
**NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS**

**Postgraduate/ Master of Science Program**

**"STRATEGIES OF DEVELOPMENTAL AND ADOLESCENT HEALTH"**

**Academic Director : Artemis Tsitsika**

# THE CORRELATION BETWEEN GIFTEDNESS AND AUTISM SPECTRUM DISORDER: A SYSTEMATIC REVIEW

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**Registration Number:**

**Medical Doctor - Pediatrician**

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**ACKNOWLEDGMENTS**

I wish to especially thank my partner in the systematic review, Georgia Dimitriou, for the excellent collaboration. We spent a lot of time together in order to complete our work and we have always been kind and supportive to each other. Through this process we have become good friends and therefore I am happy that we initially chose each other for partners in this systematic review.

Moreover, I would like to thank our professor in epidemiology, Theodoros N. Sergentanis, who took us by the hand and taught us step by step how to interpret research data and how to conduct our own research. Furthermore I would like to thank him for his assistance, guidance, support and time.

To all the members of Thesis committee I would like to express my gratitude for everything they taught us and for their support and guidance.

**To Vassilis, for giving me strength, inspiration and his unreserved support.**

**To my parents for providing me with nurturance and support throughout my life.**

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# GENERAL PART

## LITERATURE BACKGROUND

Although giftedness is usually associated with intellectual abilities, there is still no universal consensus for a single definition. According to the National Association for Gifted Children, the children who show exceptional levels of ability to learn and reason or outstanding competence in one or more domains (performance in top 10%) are considered gifted. The domain may be any structured activity such as mathematics, music and language, or sensorimotor skills such as painting, dance and sports (1). Due to the lack of a universally accepted definition, research on giftedness remains limited and its prevalence rate is considered inexact and arbitrary.

Intricate associations between giftedness children and special needs have not been fully elucidated. The term “twice exceptional” or “2e” pertains to children that are characterized by a potential for high achievement and one or more disabilities including neurodevelopmental disorders, emotional/behavioral disorders and physical disabilities. Given the fact that defining giftedness is challenging, twice exceptional children are even more difficult to identify, mostly because they often use their talent in order to compensate for their disability or their giftedness is often overshadowed by their deficit (2).

The research conducted on the association between giftedness and neurodevelopmental disorders is relatively limited. Autism Spectrum Disorder (ASD), is considered as one of the most commonly diagnosed developmental disorder. The impairment in social communication and reciprocal social interaction as well as a wide range of inflexible, recurrent and restricted behaviors, activities or interests are the main characteristics of the disorder (3). Whereas ASD refers to disabilities and impairments, giftedness refers to abilities or achievements. Therefore, it is difficult to refer to the co-occurrence of both identities as co-morbidity. However, from the educational and psychological point of view, the two conditions share two features: IG-

students and ASD-students differ from the typically developing (TD) children and therefore they require a special educational approach.

Taking all the above into consideration, it becomes obvious that gifted children with ASD compromise a unique and heterogeneous population of children: It has been suggested that specialists in ASD as well as educators are made aware of their characteristics and provide them with a tailor made approach that addresses their complex needs (4). The aim of this systematic review was to investigate the correlation between neurodevelopmental disorders and giftedness in children and adolescents. This presents the results of this systematic review considering Autism Spectrum Disorders.

## GIFTEDNESS

### Definition

Even though giftedness in children is usually associated with intellectual abilities, it may present in various ways. Despite the fact that giftedness has been studied during the last two centuries (5) scientists have still not arrived at a consensus for its definition. Different theories and definitions have been proposed over the years in order to provide a framework for gifted education programs and services and guide approach decisions. According to Renzuli, whose theory was published in 1978, gifted behavior occurs when there is an interaction among three basic clusters of human traits: above average general and/or specific abilities, high levels of creativity and high levels of task commitment (motivation) (6). Gifted and talented children are those who are capable of accomplishing or possess the above composition of traits and are able to apply them to any potential area of performance. This model, called Schoolwide Enrichment Model, allegated that gifted behaviors can be found in certain people, at certain times and under certain circumstances (6). In 1983, Gardner proposed the Theory of multiple intelligences. This theory proposed the differentiation of human intelligence into specific

“modalities of intelligence”, instead of defining intelligence as a single, general ability. The theory has been criticized by many psychologists for its lack of objective judgment and empirical evidence (7). Gagne, in 1985, proposed the differentiated model of giftedness and talent which dissociated giftedness and talent. In this model, giftedness is designated by the possession and use of untrained and spontaneously expressed natural abilities, called gifts and aptitudes, in at least one domain of ability, to a degree that places the child’s performance within the upper 10% of age-peers(8). On the other hand, the term talent indicates the superior mastery of systematically developed abilities and knowledge in at least one field of human activity to a degree that places the child among the top 10% of his/her peers. According to Gagne’s theory, there are five aptitude domains: intellectual, creative, socioaffective, sensomotor and others (e.g. extrasensory perception) (8). These natural abilities have a clear genetic substratum and can be observed in every task children are set to doing (8). The U.S. Department of Education in 1993 used the term “gifted” referring to the children and youth with outstanding talent who perform or show the potential for performing at remarkably high levels of accomplishment when compared with others of their age, experience, or environment(9). The “No Child Left Behind Act” of 2001 was a U.S. Act of Congress that reauthorized the Elementary and Secondary Education in the United states of America (U.S.A.). In this act an effort was made for the establishment of a federal definition of the terms “gifted and talented” (10). According to this act the above terms are used to describe children who give evidence of high achievement capability in such areas as intellectual, artistic, creative, or leadership capacity, or in specific academic fields. These children need services or activities that are not ordinary provided by the school in order to fully develop those capabilities (10).

According to a position statement of the the National Association for Gifted Children (NAGC), approved in 2010, the children who show exceptional levels of ability to learn and reason or outstanding competence in one or more domains (performance

in top 10%) are considered gifted. The domain may be any structured activity such as mathematics, music and language, or sensorimotor skills such as painting, dance and sports (1).

*Identification*

Gifted children are usually identified during the early or middle school years. Standardized tests are most commonly used as initial screening by schools in order to determine academic performance. Academic giftedness is often defined as the top third percentile. The Intellectual Quotient (IQ) is widely agreed upon to define giftedness and it can be determined using batteries of test such as Wechsler Intelligence Scale for Children (WISC) (11). The WISC test is the most commonly used tool to assess intelligence in children from 6 to 16 years of age. The most recent version is the WISC-Fifth Edition (11).

The WISC-V yields a Full Scale IQ (FSIQ) that depicts the individual's general intellectual ability. It also generates five index scores: Verbal Comprehension Index, Fluid Reasoning Index, Processing Speed, Index Visual Spatial Index and Working Memory Index(11). These scales provide an estimation of the child's ability in different cognitive domains. The duration of the evaluation varies depending on the testing procedures and goals. The examiner may administer the full test or a single primary index (11).

However, achievement scores and superior IQ cannot foretell academic success, due to the fact that they do not take into consideration practical intelligence, creativity or the personality characteristics that can lead to great achievements. Moreover, these methods do not succeed in identifying children who are exceptional in only one of the domain described above (9). The performance in standardized testing is also affected by sociocultural differences, because giftedness in certain domains may be valued more than others. Discrimination and poverty may also lead to limited opportunities and therefore

identification could be better made according to the potential of the child rather than according to performance (9).

Characteristics

The social, intellectual, creative, emotional and physical aspects of gifted children often develop at an uneven rate and in a way outside of norms. This pattern of development is described as asynchronous (12).

Moreover, these children have particullar personality characteristics, witch are of great importance for development of their gift. They may have remarkable diligence, enthusiasm and determination (13). They also have an insatiable curiosity, they are eager to learn and have reasoning advanced and language skills(9). They share more common interests with adults or older children rather than with their peers. They also tend to be perfectionists and they enjoy expressing and developing their gifts. They usually value relationships and they present moral sensitivity (13). On the other hand, the above characteristics may vary to a great extent, depending on the individual. Moreover, gifted children, not uncommonly, exhibit challenging personality features or susceptibilities. They may struggle with peer relationships and, as a result, they may experience social isolation (13). At times, they may present exaggerated and inexplicable by their peers emotional reactions (e.g. reaction for something they may consider unjust). Sometimes they may be so engaged with their special interests that they ignore their peers. Their extreme perfectionism may pose difficulties in failure acceptance and may lead to isolation, in cases where the child is not able to accept the other children's inconsistencies (13). Their creativity may lead to difficulties in conforming to rules and their independence may cause defiant behaviors (9). According to Dabrowski's theory, gifted students may also present more intensive and sensitive responses to the environmental stimuli. Therefore, the gifted children may give the wrong impression that they have disciplinary or behavior problems (14).

Dabrowski had described five domains of overexcitabilities: intellectual, emotional, sensual, psychomotor and imagination (14). Although most of the gifted are well adjusted, their asynchronous development may cause intense emotional distress, as they feel isolated from with their peers. Emotional distress can also be caused by excess perfectionism or difficulties with affect regulation (13).

*The need for special approach*

Taking the above into account, it becomes clear that gifted children require guidance and support in order to develop emotionally and socially as well as in the domain of their giftedness. Gifted education professionals and parents of these children should promote holistic development and the children's self-actualization (15). It is important that qualities such as social skills, emotion regulation, motivation, the ability to handle criticism and cope with challenges, self-confidence and self-perceptions are well developed, because these are the characteristics that could differentiate the children that reach excessively high levels of gift development from others who don't (15). The development of these features should be differentiated based on the type of giftedness and the stage of talent evolution (15).

Services should be provided to gifted children depending on their varying needs. Needs differ among distinct domains of giftedness, but also among the gifted children that have the same gift. The services that refer to these children should adjusted according to the current levels of achievement/potential and should also include counseling addressing their present and future needs (15). This approach aims to alleviate needs that would not otherwise be satisfied.

## AUTISM SPECTRUM DISORDER

### Definition

Leo Kanner, in 1943, described 11 children characterized by extensive deficits in social engagement and reciprocal interaction (16). More than seventy years later, the diagnostic criteria share many common characteristic with Kanner's first description.

Individuals within the Autism Spectrum Disorder are facing persistent difficulties in to initiating and to sustaining social communication and social interaction. Moreover, they exhibit a range of repetitive, inflexible and restricted patterns of activities, behavior or interests that are exaggerated or atypical for the child's age, social and cultural context (3). The signs typically appear during the first years of the child's life, but the full range of symptoms may manifest some years later, when social demands are increased and exceed the restricted capacities (3). The impairments are so severe that affect all the areas of functioning such as personal, educational, occupational, family, social and are commonly observed in all settings, despite the fact that they may vary depending on the context. Children diagnosed with ASD may exhibit a wide range of language and intellectual (3). Other impairments, such as cognitive or motor, and difficulties in adaption have a huge impact on the child's functioning and therefore they are also considered important features of the clinical presentation (17). In fifth edition of the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (DSM-5), which was published in 2013, the terms "*Asperger's disorder",* "*not otherwise specified pervasive developmental disorder* (PDD-NOS)" *"pervasive developmental disorders* and diagnostic classifications *autistic disorder", "childhood disintegrative disorder"* and *"Rett's disorder", used in DSM-IV,* were substituded by the term, *Autism Spectrum Disorder* (ASD) (18). This was caused by the fact that the subclassifications were not used reliably and had little scientific justification. The11th revision of The International Classification of Diseases (ICD), adopted in May 2019,

also incorporates the terms *"Autism"*, *"not otherwise specified pervasive developmental disorder (PDD-NOS)"* and *"Asperger syndrome* within the term "*Autism Spectrum Disorder"* (19).

Epidemiology

The Developmental Disabilities Monitoring Network (ADDM) and Centers for Disease Control and Prevention (CDC) estimated the Autism Spectrum Disorder prevalence in children 8 years of age at 1 in 68 children (1.46%) among 8 years old children and 1.7% for children aged 4 years old (20, 21). A population cohort study of 3 million subjects revealed a similar prevalence of 1.25% in the USA (22) . Slightly higher estimates have been revealed in studies, using parent's reports. The global prevalence of the disorder is estimated at 0.76% in the Global Burden of Disease Study, published in 2010 (23). National registry data in Sweden, Iceland and Denmark show prevalence higher than 1%, while the greatest prevalence estimate was 2.64% as shown by a study in South Korea that included children 7-12 years of age, (24-27). Males tend to be affected more in comparison to females. In most studies the ratio is estimated at 4:1 to 4.5:1. However, meta-analysis of studies, conducted in 2017, revealed a ratio closer to 3:1 (21, 28).

