

**Review of interventions for the management of anxiety symptoms of children  
with ASD**

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Running Head

Interventions for Anxiety of Children with ASD

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## **Abstract**

**Background:** Anxiety is a common accompanying symptom in people with Autism Spectrum Disorder (ASD).

**Objectives:** Current research aims to investigate interventions available for the management of anxiety for people with ASD internationally.

**Methods:** Research had been carried out through PubMed and National Institute of Health (NIH) publications, resources were found in the library of the University of Macedonia and the Greek National Foundation of Research.

**Results:** Several studies (n=372) were found dealing with issues of interventions world widely for students with ASD and anxiety disorders during the period 1980s to 2017. From the studies found, n=137 were reviewed. Interventions include psychosocial therapies, teaching social skills, the CBT Program, special psychosocial therapies, combination of educational, psychological and medical treatments, integrity of CBT and Social Recreational Program, pharmacological interventions and antidepressants.

**Conclusions:** Various ways of coping have been applied, pharmacotherapy, psychosocial, cognitive behavioral interventions, parent education and school based programs. A combination should be applied, selected according to each case, tailor made for every child's particular characteristics, based on assessment.

**Key words:** interventions, anxiety, autism, school, family, cognitive behavior, psychosocial, educational, medical.

## 1. Introduction

Autism Spectrum Disorder (ASD), as defined by Diagnostic and Statistical Manual of Mental Disorders (DSM-5), is characterized by qualitative weaknesses in social interaction and communication and limited, repetitive and stereotypical patterns of behavior, interests and activities (APA, 2013). The appearance of ASD has risen dramatically over the last decade, with recent estimates showing that 1 out of 88 have, with a majority of males 5: 1 at gender-centered levels (Centers for Disease Control and Prevention, 2012). A systematic review of stress studies in children and adolescents with ASD suggests that between 11 and 84% of them have experienced anxiety (White, Oswald, Ollendick, Scahill, 2009). Stereotypic behaviors, such as sound, body revolutions, shaking back, hand rotations as well as repetitive questions, often increase when children experience anxiety, stress or frustration (Howlin, 1998; Thomas et al., 1998). High rates in anxiety scales were found concerning anxiety of separation, social anxiety and persistent and compulsive disorder in children with ASD (Gillott, Furniss, Walter, 2001). Anxiety disorders are among the most prevalent (Leyfer et al., 2006) and can be debilitating for young people with ASD when they appear in an environment such as home, school, community (van Steensel, Heeman, 2017). In addition, the severity of anxiety is associated with increased aggression, reduced participation in social activities, and poor social relationships for young people with ASD (Selles & Storch, 2012; Reaven, Blakeley Smith, Beattie, Sullivan, Moody, Stern, Hepburn & Smith, 2015; Ghaziuddin, 2005; Baron, 2008; White & Roberson-Nay, 2009; White et al., 2013; Vasa et al., 2016). Anxiety obstructs people's with ASD adaptation (Hallett, Lecavalier, Sukhodolsky, et al., 2013; Skokauskas, Gallagher, 2012). For this reason, developing and testing effective treatments for anxiety in ASD is important and should be given priority for public

health. It has been suggested that deficiencies in ASD may to some extent contribute to increased anxiety and stress due to perception and communication difficulties, limited flexibility and sensory difficulties (Kerns & Kendall, 2012; Wood & Gadow, 2010). An increase in stereotypical and provocative behaviors may be a consequence of the individual's attempts to reduce the stimulation of high levels of anxiety (Hallett et al., 2013; Ozsivadjian et al., 2012).

Many different factors seem to affect the anxiety in this population. However, information and types of anxiety disorder have been extensively derived from clinical samples of people with ASD without mental disability (Kuusikko et al., 2008; Renno & Wood, 2013; White et al., 2013; MacNeil et al., 2009; VanSteensel et al., 2011). In other cases possible effect of factors such as the level of mental or adaptive capacity or the severity of autism might influence the understanding of anxiety disorder. Community surveys show that 45% to 83% of children with ASD receive drug treatment (Oswald, Sonenklar, 2007). Selected serotonin reuptake inhibitors have shown efficacy in children of typical development (TD) with anxiety disorders (Buitelaar, van der Gaag, and der Hoeven, 1998; Namerrow, Thomas, Bostic, Prince, Monteux, 2003; Martin, Koenig, Anderson, Scahill, 2003). Children with autism diagnosis are more likely to feel anxious than children of typical development. Results show that citalopram is not effective for repeated / stereotypical behavior in young people with ASD (King, Hollander, Sikich et al., 2009). After administration of non-typical antipsychotics such as risperidone (McCracken, McGough, Shah et al., 2002; Shea, Turgay, Carroll, et al., 2004) and aripiprazole (Marcus, Owen, Kamen, et al., 2009; Owen, Sikich, Marcus, et al., 2009; Stigler, Diener, Kohn, et al., 2009) a reduction of irritability in children with ASD has been reported. But they also have side effects such as metabolic abnormalities (McDougle, Stigler, Erickson, Posey,

2008). So the value of non-pharmacological interventions in ASD should be emphasized (Sukhodolsky, Bloch, Panza, Reichow, 2013).

Several studies suggest that Cognitive Behavioral Therapy (CBT) can offer a variety of forms to support children with autism for their anxiety (Vasa, Keefer, Reaven, South, White, 2017). In addition, surveys show that cognitive-behavioral intervention contributes to reducing the anxiety symptoms of children with autism because it is a structured intervention, adapted to the needs of each child and aims at modifying dysfunctional behaviors and also improving the child's skills (Wood et al., 2009; Højgaard, Skarphedinsson, Nissen, Hybel, Ivarsson, Thomsen, 2017). Parents have an integral role in managing anxiety for children with ASD. Research shows that in anxiety management programs parents take on the role of the supporter, the trainer, and the friend (Derguy, Poumeyreau, Pingault, M'bailara, 2017). A study by Spence (1998), was carried out at a school CBT program using an experimental design incorporating the Spence Children's Anxiety Scale (Spence, 1998) and the Coping Scale for Children and Youth (Brodzinsky et al., 1992). Interview data has been incorporated to help understand the change process. Children in experimental conditions had lower levels of anxiety that were maintained during their follow-up. It was, also, found changes in response behaviors such as strategies for less avoidance behaviors but more for problem-solving strategies (Clarke, Hill, Charman, 2016).

