

Gastrointestinal Abnormalities in Children with Autism
Spectrum Disorder and Typical Development. An Irish
Perspective

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Abstract

The aim of the study was to identify differences in occurrence of gastrointestinal (GI) abnormalities for children with Autism Spectrum Disorder (ASD) and children with typical development as well the most commonly occurring GI symptoms and food allergies, dislikes and diet restrictions for both groups of children. The study further examined relationships between severity of these problems and severity of ASD, insomnia symptoms and parental stress. A total of 247 parents of children living in Ireland participated in the study. Results indicate that insomnia symptoms predict ASD severity and parental stress regardless of type of development. GI symptoms predict sleep problems. Inconclusive results were obtained for food allergies, dislikes and diet restrictions. Higher frequency of insomnia symptoms and GI symptoms, mainly abdominal pain, gaseousness/bloating and constipation, were found for children with ASD. Parents of children with ASD reported higher level of stress than parents of children with typical development.

Introduction

Global mental health

“We are our brains” (Swaab, 2015, p. 3). If so, what are the implications for typically developing individuals, those with neurological and/or neurodevelopmental impairment, and in broader perspective, societies and human population? Mental health disorders are highly prevalent globally affecting people across all regions of the world (Steel et. al, 2014) and commonly occurring in many countries (Kessler et al., 2009). They are associated with all-cause mortality and cause long-term disability and dependency (Prince et al., 2007). The Global Burden of Disease Study 2016 (GBD 2016), the most comprehensive worldwide observational epidemiological study (Hay, 2017) which examined changes in health across 195 countries and territories from 1990 to 2016, reported increase of total burden and disability-adjusted life-years (DALY)¹ rates of neurological disorders by 59% and mental and substance use disorders by 47%. Mental, neurological and substance use disorders accounted for 11.13% of global DALYs and were reported to be the leading causes of years of life lived with disability (YLDs) worldwide with burden present across the lifespan (Hay, 2017). World Health Organization (WHO) estimates that mental disorders affect 450 million people constituting one of the leading cause of ill-health and disability worldwide (WHO, 2001). In Europe, estimated 83 million people are affected and neurological disorders rank as the highest cause of YLDs, accounting for 36.1% of total YLDs attributable to all causes (WHO, 2014). In Ireland 1.4% of population suffers from intellectual disability, 3.3% from learning disability and 2.6% had a psychological or emotional condition (CSO, 2016).

¹ DALY measures health loss due to disease burden. DALYs are the sum of the years of life lost (YLLs) due to premature mortality and years of life lived with disability (YLDs) (GBD, 2016)

Vigo (2016) argues that the global burden of mental illness is underestimated by more than one third and that mental disorders are the main cause of worldwide burden of disease in terms of YLDs. Prince (2007) stresses that the underestimation is attributed to low appreciation of the mutual links between mental disorders and other health conditions. At the same time, between 76% and 85% of people in low- and middle-income countries and between 35% and 50% in high-income countries do not receive any treatment (WHO, 2017) mainly due to attitudinal and structural barriers (Andrade et al., 2014). The projections for the future indicate that depressive disorders will be a second main cause of burden of disease in 2030 (Mathers and Loncar, 2006). As Vigo (2016) points out, life expectancy of the populations is on the rise, but it coincides with greater mortality and disability, including increasing prevalence of neurodevelopmental disorders. The current study will address one of the highly prevalent mental and neurodevelopmental disorders, which is of a growing concern worldwide, namely Autism Spectrum Disorder (ASD).

Neurodevelopmental Disorders

According to “Diagnostic and Statistical Manual of Mental Disorders” fifth edition (2013) (DSM-5), neurodevelopmental disorders “are a group of conditions with onset in the developmental period (...) and are characterized by developmental deficits that produce impairments of personal, social, academic or occupational functioning” (American Psychological Association [APA], 2013, p. 31), European definition somewhat overlaps with American one and refers to “disabilities in the functioning of the brain that affect a child’s behaviour, memory or ability to learn e.g. mental retardation, dyslexia, attention deficit hyperactivity disorder (ADHD), learning deficits and autism” (WHO, 2003, p.13). Bishop (2010) emphasises dual etiology of neurodevelopmental disorders, including ASD, which may be caused by known genetic or

acquired factor, or have multifactorial origin resulting in impairment of certain aspects of neurodevelopment. Apart from typically being multi-factor in origin and manifesting in early childhood, neurodevelopmental disorders are also highly heritable, commonly affect males and endure throughout their lifetime (Thapar, Cooper & Rutter, 2017).

Prevalence of neurodevelopmental disorders is high and steadily increasing. They were reported for one in six children between 2006 and 2008 in the United States and increased from 12.84% to 15.04% between 1997 and 2008 (Boyle et al., 2011). Similarly, in Ireland a number of persons with difficulty in learning, remembering or concentrating rose by 14.5% between 2011 and 2016. 3.3% of population equaling to 156,968 persons with greatest incidence among males aged 10-14 years (Central Statistics Office [CSO], 2016). Atladottir et al. (2014) argues that increase in age specific prevalence may be attributed to increase in availability and improvement of the health service, increase in awareness of developmental difficulties and broadening of the diagnostic criteria. Furthermore, the Committee on Nervous System Disorders in Developing Countries, convened by the U.S. Institute of Medicine, following review of prevalence studies published between 1970 and 1999, reported that most of the data are restricted to populations of developed countries while 80% of children were raised in low and middle-income countries. Available data on severe mental retardation from the latter suggest tendency for higher prevalence in low-income countries (Institute of Medicine, 2001). The most commonly occurring and researched conditions are intellectual disability, ADHD and ASD (Boyle et al., 2011; Bishop, 2010).

Autism Spectrum Disorder

ASD is a pervasive and life-long neurodevelopmental condition with genetic, biological, environmental and developmental etiology (Elsabbagh et al., 2012) characterized by

abnormalities in social interaction, communication and presence of stereotypical, repetitive behavior (Atladottir et al., 2014; Baxter et al, 2014). Although it is a subject to maturational change and some core symptoms may decline with age, it is considered a lifelong disorder with neurodevelopmental problems persisting into adulthood (Thapar, Cooper & Rutter, 2017). Individuals with ASD require care and support throughout life and level of support varies with severity of condition, from requiring continual care to being fully independent. The principal carers are typically parents and family members and it is important to note the significant psychological and emotional impact that raising and caring for a child with ASD has on the parents (Hare, 2016).

Definition of Autism Spectrum Disorder.

Diagnostic criteria for ASD specified in DSM-5 relate to the following symptoms: persistent deficits in social communication and social interaction across multiple contexts (criterion A) and restricted, repetitive patterns of behaviour, interests, or activities (criterion B). The symptoms must occur in early developmental period (criterion C), cause significant impairment in social, occupational or other areas of functioning (criterion D) and cannot be explained by intellectual disability (criterion E) (APA, 2013). Due to its diverse phenotypic and genotypic etiology as well as variability in intellectual, communicative and social ability, it is currently conceptualized as a spectrum disorder (McPartland, Law and Dawson, 2016).

Prevalence of Autism Spectrum Disorder.

Undoubtedly, prevalence is on the rise. WHO epidemiological data estimate global rate at one person in 160 equaling to 7.6 million DALY and 0.3% of the global burden of disease (WHO, 2013). According to GBD, in 2010 there were 52 million cases of ASD globally with prevalence of one in 132 persons and more than threefold gender difference between males and females. Following review of epidemiological surveys of autistic disorder worldwide, Elsabbagh

et al. (2012) found prevalence of 17 cases in 10,000. They observed higher ratio in males to females and increasing tendency in prevalence estimates. They further noted that such estimates are either unavailable or preliminary in many regions of the world including Africa. The prevalence of ASD in U.S. is estimated at 0.47% and has increased by 289.5% between 1997 and 2008 (Centers for Disease Control and Prevention [CDC], 2011). Similarly, in Europe the rates are high: at least 1% of children and young people in the UK (Blackburn, Read and Spencer, 2012) and at least 1% of the population in Ireland according to the study conducted in 2013 (Sweeney, Staines & Boison, 2016). Atladottir et al. reported raising tendency in ASD diagnosis in individuals up to 20 years of age in Denmark, Finland, Sweden and Western Australia and increase of 175%, 96%, 354% and 121% respectively, between 1992 and 2001. Although Faras, Al Ateeqi and Tidmarshb (2010) suggest reclassifications of disorders and improved detection as further potential reasons for reported increase, the high and rising prevalence of ASD is an undeniable fact and as such, require attention from research bodies worldwide, including Ireland.

Etiology of Autism Spectrum Disorder.

