Associations between ponderal index and hypothalamic mean diffusivity in typically developing 5-year-olds

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TURUN YLIOPISTO Lääketieteellinen tiedekunta

STÅHLBERG EMILIA: Ponderaalisen indeksin ja hypotalamuksen keskimääräisen diffuusiivisuuden yhteys tyypillisesti kehittyvillä 5-vuotiailla lapsilla.

Syventävien opintojen kirjallinen työ, s. 17, Psykiatria
Maaliskuu 2025

Lasten ylipaino ja lihavuus ovat kasvava huolenaihe erityisesti länsimaissa. Maailman terveysjärjestö (WHO) on listannut lasten ylipainon yhdeksi merkittävimmistä maailmanlaajuisista terveysriskeistä. Lapsuusiän lihavuudella on pitkäkantoisia vaikutuksia niin aikuisiän lihavuuteen sekä liitännäissairauksiin kuten tyypin 2 diabetekseen. Tässä tutkimuksesta tutkitaan 5-vuotiaiden suomalaislasten painon yhtettä hypotalamuksen rakenteeseen. Data kerättiin FinnBrain syntymäkohortin aineistosta.

FinnBrain-syntymäkohorttitutkimus on laaja monitieteellinen seurantatutkimus, jossa tutkitaan ympäristön ja perimän vaikutusta lapsen kehitykseen ja terveyteen. Tutkimukseen rekrytoitiin 3808 raskaana olevaa vuosina 2011–2015 Varsinais-Suomen ja Ahvenanmaan alueelta. Syntyneitä lapsia sekä perheitä on seurattu erilaisin tutkimusmenetelmin raskaudesta myöhempään lapsuuteen saakka. Tässä tutkimuksessa tutkittiin 5-vuotiaiden lapsien ponderaalisen indeksin ja hypotalamuksen MD-arvon (keskimääräinen diffuusiivisuus) yhteyttä. Tässä poikkileikkaustutkimuksessa satunnaisesti rekrytoitiin 147 äiti-lapsi-paria, joilla oli käytettävissä aivojen MRI-kuvaus 5 vuoden iässä.

Lapset olivat syntyneet vuosina 2012–2015, ja heistä 53 % oli poikia. Sosiodemografiset muuttujat saatiin kohorttitutkimuksen kyselylomakkeista sekä kansallisista rekistereistä. Otos vastaa hyvin Suomen väestön yleisiä piirteitä. Vanhemmat antoivat kirjallisen, tietoisen suostumuksen sekä itsensä että lapsensa puolesta, ja lisäksi varmistettiin lapsen suostumus ennen tutkimuskäyntejä.

Tässä tutkimuksessa tutkitaan miten lapsuuden ylipaino ja lihavuus sekä äidin raskautta edeltävän BMI vaikututtavat aivojen rakenteeseen. Hypoteesina on, että äidin korkeampi raskautta edeltävä BMI nostaisi lapsen hypotalamuksen keskimääräistä diffusiviteettia. Tämän tutkimuksen tuloksilla annetaan suuntaa tuleville tutkimuksille, jotta voidaan selvitettää lapsuuden ylipainon ja lihavuuden syitä ja seurauksia.

Avainsanat: lapsuus, ylipaino, lihavuus, aivokuvantaminen, hypotalamus

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Childhood overweight and obesity are growing concerns, particularly in Western countries. The World Health Organization (WHO) has identified childhood overweight as one of the most significant global health risks. Childhood obesity has long-term consequences, including an increased risk of obesity and related conditions, such as type 2 diabetes, in adulthood. This study investigates the relationship between body weight and hypothalamic structure in 5-year-old Finnish children. The data were collected from the FinnBrain birth cohort study.

The FinnBrain birth cohort study is a large, multidisciplinary longitudinal study examining the effects of environmental and genetic factors on child development and health. The study recruited 3,808 pregnant women between 2011 and 2015 from the regions of Southwest Finland and Åland. The children born into the study and their families have been followed using various research methods from pregnancy to later childhood. This study specifically examined the association between the ponderal index and the mean diffusivity (MD) value of the hypothalamus in 5-year-old children.

In this cross-sectional study, 147 mother-child pairs were randomly recruited, all of whom had available brain MRI scans at the age of 5 years. The children were born between 2012 and 2015, and 53% of them were boys. Sociodemographic variables were obtained from cohort study questionnaires and national registers. The sample is representative of the general Finnish population. Written informed consent was obtained from the parents for both themselves and their child, and the child’s assent was also ensured before the research visits.

