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Associations Between Child Characteristics and Maternal Mental Health in Families of Children With Autism, Fragile X Syndrome, and Autism Associated With Fragile X Syndrome

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ASSOCIATIONS BETWEEN CHILD CHARACTERISTICS AND MATERNAL MENTAL HEALTH IN FAMILIES OF CHILDREN WITH AUTISM, FRAGILE X SYNDROME, AND AUTISM ASSOCIATED WITH FRAGILE X SYNDROME

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ABSTRACT

The present study examined the association between various child characteristics and maternal mental health concerns in three high-risk groups of mothers – those of children with non-syndromic autism spectrum disorder (NSASD), mothers of children with fragile X syndrome (FXS), and mothers of children with fragile X syndrome and autism (FXS+ASD). Research has shown that mothers of children with NSASD and FXS are thought to share a degree of genetic vulnerability to mental health concerns it is key to examine the various other factors that may contribute to difficulties within the family system and maternal stress, depression, and anxiety.

Participants for the present study were part of a larger study (RO1MH107573) and included 31 mothers of children with NSASD, FXS-only, FXS+ASD. A secondary sample of 11 mothers of children considered to be typically developing (TD) were selected to act as a normative control group. Results indicated that mothers of children considered to be TD experienced the lowest level of mental health concern, while those with ASD and FXS+ASD experienced the highest levels. Results further indicated that while child IQ proxy, autism severity, and child problem behavior were not independently predictive of maternal mental health concerns, these factors compound and significantly influence variance in mental health concerns. Limitations of the study and potential implications are discussed.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF ABBREVIATIONS

ADOS-2……..... Autism Diagnostic Observation Schedule, Second Edition

ASD…….……..….... Autism Spectrum Disorder

BDI…….……Beck Depression Inventory

CBCL……...……. Child Behavior Checklist

DAS-II……..……Developmental Ability Scales -Second Edition

ELC……. Mullen Early Learning Composite

FXS…….…….……...……. . Fragile X Syndrome

FXS+ASD……...…….…..……. Fragile X Syndrome and Autism

GCA……..... DAS General Conceptual Ability Score

MMHC……..…….Maternal Mental Health Composite

MSEL……..……Mullen Scales of Early Learning

NSASD……. Non-Syndromic Autism Spectrum Disorder

PDD-NOS…….…..…….Pervasive Developmental Disorder – Not Otherwise Specified

PSI-4-SF……...……Parent Stress Index, Fourth Edition – Short Form

STAI…….....…….. State-Trait Anxiety Inventory

TD…….……. Typically Developing

CHAPTER ONE

INTRODUCTION

Maternal mental health concerns have been found to be more pronounced in families of children with developmental disabilities such as autism spectrum disorder (ASD) (McStay et al., 2014). However, as most of the existing literature focuses on maternal depression or stress, little is known about the extent to which various dimensions of maternal mental health may be impacted by various child characteristics such as problem behavior or ASD severity. As mothers often take on the role of primary caregiver, they seem to be particularly vulnerable to stress and difficulties that come with adapting to a child's disability. Thus, examining this relationship in families of children with developmental disorders is imperative to informing intervention and services.

Maternal mental health reflects a mother's capacity to adapt and cope (McStay et al., 2014). The association of maternal mental health and the well-being and functioning of the family system has been iterated throughout the research literature, specifically emphasizing that poor maternal mental health has a variety of effects. For instance, maternal mental health difficulties can result in lower levels of maternal engagement, less sensitivity within the parent-child relationship, and fewer positive parent-child interactions (Goelman et al., 2014; Hauser et al., 2014). These effects can be detrimental to long-term child outcomes in a bidirectional and transactional manner when compounded with negative effects of other familial risk factors (Santelices et al., 2021; White et al., 2021).

While the impact of maternal mental health concerns on child outcomes and family functioning has been well-established, literature also posits that child characteristics can likewise drive maternal mental health difficulties. For instance, studies have found that social impairments, externalizing behaviors, and emotion regulation problems are associated with higher levels of parental stress in families of children with ASD (Davis & Carter, 2008). Self-injurious behavior, conduct problems, and aggression have been found to be linked with parental depression and anxiety in both families of children with various developmental disabilities, and those of children considered to be TD (Falk et al., 2014).

The present study aims to further investigate the associations between child characteristics and overall maternal mental health concerns in families of children with developmental disorders, compared to those of families with children whom are typically developing (TD) (i.e., children without a neurodevelopmental disability) as well as the general prevalence and severity of maternal mental health concern across these high risk groups. Moreover, as child problem behavior has been found to be strongly associated with maternal stress, this study aims to assess the impact of these behaviors on a variety of dimensions of maternal mental health. Based on theories examining parent stress and attachment, we aim to further examine the potentially transactional relationship between maternal mental health, child characteristics, and child development (Goelman et al., 2014; Santelices et al., 2021).

CHAPTER TWO

LITERATURE REVIEW

2.1 Maternal Stress and Mental Health

Definition and Overview. When assessing maternal mental health and well-being, a majority of existing literature focuses solely on depression or stress. Further, in regard to families of children with developmental disabilities, most of the existing data focuses on ASD or Down syndrome. Mothers typically carry the disproportionate burden in raising a disabled child, leaving them more susceptible to caregiver related stress, frustration, and anxiety (Santelices et al., 2021). However, there is little evidence on the associations of child characteristics on a fully inclusive image of maternal mental health (i.e., the presence of stress, depression, and anxiety), specifically in families of children with low incidence developmental concerns, compared to that of children considered to be TD (Engle, 2009; Weitlauf et al., 2014).

Parenting stress, which has been defined throughout the literature as psychological distress that arises from parenting roles and responsibilities, is a complex construct thought to be influenced by a number of parent, child, and environmental characteristics (Abidin, 2012). Parental stress is further identified as an aversive psychological response to the demands of being a parent, which stems from a mismatch between parent perceptions of demands and what they perceive as available resources for dealing with those demands (Hauser et al., 2014). While a certain level of stress is considered to be healthy and

adaptive, mothers of children with developmental disabilities experience clinically significant levels of stress far more frequently and persistently than women who are not mothers, as well as compared to mothers of TD children (Goelman et al., 2014; Hauser et al., 2014).

