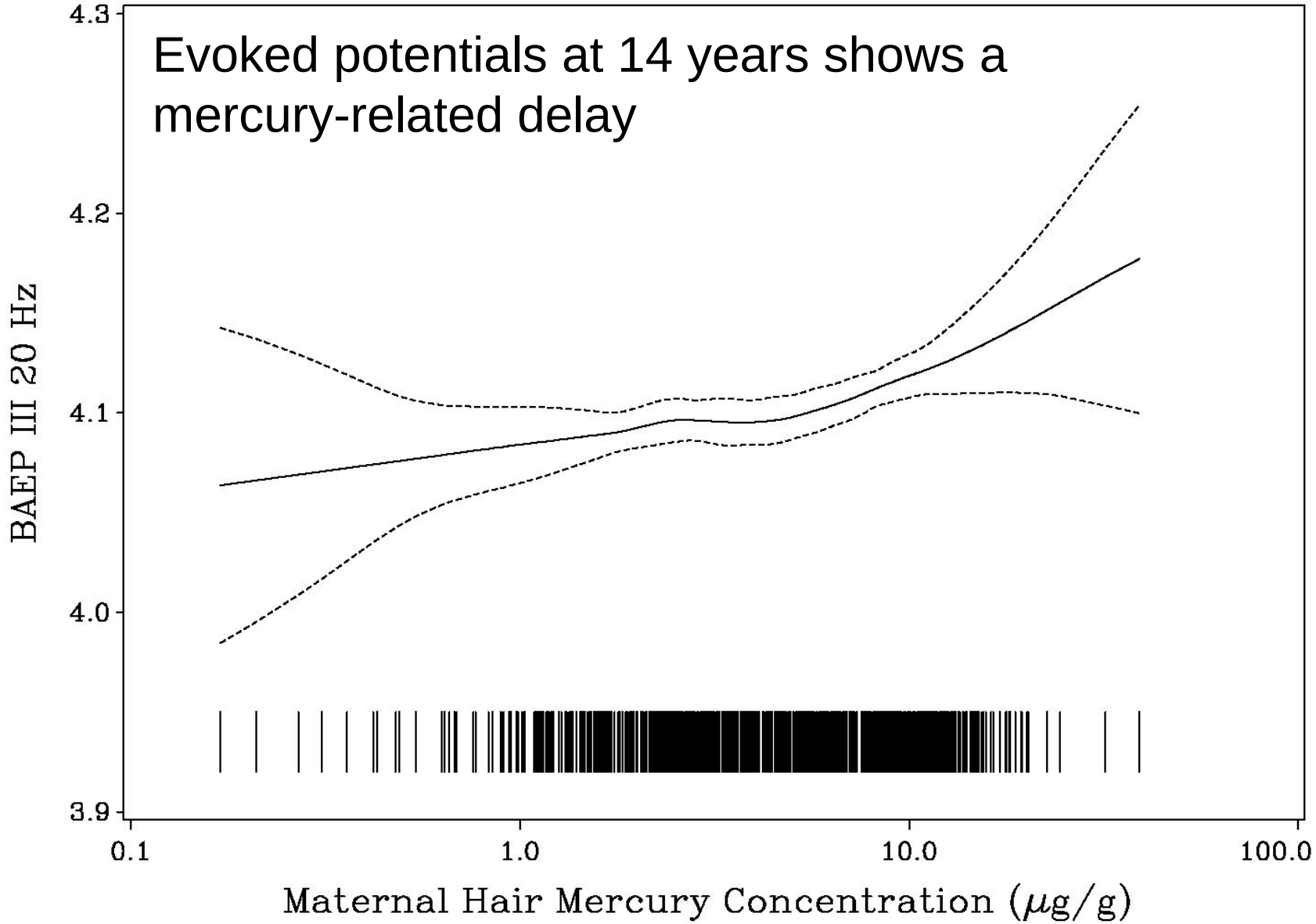
Brainstem Auditory Evoked Potentials