Etiology of ASD is currently unknown. Growing body of research points to its genetic, environmental, biological and developmental origins (Elsabbagh et al., 2012). Evidence from twin and family studies suggest that ASD is both familial and heritable with reported sibling recurrence rate of 18.7% (Ozonoff et al., 2011) and higher rate of concordance for monozygotic twins (36-95%) than dizygotic twins (31%) (McPartland et al., 2016). Although McPartland et al. (2016) argues that absence of 100% rate in monozygotic twins indicate existence of environmental influences on ASD, Tick et al. (2016) in the recent meta-analysis of twin studies provides evidence for estimated 64% to 91% heritability and stresses strong genetic influences on ASD. From a different perspective, Frith and Happé (2005) suggest that raising incidence of

ASD may point to environmental triggers, but also note that no strong evidence for any singular environmental pathogen was found. A few risk factors have been suggested to interplay with genetic vulnerability including vaccines, mercury, viral infections or exposure to certain medications during the prenatal period, gestational pesticide exposure (Shelton et al., 2012) and exposure to ambient air pollution (Weisskopf, Kioumourtzoglou and Roberts, 2015). Wasilewska and Klukowski (2015) note that current understanding of ASD pathogenesis relate to individual genetic predisposition with environment as an epigenetic phenotype trigger.

Many research also focus on exploring brain structure and functionality in the context of ASD. Frith and Happé (2005) note that no anatomical abnormalities specific or universal to ASD have been identified. Some theories point to disruption of brain connectivity whereby individuals with ASD have lower connectivity between distant brain regions (Mohammad-Rezazadeh et al., 2016) and over-connectivity in brain areas crucial for social-skill development and related to repetitive behaviors (Conti et al., 2017). Other point to under-pruning (Dixon-Salazar et al., 2015; Tang et al., 2014) or over-pruning which involve overly aggressive synaptic pruning in infancy and early childhood (Thomas et al., 2016). “Extreme male brain” hypothesis suggests that exposure to high levels of prenatal and neonatal testosterone might be a risk factor in ASD (Knickmeyer and Baron-Cohen, 2006). A recent hypothesis evaluates positive effects of oxytocin on restricted, repetitive behaviors, social interaction and communication in individuals with an ASD (Ooi, 2017). Finally, a novel theory is currently being considered suggesting that gut microbiota dysfunction may result in impairment of certain brain functions and behavioral abnormalities (Hsiao et al., 2013).

Comorbidity in Autism Spectrum Disorder.

Comorbidity, defined by Matson & Nebel-Schwalm (2007) as the co-occurrence of two or more disorders in the same person, are typically present in individuals with ASD. Gjevik et al. (2011) found that 72% of Norwegian children and adolescents with ASD were diagnosed with at least one comorbid psychiatric disorder while Amr et al. (2012) reported a figure of 63% for Arabic children. Mannion, Brahm and Leader (2014) in a comprehensive literature review identified anxiety, intellectual disability, depression, phobias and ADHD as secondary psychopathologies commonly occurring with ASD diagnosis. Also, Ming et al. (2008) found that medical co-occurrences in children with ASD included sleep disorders, food intolerance and GI dysfunction and that sleep disorders and food intolerance were associated with GI symptoms. Other comorbid disorders identified to co-occur in ASD include sleep dysfunction and gastrointestinal abnormalities. Mannion, Leader and Healy (2013) in an Irish study found that 80.9% of children and adolescents have a sleep problem and 79.3% at least one gastrointestinal symptom. Overall, they reported rate of 46.1% for comorbid diagnosis in children and adolescents with ASD. The present study will address prevalence of gastrointestinal symptoms in children diagnosed with ASD and children with typical development (TD) living in Ireland.

Gastrointestinal abnormalities and Autism Spectrum Disorder

Over the course of the last 10-20 years many studies have focused on connection between gastrointestinal (GI) abnormalities and neurological diseases, an idea derived from observation that GI abnormalities are common among patients with Parkinson (Sampson et al. 2016), Crohn's disease (Chu et al 2016), major depression, Rett syndrome, cerebral palsy and ASD (Hsiao et al., 2013).

Prevalence of GI symptoms.

Several studies have been conducted with respect to ASD to examine levels of prevalence and types of GI disorders (Parracho et al., 2005; Valicenti-McDermott, 2006; Kohane et al., 2012; Chaidez et al., 2014; Mannion, Leader & Healy, 2014; Bresnahan et al., 2015). Currently, the prevalence is estimated between 9% to 91% for children with ASD (Coury et al., 2012) and between 9% to 37% for children with TD (Wasilewska & Klukowski, 2015). However, some studies reported similar levels of GI abnormalities for children with ASD and children with TD or no association between ASD and GI symptoms (Mannion et al. (2013). More studies offering comprehensive comparison between both groups are required and the current study aims to address this gap in research. Moreover, the study will examine gender and age differences in GI symptoms across both groups of children.

A retrospective prevalence study conducted by Kohane et al. (2012) with a sample of 14,000 individuals with ASD provided evidence that GI disorders did not change significantly in age groups 0-17 and 18-34. Molloy and Manning-Courtney (2003) also reported that frequency of GI symptoms did not vary by age. On the contrary, Williams et al. (2010) in a study examining frequency of GI symptoms in 1,420 children with ASD found that parent reports of such symptoms increased with age, ranging from 39% in those under 5 years to 51% in those 7 years and older. Research in this area seem to be limited with majority of studies not investigating age differences. Similarly, for gender differences research data is not substantial as most of the comparative studies focus on children with ASD versus children with TD where age, gender and nationality are adjusted for both groups. However, Baker and Milivojevich (2013) reported that GI troubles are more prevalent among girls with ASD than boys while Williams et al. (2010) found that presence of GI problems did not differ by gender.

Core GI symptoms.

Chaidez et al. (2014) in a comparative study between children with ASD and TD indicated that frequency of GI symptoms is higher for children with ASD and correlate with maladaptive behaviors. Parent report indicated sensitivity to foods (31% for ASD vs. 4.5% for TD), constipation (15% vs. 3.5%), diarrhea (13% vs. 1.6%) and gaseousness/bloating sensation (11% vs. 2%) as most prevalent for both groups of children. A meta-analysis of 15 studies investigating GI symptoms for 2,215 children with ASD indicated higher level of same for those children in comparison with control group with TD. General odds ratios of 4.42 and specifically for diarrhea - 3.63, constipation - 3.86 and abdominal pain - 2.45 were reported. (McElhanon et al., 2014). Similarly, Williams et al. (2010) found abdominal pain (59%), constipation (51%) and diarrhea as most frequently occurring GI dysfunctions. Overall, the reported prevalence of specific symptoms ranges between 2% to 41 for abdominal pain/discomfort, 6% to 45% for constipation and 3% to 77% for diarrhea (Coury et al., 2012).

Food allergies, dislikes and diet restrictions are frequently reported GI related issues. Chaidez et al. (2014) found that children with ASD are more likely to have such issues compared with children with TD (65% vs 34%; 37.4 vs. 10.4%; 23% vs. 11% respectively). They further reported dairy/casein (14.6%) as grains category (gluten – 7.8% and nuts/soy – 7%) as most frequently occurring food sensitivity or allergy. Valicenti-McDermott (2006) found that food selectivity was higher in children with ASD (60%) than those with TD (22%). Furthermore, Ibrahim et al. (2009) indicated that children with ASD were more likely to manifest food selectivity and feeding issues arising from need for routine, ritualistic tendencies and insistence on sameness, which in turn may result in inadequate nutrition, intake of fiber and fluids. Wasilewska and Klukowski (2015) concluded that there are currently no conclusive studies confirming that food allergies are more prevalent for ASD than general population.

Finally, in Irish setting, Mannion et al. (2014) examined frequency of comorbid disorders in children and adolescents with ASD, including GI and sleep problems, and found that the most common GI symptoms were abdominal pain (51.7%), constipation (49.4%), diarrhea (45.9%), nausea (29.9%) and bloating (25.3%). Mannion and Leader (2013) also examined predictors of comorbid disorders and reported that sleep problems together with severity of intellectual disability significantly predicted GI symptoms. Moreover, GI symptoms predicted total comorbid psychopathology score, which can have impact on caregiver well-being and levels of parental stress. Following on from those findings, this study will examine GI symptoms in children with ASD and TD as well as relationships between their severity, severity of autism, sleep dysfunction and parental stress from Irish perspective. Noting that to date no research have been conducted with regards to food dislikes and diet restrictions, the study will also address those GI related symptoms.

Etiology of GI symptoms.

Notwithstanding that the underlying mechanisms and nature of GI abnormalities in individuals with ASD are yet to be determined, the current state of knowledge allows for identification of main areas of interest, including gut–brain connection, intestinal permeability, nutrition and gut microbiome (Coury et al., 2012). The latter is an interesting concept whereby gut microbiota can regulate and modulate physiological abnormalities associated with neurodevelopmental disorders (Collins and Bercik, 2009; Cryan and Dinan, 2012; Zheng et al. 2016), including ASD (Coury et al., 2012; Hsiao et al., 2013). Given that composition of intestinal microbiota is determined in pre- and post-natal period, certain environment and lifestyle factors may lead to reduced or altered intestinal flora (Wasilewska and Klukowski, 2015). Various studies suggest that commensal bacteria affect a variety of ASD-symptomatic

behaviors, including social, emotional and anxiety-like and contribute to brain development and function (Arentsen et al., 2016; Hsiao et al., 2013; Sampson et al. 2016). It is therefore possible that severity of GI symptoms may be linked to severity of ASD, a relationship which the current study aims to explore.