### **1.1 Overview of bibliography: Interventions**

Psycho-social interventions such as CBT have been recommended as effective in the treatment of anxiety symptoms among children without ASD and their families in several studies (Albano, Kendall, 2002; Flannery-Schroeder, Kendall, 2000; Kendall,

1994; Danial, Wood, 2013; Vasa et al., 2014; 2015; 2016). CBT helps the individual recognize and correct cognitive deficits and anxiety-related disorders to bring about constructive changes in behavior and feelings. Through CBT, individuals can cultivate skills, shape their thoughts and beliefs, learn problem-solving strategies to improve interaction with others in effective and appropriate ways, and promote self-regulation of behavior (Robinson et al., 2017). Children with anxiety have a way of preferring to process information in which they are selectively aware of risk-related information, resulting in the misinterpretation of strange and particular situations as dangerous (Kendall, 1985; 1994). Thus, children with ASD have weak central coherence e.g. weaknesses in integrating information into a meaningful one, leading to a misconception of the situation. Their difficulties are aggravated by the problems of processing social information (e.g. incorrect translation of ambiguity into the social context and situation context), which then causes anxiety (Frith, 1989). So recently there has been interest in the use of CBT in the management of anxiety in children with ASD and Asperger syndrome. Studies suggest that CBT can help relieve anxiety symptoms in children with ASD (Chalfant, Rapee, Carroll, 2007; Ooi et al., 2008). Findings from these studies suggest that CBT can reduce stress levels in children with ASD when compared with control groups. Parental involvement was also found as an ancillary element (Sofronoff, Attwood, Hinton, 2005). While the findings are encouraging, the control groups used in studies is likely to be affected by the contact time with the trainer and the program's structure can be improved more than its own content program only. Other intervention programs that include social recreational activities (SR: Social Recreational) can also be profitable for children with ASD. Participating in leisure and recreational social activities can provide increased opportunities for social interaction, friendship development and social skills building

in children with ASD (Favell, McGimsey, Schell, 1982; Modell, Rider, Menchetti, 1997).

Due to the frequent occurrence of anxiety in ASD, effective interventions to manage anxiety in this population are important (White, Oswald, Ollendick, Scahill, 2009). Few studies compare CBT with non-CBT forms of intervention such as recreational social activities (Sung et al., 2011). In adolescents with ASD, severe anxiety symptoms are associated with increased irritability, sleep disturbances, disordered behaviors, carelessness, attention deficit and health problems (e.g. frequent gastrointestinal problems) (Bellini, 2004; Farrugia, Hudson, 2006; Kim, Szatmari, Bryson, Streiner Wilson, 2000; Weisbrot, Gadow, DeVincent, Pomeroy, 2005). All these symptoms have a serious impact on their school performance, as well at home with their families, in addition to weaknesses and deficits associated with ASD symptoms (Bellini, 2004; Kim, Szatmari, Bryson, Streiner, Wilson, 2000; Chamberlin, Kasari, Rotheram, Fuller, 2007; Sukhodolsky, Scahill, Gadow, Arnold, Aman, McDougle et al., 2008). Cognitive-behavioral interventions that specifically target the symptoms of adolescence with autism spectrum disorders - high functioning (ASD-HF) have been designed and evaluated for the management of cognitive (e.g. anxiety cognitive factors) and behavioral (e.g. avoidance, process) factors (McKay, Abramowitz, Taylor, 2009). An application of CBT technique is avoiding fear-causing stimuli (e.g., the individual experiences a reduction in unpleasant pressure when the stimulus of fear is removed) and reinforcing future avoidance behaviors. So a way CBT treats the symptoms of anxiety is by exposing the person to fear stimuli in a gradual, progressive manner while preventing the avoidance or ritual behavior that allows the person to become accustomed to anxiety. Cognitive elements of CBT include emotion recognition, provocative conclusions, cognitive reconstruction

schemes and actions aimed at rehabilitation of distorted thoughts. Behavioral elements other than exposure to fear stimuli include activities of increased pleasure and behavioral management techniques such as reward and reinforcement (Mckay, Abramowitz, Taylor, 2009; Bogacki, Newmark, & Gogineni, 2006). When applied, the parts of CBT may vary in their emphasis on cognitive or behavioral elements and can be designed to respond to unique individual abilities and symptoms. Key developments of CBT to address the symptoms of anxiety in TD young people and young people with ASD-HF include psycho-education (e.g. the nature of the child's anxiety and the interventional rationale is explained by the therapist), cognitive therapy (e.g. fears are distorted according to how anxiety is caused to teenagers) and prevention of exposure and reaction (e.g. young people are exposed repeatedly and gradually to stimuli that cause fear and are controlled by natural stress reduction strategies) (Wood, Drahota et al., 2009; Storch, Arnold, Lewin, Nadeau, Jones, DeNadai et al., 2013). The CBT has been applied to groups (Reaven, Blakeley-Smith, Nichols, Dasari, Flanigan, Hepburn, 2009), individually and with family involvement (Wood, Drahota, Sze, Har, Chiu, Langer, 2009; Lewin, et al., 2010) or a combination of these (White, Ollendick, Albano, Oswald, Jonson, Southam-Gerow, et al., 2013; Murphy, Chowdhury et al., 2017). A combination of psychotherapy and medical care is recommended in all anxiety disorders.

