

Kviksilvurið í móðirlívi ávirkar okkum eisini sum vaksin

Fyrilestur tann 28/9 2018
á Vísindavøku í Tórshavn

Sálarfrøðingur
Fróði Debes

Inngangur



prof. Pál Weihe



prof. Philippe Grandjean



Fóru undir samarbeiði og stovnsettu fyrstu barnakohortuna í 1986- 1987

Úrslit frá føroysku kohortukanningunum

Kviksilvur í hvalatvøsti, sum ávirkar børn í móðirlívi, hevur ringt árin á:

- **nervalagið**
sæst við **7 ár** og enn við **14 ár** og við **22 ár**
- **blóðtrýstið**

Dálkandi evnir í spiki hava ringt árin á:

- **Immunverjuna**

PFAS (*Perfluoreraði alkyl evnir*) við 5 og 7 ár, hava samanhag við

- **atferðartrupulleikar**

Dálkandi evnir í hvali sýnast hjá eldri fólki at økja um vandan fyri at fáa

- **Parkinson sjúku**
- **ov høgt blóðtrýst**
- **æðrakálking**
- **Diabetes 2**
- **ov høgt fastandi blóðsukur**
- **tarnaða insulinsekretiún**

Út frá hesum kanningarúrslitum góvu Pál Weihe, Yvirlækni og Høgni Debes Joensen, Landslækni eitt kosttilmæli í 2012, sum segði, at:

grindahvalurin ikki er egnaður sum mannaføði

Arvaligt viðkvæmi fyri meHg

Epidemiology • Volume 24, Number 5, September 2013

ORIGINAL ARTICLE

Prenatal Methylmercury Exposure and Genetic Predisposition to Cognitive Deficit at Age 8 Years

Jordi Julvez,^{a,b} George Davey Smith,^c Jean Golding,^d Susan Ring,^e Beate St. Pourcain,^c Juan Ramon Gonzalez,^b and Philippe Grandjean^{a,f}

RESULTS:

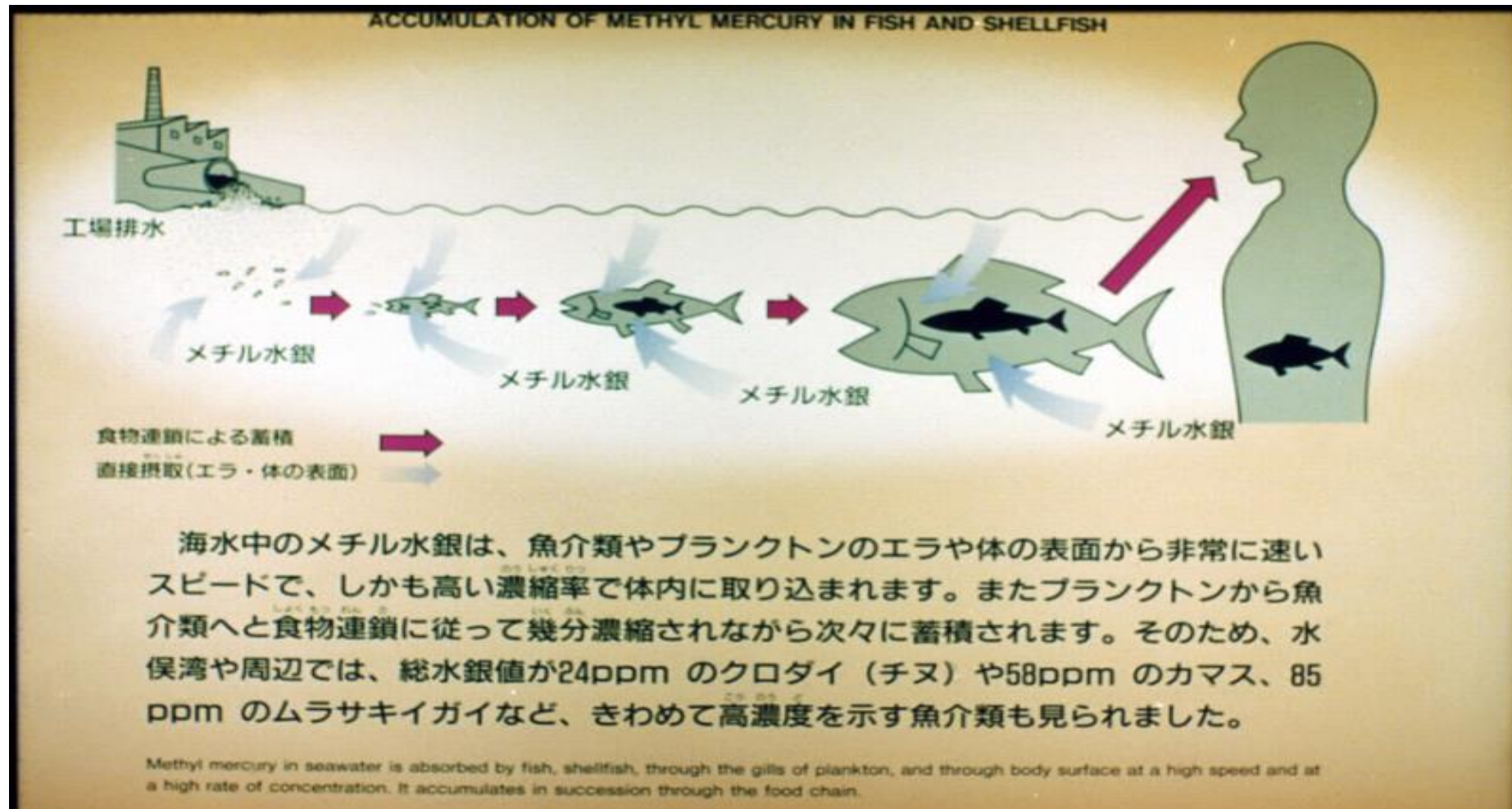
....Among 40 SNPs showing nominally significant main effects, MeHg interactions were detected for rs662 (paraoxonase 1) and rs1042838 (progesterone receptor) ($P < 0.05$) and for rs3811647 (transferrin) and rs2049046 (brain-derived neurotrophic factor) ($P < 0.10$).