It is necessary to emphasize that overall maternal mental health encompasses far more than the presence or levels of experienced stress, and more than the absence of a mental health diagnoses (Engle, 2009; Goelman et al., 2014). Rather, existing literature defines maternal mental health as a "state of well-being in which a mother can cope with the normal stressors of life, can work productively and fruitfully, and is able to make a contribution to her family and community." (Abidin, 2012). Whereas a majority of existing literature discusses only maternal stress or depression, the present study aims to encompass a more well-rounded and inclusive view of maternal mental health in terms of a composite score examining stress, depression, and anxiety.

Transactional Effects of Maternal Mental Health. There is a strong co-occurrence of maternal parenting stress, anxiety, and depression (Walker et al., 2020). Mothers who experience high levels of parenting stress typically experience depressive symptoms, anxiety, and tend to display more ineffective parenting practices (Wan & Green, 2009). Lower mental health status in mothers is also linked to lower levels of maternal engagement, lower responsivity to their child, lower warmth and sensitivity, and fewer parent-child interactions (Wan & Green, 2009). Overall, mothers with mental health concerns tend to have more difficulty adapting to a variety of parenting roles and responsibilities, which can negatively affect treatment engagement for children with developmental disorders (Rishel et al., 2006). As evidence suggests that the overall well-

being and mental health of mothers has a grave impact on the well-being and functioning of the family system, it is likely that this effect is compounded in families of children with neurodevelopmental disabilities (Santelices et al., 2021).

Research has found that children of mothers with mental health problems are at an increased risk for later psychopathology and poor functioning in a range of developmental domains including social, behavioral, linguistic and academic (Rishel et al., 2006). In 2020, Walker and colleagues reported that maternal anxiety and depression have a significant long-term impact on child development and overall family functioning. This study found that, in addition to a negative impact on the parent-child interaction, poor maternal mental health can affect functioning in domains of school readiness, verbal comprehension, expressive language, cooperation, and behavior (Goelman et al., 2014; Walker et al., 2020).

While the effects of maternal mental health concerns on child outcomes has been well documented, the impact of child characteristics on mothers has been established as well. For instance, child problem behavior, and social impairments have been found to be highly predictive of maternal stress and depression in families of children with developmental disabilities (Pozo et al., 2014; Zaidman-Zait et al., 2014). ASD symptom severity has also been linked to, heightened levels of anxiety in parents (McStay et al., 2014). Thus, the relationship between maternal mental health and child behaviors can be described as transactional and compounding, in that these factors can influence and be influenced by one another (Zaidman-Zait et al., 2014).

Theoretical Framework. Theories regarding parental mental health typically incorporate a variety of components and contexts including the parent, child, and environment (Abidin, 1992; Mash & Johnston, 1990). According to Abidin's ecological

parenting stress model, elevated parent stress levels are linked between both the parent and child, as well as the parent-child relationship (Abidin,1992). Further, this theory suggests that atypicalities and delays in children's development are reported at higher levels in families where higher levels of parent stress are reported (Abidin, 1992). A number of both parent and child factors were identified as significant influences within this framework (i.e., health, adaptability, acceptability, mood, hyperactivity, and attachment) (Abidin, 1992).

The accumulation of stressors or "mild daily hassles" has been noted to significantly impact parental mental health (Deater-Deckard & Petrill, 2004). In order to fully be classified as parental stress, the effects of these "hassles" must be serious and compromise the parent's role or identity (Deater-Deckard & Petrill, 2004). Reciprocal interactions within a family system that link child and parenting behaviors to specific long-term outcomes are highlighted throughout family systems theory (Bowen, 1978). This theory, along with Belsky's (1984) model of parenting, emphasize parental functioning as being impacted by a bidirectional process of socialization to child behaviors and interactions. Deater- Deckard and Petrill (2004) also discussed the compounding, bi-directional effects of the parent on the child and vice versa. Worth noting, this framework also emphasized that parents' poor mental health functioning can also lead to difficulties in the parent-child interaction and poor behavior management practices, resulting in heightened levels of parenting stress (Deater-Deckard & Petrill, 2004).

When examining the bi-directional impacts of maternal mental health and child characteristics, many researchers look to attachment theory (Ainsworth & Bowlby, 1991; Bretherton, 1992). A mother's relationship with her child is significantly impacted through

low levels of sensitivity and availability, which are characteristics linked to depression (Bretherton, 1992). Similarly, and reflective of neurobiological theories, a child's socioemotional development can be negatively affected by a mother's distance and avoidance (Bretherton, 1992; Santelices et al., 2021). Maternal depressive symptomology is further regarded as a potential risk factor to a child's socioemotional adjustment, problem behavior, and social acceptance (Bretherton, 1992; Santelices et al., 2021). Thus, there is theoretical relevance to the implications of the present study in that it will further inform the transactional and compounding relationship between maternal mental health and child characteristics.

2.2 Autism Spectrum Disorder

Overview. ASD is a highly prevalent and complex neurodevelopmental disorder characterized by persistent abnormalities in social-communication, social interaction, and restricted or repetitive behaviors and interests (American Psychiatric Association, 2013). Overall, deficits typically manifest differently and vary depending on age, cognitive functioning, language abilities and treatment history (American Psychiatric Association, 2013). Individuals may be diagnosed with ASD as early as 24 months, though an ASD diagnosis has been shown to be more stable at 36 months or later (American Psychiatric Association, 2013). Among other highly prevalent co-morbid disorders, approximately 31 percent of individuals with ASD have been diagnosed with an intellectual disability (Center for Disease Control and Prevention, 2021).

Maternal Mental Health and ASD. Research has consistently found that mothers of children with ASD report higher levels of stress compared to mothers of children within other disability groups (e.g., Down syndrome, Cystic Fibrosis, Cerebral Palsy, etc.) (Center

for Disease Control and Prevention, 2021; Davis & Carter, 2008). This heightened vulnerability to stress has been consistently linked to a variety of negative outcomes, including greater incidence of maternal psychopathology, lessened benefits from treatment or intervention, and failure to engage with services (Bitsika et al., 2017; Kellett, 2013). Many researchers have pointed to a heightened genetic predisposition to mental health concerns in that many of these mothers report mental health problems predating the birth and diagnosis of their children (Abbeduto et al., 2021; Kauffman et al., 2017). In addition to elevated stress, these mothers also tend to report higher levels of anxiety, and depression compared to mothers of children with other disabilities or children whom are considered to be TD (Zaidman-Zait et al., 2014).

