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Gut Health and Environmental Impact on Individuals With Autism Spectrum Disorder

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Abstract

In recent research, probable connections have been made between gut health and Autism Spectrum Disorder (ASD). Microbial imbalances within the gut were discovered in individuals with ASD, leading some researchers to think that this maladaptation may contribute to some of the impaired behaviors associated with autism. This paper seeks to answer the following questions: What evidence exists, if any, to connect gut health and environmental factors to autism? If the gut and the brain are interconnected, how can this apply to neurodevelopmental disorders? If individuals with autism could heal their bodies internally, would external behaviors and difficulties in social interaction and communication improve? If research concludes a connection exists, better solutions and treatment options could be found and implemented.

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CHAPTER I: INTRODUCTION

Personal Interview

The following text includes a personal interview.

Pseudonyms were assigned to each individual mentioned.

"Kate" is the senior vice president sales leader for a company dedicated to decreasing the use of chemicals in household products. Kate lives with her husband "Jason" and their two beautiful children, "Braden" and "Molly," in the Southeastern United States. Kate and Jason enjoy raising their kids — watching them grow up and develop into bright, talented individuals. While Molly and Braden are both very active in their day-to-day lives, Molly's health set Kate and Jason on a journey they never thought they would be on.

When Molly was born, Kate and Jason were ecstatic to welcome a baby girl into their family. Molly was a typical happy-go-lucky baby, and everything appeared normal. "She was all the things you dream about for having a kid," said Kate (Personal communication, August 17, 2019). Molly continued to meet all her developmental milestones and seemed to be as healthy as any baby could be — but then something changed. Kate and her husband had just moved into a new home and shortly before Molly's second birthday, she contracted strep and was bitten by a tic on the same day. The symptoms of these conditions, plus an ongoing ear infection and daily diarrhea, seemed to drastically alter something in Molly's body. "It was literally like one day she was gone," said Kate. "She wouldn't talk to us, her eyes glazed over and she would line up toy cars for hours" (Personal communication, August 17, 2019). To Kate, this was horrifying; she had no idea what happened to her child and started to blame herself for the alarming, sudden changes.

Kate and Jason weren't sure what to do, but they knew something was significantly wrong with their little girl. They took Molly to see her general practitioner, who prescribed antibiotics to treat the strep and ear infections. Molly completed three rounds of antibiotics, but nothing seemed to improve. The symptoms Molly experienced did not seem typical for strep or ear infections; Kate and Jason knew Molly needed further medical evaluation.

After almost five months of appointments through their county health system, Molly was diagnosed with high-functioning autism. Autism Spectrum Disorder, also referred to as ASD, is defined as "a complex developmental condition that involves persistent challenges in social interaction, speech and nonverbal communication, and restricted/repetitive behaviors" (American Psychiatric Association, 2013). Upon receiving the diagnosis, Kate questioned a lot of things. "At that point, I began to say, I know that I had a connection with this child. This doesn't just happen; there's a reason behind all of this, I know" (Personal communication, August 17, 2019).

Kate knew others would tell her that this was the age that it happens, that autism starts to show, but she was convinced there was more behind the drastic change in her daughter. Kate didn't know where to turn to next, so she started at the library to try to "figure this out" (Personal communication, August 17, 2019). It was there she found the book *Autism Breakthrough* by Raun K. Kaufman. Kate used Kaufman's suggestions to attempt various techniques to connect with Molly. When she lined up cars for hours, Kate joined her in hopes that she would feel a connection.

Not long after Molly's diagnosis, Kate and Jason took Molly to a brain restoration clinic to consult with a board-certified neurologist with qualifications in child neurology and ASD. At the appointment, the medical team retrieved a stool sample and discovered that Molly had no healthy bacteria in her gut, which also potentially explained her daily diarrhea. "She had gut

dysbiosis," said Kate. Test results showed that the strep Molly was previously diagnosed with was not only in her throat, but in her gut. The tests also revealed high numbers of inflammation markers, which indicated the only way to heal her body was to begin a detoxing process. The detoxing regimen included a gluten-free, dairy-free and sugar-free diet along with supplementing good probiotics to treat a yeast overgrowth.

The detoxing phase was rigorous, but it wasn't long before Molly made eye contact again and responded to her name. "Her eyes weren't glossy anymore," said Kate (Personal communication, August 17, 2019). At the doctor's recommendation, they continued Molly's diet protocol. Concurrently, Kate sought other professional recommendations. They found out that Molly's system was full of heavy metals and needed more detoxing. On top of all of the diet changes to help heal Molly's gut, Kate and Jason discovered a significant amount of mold in their house. Comprehensive assessment found that she had mold poisoning in her blood and nasal passages. Kate and Jason then decided they needed to move, and within three weeks of moving to a new home, Molly improved even more.

For most of Molly's life, she has been fighting for her health. The road to recovery was long and difficult not just for Molly, but for her entire family. For five years her parents have advocated for her and worked hard to heal her gut. There were seasons where Kate wanted to quit; times when she thought she would never hear her daughter talk again. But today, Molly is thriving. She is now seven years old and becoming healthier every day. She enjoys helping her mom and being a big sister to Braden.

Kate's determination for her daughter's healing was the driving force to Molly's recovery. "Every child is so different and there are so many factors involved. You have to fight for healing. If your gut is not healthy, you can't detox properly. I think we should care more

about our immune systems — play in the dirt, more probiotics, breast-feeding, cleaning your house of chemicals, etc. … It seems like we just want to kill all the germs and inject the body with toxins [vaccines] these days, and it's going to hurt the body" said Kate (Personal communication, August 17, 2019).

Although Molly is still healing, Kate is more than hopeful for a bright future. "The goal is that someday someone would come up to her and not recognize a diagnosis of autism," said Kate (Personal communication, August 17, 2019). And just like any other mom, Kate wants Molly to have the best quality of life —"going to college, getting married — all of those things." Even though every child diagnosed with ASD presents differently, Kate believes that there is healing for everyone at some level. "It's a journey that you'll have to fight your way through, but you can totally get there. It takes grit and a lot of effort," said Kate (Personal communication, August 17, 2019).

Stories like Molly's have left me contemplating the correlation between gut health and brain health. If what we eat not only affects our gut, but our brain as well, shouldn't we be more concerned with what we are essentially putting into our bodies? If the environment around us is full of pollutants and harsh chemicals, shouldn't we strive for a healthier setting? The interview with Kate motivated me to research the topic of gut health and autism because I work with individuals with neurodevelopmental disorders. If improving gut health by diet and environmental changes can work for someone like Molly, could it work for others as well?

Rationale for Gut Health and Autism

Recent research has shown probable connections between gut health and Autism Spectrum Disorder, also known as ASD (Liu et al., 2017). According to the American Psychiatric Association, ASD is defined as, "a complex developmental condition that involves persistent challenges in social interaction, speech and nonverbal communication, and restricted/repetitive behaviors" (2013). Microbial imbalances within the gut have been frequently discovered in individuals with ASD and some researchers think that this maladaptation might contribute to some of the associated impaired behaviors (Liu et al., 2017).

One theory in particular is based on the gut-brain axis. Researchers define this axis as, "the interaction between the gastrointestinal and nervous systems" (Siwek, J., Kawala-Janik, A., & Walecki, P., 2017, p.118). They have examined the association between ASD and Inflammatory Bowel Disease (IBD) and have concluded that children with autism were more likely to have Chron's disease (CD) and Ulcerative Colitis (UC) (Lee, et al., 2017). Researchers have also investigated the Intestinal Permeability (IP) or "leaky gut" and behaviors associated with gluten and dairy in children with ASD as well as other nutritional factors and interventions. According to other studies suggesting a link between diet and behavior in children with autism, parents have reported behavioral changes when their child consumed gluten and/or casein (Navarro, et al., 2014).

Environmental pollution, hormones added to the average American's food, harsh chemicals in personal products, water contamination and even poor air quality seem to cause many individuals, that would otherwise be healthy, to suffer symptoms of ailments such as gastrointestinal disorders and auto-immune diseases. But what about individuals who already have compromised immune systems? What about those with autism who typically suffer from

gastrointestinal problems? Could shifting environments and nutritional intake, which could potentially change the levels of toxicities inside the body, promote neurological changes that could alter behaviors associated with ASD (Navarro et al., 2014)? If people with autism could essentially heal their bodies from the inside out, would their behaviors and social interactions with others change? With numerous studies available connecting gut health and autism, I believe this area of research is worth evaluating.

