Autism and family health: stress, eating behavior, and health in young children with ASD and their parents

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AUTISM AND FAMILY HEALTH:

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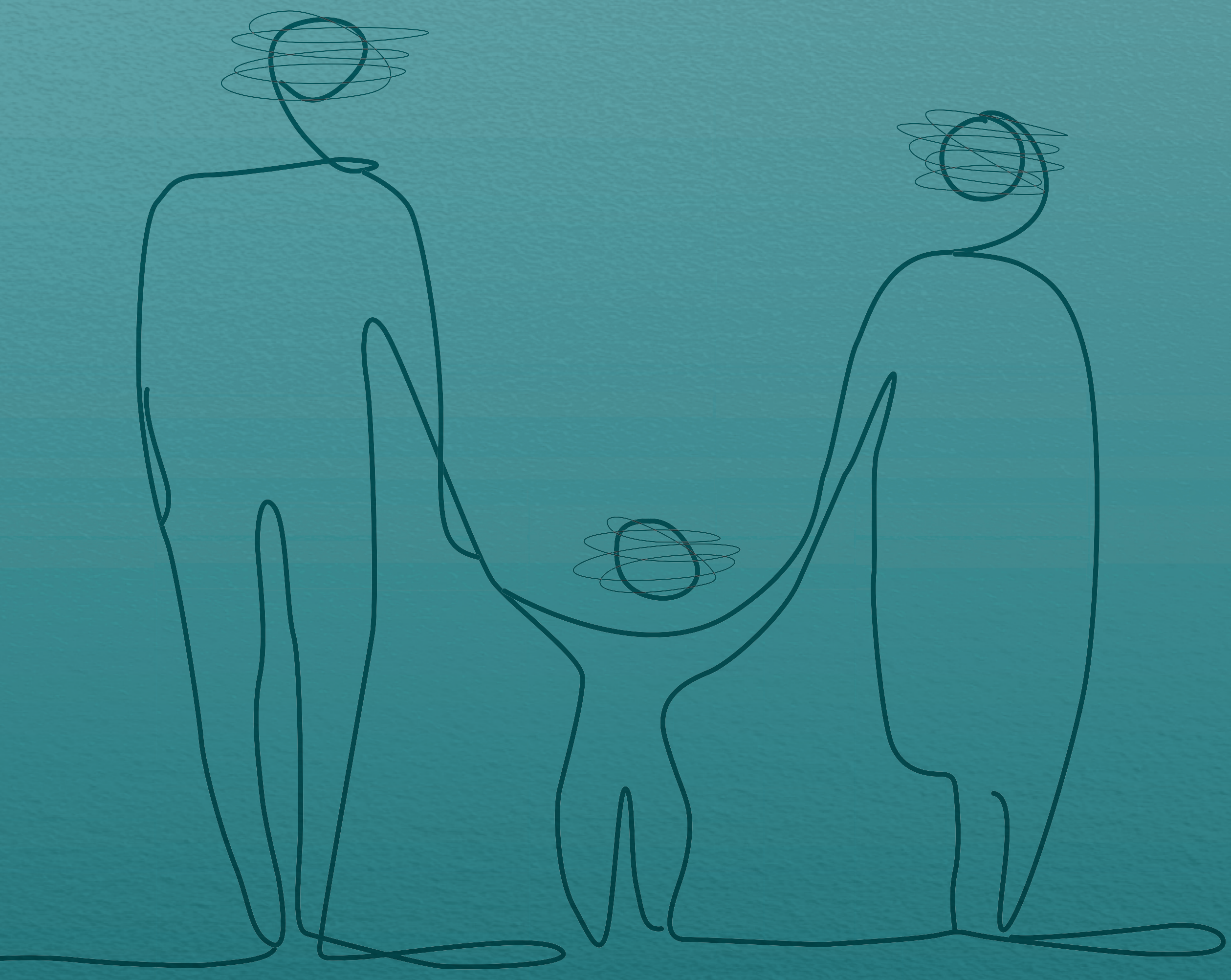

Anna van der Lubbe

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Chapter 1

General Introduction

1.1 Background

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition which is characterized by persistent deficits in social communication and interaction and the presence of restricted and repetitive behavior (American Psychiatric Association, 2013). About one in 100 children are diagnosed with ASD worldwide (Zeidan et al., 2022). Research has shown that genetic factors play an important role in autism, with both common and rare genetic variants contributing to its development (Havdahl et al., 2021). A meta-analysis of twin studies reported heritability estimates between 64% and 93% (Tick et al., 2016). Beyond the core characteristics that are outlined in the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), individuals with ASD frequently experience comorbid mental and physical health conditions (Lai et al., 2019). In addition, about one third of the individuals with ASD have co-occurring intellectual disability (Zeidan et al., 2022). While many individuals who meet the classification criteria for autism have comorbid mental and physical health problems, research into mechanisms and factors that may contribute to these additional developmental challenges in individuals with ASD is relatively sparse.

The challenges experienced by children with ASD and their parents, can significantly shape family dynamics. Difficulties in social communication, problems in interpreting social cues, and difficulty in regulating emotions, may challenge parenting and the parent-child relationship. These difficulties may coincide with high stress levels in parents, that may influence parenting behavior and may interfere with responsiveness to a child's needs (Ward & Lee, 2020). This may in turn increase stress in the child, as responsiveness and sensitivity are important in adjusting to a child's needs (Garnett et al., 2020; Ward & Lee 2020). Not only in comparison to parents of neurotypical children, but also in comparison to parents of children with chronic conditions such as cerebral palsy or Down syndrome, parents of children with ASD report higher levels of stress (Davis & Carter, 2008; Hayes & Watson, 2013). Except influencing the parent-child interaction, these high levels of stress may have negative consequences for the mental and physical health of parents of children with ASD (Dijkstra-de Neijs et al., 2020). Indeed, many studies report mental and physical health problems in parents of children with ASD (Schnabel et al., 2020; Warreman et al., 2023a). Notably, based on an Australian population study by Fairthorne and colleagues (2014), mothers of children with ASD are found to have mortality ratios that are twice as high and have a 54% higher likelihood to die from cancer compared to mothers of typically developing children. This suggests that the parents of children with ASD may have a serious health risk. Research into health risks in mothers and fathers of children with ASD, however, is sparse.

A better understanding into the relation between stress and health of children with ASD and their parents, may not only reveal mechanisms of challenged stress regulation in families of children with ASD, but may also eventually improve clinical care for children with ASD and their parents. Therefore, the studies that are part of this dissertation focus on stress in young children with ASD and their parents and the association of stress with mental and physical health.

1.2 Stress in parents of young children with ASD

Parents of children with ASD often encounter daily stressors that are related to taking care of a child with ASD. Stress is an adaptive mechanism serving as a biological response to environmental challenges, which enables individuals to respond to demanding circumstances. Although a certain amount of stress is common for all caregivers, parenting stress may shift towards chronic stress if parenting stress is persistent. Chronic stress is associated with multiple medical conditions, including obesity and metabolic syndrome (Low, Salomon, & Matthews, 2009; Tomiyama, 2019). As parents of children with ASD experience higher stress levels, they may be at risk for developing adverse health conditions. One pathway through which stress may be associated with health, is through its relationship with eating preferences. Chronic stress is associated with overeating and unhealthy eating (Adam & Epel, 2007; Torres & Nowson, 2007). Specifically, a recent meta-analysis demonstrates that stress is associated with an increased consumption of unhealthy foods and a decreased consumption of healthy foods (Hill et al., 2022). Moreover, previous research demonstrated higher levels of perceived stress, greater reward-based eating, and worse metabolic health in mothers of children with ASD compared to typically developing children (Radin et al., 2019). Based on previous research, it could be hypothesized that the high levels of mental and physical health problems in parents of children with ASD could, at least partly, be attributed to the high levels of chronic parenting stress that parents experience.

To date, most research regarding stress in parents of children with ASD is directed at mothers, while fathers are rarely included. The limited research that has been performed on fathers, suggests that fathers also experience high levels of parenting stress. For example, Davis and Carter (2008) demonstrated that 39% mothers and 28% of fathers of children with ASD scored above the 90th percentile for parenting stress. Given that both mothers and fathers play an important role in their child's life, it is important to include both parents in studies regarding parenting stress. Moreover, raising a child with ASD might affect mothers and fathers differently.

Additionally, some challenges that parents of children with ASD experience, may also be specific to the age of their child. To illustrate, some studies suggest that the level of parenting stress decreases as the child becomes older (Neece et al., 2013). Certain challenges that are specific to early childhood, may be particularly stressful for parents. For example, at this developmental stage, children have to master different developmental challenges like motor milestones, language development and learning to socially interact and meet the challenge of participation in primary education. Moreover, with the mean age of children under the age 10 receiving their diagnosis being 43.2 months, parents are often searching for the most appropriate approach for their child during this period (Van 't Hof et al., 2021). It is important to evaluate the associations between stress, eating behavior and adverse health in parents during the early developmental stage of a child, as these early associations may lay the foundation for the development of health risk of parents later in life. For example, a longitudinal study in middle-aged men showed a relationship between components of the metabolic syndrome, such as obesity, and all-cause mortality 13.6 years after the baseline measurement (Ho et al., 2008). Since the majority of research is directed at parents of children in a broader age-range, focusing on stress dynamics in parents of young children with ASD may deepen our understanding of early processes that may have lasting impact.

In summary, a gap in knowledge exists regarding stress, eating behavior and adverse health in mothers and fathers of young children with ASD.

1.3 Hair Cortisol as marker of biological Stress in parents of a child with ASD

The hypothalamic-pituitary-adrenal (HPA) axis plays an important role in the stress response by releasing cortisol during stressful situations to help to regulate stress and maintain homeostasis. On the short-term, this cortisol release can improve focus and increase alertness, providing benefits in response to environmental challenges. However, if stress becomes too strong or chronic and restoration after stress is insufficient, stress can lead to a dysregulation of the HPA-axis. The continuous high levels of cortisol may disrupt the balance of the HPA-axis, which could lead to negative health outcomes. Previous studies have related the dysregulation of the HPA-axis to adverse mental and physical health outcomes, including cardiovascular diseases, obesity, and depression (Lopez-Duran et al., 2009; van der Valk et al., 2021; van der Valk et al., 2024).

While stress is intensively investigated in parents of children with ASD, most research has focused on the self-reported stress and fewer studies have focused on (chronic) physiological stress that is associated with impact on health and wellbeing in parents of children with ASD. While self-report questionnaires are important to capture parental experiences, the use of physiological stress measures can provide a more objective understanding of the impact of parental stress in parents of children with ASD. This can be particularly useful in the understanding of the associations between stress and health in parents of children with ASD, as research in the general population associates physiological stress with various adverse health outcomes, such as abdominal obesity or cardiovascular disease (Staufenbiel et al., 2013).

The studies that compare HPA-axis activity of parents of children with ASD to parents of neurotypical children (reviewed by Padden and colleagues [2018]), demonstrate blunted cortisol responses, lower cortisol levels and lower diurnal cortisol rhythms in parents of children with ASD, which suggests a dysregulation of the HPA-axis. This pattern of blunted cortisol responses and lower cortisol levels, likely results from chronic stress and prolonged activation of the stress systems in these parents. When researching HPA-axis activity, serum and salivary cortisol are the most frequently used indicators. However, these measures present some challenges. For example, these measures reflect cortisol levels over minutes to days and are subject to variability due to factors such as circadian rhythm and food intake and, by its nature, reflect daily variability of cortisol levels that not necessarily indicate chronic stress. Cortisol levels over time are captured in hair structures, by providing a cumulative measure of cortisol over weeks to months and is less influenced by short-term fluctuations. Hair cortisol analysis therefore offers a measure of chronic stress over longer time periods. This could provide further insight into stress responses associated with challenges that are faced by parents of children with ASD. Considering that taking care of a child with ASD is a continuous responsibility, the use of hair cortisol may deepen our understanding of the physiological impact of parenting stress. Hair cortisol concentrations may be important to obtain more insights into mental and physical health dynamics in parents of young children with ASD.

To date, only one study examined hair cortisol in parents of children with ASD. Based on this study lower hair cortisol concentrations (HCC) were reported in mothers of children with ASD in comparison to mothers of typically developing children (Radin et al., 2019). However, this study only focused on mothers and did not include fathers. Additionally, this study included mothers of children in a broad age range. As the physiological responsivity to stress may change due to exposure to stress factors and to varying challenges that are associated with the developmental stage of the child, it is of value to focus on parents of children in early childhood specifically. A gap in knowledge exists regarding associations between HCC and mental and physical health of mothers and fathers of young children with ASD.

1.4 Obesity in children with ASD

Population studies show approximately two times higher morbidity and mortality rates among individuals with autism compared to the general population (Catalá-López et al., 2022; Hirvikoski et al., 2016). These higher mortality rates concern various causes of death, associated with both mental and physical conditions. Many individuals with ASD experience physical and psychological comorbidities, such as obesity, gastrointestinal problems, and problems in metabolic health (Micai et al., 2023; Sammels et al., 2022; Warreman et al., 2023b; Warreman et al., 2023c).

One condition that has frequently been associated with morbidity and mortality in the general population is obesity. Studies in non-ASD populations have associated childhood obesity with higher lifetime risk for various chronic, serious conditions, including diabetes, multiple types of cancer, cardiovascular disease, and adult obesity (Faienza et al., 2020; Hannon et al., 2005; Weihe et al., 2020). Moreover, a population study from Sweden found that individuals with obesity during childhood had three times higher risk for mortality in early adulthood compared to same-aged individuals without obesity (Lindberg et al., 2020).

Based on a recent meta-analysis it is reported that obesity rates are higher among children and adolescents with ASD (ranging from 7.9% to 31.8%), compared to those without ASD (1.4 to 23.6%) (Sammels et al., 2022). There are several factors that could play a role in connecting ASD to the higher risk for obesity. First, as many individuals with ASD have difficulties in sensory processing, some may have challenges in recognizing or interpreting hunger and satiety signals. Previous research has associated ASD with specific food approach behavior, such as eating in the absence of hunger and emotional overeating (Wallace et al., 2021). Moreover, sensory sensitivities and rigid behaviors may lead to restricted food preferences and thereby limit the exposure to a healthy, diverse diet (Baraskewich et al., 2021). In addition, many individuals with ASD experience difficulties with self-regulation, which can make it harder to regulate their eating habits (Barnard-Brak et al., 2014). Furthermore, appetite-inducing medication may also play a role in overeating in ASD (van der Valk et al., 2019). Lastly, parental stress may also play a role in obesity risk in children with ASD. As parents of individuals with ASD experience high levels of stress, it may be more difficult for them to create a healthy home environment, as they may focus primarily on managing the daily challenges that are related to having a child with ASD. Longitudinal studies in the general population demonstrated a link between parental stress and child weight, specifically in families with young children (Jang et al, 2019).

As obesity presents a significant health risk, it is important to examine obesity within the context of the health of children with ASD to understand and possibly prevent health problems in individuals with ASD. While overweight and obesity have been investigated before in individuals with ASD, the majority of studies have focused on children in a broad age range. As early development may impact the risk for obesity and other health problems in later childhood, it may be particularly relevant to study obesity during early childhood. Additionally, most studies on obesity in individuals with ASD have been conducted in the United States, where childhood obesity rates are higher compared to other Western countries (Sammels et al., 2022). Research into the obesity risk of young children with ASD in Europe is still sparse.

1.5 Stress in children with ASD

Children with ASD often struggle to adapt to changes and may perceive everyday stimuli as overwhelming, which may lead to intense and chronic stress and eventually to dysregulation of the HPA-axis. Studies in the general population demonstrate a link between stress exposure early in life and mental and physical health problems (e.g. obesity and depression) during adolescence (Danese & Tan, 2014; Hazel et al., 2008). As mentioned previously, individuals with ASD often experience additional mental and physical health issues apart from primary autism symptoms. Approximately 70% of the children with ASD are diagnosed with at least one co-morbid disorder, such as ADHD or anxiety (Mutluer et al., 2022; Simonoff et al., 2008). Additionally, studies show that compared to children from the general population, children and adults with ASD have higher rates of physical health problems, such as obesity and gastrointestinal problems (Sammels et al., 2022; Warreman et al., 2023b; Warreman et al., 2023c).

Possibly, dysregulation of the HPA-axis plays a role in the comorbid conditions that are often seen in individuals with ASD (Makris et al., 2022). For example, previous studies in non-ASD populations found an association between HPA-axis function and overweight in school-aged children and adolescents (Miller & Lumeng, 2018). As research indicates that early life stress can have an impact on the eating behavior and health of individuals, it is important to explore possible associations between stress and children's health early in life.

However, investigating stress in children with ASD can be complex. For example, some children with ASD are non-verbal, making it challenging to assess their stress levels through self-report measures. Therefore, more objective measures, such as the measurement of cortisol over a longer period of time in children with ASD can increase our understanding of stress in children with ASD. Studies comparing HCC of children with ASD to children from the general population have produced mixed findings (Lin et al., 2024; Ogawa et al., 2017). This can probably be explained by the small sample sizes that were used or by the broad age-ranges (2 to 17 years). Research regarding the associations between stress of children with autism and their parents and the health of individuals with ASD, specifically during early childhood is sparse. This is particularly important as the behavioral and emotional patterns that are formed during early childhood can have lasting effects throughout the individual's life. Therefore, a gap in knowledge exists regarding the associations between HPA-axis activity and the health of young children with ASD.

Box 1.

To illustrate the challenges that are faced by children with ASD and their parents, consider the case of Tom, a four-year-old boy diagnosed with ASD and of Emma, a five-year-old girl diagnosed with ASD. These cases demonstrate the emotional and physical stress that is experienced by parents as they try to deal with daily challenges, affecting both their child's health and the overall well-being of the family. These clinical case examples have been adapted to maintain privacy of the children.

Example 1:

Tom is a four-year-old boy who is diagnosed with ASD, which manifests in social deficits, specific habits, and routines. He often fixates on specific things and shows a strong preference for the things he is familiar with, such as his favorite toys (cars) and his favorite food. Tom also follows specific rituals throughout the day, for instance, he insists that his cars should be arranged in a precise order. If his parents touch or move his cars while tidying the living room, he dysregulates. His parents notice that Tom insists on having certain foods, crisps specifically. If Tom gets upset, he demands for crips or walks to the kitchen to take the crisps out by himself. Despite the best intentions of his parents to provide Tom with healthy food, they find it hard to, as denying his requests or taking away his food results in temper tantrums. His parents state that they do not have the energy to put up a fight so many times a day and that, while they know that complying with this eating behavior contributes to the weight gain of Tom, they view it as a temporary solution to keep Tom calm.

The parents of Tom feel overwhelmed by the constant demands that are placed on them. They experience concerns regarding the future development of Tom, particularly regarding his social ability. Due to Tom's behavior, parents avoid going to social gatherings, such as parties, as they fear that he will have temper tantrums. Parents rarely have time for themselves, and their social circle has decreased in the last few years, as they prioritize Tom's care.

Example 2:

Emma is a five-year-old girl with ASD. As she is non-verbal, she struggles to communicate her needs. Due to these communication difficulties, she often gets frustrated and ends up crying or screaming. Her parents are stressed, as they are often unsure of what Emma wants or needs. One of Emma's most notable obsessions is water: if she sees water, she gets fixated on it and tries to touch it. This requires parents to constantly supervise her, especially when outside, as she frequently attempts to approach any sources of water, such as canals or fountains. As a result, parents find it safer to stay at home, where they

are better able to control her environment. This has led to social isolation for the family.

Both of Emma's parents have demanding schedules, due to the combination of their jobs and demands in taking care of Emma. As a result, they often don't have the time or energy to cook and often order food. This has led to less healthy eating habits for the whole family. Emma also faces difficulties with eating. She does not seem to recognize when she is full and therefore, she will continue eating if food is available.

1.6 Scope and outline of this dissertation

In this dissertation we evaluate the health of young children with ASD and their parents and evaluate whether their health and eating behavior is associated with chronic stress.

In Chapter 2, results of a study are reported that addresses the questions if there are differences between mothers and fathers of children with ASD and adults from the general population regarding parenting stress, eating behavior and physical health. It is also studied whether parenting stress is associated with eating behavior and physical health in mothers and fathers of young children with ASD.

In Chapter 3, we address the question if there is an association between chronic stress (HCC) in children with ASD and chronic stress of their parents? It is also explored if chronic stress of parents is related to the mental and physical health of mothers and fathers of a child with ASD.

In Chapter 4, we report the obesity rates in a group of Dutch preschool children with ASD compared to children from the general Dutch population. Additionally, it is explored which child factors (BMI, child eating behavior and ASD severity) and which parental factors (BMI, eating behavior, parenting stress and highest completed educational level) are associated with obesity in these children.

In Chapter 5, we focus on biological stress levels of young children with ASD. The following questions are addressed: (1) Is there a difference in biological stress between children with ASD and their peers? (2) Is child biological stress associated with child mental and weight-related health? (3) Is (self-reported and biological) stress of parents associated with child mental and weight-related health?

In Chapter 6, a summary of results and a general discussion of our main findings is provided.

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Chapter 2

Stress, Eating Behavior and Adverse Health in Parents of Young Children with Autism Spectrum Disorder

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ABSTRACT

Mothers of children with Autism Spectrum Disorder (ASD) often experience chronic stress and are at risk for adverse health. However, little is known about fathers, especially when their child is in early childhood. Parenting stress, eating behavior and physical health was evaluated in mothers (n=48) and fathers (n=43) of young children (3-7 years) with ASD by questionnaires and physical measurements. Mother's prevalence rates of obesity (39.1%), abdominal obesity (59.6%) and metabolic syndrome (21.6%) were higher than the norm. In fathers, the prevalence rate of clinical parenting stress (33%) was higher than the norm. Parenting stress was positively related to disinhibited eating in mothers, not in fathers. It is crucial to monitor stress and health of parents of children with ASD.

2.1 Introduction

Parents of children with autism spectrum disorder (ASD) report considerable higher levels of stress than parents of neurotypical children and parents of children with other neurodevelopmental conditions, like Cerebral Palsy or Down Syndrome (Davis & Carter, 2008; Hayes & Watson, 2013; Hoffman et al., 2009). Stress is a biological and psychological adaption to demanding circumstances. Although a certain amount of stress is common in all caregivers, parenting stress may shift towards chronic stress if parenting stress is persistent and overwhelming. ASD is characterized by difficulties in social communication and social interaction and restricted and repetitive patterns in behaviors, interest and activities (American Psychiatric Association, 2013). Especially these core symptoms in ASD may be particularly stressful for parents. For example, studies have found high associations between experienced stress levels in parents of children with ASD and impairments in social relatedness and repetitive behaviors in the child (Davis & Carter, 2008; Gabriels et al., 2005).

Chronic stress is associated with multiple serious conditions, including obesity, metabolic syndrome and cardiovascular disease (Candola et al., 2006; Low, Salomon, & Matthews, 2009; Tomiyama, 2019). Moreover, chronic stress is related to overeating and unhealthy eating (Adam & Epel, 2007; Torres & Nowson, 2007). As parents of children with ASD experience considerable stress, they may be at risk for adverse health. Previous studies demonstrated that mothers of children with ASD reported a worse physical condition than parents of neurotypical children or children with other developmental disabilities, such as Down Syndrome (Allik et al., 2006; Fairthorne et al., 2015; Smith et al., 2013). Further insight into the connection between stress, eating behavior and adverse health may not only have implications for parents of a child with ASD, but also for parents with stress related unhealthy eating behavior in general.

Surprisingly, research into the relation between stress, eating behavior and adverse health in parents of children with ASD is sparse. A previous study showed that mothers of children with ASD report higher levels of perceived stress, greater reward-based eating and have a worse metabolic health compared to mothers of typically developing children (Radin, 2019). It was hypothesized that on the short term, chronic stress related to caring for a child with ASD promotes greater consumption of highly palatable foods in order to temporarily decrease negative affect, which may promote weight gain and subsequent worsening of metabolic components, such as LDL cholesterol, on the long-term. However, the impact of stress on eating behavior and adverse health of parents of children with ASD in early childhood is unknown, especially in fathers.