Although Wasilewska and Klukowski (2015) note that there is currently no consensus regarding nature of interconnection between GI tract and pathophysiology of ASD, they offer plausible indication of possible gut to behavior cycle: gut → blood → brain → behavior → food → gut. As this relationship is being explored, research worldwide is focusing on a better understanding of GI and ASD relationship by way of collecting data on prevalence and types of GI disorders in individuals with ASD as well as mapping mutual relationships between various comorbid disorders. The presents study aims to significantly contribute to the current state of knowledge.

GI symptoms and severity of Autism Spectrum Disorder.

Wang et al. (2011) investigated relationship between severity of ASD and GI abnormalities and reported that increased autism symptom severity was associated with higher odds of GI problems. Hsiao et al. (2013) suggested that GI dysfunction and dietary issues may contribute to manifestation of core symptoms of ASD. Chaidez et al. (2014) examined association between GI symptoms and maladaptive behaviour and found that ASD-related behaviors, i.e. stereotypy, social withdrawal, hyperactivity and irritability, were significantly higher in children with frequent occurrences of GI symptoms (abdominal pain, constipation, diarrhea and gaseousness). Nikolov et al. (2008) reported similar finding, but concluded that overall, children with GI problems were no different from children without GI problems in ASD symptom severity.

Sleep pattern disturbance and Autism Spectrum Disorder

A comprehensive review of prevalence of sleep problems in individuals with intellectual disabilities and developmental disorders provided evidence that a rate of sleep disturbance is higher for such individuals than the general population (Esbensen and Schwichtenberg, 2016). Although this group is heterogeneous in nature, individuals experience common problems including insomnia, parasomnias and circadian rhythm sleep disorders. The current study will focus on insomnia defined in DSM-5 (APA, 2013) as dissatisfaction with sleep quantity or quality, associated with difficulty initiating sleep and/or difficulty maintaining sleep due to frequent awakenings or problems returning to sleep and/or early-morning awakening with inability to return to sleep. DSM-5 definition will be adopted for the purposes of analysis of sleep symptoms in the studied sample of children with ASD and TD.

Prevalence of sleep disturbance in Autism Spectrum Disorder.

Reported rates of prevalence of sleep disorders in individuals with ASD are indicated between 50% and 80% (Esbensen & Schwichtenberg, 2016; Malow et al., 2012; Veatch et al., 2016), although some studies report smaller prevalence of 33% and 47% (Mannion & Leader, 2013). In Ireland, Mannion et al. (2013) found that 80.9% of children with ASD have sleep problems. On the contrary, the rates for children with TD were found to indicate that between 25 and 40% of individuals are affected (Cohen, Conduit, Lockley, Rajaratnam & Cornish, 2014). Insomnia is the most frequently indicated sleep problem for individuals with ASD (Goldman et al., 2014; Johnson et al., 2013; Malow et al., 2014; Veatch et al., 2016). According to Miano and Ferri (2010), insomnia is the main sleep concern in children with ASD with parents reporting difficulties with initiating and maintaining sleep, restless sleep, alterations of sleep hygiene, and early awakenings in the morning. Allik, Larsson and Smedje (2006) reported higher prevalence

of pediatric insomnia in school-age children with ASD than in school-age children with TD (31.2% and 0% respectively) with difficulties initiating sleep and daytime sleepiness as most common symptoms reported by parents. Finally, Liu, Hubbard, Fabes and Adam (2006) indicated that about 86% of children with ASD had at least one sleep problem almost every day with rate of insomnia at 56%.

Etiology of sleep disturbance in Autism Spectrum Disorder.

Although etiology of sleep problems remains uncertain, Cohen et al. (2014) suggested that they may directly originate either in the ASD condition (i.e. certain predispositions that cause chronic sleep-wake disturbances) or associated comorbidities (e.g. GI abnormalities). Similarly, Malow (2014) postulated that they can include neurotransmitter abnormalities (e.g., melatonin), medical conditions (e.g., GI disturbance), psychiatric conditions (e.g., anxiety), medication or behavioral causes including emotional regulation and difficulties with successful transition from preferred activities to sleep. Finally, Goldman (2010) suggested that underlying impairment of circadian rhythms manifested by disturbed sleep-wake cycle and hormonal abnormalities may be largely responsible for sleep disturbance in individuals with ASD.

Sleep problems seem to be associated with more severe ASD symptomology and co-occur with GI disorders that endure throughout lifespan (Esbensen & Schwichtenberg, 2016). Hollway and Aman in a comprehensive literature review examining relationships between sleep disturbance and pervasive developmental disorders found that sleep abnormalities comprise significant problem in a general pediatric population, but in particular for children with developmental disorders. They found that ASD severity and sleep abnormalities were significantly associated in 77% of 11 studies analyzed for the above-mentioned association (as cited in Mannion and Leader, 2014).

Sleep disturbance and GI symptoms in Autism Spectrum Disorder.

Cohen et al. (2014) suggested that etiology of sleep disturbance may originate in ASD associated comorbidities and as such, may be a secondary condition caused by other medical and psychiatric disorders. Mannion et al. (2013) found that GI symptoms and under-eating were significant predictors of sleep problems. Klukowski, Wasilewska and Lebensztejn (2015) reported that autistic children with GI abnormalities have higher prevalence of sleep disturbances compared with children with TD and no history of GI problems. Similarly, Hollway, Aman and Butter (2013) indicated that anxiety, ASD severity and GI symptoms were associated with sleep disturbance. Mannion and Leader (2013a) in an Irish study reported sleep disturbances in 91.1% of individuals experiencing abdominal pain, 90.9% of those with bloating, 90% with diarrhea and 83.7% of those with constipation. They further concluded that sleep problems predict GI symptoms. Despite growing body of evidence, the nature of correlation between both symptoms is yet to be determined. The current study aims to explore this relationship.

Parental stress and Autism Spectrum Disorder

The problem of parental stress is twofold. It can be considered from a broader parent and family unit perspective to identify factors which cause major stress. It can also be addressed from a child-specific perspective to determine the impact of parental stress on child's development, including in the prenatal period. Woodman, Mawdsley and Hauser-Cram (2016) propose that transactional models of development which emphasise reciprocal nature of dynamic interactions between a child and his/her environment, where the child is both the product and producer of same, may be the most effective in explaining a complex developmental course. The present study will address a relationship between GI symptoms, as significant ASD comorbidity, and parental stress. Crnic & Low (2012) proposed that stress may be conceptualized as a

circumstance which “involves an individual’s emotional and behavioral response to some unpleasant event (...) some level of distress that adversely affects subsequent behavior and functioning (...) [and] has multiple parameters (emotional, behavioral, and physiological) that affect well-being” (p. 243). This definition of stress will be adopted for the purposes of the study.

Etiology of parental stress in Autism Spectrum Disorder.

According to bidirectional theoretical model of parent-child relationship proposed by Hastings, child’s problematic behaviors lead to parental stress, which affects parenting conduct and as result, impacts and increase child’s problem behaviors (as cited in Pastor, Fernandez, Tarraga-Minguez & Navarro-Peña, 2014). The researchers note that key diagnostic traits of ASD-related symptoms are the main stressing agents for parents, but not all parents report elevated levels of stress. However, Pastor et al. indicate that parental stress was significantly higher for parents of children with ASD than TD. Similarly, Dykes (2015) following review of 173 studies (63% in relation to ASD) with respect parental stress in families of children with developmental disorders found that they experience higher levels of stress than parents of children with TD. Mancil, Boyd and Bedesen (2009) report that parental stress associated with raising a child with ASD is a consistent finding and that parents of those children are at an increased risk for high stress levels in comparison to parents of children with TD. Finally, Bonis (2016) in a comprehensive literature review of 132 studies on the subject conclude that there is a consensus among researchers that parents of children with ASD have higher levels of stress than other groups of parents. Bonis further indicates that parental stress is primarily attributed to child’s challenging behaviors, including disruptive sleep, as well as managing child’s diet and nutrition due picky eating, hyper-response to food textures and odors.