According to a very recent study, ASD prevalence in Greece was 1.15% (1.83% for males and 0.44% for females, ratio 4.14:1). The prevalence varied from 0.59% to 1.50% in Greece's distinct regions (29). It is not clear whether the observed increase in the ASD prevalence, can be attributed to a true rise in incidence cased by etiologic factors or to the contribution of non-etiological factors such as diagnostic practices, increased public awareness, changes in identification, availability of services or variation in study methods (17, 23, 30, 31).

## Etiology

A single etiology has not yet been recognised for ASD or its core behavioral components and its etiology is considered heterogeneous. However, ASD seems to be heritable, as shown by the results of family studies. These results revealed raised risk of autism in siblings of diagnosed children. Moreover, twin studies documented elevated recurrence rates for monozygotic twins compared to dizygotic twins (32-34). There is also evidence that environmental factors of pregnancy, such as multiple gestation, short interpregnancy interval, gestational diabetes, maternal obesity, exposure to maternal medications (eg, valproate), infections (eg,cytomegalovirus, rubella, influenza) and gestational bleeding may be linked to elevated risk of autism (35) (17). Exposure to toxic environmental chemicals has not been associated to ASD, however, a link between some elements (e.g. volatile organic compounds, metals, organophosphates) and ASD risk has been implicated by recent research (66, 67, (36). It has also been implied that the epigenetic changes of the exomes, probably caused by environmental factors, may also be involved in pathophysiology of autism (17, 37, 38). Epigenetic alterations are the link between environment and genes. As the etiologic and phenotypic heterogeneity of ASD indicates, no single neuropathology has been recognised (17). ASD seems to be related to alterations in the activation of many different brain regions, associated with controls on tasks assessing, executive functions, visual processing, motor skills, social perception skills and language as shown by Functional MRI (fMRI) studies (39, 40). A meta-analysis revealed some common features including decreased activation of areas of the prefrontal cortex (executive functions), lack of modulation in response to intensity of stimuli or task demands and in the preference for social stimuli. Visual-spatial systems seem to be favored instead (40). Furthermore, there is evidence for underconnectivity in frontal-posterior networks, while some studies show hyperconnectivity between sensory cortices and subcortical regions (39-41).

DSM V criteria

The DSM criteria are presented below and include the main impairments of Autism Spectrum Disorder: the deficits in social interaction and social communication, as well as the repetitive and limited interests, behaviors and activities (18). An individual should meet 3 out of 3 criteria referring to reciprocal behavior and social communication, and equal or more than 2 out of 4 criteria referring to repetitive or restricted behaviors, in order to be diagnosed with ASD (18). The impairments, caused by the symptoms, must significantly affect all the areas of the individual's functioning and must have appeared during the first years of the child's life, even though the full range of symptoms may manifest some years later, when the social demands are raised. Sometimes the deficits may be concealed by strategies acquired later in life. In children with intellectual disability (ID), the diagnosis can be made when their communication and interaction abilities are lower than what would be expected for their general level of development (18).

A. Irreversible impairment in social interaction and social communication, observed in multiple setting and circumstances, in history or at present (18):

1. Lack of social and emotional interaction, varying from abnormal reciprocal conversation or failure in social relationships to decreased shared interests emotions or affect or to inability to start, maintain and respond to social contacts(18).

2. Impairment in nonverbal communicative behavior used in order to establish social contact, such as inadequately combined nonverbal and verbal communication, restricted use and defects in comprhension of body language, gestures and facial expressions and poor eye contact (18).

3. Difficulties in developing, understanding and preserve relationships. Lack of behavior-adaption to social circumstances, difficulties in making friends or sharing play, absence of interest in other children of similar age, are some examples. (18).

B. Repetitive and restricted ways of behaving, activities or interests, by history or at present (18):

1. Repetitive or stereotyped speech, movements or use of objects: idiosyncratic phrases or echolalia, motor stereotypes, turning over or lining up objects(18).

2. Persistence on monotony, rituals of nonverbal or verbal behavior or stiff allegiance to routines, for example, excessive distress at insignificant changes and transitions, inflexible way of thinking, need for following the same path, eating the same food or having greeting rituals (18).

3. Highly fixated and restricted interests, characterized by abnormal focus or intensity, such as obsession with unusual objects or excessively circumscribed interests (18).

4. Hyporeactivity or hypereactivity to sensory stimuli or unusual interests in environmental sensory features. For example, increased tolerance to temperature or pain, aversion to particullar textures or sounds, touching or smelling objects in an excessive way, intense interest in movement or lights (18).

C. Symptoms should appear in the early period of development. However the full range of symptoms may manifest some years later, when the social demands are raised. Sometimes the deficits may be concealed by strategies acquired later in life. (18).

D. Symptoms must significantly affect all the areas of the individual's functioning such as social, occupational or other (18).

E. These deficits cannot be better explained by global developmental delay or ID. ASD and intellectual disability frequently co-exist. In order to make co morbid diagnosis of ASD and ID, communication and interaction abilities must be lower than what would be anticipated for their general level of development (18).

The severity of the disorder must be defined depending on the deficits in social communication and the repetitive and restricted patterns of behaviors (18).

Associated impairments

The clinical presentation and management of ASD is often affected by other medical and behavioral characteristics, beside its core impairments and its neuropsychological features.

**Motor Impairments.** Except motor stereotypies, children with ASD, in many cases, manifest less characteristic motor abnormalities, including impairment in motor coordination (gross and fine motor skills, gait and postural control), performance of gestures and learning of motor activities (42, 43). A main factor leading to abnormal motor functioning in autism is found to be the extreme dependence on proprioceptive feedback added together with weak assimilation of visual feedback (43). Delayed achievement of motor milestones, walking on toes, clumsiness and handwriting difficulties are not uncommon(44). Lack of motor imitation ability, hypotonia, decreased postural stability and other nearly detectable neurological manifestations, such as dysrhythmia, stressed gait maneuvers and high frequency of overflow movements of the feet and hands are often revealed in neurological examination (44). Tic disorders, such as Tourette Syndrome, may also found more often in children with autism (45, 46).

**Epilepsy.** Autism spectrum disorder is also related to elevated epilepsy hazard. The higher risk is observed in early childhood and in the period of adolescence. Any type of seizures can happen in children in the autism spectrum. However, the most common type are the complicated partial seizures leading to generalization.(47). The prevalence of seizures in autism varies and a a range from 6.6% to 22.5% is reported in the literature (48-50). The older age and the low intelligence quotient constitute the main risk factors in children with ASD. (47, 51, 52). Although the prevalence is greatest in children with known genetic etiology and severe intellectual disability, even high-functioning individuals with idiopathic ASD have an importantly higher rate of epilepsy compared to the general population. Moreover, in many autistic children interictal epileptiform activity may be obsereved during sleep on EEG, despite the fact that they never had definite clinical seizures (47).

**Behavioral Symptoms and Psychiatric Disorders.** Behaviors usually linked to ASD can lead to significant difficulties and therefore to distress. These features may be: aggression, anger outbursts, property destruction, irritability, self-injuries, mood instability, anxiety, running away, sleep disorders, inattention, hyperactivity, impulsivity, and other signs of emotional dysregulation. These behavior problems constitute a significant burden on families because they complicate every aspect functioning and in any context (53-58). Sometimes, a comorbid psychiatric identity can be reasonably diagnosed. This can be anxiety in 42%–56% of the ASD cases, attention-deficit and hyperactivity disorder (ADHD) in 28%–44% of the cases, depression in about 12%–70% of the cases, tic disorders (14%–38%), psychotic disorder (12%–17%) and oppositional defiant disorder (ODD)in 16%–28% of the ASD cases (59).

**Sleep disorders**. Sleep disturbances are described in 40% - 80% of autistic children, while in TD children the prevalence ranges between 25%–40%. They seem to be frequent at all ages and levels of IQ (60). Sleep problems contribute burden to both children and their families because they may last for years and deteriorate the children's behavioral

and emotional problems. Inadequate sleep may result in aggravation of core symptoms of the disorder, and also in tantrums, aggression and other dysfunctioning behaviors (60). Sleep problems may include bedtime resistance, lower efficiency of sleep, more frequent waking during the night, extended sleep-onset latency. The decreased sleep duration results in sleepiness during the day. (60, 61).

**Feeding and Gastrointestinal Problems.** As shown in a meta-analysis involving 2,215 subjects, individuals with ASD experience more gastrointestinal (GI) symptoms, like constipation, diarrhea and abdominal pain, compared to the normative groups.

According to the existing literature there is no evidence of a unique GI pathophysiology in ASD (62). Food selectivity, difficulties in toileting routine, delayed bowel training and other sensory and motor dysregulations seem to contribute substantially in the raised prevalence of GI symptomatology in individuals with ASD (62).

**Feeding Difficulties**. Feeding difficulties such as obsession with food presentation, food selectivity depending on texture color, texture or temperature, and compulsive consumption of certain foods, are frequent in children with autism. These children may also refuse to eat, they may hold the food in the mouth, vomit or exhibit volitional gagging. Rumination, and pica are also common among individuals with autism. (63, 64).

Surveillance and Screening

Surveillance is the method of continuously observing and identifying children at risk for neurodevelopmental disorders. On the other hand, screening involves the use of standardized instruments at particular time intervals to evaluate risk (65). Surveillance is an ongoing process that should be carried out at every pediatric care visit throughout childhood and should cover the developmental history, observations of the child, elicitation of the parents' concerns, identification of the presence of possible risk factors and protective features, and documentation of the findings (65).

The American Academy of Pediatrics (AAP) recommends developmental screening through the use of a standardized tool for children at the age of 9, 18, and 24 to 30 months or at times when there are concerns by a caregiver or professional (65).

Moreover, screening for autism spectrum disorder in particular, is suggested at the age of 18 and 24-months, or at any time caregivers express a relative concern or whenever risk factors are revealed during the process of developmental surveillance or screening (66). The fact that signs of the disorder can be identified in very young toddlers, in addition to the evidence showing that early recognition results in early intervention and improved longterm outcomes, has led to the recommendation for universal screening(66). A variety of brief developmental, autism and language-specific tools can help in order to recognize children who are at risk for ASD at any age (17). The Infant-Toddler Checklist, is a screening tool for communication impairments in children aged from 6 - 24 months, and has been proved to identify autism and language delay (67). The Modified Checklist for Autism in Toddlers (M-CHAT-R/F) is a common tool for screening toddlers for ASD. It is composed of 20 questions referred to the caregiver. A high score must be followed by a structured interview by a health care professional (68). A new tool, called PAIS, has been recently developed in Greece for screening for ASD in toddlers in Greek population (69).

Diagnosis

The diagnostic evaluation depends on which resources are available as well as the clinician's experience. The ideal approach would be made by an interdisciplinary team that specializes in neurodevelopmental disorders and autism in particular, but this is often impossible. Furthermore, there are usually delays in the appointments due to high demand (17). Most of the communities have a specialized clinician, who is able to interpret information and comfortable with making the diagnosis of autism spectrum disorder (17). This can be a child psychiatrist or neurologist, a developmental-behavioral pediatrician or a pediatric psychologist. The clinical standard for the diagnosis of autism is clinical

assessmnet and application of the criteria *according to DSM* or *ICD*. There is important overlap in symptoms among different neurodevelopmental disorders, especially in very young toddlers and children with intellectual disability or impairments in language, and it is crucial for the clinician to consider differential diagnoses(17).

Standardized rating scales, such as the assessment tools completed by caregivers, teachers, or other intervention professionals, may be used in order to collect and quantify information.

Autism Diagnostic Interview—Revised (ADI-R) and Diagnostic Interview for Social and Communication Disorders (DISCO) include structured caregiver interviews used to gather information about symptoms observed in the present or in the past. This information can help the clinician to come to a conclusion about the diagnosis (17).

The Autism Diagnostic Interview-Revised is a semi-structured diagnostic interview used to assess behaviors associated with ASD (70).

The ADI-R is based on ICD-10 and DSM-IV criteria for ASD includes questions about the child's development, social interaction, communication, and patterns of behaviors. It yields scores not only for current behaviors but also for the child’s history resulting in cutoff scores, indicative of the presence of ASD. The classification of ASD is given when scores in all of the three domains (social interaction, communication and patterns of behavior) are equal or higher than the specific cutoffs, as long as the onset of the disorder is evident by the age of three (70).