Traditionally, research on the effects of ASD in parents is directed at mothers, while fathers of these children are rarely included. Studying stress in both parents of children with ASD is important as raising a child with ASD might affect mothers and fathers differently, due to psychological, biological and social factors. First, there are differences between mothers and fathers in how they perceive their child’s problem behavior. For example, a study in parents of toddlers with ASD suggested the degree to which behavior problems and competencies are perceived as stressful varies between mothers and fathers (Davis & Carter, 2008). In addition, mothers of a child with ASD report more positive experiences compared to fathers of a child with ASD (Kayfitz et al., 2009). Second, there are biological differences between mothers and fathers. For example, a study in healthy men and women demonstrated higher hair cortisol levels in males compared to females, which may indicate a different physiological expression of long-term stress (Dettenborn et al., 2012). Lastly, raising a child with ASD might affect mothers and fathers differently due to social differences. For example, mothers of children with ASD spend 26% more time in childcare than fathers of a child with ASD, while fathers spend 41% more time in paid employment than mothers (Hartley et al. 2014). The few studies that have been performed in fathers, indicate a high level of parenting stress in fathers too: for example, Davis and Carter (2008) reported 39% of the mothers and 28% of the fathers of a child with ASD scoring above the 90th percentile for parenting stress. As mothers and fathers both play an important role in child’s life, it is important to include both parents in studies of impact of parenting stress.

As every developmental stage of a child comes with different challenges, stress experienced by parents may differ across the years. To illustrate, some studies suggest that the level of parenting stress decreases as the child becomes older (Neece et al., 2013). Some challenges that are specific to the early childhood, may be particularly stressful for parents. For example, at this developmental stage, children have to master different developmental challenges like motor milestones, language development and learning to socially interact and meet the challenge of participation in primary education. In addition, in the early school years children are often diagnosed with ASD and parents are searching for the appropriate approach for their child, since the mean age of children under the age of 10 receiving their ASD diagnosis is 43.2 months (Van 't Hof et al., 2021). Also, parents often have more than one child in their young family needing physical and emotional care during this period, while at the same time they must meet expectations in their careers as well (Frenken, 2015).

Especially during the early developmental stage of a child, it might be important to evaluate the early associations between stress, eating behavior and adverse health in parents, since these early associations may lay foundation for the health of parents later in life. To illustrate, a longitudinal study in middle-aged men showed a relationship between components of metabolic syndrome, such as obesity, hypertension and elevated cholesterol with all-cause mortality and cardiovascular mortality 13.6 years later (Ho et al., 2008). As components of metabolic syndrome, such as (abdominal) obesity, hypertension and dyslipidemia are associated with chronic stress, these components may function as an appropriate measure for stress-related health problems in parents of a child with ASD (Bergmann et al., 2014; Dijkstra- de Neijs et al., 2020). By focusing on parenting stress, eating behavior and adverse health components in parents of young children with ASD, it is possible to investigate early processes that may have lasting impact. In the current study a homogenous group of parents of young children between 3 and 7 years will be included to explore the impact of raising a young child with ASD, to investigate early associations between stress, eating behavior and adverse health.

The current study will focus on stress, eating behavior and adverse health in both mothers and fathers of young children with ASD. The first goal of the current study is to investigate whether mothers and fathers of a young child with ASD display problematic levels of stress, eating behavior and adverse health. The second goal of this study is to explore whether stress is related to eating behavior and adverse health in both mothers and fathers of a child with ASD.

2.2 Method

2.2.1 Procedure

The current study is a cross-sectional study investigating stress, eating behavior and adverse health in parents of young children with ASD. This study is part of the ongoing Tandem Study (Dutch Trial register: NL7534), a longitudinal study on the developmental impact of ASD and the effectivity of treatment, approved by the Institutional Review Board of the Leiden University Medical Center, The Netherlands.

2.2.2 Participants

Parents were recruited from Youz Parnassia Group and GGZ Delfland, both mental health care providers in The Netherlands. Parents were eligible for inclusion if: 1) their child was diagnosed with ASD and 2) their child was aged between 3 to 7 years. If parents were eligible for inclusion and agreed to be contacted by the research team, parents received an oral and written description of the study. If parents decided to participate in the study, they met with a researcher to complete the informed consent process. Data-collection took place at the study facility (Sarr Expertise Center for Autism) located in Rotterdam, the Netherlands, or at participant's homes, all located in South-Holland (see Figure 1. for a geographical map). In total, 91 parents (48 mothers and 43 fathers) of 50 children participated in this study.

Figure 1.

Geographical map of the study's location

2.2.3 Measures

2.2.3.1 Stress

Parenting stress was measured using the Parenting Stress Questionnaire (In Dutch: Opvoedbelasting Vragenlijst [OBVL]). The OBVL is a 34-item self-report measure of parenting stress (Vermulst et al., 2015). Items are answered on a 4-point Likert scale from 1 ("Not true") to 4 ("Very true"). For this study, the total score on the OBVL was used ($\alpha = .91$), in which a high score reflects a high level of parenting stress. As the response rate of fathers in the standardization study of the OBVL was minimum, the norm data of the OBVL is based on the response of mothers. For mothers and fathers in our sample, t-scores were derived from the norm tables based on data of 848 Dutch mothers of neurotypical children aged between 0 and 11 years (Vermulst, 2015). Based on their t-scores, parents were classified in one of the three following categories 1) Normal (t-score < 60), 2) Sub-clinical (t-score = 60-63) and 3) Clinical (t-score ≥ 64).

2.2.3.2 Eating Behavior

Eating behavior was measured using the Dutch Eating Behaviour Questionnaire (DEBQ). The DEBQ is a 33-item self-report measure of eating behavior consisting of 3 subscales: Emotional eating, External eating and Restrained eating (van Strien, 2015). The subscale 'Emotional eating' refers to eating in response to emotions (e.g., 'do you have the desire to eat when you are anxious, worried or tense?'). The subscale 'External eating' refers to eating in response to external food cues (e.g., 'If you walk past a snackbar, do you have the desire to buy something delicious?'). The subscale 'Restrained eating' refers to limiting food-intake to lose weight (e.g., 'Do you deliberately eat less in order not to become heavier?'). Items are scored on 5-point Likert scale from 1 ("never") to 5 ("very often"). Higher subscale scores indicate a higher level of emotional, external, or restrained eating. Cronbach's alpha value is .96 for Emotional eating, >.78 for External eating and >.90 for Restrained eating. Based on existing norms, participants were classified into two categories: 1) Normal and 2) High (≥ 80th percentile). Age and gender-appropriate norms were used of males (n = 815) and females (n = 921) aged between 21 and 70 years from the Dutch general population (van Strien, 2015).

2.2.3.3 Body Mass Index, Waist Circumference and Blood Body Pressure

Body height was measured by a stadiometer (Seca 213) and weight by a digital scale (Seca Clara 803). Body Mass Index (BMI) was calculated by dividing weight in kilograms by the square of height in meters. Participants were classified into three BMI classes: normal weight (<25 kg/m2), overweight (25-30 kg/m2) and obesity (≥30 kg/m2). The percentage of participants in each category was compared to Dutch males aged 18-59 (n = 27991) and Dutch females aged 18-49 (n = 29650) from the population-based Lifelines Cohort Study (Slagter et al., 2017).

Waist circumference (cm) was measured at the lowest point of the lowest rib and the upper border of the pelvic crest using a measuring tape. Waist circumference was also used to measure abdominal obesity. Abdominal obesity was defined according to the recommendations of the World Health Organization (WHO), with a waist circumference of 102 cm or higher for males and 88 cm or higher for females (WHO, 2008). The percentage of participants in each category was compared to Dutch males aged 18-59 (n = 27991) and Dutch females aged 18-49 (n = 29650) from the population-based Lifelines Cohort Study (Slagter et al., 2017).

We measured systolic and diastolic blood pressure using a blood pressure monitor (Omron M6). During the blood pressure measurement, parents were asked to sit still and to not speak. Blood pressure measures were done twice, and the average of the two measures was calculated. We used systolic and diastolic blood pressure to define an elevated blood pressure as follows: systolic blood pressure ≥130 OR/AND diastolic blood pressure ≥85 AND/OR use of antihypertensive drugs. Prevalence rates of elevated blood pressure in our sample were compared with prevalence rates from Dutch males aged 18-59 (n = 27991) and Dutch females aged 18-49 (n = 18-49) from the LifeLines cohort study (Slagter et al., 2017).

2.2.3.4 Cholesterol, triglycerides, and glucose

To measure cholesterol, triglycerides and glucose values, blood samples (18 ml) were drawn from participants by a phlebotomist. Parents were instructed to not eat or drink anything other than water for 8 hours before the blood test. After collection, the samples were sent to the Ijselland Hospital for laboratory analysis.

2.2.3.5 Metabolic syndrome

According to the R-NCEP-ATPIII (R-APTIII), at least three of the five metabolic risk components need to be present to diagnose MetS (Grundy et al., 2005). These metabolic risk components include: (1) elevated waist circumference (≥ 102 cm in men, ≥ 88 in women), (2) elevated triglycerides (≥ 1.7 mmol/L) and/or use of triglyceride-lowering medication-lowering medication (3) reduced HDL Cholesterol (< 1.03 mmol/L in men, < 1.3 mmol/L in women) and/or use of lipid-lowering medication, (4) elevated blood pressure (systolic blood pressure ≥130 OR/AND diastolic blood pressure ≥85 AND/OR use of antihypertensive drugs) (5) elevated fasting glucose (≥ 5.6 mmol/L) and/or use of glucose-lowering medication. We compared prevalence rates of metabolic syndrome in our sample with the prevalence rates of metabolic syndrome in same-aged males and females from the Dutch Lifelines cohort study (Slagter et al., 2017).

2.2.3.6 Smoking behavior

To estimate smoking behavior, parents filled in a demographic questionnaire. Participants were asked whether they smoked. Three answer options were possible: 1) Yes 2) No, I never smoked and 3) No, I stopped. If parents indicated to smoke, they were asked how many cigarettes they smoke during a day. If parents stopped smoking, they were asked for how long they smoked and how many cigarettes per day they smoked. Smoking status was compared to the percentage of smokers in males and females aged 18-79 from the population-based Lifelines Cohort study (Slagter et al., 2017).

2.2.3.7 Demographic variables

Parental educational levels were obtained by questionnaire and categorized as follows: low (primary education, lower vocational secondary education or lower secondary education), middle (intermediate vocational education, intermediate secondary education and higher Secondary education) and high (higher vocational education and university). Parents also filled in their marital status (married/cohabiting versus single parent), who was the primary caregiver and whether they had paid employment.

2.2.3.8 Measurements before or during COVID-19

As measurements in part of our sample were taken during the COVID-19 outbreak, we included an extra variable to control for this. In the Netherlands, the government took measures, including closing of all primary schools, on March 15th 2020 to prevent the further spread of COVID-19. All parents who filled in the questionnaires before March 15th 2020 were considered 'Before COVID-19' and all parents who filled in the questionnaires from March 15th 2020 were considered 'During COVID-19'.

2.2.4 Statistical analyses

The variables 'OBVL total', 'NVE emotional eating', 'NVE restrained eating', 'cholesterol HDL' and 'Triglycerides' were not normally distributed. Therefore, non-parametric tests were performed to evaluate these variables.

To control for parenting stress due to COVID-19, we tested whether there were differences in parenting stress between parents who participated before COVID-19 and during COVID-19 using a Mann-Whitney U test.

If height or weight data were missing, the missing value was replaced by the self-reported height and weight of the participant. Self-reported height and self-reported weight strongly correlated with measured height ($r = .98$, $p < .001$) and weight ($r = .97$, $p < .001$) in participants of which we had both self-reported and measured height ($n = 68$) and weight ($n = 64$). For the other variables, missing values were treated using pairwise deletion.

To investigate whether mothers and fathers of a young child with ASD display problematic levels of stress, eating behavior and adverse health, we used Chi-Square Goodness of Fit tests were performed to determine whether the proportion of parents scoring above a certain cut-off was different from the general population. For parenting stress, we also performed a Mann-Whitney U test to test whether there were differences in parenting stress (OBVL) between mothers and fathers of a young child with ASD regarding parenting stress.

To investigate whether stress is related to eating behavior and adverse health, we performed a Pearson's correlation analysis. For the variables that were not normally distributed, we performed a Spearman's correlation analysis. All analyses were performed in SPSS Statistics 25.

2.3 Results

2.3.1 Descriptives

In total, 91 parents (48 mothers and 43 fathers) of 49 young children with ASD (3-7 years) participated in the study. Parents were aged between 23 and 58 years old (*Mean*

= 34.9, sd = 6.0). The mother was the primary caregiver in 48 families (98%) and the father was the primary caregiver in 1 family (2%). Parents were married or co-habiting in 36 families (73.5%), the parent was a single parent in 8 (16.3%) of the families and marital status was missing in 5 families (10.2%).

Three (6.3%) mothers had a low educational level, 21 (43.8%) had a middle educational level and 14 (29.2%) had a high educational level and highest completed education was missing in 10 mothers (20.8%). In fathers, highest completed education was low in 9 (20.9%), middle in 17 (39.5%) and high in 9 (20.9%) and educational level was missing in 8 (18.6%). In total, 75% of the mothers and 97.7% of the fathers had paid employment.

In total, 36 (73.5%) families participated before COVID-19 and 13 families (16.3%) participated after COVID-19. There was no difference in parenting stress between parents who participated before COVID-19 and after COVID-19, ($U = 520,5$, $z = -.68$, $p = .50$). To our knowledge, one mother in our sample was pregnant during this study. However, excluding this mother from analysis did not make a difference in results regarding obesity and waist circumference. Therefore, analyses were performed including this mother.

2.3.2 Stress in Mothers and Fathers of a Child with ASD

2.3.2.1 Stress

As shown in Table 1, more than half of the mothers of a child with ASD scored above the 90th percentile for parenting stress, which is significantly more than mothers of neurotypical children ($\chi^2(2) = 83.88, p < .01$). In addition, 33% of the fathers in our sample scored above the 90th percentile for parenting stress, which is threefold the number of the reference mothers from the general population ($\chi^2(2) = 24.42, p < .01$). Within our sample, mothers (Median = 63.5, IQR = 21) reported significantly more parenting stress ($U = 522,5$, $z = -2.34$, $p = .02$) than fathers (Median = 55.5, IQR = 15.13).

2.3.2.2 Eating behavior

As shown in Table 1, there was no significant difference in prevalence rates of emotional eating, external eating, and restrained eating between parents of a child with ASD and same-aged individuals in the Dutch Lifelines cohort study.

2.3.2.3 Adverse health

As displayed in Table 1, more than 39% of the mothers in our sample were obese. This percentage is almost three times the percentage of obesity in same-aged females from the Dutch Lifelines cohort study ($\chi^2(2) = 23.03, p < .01$). In addition, almost 60% of the mothers of a child with ASD had abdominal obesity, which is about 1.5 times more often than females from the Lifelines cohort study ($\chi^2(1) = 10.25$, $p < .01$). Furthermore, approximately *22%* of the mothers in our sample fulfilled criteria for metabolic syndrome (at least three of the five metabolic risk components), which was about 2.5 times higher than in same-aged females from the Dutch Lifelines cohort study ($\chi^2(1) = 8.40, p = <.01$). There was no significant difference in prevalence of an elevated blood pressure ($\chi^2(1) = .37, p = .54$) *or* smoking status ($\chi^2(1) = .46, p = .50$) between mothers in our sample and the females from the Lifelines Cohort study.

In fathers, there were no significant differences between fathers in our sample and same-aged males from the Lifelines cohort study regarding obesity ($\chi^2(2) = 3.61$, $p = .17$), abdominal obesity ($\chi^2(1) = .59$, $p = .11$) blood pressure ($\chi^2(1) = 2.06$, $p = .15$), metabolic syndrome ($\chi^2(1) = .53$, $p = .47$) and smoking status ($\chi^2(1) = .88$, $p = .35$).

Table 1.
Stress, eating behavior and adverse health in parents of a child with ASD compared to males and females from the general population.

	Parents of child with ASD N	%	Norm group %	Chi-square	*p*	Comparison group
Stress						
Parenting stress (OBVL)						
Mothers				83.88	**<.001**	Dutch mothers (n = 848) of neurotypical children aged between 0-11 (Vermulst, 2015).
Normal (t-score < 60)	13	31	85			
Sub-clinical (t-score 60-63)	7	16.7	5			
Clinical (t-score ≥ 64)	22	52.4	10			
Fathers				24.42	**<.001**	Dutch mothers (n = 848) of neurotypical children aged between 0-11 (Vermulst, 2015).
Normal (t-score < 60)	17	47.2	85			
Sub-clinical (t-score: 60-63)	7	19.4	5			
Clinical (t-score ≥ 64)	12	33.3	10			
Eating behavior						
Emotional eating (NVE)						
Mothers				.95	N.S.	Females (n = 1143) from the Dutch general population aged between 21 and 70 years (van Strien, 2015)
Normal	31	73.8	80			
High (≥ 80th percentile)	11	26.2	20			
Fathers				2.97	N.S.	Males (n = 807) from the Dutch general population aged between 21 and 70 years (van Strien, 2015)
Normal	33	91.7	80			
High (≥ 80th percentile)	3	8.3	20			
External eating (NVE)						
Mothers				1.82	N.S.	Females (n = 1143) from the Dutch general population aged between 21 and 70 years (van Strien, 2015)
Normal	30	71.4	80			
High (≥80th percentile)	12	28.6	20			
Fathers				.55	N.S.	Males (n = 807) from the Dutch general population aged between 21 and 70 years (van Strien, 2015)

Normal	27	75	80			
High (≥80th percentile)	9	25	20			
Restrained eating (NVE)						
Mothers				.29	N.S.	Females (n =1143) from the Dutch general population aged between 21 and 70 years (van Strien, 2015)
Normal	35	83.3	80			
High (≥80th percentile)	7	16.7	20			
Fathers				.11	N.S.	Males (n = 807) from the Dutch general population aged between 21 and 70 years (van Strien, 2015)
Normal	28	77.8	80			
High (≥80th percentile)	8	22.2	20			
Adverse health						
Body Mass Index						
Mothers				23.03	**<.001**	Dutch females (n = 29650) aged 18-49 from the population-based LifeLines cohort study (Slagter et al., 2017)
Normal weight	18	39.1	55.9			
Overweight	10	21.7	29.8			
Obesity	18	39.1	14.3			
Fathers				3.61	N.S.	Dutch males (n = 27991) aged 18-59 from the population-based LifeLines cohort study (Slagter et al., 2017).
Normal weight	11	26.2	40.6			
Overweight	24	57.1	46.5			
Obesity	7	16.7	12.9			
Waist circumference						
Mothers				10.25	**<.01**	Dutch females (n = 29650) aged 18-49 from the population-based LifeLines cohort study (Slagter et al., 2017)
Abdominal obesity	28	59.6	37			
Fathers				.59	N.S.	Dutch males (n = 27991) aged 18-59 from the population-based LifeLines cohort study (Slagter et al., 2017).
Abdominal obesity	11	26.8	21.9			
Blood pressure						
Mothers				.37	N.S.	Dutch females (n = 29650) aged 18-49 from the population-based LifeLines cohort study (Slagter et al., 2017)
Elevated blood pressure	12	25.5	21.8			
Fathers				2.06	N.S.	Dutch males (n = 27991) aged 18-59 from the population-based LifeLines cohort study (Slagter et al., 2017).
Elevated blood pressure	25	61	49.7			

Metabolic syndrome						
Mothers				8.40	**<.01**	Dutch females (N = 29650) aged 18-49 from the population-based
Yes	8	21.6	8.4			LifeLines cohort study (Slagter et al., 2017).
Fathers				.53	N.S.	Dutch males (N = 27991) aged 18-59 from the population-based
Yes	7	22.6	17.6			LifeLines cohort study (Slagter et al., 2017).
Smoker						
Mothers				.46	N.S.	Dutch females (n =41075) aged 18-79 from the population-based
Yes	11	23.9	19.9			LifeLines cohort study (Slagter et al., 2017).
Fathers				.88	N.S.	Dutch males (n = 32189) aged 18-79 from the population-based
Yes	12	30	23.7			LifeLines cohort study (Slagter et al., 2017).

2.3.3 Stress in Mothers and Fathers of a Child with ASD

As shown in Table 2, mothers who reported a higher level of parenting stress, reported a significantly higher level of emotional eating (r = .53, p <.01) and external eating (r = .47, p <.01). This association was not found in fathers. There was no significant relationship between parenting stress and adverse health outcomes in mothers or fathers.

Table 2.
Correlations between stress, eating behavior and metabolic health in mothers and fathers of children with ASD within the Tandem study (n = 91).

	Mothers Parenting stress (OBVL)	Fathers Parenting stress (OBVL)
Emotional eating (NVE)[a]	.53**	.05
External eating (NVE)	.47**	-.03
Restrained eating (NVE)[a]	-.14	-.02
BMI	-.16	.13
Waist	-.19	.18
Systolic blood pressure (BP)	-.15	.23
Cholesterol HDL (HDL)[a]	.11	-.06
Triglycerides (Tri)[a]	-.20	.14
Glucose	-.19	-.12

[a]Variable was non-normality distributed, Spearman's correlation coefficients are displayed. *$p < .05$, **$p < .01$

2.4 Discussion

The goal of the current study was to investigate whether mothers and fathers of a young child with ASD display problematic levels of stress, eating behavior and adverse health and evaluate whether parental stress is associated with eating behavior and adverse health. While mothers of a young child with ASD experienced clinical parenting stress (above 90th percentile) five times more often than mothers of neurotypical children, this was three times more often in fathers. Regarding adverse health of mothers in our sample, prevalence rates of obesity (39.1%), abdominal obesity (59.6%) and metabolic syndrome (21.6%) were higher than in same-aged females from the general population. Interestingly, although fathers experienced higher stress as well, there were no significant differences between fathers and the general population regarding adverse health. Parenting stress was related to more emotional eating and external eating in mothers, but not in fathers.

In line with earlier studies, parents of a young child with ASD reported more parenting stress than parents of typically developing children. A meta-analysis by Hayes and Watson (2013), performed in parents of children of all ages, showed a higher experienced parenting stress in parents of a child with ASD than parents of typically developing children or children with another disability. The present study demonstrates that parents of a young child with ASD do not only experience a higher level of parenting stress on average, but also 52% of the mothers and 33% of the fathers of a young child with ASD score above the 90th percentile for parenting stress. While Davis and Carter (2008) reported a similar pattern, the percentages of clinical parenting stress in the study of Davis and Carter are somewhat lower, with 39% of the mothers and 28% of the fathers of a child with ASD scoring above the 90th percentile for parenting stress. Explanatory factors are: the children in the study of Davis and Carter were younger (between 18 and 33 months of age) than the children of the parents in our sample (between 36 and 72 months of age). As each developmental stage of a child comes with different challenges for parents, their experienced stress may differ across the years. Also, all families in the study of Davis and Carter had already received intensive intervention for autism (on average 2 months prior to joining the study), which may have decreased parenting stress in some parents.

To our knowledge, this study is the first study to demonstrate that mothers of a young child with ASD demonstrate higher rates of obesity and metabolic syndrome compared to the general population. This finding is relevant, as having obesity and metabolic syndrome substantially increases the risk for chronic diseases, such as cardiovascular disease and some types of cancer (Blüher, 2019; Galassi et al., 2006). Fairthorne and colleagues (2014) showed higher mortality hazard ratios in mothers of children with ASD and higher likelihood to die from cancer compared to mothers of typically developing children and hypothesized that this association may be mediated by increased stress levels in these mothers or maternal conditions, such as obesity. In line with that hypothesis, our study demonstrated higher rates of obesity and metabolic syndrome in mothers of a child with ASD. Possibly, the high level of stress experienced by the parents in our sample could have contributed to more aberrant eating behavior, leading to weight gain and metabolic health problems, as previous studies suggested a causal relationship between stress and weight gain. (Adam & Epel, 2007; Torres & Nowson, 2007; Wardle et al., 2011). However, based on the data of the current study, we cannot draw conclusions regarding causality of the relationships. Another possibility is that the mothers in our study were already obese before they were pregnant. A meta-analysis by Lei and colleagues (2018) demonstrated an association between maternal obesity before pregnancy and an increased risk for ASD in the child. However, the prevalence rates of maternal obesity before pregnancy in mothers of a child with ASD were lower in the meta-analysis of Lei and colleagues (ranging from 9-32%) than the obesity rates in the current study. It is likely that the high prevalence rates in the mothers in our study is due to a combination of the two: prevalence rates of obesity might have been already increased before mothers were pregnant, and mothers may have gained weight after their child was born due to stress.