This is an important topic in the field of education because if there is a connection to gut health and behaviors of individuals with ASD, then there could be a solution for improving and maybe even curing all of the components that encompass Autism Spectrum Disorder. This paper examines the following questions: Is it possible to potentially conclude that there may be a connection to the gut health of an individual with ASD and his or her behavior(s)? Could eating patterns and habits contribute to the status of one's gut health? If so, what other factors play a role? If the gut and the brain are connected, what can we learn about ASD, a neurodevelopmental disorder, and the health of one's gut (Lee et al., 2017)? Maybe it's not just the gut and nutrition, but the overall physical health of one's body. Here I would like to propose my guiding thesis question: What evidence exists, if any, to connect gut health and environmental factors and autism?

CHAPTER II: LITERATURE REVIEW

Search Parameters

For this literature review, research articles and studies were gathered from the Bethel University Library from the following online databases: EBSCO, ERIC, and PsychINFO. The search words used included the following: autism and gut health, autism and diet, autism and mercury, autism and heavy metals, autism and food, autism and toxins, autism and probiotics, autism and environment, autism and chemicals, autism and aluminum and autism and lead. Some articles were available for immediate download and others were requested through the interlibrary loan.

Gut Health, Nutrition and Autism

What does gut health and nutrition have to do with autism? Researchers have discovered that there are differences in the eating habits and the gastrointestinal health of children diagnosed with ASD. Statistics have shown that up to 80% of children with autism take dietary supplements or are on a special diet (Siwek, Kawala-Janik, & Walecki, 2017). These digestive differences have caused researchers to hypothesize a correlation between the gut and the brain and propelled them to look for more evidence regarding a link between autism and nutrition.

One theory on the etiology of autism connects ASD to disorders within the digestive system. Justyna Siwek and colleagues wanted to investigate the role of the gut-brain axis in the eating behaviors of children with ASD. The gut-brain axis refers to the communication between the central nervous system and gut intervention (Siwek, Kawala-Janik, & Walecki, 2017). The functionality of the central nervous system can be affected by the intestinal microflora, thus proving their interconnectedness. Siwek's study found that children with ASD have differences in the makeup of the intestinal and gastric flora compared to children without autism.

In this study, the most problematic concerns in ASD were the eating disorders, digestive ailments and dietary difficulties (which occur two to three times more in children with ASD) (Siwek, Kawala-Janik, & Walecki, 2017). Symptoms of these problems included constipation, diarrhea, bloating and reflux. These symptoms were evident in 70% of children with autism compared to 28% in the control group. According to this study, these symptoms had a significant influence on the neurological system, which warranted the importance of further investigation on the role of nutrition and the brain (Siwek, Kawala-Janik, & Walecki, 2017).

Siwek and colleagues wanted to reveal nutritional differences between children with autism compared to typical children. They conducted a study with 44 children diagnosed with ASD and a control group of 33 children without ASD. Information was gathered from the parents through a three-part questionnaire designed by the researchers regarding the eating habits and other dietary information of their children.

Results showed that the parents of healthy children were more interested in their child's nutritional intake compared to the parents of children with ASD; however, 40% of parents of children diagnosed with ASD indicated they believed nutrition played a big role in the behavior of their child. Deductions of this study claimed that there were differences in nutritional habits and eating behaviors of children with autism compared to children without autism. Siwek and colleagues found that children with ASD preferred to eat food of one type, color, texture and odor. These children were also prone to choose foods in similar packaging, reluctant to try unfamiliar foods and also had a tendency to eat in a ritualistic way (Siwek, Kawala-Janik, & Walecki, 2017). Common food choices for children with autism were fast-food items including burgers, fries and hot dogs—all containing preservatives (Siwek, Kawala-Janik, & Walecki, 2017). Results also concluded that children with ASD ate more red meat and giblets compared to

typical children, and that children with ASD ate more “light” bread than those without ASD, who consumed more dairy products. One reason for the high intake of giblets and red meat in children with autism may be due to the fact that these foods are are high in iron, a mineral that aids in the development of cognitive, motor and behavioral functions (Siwek, Kawala-Janik, & Walecki, 2017). According to Siwek and colleagues, children with autism are typically deficient in iron, which is still unknown as to why.

Siwek’s study found no significant difference between the two groups when comparing frequency of consumption of gluten and artificial additive products, which are both associated with nutritional factors in autism (Siwek, Kawala-Janik, & Walecki, 2017). There are still many unknowns as to why individuals with ASD have higher rates for gastrointestinal problems and more research needs to be conducted; however, the Siwek study established significant correlations and exposed specific differences in children with autism compared to children without autism.

In a journal article published in 2018 in *Psychology and Behavior,* Ceymi Doenyas shared updated perspectives on the gut-brain axis regarding dietary interventions for ASD. The study indicated that there is growing interest globally observing the gut-brain axis in correlation with typical development and neurodevelopmental disorders like autism. Although there is dabate around the topic of dietary interventions and autism, there is enough scientific evidence to merit consideration. Doenya’s article explained the importance of the intestinal barrier and its role in gut health of individuals. The microbiota aids the overall health of the intestinal barrier in the expression of neurotransmitters, modulation of brain activity and behaviors, as well as protecting the blood-brain barrier (Doenyas, 2018).

The evidence in this journal article agreed with Siwek's study that indicated a strong role of the gut-brain axis in regard to autism (Doenyas, 2018). Doenyas' study noted that one of the foundational reasons for dietary modifications for individuals with ASD is a theory known as the opioid excess theory. Incomplete digestion of opioid peptides into amino acids can cause gut permeability that allows the peptides to cross the blood-brain barrier by escaping into the bloodstream (Doenyas, 2018). According to Doenyas, dietary interventions concerning the gut-brain axis are important to consider in this topic of research.

Many nutritional interventions given to children with autism include gluten-free or case-in free diets. Doenyas explained that the peptides with opiod functions originated from these two sources are presumed to migrate through an unhealthy intestinal membrane and consequently affect the central nervous system (Doenyas, 2018). The unfinished digestion of these peptides into amino acids could cause production of gluteomorphins and caseomorphins (peptide chains resembling opiates) and could then attach to opioid neuro-receptors, resulting in ASD symptoms (Doenyas, 2018).

Another subtopic in this article considered the physiological effects restrictive diets could have on individuals because of the elimination of important nutrients. Evidence showed that the gluten-free diet may result in reducing beneficial gut bacteria and create other negative effects. It was found that the gluten-free and casein-free diets could have damaging effects on the gut microbiota and disrupt the already aggravated gut microbial composition by defecating the good gut bacteria.

According to this article, the gluten-free diet blocks fiber from products containing grain, which could lead to chronic constipation (Doenyas, 2018). Alternatively, Doenyas and other researchers have proposed supplementing with probiotics to make up for the nutritional

deficiencies of going on a restrictive diet. This study claimed that probiotics can aid in the improvements for individuals with autism because they help regulate the immune system and improve the gut microbial problems many individuals with autism have. These improvements decreased the following ASD symptoms: behaviors associated with ASD, communication difficulties, sensory and cognitive awareness and physical health, according to this study. Although this article showed evidence of reduced intestinal barrier strength in individuals with ASD, Doenyas concluded that more research is needed to confirm the validity of the opiod excess theory in the etiology of ASD (Doenyas, 2018). Gluten-free and casein-free diets may be Jasoneficial, but they also may have damaging effects on the gut health, which could affect the brain health of an individual with ASD (Doenyas, 2018).

A study published in 2016 similarly examined the gut microbiota and autism connection. Scientists from this study also agreed that there were differences in the composition of gut bacteria between children with ASD and controls (Ding, Taur, & Walkup, 2016). When researchers observed specific intestinal bacteria, they concluded that it may contribute to the development of ASD (Ding, Taur, & Walkup, 2016). The "state of unbalanced and disrupted microbial communities" is referred to by researchers as dysbiosis (Ding, Taur, & Walkup, 2016). This gut imbalance has been linked in the etiology and development of many medical conditions including autism (Ding, Taur, & Walkup, 2016).

