Title: Infancy weight faltering and childhood neurodevelopmental disorders: A general population birth-cohort study

Short title: Infancy weight faltering and childhood neuro-developmental disorders

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ABSTRACT

While it is known that intrauterine growth restriction is associated with later mental disorders it is still unclear whether similar associations exist for postnatal weight faltering, also known as ‘failure to thrive’ in infancy. This study examined the potential connection between infancy weight faltering and mental disorders diagnosed in childhood focusing specifically on neuro-developmental disorders. The Copenhagen Child Cohort (CCC2000) was used to explore weight gain in infancy assessed by community health nurses. Data from the Danish national registries were used to quantify ICD-10 mental disorders diagnosed between birth and twelve years of age, as well as potential child and family confounders. Of 4.476 children with sufficient weight data, 339 (7.3 %) children were diagnosed with a mental disorder in childhood. Both any (weight-gain < -1SD) and severe infancy weight faltering (weight-gain < -2SD) were associated with psychomotor delays, while severe infancy weight faltering was also associated with intellectual impairments. Notably, no significant associations were found between weight faltering and autism spectrum disorders or attention deficit hyperactivity disorders. Weight faltering in infancy may be an early marker of neurodevelopmental delays. This possibility should be considered when assessing infants with slow weight gain, in order to early identification and treatment of co-occurring neurodevelopmental disorders.

Keywords: Infancy weight faltering. feeding and eating problems. neurodevelopmental disorders.

Introduction

Preterm birth and intrauterine growth restriction (IUGR), defined, as substantially slower fetal weight gain than expected, has repeatedly been associated with a range of neurodevelopmental disorders in childhood [1-5]. These disorders, which include Intellectual Disability (ID), Autism Spectrum Disorders (ASD), Attention Deficit Hyperactivity Disorders (ADHD), and learning, communication, and motor disorders are characterized by an onset in early childhood and a chronic course across developmental periods in which the core features show persistency and impairment into older ages [6,7]. Apart from neurodevelopmental disorders, IUGR and low birth weight have also been associated with severe psychopathology in adulthood including schizophrenia and mayor depression [8,9]. The etiology of all these disorders seems to involve both genetic components and pre-/perinatal factors influencing early brain development [10,11]. Compared to research on mental health outcomes of IUGR, studies of postnatal weight faltering (WF), also known as 'failure to thrive' in infancy, are scarce. WF in infancy, which is defined as slow weight gain or thinness for sex and age, has consistently been linked to early feeding problems and oral motor dysfunction [12,13], and with regulatory problems of sleep, crying and feeding, which may all index early signs of neurodevelopmental problems [14]. Population-based studies have shown an increased incidence of ID and ASD in children who were never breastfeed [2,3], as well as an increased incidence of ASD and ADHD diagnosed at ages 5-7 years in children who exhibited oral-motor developmental difficulties within the first ten months of life [15]. Among the few studies exploring the link between WF and neurodevelopmental disorders in infancy, one study found slightly impaired cognitive outcomes in school-age children with previous WF [12,16] whereas another study found associations between infancy WF and social, emotional, and behavioural difficulties later in childhood which, however, diminished when adjusting for IQ, infancy feeding problems, and socio-economic factors [17]. The etiological mechanisms of neurodevelopmental disorders are suggested to involve a genetic vulnerability interacting with biological and environmental influences from early stages of brain development [18]. Both IUGR and postnatal WF may reflect congenital developmental vulnerability potentially mediated by feeding problems in the early trajectories from developmental vulnerability into neurodevelopmental disorders. Overall, the resources of the parents have important moderating functions in the developmental pathways of neurodevelopmental disorders, and maternal mental health problems and disorders have been suggested to play a key role in

risk trajectories [19]. However, research findings are scarce regarding the associations between infancy WF and childhood mental disorders, especially neurodevelopmental disorders [20]. The aim of this study was therefore to explore the early associations between infancy WF and mental disorders with a focus on neurodevelopmental disorders. We further hypothesized that potential associations might be partly explained by perinatal adversities, parental factors and early feeding and psychomotor problems.