This study examines how childhood overweight and obesity, as well as maternal pre-pregnancy BMI, influence brain structure. The hypothesis is that a higher maternal pre-pregnancy BMI is associated with increased mean diffusivity in the child's hypothalamus. The findings of this study provide direction for future research to further investigate the causes and consequences of childhood overweight and obesity.

Keywords: childhood, overweight, obesity, neuroimaging, hypothalamus

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1 Introduction

1.1 Childhood Obesity: A Global and Finnish Perspective

Childhood obesity is a growing concern worldwide, especially in western countries, with an estimated 340 million children and adolescents, from ages 5 to 19, considered overweight or obese, according to the World Health Organization *(WHO, Obesity and Overweight, 2022.)*. The WHO has identified childhood obesity as one of the major global health risks, as it is associated with higher mortality rates than underweight. In Finland when looking at 2 to 16-years old children in 2023, 17 percent of girls and 26 percent of boys were considered overweight (THL, Child and adolescent overweight and obesity 2023, Vuorenmaa et.al 2024.).

Figure 1 shows the prevalence of overweight (including obesity) among boys and girls aged 2–16 years in Finland between 2014 and 2023, based on ISO-BMI (International Obesity Task Force BMI) classifications. ISO-BMI is a standardized method for classifying BMI in children and adolescents, accounting for age and sex differences. It uses internationally recognized growth curves to define thresholds that correspond to adult BMI cutoffs for overweight (25) and obesity (30).

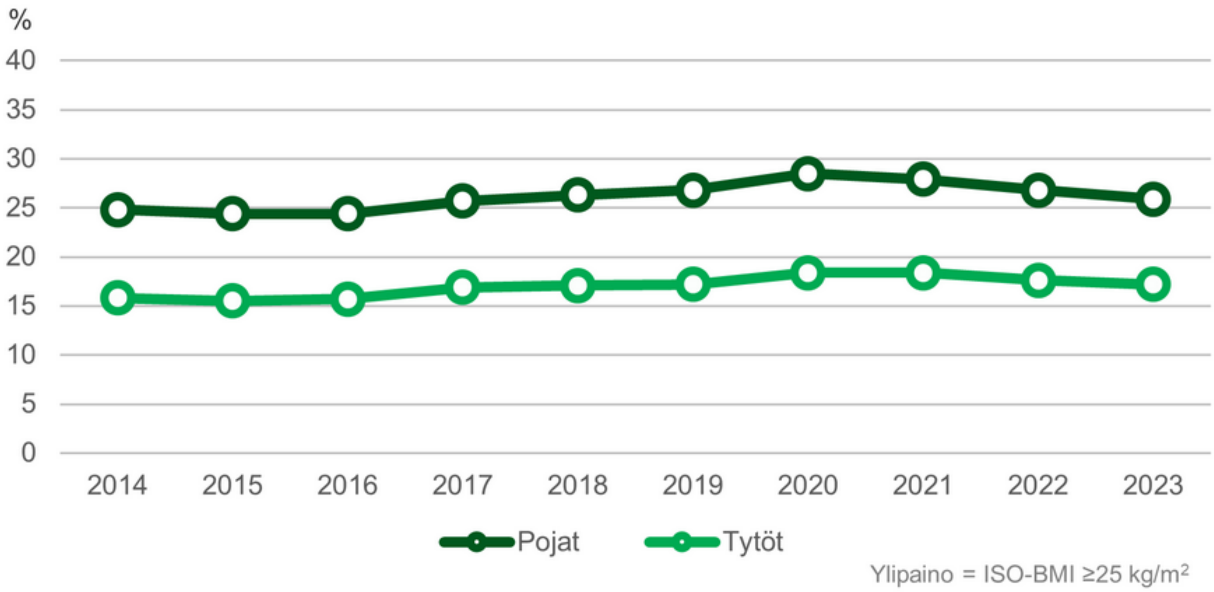

Figure 1. The prevalence of overweight (including obesity) among boys and girls aged 2-16 years in Finland between 2014 and 2023. THL, Child and adolescent overweight and obesity 2023. (Vuorenmaa et.al. 2024)

1.2 Health Consequences and Risk Factors of Childhood Obesity

The effect of childhood obesity has been studied extensively in recent years. Pulgarón (2013) concluded in a review that obesity results in an increased risk for various health problems, including cardiovascular disease, asthma, type 2 diabetes, and musculoskeletal disorders, as well as psychological and social issues (Pulgarón, 2013). A more recent review by Lister et al. (Lister et al., 2023) in *Nature Reviews Disease Primers* reaffirmed Pulgarón's findings, further emphasizing the extensive health consequences of childhood and adolescent obesity, including its links to type 2 diabetes, cardiovascular complications, and mental health disorders. Obesity is a major health problem for young and old, but one possible explanation for why obesity could be more harmful for children is that it may affect their growth and development in ways that can have lasting effects.