The Diagnostic Interview for Social and Communication Disorders (DISCO) is another diagnostic tool for ASD (71). It enables the systematic collection of information for a wide range developmental skills and behaviors and it can be used to assess children at every level of ability and at all ages. It can help the clinician to create a profile for every child and enables him to identify specific signs found in ASD (71).

The direct clinical assessment includes standardized, developmental and psychological testing, and behavioral observation. Nonverbal intellectual ability, verbal communication and adaptive behavior should also be assessed (17). The administration of standardized observation/elicitation direct assessment tool, specific for ASD, such as Autism Diagnostic Observation Schedule (ADOS) or Childhood Autism Rating Scale (CARS) is considered essential (17).

**ADOS.** The Autism Diagnostic Observation Schedule, is a standardized, semi-structured, clinical evaluation tool based on play activities. It is designed to collect information about freciprocal social interactions, communication and repetitive/restricted behaviors related to the diagnosis of autism. This specific tool yields a very precice picture of current symptoms, independently of language. It may be used to assess any individual from non-verbal 1-year-olds to verbally fluent adults (72).

**CARS.** A commonly used tool for the detection and diagnosis of ASD is the Childhood Autism Rating Scale (CARS). The CARS comprises 14 areas assessing behaviors linked to autism and a 15th area rating general impression of ASD (73).

Physical examination including assessment for dysmorphic features and extensive neurological examination should be included in the assessment. (17).

The goal should be to determine the child's diagnosis, even if ASD is excluded, and the diagnostic results should describe information for every domain of the child;s development as well as the child's functioning. (17). Children diagnosed with autism require periodic re-assessment in order to refine their weaknesses, strengths and educational needs.

Management.

The duties of the pediatric health care professionals do not end with the diagnosis of ASD. Comprehensive management of children diagnosed with ASD consists of conducting an etiological investigation and providing genetic counseling; providing health care and promoting well-being of the child, guiding families to effective medical, behavioral and educational interventions. Moreover, the pediatrician should provide support by educating the parents and giving them access to resources, in order to alleviate their stress. Lastly, primary pediatric health care professionals, besides undertaking these duties, they could also coordinate subspecialty care or other services and make the respective referrals.

**Etiologic Investigation.** There is no single consensus approach to etiological evaluation for children diagnosed with ASD, at present.

An etiologic evaluation begins with an extended family and medical history and physical examination. It is important that the child is assessed for abnormal growth (especially head circumference), congenital anomalies, skin manifestations of neurocutaneous disorders, evidence of visceral storage and neurological abnormalities (74). When a metabolic disorder or a specific syndrome is suspected, the appropriate targeted testing or referral to medical geneticist should be conducted. If not, genetic testing - starting with CMA (Chromosomal Microarray Analysis) and Fragile - X testing are recommended. If still no genetic etiology is revealed, proceeding with WES (Whole Exome Sequencing) - as described below- could help in the etiological evaluation.

Identifying a genetic etiologic diagnosis is important in order to provide accurate prognosis and counseling for recurrence risk. It would also help to recognize and treat comorbidities and to guide caregivers to specific resources. (75).

**Chromosomal Microarray Analysis.** CMA is a test aiming to reveal a certain pathogenic CNV (copy number variation), which according to clinical cohorts is found in 5% to 14% of children diagnosed with autism (76, 77). This detection rate reaches 17-24%, when cases

with revealed variants of controversial significance are added (78-80). WES is proven to be cost-efficient and useful and in the etiopathogenic investigation of individuals with developmental disorders, such as ASD (81-84).

**Fragile X Testing. Frigile X is identified fairly frequently in both males and females with autism, therefore** it is justified to routinely test both for this syndrome as a routine(85, 86). Furthermore, testing is cost-effective and provides the possibility for genetic counseling. Fragile X testing should be ordered separately from CMA or WES, due to the fact the CGG trinucleotide repeat expansion, causing fragile X syndrome, cannot be detected on these tests(17).

If the diagnosis is made by physician, he/she should also undertake the responsibility for etiological investigation. Pretest counseling should include description of the nature of the test, potential outcomes and possible effect on other members of the family.

Many pediatric subspecialists, capable of diagnosing ASD, are accustomed to ordering and explaining CMA and Fragile X testing. Many times the referral to a medical geneticist is needed in order to have a full interpretation of abnormal or equivocal results, especially if these include WES(17).

## Treatment

Currently, there is no effective treatment for ASD. Several interventions have been developed and studied for approaching young children diagnosed with ASD. The purpose of these interventions is to mitigate the core deficits (social interaction and communication and repetitive and restrictive and maladaptive behaviors) and to maximize

the individual's independence, by facilitating skill development (87). In particular the targets of interventions are:

- Building skills that are developmentally appropriate: non verbal and verbal communication, interpersonal social skills, play skills, self care skills, self regulation and emotion management skills, higher cognitive functions and preacademic/academic skills, motor skills (87).

- Reducing maladaptive behaviors such as general symptoms, difficulties in emotional regulation, non functional, restricted and repetitive patterns of behavior, activities or interests, problem behaviors that could harm the child or others and interfere with expected routines in the community (87).

The primary methods used for achieving the above goals are the non pharmacological, psychosocial interventions such as developmental, behavioral and educational interventions (87).

**Applied Behavioral Analysis (ABA).** ABA is a method of intervention based on the assumption that most behavior is learned and controlled by contingencies and that the deficits associated with ASD represent learning difficulties and the behaviors exhibited are consistent with laws of operant learning (88). ABA interventions include a variety of strategies ranging from naturalistic teaching approaches, that are child led and may be implemented in the context of play activities or play routines, to highly structured adult-directed approaches. Most of the empirically supported interventions in the current literature have their basis in the ABA method (17, 88).

**Developmental Social Pragmatic (DSP).** DSP models such as Denver model, focus on increasing caregivers's responsiveness by imitating, providing more information and joining into child-initiated play activities and on moderating the main deficits of the

disorder in the domain of affective social engagement, joint attention and imitation (17). The mitigation of these deficits is thought to help the development of reciprocal social behavior, emotional relationships, language, and cognitive abilities like theory of mind (17).

**Naturalistic Developmental Behavioral Intervention (NDBI).** NDBI strategies, such as Early Start Denver Model (ESDM), consist of both ABA and DSP components. They constitute empirically supported teaching strategies, implemented in natural settings. Shared control between therapist and child, behavioral strategies and natural contingencies, are involved so that children can learn developmentally required and appropriate skills (17, 89).

**Structured Teaching.** An example of structured teaching is the Treatment and Education of Autistic and Related Communication - Handicapped Children (TEACCH). This intervention includes devising a curriculum based on the development assessment, in order to teach children the desired skills. This curriculum is strictly structured and includes predictable activities in familiar environment, as well as the use of illustrated schedules (17). The purpose of the structure teaching is to maximize learning possibilities, ensuring optimal adaptation avoiding frustration caused by sensory dysregulation or distractions.

**Transitional Habilitative Therapies.** The intervention programs of children diagnosed with ASD also commonly include speech and occupational interventions. As speech therapy is regarded, a variety of communication modalities, such as spoken language, sign language, gestures, written language, picture communication may be used in an individualized program, based on the child's abilities and the contexts of communication (17). Occupational therapists address fine motor deficits as well as adaptive deficits interfering with achieving self-care and academic goals. They may also modify the materials of the classroom and the routines in order to increase attention and organization and promote play skills (87). Another contribution of occupational therapy in the ASD

intervention programs is the sensory processing intervention. This could be divided into sensory-based interventions and sensory integration therapies (SITs). SITs are clinic-based interventions that use sensory-rich activities, directed to the child in order to improve the child's adaptive responses to sensory experiences (90). On the other hand, Sensory Based Interventions (SBI's) are adult directed, classroom based strategies that use single sensory stimulations or a combination of them, such as massage, brushing, swinging, wearing a weighted vest or bouncing on therapy ball, to mitigate behaviors attributed to sensory modulation disorders (91).

**Medical treatment.** Psychotropic medication has not been found to correct the social and communication deficits which are the core characteristics of ASD. Their impact on repetitive and restricted behavior is also limited (92). Nevertheless, they are commonly used to target coexisting psychiatric disorders such as attention deficit hyperactivity disorder (ADHD), anxiety disorders and mood disorder(92).

**Unestablished Therapies.** Therapies based on insufficient evidence, such as facilitated communication, auditory integration training, animal-assisted interventions, floortime movement integration, concept mapping, theatre intervention, sensory intervention package, cognition intervention, social behavioral learning strategy and social thinking intervention, are considered unestablished and there is no sufficient literature to determine their effectiveness(17). Complementary and Alternative Medicine (CAM) treatments including special diets, dietary supplements, chelation (a treatment that remove heavy metals from the body), biologicals (secretin), hyperbaric oxygen therapy, detoxifying clay baths and various products, including raw camel milk, chlorine dioxide and essential oils are not only considered inefficient but also potentially dangerous, according to the FDA (U.S Food and Drug Administration)(93, 94).

The use of stem cell transplantation as a method for treating autism is a current topic of research. Preclinical evidence highlights important advances and potential benefits.

Nevertheless, the mechanisms by which stem cell transplantation could lead to a structural reorganization and functional recovery have to be better clarified. To date, the five clinical trials that have been performed are characterized by great heterogeneity regarding study design, sample, types of cells and administration route, as well as outcome measures. As a result, more extensive studies and larger trials need to be performed in order to define the cost-benefit ratio (95).

## TWICE EXCEPTIONALITY

During the last decades, a population of children that both present with extraordinary abilities as well as with learning, attention or behavioral difficulties, has engaged the attention of educators, practitioners and parents (4).

### Definition

The term “twice exceptional”, also mentioned as “2e”, is used to define children that have potential for high performance, characteristic of gifted children, and also show evidence of at least one disability (96). These disabilities may include speech and language disorders, specific learning disorders, ASD, ADHD, emotional and behavioral problems or physical disabilities (96). The above simple definitions belie the complexity and the multiple issues related to the twice exceptionality. Twice exceptional students are difficult to define as there is no universally accepted definition for giftedness or for disabilities. Just like other gifted children, twice exceptional children are highly talented or knowledgeable in at least one particular domain (96). However, their giftedness is commonly overshadowed by their difficulties or the students may mask their deficits using their talents to compensate, giving the impression of an average school performance(96). Due to the average performance in class, both giftedness and difficulties may be overlooked by the educators or the parents, as “average” is considered appropriate and does not raise any concerns (4). In reality though, this performance reflects a failure to thrive.

Twice exceptional students may face difficulties in the school environment, where long-term planning, organization and participation are important (96). They can be imaginative, highly creative, curious, with strong problem-solving ability and may have a single allconsuming interest or a wide range of interests (96). However, at school, they may fail to keep up with the course rigidity and demands or the great volume of the daily curriculum, all resulting in an inconsistent academic performance, difficulties in written expression and lastly, frustration (96). Labels as underachiever, unmotivated or lazy can be assigned to these children, affecting their self-confidence, self-efficacy and motivation(96). The excitement for school is impeded in these cases, creating a vicious cycle of underachievement and low self-esteem (96).

Approach

For the purpose of fully supporting twice-exceptional children, special arrangements should be made to address their conflicting set of needs. Children's strengths should be recognized and their abilities should be nurtured while supporting their special needs and challenges. A multifaceted approach should focus on their intellectual and social/emotional environments (96). Creativity and an open mind are often needed to dually differentiate in minimizing the effects of their difficulties while maximizing intellectual challenge (96).

**Educators.** As educators are regarded, differentiating the curriculum's content and type may be important in order to cover the 2e student's interests and nurture their strengths (97). Moreover, these students, as all students, may benefit from having varying options in demonstrating their skills and ideas These options could include alternate work products, such as art, songs, minecraft, as well as simulations, hand-on activities, problem-based learning, role playing and art integration (4). Routine and repetitive work should be abandoned. Modifications should include decreasing the amount of work, eliminating handwriting, traditional tests and class participation and mixing small group work with

independent work (4). The use of visual means such as charts and graphics is also helpful. The collaboration with parents is considered essential (96).