Methods

The study was conducted as part of the Copenhagen Child Cohort (CCC2000), which is a general population birth-cohort of 6.090 children [21, 22]. The CCC2000 comprises all children born in the year 2000 by women residing in one of 16 municipalities in the former County of Copenhagen. The catchment area consists of urban and semirural suburbs surrounding the city of Copenhagen, with a mixture of high-, moderate-, and low-income households. This cohort, which covers nearly 10% of all children born in Denmark in the year 2000, is representative of the Danish child population in terms of perinatal and sociodemographic characteristics except for a higher proportion of immigrant families and a slightly higher household income corresponding to the metropolitan area [21,22]. The CCC2000 has been followed prospectively from birth and onward using the unique civil identification number allocated to all residents in Denmark, which enables linkage with national registers. Updated analyses showed no differences when comparing the cohort with national data on parental educational level (22). The CCC2000 project at baseline included a formalized collaboration with the community health nurses (CHN) of the catchment with the aim of systematizing and standardizing their assessment of the child's health and development in the first year of living. The CHN services in Denmark, which is government financed, free of charge and well accepted, covers around 99% of infant families. In collaboration with the health nurses, and as part of the CCC2000 project, we designed a standardized record to collect data from four scheduled home visits at ages 0–4 weeks and 2–3, 4–6 and 8–10 months within the general child health surveillance [22]. For the current study, we included children with available information on birthweight measured by midwives and reported to the Medical Birth Registry, and at

least one later measure of weight assessed by the CHN at child-age between six to eleven months. The CCC2000 study was approved by the Data Protection Agency in the Capital Region (CSU-FCFS-2016-004. I-Suite 04544) and the Regional Ethic Committee (protocol 16023242).

Parameters of infancy weight status

Weights were initially converted into standard deviation scores (SD) using the WHO standard as reference [23]. Infancy weight gain was measured within the period from birth to age 11 months using the Thrive Index (TI) methodology [24]. The TI is the residual of the Z score change since birth conditional on birthweight. This adjusts for the normal phenomenon of regression to the mean, according to which children with high birthweight tend to fall on the growth curves nearer towards average, while children with low birthweight tend to catch-up [25]. A TI of null thus indicates that the weight-gain is as expected for this population when taking birth weight into account. Any infancy weight faltering (WF) was defined as TI < -1, and severe WF was defined as TI < -2.

Child mental disorders

We included all diagnoses on mental disorders diagnosed in public hospital settings (paediatric and child psychiatric in-and outpatient and emergency settings). In these settings, the diagnostic assessments are completed by medical doctors, according to defining criteria of the International Classification of Diseases, version ICD-10 [26] and afterwards recorded in the Danish National Registry of Patients and the Psychiatric Central Registry (see Supplement 1). In Denmark, the referrals to public hospitals of children with mental health problems occur via general practitioners, private specialists in pediatrics and child psychiatry, as well via other hospital departments, and from municipality psychologists and community health nurses. Very few are treated in private child psychiatric or pediatric settings. The medical services and treatment at public hospitals are free of charge to the patient, the national patient registries cover more than 98% of the Danish population and they have been found highly reliable [27]. The study sample was followed from birth to age 11-12 years corresponding to the approximate onset of puberty in Danish children; in practise till 11.6 year (hereafter 11 years)

corresponding to available data at the end of the pre-planned follow-up interval. We included all incident (i.e. first-time) ICD-10 F-diagnoses of mental disorders (F20-F99.9) except enuresis and encopresis which are now primarily considered somatic illnesses. Moreover. the ICD-10 R-diagnoses of borderline intellectual functioning (R41.8*)* and psycho-motor delay (R62.0) were also included. Disorders were sorted by diagnostic entities. The group of neurodevelopmental disorders included: disorders of intellectual disability (F70-79); specific developmental disorders (F80-83); autism spectrum disorders (F84); other and unspecified developmental disorders (F88-89); disorders of hyperactivity and inattention (F90 and F98.8; the latter is used in Denmark to classify disorders of inattention without hyperactivity); tic disorders (F95); stereotyped movement disorders (F98.4) and stuttering (F98.5); borderline intellectual functioning (R41.8*)* and psycho-motor delay (R62.0) were also included in this group. All other ICD-10 diagnoses of mental disorders were clustered in separate groups comprising: psychoses (F20-29); mood disorders (F30-39); stress-related, somatoform and anxiety disorders (F40-48); disorders of feeding and eating (F 50; F 98.2); sleep disorders (F51); childhood onset behavioral and emotional disorders (F91-93; F 98.0-98.6) and disorders of social functioning (F94); and unspecified mental disorders (F99).