Childhood obesity results from a complex interplay of environmental and genetic factors. Key risk factors include poor dietary habits, physical inactivity, family influences, socioeconomic status, and psychological factors. Genetics also plays a role, influencing metabolism, appetite regulation, and fat storage. As Brown et al. summarized it is difficult to detect the genetic role in the hereditary nature of obesity, as families often share not only genetic material but also common environments and habits (Brown et al., 2015).

1.3 Brain Structure and Function in Childhood Obesity

While genetic, environmental, and behavioral aspects have a major impact to childhood obesity, this view is challenged by new research focusing more on the brain. Childhood obesity has been shown to affect brain development, as a study from Alosco et al. (Alosco et al., 2014) found that obese children and adolescents had decreased volume of frontal and limbic cerebral grey matter regions. This is further supported by a meta-analysis by Herrmann et al. (Herrmann et al., 2018), which found that obesity is associated with decreased gray matter volume in critical areas such as the prefrontal and insular cortices, the latter of which is part of the limbic system. Together, these findings suggest that obesity may alter brain structure with potential long-term effects on cognitive and emotional development.

The hypothalamus, a small brain region situated below the thalamus and above the pituitary gland, plays a vital role in maintaining homeostasis and regulating physiological processes. It serves as a command center, controlling body temperature, hunger, thirst, sleep-wake cycles, and emotional responses (Saper & Lowell, 2014). A key function of the hypothalamus is controlling the pituitary gland, the master gland of the endocrine system. The pituitary gland releases hormones that influence growth, metabolism, and reproduction. The hypothalamus also modulates the autonomic nervous system, regulating heart rate, blood pressure, and respiration, and plays a role in the stress response. Additionally, the hypothalamus affects emotional and behavioral responses, including pleasure, reward, and mood. Hypothalamic dysfunction can lead to appetite and sleep disruptions, mood disorders, and hormone imbalances (Saper & Lowell, 2014).

The hypothalamus has a crucial role in regulating person's food intake and eating behavior, and alterations in its function and structure have been linked to obesity (Vucetic & Reyes, 2010). A large body of data from animal studies has shown the connection between high-fat diet and inflammation of the hypothalamic neurons, and a study from Thaler et al. (2012) showed that this also applies to humans (Thaler et al., 2012). Another review from Thaler (2010) concluded that microinflammation in hypothalamus can cause disruptions in person's appetite and food intake regulation through leptin and insulin signaling (Thaler & Schwartz, 2010). However, further research is needed to clarify how microinflammation of the hypothalamus can cause obesity in humans.

1.4 DTI and Hypothalamic Microstructure in Obesity

Diffusion tensor imaging (DTI) is a widely used magnetic resonance imaging (MRI) technique for examining brain microstructure, particularly white matter integrity and axon connectivity. It can provide insights into parameters such as fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). In this study, we focus on hypothalamic mean diffusivity (MD), which reflects the diffusion of water molecules within the hypothalamus. Alterations in hypothalamic MD may indicate microstructural changes, potentially resulting from inflammation, as discussed earlier. For example, previous studies have shown that obese adults have higher hypothalamic MD values than lean adults (Thomas et al., 2019), suggesting that obesity may affect hypothalamic microstructure.

The link between obesity and white matter alterations has been extensively investigated using DTI. A systematic review by Okudzhava et al. (2022) examined 31 cross-sectional studies comparing obese and lean individuals. Most studies observed a decrease in FA and an increase in MD among obese individuals, indicating potential white matter abnormalities. Notably, 22 of these studies reported significantly reduced FA, while 20 studies found altered diffusivity parameters. Despite this overall pattern, some variability in results was noted, likely due to methodological differences or sample characteristics. The authors emphasize the importance of directly assessing body fat to improve the accuracy of brain–body relationship studies.

Research on obesity-related brain changes in children has also gained attention. Ou et al. (2015) compared brain structure differences between obese and normal-weight children using MRI and DTI. In a sample of 24 children aged 8-10, the study found reduced gray matter in areas such as the thalamus and cerebellum in obese children, along with higher white matter volume in several regions. Additionally, they observed increased fractional anisotropy (FA) in specific white matter tracts, but no significant difference in mean diffusivity (MD). These findings indicate that obesity-related alterations in brain microstructure may emerge early in life, highlighting the potential developmental consequences.

