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Health Condition in Persons with Autism Spectrum Disorders

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Abstract

Introduction: Autism Spectrum Disorders (ASD) are behaviourally defined syndromes where the etiology and pathophysiology are not very well understood. If the child has been diagnosed with autism, parents already face special behavioural challenges. What makes ASD even more difficult, are the many other medical health issues that often arise in this population.

The **purpose** of this article is to summarise the latest understanding of autism's commonly associated physical and mental health conditions.

Methods: An analysis of relevant literature, sources from the internet and published literature, personal experience and observations of the author.

Recent findings: Autism is a disorder of the whole body. It is often in co-morbidity with: epilepsy, gastrointestinal disorders, neuro-inflammation and immunological disorders, asthma, eczema, sleep disturbances, eating and feeding disorders, food allergies, attention deficit and hyperactivity disorder (ADHD), headaches, anxiety disorders, bipolar disorder, depression, schizophrenia, obsessive-compulsive disorder, Fragile X syndrome, intellectual disability, nonverbal learning disorder, motor clumsiness, Tourette syndrome, sensory problems, tuberous sclerosis, oxidative stress, acquired mitochondrial dysfunction and metabolic abnormalities. Many of the issues outlined here can overlap each other.

Conclusions: Improved understanding of the underlying pathology of ASD and associated conditions, and the development of a common purpose across multiple treating sites, can improve the consistent and coordinated healthcare of children with autism. There is need for the development of improved strategies for delivering effective health education and healthcare to this large population. Improving the ability of these persons to lead relatively independent lives has a great economic impact.

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Introduction

Autism Spectrum Disorders (ASD) are a heterogeneous group of complex neurodevelopmental conditions apparent in early childhood, characterised by persistent deficits in social communication and social interaction and restricted, repetitive patterns of behaviour, interests or activities (APA, 2013). Autism is not a disease, but it is a disorder which affects the immature, developing brain. It is obvious, that for many people, autism is a whole-body disorder. Its frequent co-morbidities include gastrointestinal disorders, seizures. sleep disturbances, eating and feeding challenges, attention deficit and hyperactivity disorder (ADHD), anxiety, depression, schizophrenia and bipolar disorder (Croen, 2015). Various markers of abnormal brain development (e.g. minor and major congenital anomalies) and risk factors for brain damage (e.g. pregnancy and birth complications) were also described in the literature. Parallel developments in medical diagnostics have also lead to improvements in the detection and diagnosis of medical conditions, so the prevalence of these conditions in individuals with ASD has also increased (Bolton, 2009). Genetic research is delving into the biological causes of autism-associated health conditions. This is part of a new avenue of autism research aimed at identifying the many biological subtypes of autism and developing personalised treatments and supports (Autism Speaks, 2017).

The prevalence of ASD has been rising as the definition has evolved and awareness has increased. The most recent estimate suggests that 1 in 68 children in the United States are on the autism spectrum and that number increases in boys to 1 in 42 (CDC, 2016). To date, however, very little is known about ASD in adults, including their health status and healthcare needs (Mandell, 2013). Autism is relatively difficult to diagnose especially in developing countries. In the Republic of Macedonia, no services exist for adults with ASD. Based on the incidence of autism, there is an increased likelihood that healthcare providers will have children with autism in their practice. Current research estimates that a full-time pediatrician will have at least 20 to 25 patients on the autism spectrum (Carbone, 2013).

Comorbid conditions may be markers for underlying pathophysiology and request a more varied treatment approach. Developmental, psychiatric, and neurologic disorders frequently co-occur in children with autism spectrum disorders and may have a significant impact on the identification, treatment needs, functional status, and progress of children with ASD (Gillberg & Billstedt, 2000).