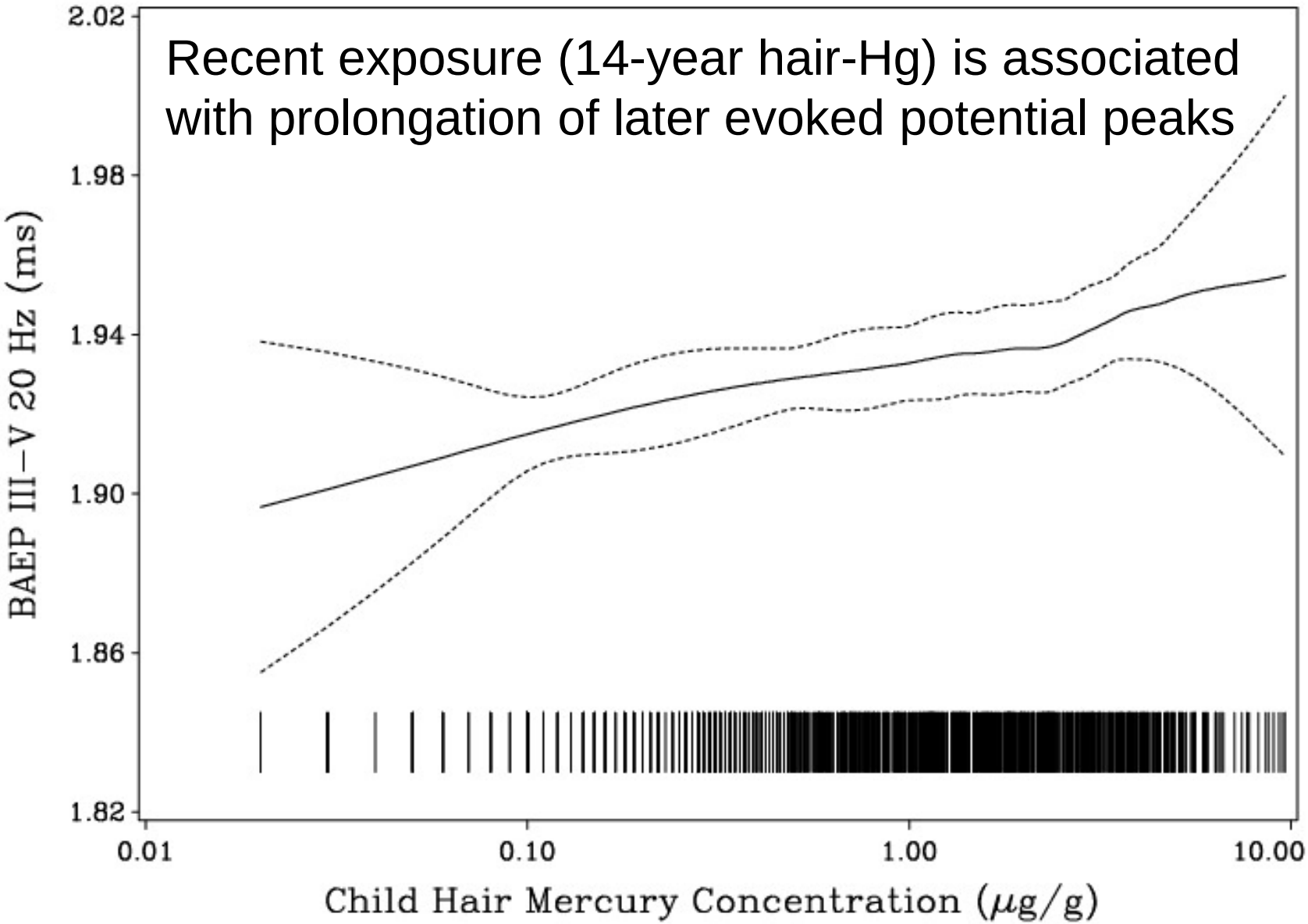
V: midbrain (inferior colliculus)

III: pons (superior olivary nucleus)