Ding and colleagues indicated the significant impact the gut microbiota has on human health. Individuals with healthy intestinal microbiota, which is made up of non-pathogenic anaerobic bacteria, are able to properly absorb nutrients and vitamins and ward off any overgrowths or infectious pathogenic bacteria that may be harmful to the gut. Individuals with unhealthy intestinal microbiota are unable to adequately absorb essential vitamins and nutrients,

thus potentially resulting in poor gut bacteria or bad gut health (Hooper et al. 2012; Sekirov et al. 2010 as cited in Ding, Taur, & Walkup, 2016). The potential hypothesis researchers stated that if an intestinal wall is leaky, the anaerobic bacteria will misbehave, leading to unwanted symptoms, some of which are common in people with autism.

Ding and colleagues also stressed the importance of gut health during developmental years of an individual. They found evidence of the evolution of GI microbiota composition during the first few years of life (Ding, Taur, & Walkup, 2016). Ding's research explained that at birth, the human gut is initially sterile and microbial colonization begins immediately after childbirth. They discovered that this colonization is influenced by many things including the route of delivery, maternal transfer, diet, environmental factors, and antibiotic usage (Sekirov et al. 2010 as cited in Ding, Taur, & Walkup, 2016). This study seems to suggest that an individual's diet is critical in the developmental years and conclusions could be made that certain nutritional deficiencies and environmental factors could rob the body of this important microbial growth.

Ding and colleagues, along with many other researchers, agreed that evidence is only increasing on the clinical importance of microbes orientating the intestinal tract. The correlation between dysbiosis and many disease states are also being formed. Within neurobehavioral disorders like autism, research seems to indicate a strong connection to the health and well-being of the intestinal microbiota. However, it remains unknown whether gut dysbiosis is secondary to altered neural regulation of vital gut functions or if it implies primary deviations that may impact brain development (Ding, Taur, & Walkup, 2016).

In a 2017 study, researchers inspected the association between ASD and Inflammatory Bowel Disease (IBD) and concluded that children with autism were more likely to have Chron's

disease (CD) and ulcerative colitis (UC), which are two diseases under the IBD umbrella (Lee, et al., 2017). According to Lee and Colleagues, these findings confirmed the link between ASD and IBD; both having multifactorial pathogenesis within the gut-brain relationship. In this study, researchers inspected this link and indicated the importance of recognizing signs and symptoms early on in children with ASD.

Lee and colleagues designed a cohort of inpatient and outpatient individuals using the TRICARE Management Activity Military Health System (MHS) database. They reduced room for selection bias due to retrieving data from a very large and diverse population, demographically, geographically and socioeconomically, thus providing a stronger correlation due to the large data set (Lee, et al., 2017). The study reported on 48,762 children diagnosed with ASD and 243,810 children considered typical. There were 344 children with an IBD diagnosis and 292,228 without (which included children with ASD). Overall results showed that the children with ASD had higher rates of IBD compared to the control group of children without ASD. (Lee, et al., 2017). Of the 344 children with IBD, 116 also had Chron's disease and ulcerative colitis. Lee and colleagues also concluded that there was a 67% increase in the odds of children with ASD also having IBD (Lee, et al., 2017).

Predictably, this study confirmed that children with IBD and ASD took more prescription drugs than the control group. Lastly, this study also mentioned the importance caretakers have on recognizing the signs and symptoms of IBD in children with autism because many children with ASD are non-verbal and cannot communicate abdominal pain or distress. Failure to thrive, down-trending growth charts and diarrhea or abdominal discomfort are some of these signs caretakers should be watching for (Lee, et al., 2017).

In addition to researchers who claimed individuals with autism had higher rates of dual diagnoses with gastrointestinal diseases like Chron's or IBD, researchers have also investigated the Intestinal Permeability (IP) or "leaky gut" and behaviors associated with gluten and dairy in children with ASD. According to other studies that suggested a link between diet and behavior in children with autism, parents have reported behavioral changes when children consume gluten and/or casein (Navarro, et al., 2014). Navarro and colleagues conducted a study that explored the effects of gluten and milk and behavioral impact in children with ASD. This study used children diagnosed with ASD whose parents were willing to follow a strict diet of gluten-free and dairy-free for a length of six weeks. The results showed that any changes in behaviors were not clinically significant to confirm specific findings; however, Navarro's study determined that they could not rule out the possibility that Intestinal Permeability and other factors connected to dairy and gluten could, in fact, impact behaviors of children with ASD (Navarro, et al., 2014).

In 2017, RuJasonstein and colleagues also examined the frequency proportion of current use of gluten-free diets among children with ASD. The children observed in the study were enrolled in the Study to Explore Early Development (SEED) program. RuJasonstein and colleagues investigated if this diet was associated with developmental regression, intellectual disabilities or gastrointestinal problems (RuJasonstein, et al., 2017). They found that within their study 50.7% of children (30-68 months) had dietary intervention prescribed by a doctor and the reason for a GF diet was associated with gastrointestinal and developmental regression (RuJasonstein, et al., 2017). The results specified that 10.3% of children with ASD in the study implemented the GFD.

Although this analysis found evidence of recommended GFD among children with ASD, data could not determine the efficiency of GFD for treating ASD or GI symptoms (Ludvigsson,

Reichenberg, Hultman, & Murray, 2013 as cited in RuJasonstein, et al., 2017). However, in another study cited within RuJasonstein, et al., 2017, scientists indicated the following: "It has been hypothesized that a genetic condition among children with ASD might lead to a 'leaky gut' where gluten or casein creates an excess of peptides, causing behavioral symptoms common to ASD (Campbell et al., 2009; Elder et al., 2015; Reichelt & Knivsberg, 2009). According to RuJasonstein and colleagues, regardless of this study's limitations, over 20% of children with ASD have tried gluten-free diets in an attempt to reduce GI or ASD symptoms.

An article published in the *Journal of Autism and Developmental Disorders,* Zimmer and colleagues discussed the frequency of selected eating and nutritional deficiencies among children diagnosed with ASD (Zimmer, et al., 2011). They examined 22 children with ASD and an age matched control group. They discovered that children with autism had poorer food variety scores and were more selective eaters, which put them at higher risk for nutritional deficiencies when compared to neurotypical children (Zimmer, et al., 2011).

The *American Academy of Pediatrics* published a journal on the assessment, diagnosis and treatment of gastrointestinal disorders on individuals with Autism Spectrum Disorders (Buie, et al., 2010). They confirmed a link between gastrointestinal disorders and associated symptoms of autism; however, Buie's research focused on the main issues regarding the prevalence and ideal treatment for these disorders and claimed they have been misunderstood (Buie, et al., 2010). Buie and colleagues presented a central factor that merits great contemplation: individuals with ASD by definition have communication barriers and cannot fully or accurately indicate their symptoms related to gastrointestinal discomfort. Buie's study explained that parents and care providers should take into consideration that problematic behaviors in children with ASD could potentially be a symptom of an underlying medical condition including one or more

gastrointestinal diseases and disorders (Buie, et al., 2010). The authors stated that it was just as important for individuals with ASD to have a thorough evaluation as individuals without ASD would. Since autism can create communication difficulties, behavioral changes may be the only indicator care providers have to realize pain or discomfort (Buie, et al., 2010).

Along with gluten-free and casein-free diets, many other dietary interventions are practiced within individuals diagnosed with autism. In a 2012 journal from the *American Academy of Special Education Professionals,* researchers reviewed background literature and researched evidence linking high fructose corn syrup with the increased diagnoses of Autism Spectrum Disorders in the United States. Ray (2008) claimed that large amounts of fructose corn syrup (HFCS) was consumed daily, especially in children (as cited in Opalinski, 2012). Default and colleagues (2009) stated that "food allergies and sensitivities have been shown to produce a variety of neurological signs associated with autism" (as cited in Opalinski, 2012, p.123). Opalinki's study also indicated that nutritional deficiencies as well as exposure to mercury have been proven to alter brain function. Interestingly, during the manufacturing process, high fructose corn syrup has been tested to show small amounts of mercury (Default, et al., 2009 as cited in Opalinski, 2012). Opalinkski and colleagues indicated that high fructose corn syrup affected behavior in both children and adults and reducing high fructose corn syrup intake could be another way to decrease or manage ASD symptoms (Wallinga, et al. 2009 as cited in Opalinski, 2012).