CONCLUSIONS:

....Heterogeneities in several relevant genes suggest possible genetic predisposition to MeHg neurotoxicity in a substantial proportion of the population.

Ymiskleikar í fleiri ávísam íløgum týða uppá eitt arvaligt viðkvæmi fyri MeHg hjá einum týðandi parti av fólkinum

Myndugleikarnir í Minamata kunnaðu almenningin



Almen kunning í Japan

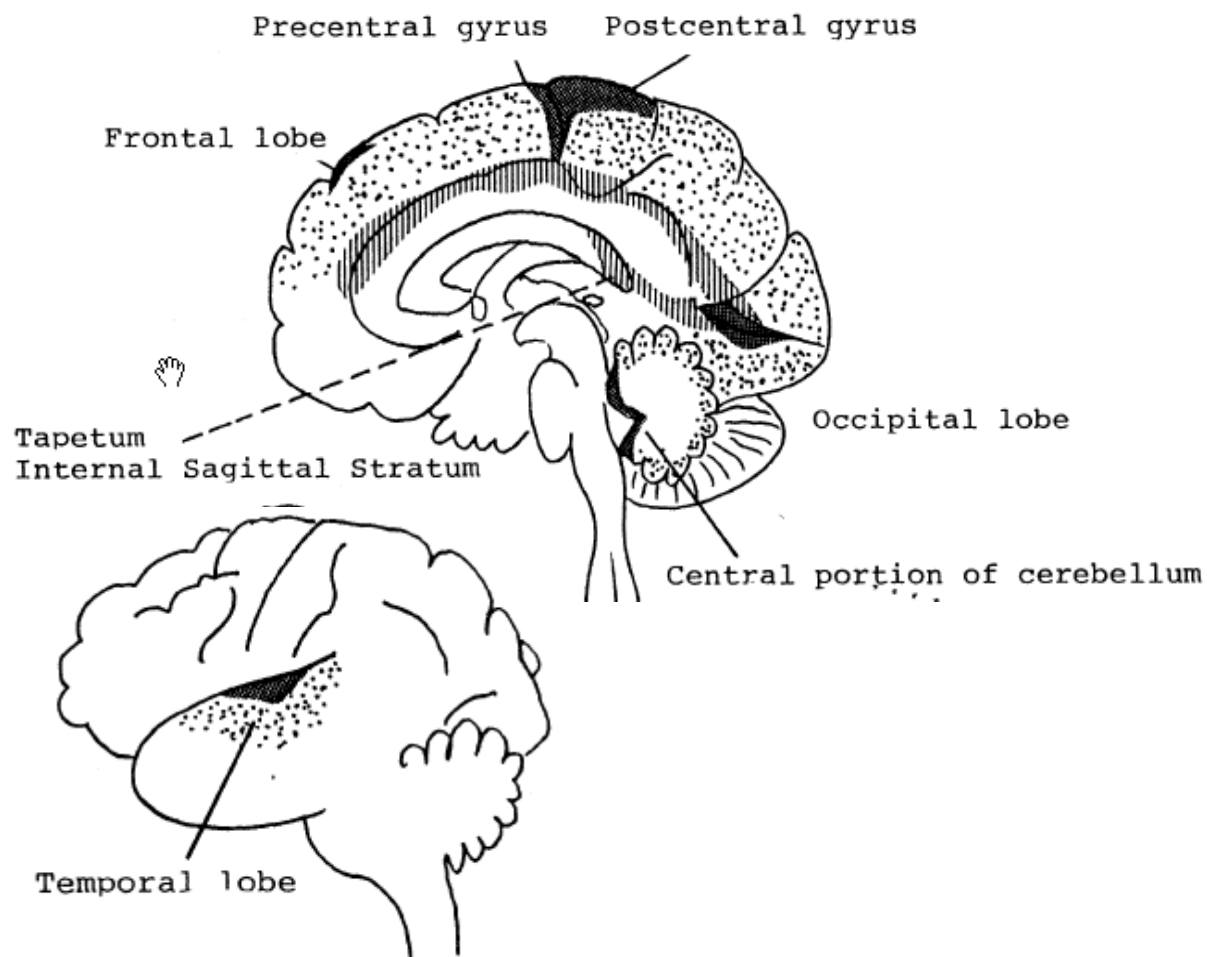
Tá ið mamman etur dálkaðan fisk, verður forstrið eisini ávirkað