I: acoustic nerve



Murata et al., submitted



Murata et al., submitted

Qaanaaq Greenland

Contrast sensitivity

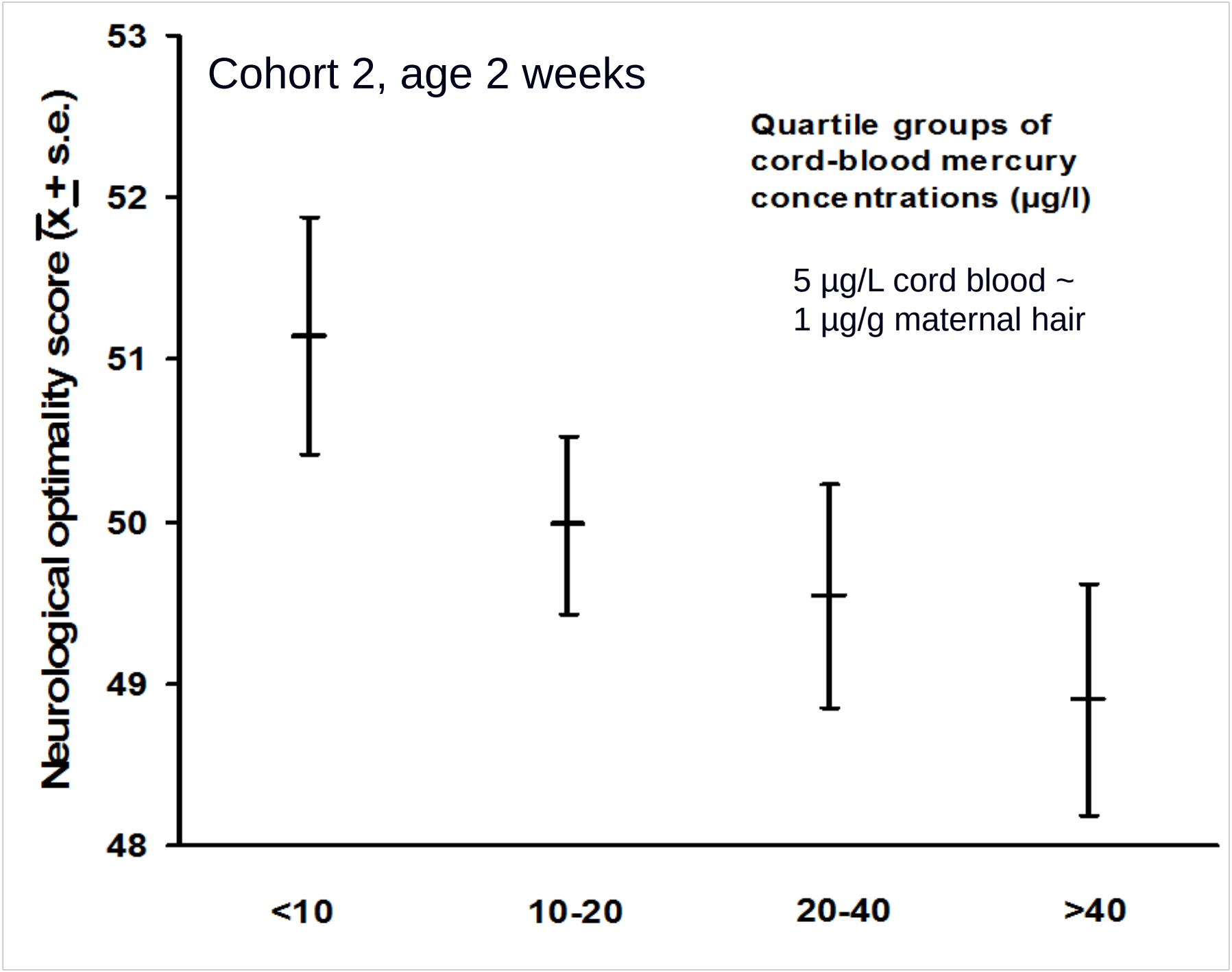
Balance

Neurological Optimality Score (NOS)