Co-variates from the CHN assessment or national registries

Oral sensory/motor difficulties and feeding problems in infancy were assessed and systematically registered as part of the CHN visits and obtained from the standardized CHN records [21-22]. From Danish national registries we obtained information on perinatal factors, serious somatic illnesses in the child's first living year, socio-economic conditions of the family, and information on parents being diagnosed with a mental disorder prior to the birth of the child [27]. Co-variates are further described in Supplement 1.

Statistics

Descriptive statistics were used to describe distributions of baseline variables and incidences of mental disorders. Crude associations were investigated using likelihood ratio chi-square and Fishers exact test. Analyses were conducted at different levels of specificity investigating, respectively, how WF

was associated with 1) any mental disorder, 2) with the two broad categories of 'neurodevelopmental disorders' and 'other mental disorders', and 3) with the specific neurodevelopmental disorders. Adjusted analyses were performed on associations that were significant in the crude analyses using logistic regression and Hosmer Lemeshow goodness of fit test, including putative confounders described in Supplement 1. Notably, we could not analyse breastfeeding as covariate due to unavailable data of sufficient validity [21-22]. To conserve power, pre-models of group-wise adjustments were done concerning, a) perinatal (e.g IUGR and preterm birth), and early somatic factors, and b) socio-economic factors. After group-wise backwards selection, sex, parental mental disorder, and child neurodevelopmental co-morbidity were added, and further backwards selection were done, leaving only influential confounders in the adjusted model. To this adjusted model, we subsequently separately added infancy feeding problems and oral sensory/motor difficulties to examine whether this would attenuate the effect of WF. Finally, we examined whether an association between WF and mental disorders was contingent upon the child's age at diagnosis. We used logistic regression with age at first time diagnosis stratified into: infancy (0 years), toddlerhood (1-3 years), and the remaining childhood (4-11 years). All analyses were in SAS version 9.4.

All analyses of the associations between WF and childhood mental disorders were adjusted for multiple testing using the Benjamini and Hochberg correction for False Discovery Rate (FDR) [28] as implemented by an online software (http://sdmproject.com/utilities/?show=FDR) which correspond to the R-codes for this analysis. Both *p*-values and the *q*-values (FDR-adjusted p-values) were presented and significant results defined as $q < 0.05$.

Results

A total of 4,476 children had data on birth weight and a postnatal weight measured around eight months (mean age 8.3 months, SD 3.2 weeks, 90%-range 7.0 to 9.5 months). Compared to the remaining cohort alive at 11-12 years the study sample included fewer children from families living in social disadvantage, fewer with congenital disorders, and slightly fewer children with a diagnosed neurodevelopmental disorder (See Supplement 1). A total of 590 children (13.2%) in the study sample had any infancy WF (TI < -1 SD), and of these 68 children (1.5% of all children) had severe infancy WF (TI < -2 SD). Table 1 shows the distribution of baseline information in the total study sample, and in the children with and without WF. Infants with WF

differed from infants without WF on some of the baseline variables such as being born with a low birth weight, be small for gestational age and have congenital disorders.

[Table 1]

Among the 4,476 children a total of 339 (7.6%) were diagnosed at hospital with any mental disorder within their first 11-12 years of life, and 268 (4.2%) were diagnosed with a neurodevelopmental disorder. The diagnostic categories and distributions of first-time diagnoses are shown in Table 2. Autism spectrum disorders (ASD) and Attention Deficit Hyperactivity Disorders (ADHD) were the overall most frequent single diagnoses, and the most frequent mental disorders among children diagnosed for the first time after three years of age (4-11 year). Among children diagnosed in early childhood (0-3 years), psychomotor delay and intellectual disability were the most frequently diagnosed neuro-developmental disorders.