Studies show that when compared to diseases treated with a combination of CBT and drugs, they experience almost twice recession rates, even when the CBT is applied by a person with little or no experience with CBT (Roy-Byrne, Craske, Stein et al., 2005). Serotonin (SSRIs) has been shown, selectively, to be a better tolerated drug, and the response rates are significantly higher than placebo for panic disorder, OCD, PTSD, social anxiety and GAD. This drug class includes fluoxetine (Prozac),

fluvoxamine (Luvox), citalopram (Celexa), escitalopram (Lexapro), paroxetine (Paxil) and sertraline (Zoloft). Benzodiazepines, which have been widely used in the past to treat anxiety disorders, continue to be useful in the short-term management of symptoms until the acceptable reduction is achieved with an SSRI or CBT. (Kalachnik, J.E., Hanzel, Sevenich, Harder, 2002).

Everyone expresses their anxiety in individual ways so the most reliable observations about the child's anxiety will be made by people who know the child better. This shows how important is to work not only with the school staff but also with the families of children with autism. There may be changes in their sleep, in the toilet or in the food. They may become less tolerant in changes or social situations. They may be less involved in communicating or emotionally. They may be overly attached to special interests or follow new or old routines. There may be evidence of anxiety-related physical symptoms such as irritable bowel or swollen swelling. They may not be able to manage well-being. They can show behaviors that avoid co-operation, this leads to the closure of the fuses or eventually they are caused by physical stimuli and some are self-inflicted. People in the autism spectrum are prone to stressful experiences. This often happens due to their difficulties in communication, in predicting results, and understanding social interaction along with differences in sensory processing (Sartorato, Przybylowski, Sarko, 2017). Environmental supports that can help are strategies that can do two things: reduce confusion and unpredictability and increase a sense of calm. The first of these two points is often desirable by using a number of strategies. This may include organizational visual information such as programs and visual modes with clarifying reminders / instructions / problem-solving strategies. It also includes ways to describe perceptual information in a visual way, such as the use of symbols to recognize and

communicate emotions. The second is about increasing awareness of the potential for overload. This can be caused by over-incoming in any way. A child may receive excessive organizational information, intense social interaction, or experience sensory overload. Supportive adults can help with having a predictable and low stimulating environment. This means that environmental stimuli such as general clutter, sensory intakes, programs, and structured educational approaches, as well as building on relaxation and emotional well-being techniques, influence the student's mood. This also means thinking about aid planning for children when they experience unmanageable levels of anxiety. Children within the autism spectrum will have personal spikes for their anxiety. Some common issues may be related to disturbed routines, changes to routine arrangements, new experiences, particular events (dentist, doctor, Christmas school events, party) changes in classes or teachers. In addition to this, there are hormonal changes and a change in mood that occurs during adolescence. Teachers can not withdraw all stress-causing situations, and maybe they do not have to. But, according to literature review, teachers can help prevent anxiety by causing conditions by doing some of the followings. They can help by making the child's daily environment predictable, giving the child opportunities for systematic relaxation in stress and at anxiety moments they can help by putting at the right moment strategies that prevent the child's anxiety so it can be understood and limit the sensory overload at the same time. One of the most important things the teacher can do to prevent anxiety from provocative situations is to get their autism learners well to be able to "read" their behavior or stress levels (Sartorato, Przybylowski, Sarko, 2017; Ashburner, Ziviani, Rodger, 2008). This will also help him to connect with a child so that he will be able to prevent or calm anxiety episodes. Something

else to be conscious of is what contributes to any difficult situation for these children, including the awareness of the impact that staff interact with.

There are areas that can be integrated into the curriculum and prevent the development of stress in the long run; there is an increased emphasis on the school curriculum to protect the children's mental and emotional health. This provides benefits to children within the autism spectrum and allows schools to increase their flexibility to meet their students' individual needs. The work of the curriculum, in USA, can be linked to Personal Health Social Education (PHSE), individual development, citizenship and career etc. Job areas that can have a benefit are the long-term barrier work that can develop self-confidence, self-knowledge, problem-solving strategies and social skills. It is also important to teach relaxation techniques and personal strategies to manage anger and anxiety (Beidas, Kendall, 2010). Space needs to be made in the school's program for additional sessions that offer emotional well-being. Some schools build on regular but short sessions with students at the beginning or end of the day, or others may use the time of gathering. The Autism Speaks Autism Treatment Network (ATN) Anxiety Workgroup authored a systematic review of pharmacologic and nonpharmacologic anxiety treatment studies in ASD that were published through June 2013. These results showed modest evidence for the efficacy of cognitive-behavioral therapy (CBT) and a lack of randomized placebo-controlled trials investigating pharmacologic treatments for anxiety in youth with ASD. The existing studies that focus on anxiety are open-label or retrospective chart reviews. This finding is in contrast to data in TD youth, which supports the use of both medications and therapy.

Aim of this study is an update on interventions of anxiety management of children with ASD that would increase their adaptation and quality of life. Also, to investigate

interventions inside and outside school social environment. The main question to be investigated is what are the current popular trends in treatment anxiety at people with ASD world wide?

## 2. Methods

The literature review was guided by the following questions:

i) What interventions, methods, approaches, have developed internationally that aim at the management and treatment of people's with ASD anxiety symptoms ?

ii) in what ways are individuals with ASD supported in order to develop skills and to be included in social and educational environments?

iii) Do students with ASD present symptoms of anxiety?

iv) How is it manifested and in which areas the stress of children with ASD in and out of school?

v) What psycho-pedagogical interventions are suggested by the international literature to support their integration into the school environment?

vi) What psycho-pedagogical interventions can be planned in the general or special school?