Another popular dietary intervention prescribed to individuals with autism is the ketogenic diet (KD); which is a diet that is high in fat and low in carbohydrates. Jacklyn Smith and colleagues wrote an article in the journal of *Behavioural Brain Research* (2016), claiming that the ketogenic diet could restore certain neurological problems. Interestingly, the KD has

been traditionally used to reduce seizure activity in epilepsy as well as autistic behaviors in humans and rodent models (Smith, Rho, & Teskey, 2016). This study discovered that the mouse model of ASD determined that dietary therapy through the ketogenic diet could reverse abnormalities in motor function as determined by increased cortical excitability (Smith, Rho, & Teskey, 2016). Smith and colleagues suggested that with growing evidence, this dietary intervention helped individuals with epilepsy and may also reduce symptoms and behaviors associated with Autism Spectrum Disorders.

Ahn and colleagues (2014) found that the ketogenic diet helped enhance mitochondrial function. They examined whether this diet could reverse deficits in social behaviors and mitochondrial dysfunction in the prenatal valproic acid (VPA) rodent model of ASD (Ahn, Narous, Tobias, Rho, & Mychasiuk, 2014). In their findings they discovered that the ketogenic diet had a positive effect on the social interactions and behaviors in the rats. "… Prenatal VPA exposure altered the biogenetic profile of mitochondria from the neocortex, and although KD was able to ameliorate some of the VPA-induced dysfunction, animals in the VPPA/KD group often failed to reach normal OCRs" (oxygen consumption rates) (Ahn, Narous, Tobias, Rho, & Mychasiuk, 2014. P.376).

In a 2018 study, Ryan W.Y. Lee and colleagues examined 15 children with ASD ages 2 to 21 years for three months. These 15 children were given a modified ketogenic and gluten-free diet with supplemental MCT (modified chain triglyceride) (Lee, et al., 2018). Lee and colleagues also noted that despite limited evidence, the KD has been prescribed in people with neurological disorders like epilepsy because this diet "alters neural cellular metabolism through the utilization of ketone bodies as an alternative for the brain" (Lee, et al., 2018. P.206).

Lee's study was conducted at Shriners Hospitals for Children in Honolulu and the scientists tested both the feasibility and efficacy of a modified KD in an attempt to improve ASD symptoms over the course of three months. The clinical study team included many professionals: a pediatric neurologist, a registered dietician/nutritionist, two pediatric nurse practitioners, a SLP (speech-language pathologist) and a behavioral neuroscientist (Lee, et al., 2018). The specifications of this diet included a protocol of limited total net carbohydrates to a daily intake of 20-25grams. Protein amounts were calculated by the dietician based on the child's age and weight. In this diet, the goal was to obtain ketosis, which is a buildup of acids (ketones) in the body, as caretakers monitored daily levels. Researchers excused the weight loss from ketosis as a positive side effect. Negative side effects, but common on a KD, were diarrhea, vomiting, fatigue, constipation, dehydration, acidosis and hypoglycemia; however, these side effects were only present within the first two to four weeks as their bodies adjusted to the diet (Lee, et al., 2018). Results of this study showed that after three months on the KD, 50% of participants showed moderate to substantial improvements on the ADOS-2 (Autism Diagnostic Observation) scores (Lee, et al., 2018). Although additional research and studies are needed, Lee and colleagues believed that components of the ketogenic diet could positively improve symptoms associated with Autism Spectrum Disorder (Lee, et al., 2018).

In a similar 2017 study, researchers examined behaviors in a maternal immune activation model of Autism Spectrum Disorder (Ruskin, Murphy, Slade, & Masino, 2017). Ruskin and colleagues claimed that prenatal factors like viral or bacterial infections during pregnancy could influence ASD in children. This study investigated pregnant mice who were injected with the viral mimic polyinosinic-polycytidylic acid after the weaning offspring were fed either a ketogenic or control diet for three weeks. Since ASD is more prevalent in males, this study was

consistent with the ASD phenotype. The KD reversed all MIA-induced abnormal behaviors partially or completely in the male mice while the females were unaffected (Ruskin, Murphy, Slade, & Masino, 2017).

While many dietary interventions exist to treat ASD symptoms, there still isn't a cure for autism. In a 2013 journal article published by the *Journal of Autism and Developmental Disorders,* researchers discussed the attitudes both parents and child health professionals hold towards dietary interventions of children diagnosed with Autism Spectrum Disorder. Winburn and colleagues found that parents and other health professionals implemented a wide range of interventions for treating autism in children, including dietary interventions not backed by research (Winburn, et al., 2013). Winburn's study wanted to investigate these attitudes towards a gluten-free, casein-free diet, so they surveyed 258 UK parents of children with ASD as well as 244 professionals. Results identified inadequate evidence and supported the need for more dietary intervention studies (Winburn, et al., 2013). As noted by more recent studies in 2017 and 2018 recorded previously in this paper, researchers have continued to examine dietary interventions for children with ASD in hopes that professionals and parents may continue to support the findings and continued research.

Besides affecting gut and brain health, food choices of individuals with autism may impact other areas of the body. In a 2017 study, 58 Pakistani children with ASD were studied in comparison to their siblings without ASD. Similar to other studies, a questionnaire was given to the parents where they indicated their children's oral hygiene measures, dietary habits and past dental experiences (Suhaib, Saeed, Gul, & Kaleem, 2017). The researchers found that the children with autism had a 50% higher rate of cavities compared to their siblings with a rate of 22.2%. Dental plaque was also recorded at a higher percentage for the children with ASD who

had 24% compared to control group who had 14%. Part of these findings potentially had to do with oral hygiene—those without ASD were more frequent and independent tooth-brushers. There was no significant difference between the two groups for sugar consumption. Overall, children with ASD needed more dental care than their siblings without ASD. While this study is not directly correlated with gut health and autism, the evidence found on oral health and individuals with autism could potentially relate to the diets of children with ASD. Food intake and dietary choices may be the root of many symptoms that result from an autism diagnosis.

Recap of Gut Health, Nutrition and Autism

Although there is currently no cure for autism, many nutritional interventions seem to have scientific evidence of improving some symptoms associated with ASD. The gut-brain axis connection has proved a correlation between the health of one's gut and the health of one's brain. While different interventions seem to affect each individual with ASD differently, there is enough research to support some trial and error in hopes of improving some autistic symptoms. The importance of early diagnosis and interventions was mentioned by the researchers as a significant part of treatment. This early diagnosis and intervention may decrease the odds of an individual having severe autistic symptoms and increase the odds of an improved outcome.

Evidence from animal models and mice investigations have confirmed these intestinal maladaptations as well (Ding, Taur, & Walkup, 2016). The relationship between the gut and the brain has been proven in many studies and there is evidence to warrant a correlation (Ding, Taur, & Walkup, 2016). Children with ASD are prone to poor eating habits which could also lead to poor oral health (Suhaib, Saeed, Gul, & Kaleem, 2017). Through dietary interventions and other forms of therapy, science shows that healing for the gut affects the brain, which may affect the behaviors associated with autism.

Researchers may have discovered ways to improve symptoms that are associated with autism through several clinical trials and studies. Even though some of the evidence does not lead to fully effective treatments for autism, enough evidence warrants further research and evaluations. According to Helen T. Ding and colleagues, “There is an emerging body of evidence linking the intestinal microbiota with Autism Spectrum Disorders (Ding, Taur, & Walkup, 2016). Many studies have revealed the differences in the gut bacteria of individuals diagnosed with ASD versus individuals without the diagnoses. This evidence has given researchers future opportunities to continue to examine the gut-brain axis in association with developmental disorders like autism. If nutrition can affect the gut, which can affect the brain, scientists are on their way to discovering more evidence on gut health, nutrition and autism.

Vitamins and Other General Health Factors and Autism

Along with dietary interventions, researchers have examined the impact vitamins and supplements could have on children diagnosed with autism. Liu and colleagues agreed that the malfunctions and deficits of the gut microbiota contributes to the impaired behaviors and other characteristics and symptoms of autism (Liu et al., 2017). They specifically wanted to study the effects Vitamin A (VA) had on children diagnosed with ASD. With VA being a significant factor in the regulation of gut microbiota, researchers hypothesized they would find evidence to show changes within the gut. Liu’s study reports data on the changes VA had on the gut microbiota as well as the impact it potentially had on symptoms of ASD (Liu et al., 2017).