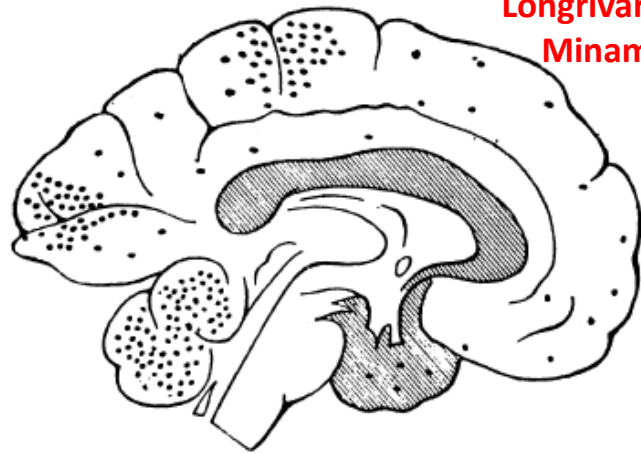
Virkning af MeHg på hjernen

Mild kronisk støða hjá vaksnum

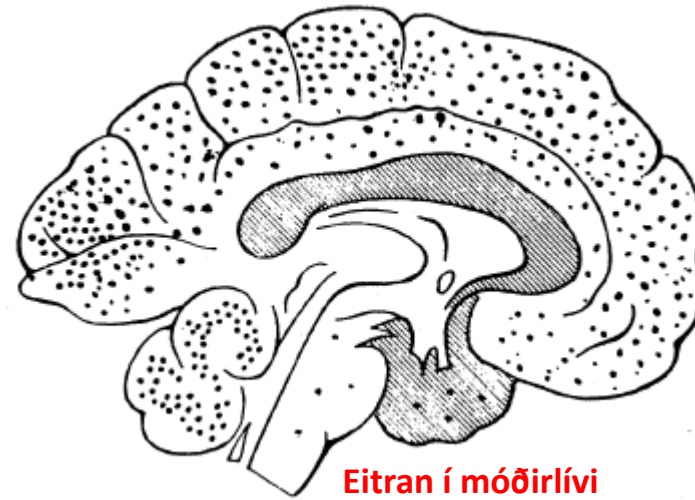
Serliga sensorisk-motorisk økir, sjón og hoyrn eru ávirkað