The selection of the studies for the purpose of this paper was based on two criteria. First, the participants in the research study sample had to be individuals with ASD and anxiety symptoms, and second, the interventions had to include the management of anxiety and the increasement of adaptation in social, family and school environments. Evidence for treatment of childhood anxiety disorders in typical

developmental children is stable and constitutes of cognitive behavioral therapies, selective serotonergic reuptake inhibitors or their combination (Walkup et al., 2008). In contrast, data on treatment of anxiety in young people with ASD is still being investigated. A number of reviews refer to treatments for the stress of young people with ASD-HF (autism spectrum disorders- high functioning). Some reviews collectively support the efficacy of cognitive behavioral therapy (CBT) for young ASD-HF (Lang et al., 2010; Moree & Davis, 2010; Nadeau et al., 2011; Wood, 2013; Rudy et al., 2013; Sukhodolsky et al., 2013). Several reviews refer to deprivation of pharmacological statistics and the need for more clinical testing (Nadeau et al., 2011; Rudy et al., 2013). A study reviewed tools used to improve the response of ASD-HF to young people (Wigham & McConachie, 2014; Guyatt et al., 2008; US Preventive Services Task Force Procedure Manual, 2008). None of the reviews focuses on both pharmacological and non-pharmacological evidence in an integrated, comprehensive way. For example, some reviews are primarily centered on CBT (Danial, Wood, 2013; Sukhodolsky et al., 2013). Others include pharmacological evidence but do not refer to detailed study information (Rudy et al., 2013) or exclusively focus on anxiety (Nadeau et al., 2011). Some reviews (Rudy et al., 2013) do not refer how anxiety was measured or the types of anxiety disorders examined or those responding to treatment. Such information is crucial about researchers and clinicians working with young people with ASD. Finally, neither of the previous reviews have organized the evidence according to a predetermined set of questions, nor have they applied a graded system to assess the validity of evidence that could help clinicians assess the bibliography based on a set of criteria, while also providing general guidelines when providing recommendations for treatment. Other reviews critically examine the literature using a clinically based framework (Vasa, Carroll, Nozolillo, Mahajan,

Mazurek, Bennett, Wink, Bernal, 2014). Cognitive-behavioral therapies (CBTs) are well-founded, well-researched, evidence-based. They are considered to be effective psychosocial interventions for anxiety (Silverman et al., 2008; Walkup et al., 2008) at least in some cases. The CBT has been extended to young people with ASD (Chalfant et al., 2007; Reaven et al., 2012; Sofronoff, et al., 2005; Storch et al., 2013; Sung et al., 2012; Wood et al., 2009). The treatment is provided individually (Wood et al., 2009) in small groups (Chalfant et al., 2007; Reaven et al., 2012; Sofronoff et al., 2005) or in a combination of both individually and in small groups (White et al., 2013). Treatment studies for children undergoing ASD and anxiety have been initially carried out at fully-controlled university clinics. This is why there is limited scope for generalizing interventions in real life situations. So the lack of empirically based school social interventions for adolescents with ASD represents a gap in the research literature. Evidence suggests that behaviorally oriented techniques such as direct feedback, behavioral appearance and role playing are key components of skill transfer laboratories (Beidas & Kendall, 2010; Heschell et al., 2010). In addition, the transfer of new therapies is often hampered by the lack of critical feedback and information from practitioners during its implementation (Hatgis et al., 2001; Reaven, Blakeley-Sith, Beattie, Sullivan, Moody, Stern, Hepburn & Smith, 2015). Cognitive-behavioral therapy is a popular treatment for anxiety in TD children, and there is evidence that CBT can be an assistance for the children's with ASD anxiety.

In TD children with anxiety disorders, CBT has been evaluated in 40 randomized studies showing a positive response in 50% to 60% of participants and a moderate to large effect. In the CBT theoretical background studies claim that pathological anxiety is the result of interaction among excessive physiological stimulation, cognitive distortions and avoidance behaviors. The basic components of the CBT include the

teaching of sensory conditioning skills to reduce normal arousal and maladaptive thoughts followed by a systematic exposure to fear situations to limit avoided behavior. In clinical trials, separation and general anxiety disorders and social phobia are often grouped together due to the large size of the coating in the symptoms and the distinction from other anxiety disorders (e.g., OCD and post-traumatic stress disorders). There is evidence that appropriate adaptation data, such as fragmenting anxiety management skills into specific small steps, adding visual aids, writing reports and giving a larger role to parents as new skill managers can make CBT helpful in reducing anxiety in children with high functioning autism (Sukhodolsky, Bloch, Panza, Reichow, 2013). Recent results show that citalopram is not effective for repeated, stereotypical behavior in young people with ASD (King, Hollander, Sikich et al., 2009). After administration of non-typical antipsychotics such as risperidone (McCracken, McGough, Shah et al., 2002; Shea, Turgay, Carroll, et al., 2004) and aripiprazole (Marcus, Owen, Kamen et al., 2009; Owen, Sikich, Marcus et al., 2009; Stigler, Diener, Kohn et al., 2009) the reduction of irritability in children with ASD has been reported. However, there are also side effects such as metabolic abnormalities (McDougle, Stigler, Erickson, Posey, 2008). Studies also put emphasis on the value of non-pharmacological interventions in ASD (Sukhodolsky, Bloch, Panza, Reichow, 2013). Children with an autism diagnosis are more likely to feel more anxious than children of typical development. (Weisbrot, Gadow, DeVincent et al., 2005; Ventola, Lei, Paisley, Lebowitz, Silverman, 2017).

Research papers were found by searching through PubMed and National Institute of Health (NIH) publications. In addition, other resources were found in the library of the University of Macedonia and the Greek National Foundation of Research. Several studies (n=137) were found dealing with issues of interventions for students with ASD

and anxiety disorders during the period 1980s to 2017. Interventions were based mainly on CBT, SR, pharmacotherapy, were identified through the literature review. The practical value of the research lies in collecting all different kind of interventions that have been applied internationally the last three decades and their comparative review that lead to recommending designs of interventions in the individuals' social environment in order to increase social and educational inclusion for individuals with ASD and anxiety symptoms.

### **3. Literature Research Results**

#### **3.1 Research Review for CBT**

Autism is categorized as a developmental disorder in DSM-5 (APA, 2013) in which a person has difficulties with social interactions, communication and stereotypes or strict behaviors and interests, also known as a triple of weaknesses. Epidemiological studies suggest that in Britain about 1% of children meet the criteria for a diagnosis of autism (Baird et al., 2006; Baron-Cohen et al., 2009). Difficulties in the social behaviors of children with autism are found when there is a risk of school failure and social isolation in the school environment, as studies show that children with autism are more likely to achieve lower scores than typical developmental children with a corresponding IQ (Ashburner et al., 2010).