For ASD severity and GI symptoms, Rivard, Terroux, Parent-Boursier and Mercier (2014) found that levels of parental stress were associated with severity of child’s autistic

symptoms, but only paternal stress was predicted by severity of ASD. Soltanifar et al. (2015) reported similar findings whereby severity of ASD was correlated with parenting stress for fathers, but not mothers. Furthermore, research by Lai (2013) indicated that autism severity was significantly correlated with parenting stress for both parents of children with autism. On the contrary, McStay et al. (2013) found that autism severity was not significantly related to parenting stress in parents of children with ASD. In GI abnormalities domain, Valicenti-McDermott (2015) reported that parental stress was related to GI problems in the studied ASD sample, but no further research seems to be available in this regard. The current study will aim to address the above-mentioned problems with respect to parental stress, specifically whether severity of ASD, GI symptoms and sleep symptoms are significantly correlated with parental stress.

Aims of the study

The study aims at identifying the following:

1. Difference in occurrence of GI problems with respect to:
 - a. children with ASD and children with TD
 - b. males and females
 - c. three age groups: 5 years and younger; 6 to 14 years and 15 years and olderas well as the most commonly occurring GI problems and food allergies, dislikes and diet restrictions for children with ASD and children with TD;
2. Whether GI problems, food allergies, dislikes and diet restrictions predict insomnia symptoms;
3. Whether GI symptoms, food allergies, dislikes, diet restrictions and insomnia symptoms predict severity of ASD; and

4. Whether GI symptoms, food allergies, dislikes, diet restrictions and insomnia symptoms predict parental stress.

Hypotheses

The following hypotheses have been formulated to address the above-mentioned aims of the study:

1. It is hypothesized that there will be a significant difference in level of GI symptoms with respect to [type of development – children with ASD and children with TD] but not [gender – males and females] and [age – three age groups: 5 years and younger; 6 to 15 years and 16 years and older];
2. It is hypothesized that GI symptoms and food allergies/dislikes/diet restrictions will be a significant prediction of insomnia symptoms;
3. It is hypothesized that GI symptoms, food allergies/dislikes/diet restrictions and insomnia symptoms will be a significant prediction of severity of ASD; and
4. It is hypothesized that GI symptoms, food allergies/dislikes/diet restrictions and insomnia symptoms will be a significant prediction of severity of parental stress.

Method

Participants

A convenience and purposive sample of 249 parents of children living in Ireland participated in the study. To ensure geographically varied and representative sampling, participants were sourced via locally established support groups for parents and via network of relatives and family members of individuals who, having gained knowledge of the study, expressed interest to participate.

Overall, 252 responses to on-line questionnaire were received, 179 from parents of children with Autism Spectrum Disorder (ASD) and 68 from parents of children with typical development (TD). 82.2% (n = 202) of the participants who specified their child's nationality (96.8%, n = 239) indicated that their children were Irish nationals and 17.8% (n = 37) that they were of other or multiple nationality, including Irish. One of the respondents did not specify their child's gender and therefore 63.4% (n = 156) of the children were reported males and 36.6% (n = 90) females. Similarly, twenty-five respondents did not indicate their child's age. The children (n = 222) were reported to be between 1.5 and 23 years of age, with an average of 8.7 years old and standard deviation of 4.41. For the purposes of the analysis, children were further divided into three age groups: 5 years and younger (27.9%, n = 62), 6 to 14 years (61.7%, n = 137), and 15 years and older (10.4%, n = 23). the sample was indicated to be geographically representative and included participants from 104 locations across Ireland. 27.1% (n = 67) of children were residents of Dublin.

Design

The study is non-experimental quantitative cross-sectional and correlational between-subjects design with qualitative component three open questions, conducted using on-line

questionnaire. Two groups of participants were identified: parents of children with ASD and parents of children with TD, with ASD diagnosis as inclusion/exclusion criteria.

Variables.

The independent variables (IV) examined in hypotheses 1 are type of child's development, gender and age. Dependent variable (DV) are GI symptoms. The predictor variables (PV) examined in hypotheses 2 are GI symptoms and food allergies/dislikes/diet restrictions, and criterion variable (CV) are insomnia symptoms. In hypothesis 3 and 4 PVs are of GI symptoms, food allergies/dislikes/diet restrictions and severity of insomnia symptoms and CV are severity of ASD and parental stress, respectively.

Materials

The on-line questionnaire prepared for the purposes of the study was a parent self-administered instrument consisting of four measures outlined below and a general information section with six questions regarding child's age, sex, nationality, place of residence and ASD diagnosis.

Childhood Autism Spectrum Test (CAST; Scott, Baron-Cohen, Bolton & Brayne, 2002).

CAST is a parent/caregiver-self completion questionnaire that enquires about various autistic traits. It was designed as an initial screening tool for ASD for use in primary-school-age children from the general population. CAST is a 39-item measure formulated as yes/no statements which includes 31 key items contributing to the total score and 8 control questions on general development. Maximum possible score is 31 with designated screening cut-off point of ≥ 15 for possible ASD or related social-communication difficulties. CAST was reported to have good accuracy for use as a screening test, with high sensitivity of 100%, 97% specificity

(Williams et al., 2005) and moderate test-retest reliability (Allison et al., 2007). In this sample CAST displayed internal consistency of .93.

CHARGE Gastrointestinal History (GIH, Chaidez et al., 2014).

GIH is a self-administrated questionnaire prepared for the purposes of The Childhood Autism Risks from Genetics and the Environment (CHARGE) study. It includes 10 Likert scale items scored never (0), rarely (1), sometimes (2), frequently (3) or always (4) for each of ten GI symptoms which may or may not have occurred in the past three months. Due to an error during questionnaire production one question was omitted from the measure (“difficulty swallowing”) and an internal consistency estimate was conducted to test reliability within the uncomplete scale. In the current sample GIH demonstrated Cronbach’s α of .82 for 9 Likert scale items and the measure was deemed reliable. The scores on GIH range from 0 to 36 and higher score indicate more frequently occurring GI symptoms. GIH also includes four questions formulated as yes/no statements regarding presence of food allergies, diet restrictions, food dislikes and whether any previous GI diagnosis has been given. Furthermore, three open-ended questions asked parents to list food allergies; reasons for food restrictions and what GI condition was diagnosed. One additional open-ended question was included in the questionnaire regarding most frequently occurring food dislikes which parents were requested to list.

Sense and Self-Regulation Checklist (SSC; Silva & Schalock, 2012).

SSC is a parent-caregiver measure of comorbid symptoms of ASD comprising of 65 items within two umbrella domains: sensory and self-regulatory, each further divided into six subdomains. Self-regulatory domain includes appetite-digestion, self-soothing, orienting-attending, aggressive behavior, self-injurious behavior and sleep. For the purposes of the current study four questions from sleep subdomain were used (“has difficulty falling asleep at bedtime”;

“has difficulty falling back asleep when awakens during the night”; “awakens very early and stays awake” and “has difficulty awakening in morning”). Items are scored never (0), rarely (1), sometimes (2) or often (3) and domain scores are obtained by summing the individual items. In the current study “often” was replaced by “frequently” to keep it consistent with GIH measure and additional score of “always” (4) was included for completeness. The scores range from 0 to 16 and higher score indicate more frequently occurring sleep problems. SSC was reported to have acceptable internal consistency for the total score with Cronbach’s α reliability of .58 for ASD group and .55 for TD group in the sleep subdomain. In this sample SSC demonstrated internal consistency of .68 for the four questions used in the questionnaire.

Autism Parenting Stress Index (APSI; Silva & Schalock, 2012).

APSI was developed in conjunction with SSC and is a measure of parenting stress specific to core and co-morbid symptoms of ASD. APSI is a parent-caregiver questionnaire comprising of 13 items ranked and scored from not stressful (0), sometimes creates stress (1), often creates stress (2), very stressful on a daily basis (3), to so stressful that sometimes we feel we cannot cope (5). The scores range from 0 to 65 and higher total score indicate higher overall perceived parental stress. APSI was reported to have acceptable internal consistency for each of ASD and TD population (Silva & Schalock, 2012). In the current sample APSI exhibited internal consistency of .92.

Procedure

An on-line questionnaire using google docs was created in consultation with supervisor. A locally established support groups for parents of children with ASD were approached and the questionnaire was emailed to representatives of those groups for posting to Facebook page or direct provision to the parents via email. In total, 52 ASD support groups were contacted.

Furthermore, 13 Facebook support groups for parents, mainly mothers, of children with ASD and TD were approached, and a browser link to the questionnaire together with information on the study was posted to Facebook pages of those groups. Also, the questionnaire and relevant information was posted on three internet fora including RollerCoaster, Schooldays and Mumstown. Separately, the questionnaire was distributed via network of relatives and family members of individuals known to the researcher who, having gained knowledge of the study and having fulfilled the inclusion criteria for one of the target groups, expressed interest to participate.

Ethical considerations

The participants were informed in advance that the questionnaire is anonymous, confidential and will take approximately 10-15 minutes to complete. They were further informed of the aims of the study and the relevant two target groups: parents of children with ASD and parents of children with TD. The questionnaire coversheet provided additional information regarding voluntary participation and right to withdrawal prior to submission of the questionnaire. Contact information of the researcher and the supervisor were also provided, both on the cover and final page of the questionnaire (see Appendix for Coversheet and Full Questionnaire). Moreover, final page included information regarding supporting services available to participants in instance when they experienced difficult feelings while completing the questionnaire or stress in relation to ASD diagnosis. The study was approved by DBS Ethics Committee.