In the study, 64 children one to eight years of age with autism were selected from six training centers in Chongqing and were observed during a six-month period. The Autism Behavior Checklist (ABC), Childhood Autism Rating Scale (CARS) and Social Responsiveness Scale (SRS) were scales used to evaluate the autism symptoms (Liu et al., 2017).

> CD38 and acid-related orphan receptor alpha (RORA) mRNA levels were used to assess autism-related biochemical indicators' changes. Evaluations of plasma retinol, ABC, CARS, SRS, CD38 and RORA mRNA levels were performed before and after six months of intervention in the 64 children. Illumina MiSeq for 16S rRNA genes was used to compare the differences in gut microbiota before and after 6 months of treatment in the subset 20 of the 64 children. After 6 months of intervention, plasma retinol, CD38 and RORA mRNA levels significantly increased. (Liu et al., 2017)

The scores of ABC, CARS and SRS scales showed no significant differences in the 64 children; however, the proportion of Bacteroidetes/Bacteroidales extensively increased and the proportion of Bifidobacterium considerably decreased in the subgroup of 20 after VA intervention. The results of this study found that VA did affect certain changes in autism biomarkers, but not necessarily any symptoms found in autism (Liu et al., 2017). Results also showed that VA could regulate gut microbiota and potentially promote changes in the gut for children diagnosed with ASD. However, the final conclusion of this study was that it is uncertain if Vitamin A is connected with autism symptoms and more research and testing needs to be done (Liu et al., 2017).

Besides Vitamin A, researchers believe folic acid also plays a role in the symptoms associated with autism (Castro, et al., 2016). Many studies have reported that supplementing with folic acid could potentially be connected with a higher chance of an ASD diagnosis. Castro and colleagues aimed to conduct a systematic review of multiple studies connecting folic acid to ASD (Castro, et al., 2016). According to their research using the MEDLINE data base, they found 60 articles regarding the correlation between folate and ASD— folate and folic acid are often used interchangeably, but they are different forms of vitamin B9. (Castro, et al., 2016).

Castro's study entitled *Folic Acid and Autism: What do we Know?* reported 11 out of 60 articles that met the inclusion criteria for the connection between autism and folate. The 11 articles addressed autism in conjunction with the use of vitamins, correlation between folic acid intake during pregnancy stages, dietary consumption and other supplementation in minors with ASD (Castro, et al., 2016). The main topic in their combined research analysis focused on the effects folic acid supplementation had on pregnancy and the higher rate of autism due to this association. Castro's research explained that children with autism have higher serum homocysteine levels, which are common amino acids associated with low levels of B vitamins/folate (Castro, et al., 2016). Since 1992, the United States Public Health Service has recommended to women of childbearing age to take 400ug of folic acid per day (Castro, et al., 2016). The results of this pooled research concluded that the number of studies were deficient to obtain a complete and accurate understanding of this topic. A larger controlled prospective assessing the levels and folic acid intake in mothers of children with ASD is needed to be certain that folic acid plays a significant role in ASD development and treatment or prevention (Castro, et al., 2016).

While there is some evidence on the potential impact of Vitamin A and folic acid in association to autism, another area of research on this topic involves the use of probiotics. In a 2018 study Tabouy and colleagues wanted to examine if probiotic supplements could be a therapeutic tool in the treatment of autism (Tabouy, et al., 2018). The researchers agreed with former evidence that when the gut microbiome is dysregulated, it has direct effects on behavior. They also explained that the microbiome is influenced by many factors including nutrition, environment, genetics and life's experiences (Tabouy, et al., 2018).

Tabouy's study wanted to investigate if the genes associated with autism could impact the gut microbiome with the use of probiotics (Tabouy, et al., 2018). SHANK3 is one of the genes researchers associate with neurodevelopmental disorders like ASD and was examined in mouse models in this study. Tabouy and colleagues reported that animal studies have suggested environmental factors that impact autism could potentially be reduced with the use of probiotics (Tabouy, et al., 2018). To determine the condition of the microbiota in the mice, the scientists extracted microbial DNA from stool samples. The SHANK3 mice had a decrease in L. reuteri, a probiotic bacterium. Considering this evidence, the scientists tested if treatment of L. reuteri would affect behaviors of both male and female mice. The adult mice were treated with this probiotic for three weeks followed by behavioral testing. The researchers discovered that the male mice had decreased antisocial behavior, but no social behavior was affected within the female mice. Anxiety levels of both male and female mice did not seem to differ with probiotic treatment. However, both the male and the female mice buried less marbles (a test for observing repetitive behaviors) with the L. reuteri treatment. The scientists also noted that the probiotics affected gamma-Aminobutyric acid (GABA) receptor gene expression and protein levels in multiple brain regions (Tabouy, et al., 2018).

In a 2019 pilot study, scientists studied the impact probiotics had on children with ASD. In their trial, Arnold and colleagues observed thirteen children ages 3 to 12 diagnosed with autism, anxiety and GI issues. The probiotic they used was called VISBIOME, which contains eight probiotic species. The 19-week trial included an eight-week treatment of the probiotic and an eight-week placebo, with a three week wash out phase. Three of the thirteen participants did not complete the study, leaving the results based on only ten children. The outcomes of the study indicated that the probiotic showed more improvement on GI symptoms than the placebo, each

outcome improved from baseline. Parents of the children did report substantial decrease in abdominal complaints during the probiotic treatment phase compared to their baseline before the study (Arnold, et al., 2019). Arnold's study concluded that VISBIOME is a safe treatment option for GI symptoms in children with ASD, but another study with a larger participant size and treatment length would provide more reliable evidence (Arnold, et al., 2019).

Recap of Vitamins and Other General Health Factors and Autism

Research has confirmed vitamins and supplements have an effect on gut health, which also impacts the brain. Liu and colleagues discovered a potential correlation between Vitamin A and the gut microbiota in regard to impaired behaviors in individuals with ASD. Tabouy's study examined the use of probiotics on model mice resulting in less repetitive behaviors and some increased social interaction. Arnold's study also found a connection with probiotics and gut health in children with ASD. While other studies found insufficient evidence on supplements like folic acid, the topic still warrants room for more research and investigation.

Heavy Metals and Autism

Along with nutrition, many researchers believe that the impact of environmental factors, including toxic heavy metals, affect the developing brain (Lanphear, 2015). In a 2015 journal article by *Annual Review of Public Health,* the author claimed that "the impact of toxins on the developing brain is usually subtle for an individual child, but the damage can be substantial at the population level" (Lanphear, 2015, p.211). Examination and investigation on this topic have been frequently challenged as numerous factors may play a part; however, many toxins have been indicated in the abnormalities of brain development in children with intellectual and mental disorders (Lanphear, 2015). In this journal review of public health, the author provided

information related to the effects of toxic chemicals and the correlation with abnormal brain development.

The history of toxic environmental adversities regarding the effects of toxins on the developing brain dates back to early 1900s. There was an epidemic of lead poisoning from paint in Queensland, Australia that caused severe conditions including anemia, paralysis of lower limbs, blindness and even death in children. In Japan in the 1950s mothers gave birth to babies with serious motor dysfunctions and other intellectual disabilities from ingesting mercury-contaminated fish. Other cases in Japan and Taiwan happened later with the ingestion of contaminated powdered milk and rice bran oil in the mid 1900s (Lanphear, 2015).

According to Lanphear, the vulnerability of the developing brain is something to pay attention to because it is especially susceptible to environmental toxins.

> The blood-brain barrier of the developing brain is not fully formed, and it is more permeable to toxins than is the mature brain (104). The rapid growth of the brain during the second trimester of fetal development is followed by neuronal migration, differentiation, proliferation, and pruning throughout early childhood. Developing cells are more vulnerable to toxins, and the brain forms over a longer period than do other organs (Lanphear, 2015, p.213).