**Parents** should act as advocates for their children, by knowing and informing the school about the child's learning style, strengths and weaknesses (96). The establishment of a collaborative rather than a combative approach in helping the educators to understand and obtain the necessary interventions needed for their child's success, is important (96). Open and positive communication and team approach is also considered useful(4, 98). Parents' acceptance and support are essential for the child's self esteem.

As it is entailed by the definition of the twice exceptionality, 2e children comprise an heterogeneous group of children, each of them idyllically needing a personalized and tailor made educational and counseling approach (98).

## GIFTEDNESS AND AUTISM SPECTRUM DISORDER

As it happens with other neurodevelopmental disorders, autism and giftedness are not mutually-exclusive. Despite the limited data documenting the co-occurring of both entities, many case studies have been published over the years. In some cases, ASD might mask giftedness or vice versa (99). On the other hand, the misdiagnosis is not rare, as gifted/talented children might display behaviors that resemble autism or children with ASD might present with behaviors that could be attributed to their giftedness (99). All of the above scenarios are unfortunate, because children do not receive the appropriate interventions.

As regards the similarities and differences between High Functioning ASD (HFASD), formerly referred as Asperger Syndrome, and giftedness, Neihart et al. pointed out that despite the fact that both groups may use the language of older children, children with HFASD tend to have more pedantic and seamless speech (100). Concerning the

response to routines, although both groups may be described as resistant to changes, ordinary gifted children are usually not as rigid as HFASD about routines (100). Moreover, gifted children are aware of their exceptionality, while children with ASD are oblivious to it (100). The attention of the gifted children is most commonly distracted by external factors, whereas the attention of the HFASD children is internally disturbed (100). Gifted individuals can be engaged in reciprocal humor. HFASD children, on the other hand, although they can be creative with words, they lack the social reciprocity that lies beneath humor (100). Affective expression could be one of the distinguishing characteristics between the two groups. HFASD children may have flattened restricted or inappropriate responses which is not the case for gifted individuals. The lack of insight of the feelings, interests and needs of other people characterizes only the ASD group. Stereotyped behaviors and motor clumsiness are not usually observed in gifted children (100).

Boschi et al. , in a relatively recent systematic review, attempted to point out the similarities between children with ASD with no language or intellectual delay, (formerly referred to as children with Asperger Syndrome) and children with High Intellectual Potential (HIP) (101). The most common similarities between the two groups (HIP and ASD) seem to be the advanced verbal skills (including extended vocabulary), the heterogenous performance in WISC test, indicating of strengths and weaknesses, atypicalities in sensory modulation, attention problems, emotion regulation difficulties, disharmonious developmental trajectory, high prevalence of lefthanders and greater involvement of the right hemisphere of the brain (101). However, according to the same study, there are also differences between the two groups, with the HIP group outclassing in FSIQ and socio adaptive skills (101). On the other hand, as expected, children with ASD had more severe symptomatology compared to the HIP groups which presented with some autistic traits (101).

Concerning gifted children with ASD, an older systematic review of the literature showed no specific pattern of characteristics (102). However, significant discrepancies between

verbal and practical IQ, asynchronous development (cognitive in opposition to social skills), advanced non-verbal skills (e.g. mathematics, computer skills), language characteristics (nearly absent prosody and pedantic speech) , restricted special interests and intense focus on details, excellent factual memory, social difficulties (difficulties in reciprocal communication and social adaption, constant talk about specific interests and unawareness of social rules) and hypersensitivity are some of the characteristics described in intellectually gifted children with ASD (102).

## RESEARCH PART

## SYSTEMATIC LITERATURE REVIEW

### MATERIALS AND METHODS

#### Literature Search Strategy

Studies were identified by searching four different electronic databases (PubMed, Google Scholar, PsycInfo and Embase) and scanning reference lists of articles. The last search was run on 31 December 2020. The following algorithm was applied to PubMed (1968 - Present) and Google Scholar (1970 - Present): (gifted OR giftedness OR talented OR "high ability" OR “high intellectual potential” OR “high IQ” OR “high intelligence quotient”) AND (("Asperger's syndrome" OR autism OR ADHD OR "attention deficit" OR “developmental disorders” OR “developmental disorder” OR “developmental disability” OR “developmental disabilities” OR “neurodevelopmental disorder” OR “neurodevelopmental disorders” OR “communication disorder” OR “communication disorders” OR “specific learning disorder” OR “specific learning disorders” OR dyslexia OR dyscalculia OR “movement disorders” OR “tic disorders” OR “tic disorder” OR “Tourette syndrome”) OR “twice exceptional”) AND (child OR children OR student OR adolescents OR adolescence OR teens OR teenagers). This algorithm was appropriately adapted for PsychInfo (1965 - Present) and Embase (1974 -Present).

#### Eligibility Criteria

The eligibility criteria were based on the PICOS (Participants, Intervention, Comparison, Outcomes, Study design) acronym (103). Regarding participants, children and adolescents up to 21 years of age were included. Neurodevelopmental disorders included Intellectual Disabilities, Communication Disorders, ASD , ADHD, Specific Learning Disorder, Motor Disorders, Other Neurodevelopmental Disorders) (18). Giftedness was defined as demonstration of outstanding levels of aptitude or competence in one or more domains ( e.g. mathematics, music, language) and/or set of sensimotor

skills (e.g. painting, dance, sports)(1). Eligible studies had to provide data about the coexistence between neyrodevelopmental disorders and giftedness.

**Outcomes.** According to a position statement of the the National Association for Gifted Children (NAGC), approved in 2010, the children who show exceptional levels of ability to learn and reason or outstanding competence in one or more domains (performance in top 10%) are considered gifted. The domain may be any structured activity such as mathematics, music and language, or sensorimotor skills such as painting, dance and sports (1).

Prospective cohorts, cross-sectional and case control studies were included. Case reports and review articles were excluded. Given the various study designs, studies comparing percentages/scores of giftedness in subjects with vs without neurodevelopmental disorders as well as studies also comparing percentages/scores of neurodevelopmental disorders in subjects with vs. without giftedness were deemed eligible.

In addition, to enrich the pool of evidence, non-comparative studies reporting percentages of giftedness in the studied disorders, or percentages of disorders in gifted youth, were eligible

Only the articles written in English language were deemed eligible. No limits were applied for publication status.

Eligibility assessment was performed independently by authors working in pairs in a blinded fashion.. Disagreements between reviewers were resolved by team consensus (Figure 1).

Data Collection Process and Assessment of Quality

A data extraction Excel sheet was developed in a structured coding scheme. From each study data considering study period, study design, sample size, gender, age, study population, matching factors, definition and technique of studying giftedness and neurodevelopmental disorders and main study findings were collected. Data abstraction was performed independently by authors working in pairs n a blinded fashion; any disagreements were resolved by team consensus.

The Newcastle-Ottawa scale was used in order to assess risk of bias of included studies, evaluating selection (representativeness, sample size, nonrespondents and ascertainment of exposure), comparability and outcome (103).

**RESULTS**

Selection and description of included studies

The literature search yielded a total of 6068 results, after removing duplicates. 5929 articles were deemed irrelevant from title and abstract, whereas 139 were evaluated in full text. Among the latter, 106 were excluded due to various reasons and ultimately a total of 32 studies (involving 9904 subjects) published between 1988 and 2020 were included in the present review. Ten of the eligible articles were investigating the correlation between giftedness and ASD (104-113). The PRISMA flowchart is presented in Figure 1, describing the successive steps in selection of studies. The general characteristics, as well as the summary findings of the quality assessment (risk of bias) of the studies concerning ASD are presented in Table 1.

A positive assosiation between ASD and giftedness was supported in two of the included studies (108, 112). Specifically, Heaton et al. compared musically naive autistic children with musically naive control subjects, matched for mental age, for their ability to identify and remember speech sounds or single-note frequencies (112). The results

revealed that although both groups identified and remembered speech sounds equally well, the autistic group compared to control subjects, showed a superior ability to identify and recall single music notes (112). The results were attributed by the authors to the predominance of local rather than global processing of stimuli as a cognitive processing strategy commonly used by autistic individuals (112). Similarly, in a more recent study, Masataka et al. investigated the ability of aesthetic perceptual judgment of music in male children diagnosed with ASD, compared to typically developing males, matched for chronological age (108). The study revealed that the ASD group preferred the aesthetic quality of the highly dissonant music, compared to the TD group, when the stimuli included consonant or dissonant musical stimuli from different composers (108). Preferring dissonant music is considered more aesthetically demanding perceptually. Therefore, these results indicated that ASD children possess an enhanced capability of aesthetic judgment of music. Subsidiary data showed that absolute pitch ability was common only in the ASD children, some of whom also possessed extraordinary musical memory (108). The authors imply that these results emphasize the notion of neurodiversity, a term used to describe potentially gifted qualities in people diagnosed with ASD (108).

On the contrary, two of the eligible studies showed a negative association between ASD and giftedness (106, 109). In particular, Craig et al., showed through three different experiments, that autism and Asperger Syndrome (AS) groups scored significantly lower than the control groups in creativity tests (106). Children with ASD were capable of generating possible novel changes to an object (106). However, the possible changes were fewer and more reality based, rather than imaginative, compared to those made by the controls. The results were attributed by the authors both to executive dysfunction and imagination deficits. Imaginative fluency was also found impaired in the ASD group (106). Furthermore, Oswald et al. studied the widely-held belief that most individuals with ASD are mathematically gifted. In this study, both the relative proportions of ASD youth

demonstrating mathematical giftedness and the cognitive/clinical characteristics best predicting mathematical achievement in ASD individuals, compared to TD peers, were assessed (109). Results indicated that a greater proportion of ASD students demonstrated math achievement suggestive of a mathematics learning disability (22%) rather than mathematical giftedness (4%). The linear regression model indicated that even after accounting for the strongest predictors of math problem solving, such as perceptual reasoning, verbal ability and test anxiety, the diagnosis of ASD was associated with a large deficit in math problem solving (109). These results update the theories of math ability in ASD individuals and emphasize the possible needs and targets for intervention, when regarding students with ASD struggling with mathematics (109).

Overall, Hetzroni et al. demonstrated that the group of children with ASD performed similarly in creativity tests to the group of TD children (104). Particularly though, Pictorial Multiple Solutions (PMS) Task indicated higher performance in fluency and originality in the TD children, while children with HFASD demonstrated higher performance in the fluency and the flexibility measures in the Creating Equal Number (CEN) test, evaluating mathematical creative thinking (104). According to Meng-Lung et al., although AS participants performed significantly higher in originality and elaboration, when assessed for creativity using the Creativity Assessment Packet (CAP), their scores in openness, flexibility and imagination were significantly lower than those of controls (107).

Other studies, found no statistically significant correlation between ASD and giftedness. Aleksandrovich et al. revealed no significant association between ASD and creativity, assessing line, size, colour and details in drawings from both ASD and TD children (105). This was also the case for Jamey et al., who studied the correlation between ASD and music perception abilities, using the Montreal Battery for the Evaluation of Musical Abilities (MBEMA) (105). The study did not record any significant difference between the ASD and TD group for melodic pitch discrimination, rhythm discrimination or melodic pitch memory, but a main effect of verbal IQ in rhythm discrimination was found

in the ASD sample (105). According to Doobay, there were no statistically significant differences in verbal and nonverbal intellectual functioning, including Verbal Comprehension, Perceptual Reasoning and Working Memory between gifted children with and without ASD, except in processing speed which was lower in the ASD group (111).

Lastly, Charman et al. in a non-comparable study, assessed the prevalence of high IQ in the ASD population, using Wechsler Intelligence Scale, Raven's Standard Progressive Matrices or Coloured Progressive Matrices for Children, and estimated it at 2,7 % (113).

## DISCUSSION

Throughout the years, several myths have arisen suggesting that children diagnosed with neurodevelopmental disorders possess unusually high abilities in specific domains, depending on the disorder. On the other hand, special skills and talents in children with developmental disorders are most commonly overshadowed by their difficulties. A lot of literature in this field focuses on the presentation of cases of twice exceptional children or on commenting on why clinical presentation of the two identities may overlap, cautioning against misdiagnosis. The present systematic review was an effort to gather and study all the existing literature and data in order to determine the association between giftedness and each neurodevelopmental disorder in particular. The results concerning giftedness and ASD are presented in this thesis.