Results

The aim of the study was to identify differences in occurrence of gastrointestinal (GI) abnormalities for children with Autism Spectrum Disorder (ASD) and children with typical development (TD) as well the most commonly occurring GI symptoms and food allergies/dislikes/diet restrictions for both groups of children. The study further examined relationships between severity of these problems and severity of ASD, insomnia symptoms and parental stress.

An on-line questionnaire was distributed to the potential participants and 252 responses were received. Five responses were excluded from the analysis for the following reasons: one of the respondent did not meet the minimum age requirement of 18 years, two respondents did not indicate whether their child was diagnosed with ASD, and two respondents indicated that their child's place of residence is outside Ireland. The final study population therefore consisted of 247 children, 179 with ASD diagnosis and 68 not diagnosed with this condition.

All participants completed four measures included in the questionnaire, namely Childhood Autism Spectrum Test (CAST), CHARGE Gastrointestinal History (GIH), four questions from Sense and Self-Regulation Checklist (SSC) and Autism Parenting Stress Index (APSI). A small number of responses from each measure were missing. Results for both groups of children based on type of developments are presented in Table 1.

Table 1: *Mean, standard deviations (SD) and scoring range of severity of ASD (CAST), GI symptoms (GIH), insomnia symptoms (SSC) and parental stress (APSI) for children with ASD and children with TD*

Variables	Children with ASD			Children with TD			
	Mean	SD	Score range	Mean	SD	Score range	Score range
Severity of ASD	21.21	4.35	7-31	5.8	6.5	0-25	0-31
GI symptoms	12.43	5.85	0-28	6.31	5.42	0-22	0-36
Insomnia symptoms	8.89	3.26	0-15	4.17	3.06	0-12	0-16
Parental stress	22.93	10.78	4-65	6.38	8.47	0-37	0-65

Results indicate that children with ASD are twice more likely to have GI symptoms and insomnia symptoms. Their parents are three times more likely to experience stress arising from parenting. For severity of ASD, which in the study was measured based on score obtained on CAST (higher score equals greater severity of ASD), ASD related symptoms are five times more frequent for children diagnosed with this condition than children with TD.

Analysis of GI symptoms from parent report

Frequency of occurrence of GI symptoms in the last three months across both groups of children was analysed. An approach previously adopted for similar analysis by Chaidez et al (2014) was also used in this study whereby items on GIH were dichotomized into symptoms which occur with “low” (items “never”, “rarely” and “sometimes”) and “high” frequency (items “frequently” and “always”). Results for low and high frequency of GI symptoms are presented in Table 2.

Table 2: *Frequency of occurrence of GI symptoms for children with ASD and children with TD*

GI symptoms	Children with ASD				Children with TD			
	Low frequency		High frequency		Low frequency		High frequency	
	N	%	N	%	N	%	N	%
Abdominal pain	117	65.4%	62	34.6	52	76.4	16	23.5
Gaseousness/Bloating ^a	118	66.3	60	33.7	60	88.2	8	11.7
Diarrhea ^b	143	79.9	36	20.1	63	94	4	6
Constipation ^a	101	57	76	42.9	62	91.2	6	8.8
Pain on stooling ^a	133	75.6	43	24.4	62	91.2	6	8.9
Vomiting ^a	164	92.7	13	7.3	67	98.5	1	1.5
Sensitivity to food	100	55.8	79	41.4	62	91.1	6	8.9
Blood in stool	177	98.9	2	1.1	68	100	0	0
Blood in vomit	179	100	0	0	68	100	0	0

^aMissing data for children with ASD

^bMissing data for children with TD

Results show that children with ASD are far more likely to have frequent GI symptoms than children with TD. Parent report for all GI symptoms, apart from blood in stool and blood in vomit, was significantly higher for children with ASD. The most commonly occurring GI symptoms regardless of type of development were abdominal pain, gaseousness/bloating, constipation, sensitivity to food and pain on stooling.

Analysis of food allergies/dislikes/diet restrictions from parent report

Both parents of children with ASD and children with TD reported presence of food allergies, dislikes and diet restrictions, and results are presented in Table 3.

Table 3: *Frequency of occurrence of food allergies, dislikes and diet restrictions for children with ASD and children with TD*

Diet related issues	Children with ASD		Children with TD	
	N	%	N	%
Food allergies ^a	34	19.3	9	13.2
Food restrictions ^a	63	35.4	9	13.2
Food dislikes	149	83.2	40	58.8

^aMissing data for children with ASD

Results show that children with ASD are three times more likely to have food allergies, dislikes and diet restrictions. Parent report indicate that the most frequently occurring food allergies and reasons for restrictions for children with TD are gluten, dairy and nut intolerance. Food dislikes include vegetables, mushrooms, fruit and meat. Similarly, parents of children with ASD list gluten, dairy and egg intolerance as main food allergies and reasons for restrictions. However, although they report dislike to vegetables, fruit and meat, majority of parents indicate that their child's diet is very restrictive with some children eating only a few products.

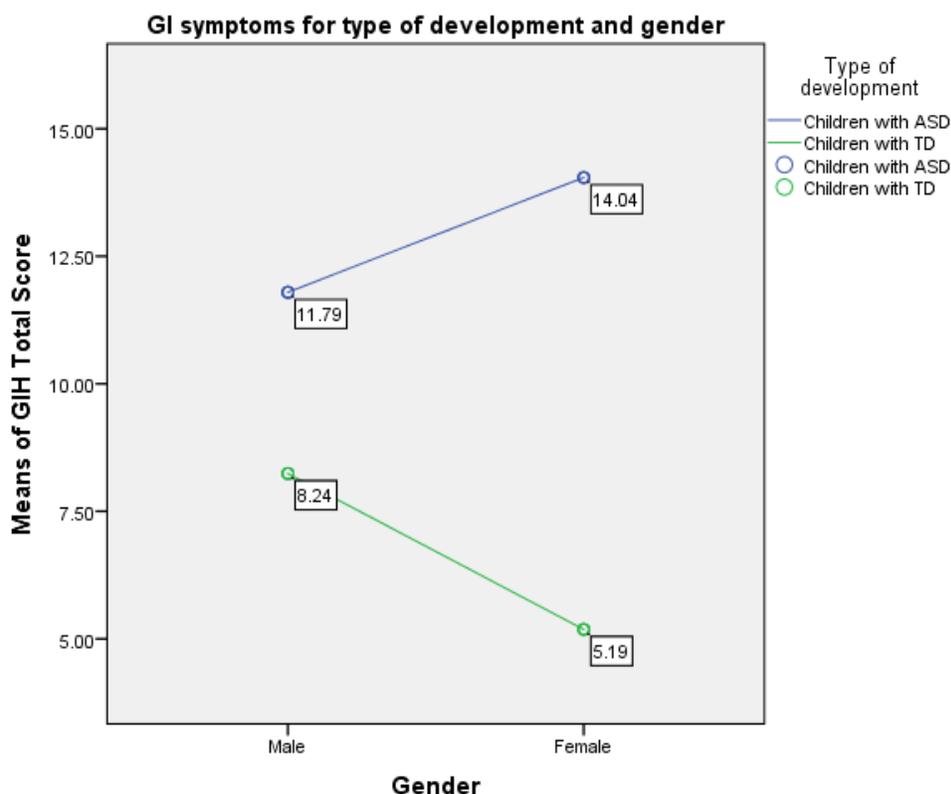
Analysis of Difference

Differences in level of GI symptoms for children with ASD and children with TD were analysed with respect to type of development, gender and age.

Difference in GI symptoms for type of development and gender.

A two-way-between groups ANOVA examined the role of type of development and gender on level of GI symptoms and found a significant interaction effect ($F(1, 242) = 9.63, p = .002$). A significant main effect was also reported for type of development effect ($F(1, 242) = 52.74, p < 0.001$) with a medium effect size (.18). No significant main effect was reported for gender ($F(1, 242) = .22, p = .638$).