In one study which examines the prevalence of co-occurring conditions across multiple organ systems among a large sample of adults with ASD, Kohane et al. reported a higher prevalence of epilepsy, schizophrenia, inflammatory bowel disease, central nervous system (CNS)/cranial anomalies, diabetes mellitus type I, muscular dystrophy, and sleep disorders among autism cases compared to controls. This study population was restricted to young adults <35 years of age. They found: 19.44% of ASD patients had epilepsy as compared to 2.19% in the overall hospital population, 2.43% of ASD with schizophrenia vs. 0.24% in the hospital population, inflammatory bowel disease (IBD) 0.83% vs. 0.54%, bowel disorders (without IBD) 11.74% vs. 4.5%, CNS/cranial anomalies 12.45% vs. 1.19%, diabetes mellitus type I (DM1) 0.79% vs. 0.34%, muscular dystrophy 0.47% vs 0.05%, sleep disorders 1.12% vs. 0.14% (Kohane et al., 2012).

The functional status of adults with ASD also remains poorly understood. In general, adaptive functioning in adults with neurodevelopmental disorders declines with advancing age in different ways from the general population, but this has not been examined in adults with ASD (Sullivan et al., 2011). Many adults with ASD develop new skills with age that allow them to thrive independently throughout life. Others require more supportive environments. Examining functional status is critical towards improving adaptive functioning and supporting independence for different cohorts of adults with ASD. Kogan et al. found that children with ASD had more difficulties accessing necessary care and had more unmet needs than other children with special healthcare needs. They also noted greater problems related to employment and family financial concerns. The documented increase in healthcare expenses, gaps in treatment, and effects on family well-being call for more attention to the major medical concerns of children with ASD (Kogan et al., 2008).

The **purpose** of this article is to summarise the latest understanding of autism's commonly associated physical and mental health conditions.

Methods

A search of the two electronic data bases PubMed and Google Scholar was performed in order to identify published papers from the field of health condition and autism from September 10th until October 12th 2018. The following keyword descriptors were used in combination: "health condition" and "autism", or "medical and "autism", or "co-morbid condition" disorders" and "autism". The search was systematically conducted on journal articles in academic peer-reviewed journals and was not limited by year. A total number of 94 articles were selected for analysis from which 33 were in the Google Scholar database and 61 were in the PubMed database. From this 47 articles (50%) have been cited as relevant literature in this paper. The majority of the articles focus on medical conditions which are associated with ASD.

Recent findings

Improved awareness of concurrent medical conditions associated with autism can increase the medical professional's index of suspicion when evaluating a child with autism (Celia, Freysteinson, & Frye, 2016).

Medical conditions in autism can be divided into two categories such as: general and specific. The category **general** consists of disorders that do not have specific cause (intellectual disability and epilepsy). The category **specific** consists of distinct conditions such as: Fragile X syndrome, tuberous sclerosis, Down syndrome, etc. (Ghaziuddin, 2018). In the following text are descriptions of several examples of comorbid medical conditions that can be easily misdiagnosed in people with autism.

1. Somatic comorbidities

1.1. Autism and Epilepsy

Epilepsy is one of the most common medical conditions associated with ASD. Epilepsy can begin at any point in the lifetime of someone with ASD but typically signs will show up by adolescence.

Epilepsy affects a 5% to 46% of people who have autism, compared to an estimated 1 to 2% of the general population (Spence and Schneider, 2009). In one of our previous studies, we found that convulsions as a symptom presented in 14% of 102 subjects with ASD (Trajkovski, 2014). The autism-epilepsy overlap appears to be most common among people who also have intellectual disability (Autism Speaks, 2017). Intellectual disability with challenges in everyday function affects an estimated 32% of those who have autism (Christensen, et al., 2016). While there are still not enough studies to conclusively determine why seizures are so common, scientists have found some evidence to support various scenarios. The risk for epilepsy appears to be higher in those children who experienced a regression of language skills before the age of three. The largest group at risk for seizure disorders appears to be those individuals diagnosed with intellectual disability in addition to ASD. Seizures appear to be more in children who have common used antipsychotic medications as part of their ASD treatment (Besag, 2018).