In addition to childhood obesity, recent studies have investigated how maternal pre-pregnancy BMI influences offspring brain development. Rasmussen and Tuulari (2023), as part of the FinnBrain birth cohort study, reported a positive association between maternal BMI and newborn hypothalamic mean diffusivity (MD). These results highlight the significant role of maternal health prior to pregnancy in influencing the brain structure and function of offspring. Specifically, pre-pregnancy weight is shown to have lasting effects on neurodevelopment. This underscores the potential for intergenerational health outcomes, where a mother's weight can impact the well-being of future generations.

Furthermore, Rosberg et al. (2025), also as part of the FinnBrain cohort, examined the effects of maternal pre-pregnancy BMI on the microstructure of the hippocampus and amygdala in infants. They identified a positive association between maternal BMI and hippocampal MD, particularly in the right hippocampus. These results suggest that different brain regions may be uniquely affected by maternal obesity, emphasizing the need to study both regional specificity and long-term consequences.

Despite these advancements, significant gaps remain in our understanding of how obesity influences hypothalamic structure and function, particularly during childhood. Further longitudinal studies are needed to determine whether the associations between maternal pre-pregnancy BMI and child brain structure persist beyond the neonatal period. This could provide valuable insights into the underlying mechanisms of the global obesity epidemic and provide new strategies for prevention and potential treatment of obese young. It also remains unstudied, whether the association between maternal pre-pregnancy BMI and child hypothalamic and hippocampal MD values are specific to neonatal period or does it persist later into the childhood.

1.5 Study Objective and Hypothesis

This MD thesis is embedded in a prospective FinnBrain Birth cohort study and carried out as part of FinnBrain neuroimaging. Here, we carried out a cross-sectional study that investigates the association between child's hypothalamic MD at the age of 5 years and maternal pre-pregnancy BMI. The hypothesis for this study is that children's hypothalamic MD values at the age of 5 increase with mother's higher pre-pregnancy BMI. The covariates included child's own weight as defined by the ponderal index, which was the secondary variable of interest in the thesis. In our study, we chose to use the ponderal index instead of BMI, inspired by the findings of Peterson et al. (2017) in their study titled "Tri-Ponderal Mass Index vs Body Mass Index in Estimating Body Fat During Adolescence." This decision was based on the Tri-Ponderal Mass Index's demonstrated ability to estimate body fat percentage more accurately, particularly during adolescence, as highlighted by Peterson et al. (2017).

2 Materials and methods

The study was approved by the Ethics Committee of the Hospital District of Southwest Finland ((07.08.2018) §330, ETMK: 31/180/2011), and performed in accordance with the Declaration of Helsinki. The methods section has been described in line with prior work (Rasmussen et al., 2023).

2.1 Participants

This study used data from the FinnBrain Birth Cohort Study. FinnBrain Birth Cohort Study (www.finnbrain.fi) was established in 2011 in Turku, Finland. The cohort study investigates effects of early life stress on child brain development and health. Families involved in the study were recruited between 2011 and 2015 in the maternity clinics in Turku during the first trimester ultrasound visits. Exclusion criteria for the children were: occurrence of any perinatal complications with potential neurological consequences (e.g., hypoxia); less than 5 points in the 5 min Apgar score; previously diagnosed central nervous system anomaly or prior clinical MRI scan at peripartum due to clinical indications.

In this present cross-sectional study 147 mother child dyads with available brain MRI scan at 5 years of age, were randomly recruited from the cohort. The children were born from 2012 to 2015 and 53% of the children were boys. Data on the sociodemographic variables were drawn from the Cohort questionnaires and from the national registries. The sample closely reflects the general Finnish population. The parents gave written informed consent on their own and on their child´s behalf, and child assent was assured prior to research visits.

Variable	*n*	*% / M*	*SD*	*Minimum*	*Maximum*
Gender	*147*	*100*			
Female	*69*	*46.94*			
Male	*78*	*53.06*			
Socioeconomic status	*141*	*0.752*	*0.434*	*0*	*1*

Table 1. Gender and Socioeconomic status of Participants

Variable	*n*	*M*	*SD*	*Minimum*	*Maximum*
Age	*147*	*5.380*	*0.112*	*5.080*	*5.790*
Ponderal index	*147*	*14.082*	*1.228*	*11.212*	*17.632*

Table 2. Age and Ponderal index of Participants

2.2 Measures and procedures

Obstetric data were obtained from the Finnish Medical Birth Register of the National Institute for Health and Welfare and included age from birth and term, gestational age when born, Apgar points at 1 and 5 min, gestational weight, head circumference, maternal age in years, race/ethnicity, maternal pre-pregnancy BMI and exposure to alcohol and/or illicit substances. DTI images were obtained in conjunction with MRI imaging of the brain of newborn children. Weight of the children was also measured at 2 and 5 years of age by recording the weight data from well-baby clinic observation charts (fin. neuvolakortti).