[Table 2]

Results of the analyses on the associations between WF and childhood mental disorders at the different levels of specificity are presented in Table 3-6. When these results were adjusted for False Discovery Rate using the Benjamini Hochberg correction, p-values ≤ 0.017 became significant corresponding to $q < 0.05$. In accordance with this, Odds Ratios were presented with wider confidence intervals (99%). In the analyses with broad outcome categories (Table 3), WF < -1 SD was not significantly associated with ‘any mental disorder’ or ‘any neurodevelopmental disorder’, while WF <-2 SD was associated with a more than two-fold increased odds of ‘any mental disorder’ (OR 2.40 [CI 1.01-5.68]) or ‘any neurodevelopmental disorders’ (OR 2.77 [CI 1.13-6.81]).

[Table 3]

In the subsequent analyses of specific neurodevelopmental disorders, WF was significantly associated with diagnoses of intellectual disability and psychomotor delay, whereas no significant associations were found with autism spectrum disorders or ADHD (See Table 4). Any WF (WF < - 1SD) was associated with a two to three-fold higher odds of (2.53[1.12-5.72]) of psychomotor delays, whereas severe WF (WF < - 2SD) was associated with a nine-fold higher odds of psychomotor delay (OR 9.38[2.92-30.1]) and an almost eleven-fold higher odds of intellectual disability (OR 10.90[3.63-32.6]. In further analysis of these associations, adjusting for perinatal and somatic factors as well as infancy feeding problems oral sensory/motor difficulties, severe WF (WF <-2SD) remained a significant independent predictor of intellectual disability (OR 7.07[1.37-36.60]), whereas associations with psychomotor delay became insignificant (See Table 5).

[Table 4, Table 5]

Finally, we examined whether the association between infancy WF and neurodevelopmental disorders was contingent upon the timing of the child's age at first diagnosis. As shown in Table 6, both any WF (WF < -1 SD) and severe WF (WF < 2 SD) were highly associated with the child being diagnosed with a neurodevelopmental disorder within the first year of life (OR 5.21 [CI 1.42-19.18]) and OR 22.89 [CI 4.99-104.90], respectively). Severe WF (WF. < -2 SD) was also associated with a diagnosis of a neurodevelopmental disorder between age of 1-3 years (OR 7.00 [1.41-34.30]), but not with first time diagnoses in the older ages (4-11 years) even though most neurodevelopmental disorders, including ID, were diagnosed in this age period. Due to the atypical growth of preterm children in early childhood and the known associations with neuro-behavioural outcomes [29], the crude and age-stratified analyses were furthermore repeated without this sub-group, showing no marked change of estimates (data not shown).

[Table 6]

Discussion

This is the first study to formally investigate and quantify associations between infancy WF and the broad spectrum of mental and neurodevelopmental disorders in childhood. We explored all major diagnostic entities of mental disorders in children referred to hospital between birth and 11 years and found that severe WF (< - 2SD) was associated overall with incident mental disorders, and in particular with neurodevelopmental disorders. Among them, a nearly seven-fold higher odds of intellectual disability (ID) was seen, even when adjusting for low birth weight for gestational age, congenital disorder, somatic illness in infancy, infancy oral sensory/motor difficulties, infancy feeding problems and neurodevelopmental co-morbidity.

In prior research, low birth weight (indicative of IUGR) has been found associated with both ASD and ADHD, but also with childhood problems of social development, attention, and adaptive behaviors [1-5], as well as schizophrenia and depression in adulthood [8,9]. Also, early feeding problems and oral motor dysfunction have been associated with disorders of neurodevelopment like ID, ASD, and ADHD [3,12,14]. In another birth cohort study, WF was associated with behavioural signs of inattention and hyperactivity later in childhood, however these associations lost significance in analyses adjusted for social confounders and IQ [17]. A previous study from the CCC2000 cohort also showed that children diagnosed with ASD and ADHD before age 8 years often had oral-motor difficulties in infancy, but that study did not include WF [15]. Notably, we did not find infancy WF to be associated with autism spectrum disorders (ASD) and attention deficit/ hyperactivity disorder (ADHD).