Interestingly, a significant, positive correlation was observed in two studies concerning ASD and music ability (108, 112). Despite the usual inability of autistic individuals to assign learned note names, an autistic tendency towards segmented information processing seemed to lead to stable long-term representations, resulting in

demonstration of advanced capacity for pitch memory and pitch labeling (112). Additionally, it seemed that children with ASD possess a more developed capability of aesthetic judgment of music even though musically untrained (108). Masataka et al. attributed this result to the fact that although individuals with ASD do not rely upon their social relationships, they are predisposed to process perceived non-social objects in more depth, which manifests itself as hyper-sensation and hyper-attention to detail (108). Lastly, only one study didn't record any significant difference between the ASD and TD group regarding musical ability (110).

Regarding creativity, among individuals with ASD, in a recent study, children with and without ASD performed overall similarly in a creativity assessment, with the ASD group slightly outperforming in mathematical creative thinking, while the control group performed better in general creative thinking (104). The above results contradicted a previous study, where children with ASD seemed to perform worse than typically developing individuals in imaginative creativity, emphasizing the role of imagination deficits in the impoverished creativity in ASD (106). Meng-Lung et al. came to ambivalent conclusions, regarding the correlation between autism and creativity, depending on the different measures of creativity assessed (107).

As regards intellectual functioning, there were found no significant differences while comparing intellectually gifted with or without ASD (111). The only exception was the processing speed, which was lower in the ASD group (111). The above study attributes to the current literature to address the characteristics of gifted children with ASD and to distinguish their characteristics from the those of gifted children without ASD (111). However, this specific field is still lacking investigation of these issues. Another study that assessed the prevalence of intellectual giftedness in children with ASD, estimated that at 2.7% (113). This proportion is equal or lower compared to the relative proportion of TD children - according to the different definitions of giftedness this varies from 3 -10 % (1). A wide disparity is observed in the literature concerning the perceptions of mathematics

abilities in the ASD population. The most dominant view is that students with autism are mathematically gifted and often have success in science, technology, mathematics, and engineering. This opinion has been further supported by the theory that ASD children have outstanding systemizing skills, which gives them the ability to outperform in fields like mathematics that depend upon rule-bound, systematic procedures and logic (114). The only eligible study concerning ASD and mathematical ability, contradicts the above theories, proving that ASD is mostly linked to disability rather than mathematical giftedness(109).

Commenting on the included literature, it should be kept in mind that children with ASD, despite their difficulties, may have special skills and talents in very specific domains which are often overshadowed. These children, as shown above, represent a very heterogeneous population. The lack of a universally accepted definition of giftedness and, consequently, of twice exceptionality, leads to underrepresentation of twice exceptional individuals in the school community. These students often experience frustration during their school years, as teachers are usually unaware of their dual exceptionalism and they might treat them as underachievers. Therefore, a very careful assessment of these children, by educators and developmental specialists, is of vital importance, in order to recognize their strengths and weaknesses and to design targeted individualized interventions that address their needs. Furthermore, counseling should be available for students, parents and educators in order to face possible psychological effects of this dual exceptionality. Policy makers should take into account the special characteristics of this group and facilitate the interventions recommended above, by endorsing individualized education programs.

The results of this review should be interpreted with caution, taking into account the limitations of the included studies. Firstly the majority of the studies are rated low in the quality assessment, as evidenced by Newcastle Ottawa scale (115). Secondly, the variability in the definition of giftedness and the tools used to assess the disorders, some

of them not validated, set more limitations in the interpretation of the results. The small size of some samples, the inclusion of studies only English written studies and the lack of multivariate adjustment contribute to these limitations. Moreover, the cross-sectional design of most studies raises limitations considering the clarification of a causal relationship between ASD and giftedness; longitudinal studies on the field are needed.

## CONCLUSION

In conclusion, this systematic review highlights potential association between specific types of giftedness and ASD. Given the variability in the definition of giftedness and the tools used to assess both entities. Further accumulation of longitudinal data on this methodologically challenging interplay are needed.

## TABLES AND FIGURES

| Study | Region | Study period | Study design | Sample size | Males, % | Mean age | Age range | Study population | Type of giftedness studied | Technique of studying giftedness | Definition of giftedness | Neurodevelopmental disorder studied | Technique of studying neurodevelopmental disorder | Matching factors | Effect sizes and interpretations of the main study findings | NOS Quality Rating |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Aleksandrovich M. (2014) | Słupsk, Poland | March-April 2013 | CS | 18 | 68 | ASD group: 6; TD group:5.9 | 4-7 y | Integrated kindergarten (for children with special and typically developing children) | Creativity | Goodenough-Harris Drawing Test (GHDT) - Auto portrait | NR | ASD | NR | Age | • No statistically significant differences between drawings of ASD and TD in line, size, color and details | 2/10 |
| Craig J. (1999) | Merseyside, Cambridgeshire and Peterborough, UK | NR | CS | 60 | NR | 10.7 | NR | Children in ASD /Asperger groups: attending special schools in Cambridgeshire or Merseyside or, UK. MLD group: attending a special school in Peterborough, UK and normal group: attending a primary school in Merseyside. | Creativity | TTCT | NR | Autism/ Asperger | NR | No matching | • Experiment-1:. ANOVA: significant group effect, F(3, 56) = 19.31, p <0 .001. Autism and AS groups scored lower than the other two groups in Condition 1 (p=0.005). In Condition 2, autism group scored lower than the control groups.<br>• Experiment-2: Significant group effect, F(3, 56) = 21.55, p<0.0001. Autism and AS groups differed from the control groups (p=0.01).<br>• Experiment-3: Significant group effect, F(3, 56) = 14.38, p<0.0001. The autism and AS groups differed from the control groups (p=0.01). | 1/10 |
| Doobay A. (2010) | Iowa, USA | Fall 2010 | CS | 81 | ASD group :85 Non ASD group :51 | ASD group:10.7; Non ASD group:9.43 | ASD group: 5-17; Non ASD group: 6-16 | School-age youth identified as intellectually gifted. | IQ | WISC-IV or WAIS III | IQ>130 | Autism | ADOS; ADI-R | NR | • No statistical difference between ASD and Non ASD group on FSIQ, Verbal Comprehension Index, Perceptual Reasoning Index, or Working Memory Index.<br>• Significant difference between the ASD group and the NonASD group on the Processing Speed Index, t(79) = 3.85, p <0.001. | 3/10 |
| Heaton P. (1998) | NR | NR | CS | 20 | 100 | Autism/ Asperger group: 9.9 ; Control group: 8.1 | Autism/ Asperger group: 7 -13; Control group: 5-11.6 | Autistic boys attending a school for able autistic children ( no visual or auditory impairments) and normal boys of average academic ability. None of them had specific musical training, or known outstanding musical ability. | Absolute Pitch (AP) (musical) ability; pitch; identification; pitch memory | Animal-tone pairs; animal-speech sound pairs | NR | Autism | NR | Chronological age to the mental ages of the autistic group | • Autistic children: superior ability for single-note identification and memory over both time intervals, F(l9 18) = 11.31, p<0.003.<br>• No significant difference between the groups for speech sounds, F(l,18) = 1.32, NS. | 2/10 |

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| Hetzroni O. (2019) | Haifa, Israel | NR | CS | 40 | 68 | 10.11 y | 9-11 y | Hebrew speaking elementary students, with no hearing, vision, language, attention, learning or intellectual difficulties, and with an average socio-economic level and family monolingualism. | General and mathematical creative thinking | PMS task, CEN task | NR | High Functional ASD | DSM-V, Childhood Autism Rating Scale, Second Edition High-Functioning (CARS2-HF) Version | NR | • ASD children performed similarly in creativity tests with TD children. TD children performed better in fluency and originality in the PMS test. ASD children performed better in the fluency and in the flexibility measures in the CEN test<br>• CEN fluency $\eta^2$: 0.104 , p=0.042<br>• CEN flexibility $\eta^2$:0.150, p=0.013<br>• PMS fluency $\eta^2$ : 0.122 , p=0.027<br>• PMS originality $\eta^2$:0.128, p= 0.024 | 5/10 |
| Jamey (2019) | Montreal, Canada | NR | CS | 64 | 100 | 10.1 | 6-12 years | Samples recruited from laboratory databases and through the local community. Participants from the TD group were excluded when having a family history of ASD. Exclusion criteria; gestational age <35 weeks and hearing impairment, missing IQ scores, or a verbal IQ >145 | Music perception abilities | Abbreviated Montreal Battery for the Evaluation of Musical Abilities (MBEMA) | NR | ASD | ADOS; ADI-R; SCQ; Social Responsiveness Scale (SRS)>13 (severity of ASD) | No matching | • The MBEMA results for the ASD-vs-TD sample : no differences in melodic pitch discrimination (F(132) = 0.67, p = 0.41, $\eta_p^2$ =0.02), rhythm discrimination (F(132) = 1.18, p = 0.29, $\eta_p^2$ = 0.01) or melodic pitch memory (F(132) = 0.03, p = 0.86, $\eta_p^2$ < 0.01<br>ASD-vs-TD sample: main effect of verbal IQ on rhythm discrimination (F(132) = 4.29, p =0 .046, $\eta_p^2$ =0 .12). | 6/10 |
| Masataka N. (2017) | NR | NR | Case control | 47 | 100 | ASD group: 5.8; TD group:5.6 | 4-7 | • Musically untrained, Japanese, auditorily normal, right-handed, attending normal classes and naïve to the purpose of this study . ASD children were verbal. The TD sample: children from a small city in Japan with no autistic traits or symptoms of other pervasive developmental disorder . | Musical pitch | • <u>Experiment 1:</u> the original, harmonic version of a Mozart's simple minuet (C major K.#1f) and its modified, inharmonic version<br>• <u>Experiment 2:</u> four musical pieces: Mozart's piano sonata K.448, Bach's toccata in G major BWV 916, Schoenberg's Klavierstuek op.33a, and Adagio in G minor for organ and strings by Albinoni.<br>In testing of AP ability (<u>Experiment 3)</u>, the participants heard 36 pure sine wave tones, in pseudorandomized order, from A3 (tuning: A4 = 440 Hz) to A5, each tone was presented once. | NR | ASD | Diagnosis by an independent child psychiatrist based on ICD-10 as well as DSM-IV; ADI-R | NR | • Experiment 1: Both samples preferred listening to the original consonant version of the minuet. One of the two main effects (STIMULUS) was statistically significant [F(1,45) =49.53, p<0.0001, $\eta_p^2$=0.299]. The other main effect (PARTICIPANT) was not significant [F(1,45) =0.84, p=0.46, $\eta_p^2$ =0.033]. The interaction between PARTICIPANT and STIMULUS was significant [F(1,45) =4.25, p=0.028, $\eta_p^2$ =0.35].<br>• Experiment 2: Absolute pitch ability was only found in ASD children, some of whom also had extraordinary musical memory. Both of the two main effects were statistically significant [F(1,45)=48.33, p<0.0001, $\eta_p^2$ =0.287 for STIMULUS and F(1,45) =9.12, p=0.009, $\eta_p^2$ =0.133 for PARTICIPANT]. The interaction between PARTICIPANT and STIMULUS was also significant [F(3,135)=4.25, p=0.012, $\eta_p^2$ =0.30].<br>• Experiment 3: some instance of extraordinary musical memory in their children was reported by six parents of the children with ASD. There was no such report by any parent of the TD children. | 5/10 |