Seizures can begin at any age, though research has identified two peaks in onset among children with autism in the preschool years and again in adolescence. Characteristic symptoms include: unexplained staring spells, stiffening of muscles, and involuntary jerking of limbs. Other lessspecific symptoms can include: sleepiness or sleep disturbances, marked and unexplained irritability or aggressiveness, and regression in normal development.

Epilepsy in autism is treated by combinations of medications and educational and social interventions. Treatment with medications, such as anti-epileptic drugs, has often been associated with improvement in behaviour and language in this population (Frye et al., 2010). Referral to a child neurologist who has experience with children with autism would be appropriate. Though diet has not been shown as a factor causing seizures, some doctors have used a ketogenic diet to significantly reduce and even eliminate seizures. This diet consists of increasing fat intake to four times the intake of carbs and proteins. Doctors still aren't sure why this works but according to the Epilepsy Foundation, up to 2/3 of patients have found some success with the diet (Autism Speaks, 2017).

1.2. Sleep disorders

Children with ASD have a significantly high rate of sleep disorders. It has been reported that up to 80% have some issue with sleep. The two most common problems are difficulty falling asleep and waking up repeatedly. Some children with ASD seem programmed to wake up early regardless of what time they go to sleep (Krakowiak et al., 2008). Sleep disorders are a common occurrence in the child with autism, compared to the non-autistic population. Individuals with autism may wake up during the night several times a week and stay awake for extensive periods of time (Bauman, 2010).

Many things can impact a child's ability to sleep. One common thread is that children with ASD often have greater anxiety and/or depression than other children. These feelings can cause a child to lay awake worrying, making it difficult for them to turn off their brain and fall asleep. If the child has a gastrointestinal disorder in addition to ASD, this can also be a factor to their ability to stay asleep throughout the night. Some sleeping problems can be attributed to behavioural problems in which the child hasn't adjusted to limits being set. Any medications that a child may be taking can affect how they sleep.

Regardless of the reason or theory for sleep disorders, it is critical that children on the autism spectrum get enough sleep. Lack of sleep can cause difficulties with attention, training, behaviours, or functioning during normal daytime hours, and can interfere with learning (Malow et al., 2012). Although there are many reported sleep problems, difficulties with obtaining proper polysomnographic studies in this population have resulted in fewer studies using objective measures to define the sleep disorder. Studies using these methods frequently find sleep abnormalities, confirming what is commonly reported by parents (Coury et al., 2009).

There are extremely limited data on circadian dysregulation in toddlers and preschoolers with ASD, derived from a small number of participants. Existing findings suggest that very young ASD children suffer from significant disturbances in sleep circadian rhythmicity, however these accounts are entirely based on parental reports and have not yet been corroborated by more objective measures of the sleep-wake cycle. ASD preschoolers appear vulnerable to circadian dysregulation at the level of hormone secretion, however it seems that circadian misalignment becomes more evident in older children. ASD research is growingly focusing on early pathophysiological and behavioural markers of the disorder from fetal life to toddlerhood. In this context, there is strong evidence that melatonin abnormalities during pregnancy and early regulatory problems during infancy may lead to increased ASD risk, suggesting that circadian abnormalities may be causally associated with ASD-specific disturbances in neurogenesis and synaptogenesis (Karaivazoglou, & Assimakopoulos, 2018).

Sleep disorders can affect the entire family but can be especially disruptive to the child, causing additional behavioural issues. Parents can establish routines to promote optimal sleeping conditions. Some common practices include: keeping the bedroom dark and cool, keeping the waking and sleeping schedule consistent – even on weekends, not allowing children to have caffeine or coca cola, to establish a bedtime routine and stick to it and to make sure children get exercise each day.