In accordance with the literature, we hypothesized that infancy WF would be overall associated with disorders of neurodevelopment, but also that these associations potential may be explained by perinatal adversities, parental factors, and early feeding/motor oral problems. Among the neurodevelopmental disorders investigated, we found that severe WF (WF <-2 SD) was associated with psychomotor delay and intellectual disability, which both manifest as delayed development. However, in contrast to psychomotor delay, which specifically involves delays in reaching psychomotor milestones, intellectual disability involves a markedly lower general cognitive ability that impair various aspect of learning and acquisition of adaptive skills. Adjusting for sociodemographic and perinatal factors did not change these findings and the limited influence in these variables within the

adjusted models resonate with findings from an evidence review which likewise did not find any associations between psycho-social factors and WF [30]. Yet, when the oral/motor difficulties were adjusted for, WF's associations were attenuated by remained significant for intellectual disability. This is also in line with prior research pointing to an overlap between WF and oral/motor problems [31-32], and may reflect a possible overlap of atypical feeding, eating and weight development in neuro-developmentally vulnerable infants. Likewise, the relation between WF and intellectual disabilities may index a common pre-natal predisposition, but still, the adjusted analyses did not support the dependence of relevant pre-, peri- and postnatal confounders. Our finding that the associations with WF were strongest for children diagnosed in the first year of life, suggests that infancy WF may coincide with rather than precede severe neurodevelopmental disorders. Thus, rather than being a part of a causal pathway, WF is probably primarily an early indicator of the most severe neurodevelopmental problems leading to early referral and diagnoses in early years [33].

The findings are also relevant to interpret with reference to Avoidant-Restrictive Food Intake Disorder (ARFID), which was first introduced in DSM-5 ([34] and subsequently included in ICD-11 ([35]. ARFID is characterized by weight loss and lack of normal weight development due to disinterest in food, aversion to food, or feared consequences of food intake not related to body image [34, 35]. Studies have found that ARFID tend to occur at a younger age than other eating disorders [36, 37]. Still, there is limited insights into its onset and longitudinal course. The identified co-occurrence between WF, feeding problems and specific neurodevelopmental disorders bear resemblance with some of the components of ARFID. It is therefore relevant to contemplate a possible connection between infancy WF and ARFID as an avenue for further investigation.

Strengths and limitations

The major strength of our study is the longitudinal, population-based birth-cohort design with information on a broad range of perinatal and infancy health parameters [25] and data on clinically diagnosed ICD-10 mental disorders [38-39]. Overall, our participation rate was high, but as in most other population-based studies, our study sample was less socio-economically disadvantaged and thus probably of somewhat lower risk of mental disorders. However, free and equal access to healthcare services in Denmark is supposed to reduce the risk of selection bias regarding diagnosed mental disorders.

Infancy weight measurements were obtained during the routines of the municipality child health surveillance by educated health nurses (CHN) and in close collaboration with the CCC200 project. However, the CHNs used transportable steelyard scales, which may influence the overall growth measurements to be less precise. Still, the Danish family nurse system ensures that the individual child is primarily assessed by the same nurse throughout infancy, hereby reducing the internal variation. In addition, solid international definitions of weight faltering were used, with the Thrive Index method reducing the likelihood of misclassification due to regression towards the mean and making unified analyses of boys and girls, and across different timespans, possible due to the use of SD-scores. Another strength of this study is the availability of CHNs' standardized recordings of their routine assessments of oral-motor and feeding abilities and difficulties in infancy in a non-selected population [21]. The diagnoses of mental disorders were discharge diagnoses made by medical doctors in agreement with the ICD-10 criteria, and overall, the Danish patient registries have been found to have good coverage and validity concerning psychiatric disorders [39-41]. However, referral bias has to be considered as infants exhibiting the combination of WF and developmental difficulties have an increased opportunity of been assessed and diagnosed earlier. However, in Denmark, teachers in kindergarten (which most children attend) and schools are aware of mental problems and guide parents concerning the need for referral. A final issue that should be considered is the data-driven approach to variable selection with regard to potential confounders. While this approach is appropriate when there is limited prior knowledge in the area, it may inflate type I errors. Moreover, as all covariates were analyzed in the same way, we were unable to distinguish confounders from possible mediators. Thus, further insights into how specific pre-/perinatal and somatic factors influence the association between WF and neurodevelopmental disorders are therefore needed.

Conclusion

The findings indicate that weight faltering in infancy may be an early marker of severe neurodevelopmental delays. This possibility should be considered when assessing infants with slow weight gain in order to identify and treat co-occurring neurodevelopmental disorders and thereby optimize child development.