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| Meng-Lung L. (2011) | Lingya District, Kaohsiung, Taiwan. | NR | Case control | 58 | 100 | Experimental group:10.6; Control group: 10.4 | Experimental group: 10.5-11.7; Control group: 10.2-11.9 | • ASD group was recruited from a local association of parents of high-functioning children with autism or Asperger syndrome (no history of other psychiatric disorders). The control group was recruited from the schools of the participants with AS (no family history of psychiatric conditions) | Creativity; Non-verbal; intelligence; Verbal ability | Creativity Assessment Packet (CAP); Test of Nonverbal Intelligence, Third Edition (TONI-3); Peabody Picture Vocabulary Test-Revised (PPVT-R) | NR | Asperger Syndrome (AS) | Diagnosis by psychiatrists according to DSM-IV criteria | NR | • The AS sample in originality ($p < 0.01$) and elaboration ($p < 0.05$) are significantly higher than the scores of the control group.<br>• The scores of AS sample, in openness ($p < 0.01$) and flexibility ($p < 0.001$) are significantly lower than those of controls. The AS sample scored ($p < 0.001$) significantly lower on a t-test than that of controls in imagination (divergent feeling).<br>• The nonverbal divergent thinking was significantly correlated to nonverbal IQ ($p < 0.05$) for participants with AS. | 5/10 |
| Oswald T.M. (2016) | California, USA | NR | Case control | 54 | 77.7 | ASD: 14.88; TD: 14.73 | ASD: 12-17.83; TD: 12.08-17.67 | • Both samples were recruited from the community through the University of California (UC) Davis MIND Institute's Subject Tracking System database, the MIND Institute's Facebook page, and fliers posted at local public middle and high schools. Both samples had a full-scale IQ > 80 on the Wechsler Abbreviated Scales of Intelligence. Exclusion criteria for ASD group: diagnoses of autism with known genetic etiologies or current diagnoses of psychosis. | Mathematically giftedness | WAIS-II; WRAML2; WIAT-III | NR | ASD | ADOS-2; SCQ-Lifetime Version (score>=15) | full-scale IQ and nonverbal IQ | • Most of the ASD students exhibited math achievement indicating mathematics learning disability (22%) rather than mathematical giftedness (4%). The ASD group consisted of a significantly greater proportion of participants with math disability than the TD group, $p=0.02$. There were no significant differences between the two groups in the proportions of participants receiving average or gifted classifications. | 6/10 |
| | Charman T. (2010) | South Thames, UK | NR | Cross sectional | 156 | 89 | NR | 9.8-14.5 | Children with ASD from the SNAP cohort study. | IQ | WISC-III; Raven's SPM or CPM, depending on the child's ability. | Above average (IQ>115) | Autism and other ASDs | • Autism Diagnostic Observation Schedule – Generic (ADOS-G); Autism Diagnostic Interview – Revised (ADI-R) | The weighted mean (S.D.) IQ for the total ASD sample was 69.4 (24.1). IQ was similar for the childhood autism [67.9 (24.0)] and other ASD [70.1 (24.2)] groups ($t=0.43$, $p=0.67$). Of the total ASD sample, 2.7% was in the above average (>115). | 4/10 |

ADI-R: Autism Diagnostic Interview-Revised; ADOS: Autism Diagnostic Observation Schedule; ASD: Autism Spectrum Disorder; CBCL: Child Behavior Checklist; CCAT: Canadian Cognitive Abilities Test; CEN: Creating Equal Number; CPS: Colorado Perceptual Speed Test, CS: Cross-Sectional; DISC: Diagnostic Interview Schedule for Children; DSM: Diagnostic and Statistical Manual; FSIQ: Full Scale Intelligence Quotient; IQ: Intelligence Quotient; K LD: Learning Difficulties; MLD: Moderate Learning Difficulties; NLD: No Learning Difficulties; NS: not significant; PMS: Pictorial Multiple Solutions; SCQ: Social Communication Questionnaire; SDQ: Strengths and

Difficulties Questionnaire; TD: Typically Developing; TRF: Teacher Report Form; TTCT: Torrance Tests of Creative Thinking; WAIS: Wechsler Adult Intelligence Scale; WIAT: Wechsler Individual Achievement Test; WISC: Wechsler Intelligence Scale for Children.

**Table 1.** Characteristics of included studies

**PRISMA Flow Diagram**

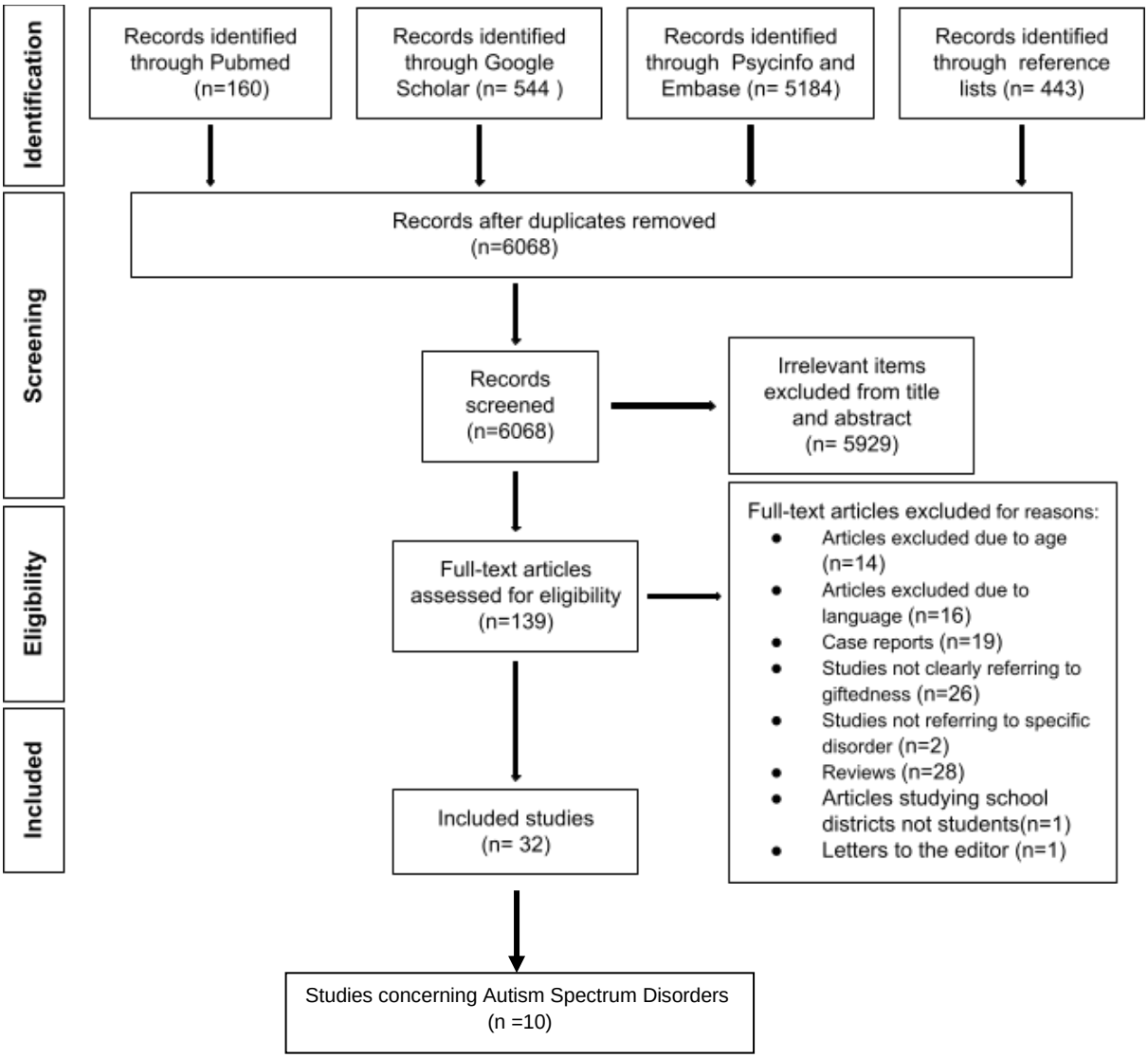


**Figure 1.** Successive steps in the selection of studies - PRISMA Flow Diagram.

**REFERENCES**


1. N.A.G.C. Redefining Giftedness fo a New Century: Shifting the Paradigm 2010 [Available from: https://www.nagc.org/sites/default/files/Position%20Statement/Redefining%20Giftedness%20for%20New%20Century.pdf.
2. N.A.G.C. Twice-Exceptional Students: N.A.G.C.; [Available from: nagc.org/resources-publications/resources-parents/twice-exceptional-students.
3. WHO. 6A02 Aytism spectrum disorder2020. Available from: icd.who.int/browse11/l-m/en#http%3a%2f%2fid.who.int%2ficd%2fentity%2f437815624.
4. Reis SM, Baum SM, Burke E. An Operational Definition of Twice-Exceptional Learners: Implications and Applications. Gift Child Q. 2014;58(3):217-30.
5. Vaivre-Douret L. Developmental and cognitive characteristics of "high-level potentialities" (highly gifted) children. Int J Pediatr. 2011;2011:420297.
6. Renzulli JS. What Makes Giftedness? Reexamining a Definition. Phi Depta Kappan. 1978;92(08):180-4.
7. Waterhouse L. Multiple Intelligences, the Mozart Effect, and Emotional Intelligence: a Critical Review. Educational Psychologist. 2006;41(4):207-25.
8. Gagne F. Giftedness and Talent: Reexamining a Reexamination of the difinitions. 1985;29(03):101-12.
9. Intagliata VJ, Scharf RJ. The Gifted Child. Pediatr Rev. 2017;38(12):575-7.
10. No Child Left Behind Act [Available from: en.wikipedia.org/wiki/No_Child_Left_Behind_Act.
11. Puttaswamy A, Barone A, Viezel KD, Willis JO, Dumont R. Whechler Intelligence Scale for Children-Fifth Edition Ancillary and Complementary Index Critical Vaues and Base Rates for the Normative Sample. Journal of Psycoeducational Assessment. 2020;38(5):1-12.
12. Guilbault K, Kane M. Asynchronous Development National Assossiation for Gifted Chidren2016 [Available from: https://www.nagc.org/resources-publications/resources-parents/social-emotional-issues/asynchronous-development.
13. Pfeiffer SI. The Gifted: Clinical Challenges for Child Psychiatry. Journal of the American Academy of Child and Adolecent Psychiatry. 2009;48(8):787-90.
14. Alias A, Rahman S, Abd Majid R, Mohd Yassin SF. Dabrowski's Overexcitabilities Profile among Gifted Students. ASS. 2013;9(16):120-5.
15. N.A.G.C. A Definition of Giftedness that Guides Best Practice N.A.G.C.2019 [Available from: https://www.nagc.org/sites/default/files/Position Statement/Definition of Giftedness (2019).pdf.
16. Kanner L. Autistic Disturbances of Affective Contact. Nervous Child. 1943;2:217-50.
17. Voigt RG, Macias MM, M. MS, Tapia CD. Autism Spectrum Disorder. Developmental and Behavioral Pediatrics. 2nd ed: AAP; 2018.
18. APA. Diagnostic and Statistical Manual of Mental Disorders. 5th ed: APA; 2013.
19. Reed GM, First MB, Kogan CS, Hyman SE, Gureje O, Gaebel W, et al. Innovations and changes in the ICD-11 classification of mental, behavioural and neurodevelopmental disorders. World Psychiatry. 2019;18(1):3-19.
20. Christensen DL, Maenner MJ, Bilder D, Constantino JN, Daniels J, Durkin MS, et al. Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 4 Years - Early Autism and Developmental Disabilities Monitoring Network, Seven Sites, United States, 2010, 2012, and 2014. MMWR Surveill Summ. 2019;68(2):1-19.
21. Christensen DL, Baio J, Van Naarden Braun K, Bilder D, Charles J, Constantino JN, et al. Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years--Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2012. MMWR Surveill Summ. 2016;65(3):1-23.