There has been an increased focus on the relationship between child behavioral characteristics and maternal mental health concerns. Further, researchers have been looking into the impact of ASD symptom severity versus more general problem behaviors, in relation to maternal stress. Research overall, noted that elevations in parent-reported stress are more directly associated with general problem behaviors, than that of ASD symptom severity (Zaidman-Zait et al., 2014). Bitsika and colleagues (2017) identified a number of child emotional and behavioral issues that are likely impacting mothers in this group, including self-injurious behavior, hyperirritability, eating problems, hyperactivity, and sleep difficulties. Investigating the bi-directional relationship between child characteristics and maternal mental health has been increasing in the ASD literature as awareness increases around the many roles these mothers take on following an ASD diagnosis (e.g., service coordinator, interventionist, advocate) (Zaidman-Zait et al., 2014).

2.3 Fragile X Syndrome

Overview. Fragile X syndrome (FXS) is a genetic, neurodevelopmental disorder that affects the population sparsely, occurring in approximately 1 in 3700 males and 1 in 6000 females (Crawford et al., 2001). FXS is caused by a unique gene mutation that results in the silencing of the Fragile X Mental Retardation-1 (*FMR1*) gene. The mutation is an expansion of a cytosine-guanine-guanine (CGG) trinucleotide repeat sequence (> 200 repeats) on the *FMR1* gene. Mothers of children with FXS carry the *FMR1* gene in a premutation state meaning that there is a presence of a CGG repeats of 50 to 200 (Crawford et al., 2001). Due to the X-linked inheritance pattern of FXS, symptoms vary according to sex, with males more severely affected (Bailey et al., 2008; Fielding-Gebhardt et al., 2020).

FXS can be diagnosed prenatally; in the absence of family history, diagnoses are usually given at 38 months or later (Roberts et al, 2016). Early signs of FXS include developmental delays (e.g., not sitting, walking, or talking at developmentally typical times), physical features (enlarged ears, long facial shape, and some connective tissue problems including high arched palate, hyper-flexible joints), learning difficulties (e.g., slow learning, trouble learning new skills), and social or behavior problems (e.g., poorly modulated eye contact, difficulties with concentration, impulsivity, hand flapping, and hyperactivity) (Falk et al., 2014; Hessel et al., 2006). The behavioral phenotype of FXS includes withdrawal, social deficits, gaze aversion, inattention, impulsivity, abnormalities in communication, atypical response to sensory stimuli, and hyperactivity (Hessel et al., 2006).

Individuals with FXS often exhibit characteristics such as intellectual disabilities, maladaptive behaviors, and symptoms of Attention-Deficit/Hyperactivity Disorder (Hessel

et al., 2009). These individuals are additionally at an increased risk for anxiety and affective disorders, as well as sensory sensitivities (Bailey et al., 2008; Hessel et al., 2006). A majority of males with FXS meet diagnostic criteria for a moderate intellectual disability, while presentation in females is far more variable, with approximately 50 percent displaying a degree of cognitive impairment, mostly falling into the mild to moderate ranges (Bailey et al., 2008; Hessel et al., 2009). Additionally, individuals with FXS are also more likely to be diagnosed with ASD, with 60 to 75 percent of males and 20 to 41 percent of females presenting with behaviors that are typical of an individual with non-syndromic autism (NSASD) (Abbeduto et al., 2021; Roberts et al., 2020).

Maternal Mental Health and FXS. Mothers of children with FXS are more likely to experience clinically significant levels of stress, with approximately 63 percent exceeding clinical thresholds (Bailey et al., 2008; White et al., 2021). Mothers of children with FXS typically report less stress than mothers of children with ASD or autism and fragile X syndrome (FXS+ASD), however, they tend to experience heightened stress compared to mothers of those considered to be TD (Abbeduto et al., 2019; Bailey et al., 2008; Fielding-Gebhardt et al., 2020). When examining the full scope of maternal mental health within this group, it was found that mothers of children with FXS report anxiety and anxiety related disorders at a rate of 3 to 5 times more than mothers of TD children (Bailey et al., 2008; Kellett, 2013). Higher rates of personality disorders and Major Depressive Disorder were also identified within this group compared to mothers of TD children (Bailey et al., 2008; Fielding-Gebhardt et al., 2020; Kellett, 2013). While the general population lifetime rates of depression fall between 10 and 12 percent, lifetime depression rates for

these mothers are estimated at 56 percent, which is also higher than that of mothers of children with Down syndrome (Bailey et al., 2008; White et al., 2021).

Specific to FXS, these mothers also overwhelmingly report earlier onset of mental health concerns (Abbeduto et al., 2021; Fielding-Gebhardt et al., 2020; White et al., 2021). Underlying mechanisms for elevations in maternal mental health concerns within this group seem to involve interactions across child, maternal, and environmental factors (Fielding-Gebhardt et al., 2020; White et al., 2021). Child characteristics, however, seem to have the most direct impact on maternal experiences with stress. Specifically, child problem behaviors such as social withdrawal, internalizing problems, aggressive behavior, etc., are reported to be the most relevant factors (Bailey et al., 2008; Kellett, 2013; Thurman et al., 2015). In 2008, Bailey and colleagues reported that, specific to FXS, there is a significant relationship between child problem behaviors and a mother's reported stress, anxiety, anger, depression, and overall quality of life.

Research has found that premutation status of mothers has been linked to increased risk of psychiatric disorders and symptoms, as well as increased vulnerability to stress (Hogan et al., 2017; Kellett, 2013; Roberts et al., 2020; White et al., 2021). Evidence suggesting a genetic predisposition to depression and anxiety disorders has also been highlighted throughout the literature (Abbeduto et al., 2019; Bailey et al., 2008; Wheeler et al., 2014; White et al., 2021). Overall maternal well-being has been found to be significantly impacted by the increased genetic susceptibility to mental health concerns, in addition to challenging child behaviors (Wheeler et al., 2014; White et al., 2021). White and colleagues (2021) highlighted the importance of understanding the genetic predisposition that these mothers carry, especially as it pertains to the experience and

likelihood of negative effects of parenting stress, compared to mothers without a genetic predisposition.