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Table 1. Baseline descriptive statistics and associations with infancy weight faltering

Baseline variables	**Available data**	**Distribution of baseline variables**		**Associations**	
		In total study sample (N = 4476)	**In subsample with Infancy Weight Faltering† (n = 590)**	**Children with versus without Infancy Weight Faltering**	
	N	***n* (%)**	***n* (%)**	**OR (99% CI)**	***p***
Sex (Boy)	4476	2277 (50.9%)	293 (49.7%)	0.95 [0.75-1.19]	0.528
Preterm (< 37 weeks)	4460	284 (6.4%)	39 (6.6%)	1.05 [0.66-1.67]	0.779
Low birth weight (< 2500g)	4476	213 (4.8%)	45 (7.6%)	1.83 [1.17-2.86]	0.001
Low BW for GA (< 10. perc.)	4460	568 (12.7%)	102 (17.4%)	1.53 [1.13-2.09]	0.001
Maternal smoking in pregnancy	4411	1037 (23.5%)	119 (20.3%)	0.81 [0.61-1.07]	0.047
Birth complications	4476	387 (8.7%)	66 (11.2%)	1.40 [0.97-2.02]	0.023
Congenital disorder	4476	97 (2.2%)	22 (3.7%)	1.97 [1.04-3.71]	0.010
Young mother < 20 years	4469	79 (1.8%)	9 (1.5%)	0.84 [0.34-2.12]	0.629
Old mother > 40 years	4469	100 (2.2%)	9 (1.5%)	0.65 [0.26-1.60]	0.189
Low maternal education	4237	996 (23.5%)	147 (26.4%)	1.20 [0.92-1.57]	0.084
Single mother	4476	313 (7.0%)	40 (6.8%)	0.96 [0.61-1.51]	0.827
Low disposable household income	4471	837 (18.7%)	116 (19.7%)	1.08 [0.81-1.43]	0.518
Immigrant parents	4476	674 (15.1%)	91 (15.4%)	1.03 [0.75-1.42]	0.790
Mental disorders in parents	4476	462 (10.3%)	66 (11.2%)	1.11 [0.77-1.60]	0.463
Serious somatic illness in infancy	4476	678 (15.2%)	103 (17.5%)	1.22 [0.90-1.65]	0.099
Feeding problems in infancy	4476	1398 (31.2%)	247 (41.9%)	1.71 [1.36-2.16]	< 0.001
Oral sensory/ motor difficulties in infancy	4476	317 (7.1%)	50 (8.5%)	1.26 [0.83-1.90]	0.167

† = Infant weight faltering defined as the thriving index < -1 SD

Table 2. Incident diagnoses of mental disorders from birth to age 11.6 years

Diagnostic group	Age of incident diagnosis		
	0-11.6 (total)	**0-3 years**	**4-11.6 years**
Any incident diagnosis	339	72	267
Incident neurodevelopmental disorder	268	48	220
Psychomotor delay (R62.0)	51	33	18
Intellectual disability (ID; F70-79)	53	16	37
Autism Spectrum Disorders (ASD; F84)	82	8	74
Attention Deficit and Hyperactivity Disorders (ADHD; F90. F98.8)	126	4	122
Other neurodevelopmental disorders[1]	110	8	102
Other mental disorders[2]	143	27	116

[1] Other neurodevelopmental disorder: Tic disorders (F95). specific developmental disorder (F80-83). other and unspecified developmental disorders (F88-89). stereotyped movement disorders (F98.4). stuttering (F98.5). borderline intellectual functioning (R41.8).
[2] Include all other incident diagnosis of mental disorders (all other ICD-10 F-codes)

Table 3. Associations between infancy weight faltering and mental disorders diagnosed from 0-11 years of age (N = 4460)

	Any mental disorder			**Main categories**					
				Any neurodevelopmental disorder			**Any other mental disorder**		
	OR [99%CI]	**p-value**	**q-value**	**OR [99%CI]**	**p-value**	**q-value**	**OR [99%CI]**	**p-value**	**q-value**
Infancy weight faltering									
< -1 SD	1.30 [0.88-1.94]	0.094	0.169	1.25 [0.80-1.96]	0.209	0.297	1.51 [0.68-3.36]	0.204	0.297
< -2 SD	2.40 [1.01-5.68]	**0.017**	**0.042**	2.77 [1.13-6.81]	**0.006**	**0.020**	#		