Toxins enter the brain through different mechanisms. When mercury enters an individual's system, it can cause cell death and alter cell migration. Toxic lead can alter synaptogenesis, synaptic trimming and neurotransmission (Lanphear, 2015). Ingesting contaminated food as well as breathing in airborne pollutants can alter the methylation pattern of the epigenome—a record of the chemical changes to DNA and proteins of an organism, which can also be passed down to offspring (Lanphear, 2015). During pregnancy, a developing fetus

could be affected by both lead and mercury toxins that increase the risk of children impacted by cognitive deficits (Lanphear, 2015). Lanphear discovered a 6.9 IQ decrement found in children who had low levels of blood concentrations of lead. Currently, no formal procedure dictates safe levels of neurotoxins in the United States. Even some pesticides have been associated with cognitive abnormalities in children. According to Lanphear, measuring the impacts of low-level exposure to toxins is challenging to do and more observational studies are needed (Lanphear, 2015). Researchers have also questioned how much evidence is necessary to prohibit, control and restrict suspected toxins from being in our food, chemicals and environment. Lanphear's article made clear that, "We can no longer deny the substantial if insidious impact that environmental toxins have on the developing brain. It is time to develop a comprehensive strategy to protect children from the impact of environmental toxins on the developing brain" (Lanphear, 2015, p.223).

Another 2005 study focused on toxic trace amounts of heavy metals found in the hair of children with autism (Fido & Al-Saad, 2005). The 40 boys with autism (ages four to seven) that were studied had higher levels of three specific toxic elements than the control group of 40 boys (ages four to eight) who did not have ASD. These individuals were studied over 12 months and all were enrolled at the Kuwait Autism Center (Fido & Al-Saad, 2005). According to this study, hair sampling is a non-invasive way to collect the best indicator of minerals in the body. The procedure included collecting untreated hair from different locations of the head. A total of eight toxic trace elements were tested: antimony, uranium, arsenic, beryllium, mercury, cadmium and aluminum. The boys diagnosed with ASD had higher levels of uranium, mercury and lead but there was no significant difference in the other elements within both groups (Fido & Al-Saad, 2005). According to Fido and colleagues, a fetus inside a mother's womb can absorb toxic heavy

metals and which can stay inside the body tissue for years. Knowing this, the toxic elements found in the hair of the 40 boys in this study could have been secondary and that their mothers were the primary carriers of these toxins.

P. Gail Williams and colleagues published a similar study testing the mercury levels in hair samples of children with ASD in the journal of *Research in Autism Spectrum Disorders* (Williams, Hersh, Allard, & Sears, 2008). In this study 15 children (two to six years old) diagnosed with ASD and a control group of same age range without ASD (including siblings of the children with autism) were tested for mercury levels in their hair. In comparison to the previous study mentioned, no significant differences were found between the two groups regarding mercury levels. This study questioned the validity of connecting mercury toxicity and autism (Williams, Hersh, Allard, & Sears, 2008). Williams and colleagues stated that the conflicting data in theories of mercury toxicity and autism in the article by Bernard et al., (2001) and the countering view of Nelson and Bauman (2003) indicated the weakness of this theory (Williams, Hersh, Allard, & Sears, 2008). Williams and colleagues argued that "The primary characteristics of mercury toxicity include ataxia, dysarthria, peripheral neuropathy, visual field constriction, hypertension, rash, thrombocytopenia and psychiatric manifestations such as anxiety and depression" (Williams, Hersh, Allard, & Sears, 2008, p.172). Their argument stated that individuals with autism did not have these other diagnoses, so therefore could not be related to mercury poisoning (Williams, Hersh, Allard, & Sears, 2008).

While blood, urine, hair and nail samples are methods to determine toxicity levels in individuals, evaluating tooth enamel is another. In a 2011 study, Maryam M. Abdullah and colleagues tested the levels of lead, mercury and manganese in prenatal and postnatal enamel of children's baby teeth (Abdullah, et al., 2011). Deciduous teeth were gathered from 84 children (9

to 14 years) some with ASD and some without. The findings of this study indicated no significant differences in the amount of metal between the children with ASD and the control group (Abdullah, et al., 2011).

In a 2008 study, Curtis and Patel reviewed literature concerning nutritional and environmental factors and autism. They concluded that many studies found evidence to support the linking of exposure of mercury, lead, pesticides and smoking in utero to higher levels of ASD and/or ADHD (Curtis & Patel, 2008). Curtis and Patel stated, "Both autism and ADHD appear to involve a broad range of genetic, prenatal, social, developmental, nutritional, and environmental factors, and it is unlikely that only a single cause will be found for either disorder" (Curtis & Patel, 2008, p.82). While larger studies are needed to draw more accurate conclusions, scientists found enough data to draw probable conclusions that nutrition and environment play a major role in the prevalence of autism (Curtis & Patel, 2008).

According to a study by Gerhard Winneke, he found existing evidence that inorganic lead, arsenic, organic mercury and polychlorinated biphenyls (PCBs) may be involved in neurodevelopmental disorders like autism (Winneke, 2011). He concluded that environmental childhood lead exposure had a significant and long-lasting impact on the brain's capabilities in regard to language function and that further research on other neurodevelopmental toxicants was needed (Winneke, 2011).

Mary Catherine DeSoto and Robert T. Hitlan published a journal article in 2010 titled: *Sorting out the Spinning of Autism: Heavy Metals and the Question of Incidence*. Their mission was to evaluate the differing opinions on the topic of autism and toxic exposures and claimed scientific research does not reject the possibility of this correlation (DeSoto & Hitlan, 2010). DeSoto and Hitlan chose to focus on the toxins of heavy metals and autism, even though there

are multiple categories of toxins related to autism in research. They do make clear that "any link between toxins and autism is almost certainly mediated by one's genetic makeup, and that other toxins, such as organophosphates likely play a role as well (DeSoto & Hitlan, 2010 as cited in Eskenazi et al. 2007)."

Over the last 30 years, the awareness of autism has increased; however, scientists still debate whether the increased awareness actually coincides with an increase in autism. DeSoto and Hitlan believe there has been a legitimate increase in ASD and argue that the increase is partly due to various contaminants in our environment (DeSoto & Hitlan, 2010). While DeSoto and Hitlan agree that some studies do not show evidence of heavy metals relating to autism, they do bring up an interesting thought for readers to consider:

> This particular controversy does have truly high stakes for many reasons. Pharmaceutical companies have been known to offer significant monetary support to the research-related endeavors of scientists whose research findings do not support a link between vaccination and autism, or which might have had relevance for evaluation of their products (vaccines) (DeSoto & Hitlan, 2010).

DeSoto and Hitlan hypothesized a high likelihood that genetic susceptibility and the ability to detoxify one's body of pollutants could be a significant reason in the correlation of environmental influences and autism symptoms. Today, many children are exposed to all sorts of neurotoxins throughout the environment and few resources are easily available to help detoxify these harsh poisons. This crisis may present a greater risk for neurodevelopmental problems for individuals who are more susceptible and vulnerable. (DeSoto & Hitlan, 2010). DeSoto's research also noted that 50 years ago there were less environmental toxins that would have caused neurological damage to one's brain, thus resulting in fewer diagnoses of Autism

Spectrum Disorder. They ended their journal article with unanswered questions but found reason and evidence to believe more research is still needed on this topic.

Recap of Heavy Metals and Autism

Many scientific studies corroborated the presence of heavy metals in the body in relation to autism. From mercury to lead, aluminum and more, there are many different metals that can toxify the body. Researchers discovered childhood lead exposure impacts the brain's ability to have proper language function. Scientists also proved that the health of the mother impacts the health of a child, but quantifiable measures were nonexistent. This is just one area of study in the wide spectrum of research on the etiology of ASD. A solid foundation exists regarding the effects heavy metals may have on neurodevelopment; however, further investigation and research are still needed.

Environmental Factors and Autism

It wasn't until the 2000s that researchers started investigating the relation between environmental factors and autism and by 2005 very little studies existed on this topic (Hertz-Picciotto, et al., 2018). This new research indicated that other influences besides genetics may be responsible for the etiology or autism (Hertz-Picciotto, et al., 2018). Researchers found evidence that prenatal factors greatly impacted the risk for having children with ASD (Hertz-Picciotto, et al., 2018). This evidence led researchers to closely examine environmental impacts like pesticide exposures (Roberts et al. 2007) and air pollution (Becerra et al. 2013 as cited in Hertz-Picciotto, et al., 2018).