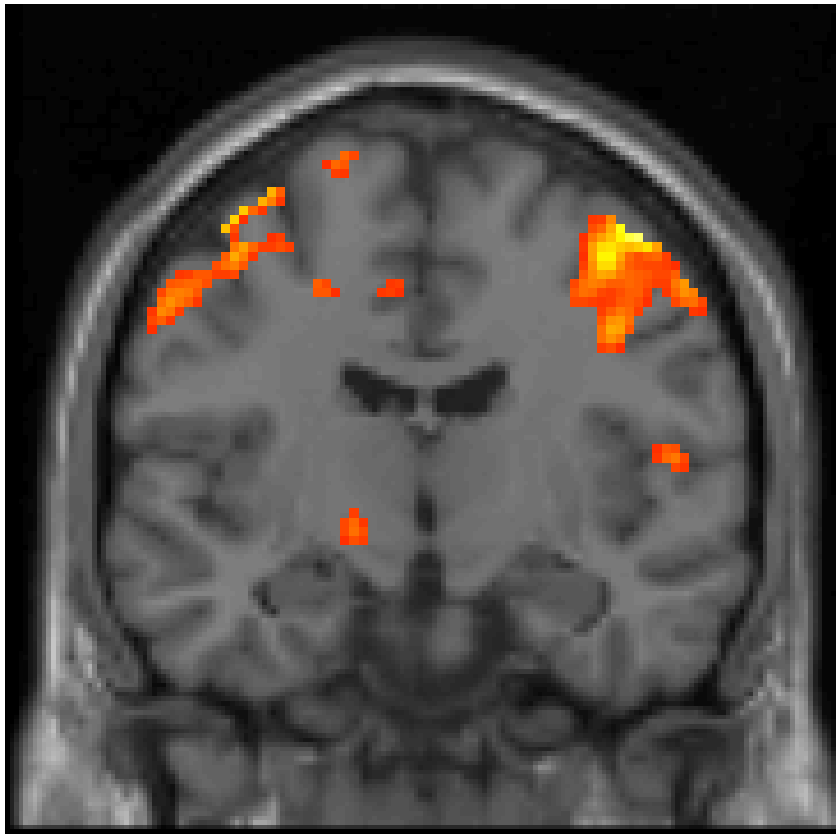
The Groningen Neonatal Neurological Examination records systematically main neurological functions, such as posture, motility, movements, tonus, responses, tendon reflexes, other reactions, reactivity, and stability of behavioral status during the examination. The technique for the examination of the children is a comprehensive age-adequate examination as described by Prechtl (Prechtl, 1977).

NOS – cont.

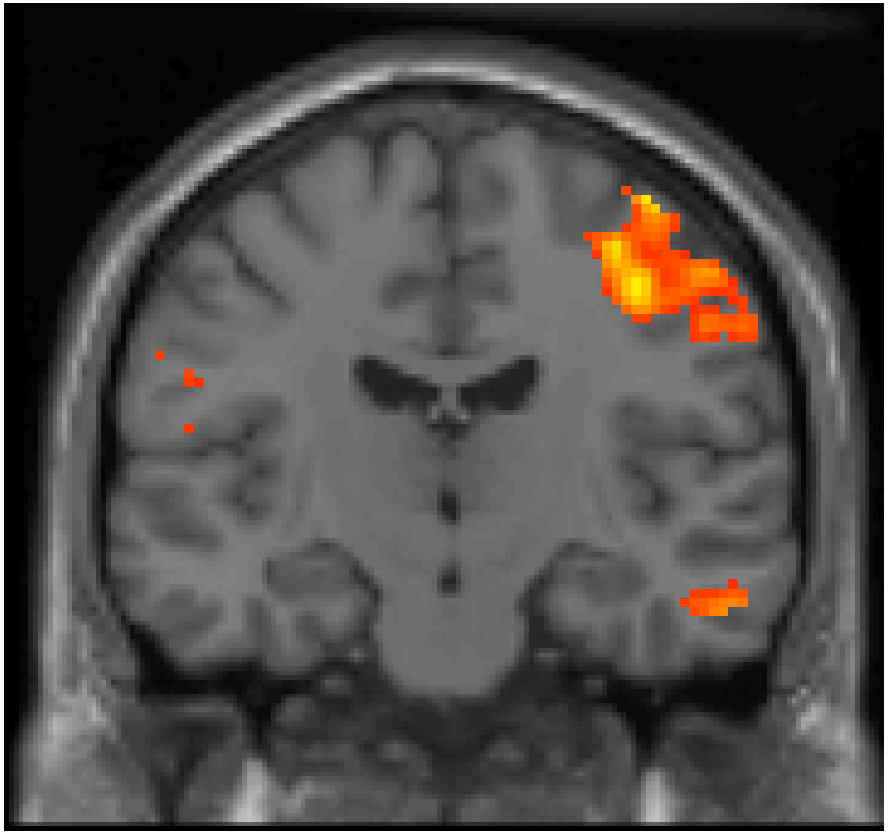
It has proven to be predictive for later major and minor neurological dysfunction. The neurological findings were summarized into a clinical diagnosis (normal, suspect and abnormal). A neurological optimality score (NOS) is generated, defined as the number of optimal items from a list of 60 items which were considered to be representative for the neurological condition (Touwen et al., 1980).