The current study was the first study to investigate adverse health in fathers of a child with ASD using physiological measures. Although we did not find a higher risk of obesity, hypertension, and metabolic syndrome in fathers of a young child with ASD than same-aged males from the general population, this does not automatically mean that fathers do not have a higher risk for adverse health. There are some other possible explanations for this finding. First, fathers of children with ASD spend approximately 26% less time in childcare than mothers (Hartley et al., 2014). Therefore, fathers could be less exposed to parenting stress than mothers. Second, fathers may have different coping mechanisms than mothers with different effects on their health. While some mothers may use (over)eating as a coping mechanism for stress, fathers may have other ways to cope with parenting stress, such as spending time in paid employment. For example, a Swedish study found a positive association between paid-employment and psychological well-being in fathers of children with an intellectual disability (Olsson & Hwang, 2006). Lastly, the observed differences between fathers of a young child with ASD and the general population may increase over time, as stress can have a long-term impact on the health via alterations in the immune system and microbiome imbalance (reviewed by Dijkstra – de Neijs et al., 2020). Therefore, it would be relevant to follow-up the fathers in our sample in a few years to investigate whether the difference between fathers of a child ASD with and the general population has increased. In addition, our finding that one third of the fathers in our sample experienced a clinical level of stress, underlines the need to draw more attention to the well-being of fathers of children with ASD in research and clinical practice.

We found a positive association between parenting stress and emotional and external eating in mothers of a young child with ASD, which is in line with earlier studies which indicated that ongoing stress can lead to chronically stimulated eating behavior (Groesz et al., 2013; Sominsky & Spencer, 2014). Previously, Radin and colleagues (2019) demonstrated a higher level of stress-related eating in parents of a child with ASD than in parents of typically developing children. Radin and colleagues (2019) theorized that chronic stress related to caring for a child with ASD may promote eating behavior on the short term, which may contribute to weight gain and worsening of metabolic components on the long-term. The current study is in line with Radin and colleagues (2019) by demonstrating a positive relationship between parenting stress and emotional eating (eating in response of emotions) and external eating (eating in response of external stimuli) in mothers of a young child with ASD. In addition, the higher rates of obesity and metabolic syndrome in mothers of a child with ASD display the same pattern as theorized by Radin and colleagues. However, as we cannot make causal conclusions based on our data, we encourage future studies to further investigate these trajectories longitudinally.

The current study had some limitations. First, the design of this study was cross-sectional and therefore, we were not able to draw causal conclusions about the development of stress and adverse health in parents of a child with ASD. Another limitation of the study was that we did not have a control group. Therefore, we used information provided by existing norm-groups or databases, which had a few drawbacks. For example, as the norm group on the OBVL consisted of mothers only, we had to compare parenting stress of fathers of children with ASD with mothers of neurotypical children. As there was no specific information available regarding family composition in the Lifelines Cohort Study, we can only draw conclusions about the difference between mothers in our sample and women from the general population (with and without children). Previous studies show that becoming a mother is associated with a larger increase in weight than remaining childless (Corder et al., 2019). However, an American National Health study did not find a difference between mothers with a young child (aged 0-5 years) versus women without children (Neshteruk et al., 2022). Given the large differences we found between mothers in our sample and the comparison group and the results from previous studies, we think it is very likely that the differences we found can (partly) be attributed to being a parent of a child with ASD specifically. Strengths of the current study were, firstly, the integrated approach, in which concurrently mental- and physical measures were examined. Such an approach allows us to not only measure experiences of parents, but also to measure adverse health in these parents by physiological measurement. A second strength of this study is that it also included fathers, which helped us to increase our knowledge of risk for stress in families of children with ASD. Lastly, all parents participating in this study had a child between 3 and 7 years old who recently received a diagnosis, which enables us to investigate the early dynamics of stress, eating behavior and adverse health in parents of a child with ASD.

In conclusion, the current study evaluated the level of stress, eating behavior and adverse health in parents of a young child with ASD at the age of 3 until 6 years. Considering more than half of the mothers and a one third of the fathers of a young child with ASD experience a clinical level of parenting stress, parents of young children with ASD are an at-risk group for stress. In mothers, we found higher rates of obesity and metabolic syndrome compared to the general population and a correlation between parenting stress and displayed eating behavior. Although we cannot make any causal conclusions based on cross-sectional data, these high parenting stress levels in both parents in combination with the high rates of obesity and metabolic syndrome in mothers are alarming. While most mothers in our sample are between 25 and 40 years old, they already display health problems which put them at higher risk for serious health conditions later in life. It could be theorized that stress, disinhibited eating behavior and adverse health in mothers are interrelated to each other: mothers may use eating as a strategy to cope with their stress, leading to weight gain and adverse health later in life. However, this should be studied longitudinally to test for causal relationships. Even though we did not find adverse health problems in fathers in the current study, this does not mean fathers are not at-risk for developing health problems, as there may be health risks that could emerge later in life. We did find a clinical level of parenting stress in one third of the fathers, which emphasizes the necessity to draw more attention to fathers in research and clinical practice, which is currently often predominantly directed at mothers. In addition, given the high level of stress in both parents, it is important to specifically target parenting stress when treating ASD, for example using group therapy for parents directed at reducing stress and preventing health problems by promoting a healthy lifestyle.

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Chapter 3

Chronic Parenting Stress in Parents of Children with Autism: Associations with chronic stress in their child and parental mental and physical health

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ABSTRACT

Purpose: Parents of children with ASD often demonstrate high levels of stress and associated health problems. A gap in knowledge exists regarding the associations between chronic stress and mental and physical health of parents of young children with ASD, in which fathers have been understudied.

Method: In 181 parents (98 mothers, 83 fathers) of 99 young children with ASD chronic stress was measured using parental self-report and hair cortisol concentration (HCC) analysis. Parental mental health and eating behavior was measured using questionnaires. Physical health was evaluated by Body Mass Index, waist circumference, blood pressure, cholesterol, triglycerides, and glucose.

Results: Parental HCC was related with child HCC ($r_{mothers} = .51$, $p < .01$; $r_{fathers} = .40$, $p < .01$). Maternal HCC was associated with lower reported parenting stress ($r = -.33$, $p < .01$). Parental mental health problems and reported parenting stress were strongly related ($r = .55$-$.61$, $p < .01$). Mental health problems were twice as frequent as in the norm-population (41.1-45.8% versus 20%). In both parents, reported parenting stress was associated with emotional eating behavior. HCC was associated with higher glucose levels in mothers. There were no associations between chronic stress and the other physical health measures in mothers and fathers.

Conclusion: Parents of young children with ASD are at high risk for chronic stress, with impact for their mental and physical health. Additionally, chronic stress of parents, cannot be perceived isolated from the stress in their children with ASD. We encourage future research to investigate whether these correlations are generalizable to the whole ASD population.

3.1 Introduction

Parents of children with autism spectrum disorder (ASD) often report considerably higher levels of stress than parents of neurotypical children and parents of children with other neurodevelopmental disorders, such as Down syndrome (Hayes & Watson, 2013; Warreman et al., 2023). Although stress in parents of children with ASD has been intensely investigated, most research has focused on the impact of subjective reports of stress. For example, perceived stress has been associated with a higher number of reported physical health problems and with a poorer health-related quality of life in parents of children with ASD (Reed et al., 2016). However, fewer studies have focused on physiological stress in parents of children with ASD. There is a gap in knowledge regarding the associations between chronic stress and the psychological and physical health of parents of young children with ASD, specifically in fathers.

Therefore, the current study will investigate associations between chronic stress in mothers and fathers of young children with ASD and their children and explore associations between chronic stress and mental and physical health in parents of children with ASD. We will give a short literature overview regarding the functioning of the HPA-associations between chronic stress in parents and stress in their children, associations between chronic stress and mental health of children with ASD and associations between chronic stress and physical health of parents of children with ASD.

3.1.1 Stress in parents of children with ASD

Previous research indicates that parents of children with ASD experience unique stressors that can significantly impact their overall well-being and family dynamics. The family system, such as the role of spouses, living conditions and social support may influence how stress affects parents of children with ASD. For example, previous studies have demonstrated an association between social support and lower levels of parenting stress, lower levels of depression and higher levels of parenting efficacy in parents of children with ASD (Ekas et al., 2010; Karst & van Hecke, 2012; Weiss, 2002). Also, families with limited socio-economic resources, poor living conditions, or weak social support networks may experience higher levels of stress (Eisenhower, Baker, & Blacher, 2005; Hayes & Watson, 2013). Parents with pre-existing psychiatric conditions might find it even more challenging to cope with the demands of raising a child with ASD, with possible effects for their mental and physical health (Olsson & Hwang, 2001). Understanding these nuanced impacts of stress is crucial for the improvement of clinical care and well-being of these families (Karst & van Hecke, 2012; Padden & James, 2017).

3.1.2 The function of the HPA-axis

A certain amount of stress is common in all individuals. The cumulative effect of experiences in daily life, as well as major challenges, is often referred to as allostatic load. However, when an individual's capacity to deal with those challenges in daily life is exceeded, this leads to allostatic overload where stress response systems are repeatedly activated (McEwen & Stellar, 1993; McEwen & Wingfield, 2003). The hypothalamic-pituitary-adrenal (HPA) axis plays a crucial role in maintaining homeostasis after stress. The HPA-axis is activated during stressful situations and forms a chain-reaction, resulting in release of the glucocorticoid cortisol. Although HPA-axis responsivity is an important mechanism in coping with challenges, chronic stress may impact adaptive functioning in response to demanding situations and may even result in impact for mental and physical health. Higher HPA-axis activity over time, indicated by higher scalp hair cortisol concentrations (HCC), has been associated with various indices of chronic stress (Dettenborn et al., 2010; Kalra et al., 2007; Staufenbiel et al, 2013, Steudte et al., 2011). Moreover, higher HCC have been associated with physical health problems, including abdominal obesity or cardiovascular disease (as summarized in Dijkstra et al., 2020; Kuckuck, Lengton et al., 2023; van der Valk et al, 2022).

Studies comparing the HPA-axis regulation activity of parents of children with ASD to parents of neurotypical children (reviewed by Padden and colleagues [2018]), demonstrated blunted cortisol responses, lower cortisol levels and lower diurnal cortisol rhythms in parents of children with ASD, indicating dysfunctional

HPA-axis regulation. However, most studies that have focused on HPA-axis activity in parents of children with ASD, have focused on short-term HPA-axis reactivity. Given that caring for a child with ASD is a long-term responsibility, investigating long-term HPA-axis activity may increase our understanding of the dynamics between chronic stress, mental health, and physical health in parents of children with ASD.

To date, to our knowledge, only one study investigated long-term HPA-axis activity in parents of children with ASD. This study demonstrated lower HCC in mothers of children with ASD compared to mothers of typically developing children (Radin et al., 2019). However, this study included mothers of children in a broad age range, while the physiological expression of stress may change over time, due to different developmental challenges or changes in the physiological reaction to stress. In addition, as this study has solely focused on mothers, the physiological expression of stress in fathers of children with ASD is unknown.

3.1.3 Associations between chronic stress in parents and children

Chronic stress in parents of children with ASD may also be associated with stress in their children. For example, a previous study in mothers of infants showed that mothers with higher HCC showed more intrusive behavior and had lower engagement with their infants (Tarullo et al., 2017). In addition, infants of mothers with higher HCC had higher salivary cortisol concentrations. Other studies found an association with parenting strategies and HCC in 6-year-olds with mild adversities (Windhorst et al., 2017). As chronic stress in parents may affect parenting strategies and cortisol levels of their children, it may be relevant to gain better insights into associations of chronic stress, especially in parents of children with ASD, as parents of these children have a high risk of being stressed. However, this association has not been investigated yet in parents and children with ASD.

3.1.4 Chronic stress and mental health of parents of children with ASD

Earlier studies demonstrate increased mental health problems in mothers and fathers of children with ASD, such as depression and anxiety. For example, Bitsika and colleagues (2013) showed that parents of children with ASD had higher rates of clinically significant anxiety and depression compared to the general population. Previously, researchers have associated blunted diurnal cortisol and a blunted cortisol awakening response with a higher level of perceived stress, eating- and anxiety disorders in parents of children with ASD (Dykens & Lambert, 2013). However, again, these measures reflect short-term HPA-axis activity, while the investigation of long-term HPA-axis activity may broaden our understanding of chronic stress in parents of children with ASD, as the long-term impact of stress may have different effects than short-term HPA-axis activity.

3.1.5 Chronic stress and physical health of parents of children with ASD

Mothers and fathers of children with ASD report more physical health problems than parents of neurotypical children (Lovell et al., 2021). Moreover, recently we found higher rates of obesity and metabolic syndrome in mothers of children with ASD in our own study (van der Lubbe et al., 2022). In addition, another study found immunological alterations in caregivers of individuals with ASD (Warreman et al., 2023). Previous studies also report associations between reported stress, disinhibited eating behavior and physical health problems in parents of children with ASD (Reed et al., 2016; van der Lubbe et al., 2022). However, the link between physiological stress and mental and physical health problems in parents of children with ASD has been understudied. One study investigating cortisol awakening responses of mothers of children with ASD, reported associations between blunted cortisol awakening responses, lower Body Mass Indices (BMI's) and hypoglycemia (Dykens & Lambert, 2014). As yet, previous research has not demonstrated a link between mental and physical health and long-term physiological stress in parents of children with ASD.

3.1.6 The current study

The current study will investigate associations of chronic stress in both mothers and fathers of young children (aged 3-7 years) with ASD. The first aim of the study is to investigate associations of chronic stress between children with ASD and their parents. The authors hypothesize that parental HCC is associated with the HCC of their children, as chronic stress may impact parenting strategies affecting parent-child interactions which may be related to stress of their children. The second aim of the study is to explore associations between chronic stress and mental health in mothers and fathers of children with ASD, evaluating mothers and fathers separately. The last aim of our study is to explore associations between chronic stress and physical health. The authors hypothesize that chronic stress is not only associated with mental health problems, but also with physical health as indicated by eating behavior and the presence of physical health problems in mothers and fathers of young children with ASD.

3.2 Method

3.2.1 Procedure

The current study is a cross-sectional study investigating the impact of chronic stress on mental and physical health in both mothers and fathers of young children with ASD. This study is part of the ongoing Tandem Study (Dutch Trial register: NL7534), approved by the Institutional Review Board of the Leiden University Medical Center, The Netherlands. Data were collected between 2018 and 2024.

For the current study, parents completed self-report questionnaires regarding their stress and mental health. In addition, a home-visit was conducted for physical measurements in parents. During this home-visit, we also collected hair samples in mothers, fathers and their children.

3.2.2 Participants

Families were recruited from Youz Parnassia Group, GGZ Delfland and Jonx Groningen, all Dutch mental health care providers. Families were eligible for inclusion if: 1) their child was diagnosed with ASD, 2) the child was aged between 3;0-6;11 years and 3) parents could understand Dutch without the help of a translator. Children who started new psychotropic medication three months prior to participating in the study were excluded.

In the Dutch healthcare system, Youth and Family Centers (YFCs) provide free preventive healthcare to all children living in the Netherlands through regular consultations with physicians and nurses, up to the age of 18. YFC's reach 94.8% of the children aged 0-18 years living in the Netherlands. Their program, which includes screening for developmental delays, also focuses on identifying potential social, psychological, and somatic disturbances (Berckelaer-Onnes et al. 2015; Centrum voor Jeugd en Gezin Rijnmond 2016). Therefore, they play an important role in screening for ASD. If a child exhibits symptoms of ASD, they are referred to mental health care for further evaluation. Additionally, only licensed professionals in mental health care can provide an ASD diagnosis in the Netherlands.

3.2.3 Measures

3.2.3.1 Chronic Stress

Hair Cortisol Concentrations (HCC) were measured as previously described by Noppe and colleagues (2015). In short, hair samples of approximately 100 hairs were cut from the posterior vertex of the scalp, as close to the scalp as possible in children and both of their parents. The most proximal 3 cm of the hair strands were used, which corresponds to a period of three months. After collection, hair samples were stored at room temperature and sent to the Erasmus Medical Centre (EMC) for laboratory analysis. At the Erasmus MC, the hair samples were weighed, washed and cortisol was extracted with methanol. Next, hair cortisol was analysed using liquid chromatography-tandem mass spectrometry (LC-MS/MS) (Noppe et al., 2015). Parents were asked to complete a questionnaire regarding hair washing frequency, usage of hair products and the use of glucocorticoids in the last three months in themselves and their children.

Reported parenting stress was measured using the Parenting Stress Questionnaire (OBVL). The OBVL is a 34-item self-report measure of parenting stress

(Vermulst et al., 2015). Mothers and fathers answered items on a 4-point Likert scale, in which 1 stands for “Does not apply” and 4 for “Applies completely”. For this study, the total score on the OBVL was used, in which a high score reflects a high level of parenting stress. Overall reliability and validity of the OBVL are good (Vermulst et al., 2015). The internal consistency, which was estimated with Cronbach’s alpha ranged from .89 to .91. for the total score and from .74 to .87 for the subscales.

3.2.3.2 Parental Mental Health

Psychopathological symptoms. The Brief Symptom Inventory (BSI) is a self-report scale comprising 53 items and is specifically designed to assess both psychopathological and psychological symptoms (Derogatis, 1993). The BSI is filled out by both parents to measure parental mental health. It measures nine dimensions (including somatization, obsession-compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism). Each item on the BSI is rated on a 5-point Likert scale, ranging from 0 ("not at all") to 4 ("extremely"). The BSI has been shown to have robust psychometric properties, with internal consistency coefficients ranging from .71 to .85 in its original administration.

3.2.3.3 Parental Physical Health

Eating behavior. Parental eating behavior was measured using the Dutch Eating Behavior Questionnaire (DEBQ) The DEBQ is a 33-item self-report measure of eating behavior consisting of 3 subscales: Emotional eating, External eating and Restrained eating (van Strien, 2015). The subscale ‘Emotional eating’ refers to eating in response to emotions. The subscale ‘External eating’ refers to eating in response to external food cues. The subscale ‘Restrained eating’ refers to limiting food-intake to lose weight. Mothers and fathers answered items on a 5-point Likert scale. Higher subscale scores indicate a higher level of the corresponding specific eating behavior. Cronbach’s alpha value is .96 for Emotional eating, .78 for External eating and .90 for Restrained eating.

Body Mass Index, Waist Circumference and Blood Pressure. Physical measurements were only performed in mothers and fathers. Body height was measured by a stadiometer (Seca 213) and weight by a digital scale (Seca Clara 803). Body Mass Index (BMI) was calculated by dividing weight in kilograms by the square of height in meters. Waist circumference (cm) was measured between the lowest point of the lowest rib and the upper border of the pelvic crest using a measuring tape. Waist circumference was also used to measure abdominal obesity. We measured systolic and diastolic blood pressure using a blood pressure monitor (Omron M6). During the blood pressure measurement, parents were asked to sit still and to not speak. Blood pressure measures were done twice, and the average of the two measures was calculated.

Cholesterol, Triglycerides and Glucose. To measure cholesterol, triglycerides and glucose values, fasting blood samples (18 ml) were drawn from parents by a phlebotomist. Parents were instructed to not eat or drink anything other than water for 8 hours before the blood test. After collection, the samples were sent to the Ysselland Hospital for laboratory analysis, using the Roche Cobas 6000 C501 module. High cholesterol, triglycerides and/or glucose levels indicate a higher risk for physical health problems, such as heart disease and diabetes.

3.2.3.4 Demographic variables

Parents indicated their highest completed education and their birth country. Parents also indicated their birthdate, birthdate of their child, ethnicity, marital status, (married/cohabiting versus single parent), who was the primary caregiver and whether they had paid employment.

3.2.4 Statistical analyses

First, an overview of characteristics of our sample will be displayed in comparison with the general population regarding parenting stress, psychopathology, eating behavior and physical health, prior to answering our research questions. To compare our sample with the general population, Chi-Square Goodness of Fit tests were performed to determine whether the proportion of parents scoring above a certain cut-off was different from the Dutch general population. Reported parenting stress, mental health problems and eating behavior scores were compared to norm-scores of the corresponding questionnaires (Derogatis, 1993; van Strien, 2015; Vermulst et al., 2015). The percentage of participants in each category of the health measurements was compared to Dutch males aged 18-59 (n = 27991) and Dutch females aged 18-49 (n = 29650) from the population-based Lifelines Cohort Study (Slagter et al., 2017).

We have performed Spearman's correlation analysis, to test for the associations between chronic stress (OBVL of both parents and HCC of both parents), chronic stress in the child (HCC child), parental mental health (BSI total score and subscales of parents) and parental physical health (DEBQ and physical measurements in both parents). We used Spearman's correlation analysis for the following reasons. First, HCC data was right-skewed and contained outlying values in mothers, fathers, and children, therefore, a nonparametric test would be more appropriate for our data. Second, given our sample size, Spearman's correlation analysis is a robust method in smaller sample sizes. To avoid measurement bias in the hair cortisol measurements, we performed two sensitivity-analyses by excluding participants with hair-strands shorter than 3 centimeters and excluding participants who have used glucocorticoids in the past three months, as this may impact HCC outcomes.

Lastly, we have tested multiple regression models to examine the significant associations from Spearman's correlation analysis. In these models, we used chronic stress variables of parents (HCC and OBVL) as predictors. The outcome variables included HCC of child, parental mental health, and parental physical health. Missing values were treated using pairwise deletion. All analyses were performed in SPSS Statistics 27.

3.3 Results

3.3.1 Descriptives

A total of 181 parents (98 mothers and 83 fathers) of 99 children with ASD participated in the study (82.8% boys). Children were aged between 3 and 7 years old (M=4.99, SD=1.2). Autism severity (ADOS) scores ranged from 1 to 10 (M = 6.31, SD = 2.2).

Mothers were between 23 and 46 years old (M=34.4, SD=5.0), fathers were between 25 and 58 years old (M=37.8, SD=6.7). The mother was the primary caregiver in 88 families (94.6%) and the father was the primary caregiver in 5 families. Further sociodemographic characteristics of the parents are displayed in Table 1.

Mothers and fathers of young children with ASD had higher levels of parenting stress and psychopathology symptoms on almost all symptom dimensions of the BSI than individuals from the population-based Lifelines cohort. In addition, obesity and metabolic syndrome was more common in the mothers in our sample than in the general population. To our knowledge, one mother was pregnant during the study. Mean scores of HCC and physical health measures of parents are displayed in Supplementary Table S1.

Six children (10.7%), 11 mothers (12.0%) and 4 fathers (5.3%) had used local (6 children, 9 mothers, 4 fathers) or systemic (2 mothers) corticosteroids during the last three months. Excluding them from Spearman's correlation analysis did not affect our results. Moreover, 12 mothers and 1 father used psychotropic medication during the study. We have listed medication type and condition in Supplementary Table S2. Excluding parents who used psychotropic medication from analysis did not affect our results. There were 26 fathers and 13 children with hair strands shorter than 3 centimeters. However, excluding these cases from the analysis did not make a difference in results regarding the association between HCC and the other variables. Therefore, analyses were performed including these cases to retain sufficient power for the study.

Table 1.
Sociodemographic characteristics and mental health, eating behavior and physical health in mothers and fathers of a young child (3-7) with ASD.