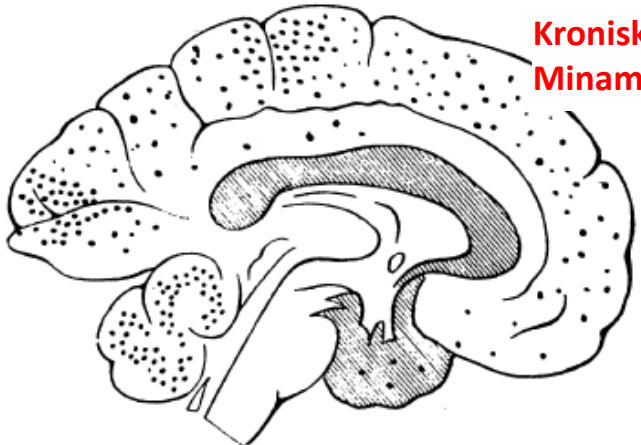
Árin av MeHg á heilan



Longrivarandi mild
Minamata sjúka



Eitran í móðirlívi



Kronisk
Minamata sjúka

Ymisk sløg av 'Minamata disease'

Álvarsom eitran í móðirlívi førir við sær
viðfevndan og spjaddan skaða á heilavevnaðin

Minamata

Minamata-offur við ávirkaðum miðnervalagi

Mynd tikin í 1995



Úrslit frá tí fyrstu føroysku kohortuni



7-ára kanningin í 1993-94



Neurotoxicology and Teratology, Vol. 19, No. 6, pp. 417-428, 1997
Copyright © 1997 Elsevier Science Inc.
Printed in the USA. All rights reserved
0892-0362/97 \$17.00 + .00

PII S0892-0362(97)00097-4

Cognitive Deficit in 7-Year-Old Children with Prenatal Exposure to Methylmercury

PHILIPPE GRANDJEAN,*† PAL WEIHE,*‡ ROBERTA F. WHITE,*†§ FRODI DEBES,‡
SHUNICHI ARAKI,¶ KAZUHITO YOKOYAMA,¶ KATSUYUKI MURATA,¶
NICOLINA SØRENSEN,‡ RASMUS DAHL* AND POUL J. JØRGENSEN**

**Institute of Community Health, Odense University, DK-5000 Odense, Denmark*

*†Departments of Neurology and Environmental Health, Boston University
Schools of Medicine and Public Health, Boston, MA 02118-2394*

*‡Department of Occupational and Public Health, Faroese Hospital System,
FR-100 Tórshavn, Faroe Islands*

*§Environmental Hazards Center and Department of Psychology, Boston Department of
Veterans Affairs Medical Center, Boston, MA 02130*

¶Department of Public Health, Tokyo University Faculty of Medicine, Tokyo 113, Japan

***Institute of Clinical Research, Odense University Hospital, Odense, DK-5000 Denmark*

Received 10 March 1997; Accepted 26 August 1997

Úrslit við 7 ár

Signifikant negativ árin av
prenatalum árinu fyri MeHg í
nalvasnórsblóði sæst í
8 av 20 royndum

TABLE 4
RESULTS OF NEUROPSYCHOLOGICAL TESTS IN CHILDREN WITHOUT NEUROLOGICAL DISEASE AND ADJUSTED REGRESSION
COEFFICIENTS (BETAS) FOR THE LOGARITHMIC TRANSFORMATION OF THE CORD BLOOD MERCURY CONCENTRATION