Melatonin, a pineal gland secretion that responds to darkness and promotes sleep in humans, is viewed by many as a natural and well tolerated treatment for sleep latency problems, where delayed or reduced melatonin release may be present. Several studies have reported on the use of melatonin in treating insomnia in children developmental with problems, with improvement in the majority of patients (Andersen et al. 2008, Johnson and Mallow, 2008). It has also shown to be effective in adults with autism and chronic sleep problems, most frequently sleep latency concerns (Galli-Carminati, Deriaz, and Bertschy, 2009). Melatonin is possibly safe when taken by mouth as a single dose. It is possibly unsafe when taken by mouth or injected into the body in multiple doses in the short-term. Because of its effects on other hormones, melatonin might interfere with development during adolescence. Melatonin might make bleeding worse in people with bleeding disorders and might make symptoms of depression worse. It also might increase blood sugar in people with diabetes. Melatonin can raise blood pressure in people who are taking certain medications to control blood pressure. Using melatonin might increase the risk of having a seizure.

1.3. Gastrointestinal disorders

The most common gastrointestinal disorders which are connected with ASD are chronic diarrhoea and constipation. Other GI issues include frequent abdominal pain, gaseousness and painful stooling. Chronic GI issues with increased severity of autism's behavioural symptoms - including repetitive behaviours, social withdrawal, hyperactivity and irritability. The association between GI issues and these autism symptoms may be particularly strong among nonverbal persons who have difficulty communicating pain and distress (Autism Speaks, 2017). Researchers have still not been able to clearly define why these children are more susceptible to GI problems but some studies suggest dietary allergies may play a role in some cases. Some children have been found to fare better when removing dairy and gluten from their diets. Others do better when processed foods with dyes are eliminated and others have added probiotics to their diet to offset symptoms. Some food elimination diets, such as glutenfree/casein-free, have gained popularity in the autistic population and have also shown some improvement with GI symptoms. Current literature does not support this as a first-line intervention (Cash, 2011) but suggests these diets may be more effective on a case-by-case basis. Food elimination diets may alleviate GI symptoms by removing an unknown allergen or item that is not well-tolerated. Theories suggest ingesting irritant foods causes inflammation in the gut lining that causes the membranes to leak, releasing particles into the body outside the GI tract (Malow et al., 2012).

Children suffering from GI problems may not exhibit typical symptoms so in some cases parents may not even know there is a problem. Some behaviours that can indicate a problem may include: coughing excessively, refusing to swallow food or difficulty swallowing, hitting self in jaw or fisting the jaw, chewing excessively, chewing on clothes, chin tapping, sleep problems, eating to relieve symptoms and unexplained changes in behaviour.

Treatment depends on identification of the underlying GI issue. Some treatments considered may be food elimination trials, as well as allergy testing, to look for possible food sensitivities. Other treatments follow the standard care for issues such as GERD, constipation or diarrhoea (Buie et al., 2010). If a GI issue is suspected and standard treatments have not shown improvement, referral to a gastroenterologist who has experience with children with autism is recommended.

One research into potential genetic causes for autism spectrum disorders has indicated a role for the autism spectrum disorder MET promoter variant rs1858830 in individuals with cooccurring ASD and gastrointestinal conditions, suggesting that there are new opportunities for research on this relationship (Campbell, 2009).

1.4. Feeding disorders

Children with sensory issues due to autism may be at risk for feeding disorders including difficulty eating or swallowing food based on the smell, texture or colour. These children tend to be picky eaters and may even throw tantrums when asked to eat certain foods. The term "feeding disorder" describes problems with eating enough or the right type of food. Among children with autism, this often involves eating only a few types of foods, eating only certain textures or colours of food, and/or disruptive mealtime behaviour. These issues have many causes, including sensory aversions, anxiety (e.g. after an incidence of choking, gagging or vomiting) and rigidity (aversion to change). Many children with autism also have motor issues that involve difficulty with chewing and swallowing. Others have digestion problems such as slow stomach emptying (Autism Speaks, 2017). One review of diagnostic records found that an estimated 70 percent of children on the autism spectrum have feeding and/or eating problems and 36 percent of these had problems classified as "severe" (Romero et al., 2016).