Figure 1: *Difference in GI symptoms for type of development and gender*



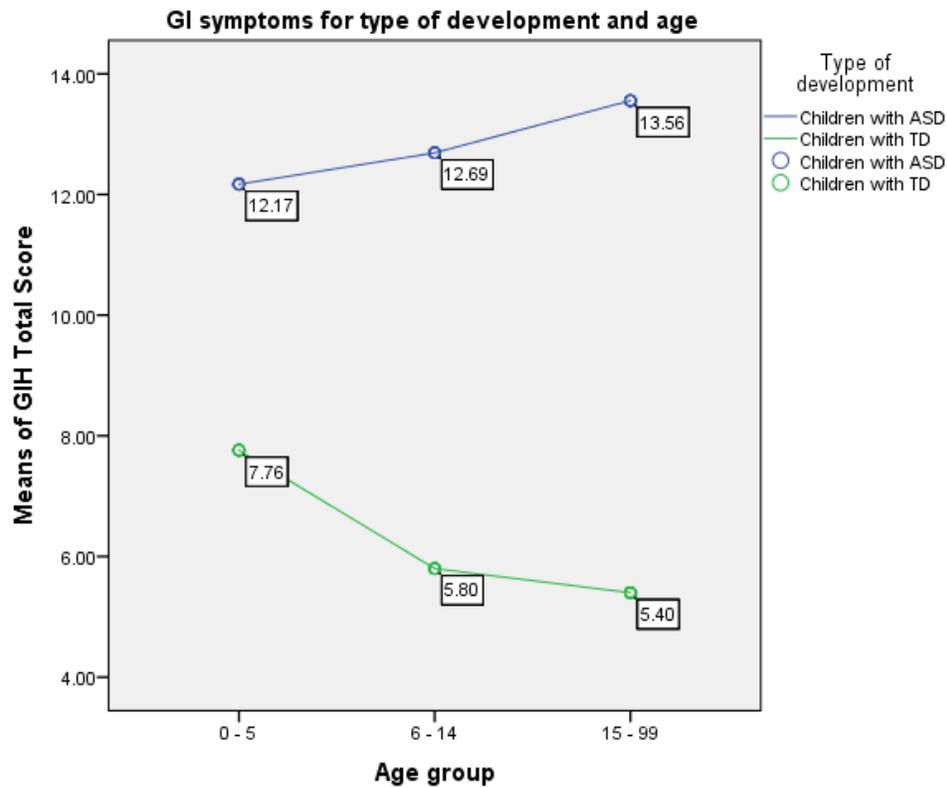
Furthermore, level of GI symptoms was indicated to be higher for females than males with ASD. On the contrary, level of GI symptoms was reported to be higher for males than females with TD. Gender as a single variable had no effect on level of GI symptoms.

Difference in GI symptoms for type of development and age.

A two-way-between groups ANOVA examined the role of type of development and age groups on level of GI symptoms and found no significant interaction effect ($F(2, 216) = 1.1, p = .338$). However, a main significant effect was reported for type of development effect ($F(2, 216) = 31.23, p < 0.001$) with a medium effect size (.13). No main significant effects were reported for age groups ($F(2, 216) = .29, p = .749$). Post hoc analysis confirmed that there were no significant

differences between the 5 years and younger group, 6 to 15 years group and 16 years and older group.

Figure 2: *Difference in GI symptoms for type of development and age*



Specifically, level of GI symptoms was indicated to have raising tendency across all age groups for children with ASD and decreasing tendency for children with TD. Age group membership as a single variable had no effect on level of GI symptoms. Thus, Hypothesis one was supported.

Analysis of Variance

GI symptoms and food allergies/dislikes/diet restrictions as predictors of insomnia symptoms.

Multiple regression was used to test whether GI symptoms and food allergies/dislikes/diet restrictions were predictors of insomnia symptoms. The results of the regression indicated that two predictors explained 31% of the variance ($R^2 = .31$, $F(2, 244) = 56.75$, $p < 0.001$). It was found that GI symptoms significantly predicted insomnia symptoms ($\beta = .49$, $p < 0.001$, 95% CI = .23 - .37) as did food allergies/dislikes/diet restrictions ($\beta = .14$, $p = .012$, 95% CI = .14 - 1.13). A strong and positive relationship suggest that severity (higher levels of occurrence) of GI symptoms correlate with severity of insomnia symptoms regardless of type of development. Moreover, a weak and positive relationship between food allergies/dislikes/diet restrictions and insomnia symptoms suggests a link between both whereby greater problems with food allergies result in a slightly greater risk of more severe levels of insomnia. Thus, hypothesis two seemed to be supported.

However, further multiple regression was performed to test how GI symptoms and food allergies/dislikes/diet restrictions predicted insomnia symptoms based on type of development. Results for children with ASD and children with TD are presented in table 4.

Table 4: *An analysis of variance values of a multiple regression for GI symptoms and food allergies as predictors of insomnia symptoms based on type of development*

Variables	Type of development	Unstandardised Coefficients		Standardised Coefficients		
		B	Std. Error	Beta β	t	p
GI symptoms	Children with ASD	.183	.040	.328	4.541	.000*
	Children with TD	.308	.063	.544	4.872	.000*
Food allergies	Children with ASD	.358	.280	.092	1.279	.203
	Children with TD	.437	.410	.119	1.064	.291

Note: * p significant at .05 level

Dependent Variable: Insomnia symptoms

Children with ASD: $R^2 = .130$, R^2 Adjusted = .120; $F = 13.142$

Children with TD: $R^2 = .372$, R^2 Adjusted = .353; $F = 19.274$

Interestingly, the results of regression indicated that both predictors together explained 12% of the variance for children with ASD ($R^2 = .13$, $F(2, 176) = 13.14$, $p < 0.001$) and 35% for children with TD ($R^2 = .37$, $F(2, 65) = 19.23$, $p < 0.001$), but only GI symptoms significantly predicted insomnia symptoms. A stronger positive relationship was found for children with TD than children with ASD, suggesting that severity of GI symptoms is a better predictor of severity of insomnia symptoms for this type of development. Those results require further investigation.

GI symptoms, food allergies/dislikes/diet restrictions and insomnia symptoms as predictors of severity of ASD.

Multiple regression was undertaken to test whether GI symptoms, insomnia symptoms, food allergies/dislikes/diet restrictions were predictors of insomnia symptoms. The results of the regression indicated that three predictors explained 42% of the variance ($R^2 = .42$, $F(3, 243) = 59.87$, $p < 0.001$). It was found that GI symptoms significantly predicted severity of ASD ($\beta = .17$, $p = .006$, 95% CI = .06 - .37) as did insomnia symptoms ($\beta = .47$, $p < 0.001$, 95% CI = .78 - 1.29) and food allergies/dislikes/diet restrictions ($\beta = .15$, $p = .005$, 95% CI = .42 - 2.4). A strong

and positive relationship between (higher levels of occurrence) of insomnia symptoms and severity of ASD and a weak and positive correlation of the latter with GI symptoms and food allergies/dislikes/diet restrictions indicate that greater insomnia symptoms, GI symptoms and food allergies result in a higher level of ASD severity. Thus, hypothesis three was supported.

GI symptoms, food allergies/dislikes/diet restrictions and insomnia symptoms as predictors of parental stress.

Multiple regression was performed to test whether GI symptoms, insomnia symptoms, food allergies/dislikes/diet restrictions were predictors of parental stress regardless of type of development. The results of the regression indicated that three predictors explained 55% of the variance ($R^2 = .55$, $F(3, 243) = 101.82$, $p < 0.001$). It was found that GI symptoms significantly predicted parental stress ($\beta = .24$, $p < 0.001$, 95% CI = .28 – .69) as did insomnia symptoms ($\beta = .54$, $p < 0.001$, 95% CI = 1.45 – 2.12) and food allergies/dislikes/diet restrictions ($\beta = .09$, $p = .049$, 95% CI = .01 – 2.66). This again indicate that insomnia symptoms are the strongest predictor among variables regardless of type of development, and that greater sleep problems correlate with higher levels of parental stress. A moderate and positive relationship for GI symptoms and a weak and positive relationship for food allergies/dislikes/diet restrictions also suggest that both can be linked to elevated levels of parental stress. Thus, hypothesis four was supported.

Further multiple regression was performed to test how GI symptoms, food allergies/dislikes/diet restrictions and insomnia symptoms predicted parental stress based on type of development. Results for children with ASD and children with TD are presented in table 5.

Table 5: An analysis of variance values of a multiple regression for GI symptoms, insomnia symptoms and food allergies/dislikes/diet restrictions as predictors of parental stress based on type of development

Variables	Type of development	Unstandardised Coefficients		Standardised Coefficients		p
		B	Std. Error	Beta β	t	
GI symptoms	Children with ASD	.368	.120	.199	3.059	.003*
	Children with TD	.659	.185	.421	3.553	.001*
Food allergies	Children with ASD	1.799	.794	.140	2.265	.025*
	Children with TD	-1.090	1.041	-.107	-1.047	.299
Insomnia symptoms	Children with ASD	1.524	.213	.460	7.155	.000*
	Children with TD	1.139	.312	.411	3.652	.001*

Note: * p significant at .05 level

Dependent Variable: Parental stress

Children with ASD: $R^2 = .370$, R^2 Adjusted = .359; $F = 34.220$

Children with TD: $R^2 = .490$, R^2 Adjusted = .466; $F = 20.516$

The results of regression indicated that all predictors together explained 36% of the variance for children with ASD ($R^2 = .36$, $F(3, 175) = 34.22$, $p < 0.001$) and 47% for children with TD ($R^2 = .47$, $F(3, 64) = 20.52$, $p < 0.001$). Food allergies/dislikes/diet restrictions significantly predicted parental stress only for children with ASD and overall are the weakest predictor across all relationships reported in this research. A strong positive relationship between GI symptoms and parental stress was found for children with TD and a weak positive one for children with ASD. Furthermore, insomnia symptoms strongly and positively correlate with parental stress for both groups of children, indicating that sleep problems are the best predictor of parental stress regardless of type of development. Thus, hypothesis four was further supported for GI symptoms and insomnia symptoms, but not for food allergies/dislikes/diet restrictions.