2.4 Overlap of Fragile X Syndrome and Autism Spectrum Disorder

FXS is the leading monogenic cause of ASD, accounting for approximately 2 to 6 percent of all ASD cases (Cohen et al., 2005). While nearly 90 percent of males and 41 percent of females with FXS display characteristics of ASD, it can be complex to adequately identify the true prevalence of fragile X syndrome and co-occurring autism (FXS+ASD) (Abbeduto et al., 2019; Harris et al., 2005). Research indicates that approximately 73 percent of males, and 29 percent of females with FXS have been identified as having comorbid ASD in studies that included direct measures of ASD in their diagnostic battery (Abbeduto et al., 2021; Roberts et al., 2020). When using parent report measures, 30 to 46 percent of children with FXS meet diagnostic criteria for co-occurring ASD or Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS) (Abbeduto et al., 2021; Roberts et al., 2020).

The relationship between FXS and ASD is often noted as complex and evolving, which is partially attributed to revisions to the definition of ASD and a growing understanding of the behavioral phenotype of FXS (Kauffman et al., 2017). The ever-present and growing debate surrounding the overlap of ASD and FXS questions whether ASD in FXS represents "true" ASD or whether it is an inherent characteristic of the FXS phenotype (Hogan et al., 2017; Kauffman et al., 2017). Consensus has not been met regarding whether there are true shared phenotypes or whether these features look similar but stem from divergent etiology. Considerable evidence has been noted in the clinical utility of using an ASD diagnosis to characterize individual variation in FXS, examining

whether a categorical diagnostic approach should be adopted in contrast to a symptom-based approach. However, many researchers have emphasized that relying solely on a categorical ASD diagnosis in FXS can potentially mask important differences between the two clinical phenotypes (Abbeduto et al., 2014; Kauffman et al., 2017).

ASD symptoms tend to emerge in the first year of life for children with FXS, and as they persist, significant differences can be identified between individuals categorized as FXS versus those whom are described as FXS+ASD (Abbeduto et al., 2019; Kauffman et al., 2017). The co-occurrence of FXS and ASD is associated with increased impairment in vocational, educational, and therapeutic domains (Abbeduto et al., 2014; Abbeduto et al., 2019; Kauffman et al., 2017). Studies have found that individuals with FXS+ASD often exhibit more attention difficulties, impulsivity, hyperactivity, aggression, and self-injurious behaviors (Abbeduto et al., 2019; Abbeduto et al., 2021; Kauffman et al., 2017; Roberts et al., 2020). Less developed language skills, lower nonverbal cognition and IQ scores, and lower adaptive skills are also highly associated with FXS+ASD (Kauffman et al., 2017; Roberts et al., 2020). These factors, coupled with more severe behavior problems, are thought to have a significant impact on parenting stress and mental health outcomes (Kauffman et al., 2017; Kellett et al., 2013; Roberts et al., 2016).

2.5 Current Study and Aims

Aims. The present study aims to examine the associations of maternal mental health and child characteristics in three groups of high-risk families; those of children with NSASD, FXS-only, and FXS+ASD, compared to that of TD children. First, this study aimed to examine group differences in maternal mental health concern (i.e. stress, anxiety, and depression). It was hypothesized that mothers in the NSASD and FXS+ASD groups

will experience higher levels of maternal mental health challenges than other groups. Further, mothers of children in the TD group are hypothesized to experience the lowest levels of concern. Next, the present study examined a variety of child characteristics and their association with maternal mental health. Specifically, correlations between child problem behavior (e.g., externalizing and internalizing behaviors), ASD symptom severity, and child IQ proxy. It was hypothesized that child problem behavior will be most highly correlated with maternal mental health difficulty, whereas ASD symptom severity will be the second most impactful factor, regardless of group. IQ proxy is hypothesized to be the weakest correlate with maternal mental health.

CHAPTER THREE

METHODS

3.1 Participants and Recruitment

Participants. Four groups of participants were included from two larger ongoing longitudinal studies regarding the emergence and stability of ASD and anxiety in early childhood. Overall, participants included 42 mothers of pre-school aged children (see Table 3.1). Participants were typically recruited into the study in infancy, though some entered later in development. These participants were recruited nationally through social media and collaborations with outside research groups. Assessments were conducted in participants' homes or at the Neurodevelopmental Disorders Laboratory at the University of South Carolina, based on parent preference. Parents provided informed consent upon enrollment. All procedures were approved by the Institutional Review Board at the University of South Carolina.

Mothers were excluded from participation if they did not complete the three questionnaires of interest for the present study (e.g., BDI-II, PSI-4-SF, STAI). Maternal ages at the time of assessment ranged from 25.72 to 48.01 years of age. To further gauge factors that may impact maternal stress and mental health outcomes, data were also collected regarding number of children in the home, and number of children in the home with a disability.

Table 3.1 *Maternal Characteristics*

	Full Sample (n=42)	NSASD (n=16)	FXS-only (n=7)	FXS+ASD (n=8)	TD (n=11)
Maternal Age, M(SD)	37.04 (5.24)	36.78 (5.33)	39.28 (4.70)	34.65 (6.24)	37.74 (4.03)
Maternal Age Range	25.72 to 48.01	27.28 to 43.61	35.55 to 48.01	25.72 to 42.56	32.12 to 45.02
Ethnicity, n (%)					
Hispanic/Latino	2 (4.76)	0	0	1 (12.50)	1 (9.09)
Not Hispanic/Latino	36 (85.72)	12 (75.00)	7 (100.00)	7 (87.50)	10 (90.91)
Unknown	4 (9.52)	4 (25.00)	0	0	0
Race, n (%)					
Black/African American	3 (7.14)	0	1 (14.29)	1 (12.50)	1 (9.09)
White	33 (78.58)	14 (87.50)	5 (71.42)	5 (62.50)	9 (81.82)
More than one race	3 (7.14)	1 (6.25)	0	1 (12.50)	1 (9.09)
Other/Unknown	3 (7.14)	1 (6.25)	1 (14.29)	1 (12.50)	0
Individuals <18 in the home, n (%)					
1-2	26 (61.90)	10 (62.50)	5 (71.43)	4 (50.00)	7 (63.64)
3-4	14 (33.33)	6 (37.50)	2 (28.57)	2 (25.00)	4 (36.36)
5+	2 (4.77)	0	0	2 (25.00)	0
Individuals <18 in home with a disability, n (%)					
0	9 (21.43)	0	0	0	9 (81.82)
1-2	30 (71.43)	15 (94.44)	7 (100.00)	6 (75.00)	2 (18.18)
3-4	3 (7.14)	1 (5.56)	0	2 (25.00)	0
5+	0	0	0	0	0

