The Mab010 data product

Original number of samples	1,104
Number of samples (per 26.02.2024)	1,099
Number of unique participants	1,096
Biological sample type	Plasma
Participant type(s)	MoBa mothers
Collection timepoint	Gestational week ~17-18
Case-control selection criteria	Cerebral palsy, autism spectrum disorder, epilepsy
Biomarker type(s)	Per- and Polyfluoroalkyl Substances (PFAS)
Original reference article	Skogheim *et al*. 2021
Analytical method(s)	LC-MS/MS
Related MoBaBIO product(s)	Mab009
FHI Project number(s)	PDB2322

The project that generated these data

Prenatal exposure to toxicants and childhood neurodevelopmental disorders and cognitive functions (NEUROTOX)

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The purpose of this study was to study whether exposure to environmental toxicants in pregnancy increases the risk for child neurological and neurodevelopmental disorders; attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), cerebral palsy (CP) or epilepsy, as well as cognitive deficits and language difficulties. Parallel analyses make it possible to evaluate whether environmental toxins have a general effect on brain development *in utero*, or whether they affect specific functions.

The present study/data is a part of **phase 2 of the NeuroTox study** (PDB1606/2322), aiming to investigate prenatal exposure to PFAS and inorganic contaminants and a wider range of neurologic and neurodevelopmental conditions in children. Data attainment was done in 2 phases; **Phase I** consisted of PDB 1606 with attainment of maternal toxicant data for NPR-ADHD cases and MoBa controls, as well as participants from the ADHD-study. **Phase II** (this dataset) consisted of PDB 2322, in which maternal toxicant data for ASD, Epilepsy and CP case groups and additional MoBa controls were attained. See Table 1 for a data overview.

Table 1: Overview of toxicant data and populations in the NeuroTox project (PDB1606/2322)

				Complete NeuroTox dataset	
NeuroTox	**PDB nu**	**Biomarker results, N**	**Mab**	**Diagnostic case groups**	**ADHD-study**
Phase I	1606	PFAS (plasma) N=2334	Mab008	Sub-population 1: ~ 700 ADHD cases ~700 controls	Sub-population 2: ~900 ADHD-study participants
		Metals/elements (whole blood), N=1872[a]	Mab007		
Phase II	2322	PFAS (plasma), N=1099	Mab010	~400 ASD cases ~300 Epilepsy cases ~170 CP cases ~300 additional controls[b] ~100 ADHD cases[c]	
		Metals/elements (whole blood), N=1045[a]	Mab009		

[a] For metals/element, NeuroTox utilized available data from the Norwegian Environmental Biobank (PDB1440) for participants that overlapped with NeuroTox participants. Thus, N with measured metals/elements are fewer than for PFAS data.
[b] To be added to controls from phase 1 (PDB1606).
[c] These ADHD cases are additional to those available from PDB1606, as they overlapped with ASD, Epilepsy and/or CP cases in the present dataset. These extra cases can be added to ADHD cases from PDB1606.

Study population

The original Mab010 biomarker data source is based on plasma samples from **1,101 mothers**. The study population was selected based on a case-control study design using the same eligible population defined using version 8 of the self-reported questionnaires in MoBa, and same selection criteria as in PDB1606 (Mab008). Cases are in this dataset are defined as MoBa mothers of children who had received a medical diagnosis through linkage to Norwegian Patient Registry (NPR) (and additional sources) of cerebral palsy (CP; ICD-10 codes G80.0, G80.1, G80.2, G80.3, G80.4, G80.8 or G80.9), epilepsy (ICD-10 codes G40.0, G40.1, G40.2, G40.3, G40.4, G40.5, G40.6, G40.7, G40.8 or G40.9) or ASD (ICD-10 codes F84.0, F84.1, F84.5, F84.8 or F84.9). The eligible for cases were identified via NPR linkage and/or clinical assessments via MoBa sub-studies of these conditions:

- the Autism Birth Cohort (ABC) Study (PDB141)
- the Cerebral Palsy study (CP-study; MOBAND) (PDB1352)
- the Epilepsy in Young Children (EPYC) Study (PDB1195)

We also identified eligible ADHD cases with ≥2 registrations of ICD-10 F90 in the NPR (linkage from January 2018; diagnoses 2008-2017) using the linkage from PDB1223.