Chronic overeating is a common issue among both children and adults on the autism spectrum. Some people with autism have poor sensitivity to internal cues such as feeling full. Autismrelated aversions to strong flavours, textures and smells can lead to overconsumption of highcalorie, low-nutrient foods. In addition, increased appetite is a common and serious side effect of the only FDA-approved medicines for autismassociated challenging behaviour (agitation) – risperidone and aripiprazole (Scahill, 2016). The result is a high incidence of obesity – often combined with nutritional deficiencies – in both children and adults on the autism spectrum (Croen et al., 2015).

Pica, the dangerous habit of eating nonfood items, is another feeding disorder long associated with autism. Anecdotally, pica appears to be concentrated among those whose autism is complicated by intellectual disability. It can include swallowing sharp objects such as nails, broken glass and pins, as well as poisonous substances such as paint chips and swimming pool chlorine tablets. Pica can place tremendous stress on caregivers by demanding their constant vigilance (Call et al., 2015). Parents dealing with these picky eaters are encouraged to offer choices while still having their child stick to the rules. Children should know that they have to eat one vegetable at dinner, but allow them to choose which one. It is also important to ensure that achild isn't avoiding a food because of an allergy.

Avoidant Restrictive Food Intake Disorder (ARFID) is a new diagnosis in the DSM-5, and was previously referred to as "Selective Eating Disorder." ARFID is similar to anorexia in that both disorders involve limitations in the amount and/or types of food consumed, but unlike anorexia, ARFID does not involve any distress about body shape or size, or fears of fatness. Although many children go through phases of picky or selective eating, a person with ARFID does not consume enough calories to grow and develop properly and, in adults, to maintain basic body function. In children, this results in stalled weight gain and vertical growth; in adults, it results in weight loss. ARFID can also result in problems at school or work, due to difficulties eating with others and extended times needed to eat. People with autism spectrum conditions are much more likely to develop ARFID, as are those with ADHD and intellectual disabilities (APA, 2013).

1.5. Immune disorders

A link between immune dysfunction and autism is further exemplified by a recent multi-genome analysis study, which found links between genes that predispose individuals to aberrant immune response to infections and risk of developing autism (Saxena et al., 2012), as well as two separate findings from large European birth cohorts, which both found perturbed immune responses and pro-inflammatory biomarkers in mothers and newborns who later develop autism (Abdallah et al., 2012; Brown et al., 2013). In autism, findings of chronic inflammation and immune dysregulation throughout the central nervous system are accompanied by serum findings, all pointing to widespread dysregulation immune mechanisms. of Individuals with autism often display immune abnormalities in the form of altered cytokine profiles, autoantibodies, changes in immune cell function and abnormal mast cell activation (Ashwood et al., 2011).

Multiple allergies are common in children with autism, which supports the theory of an underlying immune system dysfunction in this population. The combination of food and environmental allergies often results in a domino effect on other body systems, evidenced by an inflammatory response with elevated serum cytokine and immunoglobulin E (IgE) levels. This is believed to affect the neurological system in individuals with autism. Reactions to common food or environmental allergies may vary from local to systemic and manifest in some children as behavioural or sleep issues (Autism Treatment Trust, 2013). Food allergies, like autism, have an underlying link to the immune system, which is why it's possible that they may go hand in hand. In most cases the food allergies are not life-threatening for children with ASD

however certain foods may cause worsening of autistic symptoms.