The University of California Davis (UC Davis) conducted a population-based case-control study called CHARGE (Childhood ASD Risks from Genetics and Environment) in 2002 and investigated the origins and causative factors to ASD and developmental delay (DD) (Hertz-

Picciotto et al. 2006 as cited in Hertz-Picciotto, et al., 2018). Findings from the CHARGE study showed correlation with maternal prenatal vitamin supplementation (Schmidt et al. 2011, 2012), increased risk to agricultural pesticide applications (Shelton et al. 2014), traffic-related and regional air pollution (Volk et al. 2012), parental occupational exposures (McCanlies et al. 2012), maternal metabolic conditions, (Krakowiak et al. 2012), preeclampsia (Walker et al. 2015), and fever that went untreated during pregnancy (Zerbo et al. 2012) (as cited in Hertz-Picciotto, et al., 2018). CHARGE also identified immune dysregulation (Ashwood and Van de Water 2004; Braunschweig et al. 2013; Enstrom et al. 2010), mitochondrial dysfunction (Giulivi et al. 2010) and mitochondrial DNA damage (Napoli et al. 2013, 2014) (as cited in Hertz-Picciotto, et al., 2018) as potential underlying means linked to ASD.

In a 2017 study, Tara Kerin and colleagues declared that prenatal exposure to certain air pollutants was connected to children diagnosed with ASD (Kerin, et al., 2017). “Previous research suggests that neurodevelopment is adversely affected by exposure to ambient air pollutants, including particulate matter, polyaromatic hydrocarbons, diesel exhaust, nitrogen dioxide (NO_2) and the near-roadway air pollutant mixture” (Costa et al., 2015; Genkinger et al., 2015; Jedrychowski et al., 2015; Suades-Gonzalez et al., 2015 as cited in Kerin, et al., 2017, P.137). In this study, the air pollution exposure assessment was created based on parental reported residential history. Air pollution exposure was recorded starting three months before conception and continued to the most recent place of residence. Using roadway geometry, researchers were able to quantify the pollution amounts for each location the parent listed. The findings in this study confirmed the hypothesis that connected ASD and air pollutants.

Researchers agree that numerous air pollutants are linked to ASD symptoms. Exposure to nitrogen dioxide, a highly poisonous gas given off from road traffic, during the pregnancy and

during the first year of life was associated with increased cognitive impairments. Decreased language, communication, adaptive abilities, and fine motor skills were some of these impairments found (Kerin, et al., 2017).

Another study published in 2013 also examined air quality surrounding traffic-related air pollutants. Volk and colleagues found that children that lived at residences that had high amounts of exposure to traffic-related air pollution were more likely to have autism. Volk's study also reported exposure to nitrogen dioxin was specifically toxic during pregnancy and the first year of life (Volk, Lurmann, Penfold, Hertz-Picciotto, & Mcconnell, 2013).

In a 2014 study, Gong and colleagues explored the risk for autism and attention-deficit hyperactivity disorder (ADHD) in air pollution from road traffic in Sweden (Gong, et al., 2014). They drew conclusions from prenatal and postnatal exposure as they interviewed parents of 3,426 twins born between 1992 and 2000 in Stockholm. The parents were interviewed about their children at three intervals: during pregnancy, during the first year, and during the ninth year. The parents were asked about any neurodevelopmental disorders they noticed in their children. The results of this study were inconclusive and no consistent associations of road traffic pollution and neurodevelopmental disorders (Gong, et al., 2014).

According to scientists DA Rossignol and RE Frye, research identified four neurobiological areas of abnormalities in autism: immune dysregulation or inflammation, oxidative stress, mitochondrial dysfunction and environmental toxicant exposures (Rossignol & Frye, 2011). Rossignol and colleagues studied these four areas of research in literature reviews from 1971 to 2010 and ranked the studies using a validated level of evidence scale. They reported that a handful of publications indicated a link between these environmental exposures and ASD. These environmental toxins induced immune dysregulation and/or inflammation,

oxidative stress and mitochondrial dysfunction (Rossignol & Frye, 2011). Rossignol's study concluded that toxic environmental exposure plays a part in physiological abnormalities and future research should reveal additional supporting evidence (Rossignol & Frye, 2011). Rossignol and colleagues inferred the following:

> The interrelationships between these physiological abnormalities could result in an adversarial relationship such that one physiological abnormality could trigger other physiological abnormalities, which could reinforce the first, resulting in a downward spiral that could result in severe metabolic derangements. . . . further research into these areas may also provide insight into additive effect of abnormalities in critical physiological processes that contribute to ASD and other psychiatric disorders (Rossignol & Frye, 2011. P.397).

In a 2017 journal, Cindy Sage and Ernesto Burgio researched the impact technology has on the brain as it relates to electromagnetic fields (Sage & Burgio, 2017). As technology continues to rapidly advance, humans are daily exposed to the following types of EMFs: ELF EMF (electrical appliances and power lines) and RFR (wireless devices). New scientific evidence has linked EMF and RFR epigenetic changes to the neurodevelopment of a child (Sage & Burgio, 2017). According to Sage's study, cell phones and other wireless devices may have potential harmful health impacts especially in young people. These wireless devices are known to "produce electromagnetic fields (EMF) and pulsed radiofrequency radiation (RFR)" (Sage & Burgio, 2017, p.129). Sage and colleagues claimed that neurodevelopmental and neurobehavioral changes in individuals could be attributed to wireless technology. Sage's study listed the following symptoms that could result from EMF and RFR: lagging memory, learning disabilities, cognition impairment, attention deficits and behavioral problems. These symptoms are also

criteria within Autism Spectrum Disorder and Attention Deficit Hyperactivity Disorder (Sage & Burgio, 2017). As cited in Sage & Carpenter, 2012, "A comprehensive review of the scientific literature indicates that chronic exposure to even very low levels can result in biological effects that can result in diminished capacity to grow and develop normal neurologic, immune, and metabolic functions, and result in serious health and learning impairments and chronic disease" (Sage & Burgio, 2017, p.130).

While there are health risks for children exposed to EMFs, exposure in adults also may result in negative outcomes like higher cancer rates and neurodegenerative diseases. (Sage & Burgio, 2017). As cited in Sage & Carpenter, (2009, 2012),

> The 'electronic environment' has massively changed in the last three decades since wireless technologies have become deeply embedded in the lives of children. Exposures relevant to children include cell and cordless phone radiation, Wi-Fi-enabled devices like wireless iPads and other wireless tablets, wireless laptops, electronic baby monitors, and surveillance devices, among other sources. Exposure levels from these sources can result in biological effects that with chronic exposure be reasonably presumed to result in adverse health harm (Sage & Burgio, 2017).

The Kaiser Family Foundation as cited in Rideout, Foehr, & Roberts, 2010, limited screen time for children because it was connected to violent behavior, poor school performance including lower reading scores, sleep disruptions, obesity, and unhealthy eating habits (Sage & Burgio, 2017). Consequences on mental health, stress and anxiety were also linked to exposure to EMF and RFR. According to Sage and colleagues, the hope for reducing exposure and avoiding health risks associated with EMF and RFR exposure has to encourage the use of wired devices as much as possible (Sage & Burgio, 2017).

Air pollutants like as metals, solvents, nitrogen oxide and particulate matter, phthalates and pesticides were all environmental factors many scientists believe were linked to the etiology of Autism (Nowack, Wittsiepe, Kasper-Sonnenberg, Wilhelm, & Schölmerich, 2015). According to a 2015 study, endocrine disrupter chemicals called Polychlorinated diJasonzo-p-dioxins and diJasonzofurans (PCDD/Fs also known as dioxins) and polychlorinated bi- phenyls (PCBs) may have impacted fetal steroid hormone levels. These levels were potentially considered to be connected to "sex-typical development and autistic traits" (Nowack, et al., 2015, p.1). Scientists investigated associations of prenatal levels of PCDD/Fs and PCBs with autistic traits by measuring maternal blood samples. The PCDD/Fs and PCBs were discovered to be associated with lower testosterone levels which confirmed their hypothesis that ASD was linked to fetal androgen levels (Nowack, et al., 2015).

Researchers did report that exposure of the general population to these PCDD/Fs has recently decreased; however, it is still a concern because of the "accumulative character and the increased vulnerability of the immature organism" (Nowack, et al., 2015, p.2). Even though Nowak and colleagues found correlation between these dioxins and ASD, more research is needed. There was a limited number of studies that associated PCDD/F and PCB levels and autism and results are contradictory (Nowack, et al., 2015).