22. Palmer N, Beam A, Agniel D, Eran A, Manrai A, Spettell C, et al. Association of Sex With Recurrence of Autism Spectrum Disorder Among Siblings. JAMA Pediatr. 2017;171(11):1107-12.
23. Baxter AJ, Bugha T, Erskine H, Scheurer R, Vos T, Scott J. The epidemiology and global burden of Autism Spectrum Disorders. PsycolMed. 2015;45(3):601-13.
24. Idring S, Rai D, Dal H, Dalman C, Sturm H, Zander E, et al. Autism spectrum disorders in the Stockholm Youth Cohort: design, prevalence and validity. PLoS One. 2012;7(7):e41280.
25. Saemundsen E, Magnússon P, Georgsdóttir I, Egilsson E, Rafnsson V. Prevalence of autism spectrum disorders in an Icelandic birth cohort. BMJ Open. 2013;3(6).
26. Atladottir HO, Gyllenberg D, Langridge A, Sandin S, Hansen SN, Leonard H, et al. The increasing prevalence of reported diagnoses of childhood psychiatric disorders: a descriptive multinational comparison. Eur Child Adolesc Psychiatry. 2015;24(2):173-83.
27. Kim YS, Leventhal BL, Koh YJ, Fombonne E, Laska E, Lim EC, et al. Prevalence of autism spectrum disorders in a total population sample. Am J Psychiatry. 2011;168(9):904-12.
28. Loomes R, Hull L, Mandy WPL. What Is the Male-to-Female Ratio in Autism Spectrum Disorder? A Systematic Review and Meta-Analysis. J Am Acad Child Adolesc Psychiatry. 2017;56(6):466-74.
29. Thomaidis L, Mavroeidi N, Richardson C, Choleva A, Damianos G, Bolias K, et al. Autism Spectrum Disorders in Greece: Nationwide Prevalence in 10-11 Year-Old Children and Regional Disparities. J Clin Med. 2020;9(7).
30. Hansen SN, Schendel DE, Parner ET. Explaining the increase in the prevalence of autism spectrum disorders: the proportion attributable to changes in reporting practices. JAMA Pediatr. 2015;169(1):56-62.
31. Rice CE, Rosanoff M, Dawson G, Durkin MS, Croen LA, Singer A, et al. Evaluating Changes in the Prevalence of the Autism Spectrum Disorders (ASDs). Public Health Rev. 2012;34(2):1-22.
32. Georgiades S, Szatmari P, Zwaigenbaum L, Bryson S, Brian J, Roberts W, et al. A prospective study of autistic-like traits in unaffected siblings of probands with autism spectrum disorder. JAMA Psychiatry. 2013;70(1):42-8.
33. Grønborg TK, Schendel DE, Parner ET. Recurrence of autism spectrum disorders in full- and half-siblings and trends over time: a population-based cohort study. JAMA Pediatr. 2013;167(10):947-53.
34. Tick B, Bolton P, Happé F, Rutter M, Rijsdijk F. Heritability of autism spectrum disorders: a meta-analysis of twin studies. J Child Psychol Psychiatry. 2016;57(5):585-95.
35. Mandy W, Lai MC. Annual Research Review: The role of the environment in the developmental psychopathology of autism spectrum condition. J Child Psychol Psychiatry. 2016;57(3):271-92.
36. Kalkbrenner AE, Schmidt RJ, Penlesky AC. Environmental chemical exposures and autism spectrum disorders: a review of the epidemiological evidence. Curr Probl Pediatr Adolesc Health Care. 2014;44(10):277-318.
37. Tordjman S, Somogyi E, Coulon N, Kermarrec S, Cohen D, Bronsard G, et al. Gene × Environment interactions in autism spectrum disorders: role of epigenetic mechanisms. Front Psychiatry. 2014;5:53.
38. Loke YJ, Hannan AJ, Craig JM. The Role of Epigenetic Change in Autism Spectrum Disorders. Front Neurol. 2015;6:107.
39. Mahajan R, Mostofsky SH. Neuroimaging endophenotypes in autism spectrum disorder. CNS Spectr. 2015;20(4):412-26.
40. Philip RC, Dauvermann MR, Whalley HC, Baynham K, Lawrie SM, Stanfield AC. A systematic review and meta-analysis of the fMRI investigation of autism spectrum disorders. Neurosci Biobehav Rev. 2012;36(2):901-42.
41. Cerliani L, Mennes M, Thomas RM, Di Martino A, Thioux M, Keysers C. Increased Functional Connectivity Between Subcortical and Cortical Resting-State Networks in Autism Spectrum Disorder. JAMA Psychiatry. 2015;72(8):767-77.

42. Fournier KA, Hass CJ, Naik SK, Lodha N, Cauraugh JH. Motor coordination in autism spectrum disorders: a synthesis and meta-analysis. J Autism Dev Disord. 2010;40(10):1227-40.
43. Bodison S, Mostofsky S. Motor Control and Motor Learning Processes in Autism Spectrum Disorders. Handbook of Autism and Pervasive Dvelopmental Disorders. 4th ed: John Wiley and sons.inc; 2014.
44. Maski KP, Jeste SS, Spence SJ. Common neurological co-morbidities in autism spectrum disorders. Curr Opin Pediatr. 2011;23(6):609-15.
45. Canitano R, Vivanti G. Tics and Tourette syndrome in autism spectrum disorders. Autism. 2007;11(1):19-28.
46. Simonoff E, Pickles A, Charman T, Chandler S, Loucas T, Baird G. Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. J Am Acad Child Adolesc Psychiatry. 2008;47(8):921-9.
47. El Achkar CM, Spence SJ. Clinical characteristics of children nad young adults with co-occuring autism spectrum disorder and epilepsy. EPILEPSY BEHAV. 2015;47:183-90.
48. Jokiranta E, Sourander A, Suominen A, Timonen-Soivio L, Brown AS, Sillanpää M. Epilepsy among children and adolescents with autism spectrum disorders: a population-based study. J Autism Dev Disord. 2014;44(10):2547-57.
49. Mouridsen SE, Rich B, Isager T. Epilepsy and other central nervous system diseases in atypical autism: a case control study. J Neural Transm (Vienna). 2011;118(4):621-7.
50. Surén P, Bakken IJ, Aase H, Chin R, Gunnes N, Lie KK, et al. Autism spectrum disorder, ADHD, epilepsy, and cerebral palsy in Norwegian children. Pediatrics. 2012;130(1):e152-8.
51. Jeste S, Tuchman R. Autism Spectrum Disorder and Epilepsy: Two Sides of the Same Coin? JCN. 2015;30(14):1963-71.
52. Woolfelden S, Sarkozy V, Ridley G, Coory M, Williams K. A systematic review of two outcomes in autism spectrum disorder- epilepsy and mortality. Dev med Child Neurol. 2012;54(4):306-12.
53. Joshi G, Petty C, Wozniak J, Henin A, Fried R, Galdo M, et al. The heavy burden of psychiatric comorbidity in youth with autism spectrum disorders: a large comparative study of a psychiatrically referred population. J Autism Dev Disord. 2010;40(11):1361-70.
54. Simonoff E, Jones CR, Baird G, Pickles A, Happé F, Charman T. The persistence and stability of psychiatric problems in adolescents with autism spectrum disorders. J Child Psychol Psychiatry. 2013;54(2):186-94.
55. Hill AP, Zuckerman KE, Hagen AD, Kriz DJ, Duvall SW, van Santen J, et al. Aggressive Behavior Problems in Children with Autism Spectrum Disorders: Prevalence and Correlates in a Large Clinical Sample. Res Autism Spectr Disord. 2014;8(9):1121-33.
56. Gotham K, Brunwasser SM, Lord C. Depressive and anxiety symptom trajectories from school age through young adulthood in samples with autism spectrum disorder and developmental delay. J Am Acad Child Adolesc Psychiatry. 2015;54(5):369-76.e3.
57. Orinstein A, Tyson KE, Suh J, Troyb E, Helt M, Rosenthal M, et al. Psychiatric Symptoms in Youth with a History of Autism and Optimal Outcome. J Autism Dev Disord. 2015;45(11):3703-14.
58. Verheij C, Louwerse A, van der Ende J, Eussen ML, Van Gool AR, Verheij F, et al. The Stability of Comorbid Psychiatric Disorders: A 7 Year Follow Up of Children with Pervasive Developmental Disorder-Not Otherwise Specified. J Autism Dev Disord. 2015;45(12):3939-48.
59. Lai MC, Lombardo MV, Baron-Cohen S. Autism. Lancet. 2014;383(9920):896-910.
60. Cohen S, Conduit R, Lockley SW, Rajaratnam SM, Cornish KM. The relationship between sleep and behavior in autism spectrum disorder (ASD): a review. JNeurodev Disor. 2014;6.
61. Hollway JA, Aman MG. Sleep correlates of pervasive developmental disorders: a review of the literature. Res Dev Disabil. 2011;32(5):1399-421.

62. McElhanon BO, McCracken C, Karpen S, Sharp WG. Gastrointestinal symptoms in autism spectrum disorder: a meta-analysis. Pediatrics. 2014;133(5):872-83.
63. Hubbard KL, Anderson SE, Curtin C, Must A, Bandini LG. A comparison of food refusal related to characteristics of food in children with autism spectrum disorder and typically developing children. J Acad Nutr Diet. 2014;114(12):1981-7.
64. Sharp WG, Berry RC, McCracken C, Nuhu NN, Marvel E, Saulnier CA, et al. Feeding problems and nutrient intake in children with autism spectrum disorders: a meta-analysis and comprehensive review of the literature. J Autism Dev Disord. 2013;43(9):2159-73.
65. Disabilities CoCW, Pediatrics SoDB, Committee BFS, Committee MHIfCWSNPA. Identifying infants and young children with developmental disorders in the medical home: an algorithm for developmental surveillance and screening. Pediatrics. 2006;118(1):405-20.
66. Johnson CP, Myers SM, Disabilities AAoPCoCW. Identification and evaluation of children with autism spectrum disorders. Pediatrics. 2007;120(5):1183-215.
67. Pierce K, Carter C, Weinfeld M, Desmond J, Hazin R, Bjork R, et al. Detecting, studying, and treating autism early: the one-year well-baby check-up approach. J Pediatr. 2011;159(3):458-65.e1-6.
68. Oner O, Munir KM. Modified Checklist for Autism in Toddlers Revised (MCHAT-R/F) in an Urban Metropolitan Sample of Young Children in Turkey. J Autism Dev Disord. 2020;50(9):3312-9.
69. Thomaidis L, Choleva A, Kyprianou M. Age-related issues of instruments screening for autism in young children. Neuropsychiatr Dis Treat. 2016;12:3093-5.
70. Kim SHS, Ball V, Lord C. Autism Diagnostic Interview-Revised. Encyclopedia of Autism Spectrum Disorders2013.
71. Wing L, Leekam SR, Libby SJ, Gould J, Larcombe M. The Diagnostic Interview for Social and Communicational Disorders: backround, inter-rater reliability and clinical use. J Child Psychol Psychiatry. 2002;43(3).
72. Akshoomoff N, Corsello C, Schmidt H. The Role of the Autism Diagnostic Observation Schedule in the Assessment of Autism Spectrum Disorders in School and Community Settings. Calif School Psychol. 2006;11:7-19.
73. Chlebowski C, Green JA, Barton ML, Fein D. Using the childhood autism rating scale to diagnose autism spectrum disorders. J Autism Dev Disord. 2010;40(7):787-99.
74. Schaefer GB, Mendelsohn NJ, Committee PPaG. Clinical genetics evaluation in identifying the etiology of autism spectrum disorders: 2013 guideline revisions. Genet Med. 2013;15(5):399-407.
75. Savatt JM, Myers SM. Genetic Testing in Neurodevelopmental Disorders. Front Pediatr. 2021;9:526779.
76. Tammimies K, Marshall CR, Walker S, Kaur G, Thiruvahindrapuram B, Lionel AC, et al. Molecular Diagnostic Yield of Chromosomal Microarray Analysis and Whole-Exome Sequencing in Children With Autism Spectrum Disorder. JAMA. 2015;314(9):895-903.
77. Rosenfeld JA, Ballif BC, Torchia BS, Sahoo T, Ravnan JB, Schultz R, et al. Copy number variations associated with autism spectrum disorders contribute to a spectrum of neurodevelopmental disorders. Genet Med. 2010;12(11):694-702.
78. Yang Y, Muzny DM, Reid JG, Bainbridge MM, Willis A, Ward PA, et al. Clinical Whole-Exome Sequencing for the Diagnosis of Mendelian Disorders. N Engl J Med. 2013;369:1502-11.
79. Yang Y, Muzny DM, Xia F, Niu Z, Person R, Ding Y, et al. Molecular findings among patients referred for clinical whole-exome sequencing. JAMA. 2014;312(18):1870-9.
80. Lee H, Deignan JL, Dorrani N, Strom SP, Kantarci S, Quintero-Rivera F, et al. Clinical exome sequencing for genetic identification of rare Mendelian disorders. JAMA. 2014;312(18):1880-7.
81. Soden SE, Saunders CJ, Willig LK, Farrow EG, Smith LD, Petrikin JE, et al. Effectiveness of exome and genome sequencing guided by acuity of illness for diagnosis of neurodevelopmental disorders. Sci Transl Med. 2014;6(265):265ra168.