	ASD Mothers		ASD mothers vs norm group			ASD fathers		ASD fathers vs norm group			
	N	%	Expected %	Chi-Square	*p*	N	%	Expected %	Chi-Square	*p*	Comparison group
Demographic characteristics											
Highest completed education				4.14	.13				1.74	.42	Dutch females (n = 2.128.000) and males (n= 2.152.000) aged 25 to 45 years old from the Dutch general population.[a]
Low	10	11.4	10.9			12	16.0	14.5			
Middle	38	43.2	33.4			32	42.7	36.7			
High	40	45.5	55.6			31	41.3	48.9			
Paid employment				11.56	<.01				3.36	.07	Dutch females (n = 2.230.000) and males (n= 2.259.000) aged 25 to 45 years old from the Dutch general population.[b]
Yes	63	70.8	84.0			83	96.5	91.0			
Married or cohabiting				4.99	.03						The Dutch population with children living at home (n = 4.640.227).[c]
Yes	74	79.6	87.3								
Ethnic background				0.07	.97				1.40	.50	The Dutch population (n = 17.591.000).[d]
Born in the Netherlands	65	73.9	74.0			56	73.7	74.0			
Born in another European country	8	9.1	8.4			4	2.6	8.4			
Born in another non-European country	15	17.0	17.6			16	21.0	17.6			
Parenting Stress											
Total score OBVL				163.79	<.01				119.91	<.01	Dutch mothers (n = 848) of neurotypical children aged between 0-11.[e]
≥ 85th percentile	65	72.3	15.0			52	65.8	15.0			

Mental Health											
Total score BSI				26.42	<.01				16.38	<.01	Dutch females (n = 512) and
≥ 80th percentile	39	45.3	20.0			30	41.1	20.0			Dutch males (n= 535) from the
Somatization				12.42	<.01				2.74	.10	Dutch general population older
≥ 80th percentile	27	38.6	20.0			20	28.6	20.0			than 30 years.[f]
Obsession-Compulsion				38.32	<.01				11.47	<.01	
≥ 80th percentile	43	51.6	20.0			28	37.3	20.0			
Interpersonal Sensitivity				11.16	<.01				4.99	.03	
≥ 80th percentile	26	37.6	20.0			24	31.2	20.0			
Depression				34.98	<.01				12.38	<.01	
≥ 80th percentile	41	50.0	20.0			27	38.5	20.0			
Anxiety				45.16	<.01				0.25	.87	
≥ 80th percentile	45	54.2	20.0			16	20.8	20.0			
Hostility				20.65	<.01				5.83	.02	
≥ 80th percentile	37	42.0	20.0			22	28.6	20.0			
Phobic Anxiety				31.83	<.01				2.15	.14	
≥ 80th percentile	42	47.7	20.0			21	27.3	20.0			
Paranoid Ideation				7.47	<.01				2.97	.09	
≥ 80th percentile	29	33.0	20.0			22	28.6	20.0			
Psychoticism				20.65	<.01				13.93	<.01	
≥ 80th percentile	37	42.1	20.0			30	39.0	20.0			
Physical Health											
Emotional eating behavior (DEBQ)				0.01	.93				1.09	.30	Dutch females (n = 1143) and
≥ 80th percentile	18	20.5	20.0			19	25.0	20.0			Dutch males (n = 807) from the
External eating behavior (DEBQ)				5.94	.02				8.04	<.01	Dutch general population aged
≥ 80th percentile	27	31.0	20.0			26	33.8	20.0			between 21 and 70 years.[g]
Restraint eating behavior (DEBQ)				3.93	.05				0.14	.71	
≥ 80th percentile	10	11.4	20.0			14	18.2	20.0			
BMI				47.85	<.01				14.51	<.01	Dutch females aged 18-49 (n =
Normal weight	35	35.7	55.9			20	23.0	40.6			29650) and Dutch males aged
Overweight	25	25.5	29.8			47	54.0	46.5			18-59 (n = 27991) from the
Obesity	38	38.8	14.4			20	23.0	12.9			

Waist circumference				14.09	<.01				3.69	.06	population-based LifeLines cohort study.[h]
Abdominal obesity	54	53.5	37.0			27	30.3	21.9			
Blood pressure				3.73	.054				3.04	.08	
Elevated blood pressure	14	13.9	21.8			36	40.4	49.7			
Metabolic syndrome				15.55	<.01				0.06	.80	
Yes	17	20.0	8.4			14	20.0	17.6			

[a]Centraal Bureau voor Statistiek, 2022; [b]Centraal Bureau voor Statistiek, 2024a; [c]Centraal Bureau voor Statistiek, 2024b; [d]Centraal Bureau voor Statistiek, 2021; [e]Vermulst et al., 2015; [f]Derogatis, 1993, [g]van Strien, 2015, [h]Slagter et al., 2017.

3.3.2 Associations between chronic stress in parents and their children

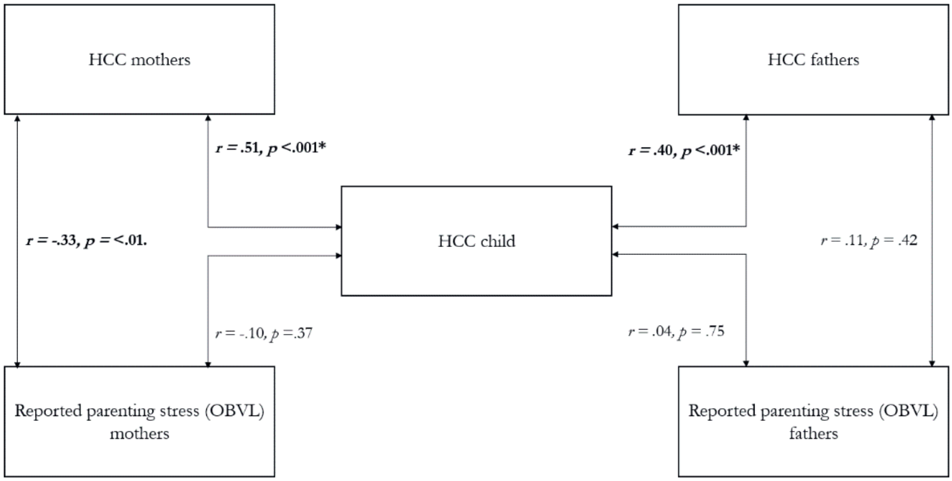
As illustrated in Figure 1, HCC of mothers correlated positively with HCC of their children (r = .51, p <.01). This association remained significant after controlling for highest completed education of mother (r = .52, p <.01), age of the child (r = .54, p <.01), employment status of mother (r = .52, p <.01), whether parents were living together (r = 51, p <.01) and after excluding mothers with a mental or physical health condition (r = .59, p <.01). We did not find a significant correlation between reported parenting stress of mothers and HCC of their children (r = -.10, p =.37). Perceived parenting stress correlated with a lower HCC in mothers of young children with ASD (r = -.33, p < .01), even after controlling for highest completed education of mother (r = -.32 p <.01), age of the child (r = -.32, p <.01), employment status of mother (r = -.33, p = <.01), whether parents were living together (r = -.35, p <.01) and after excluding mothers with a mental or physical health condition (r = -.29, p =.04).

HCC of fathers was positively correlated with HCC of their children (r = .40, p <.01). This association remained significant after controlling for highest completed education of father (r = .41, p <.01), age of the child (r = .39, p <.01), employment status of father (r = .40, p <.01) and whether parents were living together (r = .41, p < .01) and after excluding fathers with a mental or physical health condition (r = .38, p <.01). However, we did not find an association between reported parenting stress of fathers and HCC of their children (r = .04, p =.75). There was no correlation between perceived parenting stress and HCC in fathers of young children with ASD (r = .11, p =.42).

Furthermore, we tested a regression model with HCC and OBVL of parents as predictors and HCC of child as outcome variable. In line with significant associations from Spearman's correlation analysis, HCC of child was significantly predicted by HCC of mothers (B = .781, β=.490, t = 4.48, p < .01), HCC of fathers (B = .867, β=.472, t = 4.69, p < .01).

Figure 1.

Associations between chronic stress of parents and chronic stress in their children with ASD.



3.3.3 Correlation chronic stress and parental mental health

Reported parenting stress correlated with more total psychopathology symptoms in mothers ($r = .55$, $p < .01$) and fathers ($r = .66$, $p < .01$). In addition, as shown in Table 2, there was a correlation between reported parenting stress and all subscales of the BSI in mothers and fathers. All associations remained significant after controlling for highest completed education of the parent, age of the child, employment status of the parent, whether parents were living together, and after excluding mothers and fathers with a mental or physical health condition.

Additionally, we tested two regression model with HCC and OBVL as predictors and BSI total scores as outcome variable for mothers and fathers separately. In line with significant associations from Spearman's correlation analysis, OBVL scores significantly predicted BSI sores in both mothers (B = .02, β = .59, t = 5.85, p <.01) and fathers (B = .02, β =.62, t = 5.83, p < .01).

Table 2. Spearman's correlations between chronic stress and mental health.

	Mothers		Fathers	
	HCC	Reported parenting stress (OBVL)	HCC	Reported parenting stress (OBVL)
Total symptoms (BSI)	-.16	**.55*** **	.01	**.66*** **
Somatization	-.04	**.53*** **	.06	**.43*** **
Obsession-Compulsion	-.20	**.57*** **	-.05	**.54*** **
Interpersonal Sensitivity	-.07	**.39*** **	.08	**.53*** **
Depression	-.20	**.45*** **	.09	**.60*** **
Anxiety	-.20	**.50*** **	-.04	**.56*** **
Hostility	-.11	**.43*** **	-.05	**.59*** **
Phobic Anxiety	-.15	**.37*** **	.02	**.36** **
Paranoid Ideation	-.10	**.38*** **	.04	**.51*** **
Psychoticism	-.07	**.40*** **	.06	**.49*** **

BSI = Brief-Symptom Inventory; HCC = Hair Cortisol Concentrations; OBVL = Parenting Stress Questionnaire. *p < .05, **p < .01, ***p < .001.

3.3.4 Correlation chronic stress and parental physical health

In mothers, there was a positive association between reported parenting stress and emotional eating behavior (r = .29, p = .01) and external eating behavior (r = .30 p = .01), also after controlling for highest completed education of the mother, age of the child, employment status of mother, whether parents were living together and after excluding mothers with a mental or physical health condition. In fathers, reported parenting stress correlated with emotional eating (r = .36, p = .01), but not with external eating behavior (r = .22, p =.06). The correlation remained significant after controlling for highest completed education of father, age of the child, employment status of father, whether parents were living together and after excluding fathers with a mental or physical health condition. We did not find an association between eating behavior and HCC in mothers and fathers of young children with ASD (see Table 3).

In mothers, fasting glucose levels correlated positively to scalp hair cortisol (r = .24, p = .04), also after controlling for highest completed education of the mother, age of the child, employment status and whether parents were living together, but not after excluding mothers with a mental or physical health condition (r = .23, p = .16), excluding mothers who used glucocorticoids (r = 24, p = .053) or mothers who used psychotropic medication (r = .23, p = .07) . As shown in Table 3, the other physical health measures did not correlate with HCC and reported parenting stress in mothers and fathers of young children with ASD.

Lastly, we tested significant associations using multiple regression analysis. In line with significant associations from Spearman's correlation analysis, Total OBVL scores of mothers significantly predicted emotional eating behavior (B = .24, β= .25, t = 2.15, p =.04) and external eating behavior (B = .18 β= .34, t = 2.87, p <.01) of mothers. Furthermore, total OBVL scores of fathers significantly predicted emotional eating behavior of fathers (B = .25, β= .33, t = 2.58, p =.01).

Table 3.
Spearman's correlations between chronic stress and physical health.

	Mothers		Fathers	
	HCC	Reported parenting stress (OBVL)	HCC	Reported parenting stress (OBVL)
Emotional eating (DEBQ)	-.16	**.29***	-.08	**.36****
External eating (DEBQ)	-.08	**.30***	-.16	.22
Restraint eating (DEBQ)	.03	-.09	-.14	.07
BMI	-.04	-.12	-.12	<.01
Waist circumference	-.09	-.07	-.11	.14
Systolic blood pressure	.07	-.04	-.19	.04
Cholesterol HDL	-.13	.14	-.21	-.05
Triglycerides	.07	-.04	.10	.10
Glucose	**.24***	-.11	-.21	-.07

DEBQ = Dutch Eating Behavior Questionnaire; HCC = Hair Cortisol Concentrations; NVE = OBVL = Parenting Stress Questionnaire. *p < .05, **p < .01, ***p < .001.

3.4 Discussion

The current study investigated associations of chronic stress between children with ASD and their parents and explored associations between parental chronic stress and parental mental and physical health. Mothers and fathers with a higher HCC, had children with higher HCC. In addition, maternal HCC was associated with lower reported parenting stress. Mothers and fathers who reported more parenting stress, reported a worse mental health. In mothers and fathers, HCC and psychopathology symptoms were not related. We found an association between reported parenting stress and disinhibited eating behavior in mothers and fathers. In addition, mothers with a higher HCC had higher levels of glucose, indicating higher risk for diabetes. This was not found in fathers. We did not find an association between HCC and mental health problems, eating behavior, and other measures of physical health in mothers and fathers.

In mothers, higher parenting stress scores were associated with lower maternal HCC. This is in line with the study by Radin and colleagues (2019), that consequently found lower HCC levels in mothers of children with ASD compared to mothers of typically developing children longitudinally. Based on these findings, it could be theorized that in these specific populations chronic stress may be associated with dampening of the HPA-axis on the long-term, resulting in a lower level of HCC. This hypothesis is in line with previous studies that investigated short-term HPA-axis activity in parents of children with ASD. For example, Dykens and Lambert (2013) associated a blunted diurnal cortisol and a blunted cortisol awakening response with a higher level of perceived stress in parents of children with ASD. However, these studies have investigated short-term HPA-axis activity (as opposed to hair cortisol, which is a measure of longer term stress). On the contrary, there are other studies that have associated higher HCC with stress-related conditions, such as caregivers of adults with dementia (Stalder et al., 2014). Additionally, Radin and colleagues (2019) did not find an association between HCC and reported stress. It must be noted that the association between reported stress and HCC may depend on other factors too, such as glucocorticoid sensitivity, duration of stress, and psychological resilience (Lehrer et al., 2020; Luo et al., 2012; Walsh et al., 2017). However, previous studies have consequently demonstrated a correlation between HCC and stress exposure, such as unemployment and post-traumatic stress disorder (Stalder et al., 2017; Staufenbiel et al., 2012). We encourage future studies to further explore the long-term functioning of the HPA-axis in parents of children with ASD in combination with possible moderating factors to gain better understanding of the association between high reported stress and lower HCC.

Our results demonstrate a positive association between HCC of parents and HCC in their children. To our knowledge, this study is the first study to investigate associations between HCC of parents and children with ASD. The positive link between HCC of parents and HCC of children stands out, especially when considering the negative association between maternal HCC and reported parenting stress. A previous study in neurotypical mother-daughter dyads yielded similar results (Ouellette et al., 2015). This study found that the mothers who reported higher stress had lower HCC compared to the mothers that reported lower stress. Additionally, they found a positive correlation between maternal HCC and HCC of their daughters. Interestingly, Ouellette and colleagues (2015) found a stronger association between maternal HCC and child HCC in mothers who used lower quality parenting strategies. This is in line with another study, that demonstrated a relationship between maternal HCC and infant salivary cortisol concentrations and maternal HCC and mother-child interaction quality (Tarullo et al., 2017). Based on our results and previous studies, it could be theorized that the association between HCC in parents and child HCC could, at least partly, be explained by parenting strategies. More specifically, highly stressed parents may use lower quality parenting strategies which results in stress in their children. It could be speculated that through parenting, chronic stress in parents of children with ASD may also result in the dampening of the HPA-axis of their children. As we were not able to test this theory in our study, we encourage future studies to further investigate this topic. An alternative explanation could be that HCC of parents and children correlate due to genetic factors, which could also explain why we did not find a correlation between reported parenting stress and child HCC. For example, genes that play a role in the HPA-axis regulation are the glucocorticoid receptor gene (NR3C1), POMC, FKBP5, and many more (Gerritsen et al, 2017). Gerritsen and colleagues have also associated these genes with the susceptibility for stress-related disorders. However, less is known about the role of these genes in ASD. Thus, the association between HCC of parents and children may partly be explained by environmental factors and shared genes between parent and child.

While we did find an association between psychopathology symptoms and reported parenting stress in mothers and fathers, we did not find this correlation for psychopathology symptoms and HCC. While these associations have not been investigated before in parents of children with ASD, previous studies investigating the relationship between HCC in individuals with mental health problems (e.g. depression or anxiety), did find contrasting results, depending on the type or age-of-onset of the psychiatric disorder. For example, Staufenbiel and colleagues (2013) found increased HCC in patients with major depression and patients with late-onset bipolar disorder, while they found decreased HCC in patients with anxiety disorders. Another study in individuals with a major depression demonstrate a cortisol increase in some days and a corrective decrease in other days, which results in normal HCC levels (Herane-Vives et al., 2020). Additionally, timing also seems to play a role. To illustrate, a study in individuals with post-traumatic stress disorder (PTSD), showed increased HCC one month after the traumatic event and decreased HCC 7 months following the event (Luo et al., 2012). It is possible that we did not find an association in the current study, due to a combination of heterogeneity in psychiatric complaints, timing and variation in the effect on the HPA-axis.

In mothers and fathers, reported parenting stress was associated with more emotional eating behavior and in mothers, higher HCC was associated with higher fasting blood glucose levels. To our knowledge, this is the first study that finds this association in mothers of children with ASD. Previous studies reported associations between high HCC and an increased risk of type 2 diabetes mellitus and metabolic syndrome (Kuckuck, Lengton et al., 2023, Stalder 2013, Manenschijn et al., 2013). It could be theorized that parents demonstrated more disinhibited eating behavior because of their higher levels of stress, which may put them at higher risk for weight gain and type 2 diabetes. This is in line with the results of our previous study, demonstrating high rates of obesity (39.1%) and a positive association between reported parenting stress and disinhibited eating behavior in mothers of young children with ASD (van der Lubbe, 2022). In addition, chronic stress has previously been associated with a preference for highly caloric food intake through cortisol, which could lead to changing eating patterns (Kuckuck, van der Valk et al., 2023). However, we did not find associations between HCC and obesity in this study. Since mean BMI and in particular also waist circumference, was high in these mothers and fathers, the lack of an association with BMI and waist may be due to a "ceiling effect”. The abdominal obesity present in many mothers suggests that on average most had high visceral adipose tissue, which is important for local cortisol production (Rask et al, 2001). Other possibilities are that the high prevalence of obesity was related to other factors, e.g. lifestyle, environmental and /or genetic factors. However, as the current study was a cross-sectional study, further prospective research is necessary to gain better understanding into those relationships.

There were differences in associations between chronic stress and mental- and physical health in mothers and fathers. For example, while we did find an association between reported parenting stress and external eating behaviors in mothers, we did not find this association in fathers. A previous study that investigated the relationship between stress and eating behavior in students, reported a relationship between perceived stress and emotional eating behavior in both males and females (Du et al., 2022). However, other studies indicate that stress-induced eating is more common in women than in men (Beydoun, 2014). Possible explanations for these differences found in our study could be variation in exposure to parenting stress in mothers and fathers or differences in coping strategies to deal with stress. Previous research demonstrated that fathers of children with ASD spend approximately 26% less time in childcare than mothers (Hartley et al., 2014). Another study found a positive association between time spend in paid employment and physical well-being of fathers of children with an intellectual disability (Olsson & Hwang 2006). Nevertheless, the increased scores of parenting stress and mental health problems in mothers as well as fathers, underlies the importance to pay close attention to both in research and clinical practice.

Interestingly, our results remained significant after controlling for demographic factors such as, age of the child, highest completed education of parents, paid employment, marital status and the presence of a mental or physical health condition. The associations between chronic stress and health factors are significant, regardless of individual differences in background. However, it is important to acknowledge that other factors that were not measured in this study, such as social support and living conditions may potentially affect these associations. Therefore, we encourage future research to examine these factors as potential moderators of the associations identified in our study.

The current study had some limitations. For example, our study design was cross-sectional and therefore, we cannot make conclusions about causality based on our results. It is important to acknowledge that the stress level of parents may be associated with many other underlying factors, such as parental health conditions and other socio-economic circumstances. However, we due to power we were not able to include every potential underlying factor in our study. That being said, in line with our findings, Radin and colleagues (2019) longitudinally demonstrated decreased HCC levels in mothers of children with ASD over a period of two years. In addition, another study by Warreman and colleagues (2023) found higher levels of stress and higher prevalence rates of anxiety and depressive disorders in caregivers of individuals with an autism spectrum disorder (n = 722) compared to people who provide care for individuals with other chronic conditions (n = 2632), even after controlling for demographic variables such as age, sex and socio-economic status. Also, they found associations between reported stress and physical health of caregivers of children with ASD. While the study of Warreman was cross-sectional, that study included caregivers that were caregiving for 5 years or longer to ensure the caregiving exposure began prior to the measurements of parenting stress. Compared to our sample, the mean age of the sample of Warreman and colleagues was 50.8 years old, so about 15 years older than the parents in our study (mean age mothers 34.4 years and fathers 37.8 years). Therefore, we foresee that the associations between chronic stress and mental and physical health will also be found longitudinally. We encourage future studies to elaborate on this topic by investigating these associations longitudinally, before and after receiving interventions to enhance tailored interventions to the children with ASD and their parents. Additionally, quantitative studies regarding the experiences of parents of children with ASD could deepen our understanding of what experiences or elements of having a child with ASD impacts parents the most.

We consider it a strength of our study that we used an integrated approach, in which concurrently mental and physical measures were examined in both parents and children. Both methods have different potential biases. For example, the self-report measures may have social desirability bias and recall bias, which may lead to over- and underreporting of stress and mental and physical health problems, while the physiological measurements could have other potential biases, such as individual differences in hair treatment or medication use, which could also lead to an over- and underestimation of stress. Nevertheless, we think both instruments are important in measuring stress. Specifically, self-reporting is a valuable tool for capturing the subjective parental experiences. A previous study found a strong correlation between self-rated health and all-cause mortality, which emphasized the importance of investigating self-report measurements in relation to health outcomes (Lorem et al., 2020). Also, physiological measurements provide a more objective perspective on stress and may capture biological processes that may not be fully reflected in self-reported data. Therefore, using both methods strengthens our understanding of the associations between chronic stress and mental- and physical health in parents of young children with ASD.

Interestingly, twice as many parents scored above the 80^{th} percentile for mental health problems compared to the norm-group. In addition, reported parenting stress was highly correlated with mental health problems in in both fathers and mothers. Therefore, it would be relevant to screen highly stressed parents in clinical care for symptoms of psychopathology. In addition, screening for obesity and metabolic comorbidities is also important since the prevalence of obesity was also alarmingly high in mothers of children with ASD, as it is known that obesity and mental health are bidirectionally related (Milaneschi et al., 2018).

Parents of children with ASD demonstrate high levels of reported stress and this stress is related to their mental and physical health. Therefore, it is important to pay attention to parental stress, mental and physical health in clinical care of mothers, fathers and children with ASD. These results promote a preventive approach in clinical care aimed at improving mental and physical health of mothers and fathers. For example, by training general practitioners and pediatricians to explicitly ask about mental- and physical stress in parents of children with ASD. For parents of children with ASD who are in mental health care, this could be done by specifically targeting mental stress, for example by mindfulness training and focus on peer support for parents in groups. As the Dutch health care system emphasizes on empowering parents through educational programs or training sessions to manage challenges associated with ASD, parental stress and health could also be an important topic in these sessions, for example by lifestyle education and if necessary, interventions aimed at improving physical health. Thus, an integrative and intergenerational approach to alleviate distress in parents and children with ASD could benefit families of children with ASD. In addition, we encourage researchers in this field to further explore this topic longitudinally to gain better understanding in the long-term effects of chronic stress on mental and physical health in parents of children with ASD.