In the Macedonian study we examined specific IgA, IgG, and IgE antibodies to food antigens in 35 participants with an autism spectrum disorder and 21 of their siblings. A statistically significant higher plasma concentration of IgA antibodies against alpha-lactalbumin, beta-lactoglobulin, casein, and gliadin were found in the children with a ASD. Plasma concentrations of IgG antibodies against alpha-lactalbumin, betalactoglobulin, and casein in participants with ASD were significantly higher. IgE-specific (alpha-lactalbumin, antibodies betalactoglobulin, casein, and gluten), as well as plasma concentration of total IgE, also were statistically significantly higher in the participants with ASD (Trajkovski et al., 2008). Both IgE and non-IgE mediated allergic reactions are increasingly recognised causative factors of anxiety and mood disorders. As well, these allergic reactions contribute to difficulty focusing, irritability, tics, daytime fatigue and sleep problems in both children and adults. In this survey it was found that approximately 16% of people with autism suffer from some kind of allergy to food, inhalants, etc. These findings indicate intestinal immunological disturbances and the need for gluten-casein free diets in this (Trajkovski, population 2013). Current treatment recommendations for allergies include avoiding the allergen (if known), testing for allergens, and evaluation by an allergy specialist. Antihistamines may be given to treat symptoms. between autism The connection and autoimmune disorders is gaining increasing support with a number of studies demonstrating a high incidence of autoimmune conditions in autism and an association between serum levels of various autoantibodies and severity of autistic symptoms (Chen et al., 2013). Autoantibodies to folate receptors for example are suspected to play a pathological role in some forms of idiopathic autism because of their negative effects on cerebral folate metabolism and wellknown involvement in other neurodevelopmental syndromes (Ramaekers et al., 2012). Family history of autoimmune diseases is significantly higher in autistic children than in the general population

(McDougle and Carlezon, 2013). The combination of these findings has led many researchers and clinicians to suggest that autoimmune mechanisms could be a causative or contributing factor in at least a subset of individuals with autism.

1.6. Autism and infections

Vulnerability to infections is high in children and pregnant women. If infection occurs during pregnancy, the outcome depends on the immune status of the mother, the type and strain of the virus and the development stage of the fetus. Other factors, such as generic predisposition to autism may be important. Viral infections lead to the production of cytokines which can destroy neurons and damage fetal development. Depending on the virus and the site where the infection occurs, the cytokines could be produced directly in the brain or gain access to it through the blood-brain barrier. The most described viruses associated with the etiology of ASD are: herpes virus, cytomegalovirus, measles virus and rubella virus (Ghaziuddin, 2018). In the Macedonian sample, the most prevalent medical condition was the acute infectious disease varicella in (34.5%) and measles in (6.5%) of the people with autism (Trajkovski, 2013).

1.7. Headaches

One of the less common ASD symptoms is headaches. One reason may be because ASD can be associated with pain insensitivity. This means that the child may just not feel the pain of a typical headache the same way a child without ASD would. Research has however indicated a link between migraines and ASD. One study found that children with sensory hyperactivity were more likely to experience migraines. Additionally those children with higher levels of anxiety are more likely to have migraines or cluster headaches than others (Sullivan et al., 2013).

Children with ASD may also suffer from headaches if they are head bangers. Children who bang their heads may be doing so in an attempt to limit the pain signals that are being delivered to their brains. Inflammation caused by GI disorders can also cause headaches in a child. Nutritional changes, behavioural therapies and other treatments to reduce anxiety can play a significant role in reducing these symptoms.

1.8. Oxidative stress, mitochondrial dysfunction and metabolic abnormalities

There is increasing evidence that mitochondrial dysfunction, perturbation in sulfur and amino acid metabolism, and high levels of oxidative stress are common in people affected by autism. Elevations in metabolic markers of oxidative stress as well as reduced levels of glutathione and other cellular antioxidants have been found in many areas of the body, including the brain and primary immune cells (Rose et al., 2012). Reactive oxygen species are destructive to cells and organs and elevated oxidative stress has been implicated in autoimmune, inflammatory, cardiovascular and neurodegene-rative diseases and cancer. A substantial percentage of autistic display markers of patients abnormal mitochondrial energy metabolism, such as elevated lactate, pyruvate, and alanine in blood, urine and/or cerebrospinal fluid, as well as serum carnitine deficiency (Frye et al., 2013). In the majority of cases this abnormal energy metabolism cannot be linked to specific inborn mitochondrial disease, or another primary inborn error of metabolism. It has therefore been suggested that in autism, abnormalities in mitochondrial function could be a downstream consequence of immune dysfunction (Rossignol and Frye, 2011). Insufficient mitochondrial energy production could both result from and contribute to cellular oxidative stress and chronic inflammation in autism. Raising antioxidant and/or metabolic precursors and levels supporting mitochondrial function have been treatment avenues. Routine proposed as metabolic screening mitochondrial and functional studies required for the diagnosis of mitochondrial disease are rarely performed for patients with autism, and the hypothesis of an etiological link between autism and mitochondrial dysfunction has therefore not properly been assessed. Mitochondrial dysfunction contributes to a number of language deficits, abnormal energy metabolism, chronic gastrointestinal problems, abnormalities in fatty acid oxidation, and increased oxidative stress.