Test	N	Mean	Interquartile Range	Multiple Regression		Peters-Belson Adjustment		Low-Level Exposure*	
				Beta	p-Value	Beta	p-Value	Beta	p-Value
NES2 Finger Tapping (maximum in 15 s)									
Preferred hand	901	42.9	39–47	-1.10	0.05	-1.18	0.03	-0.68	0.29
Other hand	901	41.2	37–45	-0.39	0.46	-0.37	0.47	-0.13	0.83
Both hands	895	55.5	47–64	-1.67	0.14	-1.86	0.08	-0.62	0.63
NES2 Hand-Eye Coordination (average of best two trials)									
Error score	897	2.60	2.41–2.80	0.034	0.19	0.033	0.20	0.033	0.28
Tactual Performance Test (s)									
Preferred hand	852	466	231–583	-14.3	0.63	-18.8	0.60	-11.3	0.76
NES2 Continuous Performance Test (first year only)									
Ln total missed responses	431	6.79	2–10	0.12	0.02	0.14	0.007	0.21	0.0005
Average reaction time (ms)	428	759	705–809	40.3	0.001	38.2	0.0002	46.9	0.0003
Wechsler Intelligence Scale for Children—Revised									
Digit Spans	889	3.8	3–5	-0.27	0.05	-0.27	0.05	-0.31	0.05
Similarities	746	7.4	5–10	-0.05	0.90	0.14	0.70	0.65	0.15
Squareroot Block Designs	888	14.6	7–20	-0.17	0.11	-0.25	0.02	-0.13	0.27
Bender Visual Motor Gestalt Test									
Errors on copying	895	29.4	26–33	0.67	0.15	1.04	0.03	0.71	0.19
Reproduction	841	3.0	2–4	-0.25	0.10	-0.16	0.31	-0.43	0.02
Boston Naming Test									
No cues	866	25.0	21–28	-1.77	0.0003	-1.66	0.0007	-1.42	0.01
With cues	865	27.5	24–31	-1.91	0.0001	-1.82	0.0002	-1.57	0.005
California Verbal Learning Test (Children)									
Learning	879	27.9	22–34	-1.25	0.12	-1.30	0.11	-1.55	0.10
Short-term reproduction	867	4.0	2–6	-0.57	0.02	-0.63	0.009	-0.74	0.009
Long-term reproduction	837	4.4	2–7	-0.55	0.05	-0.64	0.02	-0.56	0.08
Recognition	830	10.4	10–12	-0.29	0.15	-0.28	0.15	-0.22	0.34
Nonverbal Analogue Profile of Mood States									
Average positive moods	825	59.8	48.0–80.5	2.61	0.31	2.39	0.34	3.66	0.20
Average negative moods	825	36.0	16.3–52.6	-0.04	0.99	0.17	0.94	1.83	0.51

* Maternal hair-mercury below 10 µg/g.

14-ára kanningin í 2000-2001



Available online at www.sciencedirect.com



Neurotoxicology and Teratology 28 (2006) 363–375

NEUROTOXICOLOGY
AND
TERATOLOGY

www.elsevier.com/locate/neutera

Impact of prenatal methylmercury exposure on neurobehavioral function at age 14 years

Frodi Debes^a, Esben Budtz-Jørgensen^{b,c}, Pal Weihe^{a,c},
Roberta F. White^d, Philippe Grandjean^{c,e,*}

^a *Faroese Hospital System, FR-100 Tórshavn, Faroe Islands, Denmark*

^b *Department of Biostatistics, University of Copenhagen, DK-2200 Copenhagen N, Denmark*

^c *Institute of Public Health, University of Southern Denmark, DK-5000 Odense, Denmark*

^d *Department of Environmental Health, Boston University School of Public Health, Boston, MA 02218, USA*

^e *Department of Environmental Health, Harvard School of Public Health, Boston, MA 02215, USA*

Received 26 August 2005; received in revised form 6 December 2005; accepted 10 February 2006

Available online 2 May 2006

Table 5

Test score change in percent of test score standard deviation associated with doubling in exposure, as indicated by multiple regression analysis with adjustment for covariates^a