The current study explored associations between chronic stress of the parents and their children, and mental and physical health in mothers and fathers of young children with ASD. It is important to recognize that the chronic stress experienced by parents may be interconnected with the chronic stress of their children with ASD. We encourage future research to investigate whether this correlation is generalizable to the whole ASD population. Furthermore, the current study addressed the gap in knowledge regarding the relationship between chronic stress and mental and physical health problems in parents of young children with ASD. Our findings indicate that chronic stress is associated with a higher level of mental health problems in parents of children with ASD, while its association with physical health is less consistent. The positive association between HCC and glucose levels in mothers suggests an association between chronic stress and physical health, but we did not find an association between chronic stress and the other physical health measures. It must be noted that the current study is cross-sectional and therefore, we cannot make any causal conclusions. However, as parents of young children have higher risks for chronic stress and mental- and physical health problems, preventive measures could improve parental care, by preventing the development of mental and physical health disorders and providing necessary parenting support in parents of children with ASD.

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3.6 Supplementary Material

Table S1.
Descriptive values of Hair Cortisol Concentrations and Physical Health Measures of Mothers and Fathers of Young Children with ASD.

	Mothers		Fathers	
Measure	**n**	**M (SD)**	**n**	**M (SD)**
Hair cortisol concentration (pg/mg)[a]	90	3.40 (2.72)	64	3.13 (1.95)
BMI (kg/m^2)	94	28.88 (6.12)	84	27.73 (4.14)
Waist circumference (cm)	97	91.28 (13.86)	86	97.44 (12.01)
Systolic blood pressure (mmHg)	97	114.77 (12.23)	86	127.30 (14.35)
Cholesterol HDL (mmol/l)	84	1.40 (0.32)	70	1.18 (0.25)
Triglycerides (mmol/l)[a]	84	0.90 (0.20)	70	1.26 (1.10)
Glucose (mmol/l)	81	5.08 (0.56)	69	5.09 (0.57)

[a]Variable was non-normally distributed, median and IQR's are displayed.

Table S2.
Diagnosis of mental and physical health conditions and use of psychotropic medication in parents of children with ASD.

	n	%
Mothers		
Diagnosis of mental or physical health condition		
No	50	56.2
Yes, mental health condition(s), namely:	12	13.5
Anxiety disorder	3	
Attention deficit hyperactivity disorder	5	
Autism spectrum disorder	1	
Depression	6	
Eating disorder	1	
Post-traumatic stress disorder	3	
Personality disorder	1	
Yes, physical health condition(s), namely:	20	22.5
Diabetes	4	
Liver disease	1	
Thyroid disease	3	
Other condition(s)	22	
Yes, mental- and physical health condition(s)	6	6.7
Use of psychotropic medication		
No	80	87.0
Yes, namely:	12	13.0
Antidepressants	4	
Anti-epileptics	1	
Antipsychotics	1	
Benzodiazepine receptor agonists	2	
Selective serotonin reuptake inhibitors	6	
Fathers		
Diagnosis of mental or physical health condition		
No	62	78.5
Yes, mental health condition(s), namely:	6	7.6
Anxiety disorder	1	
Attention deficit hyperactivity disorder	2	
Autism spectrum disorder	2	
Depression	1	
Dyslexia	1	
Yes, physical health condition(s), namely:	11	13.9
Diabetes	1	
Kidney disease	1	
Liver disease	1	
Thyroid disease	1	
Other condition(s)	7	
Use of psychotropic medication		
No	79	98.7
Yes, namely:	1	1.3
Psychostimulants	1	

Chapter 4

Novel insights into Obesity in Preschool Children with Autism Spectrum Disorder

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ABSTRACT

Obesity is present in 8-32% of the children with Autism Spectrum Disorder (ASD). However, most studies are performed in school-aged children from the USA. The current study compares obesity rates of Dutch preschoolers with ASD with children from the Dutch general population and explores which child- and parental factors are related to obesity in children with ASD. This cross-sectional study is part of the ongoing Tandem Study (Dutch Trial register: NL7534). Seventy-eight children with ASD aged 3-7 years and their parents (77 mothers, 67 fathers) participated. Child factors are: Body Mass Index (by physical measurement), child eating behavior (Child Eating Behavior Questionnaire), child problem behavior (Child Behavior Checklist), and ASD severity (Autism Diagnostic Observation Scale 2). Parental factors are: BMI (by physical measurement), parental eating behavior (Dutch Eating Behavior Inventory), parenting stress (The Parenting Stress Questionnaire) and highest completed educational level (SES). Children with ASD were 8 times more often obese (16.8%) than children from the general population (2.0%). Child BMI correlated positively with child food approach behavior and maternal BMI, and correlated negatively with child 'Slowness in eating'. There was no correlation between child BMI and ASD severity, problem behavior, parental eating behavior, parental stress and SES. Thus, Dutch, preschool children with ASD have 8 times higher obesity rates than children from the general population. More attention to obesity risk in research and clinical care could contribute to the quality of life of individuals with ASD and their families.

4.1 Introduction

Previous studies show that individuals with Autism Spectrum Disorder (ASD) may have a two to three times higher risk for morbidity and early mortality than individuals from the general population (Catalá-López et al., 2022; Hwang et al., 2019). One condition that has frequently been associated with morbidity and mortality is obesity. A Swedish population study (n = 41,359) demonstrated that individuals who were obese during childhood, had a three times higher risk for mortality during early adulthood compared to same-aged individuals from the general population (0.55% vs 0.19%) (Lindberg et al., 2020). Moreover, other studies in non-ASD populations have associated childhood obesity with high life-time risk for various chronic conditions, including diabetes, multiple types of cancer, cardiovascular disease and adult obesity (Faienza et al., 2020; Hannon et al., 2005; Weihe et al., 2020). Research suggests that childhood obesity is preventable and treatable (Pamungkas & Chamroonsawasdi, 2019). Therefore, it may be particularly important to focus on childhood obesity to understand and possibly prevent health problems in individuals with ASD.

Recent meta-analyses indicate that children and adolescents with ASD have higher prevalence rates of obesity, ranging from 7.9-31.8% compared to 1.4-23.6% among individuals without ASD (Kahathuduwa et al., 2019; Sammels et al., 2022). Learning more about obesity in individuals with ASD is relevant from several perspectives. First, high obesity rates can be considered as a risk factor for future health problems. From this perspective, research focusing on obesity may support the development of future prevention strategies of health problems in children with ASD. Second, it could be theorized that a high risk for obesity reflects a genetic disposition that may put individuals with ASD at higher risk for obesity and other health problems as well. For example, some genomic imbalances that have been associated with ASD have also been associated with childhood obesity (Curtin et al., 2014). From this point of view, research focusing on obesity in early childhood may increase the understanding of pathways to physical health problems in general in individuals with ASD by identifying possible vulnerability already at an early age.

While overweight and obesity in children with ASD have been investigated before, most studies so far have focused on obesity in children of a broad age-range, mostly school- age. Early childhood may be a particularly relevant period to study obesity, since early development may impact the risk for obesity and other health problems in later childhood, adolescence and adulthood (Singh et al., 2008). In addition, most studies have been performed in the United States. Since childhood obesity is more prevalent in the United States than in other Western countries, it could be argued that the prevalence rates of obesity in children with ASD might be different in other countries (Ng et al., 2014).

Previous studies have demonstrated several factors associated to overweight or obesity in children with ASD, such as lower parental education levels and sleep problems (Hill et al., 2015). However, again, most studies focused on older children with ASD or children in a broad age-range. Furthermore, less attention has been directed at parental health factors that may be related to their child's health. This may be particularly important for children with ASD, as a recent study demonstrated higher rates of obesity in mothers of children with ASD and higher rates of clinical parenting stress in both mothers and fathers of a child with ASD compared to the general population (van der Lubbe et al., 2022). This may be relevant for the health of their children, as previous studies have associated parenting stress and parental obesity with the risk for childhood obesity (Jang et al., 2019; Lee et al., 2022).

The first goal of the current study is to investigate whether Dutch, preschool children with ASD show higher obesity rates compared to children from the general Dutch population. The second goal of the study is to explore which child factors (ASD severity, eating behavior and problem behavior) and parental factors (eating behavior, BMI, parenting stress, demographics) are associated with obesity in Dutch, preschool children with ASD.

4.2 Method

4.2.1 Procedure

The current study is a cross-sectional study investigating obesity in preschool children with ASD. This study is part of the ongoing Tandem Study (Dutch Trial register: NL7534), approved by the Institutional Review Board of the Leiden University Medical Center, The Netherlands. Data were collected between 2018 and 2022.

4.2.2 Participants

Families were recruited from Youz Child and Adolescent Psychiatry (Parnassia Group), GGZ Delfland and Jonx, which are large mental health care providers with multiple locations throughout the west, middle or north of the Netherlands. Families were eligible for inclusion if: 1) the child was diagnosed with ASD, 2) the child was aged between 3-7 years and 3) parents could understand Dutch or English without the help of a translator. Children who started new psychotropic medication three months prior to participating in the study were excluded. If parents were eligible for inclusion and agreed to be contacted by the research team, parents received an oral and written description of the study. If parents decided to participate in the study, they met with a researcher to complete the informed consent process.

4.2.3 Measures

4.2.3.1 Obesity

Body height was measured using a stadiometer (Seca 213), and body weight by a digital scale (Seca Clara 803) in all participants. Body Mass Index (BMI) was calculated by dividing weight in kilograms by the square of height in meters. Child BMI was standardized to BMIz, using Growth Analyser Software Research Calculation Tools version 4.1.5 with the Fifth National Dutch Growth Study as a reference group. Based on international cut-off points by Cole and colleagues (2000), children were classified into three BMI classes: healthy weight, overweight and obese. The percentage of participants in each category was compared to Dutch children aged 2-21 years (n =

20.867) from the Fifth Dutch Growth Study, the actual standard of comparison in Dutch pediatric health care (Schönbeck & Van Buuren, 2010). In addition to physical measurements, parents also reported their own height and weight as part of the Dutch Eating Behavior Questionnaire.

4.2.3.2 ASD severity

ASD severity was measured using the Autism Diagnostic Observation Scale (ADOS-2; de Bildt et al., 2014). The ADOS-2 is a standardized, semi-structured observational measure of ASD symptoms. For this study, we used the standardized ADOS severity score, ranging from 0 (minimal) to 10 (high), representing the severity of autism symptoms.

4.2.3.3 Children's eating behavior

Child eating behavior was measured using the Child Eating Behavior Questionnaire (CEBQ). The CEBQ is a 35-item questionnaire consisting of 8 subscales measuring food approach behaviors (subscales: Food Responsiveness, Enjoyment of Food, Emotional Overeating and Desire to Drink) and food avoidant behaviors (subscales: Satiety Responsiveness, Slowness in Eating, Emotional Under-Eating and Food Fussiness). Mothers rated items on a 5-point Likert scale, with higher scores indicating a higher level of the specific behavior. The CEBQ has good psychometric properties in terms of factor structure, internal reliability and correlations between subscales (Sleddens et al., 2008; Wardle et al., 2001). Cronbach's alpha values for the subscales range from .75 to .91.

4.2.3.4 Behavior problems

Behavior problems were measured using the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2000, 2001). The CBCL is a caregiver report form targeting problem behavior in children, using two versions: the preschool version (CBCL/1½-5), containing 100 problem behavior questions and the school-age version (CBCL/6-18), containing 118 problem behavior questions. Mothers rated their child's problem behavior on a 3-point scale, with higher scores reflecting a higher level of the corresponding behavior. For the current study, the total raw score and the raw scores on the subscales Internalizing and Externalizing problems were used. As both versions have a different number of items, the total raw score on each subscale was divided by the number of items for comparability between the two versions.

4.2.3.5 Parental eating behavior

Parental eating behavior was measured using the Dutch Eating Behavior Questionnaire (DEBQ; van Strien, 2015). The DEBQ is a 33-item self-report measure of eating behavior consisting of 3 subscales: Emotional eating, External eating and Restrained eating. Items are scored on 5-point Likert scale. Higher subscale scores indicate a higher level of the corresponding specific eating behavior. Cronbach's alpha value is .96 for Emotional eating, >.78 for External eating and >.90 for Restrained eating.

4.2.3.6 Parental stress

Parenting stress was measured using the Parenting Stress Questionnaire (OBVL). The OBVL is a 34-item self-report measure of parenting stress (Vermulst et al., 2015). Items are answered on a 4-point Likert scale. For this study, the total score on the OBVL was used ($a = .91$), in which a high score reflects a high level of parenting stress.

4.2.3.7 Demographic variables

Parents indicated their highest completed education and their birth country. The highest completed education of mother was used as a measure of Social Economic Status (SES). To be consistent with our comparison group, the participants of the Fifth Dutch National Growth Study, an indication of ethnic background of the child was derived based on the birth country of parents. Children were categorized into one of the two categories: (1) Non migration background and (2) Migration background (if one- or both parents was born outside the Netherlands). Parents also reported their child's medication use and whether their children had any other physical or psychiatric health problems. Parents filled in their marital status (married/cohabiting versus single parent), the primary caregiver and whether they had paid employment.

4.2.4. Statistical analyses

We used a chi-square test of independence to determine whether the proportion of children scoring above the previously mentioned weight cut-offs was different from the reference population. As the reference population consisted only of Dutch children without a migration background, we performed an additional analysis excluding the children in our sample with a migration background to test whether this would affect our results. Moreover, we performed an additional analysis excluding the children who used appetite-inducing medication.

To explore which factors are associated with child BMIz in children with ASD, we performed a Pearson's or Spearman's correlation analysis, depending on the (normal) distribution of the variables. In addition to zero-order correlations, partial correlation coefficients were also calculated controlling for SES and ethnic background.

If BMI values were missing in children, BMI values were collected during the next visit 6 months later. If physical height or weight data was missing in fathers and mothers, parental self-reported height and weight measures were used. If total scores or subscale scores were missing, pairwise deletion in analyses was used. All analyses were performed in SPSS Statistics 25.

4.3 Results

4.3.1 Descriptives

Seventy-eight children with ASD aged 3 to 7 years (Median = 5.2; IQR = 2.2) and their parents (77 mothers, 67 fathers) participated. The demographic characteristics of the children are displayed in Table 1. Medication used is listed in Table S1. There was one child in our sample with a sex chromosome abnormality, the rest of our sample did not have any (known) genetic disorder. To our knowledge, one mother was pregnant during the study. Excluding her from analysis did not affect our results. Data was collected between November 2018 and March 2023.

As three children refused physical measurements, the missing BMI values were replaced by child BMI values that were measured during the next visit 6 months later (r = .89, p = <.001). These children did not use medication. Parental height was missing in 3 parents and parental weight was missing in 1 parent and were replaced by self-reported height (r = .97, p < .001) and weight (r = .99, p < .001).

Parents were married or co-habiting in 57 families (73.1%), the parent was a single parent in 16 of the families (20.5%) and marital status was missing in 6 families (6.4%). In total, 78.3% of the mothers and 95.7% of the fathers had paid employment.

Table 1. Sociodemographic characteristics of children with ASD aged 3-7 years (n = 78)

		n	%
Child gender			
	Boy	64	82.1
	Girl	14	17.9
Child use of medication			
	Yes, appetite inducing medication	7	12.5
	Yes, appetite reducing medication	1	1.8
	Yes, but without effect on appetite	3	5.4
	No	55	77.5
Highest completed educational level of mother			
	Primary school	1	1.4
	Lower vocational secondary education	5	7.2
	Lower secondary education	1	1.4
	Intermediate vocational education	29	42.0
	Intermediate secondary education	2	2.9
	Higher secondary education	1	1.4
	Higher vocational education	22	31.9
	University	8	11.6
Ethnic background of the child[a]			
	Dutch	47	64..4
	Migration background	26	35.6

[a.] Children were classified with a migration background if one or more parents were born in a different country than the Netherlands.

4.3.2 Obesity rates

As shown in Table 2, almost 17% of the children with ASD were obese, which is more than 8 times higher than the rates of obesity (2%) of Dutch children from the Fifth National Growth Study ($\chi^2(3) = 81.5, p < .001$). This difference remained significant after excluding children using medication or children from a migration background (see Table S2). Furthermore, 9% of the children with ASD were overweight, while the national prevalence rate is about 12%.

Table 2. Overweight and obesity in children with ASD (3-7 years) compared to Dutch children aged 2-21 years from the Fifth National Growth Study (Schonbeck & van Buuren, 2010).

	Children with ASD (n = 78)		Reference group (n = 12,151)		
	N	%	%	Chi-square	*P*
Not overweight	58	74.4	85.9	81.5	<.001
Overweight	7	9.0	12.1		
Obese	13	16.7	2		

4.3.3 Correlation between Body Mass Index, child- and parental factors

4.3.3.1 Child factors

As displayed in Table 3, a higher BMIz was related to more food responsiveness (r = .43, p <.001), emotional overeating (r = .30, p =.011), enjoyment of food (r = .36, p = .002) and desire to drink (r = .28, p =.019) in children with ASD. In addition, child BMIz correlated negatively with slowness in eating (r = -.32, p = .006). There was no significant correlation between child BMIz and the other food avoidance scales of the CEBQ. Child BMIz did not correlate significantly with autism severity and behavior problems. All correlations remained significant after controlling for SES and ethnic background (see Table S3).

Table 3.
Correlations between BMIz of children with ASD and autism severity, eating behavior and behavior problems.

	BMIz Child 3-7 years of age
Autism severity (ADOS-2)	
Autism Severity[a]	-.08
Child eating behavior (CEBQ)	
Food responsiveness[a]	**.43*** **
Emotional overeating[a]	**.30***
Enjoyment of food	**.36****
Desire to drink	**.30***
Satiety responsiveness	-.23
Slowness in eating	**-.32****
Emotional undereating[a]	-.10
Food fussiness[a]	-.04
Child problem behavior (CBCL)	
Externalizing behavior problems	.10
Internalizing behavior problems	.09
Total behavior problems	.22

Abbreviations: BMIz = Standardized Body Mass Index; ASD = Autism Spectrum Disorder; ADOS = Autism Diagnostic Observation Scale; CEBQ = Child Eating Behavior Questionnaire; CBCL = Child Behavior Checklist.. [a]Variable was non-normally distributed, Spearman's correlation coefficients are displayed. *$p < .05$, **$p < .01$, ***$p < .001$.

4.3.3.2 Parental factors

As presented in Table 4, there was a significant correlation between child BMIz and mother's BMI ($r = .29$, $p = .011$), which remained significant after controlling for SES and ethnic background (see Table S4). Child BMIz did not correlate significantly with father's BMI, parental eating behavior, parenting stress and parental educational level.

Table 4.
Correlations between BMI of children with ASD and parental BMI, eating behavior and SES.

	BMI Child
Mothers	
BMI[a]	**.29***
Emotional eating (DEBQ)[a]	.05
External eating (DEBQ)	.05
Restraint eating (DEBQ)[a]	.19
Parenting stress (OBVL)	.04
Highest completed education[a]	-.17
Fathers	
BMI[a]	.20
Emotional eating (DEBQ)[a]	.04
External eating (DEBQ)	-.21
Restraint eating (DEBQ)[a]	-.20
Parenting stress (OBVL)	-.01
Highest completed education[a]	-.15

Abbreviations: ASD = Autism Spectrum Disorder; BMI = Body Mass Index; SES = Social Economic Status; DEBQ = Dutch Eating Behavior Questionnaire; OBVL = Parenting Stress Questionnaire; SES = Social Economic Status. [a]Variable was non-normally distributed, Spearman's correlation coefficients are displayed. *p < .05, **p < .01, ***p < .001.

4.4 Discussion

The current study investigated rates of obesity in preschool children with ASD living in the Netherlands and explored several possible contributing child and parental factors. Almost 17% of the children with ASD was obese, which is more than 8 times higher than the national prevalence rates of childhood obesity (2%). Children with a higher BMI showed more food approach behavior and less slowness in eating. Child BMI correlated positively with maternal BMI. We did not find an association between child BMI, child problem behavior, autism severity, parental disinhibited eating behavior, BMI of fathers and SES.

The higher rates of obesity in children with ASD compared to the general population is in line with previous studies from the USA (Sammels et al., 2022). On the contrary, none of the European studies that were included in the meta-analysis of Sammels and colleagues found a significant difference between the obesity rates of children with ASD and those of non-ASD individuals (de Hoogd et al., 2012;

Esteban-Figuerola et al., 2021; Healy et al., 2017). They propose several explanations for this, such as the use of a psychiatric control group and inadequate power. However, obesity rates in our study are in line with age-specific obesity rates as reported by the meta-analysis of Li and colleagues (2020) reporting obesity in 16.7% of the children with ASD between 2 and 5 of age.

We found an association between BMI and food approach behavior in children with ASD, which is in line with earlier studies in neurotypical children (Sleddens et al., 2008). This association may be particularly important for children with ASD, as previous studies suggest that compared to their neurotypical peers, children with ASD are more likely to engage in food approach behavior, including emotional overeating (Hess et al., 2010; Wallace et al., 2021). We did not find an association between BMI and autism severity or child problem behavior. Previous studies that have investigated the association between BMI and autism severity displayed contrasting results. While some studies associated autism severity with higher odds of being overweight in children and adolescents with ASD, some studies found an inverse relationship between autism severity and BMI in girls with ASD, or no association (Hill et al., 2015; Levy et al., 2019; Mccoy et al., 2016; Memari et al., 2012). Therefore, we encourage future studies to further investigate this association by including possible moderating factors, such as gender or age-group.

Children with a higher BMI had mothers with a higher BMI, also after controlling for SES and ethnicity. This is in line with an earlier American study, indicating parental obesity as a strong predictor for obesity in children with ASD (Dempsey et al., 2017). Possible explanations for this are genetic susceptibility, shared environment, or a combination of both. Child BMI was not associated with the educational level of their parents, which contrasts with international studies that observe a negative relationship between SES and the prevalence of childhood BMI in high-income countries (Buoncristiano et al., 2021). Therefore, the high levels of obesity in our sample may reflect a health-risk that is specific for (families of) children with ASD.

The current study had some limitations. We used a national reference group to compare obesity rates. One might consider this a limitation, as the Fifth National Growth study did not include children with a migration background and in our study population 36% of the ASD children had a migration background. However, we showed that obesity rates in our population remained significantly higher than the comparison group after excluding children with ASD with a migration background, indicating the robustness of the finding. In addition, there was a difference between comparison samples in age-range, as our comparison group was aged between 2 and 21 years, while our sample was aged between 3 and 7 years. However, Schönbeck and colleagues (2011) reported age-specific obesity rates of our reference group that range from 0.8% to 3.4% in children aged 3-6 years, which is 5-21 times lower than the obesity rates we found in children with ASD. Therefore, we think it is likely that observed differences cannot be attributed to age differences. We consider it a strength of the study that we used an integrated approach, in which concurrently mental- and physical measures were examined of both parents and children. Furthermore, all children that participated in this study were between 3 and 7 years old and recently received an ASD diagnosis, which allowed us to investigate obesity during an early developmental stage.

The current study evaluated obesity rates in preschool children with ASD and explored possible factors associated with obesity. Almost 17% of the children in our study was obese, which is more than 8 times higher than in the Dutch general population. Moreover, almost 9% of the children with ASD were at risk for obesity and classified as overweight. Children with a higher BMI showed more food approach behavior and less slow eating behavior. In addition, children with a higher BMI had mothers with a higher BMI. We did not find a significant association between child BMI and ASD severity, problem behavior, parental eating behavior, parental stress and SES.

To better understand underlying mechanisms, more research is needed. As childhood obesity can profoundly affect children's physical- and psychological well-being, it is important to target obesity and obesity related behavioral factors like food approach behavior in the treatment of ASD. We encourage professionals to screen for (risk for) obesity during standard clinical care of individuals with ASD. Some studies have demonstrated weight loss after intervention in children with ASD, which suggests that improvement is possible (Healy et al., 2017). However, it would be even better to prevent obesity by educating parents of young children with ASD about the risk for obesity and the associated health risks and guiding them to a healthy lifestyle, as breaking habits is more difficult than learning healthy patterns right away.

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4.6 Supplementary Material

Table S1.
Medications taken by children with ASD aged 3 – 7 years (n = 16).