Cases and *control* mother-child pairs were selected by the following **criteria**:

- Non-withdrawals from MoBa
- Singleton pregnancies
- Child born in 2001 or later
- Available records from the Medical Birth Registry of Norway (MBRN)
- Mother's questionnaire 1 available (week 17)
- No child serious malformation or affected by Down's syndrome (except for the CP case group)
- Available maternal plasma and whole blood sampled during the routine ultrasound assessment (K1) approximately 17-18th week of pregnancy (for CP cases: available maternal plasma or whole blood).

Controls were comprised of a randomly-selected sample from MoBa of the same eligible group as cases, and frequency matched to cases by child sex and year of birth.

Available biomarker measures (variable names in bold)

Perfluoroheptanoic acid (**PFHpA**)
Perfluorooctanoic acid (**PFOA**)
Perfluorononanoic acid (**PFNA**)
Perfluorodecanoic acid (**PFDA**)
Perfluoroundecanoic acid (**PFUnDA**)
Perfluorotridecanoic acid (**PFTrDA**)
Perfluorohexan sulfonic acid (**PFHxS**)
Perfluorohepane sulfonic acid (**PFHpS**)

Perfluorooctane sulfonic acid (**PFOS**)
Perfluorooctane sulfonamide (**PFOSA**)

Definition of cases and controls in the dataset

There are two case/control variables that are provided with the Mab010 dataset, **CaseControlGrpAlt1** and **CaseControlGrpAlt2**. Each of these subcategorizes cases and controls into the specific selection groups to which they belong and from which they were derived for inclusion in this study. A variable key with associated descriptions is provided below.

CaseControlGrpAlt1 (Retrieval ID: 965 & 967)

- Case_ASD: *Mother-child pairs where the child was diagnosed with ASD.*
- Case_CP: *Mother-child pairs where the child was diagnosed with CP.*
- Case_Epilepsy: *Mother-child pairs where the child was diagnosed with Epilepsy.*
- Control: *Mother-child pairs that were randomly selected from MoBa, frequency matched ASD, CP and Epilepsy case groups on child sex and birth year*.
- Case-ADHDNPR: *Mother-child pairs where the child was registered with ≥ 2 ADHD diagnoses.*

Variable describing the overlap between groups:

- Case_ASD (+ Case_ADHDNPR)
- Case_ASD + Case_CP
- Case_ASD + Case_CP (+ Case_ADHDNPR)
- Case_ASD + Case_CP + Case_Epilepsy
- Case_ASD + Case_CP + Case_Epilepsy (+ Case_ADHDNPR)
- Case_ASD + Case_Epilepsy
- Case_ASD + Case_Epilepsy (+ Case_ADHDNPR)
- Case_ASD + Control
- Case_ASD + Control (+ Case_ADHDNPR)
- Case_CP (+ Case_ADHDNPR)
- Case_CP + Case_Epilepsy
- Case_CP + Case_Epilepsy (+ Case_ADHDNPR)
- Case_CP + Case_Epilepsy + Control
- Case_CP + Control
- Case_Epilepsy (+ Case_ADHDNPR)
- Case_Epilepsy + Control
- Case_Epilepsy + Control (+ Case_ADHDNPR)
- Control (+ Case_ADHDNPR)

CaseControlGrpAlt2

- Case_Neurotox*: Mother-child pair where child had at least one diagnoses (ASD, CP or Epilepsy).*
- Control: *Mother-child pairs that were randomly selected from MoBa, frequency matched ASD, CP and Epilepsy case groups on child sex and birth year*
- Control (+ Case_Neurotox): *Mother-child pairs where the child had at least one diagnosis (ASD, CP or Epilepsy) and was selected as a control*

Biological sampling and processing

Non-fasting blood samples were collected from mothers at 17-18 weeks' gestation into ethylenediaminetetraacetic acid (EDTA) tubes, centrifuged within 30 minutes, and temporarily placed in a refrigerator at 4 °C. They were shipped from the collecting hospital overnight to MoBa's biobank at the Norwegian Institute of Public Health (NIPH). The samples most often arrived at the biobank within 1–2 days of blood donation, where EDTA plasma were aliquoted onto polypropylene microtiter plates (96-well format, 300 µL per well), sealed with the use of heat-sealing foil sheets, and placed in long-term storage at −80 °C.