2.3 MRI data acquisition

MRI scans were conducted on a Siemens Magnetom Verio 3T MRI scanner (Siemens Medical Solutions, Erlangen, Germany) equipped with a 12-element Head Matrix coil.

The MRI data utilized in this study was obtained from the FinnBrain Birth Cohort Study. Data pre-processing pipelines for time series correction were developed independently and performed by respective data collection sites prior to the initiation of the current study (Figure 2. Rasmussen and Tuulari (2023)). In brief, while they were broadly overlapping (FSL's *eddy* for motion and eddy current correction, *dtifit* for diffusion parameter fitting, *flirt* for spatial normalization, and image derived phenotype extraction based on a high-resolution HTH mask), they differed in approach to quality control (QC). Specifically, site 1 used a prospective data censoring approach and site 2 used a retrospective data replacement/correction approach with statistical adjustment for potential confounding, as described below. Brain masks were generated using the participant average b=0 s/mm^2 volume (site 1: range = 2–8 b0 volumes available, median = 5, site 2: 3–7 b0 volumes available, median=7). Following time series correction, all processing steps were harmonized for the purpose of this study. Scalar maps (fractional anisotropy [FA] and MD) were fit to the corrected time series using FSL's *dtifit*. Spatial registration to a common template was performed using FSL's TBSS procedure via *fnirt* in a two-stage process beginning with the generation of a sample-based template followed by non- linear registration to the sample-based template in MNI space. The adult template was used to initialize the creation of the sample template and MNI space was used as a common reference space between the templates and the probabilistic HTH mask. Finally, individualized deformation fields were then retrospectively applied to MD maps and bi-lateral median HTH MD was extracted based on the application of a binary HTH mask. The binary mask was thresholded at a value of 0.6 and median statistics were used to minimize the potential impact of partial volume effects. Qualitative assessment of registration consistency in the vicinity of the HTH was used to verify proper alignment of data across both sites.