OR = Odds ratio, CI = Confidence Intervals, p-value = raw p-value, q-value = Benjamini Hochberg corrected p-value, # = presenting results prohibited due to microdata
Significant results after Benjamini Hochberg adjustment are highlighted in bold

Table 4. Infancy weight faltering predicting specific neurodevelopmental disorders 0 to 11.6 years of age (N = 4460)

	Psycho-motor Delay (R62.0)			Mental retardation (F70-79)			Autism Spectrum Disorders (F84)			ADHD/ADD (F90. F98.8)			Other neurodevelopmental disorders		
Predictors	**OR[99%CI]**	**p-value**	**q-value**	**OR[99%CI]**	**p-value**	**q-value**	**OR[99%CI]**	**p-value**	**q-value**	**OR[99%CI]**	**p-value**	**q-value**	**OR[99%CI]**	**p-value**	**q-value**
Infancy weight faltering															
< - 1 SD	2.53[1.12-5.72]	**0.006**	**0.020**	1.95[0.83-4.57]	0.058	0.112	1.02[.44-2.37]	0.949	0.949	1.03[0.52-2.03]	0.917	0.949	0.98[0.47-2.07]	0.949	0.949
< -2 SD	9.38[2.92-30.1]	**< 0.001**	**< 0.001**	10.90[3.63-32.6]	**< 0.001**	**< 0.001**	1.64[.25-10.7]	0.526	0.617	1.61[0.35-7.49]	0.457	0.561	0.66[0.05-8.93]	0.337	0.433

ADHD = Attention Deficit Hyperactivity Disorder, ADD = Attention Deficit Disorder, OR = Odds ratio, CI = Confidence Intervals
p-value = raw p-value, q-value = Benjamini Hochberg corrected p-value
Significant results after Benjamini Hochberg adjustment are highlighted in bold

Table 5. Adjusted analyses of significant associations between infancy weight faltering and neurodevelopmental disorders (N = 4460)

	Mental retardation (F70-F79)						Psychomotor delay (R 62.0)					
	Model 1 *Adjusting for perinatal and somatic factors*			**Model 2** *Adding oral/motor difficulties*			**Model 1** *Adjusting for perinatal and somatic factors*			**Model 2** *Adding oral/motor difficulties*		
Predictors	**OR [99%CI]**	**p-value**	**q-value**	**OR [99%CI]**	**p-value**	**q-value**	**OR [99%CI]**	**p-value**	**q-value**	**OR [99%CI]**	**p-value**	**q-value**
Infancy weight faltering												
< -1 SD	2.10 [0.85-5.02]	0.036	0.081	1.67 [0.66-4.24]	0.158	0.267						
< -2 SD	7.43 [1.44-38.3]	**0.002**	**0.009**	7.07 [1.37-36.6]	**0.002**	**0.009**	4.30 [1.00-18.8]	**0.012**	**0.032**	3.27 [0.72-14.9]	0.044	0.091

Model 1: Including: Low birth weight for gestational age, congenital disorder, neurodevelopmental co-morbidity
Model 2: Adding infancy oral sensory/motor difficulties
OR = Odds ratio, CI = Confidence Interval, p-value = raw p-value, q-value = Benjamini Hochberg corrected p-value, Significant results after Benjamini Hochberg adjustment are highlighted in bold

Table 6. Associations between infant weight faltering and neurodevelopmental disorder by age of incident diagnosis (N = 4460)

	First year of life (0 years) (n = 16)			1-3 years of age (n =32)			4-11.6 years of age (n = 267)		
Predictors	**OR [99%CI]**	**p-value**	**q-value**	**OR [99%CI]**	**p-value**	**q-value**	**OR [99%CI]**	**p-value**	**q-value**
Infancy Weight Faltering:									
< -1 SD	5.21 [1.42-19.18]	**0.002**	**0.009**	1.87 [0.62-5.65]	0.180	0.286	0.97 [0.57-1.65]	0.866	0.949
< -2 SD	22.89 [4.99-104.90]	**< 0.001**	**< 0.001**	7.00 [1.41-34.30]	**0.012**	**0.032**	0.89 [0.19-4.12]	0.226	0.305

OR = Odds ratio, CI = Confidence Intervals, p-value = raw p-value, q-value = Benjamini Hochberg corrected p-value, Significant results after Benjamini Hochberg adjustment are highlighted in bold