For more information on biological sampling, processing and storage, please refer to the original reference articles for NIPH's biobank by Rønningen *et al*. 2006 and Paltiel *et al*. 2014.

Analytical methodology

Data on Per- and Polyfluoroalkyl Substances (PFAS) were measured by **liquid chromatography-triple quadruple mass spectrometry (LC-MS/MS)**. For more information on this analytical method, refer to the original reference article by Haug *et al*. 2009.

Measurement units:

Concentration in ng/mL for all included variables.

Limit of quantification (LOQ):

Perfluoroheptanoic acid (PFHpA): 0.05 ng/ml
Perfluorooctanoic acid (PFOA): 0.05 ng/ml
Perfluorononanoic acid (PFNA): 0.05 ng/ml
Perfluorodecanoic acid (PFDA): 0.05 ng/ml
Perfluoroundecanoic acid (PFUnDA): 0.05 ng/ml
Perfluorotridecanoic acid (PFTrDA): 0.05 ng/ml
Perfluorohexan sulfonic acid (PFHxS): 0.05 ng/ml
Perfluorohepane sulfonic acid (PFHpS): 0.05 ng/ml
Perfluorooctane sulfonic acid (PFOS): 0.05 ng/ml
Perfluorooctane sulfonamide (PFOSA): 0.05 ng/ml

Published articles using Mab010

Note: This section also includes publications that used Mab008, as these datasets were often combined and analyzed together

This section also includes articles related to study design, sampling, and data collection.

- Skogheim TS, Weyde KVF, Aase H, Engel SM, Surén P, Øie MG, Biele G, Reichborn-Kjennerud T, Brantsæter AL, Haug LS, Sabaredzovic A, Auyeung B, Villanger GD. Prenatal exposure to per- and polyfluoroalkyl substances (PFAS) and associations with attention-deficit/hyperactivity disorder and autism spectrum disorder in children. Environ Res. 2021 Nov;202:111692.
- Skogheim TS, Villanger GD, Weyde KVF, Engel SM, Surén P, Øie MG, Skogan AH, Biele G, Zeiner P, Øvergaard KR, Haug LS, Sabaredzovic A, Aase H. Prenatal exposure to perfluoroalkyl substances and associations with symptoms of attention-deficit/hyperactivity disorder and cognitive functions in preschool children. Int J Hyg Environ Health. 2020 Jan;223(1):80-92

Restrictions for use

The NeuroTox study is continued in NeuroTox-CHAIN (PDB3144) and has not yet published any data on the relationship between PFAS exposure and child epilepsy or CP as outcomes. We kindly ask researchers with the intention to look at these specific outcomes to contact us first at Gro.Dehli.Andersen@fhi.no. No other restrictions are currently known.

Acknowledgements recommended for use

We recommend that any use of these data in analyses that are presented in peer-review publications acknowledges the original articles describing sampling and data collection:

Skogheim TS, Weyde KVF, Aase H, Engel SM, Surén P, Øie MG, Biele G, Reichborn-Kjennerud T, Brantsæter AL, Haug LS, Sabaredzovic A, Auyeung B, Villanger GD. Prenatal exposure to per- and polyfluoroalkyl substances (PFAS) and associations with attention-deficit/hyperactivity disorder and autism spectrum disorder in children. Environ Res. 2021 Nov;202:111692.

Disclaimer

The data in Mab010 that are available for use are provided by MoBa on an *as is* basis as they were received from the generating laboratory and have not been curated or quality controlled prior to release. FHI does not provide any guarantees related to data quality and assurance of the original dataset. We reserve the right to periodically remove samples from the dataset belonging to participants who have retracted their consent to participate in this cohort study, and may alter the contents of the associated documentation accordingly.