Nutritional supplementation to decrease oxidative stress along with factors to improve reduced glutathione, as well as hyperbaric oxygen therapy represent supported and rationale approaches. There is a need for reliable laboratory markers to detect abnormalities of mitochondrial function, which will then facilitate further clinical investigations in this subgroup of children with autism.

2. Mental health comorbidities

Epidemiological studies suggest that between 54 and 70% of people with autism also have one or more other mental health conditions (Romero, 2016). Like autism, ADHD, schizophrenia and bipolar disorder are neurodevelopmental conditions that appear to have roots in early brain development. Among people with autism, anxiety and depression may stem, at least in part, from autism-related impairments that increase daily stress and social isolation and decrease overall quality of life (Vasa et al., 2016). Untreated health mental conditions can profoundly worsen autism's behavioural challenges. But because of overlapping symptoms, they can be particularly difficult to identify in someone who has autism (Sikora et al., 2012). The social withdrawal associated with depression or schizophrenia, for example, can be difficult to distinguish from autism-related social impairments. In addition, many people with autism have difficulty identifying and expressing emotions and other internal feelings. Autism specialists have developed guidelines for diagnosing and treating some of the most common mental health conditions affecting children, and adults who have autism.

2.1. Autism and ADHD

Over the last decade, studies have suggested that between 30 and 61 percent of people with autism also have symptoms of ADHD (Romero, 2016). Symptoms of ADHD include a persistent pattern of inattention, hyperactivity and/or impulsivity that interferes with daily life, social development and learning. People with ADHD often fail to pay close attention to details and make careless mistakes at school or work. Often, they don't appear to listen when spoken to, have trouble organizing tasks and fail to follow through on instructions and assignments, especially those that require sustained attention.

2.2. Autism and anxiety disorders

Studies suggest that between 11 and 42% of people with autism struggle with one or more anxiety disorder (Vasa et al., 2016). These disorders include separation anxiety, panic disorder and phobias (extreme fear of certain noises, places). Most research on anxiety in autism has focused on children and adults who are verbal and have normal to high intelligence. Experts agree on the need for more studies involving the one-third of people with autism who are nonverbal or minimally verbal and/or have intellectual disability. Anxiety can trigger strong internal sensations of tension that include a racing heart, muscle tightness and stomach ache. In someone with autism, these feelings can prompt an increase in self-soothing, repetitive behaviours (flapping, rocking, spinning, etc.) and/or destructive or self-harming behaviours (shredding, clothing, head banging, etc.). Similarly, anxiety can be the underlying cause of new resistance to what had been an enjoyed activity (e.g. a trip to the beach, a birthday party, school, etc.) (Autism Speaks, 2017).

2.3. Autism and depression

Depression affects an estimated 7% children and 26% of adults with autism (Croen, 2015). This compares to 2% of children and close to 7 percent of adults in the general U.S. population. A recent report in the journal Pediatrics found that the rate of depression among children with autism rose dramatically with age, from just under 5 percent in grade-schoolers to just over 20% in teenagers. It likewise rose with intellectual ability (IQ), as well as the presence of one or more of the medical conditions that commonly accompany autism - particularly seizures and gastrointestinal issues. That depression rates rise with age and intellectual ability suggests a painful awareness of autism's social challenges and isolation, the researchers propose. That the rates increase with associated medical conditions may demonstrate their profound effect on quality of life. The authors called on healthcare professionals to consider screening for depression as a routine part of care

for teens and adults who have autism – particularly those with normal to high IQ and those with additional medical issues. Signs and symptoms of depression include chronic feelings of sadness, hopelessness, worthlessness, emptiness and/or irritability. Also common: social isolation, moving or talking slowly, feeling restless, and having trouble sitting still or concentrating. At its most serious, depression can include frequent thoughts about death and/or suicide (Autism Speaks, 2017).