Medication name		N
Appetite inducing medication		
Anti-epileptics		
	Valproic acid	2
Antihistamines		
	Desloratadine	2
	Yes, name of medicine not specified	2
Antipsychotics		
	Aripiprazole	3
Corticosteroids		
	Dexamethasone	1
	Triamcinolone Acetonide Cream	1
	Hydrocortisone cream	1
Appetite reducing medication		
Amphetamines		
	Methylphenidate	1
	Dexamphetamine	1
Medication without effect on appetite		
Acetanilide Derivative		
	Paracetamol	1
Benzodiazepine		
	Midazolam	1
	Clobazam	1
Beta-2 adrenergic receptor agonist		
	Ventolin	1
Leukotriene receptor antagonists		
	Montelukast	1
Melatonin receptor agonists		
	Melatonin	1
Other		
	Vaseline cetomacrogol cream	1

Table S2.
Overweight and obesity in children with ASD (3-7 years) compared to Dutch children aged 2-21 from the Fifth National Growth Study, excluding children with ASD that use appetite inducing medication or have a migration background (Schonbeck & van Buuren, 2010).

	Children with ASD		Reference group		
	N	%	%	Chi-square	*p*
Children with ASD (3 – 7 years) using appetite inducing medication excluded					
Healthy weight	48	75	85.9	45.86	<.001
Overweight	7	10.9	12.1		
Obesity	9	14.1	2		
Children with ASD (3 – 7 years) from a migration background excluded					
Healthy weight	40	76.9	85.9	60.96	<.001
Overweight	3	5.8	12.1		
Obesity	9	17.3	2		

Table S3.
Correlations between BMIz of children with ASD and autism severity, eating behavior and behavior problems controlled for SES mother and ethnic background.

	Controlling for SES	Controlling for ethnicity
	BMI child	BMI child
Autism severity (ADOS-2)		
Autism severity[a]	-.08	-.07
Child eating behavior (CEBQ)		
Food responsiveness[a]	**.42*** **	**.44*** **
Emotional overeating[a]	**.32** **	**.30* **
Enjoyment of food	**.39*** **	**.36** **
Desire to drink	**.25* **	**.27* **
Satiety responsiveness	**-.25* **	-.23
Slowness in eating	**-.32** **	**-.32** **
Emotional undereating[a]	-.09	-.09
Food fussiness[a]	.04	.04
Child problem behavior (CBCL)		
Externalizing behavior problems	.10	.10
Internalizing behavior problems	.09	.09
Total behavior problems	.21	.22*

Abbreviations: BMIz = Standardized Body Mass Index; ASD = Autism Spectrum Disorder; ADOS = Autism Diagnostic Observation Scale; CEBQ = Child Eating Behavior Questionnaire; CBCL = Child Behavior Checklist.. [a]Variable was non-normality distributed, Spearman's correlation coefficients are displayed. *$p < .05$, **$p < .01$, ***$p < .001$.

Table S4.
Correlations between BMI of children with ASD and parental BMI, eating behavior and SES controlled for SES and Ethnic background.

	Controlling for SES	*Controlling for ethnic background*
	BMI Child	BMI Child
Mothers		
BMI[a]	**.29***	**.28***
Emotional eating (DEBQ)[a]	.10	.06
External eating (DEBQ)	.08	.06
Restraint eating (DEBQ)[a]	.23	.19
Parenting stress (OBVL)	.06	.04
Fathers		
BMI[a]	.22	.21
Emotional eating (DEBQ)[a]	<.01	-.05
External eating (DEBQ)	-.19	-.20
Restraint eating (DEBQ)[a]	-.15	-.19
Parenting stress (OBVL)	<.01	-.01

Abbreviations: ASD = Autism Spectrum Disorder; BMI = Body Mass Index; SES = Social Economic Status; DEBQ = Dutch Eating Behavior Questionnaire; OBVL = Parenting Stress Questionnaire; SES = Social Economic Status. [a]Variable was non-normally distributed, Spearman's correlation coefficients are displayed. *p < .05, **p < .01, ***p < .001.

Chapter 5

Hair Cortisol in Young Children with Autism and their Parents: Associations with child mental health, eating behavior and weight status

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ABSTRACT

Purpose: Children with autism and their parents face daily challenges that may be stressful for both. However, little is known about biological stress (hair cortisol concentrations [HCC]) in these families and its connection to children's health outcomes. This study investigates biological stress in children with autism and their parents and its associations with child mental health, eating behavior and BMI.

Method: Stress was measured in 102 young children with autism and their parents (101 mothers, 86 fathers) using HCC and self-reported parenting stress (OBVL). Child mental health was measured through autism symptoms (ADOS-2, SRS-2) and problem behavior (CBCL). Child eating behavior (CEBQ) and BMIz were also measured.

Results: Children with autism had higher HCC than their peers. Child HCC was not linked to mental health, eating behavior, or BMIz. Maternal stress (self-reported and HCC) was associated with child problem behavior. In fathers, self-reported parenting stress correlated with child autism symptoms (SRS-2) and behavior problems. Both parents' self-reported stress was associated with child eating behavior, specifically emotional undereating and overeating.

Conclusion: In conclusion, higher HCC levels in children with autism in comparison to children from the general population, suggest differences in stress-regulation in children with autism. Given these findings, monitoring HCC in research and clinical practice could improve our understanding of stress-regulation in children with autism. The association between parental stress and children's mental health and eating behaviors, underscores the importance of considering family dynamics in clinical (preventive) interventions and in further research that addresses the mental and physical health of children with autism.

5.1 Introduction

Children with Autism Spectrum Disorder (ASD) face everyday challenges that may impact family life, which may be stressful for both children and their parents. Extensive research demonstrates that stress can have a negative impact on health, by triggering autonomic and hormonal responses and by influencing health-related behavior (O'Connor et al., 2021). Moreover, parental stress may elevate these effects, as it can negatively affect the child's mental and physical health. A meta-analysis demonstrated the association between parental stress and children's emotional and behavioral problems in school-aged children (Ribas et al., 2024). Recent studies show that children with autism and adults have higher rates of physical health problems than children from the general population, such as obesity, gastrointestinal problems, and worse perceived metabolic health (Sammels et al., 2022; Warreman et al., 2023). In addition, comorbid mental health problems are common in individuals with autism. To illustrate: about 70% of the children with autism have at least one comorbid disorder (Simonoff et al., 2008). Studies also demonstrate higher mortality risks in individuals with autism (Catalá-López et al., 2022). As stress may contribute to both mental- and physical health problems, it is important to further investigate how these are related to each other. However, research regarding the associations between stress of children with autism and their parents and the health of individuals with autism, specifically during early childhood is sparse. This is particularly important as the patterns that are formed during early childhood can have lasting effects throughout the individual's life. Therefore, the current study will investigate biological stress in children with autism and their parents and explore its relationship to the mental health, eating behavior and BMI in children with autism.

The hypothalamic-pituitary-adrenal (HPA) axis is activated during stressful situations and forms a chain reaction, which results in the release of the glucocorticoid cortisol. The HPA-axis is in important mechanism for coping with challenges. However, if challenges become overwhelming or chronic, this can lead to a dysregulation of the HPA-axis. Previous studies associate higher HPA-axis activity with various indices of chronic stress and physical health problems, including obesity (Dettenborn et al., 2010). When studying biological stress, serum and salivary cortisol are the most common measures. However, these measures only reflect short-term HPA-axis activity. Given that individuals with autism and their parents face ongoing daily challenges, investigating long-term HPA-axis activity may increase our understanding of the biological stress in children with autism and their parents.

Studies that have compared HCC of children with autism to same-aged children from the general population have produced mixed findings (Lin et al., 2024; Ogawa et al., 2017). The study of Ogawa and colleagues (2017) found higher HCC levels in children with autism than same-aged typically developing children, but this study was performed in a small sample of 28 children with autism . Lin and colleagues conducted a larger study that did not find differences between children with autism (n = 307) and without autism (n = 282). However, this study was performed in a broad age-range (2 to 17 years). Investigating stress in young children specifically may be valuable, as this may provide insights on how stress may impact the development of children's health at an early age. Currently, no studies have specifically investigated HCC in young children with autism.

Previous studies in the general population show a link between stress exposure in early childhood and mental and physical health problems during adolescence, such as depression and obesity (Danese & Tan, 2014; Hazel et al., 2008). Stress could be connected to children's health through biological mechanisms. For example, previous studies found associations between HPA-axis functioning and overweight in school-aged children and adolescents (Miller & Lumeng, 2018). Another mechanism through which stress could be related to the health of children with autism, is through behavioral pathways. Children may use eating behavior to cope with stress, resulting in unhealthy eating habits. In our previous study, we found a positive association between child BMIz and food approach behavior in the child (van der Lubbe et al., 2024). Notably, we found 8 times higher obesity rates in children with autism compared to the general population (van der Lubbe et al., 2024). In addition, previous studies demonstrate that individuals who have experienced high levels of stress in early childhood are at risk for later behavioral problems (Rudd et al., 2021). As research indicates that early life stress can have an impact on the health of individuals, it is important to explore possible associations between stress and children's health early in life.

Another factor that may be associated with child health, is the stress of their parents. For example, a previous study found a link between reported parenting stress in mothers and internalizing and externalizing problem behavior of their children with autism (Zaidman-Zait et al., 2014). Furthermore, stress of parents may be associated with the health of their children in various ways. First, health problems of children may increase stress of their parents. On the other hand, parenting stress may also increase health problems in their children. In a previous study, we found an association between self-reported parenting stress and disinhibited eating behavior of mothers of young children with autism (van der Lubbe et al., 2022). Additionally, another study demonstrated a negative relationship between parental stress and healthy food availability at home, which may impact healthy eating behavior of their children (Jang et al., 2021). While most research on this subject has focused on subjective reports of parental stress, fewer studies have examined the incidence of biological stress. A previous study in children susceptible to obesity, reported an association between high maternal scalp hair cortisol concentrations (HCC) and high fat mass as well as low fat free mass in their children (Larsen et al., 2016). However, less is known about the associations between stress of parents and the mental health, eating behavior and BMI of their children with autism. Furthermore, most research has focused on mothers, while there may be associations of child health with stress in fathers as well. A better understanding of these associations is specifically important, as mothers and fathers of young children with autism report high rates of clinical parenting stress compared to parents of neurotypical children (van der Lubbe et al., 2022).

The current study investigates stress of young children with autism and will explore associations between stress of children with autism with stress of their parents and child mental health, eating behavior and BMI. The first goal of this study is to investigate whether biological stress levels of children with autism differ from same-aged children from the general population. The second goal of this study is to explore associations between biological stress of children with autism and their mental health, eating behavior and BMI. The third goal of the study is to explore associations between stress (self-reported and biological) of parents of children with autism and their children's mental health, eating behavior and BMI.

5.2 Method

5.2.1 Procedure

The current study is a cross-sectional study investigating stress in young children with autism and their parents. This study is part of the ongoing Tandem Study (Dutch Trial register: NL7534), approved by the Institutional Review Board of the Leiden University Medical Center, The Netherlands. Data were collected between 2018 and 2024.

5.2.2 Participants

As the current study is part of an ongoing randomized controlled trial (RCT), the participants in the current study overlap with those reported in our previous study (van der Lubbe et al., in press). Families were recruited from Youz Parnassia Group, GGZ Delfland and Jonx, all Dutch mental health care providers. Families were eligible for inclusion if: 1) the child was diagnosed with ASD, 2) the child was aged between 3-7 years and 3) parents could understand Dutch without the help of a translator. Children who started new psychotropic medication three months prior to participating in the study were excluded.

5.2.3 Measures

5.2.3.1 Stress

Hair Cortisol Concentrations (HCC). Hair samples of approximately 100 hairs were cut from the posterior vertex of the scalp, as close to the scalp as possible in children and their parents. The most proximal 3 cm of the hair strands were used, which corresponds to a period of three months. After collection, hair samples were stored at room temperature and sent to the Erasmus Medical Centre (EMC) for laboratory analysis. At the EMC, the hair samples were weighed, washed and cortisol was extracted with methanol. Next, hair cortisol was analysed using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Parents were asked to complete a questionnaire regarding hair washing frequency, usage of hair products and the use of glucocorticoids in themselves and their children.

The reference intervals that were provided by the study of Kruijf and colleagues (2020) for children aged 3 to 7 years (n = 82) were used to determine cut-off scores for high and low HCC and used to compare our sample with the norms of de Kruijf and colleagues. This study focuses on an age-selected subgroup drawn from a general population sample of children aged 0 to 18 years (n = 625), who were recruited through infant-welfare centres and schools. We will refer to this subgroup as 'peers'.

Reported parenting stress. Reported parenting stress was measured in mothers and fathers using the Parenting Stress Questionnaire (OBVL). The OBVL is a 34-item self-report measure of parenting stress (Vermulst et al., 2015). Mothers and fathers scored items on a 4-point Likert scale. For this study, the total score on the OBVL was used (Cronbach's alpha = 0.91), in which a high score reflects a high level of parenting stress.

5.2.3.2 Child mental health

Autism symptoms. Autism severity was measured using the Autism Diagnostic Observation Scale (ADOS-2; de Bildt et al., 2008). The ADOS-2 is a standardized, semi-structured observational measure of ASD symptoms. For this study, we used the standardized ADOS severity score, ranging from 0 (minimal) to 10 (high), representing the severity of autism symptoms. The ADOS-2 consists of 4 modules, administered according to the level of expressive language of individuals. Modules 1, 2 and 3 were used for the current study.

Social Ability of the child was measured using the Social Responsiveness Scale – second edition (SRS-2; Constantino & Gruber, 2012). The SRS-2 is a 65-item questionnaire consisting of 5 subscales (Social Awareness, Social Cognition, Social Communication, Social Motivation, Restricted Interests and Repetitive Behavior) and a total-score measuring the severity of social deficits in children with autism. The SRS-2 was completed by both parents. The Dutch version of the parent report SRS-2 demonstrated high internal consistency (Cronbach's alpha = 0.92-0.95).

Child problem behavior. Child problem behavior was measured using the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2000; Achenbach & Rescorla, 2001). The CBCL is a caregiver report form targeting problem behavior in children, using two versions: the preschool version (CBCL/1½-5), containing 100 problem behavior questions and the school-age version (CBCL/6-18), containing 118 problem behavior questions. Parents rated their child's problem behavior on a 3-point scale, with higher scores reflecting a higher level of the corresponding behavior. For the current study, the total raw score and the raw scores on the subscales Internalizing and Externalizing problems were used. As both versions have a different number of items, the total raw score on each subscale was divided by the number of items for comparability between the two versions. The CBCL demonstrates strong internal consistency (Cronbach's alpha >.80) and has been validated for use with children with autism (Pandolfi et al., 2009; Pandolfi et al., 2012).

5.2.3.3 Child Eating Behavior and Body Mass Index

Child eating behavior. Child eating behavior was measured using the Child Eating Behavior Questionnaire (CEBQ). The CEBQ is a 35-item questionnaire consisting of 8 subscales measuring food approach behaviors (subscales: Food Responsiveness, Enjoyment of Food, Emotional Overeating and Desire to Drink) and food avoidant behaviors (subscales: Satiety Responsiveness, Slowness in Eating, Emotional Under-Eating and Food Fussiness). Mothers rated items on a 5-point Likert scale, with higher scores indicating a higher level of the specific behavior. The CEBQ has good psychometric properties in terms of factor structure, internal reliability and correlations between subscales (Sleddens et al., 2008). Cronbach's alpha values for the subscales range from .75 to .91 (Wardle et al., 2001).

Body Mass Index. Body height was measured using a stadiometer (Seca 213), and body weight by a digital scale (Seca Clara 803) in all children. Body Mass Index (BMI) was calculated by dividing weight in kilograms by the square of height in meters.

Child BMI was standardized to BMIz, using Growth Analyser Software Research Calculation Tools version 4.1.5 with the Fifth National Dutch Growth Study as a reference group. Based on international cut-off points by Cole and colleagues (2000), children were classified into three BMI classes: healthy weight, overweight and obese. The percentage of participants in each category was compared to Dutch children aged 2-21 years (n = 20.867) from the Fifth Dutch Growth Study, the actual standard of comparison in Dutch pediatric health care.

5.2.3.4 Demographic variables

Parents indicated their highest completed education and their birth country. The highest completed education of mother was used as a measure of Social Economic Status (SES). Children were categorized into one of the two categories: (1) Non migration background and (2) Migration background (if one- or both parents was born outside the Netherlands).

5.2.4 Statistical analyses

To investigate whether children with autism show differences to their peers regarding biological stress, Chi-Square Goodness of Fit tests were performed. The reference intervals that were provided by the study of de Kruijf and colleagues (2020) were used to determine cut-off scores for high and low HCC and used to compare our sample with the norms of de Kruijf and colleagues. Additionally, we used the Mantel-Haenszel test to control for sex and age of the children.

For our next research question, we explored whether biological stress of the child was associated with child mental health, eating behavior and BMI. As child HCC was right-skewed, we performed a Spearman's correlation analysis. We used maternal reports of the SRS, CBCL and CEBQ. If mothers did not complete questionnaires, we used the questionnaires of fathers.

For our last research question, we explored whether stress (self-reported and biological) of the parents was associated with child mental health, eating behavior and

BMI. As HCC of mothers and fathers was right-skewed, we performed a Spearman's correlation analysis. For associations between maternal HCC and the SRS, CBCL and CEBQ, we used maternal reports. We used paternal reports for correlations between HCC of fathers and SRS, CBCL and CEBQ.

For each analysis, we performed a sensitivity analysis by excluding the HCC of individuals who used corticosteroids. Missing values were treated using pairwise deletion. All analyses were performed in SPSS Statistics 27.

5.3 Results

5.3.1 Descriptives

One hundred two children with autism (85 boys, 17 girls) aged 3 to 7 years (Median = 5.1, IQR = 2.1) and their parents (101 mothers, 86 fathers) participated. Autism severity scores (ADOS) raged from 1 to 10 (Median = 6, IQR = 3). In our sample, 11.3% of the children was overweight and 13.4% of the children was obese. Additional details regarding weight-classes and sociodemographic characteristics of our sample, compared to the general population, are displayed in Table 1. Additionally, mean and median values of HCC and the mental health, eating behavior and BMI measures are displayed in Supplementary Table 1.

There were 11 children, 3 fathers and 11 mothers who used corticosteroids and there were 13 children and 26 fathers with hair strand shorter dan 3 centimeters. However, excluding these cases from analysis did not make a difference in results regarding the association between HCC and the other variables. Therefore, analyses were performed including these cases to have sufficient power for the study. Data was collected between November 2018 and April 2024.

Table 1.
Sociodemographic characteristics and weight-status of children with autism aged 3-7 years (n = 102) compared to the general population.

	Children with autism		Comparison group			
	N	%	%	Chi-square	*p*	Reference group
Highest completed educational level of mother				3.85	.15	Dutch females (n = 2,218,000) aged 25 to 45 years from the Dutch general population[b]
Low	11	12.2	10.9			
Middle	38	42.2	33.4			
High	41	45.6	55.6			
Ethnic background of the child[a]				8.21	<.001	The Dutch population (n = 17,591,000)[c]
Dutch	60	63.2	75.8			
Migration background	35	36.8	24.2			
Weight-status				61.17	<.001	Dutch children aged 2-21 years from Fifth National Growth Study[d]
Overweight	11	11.3	12.1			
Obesity	13	13.4	2			

[a]Children were classified with a migration background if one or more parents was born in a different country than the Netherlands; [b]Centraal Bureau voor Statistiek, 2021; [c]Centraal Bureau voor Statistiek, 2022; [d]Schönbeck & van Buuren, 2020.

5.3.2 Biological stress in children with autism versus peers

As shown in Table 2, 15.3% of the children with autism scored above the 97.5th percentile for scalp hair cortisol, while 2.5% of the children in the reference group scored above the 97.5th percentile ($\chi2 = 8.92$, $p < .01$). The difference remained significant when children who used corticosteroids or with hair strands shorter than 3 cm were excluded from analysis. Differences between children with autism and the reference group remained significant if controlled for gender ($\chi2 = 4.88$, $p = .01$) and age ($\chi2 = 7.34$, $p <.01$) of the children by using the Mantel-Haenszel test. Frequencies and percentages of children with autism above the 97.5th percentile are summarized in Supplementary Table 2.

Table 2.
Scalp hair cortisol in children with autism (3-7 years) compared to their peers (de Kruijf et al., 2020).

	Children with autism (n = 98)		Reference group (n=82)		
	n	%	%	χ^2	*p*
Normal range	83	84.7	97.5	8.92	<.01
≥ 97.5th age percentile	15	15.3	2.5		

5.3.3 Associations between child stress and their mental health, eating behavior and BMI.

As presented in Table 3, child HCC was not associated with autism symptoms and problem behavior in young children with autism. Furthermore, as shown in Table 4, there was no significant correlation between child HCC, eating behavior and BMIz.

Table 3.
Spearman's correlations between HCC of children with autism and autism severity and behavioral problems.

	HCC Child 3-7 years of age	
Autism Symptoms	R	*p*
Autism Severity (ADOS-2)	.03	NS
Social Awareness (SRS-2)	.02	NS
Social Cognition (SRS-2)	.01	NS
Social Communication (SRS-2)	.10	NS
Social Motivation (SRS-2)	.05	NS
Restricted Interests and Repetitive Behavior (SRS-2)	.01	NS
Total autism symptoms (SRS-2)	.02	NS
Child problem behavior		
Externalizing behavioral problems (CBCL)	-.05	NS
Internalizing behavioral problems (CBCL)	-.05	NS
Total behavioral problems (CBCL)	-.08	NS

Abbreviations: ADOS-2 = Autism Diagnostic Observation Scale-Second Edition; CBCL = Child Behavior Checklist; NS = Non-significant; HCC = Hair Cortisol Concentration; = Social Responsiveness Scale-2. *p < .05, **p < .01, ***p <.001.

Table 4.
Spearman's correlations between HCC of children with autism and eating behavior and Body Mass Index.

	HCC Child 3-7 years of age	
Child eating behavior (CEBQ)	R	*p*
Food responsiveness	-.07	NS
Emotional overeating	.11	NS
Enjoyment of food	-.03	NS
Desire to drink	-.02	NS
Satiety responsiveness	-.07	NS
Slowness in eating	-.10	NS
Emotional undereating.	-.02	NS
Food fussiness	.01	NS
Physical Measurements		
Body Mass Index – SD	.05	NS

Abbreviations: BMIz = Standardized Body Mass Index; CEBQ = Child Eating Behavior Questionnaire; NS = Non-significant; HCC = Hair Cortisol Concentration.

5.3.4 Associations between parental stress and child mental health, eating behavior and BMI.

As shown in Table 5, there was a negative association between maternal HCC and externalizing problem behavior ($r = -.29$, $p < .01$), internalizing problem behavior ($r = -.22$, $p = .04$) and total problem behavior ($r = -.25$, $p = .02$) of their children, while we found a positive correlation between reported parenting stress of the mothers and externalizing problem behavior ($r = .37$ $p < .01$), internalizing problem behavior ($r = .29$, $p = <.01$) and total problem behavior ($r = .38$, $p < .01$) of their children. Associations between maternal HCC and child mental health remained significant after excluding mothers who used corticosteroids from HCC analysis. Stress of mothers was not significantly associated with autism symptoms of their child.

In fathers, we did not find a significant correlation between HCC and child problem behavior or autism symptoms. Reported parenting stress of the fathers was positively associated with reported autism symptoms of the child all domains of the SRS-2 ($r = .24$-$.40$, $p <.05$). Furthermore, reported parenting stress of fathers correlated positively with externalizing problem behavior (r = .47, p <.01), internalizing problem behavior (r = .40, p <.01) and total problem behavior (r = .49, p < .01) of their children.

Table 5.
Spearman's correlations between stress of parents and autism severity and behavioral problems of the child.