Cohort 2, age 2 weeks
Quartile groups of cord-blood mercury concentrations (µg/l)
5 µg/L cord blood ~
1 µg/g maternal hair
Neurological optimality score (x̄ ± s.e.)
53
52
51
50
49
48
<10
10-20
20-40
>40

Functional MRI: Finger tapping with left hand*



High developmental exposure to methylmercury



Low developmental exposure to methylmercury (control)

*Averages for three 15-year old boys in each group, White et al. (to be submitted)

W-179

Underestimation of adverse effects of mercury exposure unadjusted for beneficial effects of seafood consumption

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Background

Methylmercury is a common contaminant of seafood and occurs in varying concentrations in different types of seafood, which also contain essential nutrients. Subjects exposed to methylmercury from their diet are therefore likely to differ in regard to intake of nutrients which may have beneficial effects that could perhaps compensate for the toxic effects of mercury. We have examined this issue in a birth cohort from the Faroe Islands.

The Faroese Mercury Study

Bias due to confounder imprecision

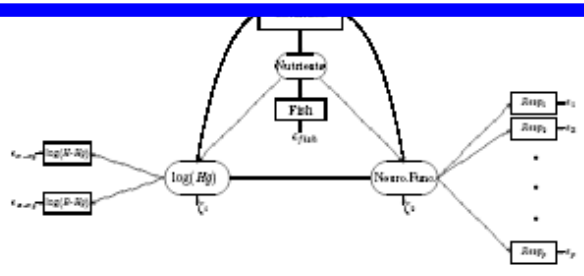
In a regression model with exposure X and true confounder Z: $Y = \beta_0 + \beta_x X + \beta_z Z + \epsilon$, if the observed confounder V has additive error: $V = Z + U$ and Z is naively replaced by V in the analysis, then the exposure effect estimate is affected by an additive bias term, i.e.,

$$\hat{\beta}_x \rightarrow \beta_x + \beta_z \cdot [cov(X,Z)/var(X)] \cdot [var(U)/var(V|X)]$$

In the case where X is mercury exposure and Z nutrients from fish, the effect of Z on Y (β_z) is positive and so is the covariance between mercury exposure and nutrients intake $cov(X,Z)$. Therefore, the bias term is positive and the adverse effect of mercury is underestimated.

Without mutual adjustment for beneficial and toxic effects, and without allowance for imprecision, the opposite effects of mercury and nutrient intakes from seafood are underestimated. Assessment of adverse effects caused by toxicants therefore needs to adjust for both confounding and imprecision of the exposure variables.