Test	Cord blood			Maternal hair			Cord tissue		
	<i>N</i>	Change	<i>p</i>	<i>N</i>	Change	<i>p</i>	<i>N</i>	Change	<i>p</i>
NES2 Finger Tapping									
Preferred hand	758	-4.18	0.16	776	-6.01	0.052	379	-5.43	0.19
Non-preferred hand	758	-4.15	0.16	776	-7.15	0.020	380	-5.36	0.23
Both hands	757	-6.41	0.033	775	-7.22	0.022	379	-6.42	0.17
CATSYS									
Mean tapping maximum	759	-1.59	0.61	777	-0.21	0.95	380	-8.35	0.087
Supination-pronation	758	-2.83	0.36	776	-1.91	0.56	380	-2.16	0.66
Mean reaction time (ms) ^b	758	3.96	0.19	776	5.97	0.062	379	4.89	0.29
NES2 Continuous Performance Test									
Average reaction time (ms) ^b	761	7.44	0.018	779	6.30	0.055	381	2.35	0.63
Number of false positives ^b	761	-0.97	0.75	779	-1.18	0.71	381	-5.98	0.20
Number of false negatives ^b	761	0.72	0.82	779	-1.95	0.55	381	-6.66	0.16
Digit Spans	761	0.22	0.94	779	-0.96	0.76	381	0.35	0.94
Spatial Span	761	7.25	0.019	779	7.51	0.021	381	4.48	0.37
Stanford-Binet Copying									
Total copying score	757	-2.99	0.33	775	-4.12	0.20	378	-0.62	0.90
Sum of most difficult 5	757	-5.89	0.056	775	-6.19	0.055	378	-5.09	0.28
Recall number correct	755	0.62	0.84	773	3.04	0.35	378	-3.36	0.48
Block Design, WISC-R	761	3.65	0.22	779	2.96	0.38	381	6.94	0.15
Block Design, WISC+WAIS	276	3.46	0.48	283	6.29	0.24	214	9.76	0.11
Children's Category Test ^b	761	0.49	0.87	779	1.98	0.53	381	-0.70	0.88
Similarities	761	-0.38	0.90	779	2.01	0.52	381	1.76	0.69
Boston Naming Test									
Correct without cue	761	-4.79	0.11	779	-3.39	0.28	381	-6.71	0.14
Total correct w/cues	761	-5.90	0.048	779	-4.21	0.18	381	-9.75	0.036
California Verbal Learning Test									
Learning, total correct, 5 trials	761	-2.84	0.34	779	0.61	0.84	381	-9.01	0.044
Short delay, free recall	761	1.45	0.63	779	4.79	0.13	381	-4.33	0.35
Long delay, free recall	760	-0.42	0.89	778	2.42	0.45	380	-7.43	0.11
Long delay, recognition	759	-2.94	0.35	777	0.08	0.98	379	-6.01	0.19

^a Age, sex, maternal Raven score, residence in town/village, school grade, maternal and paternal employment, time of day, language, and computer experience (for computer tests only).

^b An increase in the test parameter denotes a deficit.

**Signifikant negativ árin af prenatalum árinu fyri metylkviksilvuri í:
Navlesnorsblóði 5/24; Móðirhár: 7/24; Navlesnórsvevnaður: 3/24**

22-ára kanningin í 2008-2009

CORTEX 74 (2016) 358–369



Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex



Special issue: Research report

Cognitive deficits at age 22 years associated with prenatal exposure to methylmercury



Frodi Debes^a, Pal Weihe^a and Philippe Grandjean^{b,c,}*

^a Faroese Hospital System, Torshavn, Faroe Islands

^b Department of Environmental Health, Harvard School of Public Health, Boston, MA, USA

^c Institute of Public Health, University of Southern Denmark, Odense, Denmark

22-ára kanningin í 2008-2009

Eyeballing long list of numerous independent regressions

- Looking for significance!

Cognitive domain	Test variable	N	Change associated with 10-fold increase	Standardized coefficient (Beta)	p
Gf	WJ III Concept Formation	662	-.284	-.022	.585
	Raven Standard Progressive Matrices Plus	661	-.990	-.048	.235
Gc	Boston Naming Test, without cues	662	-1.295	-.079	.046
	Boston Naming Test, with cues	662	-1.382	-.097	.014
	Synonyms, WJ III	662	-.769	-.112	.005
	Antonyms, WJ III	662	-.453	-.080	.046
	Verbal Analogies, WJ III	662	-.137	-.024	.547
Gv	Block Design WISC-R	659	.015	.001	.986
	Block Design WISC-R + 3 WAIS-R	333	-1.579	-.065	.247
	Spatial Relations, WJ III	657	-.551	-.043	.290
Gsm	Numbers Reversed, WJ III	659	-.289	-.028	.491
	Memory for words, WJ III	659	-.196	-.034	.403
	Spatial Span Forward, WMS-III	659	.266	.052	.197
	Spatial Span Backwards, WMS-III	659	.073	.016	.696
Glr	CVLT, Trial 1, Correct	662	-.489	-.097	.015
	CVLT, Learning trials 1-5	662	-.170	-.006	.869
	CVLT, List B, Correct	662	-.081	-.015	.706
	CVLT, Short Delay, Free Recall	662	-.135	-.018	.657
	CVLT, Long Delay, Free Recall	662	-.093	-.013	.751
	CVLT, Long Delay, Recognition	659	-.157	-.043	.293
	Incidental Memory for Boston Naming and Picture Vocabulary, WJ-III	662	-.517	-.047	.248
	Warrington's Face Recognition Test, Set2, Immediate Recall	656	-.476	-.041	.319
	Warrington's Face Recognition Test, Set 2, Delayed Recall	656	-.056	-.004	.918
	Gs	Visual Matching, WJ III	659	-.748	-.043
Decision Speed, WJ III		659	.926	.049	.225
Gt	CPT, NES II, Mean RT of 4 last Blocks	656	4.082	.033	.432
	CPT, NES II, SD of 4 last Blocks	656	.861	.017	.685
	CPT, NES II, false negative errors last 4 blocks	656	.047	.016	.693
	CPT, NES II, false positive errors last 4 blocks	656	-.066	-.019	.645
	CPT-90, Proportion correct non-target (minus first 20 stimuli)	641	-.022	-.033	.419
	CPT-90, Noise corrected proportion correct non-target (minus first 20 stimuli)	641	-.019	-.028	.491
Gps	Finger Tapping, NES2, preferred hand	656	-1.218	-.041	.275
	Finger Tapping, NES2, non-preferred hand	656	-1.381	-.035	.338
	Finger Tapping, NES2, alternate hands	656	-1.199	-.023	.551