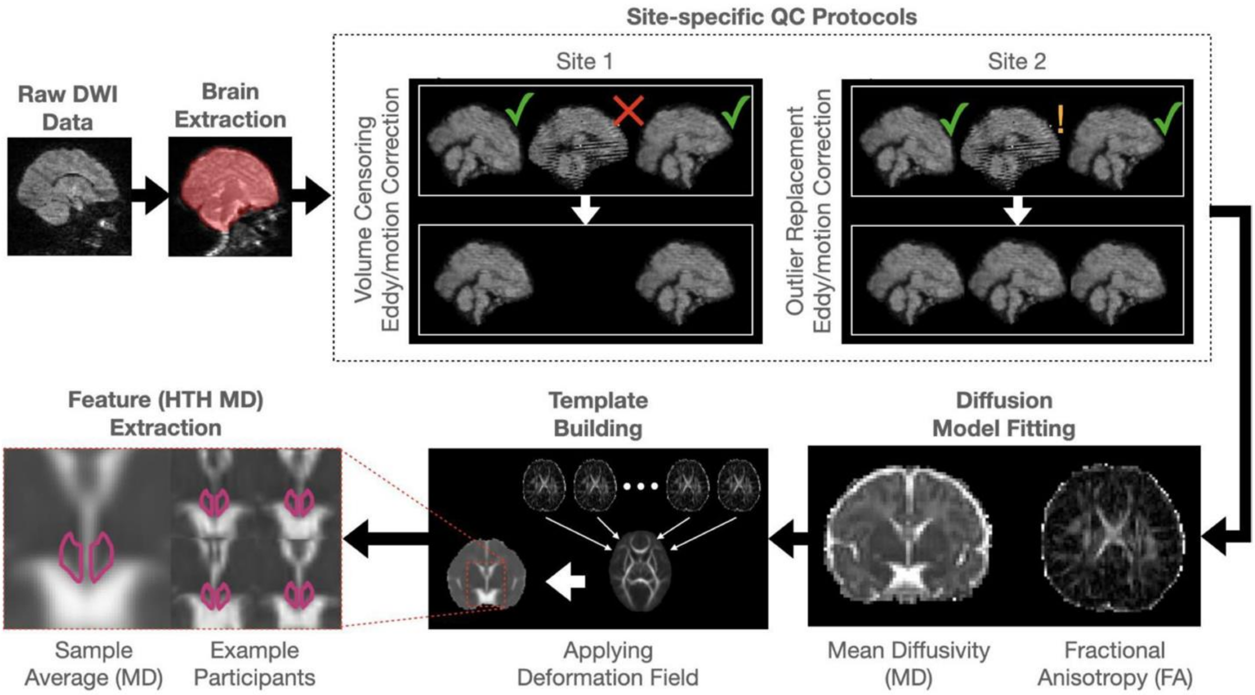

Figure 2. Site-specific image processing overview. Rasmussen and Tuulari (2023). This figure is reproduced with permission under the terms of the Creative Commons Attribution 4.0 International License, which allows use, sharing, adaptation, distribution, and reproduction, provided appropriate credit is given to the original authors and source, and any changes are noted.

2.4 Statistical analysis

All statistical analyses were performed with JASP version 0.16.2. Linear regression models were used to examine the association between ponderal index and hypothalamic MD values in 5-year-old children. The dependent variable was the hypothalamic MD value and other covariates included the maternal pre-pregnancy BMI, sex of the child, the age of the child at the time of MRI scanning, and the mother's pre-pregnancy BMI.

3 Results

Multiple linear regression was used to test if ponderal index, gender of the child, Mother's pre-pregnancy BMI and age of the child significantly predicted hypothalamic mean diffusivity values. The overall regression was not statistically significant (R^2 = [0.047], F (4, 141) = 1.729, p = 0.147). It was found in the parsimonious regression model that Ponderal index did not significantly predict MD values of the hypothalamus (ß = 0.096, p = 0.272). It was also found that gender of the child, Mother's pre-pregnancy BMI and age of the child did not significantly predict hypothalamic mean diffusivity values (p (gender) = 0.447, p (ABMI) = 0.108, p (age) = 0.058)

Regression Statistics

Model	**R**	**R^2**	**Adjusted R^2**	**RMSE**
H_0	0.000	0.000	0.000	9.025e-5
H_1	0.216	0.047	0.020	8.935e-5

Table 3. Multiple regression model. Ponderal Index and hypothalamic (HTH) mean diffusivity (MD) of the child at 5 years of age.

ANOVA

Model		Sum of Squares	df	Mean Square	F	p
H_1	Regression	5.522e-8	4	1.380e-8	1.729	0.147
	Residual	1.126e-6	141	7.984e-9		
	Total	1.181e-6	145			

Table 4. Analysis of Variance. Overall significance of the regression model in predicting hypothalamic mean diffusivity (MD) values based on the included predictors (ponderal index, gender of the child, mother's pre-pregnancy BMI, and age of the child).

Coefficients

Model		Unstandardized	Standard Error	Standardized	t	p	95% CI Lower	95% CI Upper
H_0	(Intercept)	0.001	7.469e-6		151.666	< .001	0.001	0.001
H_1	(Intercept)	4.420e-4	3.649e-4		1.211	0.228	-2.793e-4	0.001
	Age	1.272e-4	6.658e-5	0.158	1.911	0.058	-4.387e-6	2.589e-4
	Mother's pre-pregnancy BMI (ABMI)	-3.138e-6	1.940e-6	-0.141	-1.617	0.108	-6.973e-6	6.978e-7
	Gender	-1.129e-5	1.482e-5	-0.063	-0.762	0.447	-4.059e-5	1.801e-5
	Ponderal index	7.021e-6	6.367e-6	0.096	1.103	0.272	-5.567e-6	1.961e-5

Table 5. Full model. Ponderal Index and hypothalamic (HTH) mean diffusivity (MD) of the child at 5 years of age with covariates.