Children with autism are not only at risk of school failure and social isolation but also at risk of mental health difficulties. Simonoff et al., (2008) and Kussikko et al. (2008) found that children with autism were more likely to have co-morbidity with social

anxiety disorders in comparison with TD children. Specifically a meta-analysis reports that 40% of children with autism presenting an anxiety disorder (van Steensel et al. 2010), and the level of social anxiety is related to the child's loneliness.

A study by Simonoff et al., (2012) shows that concomitant difficulties were moderately stable over a period of 4 years but the risk factors which are associated with mental health difficulties in the general population were poor predictors of mental health difficulties for children with autism, suggesting different developmental trajectories. Research has attempted to distinguish co-morbidity between autism and anxiety. Wood & Gadow (2010) highlight the difficulty of assessing autism and anxiety. Some autism symptoms (such as unwillingness to get in or out of social interactions) that are reflected in the anxiety questionnaires may confuse the co-morbidity of children with autism, leading to high rates of co-morbidity. They suggest that anxiety in children with autism exists for three reasons: (a) continuous social rejection leading to an increase in stress levels where the main symptoms of autism can rise from stress factors and as an alternative measurement of the main symptoms of anxiety (b) awareness of social deficiencies (c) lack of flexibility in social situations, confusion of social stimuli. Some authors have also raised the question of whether anxiety in children with ASD is atypical in comparison to that of TD children (Kerns & Kendall, 2012). Cognitive Behavioral Therapy (CBT) has shown in researches to have positive results supporting young people with anxiety (Chu & Harrison, 2007; Okuda, Asano, Numata, Hirano, Yamamoto, Tanaka, Matsuzawa, Shimizu, Iyo, Nakazato, 2017), producing moderate to significant results. It initially focuses on both cognition and behaviors. However, professionals may place more emphasis on the behavioral or cognitive aspects of the treatment according to each one's abilities and experience (Graham, 2005). The CBT supports one's

understanding of anxiety environments and content (psycho-educational component) and helps to provoke an individual's knowledge of these contents through strategies such as taking a view and behavioral strategies such as exposure to help rebuild and reflect thoughts and feelings towards some situations (Drmic, Aljunied, Reaven, 2017). An advantage of CBT is that it can be provided in one to one or small groups. It can also be provided as part of a modular system or of a program in a number of weeks or through continuous support until specific results to be achieved.

The flexibility of CBT allows it to be specifically researched through empirical means. There are researches suggesting that CBT is an effective treatment for use by children with autism with anxiety (Chalfant et al., 2007; Sofronoff et al., 2005; Sze & Wood, 2007; White et al. al., 2009). These studies have incorporated simple and multiple case studies (Sze & Wood, 2007; White et al., 2009) and controlled trials (Chalfant et al., 2007; Sofronoff et al., 2005).

Research shows that children receiving CBT respond well to treatments ranging from 6 weeks (Sofronoff et al., 2005) to 16 weeks (Wood et al., 2009) and those who received a vertebrate CBT program (White et al., 2009) or a manual and supervisor-based treatment program (Sofronoff et al., 2005). The study also shows that the effects of CBT are maintained in post-intervention at 6 (Sofronoff et al., 2005) and at 12 weeks of follow-up (Chalfant et al., 2007). There are studies suggesting that CBT programs can be used to support children with autism to manage their anxiety (McConachie et al. 20014; Reaven et al., 2012). Research is encouraging and provides support for the use of CBT as an effective program for children with autism. However, current research, which is mainly empirically based, does not provide detailed information about the change process, or factors that affect change when children with autism are included in CBT.

Kazdin (2000) suggested that research into treatment approaches used with children should focus on what mechanisms they cure, rather than concentrating on symptom reduction. Excessively stressed children often perceive themselves as incompetent to cope with demanding situations, preferring avoidance as a basic management response (Ollendick et al., 2011), but changes in children's styles that cope with avoiding more active approaches, which (Compas et al., 2001) are still to be understood (Prints & Ollendick, 2003). Restriction of research is the content within which studies take place, and are often clinically based. The advantage of CBT is that programs with manual from a range of professionals to a variety of different contents can be provided. Improving these interventions in other contexts can lead to support more community programs for the children's with autism mental health. Schools have the potential to be important and accessible bases, customized environments in which CBT programs are provided. Schools require a high degree of social skills that can increase the levels of anxiety in children with a diagnosis of autism. Providing interventions within schools can help to generalize skills from one context to another and reduce the disruption of education for children and young people who need to move to clinics. (Clarke, Hill, Charman, 2016). It is important to investigate the use of CBT in schools, in order to help schools promote mental health in their students and identify and deal with fewer problems at a later stage and to build their resilience and flexibility. A meta-analysis of CBT used with stress-stricken young people found different results depending on whether the intervention took place in a university or other clinical setting (Ishikawa et al., 2007). Interaction, treatment reliability, supervision and the level of therapists' experience can affect the overall efficacy. In addition, conducting research in a school environment affects its outcomes, as children are in a socially demanding context before taking part in the CBT. The

completion of the treatment and the child's initial anxiety levels may be different in a school than in a clinic, which may have an impact on the effectiveness of the treatment (Clarke, Hill, Charman, 2016).

### **3.2 The CBT Program**

The CBT program has been developed by Child Guidance Clinic (CGC) psychologists and the Autism Resource Center in Singapore. Modifications and adjustments have been made to various CBT programs such as The Coping Cat Program, Exploring Feelings, and unpublished anxiety management programs from the CGC and the Autism Resource Center. For example, strategies that were found to be effective with children with ASD such as structure use, visual strategies, role plays and social stories were incorporated. The CBT program was also designed to meet the cultural and developmental profiles of children with ASD in the Asian population. Scriptural examples and worksheets were also a package of content that was most understandable to children in Asia. Also, the use of the toolbox from the Exploring Feelings program in the Cleaning Toolbox was modified. (Storch et al., 2013).