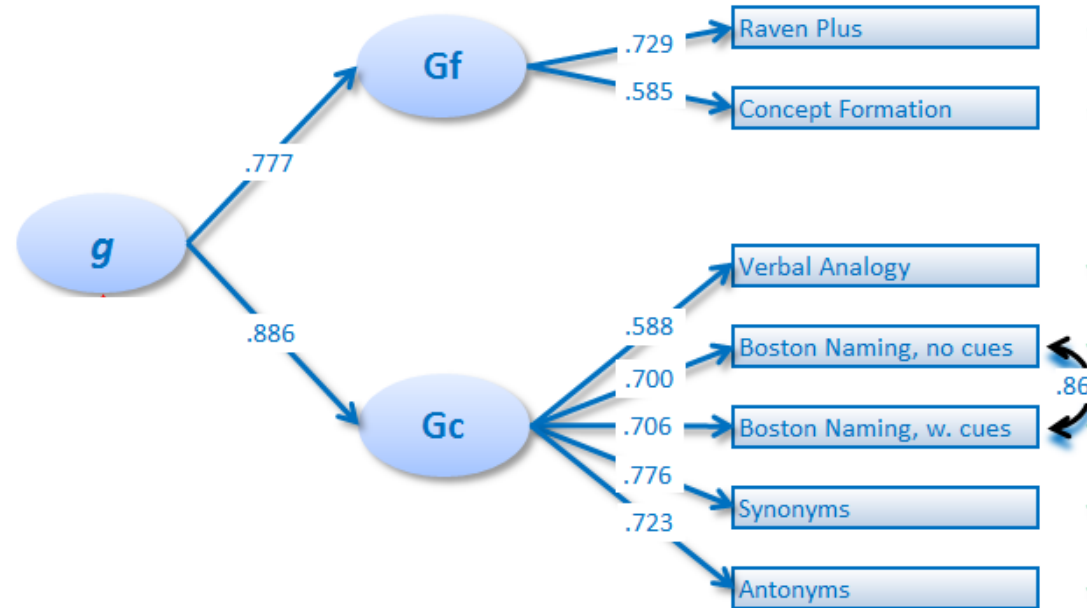
For explanation of acronyms, see [Table 3](#).

Covariates: Sex, Maternal fish dinners during pregnancy, Maternal Raven, Mother employed (age 14), Father employed (age 14), Age at examination, Tested in language, School grade (age 14), Lead logarithmic, PCB's logarithmic.