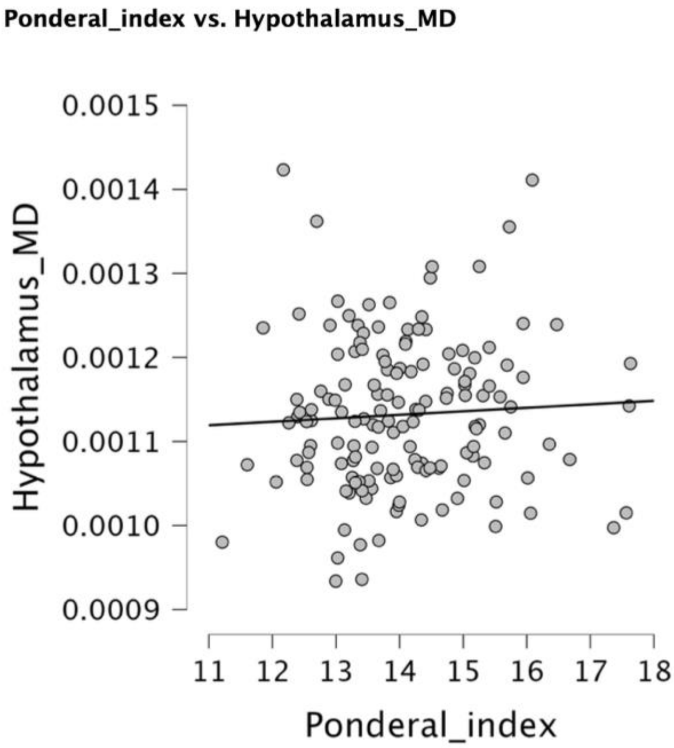

Figure 3: Ponderal index is not significantly associated with hypothalamic mean diffusivity

(ß = 0.096, p = 0.272).

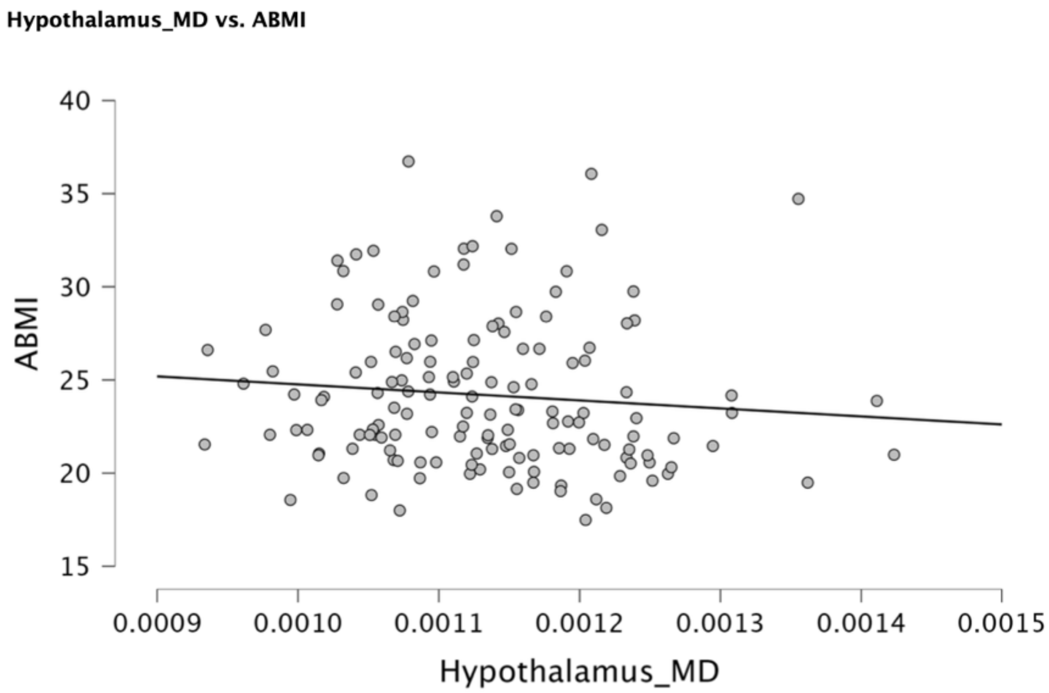

Figure 4: Mother's pre-pregnancy BMI and age of the child does not significantly predict hypothalamic mean diffusivity values (p (ABMI) = 0.108, p (age) = 0.058)

4 Discussion

4.1 Main findings

Childhood obesity is a complex and multifactorial issue that continues to draw attention globally due to its significant impact on long term health outcomes and quality of life. This study aimed to investigate the potential correlation between a child's weight at 5 years of age and the hypothalamic mean diffusivity of the brain. However, contrary to our initial hypothesis, we did not find significant correlation between these two variables. While previous research has established links between obesity and alterations in brain structure and function, including changes in grey matter volume and white matter integrity (Alosco et al., 2014; Thomas et al., 2019), our study suggests that the relationship between weight status and hypothalamic microstructure may be more nuanced than previously assumed.

The study by Rasmussen and Tuulari (Rasmussen et al., 2023) found a positive association between maternal BMI and newborn hypothalamic mean diffusivity (MD), suggesting that maternal factors may have an influence on early brain development. In our study, we examined whether this relationship persisted into early childhood but found no strong evidence of a lasting association at age five. While the observed trend was in the same direction as previous findings as expected, it did not reach statistical significance. The absence of a statistical significance may indicate that early influences on hypothalamic structure diminish over time or are shaped by other environmental and genetic factors. Rather than contradicting earlier research, these findings highlight the need for further studies to better understand how early-life exposures shape brain development across different stages of childhood. Despite the non-significant findings of our study, it is important gain more understanding of how neural function affects childhood obesity. Furthermore, it is important for clinical practitioners to identify children at risk for obesity and start intervention early to prevent obesity-related complications.