	Mothers		Fathers	
	HCC	OBVL	HCC	OBVL
Child Autism Symptoms				
Autism Severity (ADOS-2)	.00	-.06	-.16	-.15
Social Awareness (SRS-2)	.00	.19	.08	**.29***
Social Cognition (SRS-2)	.04	.01	-.12	**.24***
Social Communication (SRS-2)	.03	.10	-.03	**.28***
Social Motivation (SRS-2)	-.01	**.22***	-.01	**.40*****
Restricted Interests and Repetitive Behavior (SRS-2)	-.04	.11	-.01	**.38*****
Total autism symptoms (SRS-2)	-.01	.16	-.03	**.36****
Child problem behavior				
Externalizing behavioral problems (CBCL)	**-.29****	**.37*****	-.11	**.47*****
Internalizing behavioral problems (CBCL)	**-.22***	**.29****	.07	**.40*****
Total behavioral problems (CBCL)	**-.25***	**.38*****	-.01	**.49*****

Abbreviations: ADOS-2 = Autism Diagnostic Observation Scale-Second Edition; CBCL = Child Behavior Checklist; HCC = Hair Cortisol Concentration; OBVL = Parenting Stress Questionnaire; SRS-2 = Social Responsiveness Scale-2. **p* < .05, ***p* < .01, ****p* <.001

As displayed in Table 6, there was a positive correlation between reported parenting stress of mothers and both emotional overeating of the child (r = .22, p = .03) and emotional undereating of the child (r = .42, p <.01). Reported stress of mothers did not correlate with any of the other subscales of the CEBQ and child BMIz. Additionally, there was no correlation between maternal HCC and eating behavior or BMIz of the child.

In fathers, there was a positive association between reported parenting stress and child eating behavior on the following subscales of the CEBQ: food responsiveness (r = .25, p = .02), emotional overeating (r =.27, p = 02), satiety responsiveness (r = .22, p = .05) and emotional undereating (r =.35, p <.01). Reported stress of fathers did not correlate with any of the other subscales of the CEBQ and child BMIz. Additionally, there was no correlation between HCC of fathers, child eating behavior and BMIz.

Table 6.
Spearman's correlations between stress of parents and eating behavior and Body Mass Index of the child.

	Mothers		Fathers	
	HCC	OBVL	HCC	OBVL
Child eating behavior (CEBQ)				
Food responsiveness	-.09	.12	.00	**.25***
Emotional overeating	-.02	**.22***	-.17	**.27***
Enjoyment of food	.13	-.06	.05	.08
Desire to drink	-.02	-.01	-.03	-.07
Satiety responsiveness	-.17	.12	.01	**.22***
Slowness in eating	-.10	.17	.13	.22
Emotional undereating.	-.20	**.42*****	-.19	**.35****
Food fussiness	-.15	.11	-.03	.05
Physical Measurements				
BMIz	-.07	-.00	.09	.05

Abbreviations: BMIz = Standardized Body Mass Index; CEBQ; Child Eating Behavior Questionnaire; HCC = Hair Cortisol Concentration; OBVL = Parenting Stress Questionnaire;. *$p < .05$, **$p <.01$

5.4 Discussion

The current study investigated stress in children with autism and their parents and explored associations between stress and child mental health, eating behavior and BMI. While children with autism had higher HCC than their peers, biological stress of children with autism was not associated with their mental health, eating behavior and BMI. Stress of mothers, as well as stress of fathers, was related to child mental health, eating behavior and BMI.

Compared to their peers, children in our sample exhibited higher HCC, with 15.3% of the children scoring above the 97.5th percentile. This finding is in line with the study of Ogawa and colleagues (2017), that reported higher HCC in children with autism compared to same-aged typically developing children. However, their sample size was smaller than ours (34 children with autism versus 102 in our study) and the children were older than the children in our group (mean age = 11.9 years versus 5.1 years in our study). Another recent study did not find differences between HCC of children with and without autism (Lin et al., 2024). The age range of the study by Lin and colleagues was broader than ours, with children who were aged between 2 and 17 years old, compared to the 3 to 7 years old age range in our study. Furthermore, the autistic group was significantly older than the non-autistic group in the study by Lin and colleagues. This age difference could explain why they did not find differences between the two groups, although their results indicated higher HCC concentrations in younger children. The age-related differences in HCC could be explained by both biological changes as well as psychosocial factors, such as family stress and socio-economic differences (Perry et al., 2022). In addition, the studies of Ogawa (2017) and Lin and colleagues (2024) used another, less sensitive, analysis method for cortisol analysis (ELISA method) than our study (LC-MS method), which may explain differences in findings. The current study is the first study to demonstrate a difference between young children with autism and their peers. Further research is needed to better understand biological stress of children with autism.

While we did observe higher HCC values in children with autism compared to their peers, we did not find any associations between HCC of children with autism and their mental health, eating behavior or BMI. These results suggest that while children with autism may demonstrate elevated biological stress levels, the relationship with mental health, eating behavior and BMI measures may be more complex and needs further investigation. Given that the children in our study were aged between 3 and 7 years old, a developmental stage where children are still very dependent on their parents, it could be hypothesized that parents, rather than children themselves, may have a large impact on the mental- and physical wellbeing of young children. As parental stress may affect parenting behavior and family environment, it could possibly play a more important role in shaping the child's mental health and eating behavior than the child's own stress levels. This is in line with a study by Perry and colleagues (2022) that found an association between HCC of mothers and that of their children, especially in young children. This hypothesis is supported by our previous study in the same sample, that found a significant correlation between HCC of parents and HCC of children with autism (van der Lubbe et al., under review). Therefore, longitudinal research is warranted to further investigate these multifactorial relationships.

We found an association between reported parenting stress in mothers and fathers and problem behavior of children with autism. This is in line with previous research, that demonstrates an association between parental stress and externalizing and internalizing behavioral problems of the child (Barraso et al., 2018). Hasting (2002) proposes a bidirectional model in which behavioral problems elevates parenting stress, which disrupts parenting behavior, further elevating the behavioral problems of the child. This bidirectional model is inconsistently supported by research, with some studies finding evidence for a bidirectional relationship between parenting stress and behavioral problems in children with autism, while others support a unidirectional model in which parental stress predict later behavioral problems of the children or vice versa (Yorke et al., 2018; Zaidman-Zait et al., 2014).

Interestingly, children with a higher level of behavioral problems had mothers with lower HCC. In other words, the biological stress response of mothers seems to be lower when their children demonstrate more behavioral problems. A possible explanation is that chronic stress leads to a dampening of the HPA-axis. This is in line with our previous study in the same sample, that demonstrated a negative correlation with reported parenting stress and HCC of parents (van der Lubbe, under review). Moreover, Radin and colleagues (2019) found lower HCC in mothers of children with autism compared to mothers of typically developing children. These findings demonstrate the complex interplay between maternal stress regulation and child behavioral problems, suggesting that behavioral problems in children may be associated with a dampened physiological stress response in mothers. However, as the current study was cross-sectional, it is relevant to further investigate these relationships longitudinally.

While self-reported parenting stress for both mothers and fathers correlated with mental health of their children, and maternal HCC was associated with mental health of their child, we did not find this correlation for HCC of fathers. This means that while behavioral problems and autism symptoms are associated with reported parenting stress in fathers, they are not necessarily associated with biological stress in fathers. Possibly, the psychological response to behavioral problems of the child may precede the biological response, therefore it may be that the connection develops later in time. Additionally, differences in exposure to childcare responsibilities among fathers could influence the extent to which the parenting stress translates to a biological stress response. Previous research demonstrated that fathers of children with autism spend approximately 26% less time in childcare than mothers (Hartley et al., 2024). Another explanation is that the biological response of the HPA-axis may differ between fathers and mothers. Previous studies in various species suggest that the physiological reactivity to stress is greater in females than in males (Goel et al., 2014). This could explain why we found a correlation between reported parenting stress and mental health problems of the child, but not between these factors and HCC of fathers.

Although almost 25% percent of the children in our study were overweight or obese, BMI was not related to children's or parents' stress levels. However, in both mothers and fathers, we found associations between reported parenting stress and eating behavior of the child. This is in line with previous research in children without autism, that found a correlation between parenting stress and child's eating behavior (Jang et al., 2021). Interestingly, parenting stress was associated with emotional overeating and emotional undereating of the child. It is possible that both emotional overeating and emotional undereating leads to increased parenting stress, due to the health risks that are associated with both eating behaviors. On the other hand, it is also possible that both emotional overeating and emotional eating is a reaction of the children to the stress they experience due to the stress of their parents. Our previous study in the same sample indicated a correlation between HCC of parents and HCC of children with autism (van der Lubbe et al., under review). While children may react to stress by using food as a source of comfort, leading to overeating, children may also experience reduced appetite, leading to undereating. As stress may influence children's behavior in diverse ways, this may explain why we did not observe a relationship between BMI and the stress levels of children with autism and their parents.

The current study has some limitations. One limitation is that our study design was cross-sectional and therefore, we cannot make conclusions about causality based on our results. Additionally, for future research it is important to acknowledge that the mental health, eating behavior and BMI of children with autism may be associated with other underlying factors too, such as genetic health conditions. For example, a previous twin-study in children with autism found that shared genetic factors may contribute to both ASD and emotional symptoms (Tick et al., 2015). However, as the mental health, eating behavior and BMI of young children with autism is a complex interplay of genetic, environmental and developmental factors, the current study may help by identifying specific factors that are associated with the mental health, eating behavior and BMI of children with autism. We consider it a strength of the study that we used an integrated approach, in which concurrently mental- and physical measures were used.

The current study investigated biological stress of children with autism and explored associations between stress of children with autism and their parents, as well as child mental health, eating behavior, and BMI. First, we found higher levels of HCC in children with autism compared to their peers. Second, we did not find associations between child HCC, mental health, eating behavior and BMI. Third, parenting stress was associated with behavioral problems of the child, autism symptoms and with child eating behavior. Differences in mothers and fathers between their associations of stress with child factors motivate the urge to better understand underlying mechanisms in further research. We encourage future studies to examine longitudinal effects of stress on mental health, eating behavior and BMI of children with autism. For example, it would be relevant to further investigate whether the amount of time attributed to parenting tasks, such as time spent caregiving or other parenting tasks, may impact parental stress or health. Additionally, it would be significant to investigate the effect of interventions on (parenting) stress and mental health, eating behavior and BMI of children with autism.

In the current study, differences in HCC between young children with autism and their peers were found, suggesting potential alterations in stress-regulation of young children with autism. While the associations between biological stress and child mental health, eating behavior and BMI were not observed, we found a significant relationship between stress of parents (self-reported and biological) and child mental health and eating behavior.

These findings demonstrate the importance of addressing stress of parents in research and clinical care of children with autism, as this may have an impact on the mental health and eating behavior of their children. For example, interventions directed at reducing parenting stress could be beneficial for the mental and physical health of both parents and children. Additionally, it could be beneficial to monitor HCC in research and clinical practice, as this could improve our understanding of stress-regulation in children with autism.

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5.6 Supplementary material

Table S1. Descriptive values of hair cortisol concentrations and mental health, eating behavior and BMI of young children with autism.

Measure	**n**	**M (SD)**
Hair cortisol concentration (pg/mg)[a]	95	2.1 (6.03)
Autism Severiy Score (ADOS-2) [a]	97	6.0 (3.00)
Total score SRS-2	90	93.8 (2.58)
Total behavioral problems (CBCL)	94	67.4 (9.01)
Food Responsiveness (CEBQ)[a]	92	11.0 (8.00)
Emotional Overeating (CEBQ)[a]	92	6.0 (4.75)
Enjoyment of Food (CEBQ)[a]	92	13.0 (5.00)
Desire to Drink (CEBQ)[a]	94	7.0 (4.00)
Emotional Undereating (CEBQ)[a]	92	11.0 (8.00)
Satiety Responsiveness (CEBQ)	91	14.2 (4.11)
Slowness in Eating (CEBQ)[a]	91	12.0 (7.00)
Food Fussiness (CEBQ)[a]	92	22.0 (9.00)
BMIz	97	0.9 (1.52)

[a]Variable was non-normally distributed, median and IQR's are displayed.
Abbreviations: ADOS-2 = Autism Diagnostic Observation Scale-Second Edition; BMIz = Standardized Body Mass Index; CBCL = Child Behavior Checklist; CEBQ; Child Eating Behavior Questionnaire; HCC = Hair Cortisol Concentration; M = Mean; SD = Standard Deviation; SRS-2 = Social Responsiveness Scale-2.

Table S2. Frequencies of children above the 97.5th percentile for hair cortisol categorized by sex and age-group.

	Above the 97.5th percentile (%)	Within the normal range
Boys	14 (17.1)	68 (82.9)
Girls	1 (6.3)	15 (93.8)
3-year-olds	4 (16.7)	20 (83.3)
4-year-olds	3 (12.0)	22 (88.0)
5-year-olds	3 (15.0)	17 (85.0)
6-year-olds	5 (17.9)	23 (82.1)
7-year-olds	0 (0.0)	1 (100.0)

Chapter 6

General Discussion

6.1 General discussion
6.1.1 Aim

The aim of this dissertation was to examine associations between stress, eating behavior and physical and mental health in young children with ASD and their parents. The following questions were addressed:

1) Are there differences between parents of children with ASD and adults from the general population regarding parenting stress, eating behavior and physical health, and are these factors interrelated?
2) Is parental chronic stress related to chronic stress of their children, and to the mental and physical health of mothers and fathers of children with ASD?
3) What are obesity rates and associated child and parental factors in young, Dutch children with ASD?
4) How do chronic stress levels of young children compare to those of their peers, and how are they related to child mental and weight-related health?

Those questions were addressed in a large sample of young children with ASD and their parents.

6.1.2 Stress in parents of young children with ASD

In the study presented in Chapter 2, we addressed the question whether there are differences between mothers and fathers of children with ASD and adults from the general population regarding parenting stress, eating behavior and physical health. Also, we studied whether parenting stress was associated with eating behavior and physical health in both mothers and fathers. We studied this in families of young children with ASD, as previous studies demonstrated higher levels of perceived stress, higher incidence of reward-based eating and high levels of self-reported health problems in mothers of children with ASD compared to mothers of typically developing children. Moreover, in a study by Fairthorne and colleagues (2014) higher morbidity and mortality ratios were found in mothers of children with ASD. However, to date, most research regarding parenting stress in parents of children with ASD is directed at mothers, while limited research has been performed on fathers. In addition, most research is performed in parents of children in a broad age range. We chose to study children in early childhood, as dynamics in early childhood may shape long-term health risks, laying the groundwork for health outcomes later in life.

The findings demonstrate that both mothers and fathers experience high levels of parenting stress. This indicates that elevated parenting stress levels are already present while their children are at an early age in both mothers and fathers. In addition, we found higher rates of obesity and metabolic syndrome in mothers of young children with ASD compared to females from the general population. This finding is noteworthy, as both conditions are known to elevate the risk of chronic illnesses, including cardiovascular disease and certain types of cancer. This finding is in line with the hypothesis proposed by Fairthorne and colleagues (2014), who observed higher mortality rates in mothers of children with ASD and suggested that this link may be mediated by increased maternal stress levels or health conditions, such as obesity.

We did not observe higher rates of obesity, hypertension, and metabolic syndrome in fathers of young children with ASD. Several factors could explain these different findings for fathers compared to mothers. One might hypothesize that there may be differences in the amount of time spent with their children, potentially resulting in less exposure to parenting stress in fathers. Variations in coping mechanisms between mothers and fathers can also explain differences. Another explanation may be that health disparities between fathers of children with ASD and the general population may emerge over time, as chronic stress can have a long-term impact on health through alterations in the immune system and microbiome imbalance (reviewed by Dijkstra–de Neijs et al., 2020).

We found a positive association between parenting stress and emotional and external eating in mothers of young children with ASD, indicating that the mothers who reported high levels of stress were also more likely to engage in disinhibited eating behavior, such as eating in response to emotions or external food cues. This finding is in line with earlier studies in the general population, that suggested chronic stress can increase food consumption (Sominsky & Spencer, 2014). Radin and colleagues (2019) theorized that chronic stress related to taking care of a child with ASD may promote disinhibited eating behavior in the short term, which may potentially contribute to weight gain and negative changes in metabolic health, such as altered lipid profiles in the long-term. The current study supports this hypothesis, by demonstrating a positive relationship between parenting stress and disinhibited eating behavior. However, as we cannot draw causal conclusions based on our cross-sectional data, our findings point to the need for future longitudinal studies to further investigate these trajectories.

6.1.3 Hair cortisol as a biological marker of chronic stress in parents and children with ASD

In Chapter 3, we describe the findings of a study that examined physiological stress levels, using Hair Cortisol Concentrations (HCC), and the associations with mental and physical health in parents of young children with ASD. While most research on stress in these parents has focused on self-reported stress or short-term physiological stress levels, fewer studies have focused on chronic stress. Using HCC as a measure of chronic stress may provide further, objective insights into long-term stress of parents of children with ASD. To our knowledge, only one other study examined HCC in parents of children with ASD so far. This study demonstrated lower HCC levels in mothers of children with ASD compared to mothers of typically developing children, suggesting a dampening of the HPA-axis reactivity due to prolonged stress exposure (Radin et al., 2019).

In line with the study by Radin and colleagues (2019), we found that mothers of children with ASD who reported high levels of parenting stress demonstrated lower HCC. Previous studies that investigated short-term HPA-axis activity are in line with the findings of the current study, as these studies found an association between a higher level of perceived stress and a blunted cortisol response in mothers of children with ASD (Padden et al., 2019). Based on these findings, it could be suggested that chronic stress in mothers of children with ASD may be associated with a dampening of the HPA-axis reactivity, resulting in lower HCC, potentially as a biological adaptation to the prolonged stress exposure. This blunted HPA-axis reactivity could reflect an adaptation of the body that is directed at protecting the body from the negative effects of sustained HPA-axis activation. However, a blunted HPA-axis response is also related to health risks, such as an impaired immune response (Tsigos et al., 2020).

Our findings reveal a positive connection between HCC of parents and HCC of their children with ASD. To our knowledge, this is the first study of these associations in families of children with ASD. This finding is significant, as it demonstrates how chronic stress may be shared within the family and may be associated with overall family well-being. We encourage future researchers to investigate whether this correlation is generalizable to older children with ASD. Moreover, it could be speculated that the connection is influenced by parenting strategies. For example, Ouellette and colleagues (2015) found a stronger association between HCC of mothers and their infants in mothers who used lower quality parenting strategies. Furthermore, genes could also play a role in this association. For example, some genes play a role in the HPA-axis regulation (Gerritsen et al., 2017). Therefore, we encourage future studies to explore the role of genetics and parenting strategies to better understand the dynamics of stress regulation within families.

While we did find a strong correlation between self-reported parenting stress and parental psychopathology symptoms, we did not find this connection between parental HCC and psychopathology symptoms. There could be different explanations for this discrepancy. For example, it is possible that variation within psychopathology symptoms could hide specific associations. It is possible that some behavioral or emotional problems are associated with a higher HCC, while others are associated with a lower HCC. For example, Staufenbiel and colleagues (2013) found increased HCC in patients with major depression, while they found lower HCC in individuals with anxiety disorders.

Our findings highlight that chronic stress may play a significant role in shaping family dynamics. This emphasizes the importance of future research to understand how these patterns emerge and whether these are generalizable to the whole ASD population and to each developmental stage. The current study also addressed a gap in knowledge regarding the relationship between chronic stress and mental and physical health problems in parents of young children with ASD. The results reveal that self-reported parenting stress is strongly associated with increased mental health problems in parents of children with ASD, whereas the association with physical health problems is less consistent. Notably, the positive correlation between HCC and glucose levels in mothers suggests a potential link between chronic stress and physical health, but we did not find an association between chronic stress and the other physical health measures. It must be noted that the current study is cross-sectional and therefore we cannot make any causal conclusions. However, as parents of young children have higher risk for chronic stress and mental and physical health problems, preventive measures like parenting support, could improve parental care, by preventing the development of mental and physical health disorders in parents of children with ASD.

6.1.4 Obesity in children with Autism Spectrum Disorder

In Chapter 4, we evaluated obesity rates in young children (3 to 7 years) with ASD and explored possible factors associated with obesity. Given the significant health risks that are associated with obesity, examining the risk of obesity and associated factors in young children with ASD is crucial for understanding and potentially preventing health problems in this population. While obesity has been investigated before in children with ASD, most studies have focused on children across a wide age range. Early childhood may be a particularly important period to investigate obesity and related health problems, since early development may impact the risk of obesity and other health problems later in childhood, adolescence, and adulthood. Additionally, most research on obesity in children with ASD has been conducted in the United States, where obesity rates are higher than in other Western countries (Sammels et al., 2022).

In line with studies from the United States, we found higher obesity rates in Dutch children with ASD (17%) compared to same-aged children from the Dutch population (2%). Moreover, almost 9% of the children with ASD were classified as overweight, placing them at increased risk for obesity. As childhood obesity is associated with various health risks later in life, it is important to target obesity and obesity-related factors in treatment and research of children with ASD.

We explored possible factors that could be associated with obesity in young children with ASD. First, we found an association between BMI and food approach behaviors in young children with ASD. While studies in neurotypical children yielded similar results, we think this is a particularly important finding, as studies demonstrate that children with ASD are more likely to engage in food approach behavior (Hess et al., 2010; Wallace et al., 2021). Secondly, we found that children with a higher BMI had mothers with a higher BMI. This is also in line with an earlier American study, identifying parental obesity as a strong predictor for obesity in children with ASD (Dempsey et al., 2017). Possible explanations for this could be genetic susceptibility, shared environment, or a combination of both. Again, this finding may be particularly important, given our previous study that demonstrated that 39.1% of the mothers of a young child with ASD had obesity and another 21.7% of the mothers were overweight. Similar to stress, the risk for obesity may not be an individual characteristic but could be significantly shaped by family dynamics. To better understand underlying mechanisms of obesity in families of children with ASD, more research is warranted.

6.1.5 Stress in children with Autism Spectrum Disorder

We evaluated differences in HCC between young children with ASD and same-aged children from the general population in the studies that are described in **Chapter 5.** To date, no studies have specifically investigated HCC in young children with ASD. Investigating HCC in this population could offer new insights into their biological susceptibility for stress. Also, we have explored associations between biological stress of children with ASD and their mental health, eating behavior and BMI. Lastly, we investigated associations between stress (self-reported and HCC) of parents of children with ASD and their children's mental health, eating behavior and BMI. A deeper understanding of these associations could provide valuable insights into the role of stress in the health of families of children with ASD. Such knowledge has the potential to enhance clinical care and support for children with ASD and their families.

We found that individuals with ASD had high HCC more often (15.3%) than same-aged children from the general population (2.5%), which could suggest a dysregulation of the HPA-axis. This finding is in line with the study by Ogawa and colleagues (2017), which was performed in a smaller sample (n = 34 versus n = 102 in our study) of older children (mean age = 11.9 years) with ASD. Further research into the trajectories and mechanisms behind HPA-axis dysregulation and its potential effects on mental and physical health could further enhance our understanding of chronic stress in children with ASD.

We found no associations between HCC of children with ASD and their mental health, eating behavior, or BMI. This suggests that while children with ASD may demonstrate higher stress levels, the relationship with these factors may be more complex and needs further investigation. Interestingly, we found associations between mental health of children with ASD and their parents' stress levels. More specifically, children who exhibited more behavioral problems had mothers and fathers who reported more parenting stress, and mothers who demonstrated lower HCC. A possible explanation for this could be that children with behavioral problems increase stress in their parents and that this stress leads to a dampening of the HPA-axis. This is in line with the study we described in **Chapter 3**, that demonstrates a negative correlation between reported parenting stress and HCC of parents. However, as the current study was cross-sectional, it is relevant to further investigate these relationships longitudinally.