Selection Criteria. The primary purpose of this study necessitated focus on pre-school aged children (range = 3.19 to 6.18 years). Participants in the ASD group were required to have a previous diagnosis of ASD, which was confirmed through the clinical best estimate (CBE) procedure outlined below. Individuals for whom an ASD CBE was not available, were excluded. Participants in the FXS-only group had completed previous genetic testing to confirm the presence of the full *FMR1* mutation (>200 CGG repeats),

and FXS was confirmed through the review of these reports provided by the parents. Exclusionary criteria for the ASD group included prematurity (<37 weeks gestation) or any known genetic or neurological condition (e.g., tuberous sclerosis, seizure disorder, FXS) that may affect development.

As participants with FXS were nationally recruited for participation in two larger studies, it should be noted that many parents have multiple children for which data is collected. However, for the purpose of this study, only the oldest child for each family was included to avoid unnecessary compounding affects. As the primary focus of this study investigated maternal outcomes, any participants for whom data was provided by the father (n = 1), were excluded. Assessment timepoints include 6 months, 9 months, 12 months, 18 months, 24 months, and then every 12 months until the child reached 72 months of age. Only assessments completed between the ages of 2 and 6 years of age were considered for this particular study. Further, only the youngest timepoint with the most data available was included in the analyses.

Clinical Best Estimate (CBE) Procedures. For the purpose of this study, primary diagnostic labels of ASD versus non-ASD were included for the first available timepoint at or after 36 months of age. A CBE diagnosis was assigned via case review by a multidisciplinary team that included a licensed psychologist with expertise in differential diagnosis of ASD in young children and individuals who conducted the assessments. In order to receive an ASD diagnosis, children were required to meet DSM-5 criteria for ASD (American Psychological Association, 2013). Information used to inform CBE diagnoses was gleaned from: adaptive functioning as measured by the Vineland Adaptive Behavior Scale-2nd Edition (VABS-2) (Sparrow et al., 2005) and ASD symptom severity as

measured by the ADOS-2 (Lord, et al., 2012), ADI-R (Lord et al., 1994), and Childhood Autism Rating Scale – Second Edition (Schopler et al., 2010).

Child Demographics. Children were only considered to be participants in the present study if all measures of interest were available for their mothers. Inclusion in the relevant disability categories required a confirmed diagnosis of NSASD, FXS-only, or FXS+ASD. Specifically, participants included 11 typically developing children, 16 children with NSASD, and 7 children with FXS-only. Further, a fourth group of 8 participants was defined for individuals who were confirmed to have both FXS and ASD (FXS+ASD). Child participants ranged in age from 3.19 to 6.18 years. A comprehensive breakdown of demographics for these children is available in Table 3.2.

Table 3.2 *Child Demographics*

	Full Sample (n=42)	NSASD (n=16)	FXS-only (n=7)	FXS+ASD (n=8)	TD (n=11)
Child Sex (male), n (%)	33 (78.57)	14 (87.50)	4 (57.14)	8 (100.00)	7 (63.64)
Child Age, M(SD)	5.19 (0.78)	5.06 (0.99)	5.35 (0.46)	5.12 (0.82)	5.33 (0.59)
Age Range	3.19 to 6.18	3.19 to 6.18	4.98 to 6.03	3.65 to 5.95	4.09 to 6.05
Child Ethnicity, n (%)					
Hispanic/Latino	1 (2.08)	0	0	0	1 (9.09)
Not Hispanic/Latino	41 (97.92)	16 (100.00)	7 (100.00)	8 (100.00)	10 (90.91)
Unknown	0	0	0	0	0
Child Race, n (%)					
Black/African American	2 (4.76)	0	0	1 (12.50)	1 (9.09)
White	32 (76.19)	15 (93.75)	4 (57.14)	4 (50.00)	9 (81.82)
More than one race	7 (16.67)	1 (6.25)	3 (42.86)	2 (25.00)	1 (9.09)
Other/Unknown	1 (2.38)	0	0	1 (12.50)	0

3.2 Measures

Parenting Stress Index, Fourth Edition Short Form (PSI-4-SF). The PSI-4-SF is a self-report screening tool that is used to identify types and sources of stress that come with parenting. Parents are asked to rate their level of agreement with 36 items that are fall under three subscales; Parental Distress (PD), Parent-Child Dysfunctional Interaction (P-CDI), and Difficult Child (DC) (Abidin, 2012). The Parental Distress subscale measures the extent to which a parent perceives themselves as competent, conflicted, supported, restricted, and/or depressed in their parenting role (Abidin, 2012). Parent satisfaction with their interactions with their child is measured using the Parent-Child Dysfunctional Interaction subscale (Abidin, 2012). The Difficult Child subscale examines a parent's perception of their child in terms of how easy or difficult they are to care for (Abidin, 2012). Further, the PSI-SF provides an overall score that indicates the level of stress a parent is experiencing (Abidin, 2012).

Beck Depression Inventory - II (BDI-II). Consisting of 21, multiple choice items, the BDI-II was used to assess parental depression, depressive ideation, and intensity of depression symptoms (Beck, et al., 1996). Respondents rate each item based on four differential responses ranging from 0 to 3, gauging the severity of depressive symptoms, specifically from absent to intense presence, within the past two weeks. The BDI-II is further comprised of both an Affective and Somatic subscale which together assess feelings of hopelessness, irritability, guilt, and physical symptoms (Beck, et al., 1996). The respondent's ratings are combined into a Total Score, which is then classified as minimal (0-13), mild (14-19), moderate (20-28), or severe (29 or higher).