The manual CBT program consists of 90-minute weekly sessions distributed in small groups with 3-4 participants. Each group is coordinated by 2 therapists trained to coordinate the program. The CBT program includes 3 key parts. The first part (sessions 1-3) focuses on recognizing and understanding emotions within the participant itself and others. Participants were taught to recognize different types of feelings (e.g., happy, sad and angry) with an emphasis on stress. Differences in the challenges of situations, facial expressions, behaviors and gestures, reason,

physiological reactions and thoughts associated with various feelings were stressed. Participants also recognized what triggered their own anxiety.

The second part (4-9 sessions) focused on anxiety management techniques. Participants have been taught techniques in hierarchical levels of difficulty, such as relaxation in the form of physical activities, relaxation skills (breathing exercises and muscle relaxation techniques), recruiting help from others (including social opinion) and cognitive reconstruction (by identifying and replacing cognitive errors with positive and auxiliary ways of thinking). These strategies and skills were presented to the participants with the support of visual representation in the form of "cleansing tools" in order to facilitate retraction. The participants practiced with therapists and were provided with residential and clues to encourage generalization and practice outside the therapeutic setting.

The third part (sessions 10-16) focuses on problem-solving strategies based on STAR's strategy, which has been used by the Child Psychiatric Service at the University Hospital & Iowa Clinic since 1980. STAR is an acronym for STOP THINK (think about possible ways to calm down and / or solve the problem) ACT (execute a selected plan and design) and REFLECT (evaluate the result from the selected design, and do the appropriate adapters ). Participants were practiced using problem-solving strategy at different levels such as theory, imagination, role playing, and in-vivo real situations wherever possible. This was repeated for various stress-inducing traits found by participants in the first part of the program.

It is important that the method of instructions was flexible and allowed for various treatment facilities between the younger group (9-12 years) and the older group (13-16 years). Therapists must be sensitive to the developmental differences between

children of different ages. Also, mental, cognitive maturity for treatment is important. While games and activities were built to increase learning, their complexity and goals vary according to the learners' learning pace. For the younger group, concepts were interpreted or depicted in simple terms. The older children were capable and encouraged to rationalize their thoughts or problems. Strategies were also discussed and taught at an appropriate level, for example a 9-year-old may have been encouraged to approach a teacher when it was bullied by classmates, and a 15-year-old with a similar problem could have been encouraged to deal with a "smart" or seek comfort from the grown-ups. Problem solving practices depend on individuals' issues and content that allow program's flexibility and adaptation according sensitive to each child's needs (Clarke, Hill, Charman, 2016; Danial, Wood, 2013).

### **3.3 Teaching social skills**

Teaching Social Skills is a method used for adolescents with ASD. Although few studies exist to improve social skills for highly functional teenagers in the spectrum and even fewer studies have examined the effectiveness of teaching social skills in the classroom. This study examines the change in the adolescents' with ASD-HF social function following the implementation of a school intervention, such as PEERS and Program Support for Education and Enrichment of Relational Skills (PEERS) (McNally et al., 2013; Drmic, Aljunied, Reaven, 2017).

### **3.4 Psychosocial Therapies**

The use of psychosocial therapies includes more cognitive and behavioral therapy (CBT) and approaches for children and adults with anxiety. It has been well

documented, but the application of these therapies and approaches to patients with developmental disorders and anxiety is limited. Children with anxiety have benefited from parental involvement in the treatment (Suveg, Roblek, Robin et al., 2006) as increased parental involvement in the treatment of children with developmental disorders and anxiety can be beneficial (Reaven, Hepburn, 2006).

Interventions involving multiple treatment components including behavioral, psychosocial and pharmacological may be appropriate for the treatment of adults in the community, in care settings, and working with their carers (Bogacki, Newmark, Gogineni, 2006). Some research has been done to implement CBT models for treating social phobia in people with intellectual disabilities (Dagnan, Jahoda, 2006).

Improving social skills for children with Asperger's syndrome have been examined in a number of studies and these can reduce the severity of anxiety and especially social anxiety, in these children through improved social interactions and relationships (Elder, Caterino, Chao et al., 2006). Modifications, of psychosocial interventions for anxiety may be necessary for patients with developmental disorders. Some of these modifications have been described in several studies.

### **3.5 Studies for Special Psychosocial Therapies**

Most studies concerning psychosocial anxiety therapies are case studies with a small sample. A review of 8 studies identified in the literature is shown in Table 1 below.

INSERT TABLE 1 SOMEWHERE AROUND HERE

Two studies involving treatment with control groups and culture of relaxation skills in patients with mental retardation were identified in the literature. These studies were carried out on the same subject (Lindsay, Baty, Michie et al., 1989; Lindsay, Morrison, 1996). A multi-group study involving 50 mentally retarded patients divided into 4 groups using different forms of relaxation techniques. Stress and cardiac pulse rates were evaluated before and after the intervention. They were compared with a control group which was not trained in relaxation techniques (Lindsay, Baty, Michie, et al., 1989). A second case study with adults with mental retardation showed that behavioral relaxation reduced anxiety during several sessions. Also it seems that anxiety could be reduced with controlled signs of reduction after previous behavioral training (Lindsay, Fee, Michie et al., 1994). Other studies point out that some of the developmental disorders require specific modifications to standard behavioral and cognitive approaches to anxiety. The third study examined the education's effect on relaxation by cognitive approaches and methods in adults with mental retardation and showed improved concentration in intervention procedures necessary for patients with developmental disorders. Generally, patients with developmental disorders may need more specific advice and guidelines, a focus on more repetition, a greater number of meetings, more use of behavioral enhancers and patterns, and more involvement of parents and guardians. In a case study with CBT intervention for a 7-year-old child with water- and elevation- phobia, it was treated with the use of a fast, one-session therapeutic intervention for each phobia, which was repeated with a difference of 2 months. The treatment included mass exposure, in vivo exposure, standard participant, cognitive challenges, reinforcement and other techniques. The study revealed that the child, after intervention, showed reduced or limited avoidance, fear, negative voice, and other phobic symptoms (Davis, Kurtz, Gardner et al., 2007).