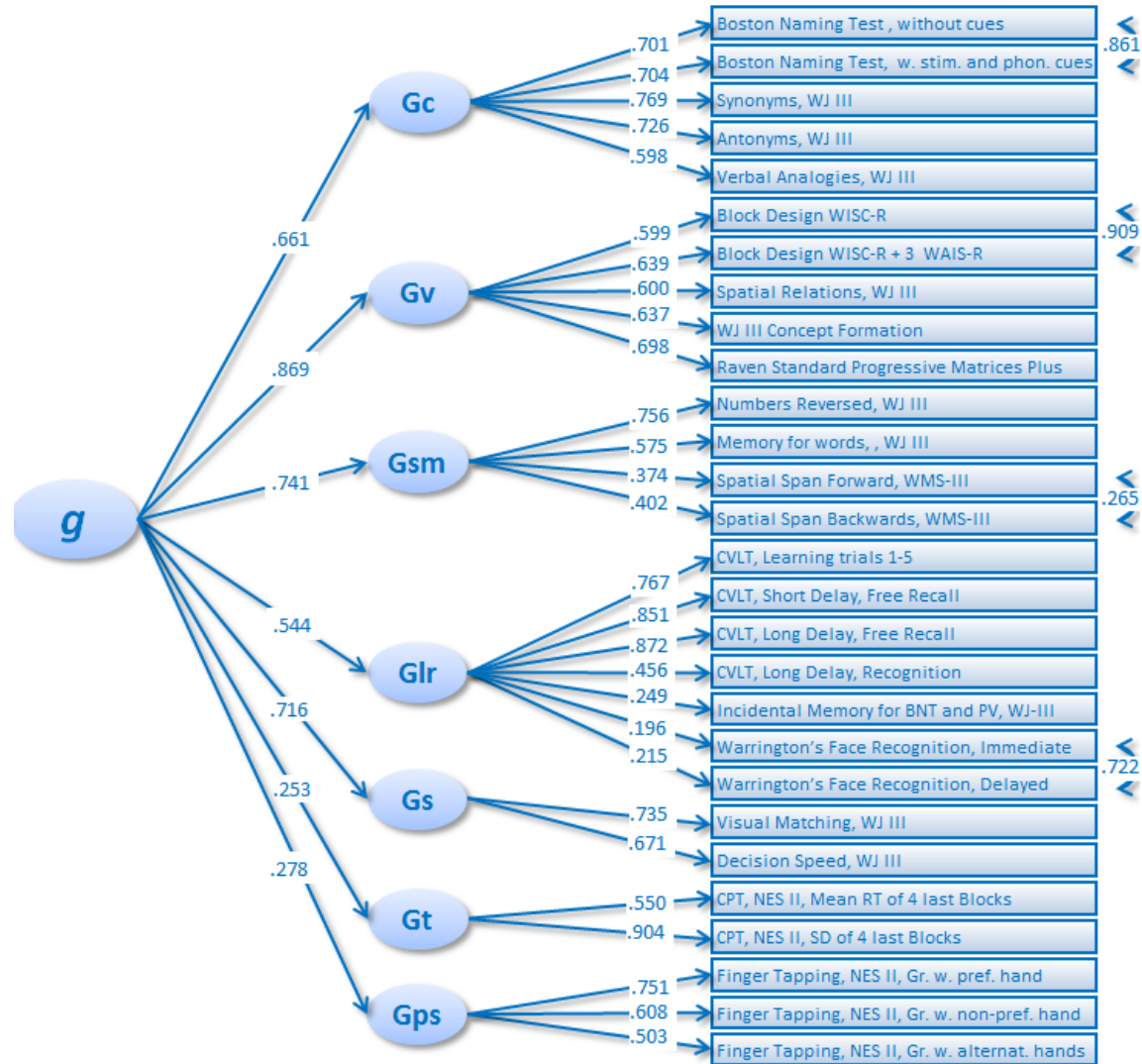


4/34 test variablar eru signifíkant ávirkaðir av prenatalari eksponering fyri MeHg i navlesnorsblóði

SEM at 22 years – Brief Model



SEM at 22 years – Broad Model



SEM med en ortogonal førsteordens faktormodel ved 22 år

Cognitive domain	Standardized coefficient (Beta)	p	IQ
Gc	-0.164	0.000	-2.5
Gv	-0.093	0.057	-1.4
Gsm	-0.062	0.198	-0.9
Glr	-0.075	0.079	-1.1
Gs	-0.037	0.457	-0.6
Gt	-0.025	0.582	-0.4
Gps	-0.052	0.260	-0.8

Covariates: Sex, Maternal fish dinners during pregnancy, Maternal Raven, Mother employed (age 14), Father employed (age 14), Age at examination, Tested in language, School grade (age 14), Lead logarithmic, PCB's logarithmic. N = 814, RMSEA = 0.064, CFI = 0.875, SRMR = 0.098

Den latente variabel for prenatal eksponering for metylkviksølv har en **negativ effect på alle syv evnedomæner**, og manifesteres **signifikant i Gc, nær-signifikant in Gv og Glr**, men kun svagt og ikke-signifikant i de andre fire evnedomæner

Takk fyri áhugan!



Deildin fyri Arbeiðs-
og Almannaheilsu



SYDDANSK UNIVERSITET