> The exact mechanisms how PCDD/Fs and PCBs are related to neurodevelopment are yet unknown, however, numerous possible explanations for an association between these POPs and autistic traits exist. Recent research has provided convincing evidence for a link between steroid hormones, i.e. androgens and estrogens, and autism (Nowack, et al., 2015, p.11).

Another element researchers have related to autism to is the genetic and environmental component of oxidative stress, which is the imbalance of free radicals and antioxidant defenses in one's body (Mandic-Maravic, et al., 2019). A 2019 study investigated the potential role of common polymorphisms in genes for glutathione transferase A1, M1, T1 and P1 in vulnerability to ASD. They also explored the possible risk of ASD with oxidative stress, which is the imbalance of free radicals and antioxidants in the body, regarding GST polymorphisms and mothers smoking while pregnant (Mandic-Maravic, et al., 2019). This study included 113 children with ASD and 114 in the control group. Surprisingly, smoking while pregnant was not significant for the risk of ASD (Mandic-Maravic, et al., 2019).

Recap of Environmental Factors and Autism

Many studies confirmed a link between environmental factors like air pollution and autism. Living near high-trafficked areas created a more toxic environment and poorer air quality for children and increased their potential risk for ASD and other cognitive disabilities (Kerin, et al., 2017). As technology has advanced, EMFs and RFR exposure have also raised questions and propelled scientific research on the effects they have on the human brain. The evidence has linked EMF and RFR epigenetic changes that could alter a child's neurodevelopment (Sage & Burgio, 2017). Exposure to Nitrogen Dioxide during pregnancy and first year of life increased cognitive impairments (Kerin, et al., 2017). Rossignol and colleagues said that "environmental toxicant exposure is a ripe area of research for triggering additional physiological abnormalities" (Rossignol & Frye, 2011, p.397). Removing or restricting these environmental influences could help in the treatment of ASD.

Chapter III: Discussion and Conclusion

Summary of Literature

In chapter one of this paper, readers were invited into the lives of Kate and Jason and the health challenges they faced with their daughter, Molly, and her diagnosis of autism. Molly's parents advocated for her and got her the help she needed. Through healing her gut and changing her environment, they saw improvements in not only her physical health, but her ability to communicate with others. Her story and many others are the reason scientists and researchers have studied and investigated the impact gut health has on the brain as well as environmental factors that contribute to neurodevelopment.

Through multiple studies, scientists have found some answers to the etiology of autism and continue to examine different factors that contribute to one's neurological and developmental health. Studies confirmed a possible link between gut health and autism. Justyna Siwek and colleagues explored the role of the gut-brain axis in the eating behaviors of children with ASD. The results from this study indicated that children with gastrointestinal diagnoses experienced constipation, diarrhea, bloating, and other digestive-related disorders (Siwek, Kawala-Janik, & Walecki, 2017). They found that up to 70% of children with autism were diagnosed with digestive system problems compared to only 28% in the control group (Siwek, Kawala-Janik, & Walecki, 2017). Probable connections between gut health and Autism Spectrum Disorder were confirmed with microbial imbalances within the gut discovered in individuals with ASD (Liu et al., 2017). Some researchers think that this maladaptation might contribute to some of the impaired behaviors associated with ASD (Liu et al., 2017).

Along with gut health correlations and ASD, research has also indicated connections with environmental health including exposure to poor air quality and heavy metals like mercury, lead

and aluminum. The association between air pollution exposure and cognitive function was examined by Tara Kerin and colleagues in a 2017 study. They declared that prenatal exposure to some air pollutants was connected with children diagnosed with ASD (Kerin, et al., 2017). "Previous research suggests that neurodevelopment is adversely affected by exposure to ambient air pollutants, including particulate matter, polyaromatic hydrocarbons, diesel exhaust, nitrogen dioxide and the near-roadway air pollutant mixture (costa et al., 2015; Genkinger et al., 2015; Jedrychowski et al., 2015; Suades-Gonzalez et al., 2015 as cited in (Kerin, et al., 2017).

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> The blood-brain barrier of the developing brain is not fully formed, and it is more permeable to toxins than is the mature brain. The rapid growth of the brain during the second trimester of fetal development is followed by neuronal migration, differentiation, proliferation, and pruning throughout early childhood. Growing cells are more vulnerable to toxins, and the brain forms over a longer period than do other organs (Lanphear, 2015, p.213).

Toxins enter the brain through different mechanisms. When mercury enters an individual's system, it can cause cell death and alter cell migration. Toxic lead can alter synaptogenesis, synaptic trimming and neurotransmission. Whether airborne pollutants or ingested contaminated food, can alter the methylation pattern of the epigenome—a record of the

chemical changes to DNA and proteins of an organism, which can also be passed down to offspring (Lanphear, 2015).

There is a lot of research on the effects of nutrition and environmental factors and its role on the brain. The connection between the gut and the brain have caused scientists to look deeper into the cause of neurodevelopmental disorders like autism. The good news is that as technology increases, more scientifically backed research is able to happen.

Professional Application

Working with individuals with developmental conditions like Autism Spectrum Disorder has given me insight into the field of special education and the psychology of developmental disorders. Although researchers cannot identify the reason behind autism's rise globally, the increased awareness of this disorder should intrigue professionals to seek more understanding. From in-home treatment, special education classrooms, transition schools and adult daycare programs, individuals with developmental disabilities need support and care for their entire lives. While many of these individuals, specifically with autism, are unable to verbally communicate, it is up to parents, caretakers and educators to advocate for their needs and help them in obtaining the best quality of life.

Understanding both the positive and negative impacts nutrition and environmental factors have on one's health can allow parents, teachers and health professionals to make progressive modifications in the lives of vulnerable individuals with developmental disorders. Staying informed with the latest research is vital in addition to seeking professional recommendations for interventions. Improving the symptoms of autism is a team effort: strong communication and a willingness to maintain awareness of how food choices and specific environmental conditions

affect individuals with ASD is indispensable. Only together, we can continue to help people with neurodevelopmental disorders like autism thrive in their daily lives.

Limitations of the Research

While almost every individual study has its limitations, it is important to note that research as a whole does as well. I chose not to cover the topic of vaccinations and autism because of limited and contradictory research as well as the massive controversy it holds. Regardless of one's beliefs on this subject, it is an area that could have been included in this literature review. Anything that goes into the bloodstream can also have an effect on the gut. If anything, my hope is that parents complete their own research and draw their own conclusions when it comes to caring for their children.

In regard to the studies discussed in this paper, researchers found evidence both supporting and contradicting a potential link to gut health and environmental factors in autism. In my experience researching this topic, I was glad to find many studies that applied to my leading thesis question. When I chose this topic, I did not know what information was available or what research existed on this topic. Regardless of all of the studies that either confirm or deny certain correlations between autism and specific health factors, the real application is in caring for our friends diagnosed with ASD. Personal relationships with individuals on the spectrum trump any amount of dietary or behavioral interventions and I believe it is our job as teachers, caretakers, parents and other health professionals to create a protected environment where a child feels safe, healthy and loved.

Implications for Future Research

I think research in this area has a tremendous way to go. While there are many studies regarding gut health and autism, as well as research on environmental factors, there is so much

left undiscovered. I am excited to see more scientific evidence in the next five to ten years and how special education curriculum will expand in the school systems. In the last few decades, researchers have made great strides in understanding this disorder, yet so many questions remain unanswered. What if new research gave more insight about how to change the trajectory of an individual's development by incorporating nutritional and environmental changes? What natural substances have not yet been explored that could help individuals with autism? What other behavioral therapies have scientists and psychologists not cracked the surface on? What scientific information on brain development and functions do we still have yet to discover?

Conclusion

What evidence exists, if any, to connect gut health and environmental factors and autism? According to research, there is in fact evidence that connects gut health and autism. Studies have proven connections between autism and environmental factors including exposure to poor air quality and heavy metals. Scientists still do not entirely know the full extent of how these factors contribute to the diagnosis of autism or the rate at which symptoms of autism can be reversed. However, practical applications of this research can be implemented right away: better food choices, removal of toxic environments and supplementing with probiotics. Parents and caretakers of children with ASD have numerous options for treatment and interventions for their loved ones with Autism Spectrum Disorder.

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