Another case study describes a modified CBT 20-sessions approach for an 8-year-old girl with cognitive retardation and social phobia, selective suicide and GAD (Suveg, Comer, Furr et al., 2002). Therapists used multiple assessment forms including a structured diagnostic interview, self-reports, parent and teacher reports. They showed a significant reduction in anxiety and other symptoms, and the child no longer met the criteria for GAD and selective mood during the post-intervention period. In the adaptation of intervention for the child with mental retardation, the therapists presented the concepts in particular, emphasized the cognitive psychology, made a number of meetings and gave more practice to skill development (Suveg, Comer, Furr, et al., 2002). A case study on the use of graded exposure to skin care products in two 4-year-old boys with autism who had despair, fear and anxiety was treated with skin care products (Ellis, Ala'i-Rosales, Glenn, et al., 2006). They note that the use of standard therapies and treatment took place during a number of 30-60 minute meetings and used a number of stimulus exposure tests (44 for the child with moderate to severe autism and 24 for the child with mild to moderate autism). Some of the trials were completed with the participation of the mother and some with the therapist (Ellis, Ala'i-Rosales, Gless, et al., 2006). Another study describes CBT with a 7-year-old Asperger and OCD child during 14 sessions for 5.5 months using exposure and response prevention. Modifications were used, the parents were involved in each session, reconciling the child's preferences for formal language, using lists, score sheets, visual support, and including the child's preferences for creating names for things. They reported that most of the OCD symptoms had been disappeared at the end of the intervention. They also performed a series of consecutive 3-4 week sessions where the authors noted that the profits of the interventions were maintained (Raven, Hepburn, 2003). Other creative therapeutic approaches have

included the use of mutual restraint / obstruction with music therapy in a case study that involved the use of a lung instrument to attenuate fear and anxiety and to avoid a reaction from the child with ASD (Hoelzley, 1991).

In conclusion, a significant number of people with developmental disorders have comorbid anxiety disorders. Greater anxiety appears to be associated with higher levels of cognitive function. Lower levels of anxiety were detected in people with mental retardation and higher levels in those with autism and Asperger syndrome (Dagnan, 2007; Skokauskas, Gallagher, 2012; King, 2007). Anxiety disorders in patients with developmental disorders may be difficult to detect and diagnose due to overstimulation of stress symptoms associated with special developmental disorders and due to the fact that people with developmental disorders often lack communication skills to describe their symptoms well.

Some research evidence points out the physiological abnormalities in stress-related and brain-related areas that are associated to developmental disturbances and anxiety, which can explain biological divides and provide indications for improved intervention (Wood, Gadow, 2010). Several clinical practices in the treatment of comorbid developmental disorders and anxiety are based on the modification of interventions used in patients with anxiety but without developmental disorders for which there is a significant research. There is research on the treatment of stress comorbidity in developmental disorders, using pharmacological and psychological approaches, although more research is needed. Concerning pharmacological treatments, there are findings that anti-depressant buspirone and non-standard antipsychotics, risperidone are effective. However, many of the evidence is based on uncontrolled trials, and there are serious difficulties in identifying therapies and side effects on patients participating in them (Kalachnik, Hanzel, Sevenich, Harder, 2002;

Kamimura-Nishimura et al., 2017). As for psychological interventions, many of the evidence is based on case study reports with a small sample. Although it appears that modified versions of standard stress interventions such as relaxation, gradual exposure and exposure and prevention of reaction used with patients without developmental disorders may be effective, more research should be conducted with larger samples, weighted measurement means and control groups. In reviewing research on drug therapies and psychosocial treatments for anxiety in developmental disorders, it is clear that there is a need for more research into treatments that compare results with control groups, especially in studies using virtual treatments for therapies medicines and control groups and in control group studies and a larger sample for psychosocial interventions (Aman, 2009).

Studies involving drugs and psychosocial treatments would be particularly valuable because this is consistent with current practice. To evaluate the outcome and change, many studies that have been reviewed are based on overall rates. Although some have used weighted tests with appropriate validity and reliability, only a few have used tools developed specifically for use in patients with developmental disorders. Further use of these weighted instruments would provide valuable data for the benefit of treatments. Moreover, it should be noted that developmental disturbances have lifelong consequences and may continue to be more at risk for stress and relapse (Tables 2, 3).

INSERT TABLES 2 & 3 SOMEWHERE AROUND HERE

### **3.6 Combination of educational, psychological and medical treatments**

An important part of any intervention with a patient with an anxiety disorder is education. A practical guide to panic disorder suggests family education as well. Symptoms and behavior might not be clear but confusing. People with anxiety symptoms that seek treatments need to know that they are not alone and that there are effective interventions. The persons who would seek for appropriate medical care, should perform medical tests for thyroid hormones and electrocardiogram when indicated. After medical examinations, the development of a "labor ally" model with the patient provides a basis for continuous management and limits or excludes the use of medical methods.

A combination of psychotherapy and medical care is recommended in all anxiety disorders. CBT is claimed to provide support but requires commitment to treatment by the patient. Its effectiveness may lie in the therapist's capacity and duration of treatment. Studies show that when compared to diseases treated with a combination of CBT and drugs, they experience almost twice recession rates, even when the CBT is applied by a person with little or no experience with CBT (Roy-Byrne, Craske, Stein et al., 2005). Serotonin (SSRIs) has been shown, selectively, to be a better tolerated drug, and response rates are significantly higher than placebo for panic disorder, OCD, PTSD, social anxiety and GAD. This drug class includes fluoxetine (Prozac), fluvoxamine (Luvox), citalopram (Celexa), escitalopram (Lexapro), paroxetine (Paxil) and sertraline (Zoloft). Some improvement should be noted within 3 or 4 weeks and the dose should be increased if improvement does not appear. OCD symptoms can take 8 to 12 weeks to respond to treatment. These patients often require doses at a higher level than the usual dosage, in which case the dose is increased. It is also rare to achieve complete analysis of OCD symptoms and a partial reduction is the typical response. In all anxiety disorders, SSRIs should start at low doses and gradually