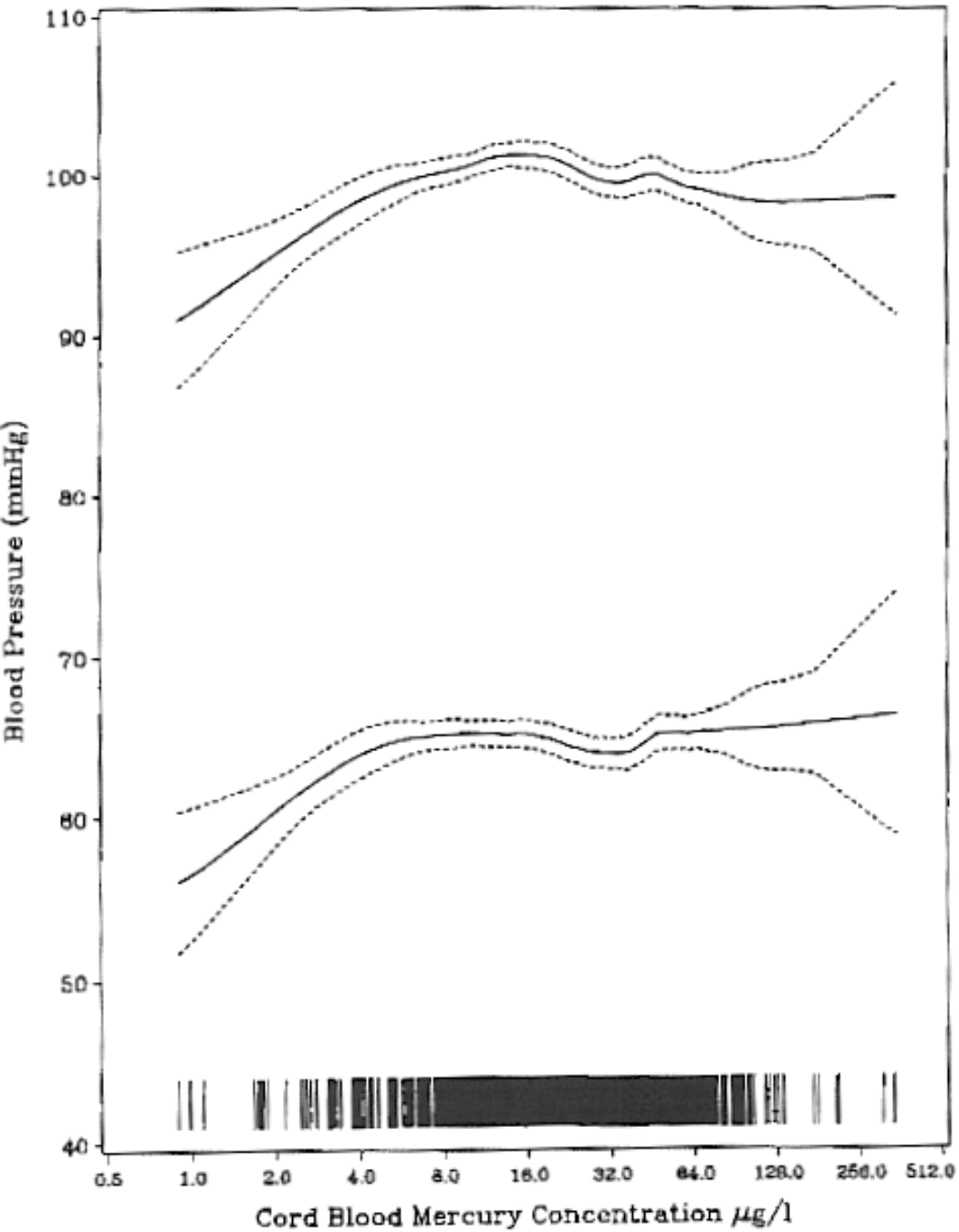
hair were assumed to be manifestations of an underlying true exposure. Similarly, outcome variables were grouped into motor functions and verbally-mediated functions that were each joined into a latent variable [3]. Tests conducted at 14 years were also split into groups. The latent exposure and potential confounders were assumed to affect each of the latent outcome functions [2]. Frequency of maternal fish dinners was added as a separate covariate (Figure 1).



Selenium

- On the average, Se was present in cord blood in a molar excess of about 10-fold above Hg
- Se concentrations suggested all children were Se sufficient
- No evidence that Se was a significant protective factor against MeHg neurotoxicity
- Selenium intake can therefore not explain the significant benefits associated with fish intake
- Preventive methods are needed to address MeHg exposures, rather than Se intakes, while maintaining a high fish/seafood intake

Blood pressure at 7 years:



The increase appears at cord blood mercury concentrations below 10 µg/l

Sørensen et al., 1999

Heart rate variability in Faroese children at age 14 years

Methylmercury exposure was associated with decreased sympathetic and parasympathetic modulation of the HRV. Parallel MeHg-related delays of BAEP latencies may be caused by underlying MeHg neurotoxicity to brainstem nuclei

(J Pediatr 2004;144:169-76)

Conclusions on developmental neurotoxicity related to MeHg

- Neurobehavioral effects most clearly on attention, memory and language, but also visuospatial and motor functions
- Parallel neurophysiological findings
- Prenatal generally more toxic than early postnatal exposure
- Results from age 14 and 22 years suggest that effects are permanent

Committee on the Toxicological Effects of Methylmercury, Board on Environmental Studies and Toxicology, US-National Research Council concluded in 2000:

Based on cord blood analyses from the Faroe Islands study, the lowest BMD (Benchmark Dose) for a neurobehavioral end point the committee considered to be sufficiently reliable is for the Boston Naming Test.

That approach estimates a BMDL (BMD lower confidence limit) of 58 ppb of Hg in cord blood (corresponding to a BMDL of 12 ppm of Hg in hair) as a reasonable point of departure for deriving a RfD.

A safety factor of 10 leads to a limit value in hair of only 1,2 ppm. This value not only some of the arctic populations will exceed, e.g. in Greenland and the Faroes, but even non-arctic areas.