4.2 Understanding Obesity Beyond Stereotypes and Weight Stigma

In addition to obesity, weight stigma remains a widespread issue in society, with far-reaching consequences for children's physical and mental health. In society, weight stigma can be seen through negative stereotypes and discrimination directed towards overweight individuals. These biases are seen in media, cultural norms and even in healthcare, and they lead into misconceptions about the causes of obesity. Our study contributes to reinforce the idea that obesity is simply not a matter of personal choice. Weight stigma is a pervasive issue that affects individuals of all age groups, but children are particularly vulnerable because of their developmental stage. The study by Tanas (Tanas et al. 2022) highlights the detrimental impact of weight stigma on children, demonstrating its negative effects, for example unhealthy weight control behaviors, increased stress, elevated cortisol levels and depression. By researching the hypothalamic function and its connection to obesity, we can tackle weight stigma by emphasizing that obesity is not only based on individual decisions and will-power, but more over is a diverse issue that needs more research.

Healthcare providers have a crucial role in tackling the issue of weight stigma. Biases about weight and obesity can lead to false assumptions about patient's lifestyle and can prevent individuals from seeking care and so contribute to poorer outcomes in health. To combat this, healthcare providers should be educated about the complexity of obesity. Addressing obesity effectively as a medical practitioner requires a compassionate approach that considers the complex nature of the condition. It is essential to understand the health risks behind obesity and offer a broad spectrum of medical interventions including behavioral, pharmacological, and surgical options, while ensuring that care is delivered free from judgment and biases. To have successful outcomes with care it is crucial to educate and motivate the patient. Creating a supportive environment is vital for sustaining the motivation of the patient and that requires a non-judgmental approach, which is free from weight-stigma.

4.3 Strengths and limitations

Several limitations of this study should also be acknowledged. Firstly, the sample size of this study is relatively small. Future studies with larger participant numbers are needed to provide more significant information on this topic. Secondly the mean ponderal index of the participants, 14, was in relatively normal limits, with maximum ponderal index being only 17. In future studies if the participants included more severely obese children results might be more significant and results might provide a more comprehensive understanding of the relationship between childhood obesity and hypothalamic microstructure. Early identification of children at risk for obesity remains crucial. Our findings suggest that neural indicators alone may not be sufficient without more future research. Intervention strategies should now continue to focus on promoting healthy eating habits, physical activity, and mental well-being, both for the child and mothers to come.

The findings of this study highlight the complexity of the factors contributing to childhood obesity and the need for further research with larger sample sizes to understand the underlying mechanisms of this worldwide health problem. Such knowledge could provide essential insights for developing targeted interventions and preventive strategies to effectively reduce the risk of obesity in children. Addressing these limitations and building upon our findings, future research can contribute to a deeper understanding of childhood obesity.

4.4 Conclusions and future directions

This study did not find correlation between hypothalamic mean diffusivity and children's ponderal index at 5 years old. Although we hypothesized that the microstructure of the hypothalamus ponderal index would relate to ponderal index, the results suggest that the relationship between body weight and hypothalamic function may be more complex than we anticipated. Despite the lack of significant findings, this study gives valuable information to the ongoing investigation of how childhood obesity affects the developing brain.

The hypothalamus plays a key role in regulating hunger, metabolism, and energy balance in the brain, all of which are critical in the context of obesity. However, our results suggest that hypothalamic MD alone may not be a reliable marker for obesity risk in children at this young age. It remains possible that other factors, such as the duration and severity of obesity or environmental factors might mediate this relationship in ways that were not captured by this study. The relatively normal distribution of ponderal index values within our sample may have limited our ability to detect more pronounced effects on brain structure. Investigating a study population that includes children with more extreme weight variations, particularly those in higher obesity risk categories, could help clarify whether hypothalamic MD changes are present in more severely overweight or obese children.

In conclusion, more research is needed to understand the underlying mechanisms and identify more accurate predictors of obesity risk in children, so that in the future we can develop more targeted interventions to improve long-term health for children. The complexity of this issue underscores the need for more comprehensive approaches to childhood obesity in future research, including biological, social, and environmental factors. By deepening our understanding of these different factors, we can develop more effective and compassionate public health strategies to address the global obesity challenge.

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