Discussion

The aim of the study was to identify differences in occurrence of gastrointestinal (GI) abnormalities for children with Autism Spectrum Disorder (ASD) and children with typical development (TD) as well the most commonly occurring GI symptoms and food allergies, dislikes and diet restrictions for both groups of children. The study further examined relationships between severity of these problems and severity of ASD, insomnia symptoms and parental stress. Four hypotheses were formulated to address the above-mentioned aims. Several multiple regressions and analysis of variance were performed to test the assumptions of the study. Furthermore, analysis of parent reports of the most frequently occurring GI symptoms and three open questions with regards to food allergies, dislikes and diet restrictions provided insight into nature and scale of both problems for ASD and TD type of development.

Difference in GI symptoms for type of development, gender and age

The research hypothesis expected that there will be a significant difference in level of GI symptoms depending on type of development, but not on gender and age. The hypothesis was supported in line with previous research which indicate that frequency of occurrence of GI symptoms for children with ASD is higher than for children with TD (Kohane et al., 2012; Chaidez et al., 2014; Bresnahan et al., 2015; Parracho et al., 2005). Court et al. (2012) conducted analysis of the relevant studies undertaken prior to 2012 and reported that prevalence of GI disorders in children with ASD ranges from 9% to 91%. They further observed that the results indicate unusually high rates of GI symptoms for this type of development. To date only a few studies have been conducted where a control population of children with TD was employed alongside children with ASD, and none in the Irish setting. The current study addressed this gap in research.

Parent report of most frequently occurring GI symptoms indicated abdominal pain, gaseousness/bloating, constipation, sensitivity to food and pain on stooling among those most prevalent regardless of type of development. Children with ASD were reported to have far more frequent GI symptoms than children with TD which is consistent with majority of the previous studies (Chaidez et al., 2014; McElhanon et al., 2014; Valicenti-McDermott, 2006). Also, from Irish perspective, Mannion et al. (2014) found that abdominal pain, constipation and bloating were frequently experienced by children with ASD and those findings were confirmed by the present study. However, it is important to note that some studies reported similar levels of GI symptoms occurrence for both types of development (Ibrahim et al., 2009; Black, Kaye & Jick, 2002), which may be attributed to small sample sizes or inconsistent methodological approaches. Chaidez et al., 2014 further points out that in absence of standardized definition of GI symptoms, it is difficult to make comparisons across studies.

Results of current research indicate that both gender and age as individual variables have no effect on level of GI symptoms. Similar findings were reported by Kohane et al. (2012) who conducted a study based on electronic health records of 14,000 individuals with ASD across four hospitals in U.S.A. and Molloy and Manning-Courtney (2003). Both concluded that frequency of GI symptoms did not vary by age. Furthermore, Williams et al. (2010) found that presence of GI problems did not differ by gender. However, research in this area is limited and majority of studies employ small number of participants and/or focus only on children with ASD with no comparative data available for children with TD. Overall, in the current sample, hypothesis one was confirmed for all three independent variables: type of development, age and gender.

GI symptoms and food allergies/dislikes/diet restrictions as predictors of insomnia symptoms

The second research hypothesis predicted that GI symptoms and food allergies/dislikes/diet restrictions will be a significant prediction of insomnia symptoms. A strong and positive relationship was found between GI symptoms and insomnia symptoms regardless of type of development. Interestingly, GI symptoms are reported to be strongly correlated with insomnia symptoms for children with TD and moderately for children with ASD. This may be presumably attributed to the small sample of children with TD or to more clear-cut and apparent relationship between both disorders when assessed by parents. Previous studies provided similar evidence with respect to GI symptoms (Klukowski et al., 2015; Hollway et al., 2013; Mannion and Leader, 2013). Food allergies/dislikes/diet restrictions were correlated with insomnia symptoms only for the entire sample and not for different types of development. No studies addressing food allergies-insomnia relationship with respect to children with ASD and TD are currently available. It was determined that hypothesis two was partially supported.

GI symptoms, food allergies/dislikes/diet restrictions and insomnia symptoms as predictors of severity of ASD

The third research hypothesis presumed that GI symptoms, food allergies/dislikes/diet restrictions and insomnia symptoms will significantly predict severity of ASD. In the current study insomnia symptoms are indicated to have the strongest impact on same. A positive relationship was observed whereby more frequent occurrence of insomnia symptoms results in greater manifestation of ASD symptoms. Also, food allergies/dislikes/diet restrictions significantly predicted severity of ASD, but the correlation was weak. For GI symptoms, similar findings have been previously reported by Esbensen & Schwichtenberg (2016) and Hollway and Aman who indicated that sleep abnormalities were significantly associated with developmental

disorders (as cited in Mannion and Leader, 2014). Again, no studies are currently available with respect to food allergies. To sum up, hypothesis three was supported.

GI symptoms, food allergies/dislikes/diet restrictions and insomnia symptoms as predictors of parental stress

Finally, the fourth research hypothesis stated that GI symptoms, food allergies/dislikes/diet restrictions and insomnia symptoms will significantly predict severity of parental stress. As expected, the hypothesis was confirmed in line with previous research (Dykes, 2015; Mancil, 2009; Bonis, 2016). In addition, insomnia symptoms are indicated to have the strongest impact on parental stress regardless of type of development. A positive relationship was observed between insomnia symptoms and GI symptoms whereby greater sleep and GI problems correlate with higher levels of parental stress. Interestingly, food allergies/dislikes/diet restrictions were correlated with stress only for the entire sample and children with ASD, and no result was observed for TD sample alone. Overall, this variable significantly predicted all tested relationships only when measured alongside other variables.

For severity of ASD, Rivard et al. (2014) and Soltanifar et al. (2015) reported that it was correlated only with paternal stress and McStay et al. (2013) that autism severity was not significantly related to parenting stress. It is presumed that in the current research parent report of ASD-related symptoms and comorbidities was provided by mothers, and therefore the findings contradict the above findings. However, they may support findings of Hickson (2013) who reported that autism severity was significantly correlated with parenting stress for both parents of children with ASD. Nonetheless, hypothesis four was deemed to be partially supported.

Strengths of the study

Given the raising prevalence of neurodevelopmental disorders and ASD, the present study addresses a very current and future-focused issue. A large, geographically and demographically varied sample of children with ASD offers a good insight into hypothesized relationships between GI symptoms, sleep symptoms, severity of ASD and parental stress. It supports and substitutes other studies conducted in Irish setting and provides guidance for future line of research. It contributed, and is expected to further contribute, to raising awareness of prevalence and role of GI symptoms in ASD in the general public. Many members of the support groups who were approached in connection with the research, regardless of type of development, expressed interest in broadening their knowledge in this area and are awaiting to receive the final findings.

Limitations of the study and recommendations for future research

The study presents some limitations. First, sample of children with TD was smaller than children with ASD. Although assumptions for Cohen's effect size were met, it may be deemed insufficient to observe relationships representative of the general population. Second, although the used instruments have good reliability, they were self-report measures and therefore subjective in nature and prone to biases. Third, it is presumed that in most cases the questionnaire was completed by mothers since mainly mother's support groups were targeted. Fourth, the study employed only cross-sectional data and as such, did not examine the variables over time. Fifth, CAST measure was designed for high-functioning ASD and GIH measure may be suitable mainly for verbal children with ASD. It does not seem to relate explicitly to non-verbally expressed abdominal behaviors. Finally, only very limited data with regards to diet have been collected and it was not possible to examine if diet quality and quantity plays a role in

prevalence of GI symptoms. As observed by Wasilewska and Klukowski (2015), the gut ecosystem closely reflects diet quality and as result of food selectivity, children with ASD may not meet dietary allowances for many nutrients.

Future recommended line of research mainly arises from the above-mentioned limitations. It would be desirable to conduct similar study with bigger sample of children with TD, with measures better suited for full ASD spectrum and distributed to fathers to determine differences in perceived severity of ASD-related symptoms and parental stress. Finally, a future comprehensive study would be recommended to address dietary habits of both children with ASD and their mothers in pre- and post-natal period to determine impact on nutrition on gut microbiota, gut functioning and as result, on ASD-associated behaviors.