The State-Trait Anxiety Inventory (STAI). The STAI is a psychological inventory that measures two types of anxiety; state and trait. State anxiety is defined as anxiety about an event, whereas trait anxiety is considered a personal characteristic (Spielberger, et al., 1983). The S-Anxiety scale, looking at state anxiety, measures how the respondent feels in that specific moment (Spielberger, et al., 1983). Conversely, the T-Anxiety scale, assessing at trait anxiety, measures how the respondent generally feels (Spielberger, et al., 1983). The STAI consists of 40 self-report items to which responses are provided on a four-point Likert scale (Spielberger, et al., 1983). Higher scores on this measure are considered to be positively correlated with, and reflective of, higher level of anxiety (Spielberger, et al., 1983).

Maternal Mental Health Scores. For the purpose of this study, a composite maternal mental health score was produced through the sum of each mother's raw scores on the BDI-II, the PSI-4-SF, and the STAI. As the raw or overall scores for each of these measures are associated with higher levels of depression, stress, and anxiety, respectively, higher maternal mental health composite (MMHC) scores are associated with poor maternal mental health and more symptomology of the above concerns. This score will be useful in assessing a mother's overall severity of mental health concerns and providing a more well-rounded image of the dimensions of maternal mental health that are being impacted.

Autism Diagnostic Observation Schedule - Second Edition (ADOS-2). The ADOS-2 is considered to be the "gold standard" of autism diagnostic measures for individuals age 12 months and above (Lord, et al., 2012). Divided into four diagnostic modules dependent on the developmental and language level of the individual being

assessed, the protocol for this measure includes several structured and semi-structured tasks that are used to urge social interaction and communication between the child being assessed and the examiner (Lord, et al., 2012). Modules were selected per participant using the guidelines detailed within the manual. Behavior and communication observations are categorized and combined to provide scores that the examiner will use to inform a diagnosis and severity level for each individual (Maddox et al., 2017). For the purpose of this study, ASD severity is measured using the total calibrated severity score provided by the ADOS-2.

Child Behavior Checklist (CBCL). The CBCL is a parent-report form that is used to identify problem behavior and social competencies in children (Achenbach & Rescorla, 2000). The CBCL is composed of 113 items, scored on a three-point Likert scale, for which parents consider their child's behaviors in the last 6 months. There are 8 syndrome scales of the CBCL: Depressed, Anxious/Depressed, Social Problems, Attention Problems, Somatic Complaints, Rule-Breaking Behavior, Thought Problems, and Aggressive Behavior. Additionally, there are two higher order factors, Internalizing and Externalizing Factors, that are composed of these scales. The CBCL also provides six scales that evaluate consistency with DSM diagnostic categories (i.e., Affective Problems, Anxiety Problems, Somatic Problems, Conduct Problems, Oppositional Defiant Problems, and Attention-Deficit/Hyperactivity Disorder). For the purpose of this study, children's problem behaviors were examined by externalizing and internalizing categories, and measured using the raw scores from both of these scales.

Developmental Level. Two standardized measures of development were used to examine participants general cognitive abilities. Which measure was used depended on the

participant's age at the timepoint utilized for the purpose of this study. Scores for children aged 68-months of age or younger were obtained via the Mullen Scales of Early Learning (MSEL) (Mullen, 1995). Children evaluated using the MSEL were assigned an IQ proxy referred to as the Mullen Early Learning Composite (ELC). The lowest possible ELC is 49. Conversely, children aged 69 to 83-months were evaluated using the Differential Ability Scales, Second Edition (DAS-II) via the Early Years Battery (Elliot, 2007). Children evaluated using the DAS-II were assigned an IQ proxy referred to as the DAS General Conceptual Ability Standard Score (GCA).

3.3 Procedures

The author and primary investigator in this study was approved access to extant data through the Neurodevelopmental Disorders Laboratory at the University of South Carolina and is included as a member of Dr. Jane Roberts' research team under Institutional Review Board approval. A dataset was compiled for the present study based on predetermined inclusion criteria. Assessments were completed by a team of two or three trained research specialists, and typically took place in a participants' home or at the research laboratory at the University of South Carolina, dependent on parent preference. Upon completion of the assessment, a brief developmental summary was collected, and monetary compensation was provided to the family.

Statistical Analysis. To determine whether maternal mental health significantly differed across groups, a one-way ANOVA was used to examine differences in MMHC scores across all four groups of mothers (ASD, FXS-only, FXS+ASD, and TD). Bonferroni-adjusted post-hoc analyses were completed to determine specific group differences, as needed. Next, Pearson correlations were employed to examine the

associations between MMHC scores and child characteristics, including ASD severity, child problem behaviors, and IQ proxy. A linear regression model was also used to determine whether these child characteristics predict MMHC scores across all four groups of participants. Specifically, child problem behaviors, ASD severity as measured by the ADOS-2, and child IQ proxy were regressed in order to determine their role as predictors of MMHC.

CHAPTER FOUR

RESULTS

Each mother's obtained scores on the PSI-4-SF, BDI-II, and STAI were used to produce MMHC scores, as outlined in the section above (Table 4.1). An overall one-way ANOVA examining group differences in MMHC scores indicated that there were statistically significant differences in MMHC scores between groups (F (3, 38) = 6.83, p= <.01). Bonferroni-adjusted post-hoc analyses further indicated that the TD group differed significantly from the both the NSASD and FXS+ASD groups, ps < .05. No other pairwise comparisons were statistically significant, ps > .05 (see Figure 4.1).

Table 4.1 *Maternal Measure Scores*

	Full Sample (n=42)	NSASD (n=16)	FXS-only (n=7)	FXS+ASD (n=8)	TD (n=11)
PSI-4-SF, M(SD)	79.52 (29.17)	94.94 (25.80)	68.71 (16.31)	92.50 (31.74)	54.55 (18.50)
BDI-II, M(SD)	6.88 (8.46)	11.75 (9.63)	1.57 (2.82)	9.00 (8.80)	1.64 (1.96)
STAI State, M(SD)	33.38 (11.21)	38.38 (11.01)	29.00 (8.33)	35.13 (15.10)	27.64 (6.36)
STAI Trait, M(SD)	37.21 (10.65)	41.25 (10.46)	35.29 (10.23)	39.63 (12.87)	30.82 (6.65)
MMHC, M(SD)	157.00 (52.75)	186.31 (48.31)	134.57 (32.85)	176.25 (61.30)	114.64 (25.12)