1,2 ppm in hair corresponds to an intake of 0,1 µg per kg body weight per day (RfD - Reference Dose)

NRC exposure limit calculated from the benchmark dose (and our update)

Mercury concentrations	NRC	Updated
BMDL (µg/L cord blood)	58	43+
Cord blood adjustment (1.5*)	-	29
Uncertainty factor	(10)	(10)
Exposure limit (µg/L blood)	5.8	2.9
Converted to µg/kg*d	0.1	0.05

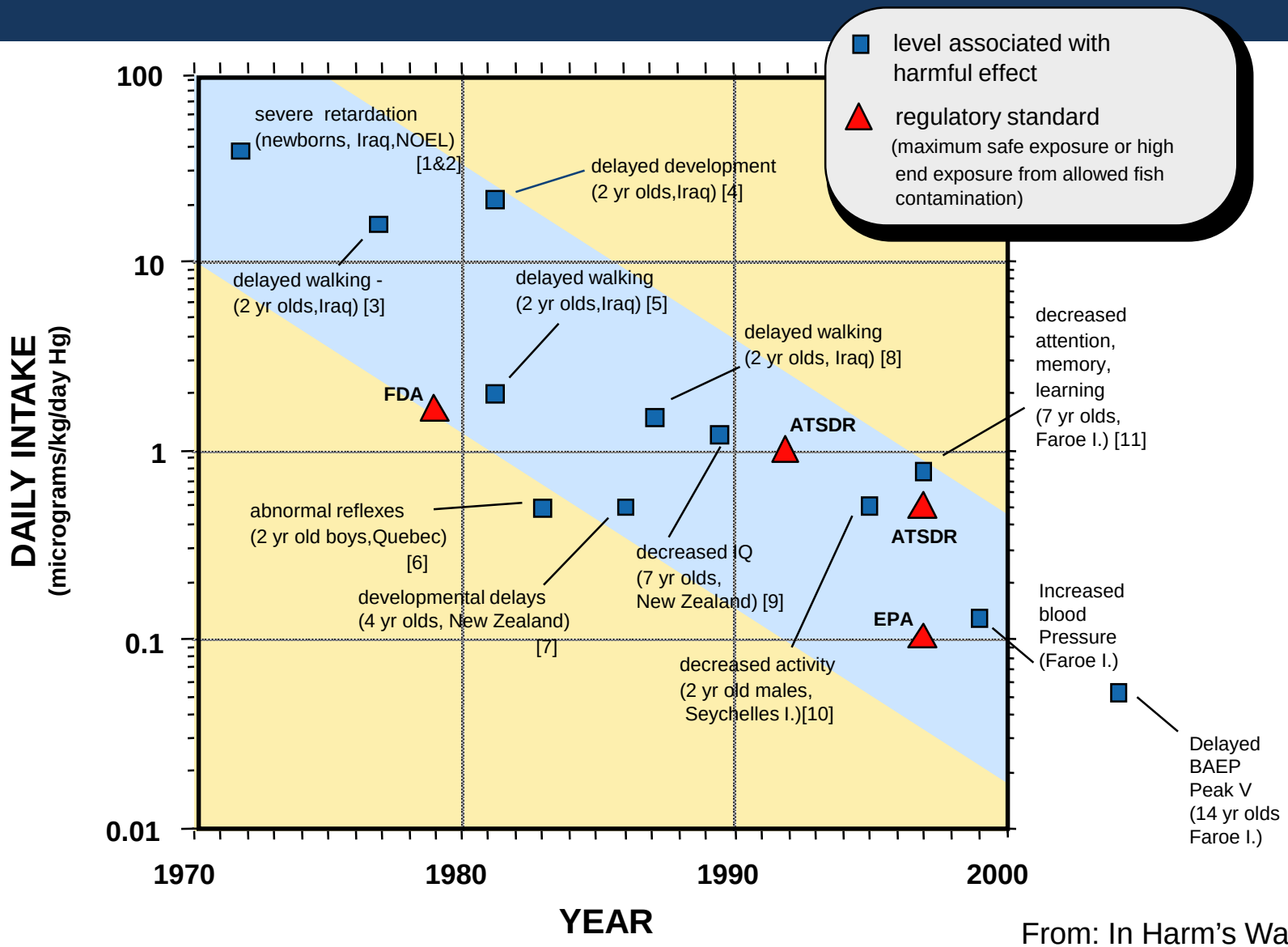
EPA RfD

BMDL: P_0 = 0.05, BMR = 0.05, linear slope for BNT

+Adjusted for exposure assessment imprecision by SEM

*Based on hair-to-blood ratios in pregnant and non-pregnant subjects

Regulatory standards declining



From: In Harm's Way, 2002