82. Valencia CA, Husami A, Holle J, Johnson JA, Qian Y, Mathur A, et al. Clinical Impact and Cost-Effectiveness of Whole Exome Sequencing as a Diagnostic Tool: A Pediatric Center's Experience. Front Pediatr. 2015;3:67.
83. Monroe GR, Frederix GW, Savelberg SM, de Vries TI, Duran KJ, van der Smagt JJ, et al. Effectiveness of whole-exome sequencing and costs of the traditional diagnostic trajectory in children with intellectual disability. Genet Med. 2016;18(9):949-56.
84. Nolan D, Carlson M. Whole Exome Sequencing in Pediatric Neurology Patients: Clinical Implications and Estimated Cost Analysis. J Child Neurol. 2016;31(7):887-94.
85. Roesser J. Diagnostic yield of genetic testing in children diagnosed with autism spectrum disorders at a regional referral center. Clin Pediatr (Phila). 2011;50(9):834-43.
86. Tassone F, Choudhary NS, Durbin-Johnson B, Hansen R, Hertz-Picciotto I, Pessah I. Identification of expanded alleles of the FMR1 Gene in the CHildhood Autism Risks from Genes and Environment (CHARGE) study. J Autism Dev Disord. 2013;43(3):530-9.
87. Myers SM, Johnson CP, Disabilities AAoPCoCW. Management of children with autism spectrum disorders. Pediatrics. 2007;120(5):1162-82.
88. Smith T. Applied Behavior Analysis and Early Intencive Behavioral Intervention. Autism Spectrum Disorders2011. p. 1036-55.
89. Schreibman L, Dawson G, Stahmer AC, Landa R, Rogers SJ, McGee GG, et al. Naturalistic Developmental Behavioral Interventions: Empirically Validated Treatments for Autism Spectrum Disorder. J Autism Dev Disord. 2015;45(8):2411-28.
90. Zimmer M, Desch L, Medicine SOCAI, Disabilities CoCw, Pediatrics AAo. Sensory integration therapies for children with developmental and behavioral disorders. Pediatrics. 2012;129(6):1186-9.
91. Wan Yunus F, Liu KP, Bissett M, Penkala S. Sensory-Based Intervention for Children with Behavioral Problems: A Systematic Review. J Autism Dev Disord. 2015;45(11):3565-79.
92. Farmer C, Thurm A, Grant P. Pharmacotherapy for the core symptoms in autistic disorder: current status of the research. Drugs. 2013;73(4):303-14.
93. Center NA. National Standard's Project - Phase 2 National Autism Center in May Institute2015 [Available from: http://www.nationalautismcenter.org/national-standards-project/phase-2/.
94. FDA. Be Aware of Potentially Dangerous Products and Therapies that Claim to Treat Autism FDA2019 [Available from: https://www.fda.gov/concumers/concumer-updates/be-aware-pottentially-dangerous-products-and-therapies-claim-treat-autism.
95. Ichim TE, Solano F, Glenn E, Morales F, Smith L, Zabrecky G, et al. Stem cell therapy for autism. J Transl Med. 2007;5:30.
96. N.A.G.C. Twice-Exceptionality N.A.G.C.2009 [Available from: https://www.nagc.org/sites/default/files/Position%20Statement/twice%20exceptional.pdf.
97. Nicpon MF, Allmon A, Sieck B, Stinson RD. Empirical Investigation of Twice-Exceptionality:Where Have We Been and Where Are We Going? Gift Child Q. 2011;55(1):3-17.
98. N.A.G.C. Twice-Exceptional Students: N.A.G.C.; [Available from: https://nagc.org/resources-publications/resources-parents/twice-exceptional-students.
99. Assouline S, Nicpon MF, Colangelo N, O'Brien M. The Paradox of Giftedness and Autism The Univercity of Iowa2008 [Available from: https://www.files.eric.ed.gov/fulltext/ED535140.pdf.
100. Neihart M. Gifted Children With Asperger's Syndrome. Gift Child Q. 2000;44(4):222-30.
101. Boschi A, Planche P, Hemimou C, Demily C, Vaivre-Douret L. From High Intellectual Potential to Asperger Syndrome: Evidence for Differences and a Fundamental Overlap-A Systematic Review. Front Psychol. 2016;7:1605.
102. Burger-Weltmeijer A, Minnaert A, Bosch V-H-Vd. To co-occurence of intellectual Giftedness and Autism Spectrum Disorders. EducResRev. 2011;6(1):67-88.
103. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009;339:b2700.

104. Hetzroni O, Agada H, Leikin M. Creativity in Autism: An Examination of General and Mathematical Creative Thinking Among Children with Autism Spectrum Disorder and Children with Typical Development. J Autism Dev Disord. 2019;49(9):3833-44.
105. Aleksandrovich M, Zoglovec H. Autistic Spectrum Disorders and Creativity: Comparative Study of the Art Works. JEE. 2014;3(4):5-16.
106. Craig J, Baron-Cohen S. Creativity and imagination in autism and Asperger syndrome. J Autism Dev Disord. 1999;29(4):319-26.
107. Meng-Lung L, Wei-Lin S, Le-Yin M. Are children with Asperger syndrome creative in divergent thinking and feeling?Abrief report. ResAutism Spectr Disord. 2011;5(1):294-8.
108. Masataka N. Neurodiversity, Giftedness, and Aesthetic Perceptual Judgment of Music in Children with Autism. Front Psychol. 2017;8:1595.
109. Oswald TM, Beck JS, Iosif A-M, McCauley JB, Gilhooly LJ, Matter JC, et al. Clinical and Cognitive Characteristics Assosssiated with Mathematics Problem Solving in Adolescents with Autism Spectrum Disorder. Autism Res. 2015;9(4):480-90.
110. Jamey K, Foster N, Sharda M, Tuerk C, Nadig A, Hyde KL. Evidence of intact melodic and rythmic perception in children with Autism Spectrum Disorder. Res Autism Spectr Disord. 2019;64:1-12.
111. Doobay A. Comparison of cognitive, psychosocial, and adaptive behavior profiles among gifted children with and without Autism Spectrum Disorder. Iowa Research Online2010.
112. Heaton P, Hermelin B, Pring L. Autism and Pitch Processing: A Precursor for Savant Musical Ability? Music Perception: An Inderdisciplinary Journal. 1998;15(3).
113. Charman T, Pickles A, Simonoff E, Chandler S, Loucas T, Baird G. IQ in children with autism spectrum disorders: data from the Special Needs and Autism Project (SNAP). Psychol Med. 2011;41(3):619-27.
114. Baron-Cohen S, Ashwin E, Ashwin C, Tavassoli T, Chakrabarti B. Talent in autism: hyper-systemizing, hyper-attention to detail and sensory hypersensitivity. Philos Trans R Soc Lond B Biol Sci. 2009;364(1522):1377-83.
115. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25(9):603-5.

**ABSTRACT**

**Objective:** Throughout the years, several myths have arisen suggesting that children diagnosed with neurodevelopmental disorders possess unusually high abilities in specific domains, depending on the disorder. On the other hand, special skills and talents in children with developmental disorders are most commonly overshadowed by their difficulties and overlooked. The purpose of this systematic review was to examine the association between giftedness and each neurodevelopmental disorder in particular. The present study focuses on the correlation between giftedness and Autism Spectrum Disorders (ASD) and presents the results of the above systematic review concerning the two identities.

**Materials and Methods:** The related articles published in PubMed, Google Scholar, PsycInfo and Embase up to 31 December 2020, as well as their reference lists, were reviewed systematically.

**Results:** A total of 6069 studies were scanned and 32 of them (9904 subjects) were deemed eligible for this systematic review. Ten of the eligible articles were investigating the correlation between giftedness and ASD. Studies have supported associations between Autism Spectrum Disorders and music ability.

**Conclusion:** More research is needed to investigate the field of dual exceptionality in children with ASD. Longitudinal studies are needed, overcoming methodological challenges related to variability in the definition of giftedness.

Key-terms: giftedness, neurodevelopmental disorders, Autism Spectrum Disorders, children, adolescents

**ΣΥΣΧΕΤΙΣΗ ΧΑΡΙΣΜΑΤΙΚΟΤΗΤΑΣ ΜΕ ΔΙΑΤΑΡΑΧΗ ΑΥΤΙΣΤΙΚΟΥ ΦΑΣΜΑΤΟΣ ΣΕ ΠΑΙΔΙΑ ΚΑΙ ΕΦΗΒΟΥΣ: ΣΥΣΤΗΜΑΤΙΚΗ ΑΝΑΣΚΟΠΗΣΗ**

**Σκοπός:** Κατά την πάροδο των ετών, πολλοί μύθοι έχουν συσχετίσει την ύπαρξη νευροαναπτυξιακών διαταραχών με εξαιρετικές ικανότητες σε συγκεκριμένους τομείς, ανάλογα με τη διαταραχή. Από την άλλη μεριά, όπως περιγράφεται στη βιβλιογραφία, οι ιδιαίτερες ικανότητες και ταλέντα που μπορεί να κατέχουν παιδιά με νευροαναπτυξιακές διαταραχές συχνά επισκιάζονται από τις δυσκολίες τους και παραβλέπονται, τόσο από τους γονείς όσο και από τους εκπαιδευτικούς. Σκοπός της συστηματικής αυτής ανασκόπησης ήταν η συλλογή και μελέτη της υπάρχουσας βιβλιογραφίας, προκειμένου να διερευνηθεί η συσχετιση της χαρισματικότητας με κάθε είδους νευροαναπτυξιακή διαταραχή. Η παρούσα μελέτη παρουσιάζει τα αποτελέσματα της συστηματικής ανασκόπησης που φορούν στη συσχέτιση μεταξύ χαρισματικότητας και Διαταραχής Αυτιστικού Φάσματος (ΔΑΦ).

**Υλικά και Μέθοδος:** Έγινε συστηματική ανασκόπηση των άρθρων έχουν δημοσιευτεί στα PubMed, Google Scholar, PsycInfo και Embase έως τον Δεκέμβριο του 2020, καθώς και των βιβλιογραφικών αναφορών τους.

**Results:** Συνολικά 6069 αξιολογήθηκαν και 32 από αυτά (συνολικά 9904 υποκείμενα) κρίθηκαν επιλέξιμα για τη συγκεκριμένη συστηματική ανασκόπηση. Δέκα από τις επιλέξιμες μελέτες μελετούσαν τη συσχέτιση μεταξύ χαρισματικότητας και Διαταραχής Αυτιστικού Φάσματος (ΔΑΦ). Από τις ανωτέρω μελέτες διαφαίνεται συσχέτιση μεταξύ ΔΑΦ και μουσικής αντίληψης,

**Conclusion:**. Περισσότερη έρευνα πάνω στο συγκεκριμένο θέμα κρίνεται απαραίτητη. Απαιτείται η διενέργεια διαχρονικών μελετών, ώστε ξεπεραστούν μεθοδολογικές δυσκολίες που σχετίζονται με την ετερογένεια των ορισμών της χαρισματικότητας.

# APPENDIX

## LIST OF ABBREVIATIONS

**AAP** : American academy of pediatrics

**ABBA** : Applied Behavioral Analysis

**ADI-R** : Autism Diagnostic Interview—Revised

**ADOS** : Autism Diagnostic Observation Schedule

**ADHD** : Attention Deficit Hyperactivity Disorder

**CAM :** Complementary and Alternative Medicine

**CAP** : Creativity Assessment Packet

**CARS :** Childhood Autism Rating Scale

**CMA** : Chromosomal Microarray Analysis

**CNV** : Copy-Number Variation

**DISCO** : Diagnostic Interview for Social and Communication Disorders

**DSM V :** Diagnostic and Statistical Manual of Mental Disorders - 5th edition

**DSP :** Developmental Social Pragmatic

**2e** : Twice Exceptional

**ESDM** : Early Start Denver Model

**fMRI** : Functional MRI

**FDA :** Food and Drug Administration

**GI :** Gastrointestinal

**HFASD** : High Functioning Autism Spectrum Disorders

**HIP** : High Intellectual Potential

**ICD11** : International Statistical Classification of Diseases

**ID** : Intellectual Disability

**IQ** : Intelligence Quotient

**M-CHAT-R/F** : Modified Checklist for Autism in Toddlers, Revised, with Follow-Up

**MBEMA** : Montreal Battery for the Evaluation of Musical Abilities

**NAGC** : National Association for Gifted Children

**NDBI :** Naturalistic Developmental Behavioral Intervention

**SITs** : Sensory Integration Therapies

**SBI's** : Sensory BAsed Interventions

**TEACCH** : Treatment and Education of Autistic and Related Communication - Handicapped Children

**U.S.A** : United States of America

**WAIS** : Wechsler Adult Intelligence Scale

**WISC** : Wechsler Intelligence Scale for Children

**WPPSI** : Wechsler Preschool and Primary School Intelligence

**WES** : Whole Exome Sequencing