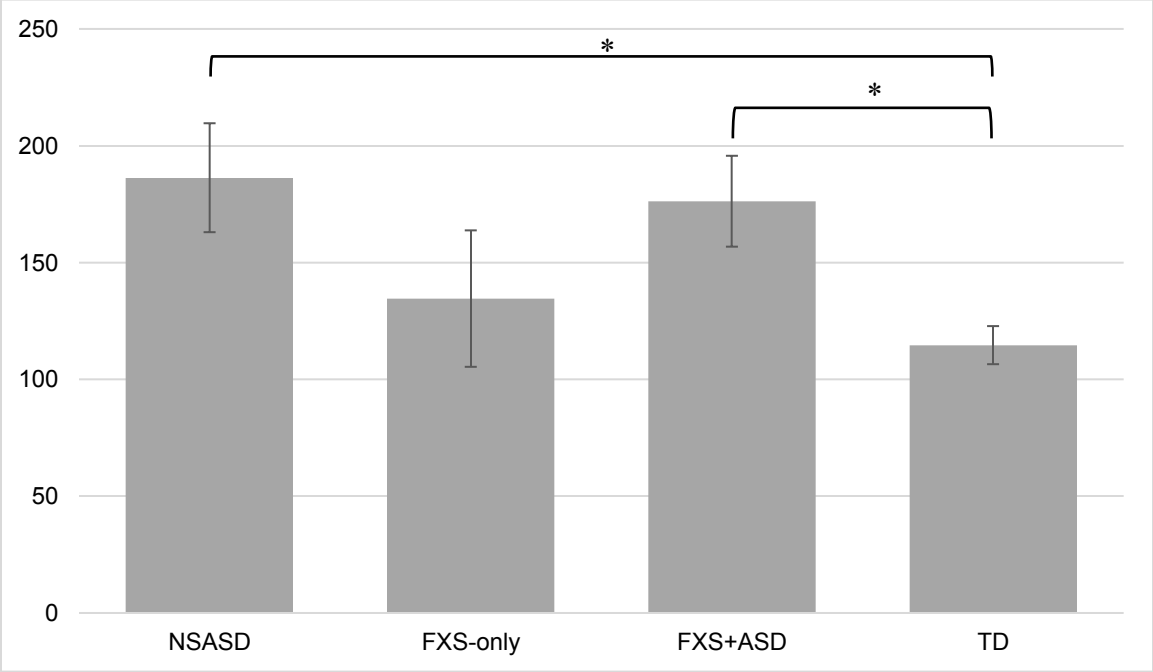

Figure 4.1 *MMHC Score Differences Across Groups*

Note: (*) represents a significant group difference at the .05 level

A comprehensive breakdown of scores for each group across the ADOS-2, measures of child IQ proxy, and externalizing and internalizing behaviors as measured by the CBCL are available below (Table 4.2). Pearson correlations were used to examine the associations between MMHC scores, ASD severity, child IQ proxy, internalizing behavior, and externalizing behavior with results indicating that all variables were significantly correlated with MMHC scores, $p < .01$(see Table 4.3). This suggests that there is a strong relationship between child characteristics and more significant levels of maternal mental health concerns. Upon further examination of these variables, results suggested that the strongest correlation to MMHC scores is found in child internalizing behavior ($r = 0.65$).

Additionally, it should be noted that the relationship between child IQ proxy, and MMHC was found to be significant in a negative direction (r = -0.54).

Table 4.2 *Child Scores by Measure*

	Full Sample (n=42)	NSASD (n=16)	FXS-only (n=7)	FXS+ASD (n=8)	TD (n=11)
ASD Severity n(%)	42.00 (100.00)	16.00 (100.00)	7.00 (100.00)	8.00 (100.00)	11.00 (100.00)
M(SD)	5.00 (3.00)	7.25 (1.88)	2.71 (1.80)	6.25 (2.61)	2.27 (1.95)
IQ Proxy n(%)	42.00 (100.00)	16.00 (100.00)	7.00 (100.00)	8.00 (100.00)	11.00 (100.00)
M(SD)	72.29 (24.74)	65.38 (16.80)	72.00 (19.75)	46.45 (5.47)	101.45 (16.60)
Internalizing Behavior n(%)	41.00 (97.62)	15.00 (93.75)	7.00 (100.00)	8.00 (100.00)	11.00 (100.00)
M(SD)	11.83 (10.86)	17.67 (12.20)	4.43 (2.70)	19.75 (5.97)	2.82 (2.40)
Externalizing Behavior n(%)	41.00 (97.62)	15.00 (93.75)	7.00 (100.00)	8.00 (100.00)	11.00 (100.00)
M(SD)	14.73 (9.01)	18.87 (9.51)	10.57 (2.88)	20.38 (5.73)	7.64 (7.16)

Table 4.3 *Correlations of Variables*

Variable	1	2	3	4
1. MMHC Score	1			
2. Child IQ Proxy	-0.54**	1		
3. Child Externalizing Behavior	0.57**	-0.55**	1	
4. Child Internalizing Behavior	0.65**	-0.54**	0.80**	1
5. Child ASD Severity	0.58**	-0.53**	0.58**	0.70**

Note: (**) represents a significant correlation at the .01 level

Further, a multiple linear regression model was run with ASD severity, child IQ proxy, child problem behavior (i.e. externalizing and internalizing behaviors) entered as predictors of the MMHC score. The overall model explains 49% of the variance in MMHC ($F(4, 36) = 8.62$, $p < .001$, $R^2 = .49$). These results suggest that when evaluated together, these variables are predictive of increases in MMHC scores. However, no individual child characteristic was found to be a significant predictor of MMHC scores in that all *p*s > .05 (see Table 4.4).

Table 4.4 *Multiple Linear Regression*

	β	*t*	*p*
Child ASD Severity	0.17	1.00	0.33
Child Internalizing Behavior	0.37	1.63	0.11
Child Externalizing Behavior	0.05	0.22	0.83
Child IQ Proxy	-0.23	-1.52	0.14

CHAPTER FIVE

DISCUSSION

Mothers often take on the role of primary caregiver, seemingly increasing their vulnerability to the stressors and difficulties of adapting to and managing a child's disability. Lower maternal mental health status is found to negatively impact the functioning of the family system, as well as the fidelity and efficacy of treatment for children with developmental disorders. As this is likely compounded in families of children with disabilities, understanding the potentially transactional associations between child characteristics and maternal mental health outcomes across several high-risk groups will aid in targeting and facilitating early intervention, better inform family systems support, and mitigate negative long-term outcomes.