2.4. Autism and schizophrenia

In terms of symptoms, autism and schizophrenia both involve impairments in processing language and understanding other people's thoughts and feelings. Clear differences include schizophrenia's hallmark psychosis, which often involves hallucinations. In addition, autism's core symptoms typically emerge between ages 1 and 3 years; schizophrenia's in early adulthood. Many clinicians have reported identifying autism at high rates in adults already diagnosed with schizophrenia and vice versa. Investigations looking at how commonly these two conditions occur together vary widely in their findings. Taken together, the studies found schizophrenia in 4 to 35% of adults who have autism and found autism in 4 to 60% of those who have schizophrenia. Many of the same gene

changes known to increase risk of autism also increase the risk of schizophrenia (Autism Speaks, 2017).

2.5. Autism and bipolar disorder

Bipolar disorder is a mood disorder also known as "manic depression". People with bipolar disorder tend to alternate between a frenzied state known as mania and episodes of depression. While some people experience only the manic episodes, most alternate between these two states and can show extreme irritability. Research shows that children and adults with autism are at increased risk for bipolar disorder. However, studies vary widely in estimating the prevalence of bipolar disorder among people with autism, ranging from 6 to 27%. Bipolar disorder affects around 4% of the general population. Some leading experts propose that bipolar disorder may be over-diagnosed in those who have autism, due to overlapping symptoms such as hyperactivity, irritability and disturbed sleep. They caution mental health providers to tease apart the symptoms of true bipolar disorder from those of autism by looking at when the symptoms appeared and how long they lasted. The antipsychotics risperidone and aripiprazole can treat irritability in children with autism, though both tend to produce significant weight gain and diabetes risk (Autism Speaks, 2017).

Conclusions

Autism can affect the whole body. An increasing number of medical disorders are being identified in individuals with ASD and studies are starting to identify the conditions that probably play a causal role in etio-pathogenesis. People identified with autism spectrum disorders have high frequencies of one or more co-occurring developmental, psychiatric, non-ASD neurologic, metabolic, immune, gastrointestinal and possibly causative medical diagnoses. Seizures, disturbed sleep and painful gastrointestinal disorders are some of the health conditions commonly associated with autism. Autism is also frequently accompanied by mental health conditions including anxiety, depression, and ADHD. Medical conditions and consecutive pathological processes can negatively impact behaviour, socialisation, communication, cognitive function and sensory processing of individuals with autism. It is also becoming increasingly clear that the medical comorbidities that underlie autism are not stagnant or transient, but tend to be chronic and in many cases, if left unrecognised and untreated, progressive. Accurate diagnosis and treatment often results in improved level of functioning and decreased severity of symptoms. Healthcare providers should be aware of the medical conditions that occur with ASD. Children with autism do not have typical presentations for medical illnesses and that's why careful assessment and attention should be paid to the subtlest differences that occur.

Autism-associated health problems extend across the life span – from young children to senior citizens. A better understanding of the possible mechanisms leading to poorer health status will enable improved patient care and ultimately enhance the quality of life for people with autism spectrum disorders. Despite the prevalence of these health conditions, more systematic research is needed to understand their manifestation in people with ASD and the best practices for identifying and treating them. Specialists at autism care centres are working with patients and their families to improve the health and quality of life of all those with ASD by developing and disseminating evaluation and treatment guidelines for healthcare providers. Appropriate and individualised medical assessments must be carried out in all cases, including a documented clinical examination. Autism spectrum disorder usually occurs with medical or psychiatric health conditions.

Treatment should address not only the symptoms of autism but also those of the associated comorbidities.

Conflicts of interests

The author declares no conflict of interests.

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