Conclusion

The present study addressed certain aspect attributable to a neurodevelopmental disorder of the future, Autism Spectrum Disorder (ASD). Prevalence and relationships between gastrointestinal symptoms (GI), food allergies and dislikes, sleep symptoms and parental stress were studied in conjunction with ASD severity. Current results indicate that all variables are interrelated with different magnitude. Sleep problems are reported to have the strongest impact on ASD severity and parental stress regardless of type of development. In turn, GI symptoms were determined to be the stronger predictor of insomnia symptoms. Although underlying mechanisms associated with ASD and GI disorders are yet to be determined, the present study provides evidence that exploration of relationships between both may contribute to understanding of basic principles and complex nuances of their, presumably, epigenetic origin.

Appendix

Gastrointestinal Abnormalities in Children with Autism Spectrum Disorder and Typical Development. An Irish Perspective

Dear Participant,

Thank you for considering taking part in the study.

My name is Anna Lezanska-Toma and I am a final year student in the Department of Psychology at Dublin Business School. I am conducting research that explores relationship between occurrence of gastrointestinal problems for children with autism spectrum disorder and children with typical development as well as relationship between severity of these problems and severity of autism. This research is being conducted as part of a Higher Diploma in Psychology and will be submitted for examination.

You are invited to take part in this study and participation involves completing and returning the attached anonymous survey. While the survey asks some questions that might cause some minor negative feelings, it has been used widely in research. If any of the questions do raise difficult feelings for you, contact information for support services are included on the final page.

Participation is completely voluntary and so you are not obliged to take part. Participants have the right to withdraw from the study at any time for whatever reason before the questionnaire is submitted.

Participation is anonymous and confidential. Thus, responses cannot be attributed to any one participant. For this reason, it will not be possible to withdraw from participation after the questionnaire has been submitted.

Your responses and data will be kept strictly confidential, and the data from the questionnaire will be securely stored on a password protected computer. Findings from this study will be published in a thesis and may be presented at conferences and submitted for publication in peer-reviewed journals. However, no participants will be identifiable in any publication or presentation.

It is important that you understand that by completing and submitting the questionnaire that you are consenting to participate in the study.

Should you require any further information about the research or would like to obtain details of the results, please contact Anna Lezanska-Toma, [REDACTED]. My supervisor Dr. Garry Prentice can be contacted at [REDACTED].

Thank you for taking the time to complete this survey.

1. General Questions

Child's Age:

Child' Sex: Male / Female

Nationality

Place of residence (town/village)

Was Child diagnosed with ASD Yes / No

If Yes, when was child assessed

2. The Childhood Autism Spectrum Test (CAST)

Please read the following questions carefully, and circle the appropriate answer. All responses are confidential.

- | | | |
|--|-----|----|
| 1. Does s/he join in playing games with other children easily? | Yes | No |
| 2. Does s/he come up to you spontaneously for a chat? | Yes | No |
| 3. Was s/he speaking by 2 years old? | Yes | No |
| 4. Does s/he enjoy sports? | Yes | No |
| 5. Is it important to him/her to fit in with the peer group? | Yes | No |
| 6. Does s/he appear to notice unusual details that others miss? | Yes | No |
| 7. Does s/he tend to take things literally? | Yes | No |
| 8. When s/he was 3 years old, did s/he spend a lot of time pretending (e.g., play-acting being a superhero, or holding teddy's tea parties)? | Yes | No |
| 9. Does s/he like to do things over and over again, in the same way all the time? | Yes | No |
| 10. Does s/he find it easy to interact with other children? | Yes | No |
| 11. Can s/he keep a two-way conversation going? | Yes | No |

- | | | |
|---|-----|----|
| 12. Can s/he read appropriately for his/her age? | Yes | No |
| 13. Does s/he mostly have the same interests as his/her peers? | Yes | No |
| 14. Does s/he have an interest which takes up so much time that s/he does little else? | Yes | No |
| 15. Does s/he have friends, rather than just acquaintances? | Yes | No |
| 16. Does s/he often bring you things s/he is interested in to show you? | Yes | No |
| 17. Does s/he enjoy joking around? | Yes | No |
| 18. Does s/he have difficulty understanding the rules for polite behaviour? | Yes | No |
| 19. Does s/he appear to have an unusual memory for details? | Yes | No |
| 20. Is his/her voice unusual (e.g., overly adult, flat, or very monotonous)? | Yes | No |
| 21. Are people important to him/her? | Yes | No |
| 22. Can s/he dress him/herself? | Yes | No |
| 23. Is s/he good at turn-taking in conversation? | Yes | No |

- | | | |
|---|-----|----|
| 24. Does s/he play imaginatively with other children, and engage in role-play? | Yes | No |
| 25. Does s/he often do or say things that are tactless or socially inappropriate? | Yes | No |
| 26. Can s/he count to 50 without leaving out any numbers? | Yes | No |
| 27. Does s/he make normal eye-contact? | Yes | No |
| 28. Does s/he have any unusual and repetitive movements? | Yes | No |
| 29. Is his/her social behaviour very one-sided and always on his/her own terms? | Yes | No |
| 30. Does s/he sometimes say “you” or “s/he” when s/he means “I”? | Yes | No |
| 31. Does s/he prefer imaginative activities such as play-acting or story-telling, rather than numbers or lists of facts? | Yes | No |
| 32. Does s/he sometimes lose the listener because of not explaining what s/he is talking about? | Yes | No |
| 33. Can s/he ride a bicycle (even if with stabilisers)? | Yes | No |
| 34. Does s/he try to impose routines on him/herself, or on others, in such a way that it causes problems? | Yes | No |

- | | | |
|--|-----|----|
| 35. Does s/he care how s/he is perceived by the rest of the group? | Yes | No |
| 36. Does s/he often turn conversations to his/her favourite subject rather than following what the other person wants to talk about? | Yes | No |
| 37. Does s/he have odd or unusual phrases? | Yes | No |

SPECIAL NEEDS SECTION

Please complete as appropriate

- | | | |
|--|-----|----|
| 38. Have teachers/health visitors ever expressed any concerns about his/her development? | Yes | No |
|--|-----|----|

If Yes, please specify.....

- | | | |
|---|-----|----|
| 39. Has s/he ever been diagnosed with any of the following? | | |
| Language delay | Yes | No |
| Hyperactivity/Attention Deficit Disorder (ADHD) | Yes | No |
| Hearing or visual difficulties | Yes | No |
| Autism Spectrum Condition, incl. Asperger's Syndrome | Yes | No |
| A physical disability | Yes | No |

Other (please specify)

Yes

No

3. CHARGE Gastrointestinal History (GIH)

A. Please read the following questions carefully and place an X in the appropriate box.

In the last three months how often did your child experienced the following:

	Never	Rarely	Sometimes	Frequently	Always
Abdominal pain					
Gaseousness/Bloating					
Diarrhea					
Constipation					
Pain on stooling					
Vomiting					
Sensitivity to food					
Blood in stool					
Blood in vomit					

B. Please circle the response that most accurately describes your child:

- A. Does your child has any food allergies Yes / No
- B. Does your child has any diet restrictions Yes / No
- C. Does your child has any food dislikes Yes / No
- D. Has any gastrointestinal diagnosis been given to your child Yes / No

C. Please list the following, if applicable to your child:

- A. Food allergies
- B. Reasons for diet/food restrictions
- C. Reasons for food dislikes
- D. What gastrointestinal condition was diagnosed

4. Sleep pattern disturbance

Please read the following questions carefully and place an X in the appropriate box.

In the last three months how often did your child experienced the following:

	Never	Rarely	Sometimes	Frequently	Always
Difficulty falling asleep at bedtime					
Difficulty falling back asleep when awakened during the night					
Awakened very early and stayed awake					
Difficulty awakening in morning					

5. Autism Parenting Stress Index (APSI)

Please rate the following aspects of your child's health according to how much stress it causes you and/or your family by placing an X in the box that best describes your situation

Stress Ratings					
	Not stressful	Sometimes creates stress	Often creates stress	Very stressful on a daily basis	So stressful sometimes we feel we can't cope
Your child's social development					
Your child's ability to communicate					
Tantrums/meltdowns					
Aggressive behavior (siblings, peers)					
Self-injurious behavior					
Difficulty making transitions from one activity to another					
Sleep problems					
Your child's diet					
Bowel problems (diarrhea, constipation)					
Potty training					
Not feeling close to your child					
Concern for the future of your child being accepted by others					
Concern for the future of your child living independently					

Thank you for taking the time to complete this survey.

If any of the questions have raised difficult feelings for you, or if you are experiencing stress in relation to autism spectrum disorder diagnosis, the following support services can be contacted:

- Carecall: www.carecallwellbeing.ie
- The Samaritans: www.samaritans.org
- My Mind: www.mymind.org
- Aware: www.aware.ie

Should you require any further information regarding the research, please do not hesitate to contact Anna Lezanska-Toma at the following email address: [REDACTED].

My supervisor Garry Prentice can be contacted at [REDACTED].

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