Whereas a majority of existing literature discusses only maternal stress or depression, the present study examines maternal mental health and its association to child characteristics in a more inclusive manner through the use of a composite score examining stress, depression, and anxiety. This approach to the examination of overall maternal mental health is better aligned with the existing literature defines it, whereas it aims to encompass more than just the presence or absence of a diagnosis of set of symptoms. Specifically, the present approach allows for a tangible representation of maternal mental health that encompasses far more than the presence or levels of experienced stress, and more than the absence of a mental health diagnoses. The utilization of a maternal mental

health composite is novel in that it encompass a more well-rounded and inclusive view of maternal mental health in terms of a composite score examining stress, depression, and anxiety.

Results from the present study highlight the importance of considering the transactional relationship between child characteristics and maternal mental health, and the way difficulties may be uniquely compounded in families of children with developmental disabilities. Upon examining group differences in maternal mental health concerns, results indicated that MMHC scores were significantly elevated in families of children with NSASD and FXS+ASD. While the scores from the FXS-only group were not found to be significantly different from??, it is worth noting that these scores were still considered to be elevated compared to that of mothers in the TD group. Confirming the initial hypotheses, MMHC scores following an expected trend with all three disability groups showing higher MMHC scores. Further, MMHC scores were found to be highest in families of children considered to be NSASD or FXS+ASD, supporting the notion that an ASD diagnosis was the most relevant predictor of maternal mental health challenges.

The examination of existing literature revealed that biological risk factors (i.e., genetic predisposition) increase maternal vulnerability to mental health concerns in families of children with FXS and ASD, which is explanative of the significant elevations in MMHC scores for the NSASD, and FXS+ASD groups. These results were found to support existing literature and research. However, there are a number of factors outside of an ASD diagnosis that could have driven this shift that were not directly measured by the present study. For example, families with more children in the household, or with more children with disabilities in the household (which is common in ASD and FXS considering

the heritability of these diagnoses), may experience more elevated levels of mental health concern. Thus, it is suggested that future studies consider additional factors within the family system that may influence these mental health concerns such as the number of children in the home, household income, etc..

These results have important implications. First, mothers of children with NSASD or FXS+ASD should be more closely monitored for maternal mental health concerns than mothers of TD children or children with FXS-only. It is worth noting that the mean MMHC score for the FXS-only group were higher than those of the scores in the TD group, though this difference was not statistically significant. These findings have the potential to inform earlier intervention and strengthen supports for these families in that service providers can more clearly identify families considered to be 'at-risk'. Specifically, as results suggested that the FXS+ASD and NSASD groups reported the highest MMHC scores, intervention and services for groups of mothers who are likely facing genetic predisposition to poor mental health are highlighted in that they may necessitate additional and more personalized services to cope with the demands of parenting. Overall, results from the present study can inform early intervention services, not only for children, but for mothers of children with developmental disabilities. Identifying mothers who may experience negative mental health outcomes early-on, particularly when a genetic predisposition is likely, will strengthen future treatment efficacy and engagement, as well as strengthen the family system.

Examining specific child characteristics and how they may impact and predict maternal mental health outcomes yielded overall significant results. Specifically, the overall model examining the associations of child IQ proxy, child problem behavior, and

ASD severity were found to be significantly positively associated with MMHC, as well as these factors individually. Child internalizing behavior was found to yield the strongest relationship to MMHC. Further examination, however, found that no independent variable alone was found to significantly predict MMHC score variance. These findings align with existing literature in that ASD severity does not alone predict maternal mental health concerns, nor does child problem behaviors. Rather, these factors are simply positively associated with maternal stress, depression and anxiety. This suggests that while none of the explicitly examined variables may predict maternal mental health concerns alone, it is essential to a utilize broader, more overarching perspective of these families in order to identify potential risk factors, effectively informing interventions and treatment. In sum, as results indicate that child characteristics can compound to drive significant negative impacts on maternal mental health, results are suggestive of the potential benefits of multimodal intervention and treatment targeting a number of risk factors.

Findings from the present study support the initial hypothesis mothers of children in the NSASD and FXS+ASD groups experiencing more negative mental health outcomes than other groups. It was further hypothesized and confirmed that mothers of TD children experience the lowest level of mental health concern. These results additionally supported the hypothesis that other factors predictive of maternal mental health concern would be child problem behavior, ASD severity, and child IQ proxy, respectively. However, these factors were only found to yield a significant positive association with MMHC scores and were not individually predictive of change.

Strengths of this study include the examination of maternal mental health concern as a composite variable as opposed to simply considering depression, stress, and anxiety

individually. Another strength of the present study can be found in the number of comparison groups; NSASD, FXS-only, FXS+ASD and TD groups were all included in this examination to allow for informing group differences and normative level considerations. Despite these strengths, this study is limited by the small number of participants in groups. This makes results difficult to generalize, as there may not have been an appropriate level of normative variance. Another limitation to the present study is the imbalance of biological sex of children across groups, which may have impacted the variance in children's symptom profiles. Future studies should aim to explore these questions using a larger, more diverse sample in terms of biological sex of child subjects. Further, this study was limited by the lack of consideration for the heritability of FXS and ASD. Specifically, many families involved in this study have several children in the home, and some have multiple children with disabilities. These circumstances may further compound influences of maternal mental health outcomes. Future studies should examine these questions while controlling for the relationship between number of children in the home, or number of children in the home with a disability.

In conclusion, the present study is the first to examine maternal mental health across three high-risk groups in an inclusive and overarching manner using a composite score that includes measures of maternal stress, anxiety, and depression. Findings suggest that mothers of children with FXS and ASD present with higher levels of mental health difficulties than those of TD children. Additionally, findings suggest that the compounding of child characteristics such as problem behavior, ASD severity, and IQ proxy are significantly associated with maternal mental health outcomes. These findings aid in the early identification of vulnerabilities within the family systems of children with

developmental disabilities, and allows for intervention that will strengthen treatment efficacy and parent-child interactions.

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