6.1.6 Strengths and limitations

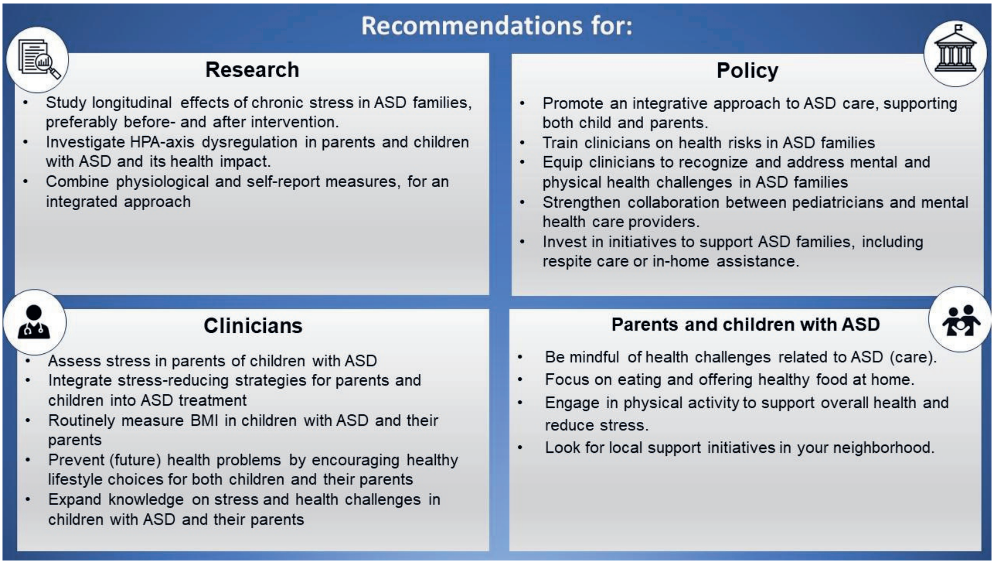
The key strengths of the studies described in this dissertation are the integrated approach, in which subjective self-report measures are combined with objective physiological and physical data in a large group of young children with ASD and their parents. This approach provides a more comprehensive picture of stress and its associations with mental and physical health in children with ASD and their parents. Additionally, including fathers in our sample addressed a significant gap in knowledge and enhanced our understanding of stress and health dynamics of fathers of young children with ASD. Another strength is the focus on young children (aged 3-7 years) specifically, which allowed us to examine early developmental stages and gain insights into the early experiences of parenting a child with ASD. Having a better understanding of early processes can shape longitudinal studies and provide further understanding of the relevance of prevention and early intervention. Additionally, the associations between stress and health may be relevant for a broader group beyond children with ASD and their parents, extending to families facing other parenting challenges, such as raising a child with an atypical (neuro)developmental condition.

The current study has some limitations too. First, due to the cross-sectional design of the study, we cannot make any causal conclusions based on our data. However, our findings offer a valuable starting point for future longitudinal research, which is crucial for exploring how these associations evolve over time, particularly before and after interventions. For example, it may be relevant to study whether reducing parental stress through intervention has lasting effects on parental health in the years that follow. Furthermore, as we did not have a control group, we relied on normative data from the general population for comparison, which had some limitations. For example, some reference groups, such as those used for the Parenting Stress Questionnaire (OBVL) norms, consisted only of mothers. Future research could strengthen these findings by incorporating longitudinal designs and control groups to further validate the results.

6.1.7 Implications

The findings of this dissertation may have important implications for four domains: research, healthcare policy, prevention and intervention designed by clinicians that work with children with ASD and their parents and for daily family life. These implications are aimed to improve the lives of children with ASD and their parents, offering insights that could guide research, policy, clinical care, and families. The recommendations for each domain are summarized in Figure 1.

Figure 1. Recommendations for research, policy, clinicians, and families.



6.1.7.1 Future research

We encourage future studies to explore the longitudinal effects of chronic stress in children with ASD and their parents. Understanding how associations between stress, mental and physical health may develop over time, could help us to form more targeted and effective treatments for both parents and children. Furthermore, further research into HPA-axis dysregulation in parents and children with ASD can offer more insights into the stress regulation. Future studies could focus on possible factors that may play a role in stress dysregulation, such as coping strategies, chronicity of stress and glucocorticoid sensitivity. Lastly, parental stress should be considered as an outcome variable when evaluating the effectivity of interventions. As parental stress is linked to stress in the children and overall family health, reducing parental stress may improve well-being of the whole family.

6.1.7.2 Policy and clinical implications

The findings of this dissertation demonstrate the interrelated nature of stress and health in families of children with ASD. Therefore, there is a need for policy initiatives from various stakeholders, including governments and health care institutions to promote an integrative approach to ASD care, focusing on both the child and their parents. Healthcare policies should encourage comprehensive screening for stress, mental health and physical health in both parents and children with ASD. Additionally, health professionals, such as psychologists, general practitioners, pediatricians, and psychiatrists, should be trained to recognize and address the mental and physical health challenges faced by parents of children with ASD. This could improve overall family health and contribute to a more holistic approach for children with ASD and their families. Moreover, the collaboration between health care professionals should be strengthened. For example, a consultation possibility where professionals from different fields (e.g. psychiatrist and pediatrician) see clients together, integrating their knowledge and combining their expertise to help individuals with ASD and their parents. Lastly, to alleviate stress in parents of children with ASD, the government should invest in local initiatives to support ASD families, such as respite care or in-home assistance.

Given that half of the mothers and one third of the fathers in our sample experienced parenting stress levels in the clinical range, it is crucial to draw attention to the well-being of both mothers and fathers of children with ASD in clinical settings, such as in mental health care institutions. Incorporating stress-reducing strategies in clinical practice, such as mindfulness-based interventions, could significantly benefit parents and may even positively impact their children's outcomes. Furthermore, addressing obesity risk factors and promoting healthy lifestyle choices for both parents and children with ASD should be a focus in clinical care of individuals with ASD. For example, it may be helpful to routinely measure BMI in children with ASD and their parents during intake. Early interventions, including psychoeducation on the risk of obesity and behavioral strategies for promoting healthy eating behavior and other healthy coping mechanisms may have long-term benefits for both children with ASD and their parents.

We encourage children with ASD and their parents to focus on providing healthy food at home. While this may be challenging, due to factors such as selective eating, or limited time for meal preparation, offering healthy options more frequently and limiting unhealthy snacks may be beneficial. Seeking guidance from a dietitian with expertise in children with ASD could also be helpful. Additionally, engaging in physical activity to support both mental and physical health may reduce stress and improve family well-being. For the families that may find it difficult to make time for physical activity, small adjustments in daily routines, such as taking the stairs more often, or cycling or walking short distances – can still have a positive impact.

6.1.8 General conclusion

The findings of the current study reveal differences between children with ASD and their peers regarding biological stress and obesity. In addition, we observed elevated stress levels in both their mothers and fathers and found high rates of obesity and metabolic syndrome among mothers. It is important to recognize that the chronic stress and health risks that children with ASD and their parents experience may be interconnected. Considering these findings, it is crucial for preventive support and clinical care to address stress and health within families adopting a family-centered approach rather than focusing on individuals. This could involve promoting a health promoting lifestyle that benefit both parents and their children with ASD. To further understand the long-term effects of chronic stress on family health, future research is needed.

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6.2 Summary

In this dissertation, the question is addressed if stress, eating behavior and health are interrelated in young children with ASD and their parents. To gain a comprehensive understanding, an integrated approach is used, including children with autism and their parents in other to shed light on family dynamics on stress, eating behavior and somatic and mental health risk by use of self-reflection (questionnaires), physical assessments (Body Mass Index, blood pressure, waist circumference) and physiological measures (blood tests and hair cortisol).

In **Chapter** 1, the importance of studying stress, eating behavior, and health in young children with ASD and their parents is discussed. Children with autism and their parents face substantial daily challenges, and early stress may shape long-term mental and physical health. Although research demonstrates elevated stress levels in mothers, research regarding fathers, early childhood and long-term physiological stress markers is limited. Including fathers is essential, as they also play a unique role in their child's development. Early childhood is a particularly important period, as the behavioral and emotional patterns that are formed during this stage can have lasting effects throughout the individual's life. Research on how stress relates to eating behavior and health in individuals with autism and their parents may increase our understanding of associated factors and dynamics within the family, which may guide future research, strengthen clinical care and support the families in the long term.

In **Chapter 2**, it is addressed whether mothers and fathers of young children with ASD differ from adults from the general population regarding parenting stress, eating behavior and physical health. Both mothers and fathers of young children with ASD report high levels of parenting stress. Mothers of young children with ASD also demonstrate higher rates of obesity and metabolic syndrome compared to females from the general population, indicating an elevated risk for chronic illnesses. Parenting stress in mothers is positively associated with disinhibited eating behavior. Fathers do not demonstrate higher rates of obesity or metabolic syndrome.

In **Chapter 3**, both self-reported and physiological stress levels, as indicated by hair cortisol concentrations (HCC), in parents of children with ASD are examined. It is found that mothers of children with ASD who report high levels of stress, demonstrate lower HCC. Furthermore, a positive connection is found between HCC of parents and HCC of their children, suggesting that stress may be shared within the family. Parents of children with autism also show higher levels of psychopathology symptoms, such as depression and hostility, compared to same-aged males and females from the Dutch population. Moreover, a strong correlation between self-reported parenting stress and parental psychopathology symptoms is found. These findings indicate that stress levels of parents and their children are interrelated and demonstrates a link between parental stress and mental health, which emphasizes the importance of a family-focused approach in research and clinical care, as well as the need to monitor parental mental health.

In **Chapter 4**, obesity rates of young children with ASD are compared to those of their peers and it is explored which child- and parental factors are associated with obesity in these children. Compared to same-aged children from the Dutch population, children with ASD demonstrate higher obesity rates. Child Body Mass Index (BMI) is associated with food approach behavior and maternal BMI, suggesting that, in young children with ASD, shared environment, genetics, and family dynamics, may contribute to obesity risk. These findings highlight that early childhood may be an important period for identifying and supporting children with ASD at risk for obesity and for guiding families toward health lifestyle habits. making early childhood an important period for intervention and support.

In **Chapter 5**, HCC of young children with ASD and same-aged children from the general population is compared. In addition, associations between HCC of children with ASD and their mental health (autism symptoms, internalizing problem behavior, externalizing problem behavior), eating behavior and BMI are explored. Also, associations between stress (self-report and HCC) of parents of children with autism and their child's health, eating behavior and BMI are described. It was found that young children with autism more often show high HCC than same-aged children from the general population. Child HCC is not directly associated with their mental health or BMI, indicating that biological stress of the child may not directly reflect these outcomes at this early age. However, maternal HCC is associated with behavioral problems in their children with autism. Additionally, self-reported stress of mothers and fathers is correlated with autism symptoms, behavior problems and eating behavior of their children with autism. This underscores how stress of parents are linked to specific aspects of child functioning in families of children with ASD, highlighting the relevance of assessing both parent and child factors in research and clinical context.

In **Chapter 6,** the implications of our findings and the strengths and limitations of the reported studies are addressed. The main strength is the family approach, combining self-reflection questionnaires, physical assessment and physiological measures in children, mothers and fathers. In addition, the focus on early childhood, offers insights into family dynamics during this specific developmental period in children with ASD. A limitation is the cross-sectional design, which prevents causal conclusions, leaving the direction of the associations unknown. Nevertheless, the observed associations provide valuable information for future studies that can further examine the relation between stress and health in families of children with ASD.

Implications of these findings are relevant for further research, clinical care, policy and daily family life. In future studies it might be important to further evaluate the dynamics of stress and health in children with ASD and their parents using longitudinal design, while also evaluating the impact of interventions that address stress regulation in parents on family well-being. The findings in this dissertation support a family-centered approach in clinical support that combines mental and physical care, monitors BMI, promotes a healthy lifestyle, and addresses parental stress, next to evaluation of psychological and social emotional impact. Policy initiatives could stimulate multidisciplinary interventions, targeted at reducing parental stress and supporting parental mental and physical health outcomes. For families, it is important to recognize the mental and physical health risks associated with (raising children) with autism. While our study did not examine causal effects, supporting healthy lifestyle habits, such as balanced nutrition and frequent physical activity, may promote mental and physical health and could positively impact well-being of both children with ASD and their parents.

Taken together, the findings of the studies highlight the mental and physical vulnerabilities of young children with ASD and their parents, including an increased risk for chronic stress and obesity. Importantly, differences between mothers and fathers were observed, suggesting that parental stress may relate to child and parent health in distinct ways for mothers and fathers, highlighting the need to consider both parents in research and clinical practice. The findings emphasize the importance of addressing stress within the family system to promote health and well-being of both children with autism and their parents.

6.3 Nederlandse samenvatting

In dit proefschrift wordt onderzoek beschreven naar de vraag of stress, eetgedrag en gezondheid samenhangen bij jonge kinderen met autisme en hun ouders. Deze vraagstelling werd gemotiveerd vanuit de veronderstelling dat er samenhang kan bestaan tussen ouderlijke stress en mentale gezondheid van kinderen met autisme en hun ouders. Er is een geïntegreerde aanpak gebruikt, waarbij zowel kinderen met autisme als hun ouders zijn betrokken om zicht te krijgen op de familiedynamiek rond stress, eetgedrag en mentale en fysieke gezondheidsrisico's. Hiervoor zijn zelfrapportages (vragenlijsten), lichamelijke metingen (Body Mass Index, bloeddruk, middelomtrek) en fysiologische maten (bloedonderzoek en haarcortisol) gebruikt.

In **Hoofdstuk 1** wordt het belang van onderzoek naar stress, eetgedrag en gezondheid in jonge kinderen met autisme en hun ouders besproken. Kinderen met autisme en hun ouders ervaren dagelijkse uitdagingen, en vroege stress kan een effect hebben op hun mentale en fysieke gezondheid op de lange termijn. Hoewel er uit onderzoek blijkt dat moeders verhoogde stressniveaus hebben, is er beperkt onderzoek beschikbaar naar vaders, de vroege kindertijd en lange termijn fysiologische stressmarkers. Het betrekken van vaders is belangrijk, omdat zij ook een unieke rol spelen in de ontwikkeling van hun kind. De vroege kindertijd is daarnaast een belangrijke periode, omdat de patronen in die fase ontstaan, de basis kunnen leggen voor later. Onderzoek naar hoe stress samenhangt met eetgedrag en gezondheid bij jonge kinderen met autisme en hun ouders kan ons begrip van relevante factoren en dynamieken binnen het gezin vergroten, wat toekomstig onderzoek kan sturen, de klinische zorg kan versterken en gezinnen op de lange termijn kan ondersteunen.

In **Hoofdstuk 2** wordt onderzocht of moeders en vaders van jonge kinderen met autisme verschillen van volwassenen uit de algemene populatie op het gebied van ouderlijke stress, eetgedrag en lichamelijke gezondheid. Zowel moeders als vaders van jonge kinderen met autisme rapporteren hoge niveaus van ouderlijke stress. Deze moeders laten daarnaast een hogere percentages obesitas en metabool syndroom zien vergeleken met vrouwen uit de algemene populatie, wat kan wijzen op een verhoogd risico op chronische ziekten op latere leeftijd. Ouderlijke stress bij moeders is positief geassocieerd met ongeremd eetgerag. Vaders laten geen verhoogde percentages obesitas of metabool syndroom zien.

In **Hoofdstuk 3** worden de resultaten beschreven van het onderzoek naar stress bij ouders van kinderen met autisme, met behulp van vragenlijsten en haar cortisol concentraties (HCC) en de relatie met de mentale gezondheid bij ouders en kinderen met autisme. Moeders met een hoog niveau aan zelfgerapporteerde stress, hadden lagere HCC. Daarnaast is er een positief verband gevonden tussen HCC van ouders en HCC van hun kinderen, wat suggereert dat stress wordt gedeeld binnen het gezin. Daarnaast rapporteren ouders van kinderen met autisme hogere niveaus van psychopathologische symptomen, zoals depressie, vergeleken met mannen en vrouwen van dezelfde leeftijd uit de Nederlandse populatie. Ook wordt er een sterke correlatie gevonden tussen zelfgerapporteerde ouderlijke stress en psychopathologische symptomen bij ouders. Deze resultaten laten zien dat stressniveaus van ouders en hun kinderen met elkaar samenhangen en dat er een verband is tussen ouderlijke stress en hun mentale gezondheid, wat het belang onderstreept van een familie gerichte aanpak in onderzoek en klinische zorg, en daarnaast de noodzaak laat zien om de mentale gezondheid van ouders te monitoren.

In **Hoofdstuk 4** worden de obesitas percentages van jonge kinderen met autisme vergeleken die van hun leeftijdsgenoten, en wordt er onderzocht welke kind- en ouderfactoren samenhangen met obesitas bij deze kinderen. Vergeleken met leeftijdsgenoten uit de Nederlandse populatie, laten kinderen met autisme hogere obesitaspercentages zien. Het Body Mass Index (BMI) van kinderen met autisme is gerelateerd aan voedseltoenaderingsgedrag en het BMI van moeder, wat wijst op een mogelijke bijdrage van de gedeelde omgeving, genetica en gezinsdynamiek aan het risico op obesitas. Deze bevindingen benadrukken dat de vroege kindertijd een belangrijke periode kan zijn om kinderen met autisme die risico lopen op obesitas te identificeren en te ondersteunen en om gezinnen te begeleiden naar gezonde leefgewoonten.

In **Hoofdstuk 5** wordt HCC van jonge kinderen met autisme vergeleken met HCC van leeftijdsgenoten uit de algemene populatie. Daarnaast wordt onderzocht welke verbanden bestaan tussen HCC van kinderen met autisme en hun mentale gezondheid (autisme symptomen, internaliserende gedragsproblemen, externaliserende gedragsproblemen), eetgedrag en BMI. Ook worden de associaties tussen stress van ouders van kinderen met autisme (zelfgerapporteerde en HCC) en mentale gezondheid, het eetgedrag en BMI van hun kind beschreven. Uit de resultaten blijkt dat jonge kinderen met autisme vaker een hoog HCC laten zien dan leeftijdsgenoten uit de algemene populatie. Het HCC van kinderen met autisme is niet geassocieerd met hun mentale gezondheid, eetgedrag of BMI. Het HCC van moeders is echter wel gerelateerd aan gedragsproblemen bij hun kinderen met autisme. Daarnaast correleert de door moeders en vaders zelfgerapporteerde stress met autisme symptomen, gedragsproblemen en eetgedrag van hun kinderen met autisme. Dit benadrukt dat ouderlijke stress gekoppeld is aan het functioneren van het kind met autisme, en onderstreept het belang van het meenemen van zowel ouder- als kind factoren in onderzoek en de klinische praktijk.

In **Hoofdstuk 6** worden de implicaties en de sterke en zwakke punten van de gerapporteerde onderzoeken besproken. De belangrijkste sterkte van het onderzoek is de familiegerichte benadering, waarbij zelfrapportage vragenlijsten, lichamelijke metingen en fysiologische metingen bij kinderen, moeders en vaders werden gecombineerd. Daarnaast biedt de focus op de vroege kindertijd inzicht in de familiedynamiek tijdens deze specifieke ontwikkelingsfase bij kinderen met autisme. Een beperking is het cross-sectionele onderzoeksopzet, waardoor er geen causale conclusies kunnen worden getrokken en de richting van de geobserveerde associaties onbekend blijft. Desondanks bieden deze bevindingen waardevolle informatie voor toekomstig onderzoek naar de relatie tussen stress en gezondheid in gezinnen van kinderen met autisme.

Implicaties van deze bevindingen zijn relevant voor verder onderzoek, de klinische praktijk, beleid en het dagelijkse gezinsleven. In toekomstige studies is het belangrijk om de dynamiek tussen stress en gezondheid bij kinderen met autisme en hun ouders longitudinaal te onderzoeken, terwijl ook de impact van interventies gericht op stressregulatie bij ouders op het gezinswelzijn wordt onderzocht. De bevindingen in dit proefschrift ondersteunen een gezinsgerichte benadering in de klinische praktijk, waarbij mentale en fysieke gezondheidszorg wordt gecombineerd, BMI wordt gemonitord, een gezonde leefstijl wordt bevorderd en ouderlijke stress wordt meegenomen, naast de evaluatie van de psychologische en sociaal-emotionele effecten. Beleidsinitiatieven kunnen multidisciplinaire interventies stimuleren, gericht op het verminderen van ouderlijke stress en het ondersteunen van ouderlijke mentale en lichamelijke gezondheid. Voor gezinnen is het belangrijk om zich bewust te zijn van de mentale en fysieke gezondheidsrisico's die gerelateerd zijn aan (het opvoeden van een kind met) autisme. Hoewel ons onderzoek geen causale verbanden heeft onderzocht, kan het stimuleren van een gezonde leefstijl, zoals een evenwichtige voeding en regelmatige fysieke activiteit, de mentale en fysieke gezondheid bevorderen en mogelijk het welzijn van zowel kinderen als hun ouders positief beïnvloeden.

Samenvattend tonen de onderzoeken de mentale en fysieke kwetsbaarheden van jonge kinderen met autisme en hun ouders, waaronder een verhoogd risico op stress en obesitas. Belangrijk is dat er verschillen tussen moeders en vaders werden gevonden, wat suggereert dat de manier waarop ouderlijke stress samenhangt met de gezondheid van het kind en van de ouder zelf verschilt tussen moeders en vaders. Dit onderstreept de noodzaak om beide ouders mee te nemen in onderzoek en de klinische praktijk. De resultaten benadrukken het belang van het aanpakken van stress binnen het gezinssysteem om gezondheid en het welzijn van zowel kinderen met autisme als hun ouders te bevorderen.

Chapter 7

About the Author

7.1 Acknowledgements

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7.2 Curriculum vitae

Anna van der Lubbe werd op 13 december 1993 geboren in Den Haag. Na het behalen van haar atheneumdiploma aan het Grotius College in Delft (2006-2013), volgde zij van 2013 tot 2016 de bacheloropleiding *Pedagogische Wetenschappen* aan de Universiteit Leiden. In 2016 begon Anna met de Research Master '*Development Psychopathology in Education and Child Studies'* eveneens aan de Universiteit Leiden. Tijdens haar studie was Anna betrokken bij diverse onderzoeksprojecten als student-assistent, waaronder de "TRIXY studie: opgroeien met een extra X of Y chromosoom". In deze periode werkte zij ook als testleider voor Pearson, waar zij ervaring opdeed met diverse klinische instrumenten, zoals de Wechsler-tests. In 2018 ronde zij haar master cum laude af.
Na een jaar als onderzoeksassistent te hebben gewerkt aan de Erasmus Universiteit, werd Anna in 2020 promovendus aan de Universiteit Leiden, onder begeleiding van prof. dr. Hanna Swaab, prof. dr. Robert Vermeiren en dr. Wietske Ester. Haar promotieonderzoek vond plaats binnen Sarr Autisme Rotterdam, binnen Youz Kinder- en Jeugdpsychiatrie, onderdeel van de Parnassia Groep. Het promotietraject maakte deel uit van de Tandem-studie: een gerandomiseerd onderzoek naar de effectiviteit van Theraplay bij jonge kinderen met autisme en hun ouders. Tijdens het promotietraject behaalde Anna haar basisaantekening diagnostiek (NVO), voltooide zij de eBROK-cursus en werd zij gecertificeerd in het afnemen van de ADOS-2. Anna heeft de resultaten van haar onderzoek op verschillende congressen gepresenteerd, waaronder de International Society for Autism Research (INSAR) in Stockholm en het voorjaarscongres van de Nederlandse Vereniging voor Psychiatrie (NVVP). Momenteel werkt Anna als orthopedagoog bij Youz Kind- en Jeugdpsychiatrie binnen een wijkteam.

7.3 List of publications

1. van der Lubbe, A., Swaab, H., Vermeiren, R. R., & Ester, W. A. (2024). Stress, eating behavior and adverse health in parents of young children with autism spectrum disorder. Journal of Autism and Developmental Disorders, 54(2), 662-672. https://doi.org/10.1007/s10803-022-05825-3
2. van der Lubbe, A., Swaab, H., Vermeiren, R., van den Akker, E., & Ester, W. (2024). Novel insights into obesity in preschool children with autism spectrum disorder. *Child Psychiatry & Human Development*, 1-8. https://doi.org/10.1007/s10578-024-01679-1
3. van der Lubbe, A., Swaab, H., van den Akker, E., Vermeiren, R., & Ester, W. A. (2025). Hair Cortisol in Young Children with Autism and Their Parents: Associations with Child Mental Health, Eating Behavior and Weight Status. *Journal of Autism and Developmental Disorders*, 1-10. https://doi.org/10.1007/s10803-024-06672-0
4. van der Lubbe, A., Swaab, H., Vermeiren, R., van Rossum, E. F., van Balkom, I. D. C., & Ester, W. A. (2025). Chronic parenting stress in parents of children with autism: Associations with chronic stress in their child and parental mental and physical health. *Journal of Autism and Developmental Disorders*, 1-15.