increase therapeutic levels to avoid an initial worsening of anxiety (Kalachnik, 2002; Kamimura-Nishimura, 2017). Benzodiazepines, which have been widely used in the past to treat anxiety disorders, continue to be useful in the short-term management of symptoms until the acceptable reduction in symptoms is achieved with an SSRI or CBT. Tolerance and lack of addiction initially makes SSRIs more desirable for long-term management, but the delay in response makes relief from the short-term symptom of benzodiazepine desirable for those with greater disability. Because of the risk of increased stress when withdrawing from short-term benzodiazepines, such as alprazolam (Xanax), many psychiatrists prefer longer-acting benzodiazepines such as clonazepam (Klonopin). If the patient does not respond to the combination of CBT and medication, a re-evaluation of the symptoms may reveal a co-morbid disorder received at the first examination. Emotional psychiatric disorders reduce significantly the likelihood of anxiety recovery and increase repeat rates (Bruce, Yonkers, Otto et al., 2005). Many clinicians try to avoid selective serotonin reuptake inhibitors (SSRIs) before deciding on the next step in treatment. A referral to the psychiatrist for (more) further evaluation and management may be necessary if none of these strategies work. Strict therapies for stress can be too debilitating for both the patient and the therapist. This can lead to an increase in dependence on benzodiazepines and the escalation of doses required for the same effect. Sometimes when treatment is started although the therapist can assure the patient that there is proper treatment it is necessary to experiment with various combinations until the appropriate one is found. Although all anxiety disorders seem to require a long duration, most patients improve their condition with the appropriate treatment. Response rates are improved when co-morbidity is low. Patients with an early onset of symptoms (childhood or adolescence) can generally expect a more time-consuming course and may be more

difficult to cope with. In some of the disorders (PTSD, panic disorder), patients sometimes have an auto recession or can operate despite symptoms. Although the time for withdrawal of symptoms is shortening, all of the function can be improved with the treatment (Oswald, Sonenklar, 2007; Owen et al., 2009; Reaven et al., 2015). Pharmacotherapy often helps when effective treatment is continued for 12 months. When it is about to stop pharmacological treatment, the risk should be discussed with the patient. When SSRIs are to be discontinued, slow, gradual, reduction is recommended, with monitoring for any signs of recovery. Lifelong management with pharmacotherapy or psychotherapy, or both, is not uncommon for many patients. For many a maximum reduction of symptoms, than a full recovery is an acceptable result. Individuals's education is as crucial as family's for realistic treatment expectations. Treatment includes a selective serotonin reuptake inhibitor, starting at low doses with careful volumetric analysis so as not to stimulate anxiety symptoms. Starting cognitive-behavioral therapy along with pharmacotherapy to significantly increase response rates is also important. Short-term benzodiazepines should be considered appropriate in more serious cases. Long-term use of the drug involves reducing the impact of its gradual withdrawal. Usually they concern mental health professionals in difficult cases or for patients with less than expected response to treatment (Oswald, Sonenklar, 2007; Owen et al., 2009; Reaven et al., 2015).

### **3.7 Social Recreational (SR ) Program**

The group received 16 weeks in a SR program developed by psychologists and research assistants at the Child Guidance Center (CGC). It consists of 90-minute weekly meetings, divided into small groups of 3-4 participants. Each team worked with 2 therapists trained to run the program. Similar to the CBT program, common strategies have been found to be effective with children with ASD such as the use of

structure and visual indications to encourage behavioral adjustment expected in a group. The range of activities in the SR program is designed with activities for children with typical neurodevelopment in age groups. These activities were categorized into individual or group activities. Individual activities intended to cultivate self-development skills, such as teaching the child to prepare a simple meal, and self-stimulation behaviors such as doing works (such as cutting paper). Other activities were intellectual simulation (e.g. word puzzles) or intended to improve coordination skills (e.g. magic tricks). Group activities provided participants with opportunities to learn and practice pre-social skills through collaborative games such as board games and treasure hunting. When interacting with others, participants were reminded of a social lesson such as changing rows and playing fairly. Homework included activities that participants could try out of the treatment's context. The SR team participants did not receive any specific instruction (representing the basic components of the CBT program) in STAR, repeat practice and exposure activities. Social skills can be taught according to the opportunities available, for example, the therapist points out the child's inappropriate behaviors when they appear. But this is the case for example in group lessons following the application of structured classes (Wigham, McConachie, 2014; Rudy, Lewin, Storch, 2013).

### **3.8 Integrity of CBT & SR programs**

The integrity of the CBT program and SR program was evaluated in the following ways. First, both programs were manual programs to increase adherence to intervention procedures. Second, the sessions were videotaped and viewed by an independent statistician who completed checklists describing the specific topics to be

covered by each session. The results showed that adherence and attachment to both programs was over 95%. In the study of Sung, Phaik, Ooi, Jui Goh, Pathy, Fung, Ang, Chua, Lam (2011) CBT refers to cognitive deficits and disorders that can cause social and communication, behaviors and feelings difficulties. Practical strategies such as problem solving skills and relaxation techniques were integral to helping these children interact with others effectively, and to promote self-regulation. Activities in SR groups are recreational activities. Nuelinger (2012) defined leisure activity as a situation characterized by lack of meaning and non-utilitarian activity. The lack of importance in leisure activity is good to promote mental health even of people with ASD. Evidence suggests that self-stimulating and self-traumatic behaviors can be prevented by providing a different sensory stimulus, and in this case, leisure activity offers this possibility. While the SR program does not incorporate CBT strategies, it contains common strategies found effective in children with ASD, such as the use of structured and visual indicia that encourage behavioral regulation. In addition, there were opportunities to learn and practice social and prosocial skills through some collaborative games facilitated by therapists. Children in the SR program also had opportunities to learn self-help skills such as preparing a simple meal. So the SR program, although it did not directly introduce stress management, can be seen as an alternative treatment. The SR program may address some weaknesses related to ASD and promote behavioral conditioning and positive social skills in these children through a variety of leisure activities, thus reducing stress levels (Sung et al., 2012).

The CBT and SR programs share common elements, i.e. regular sessions in a structured environment, consistent therapists, social exposure and the use of useful strategies for children with ASD (e.g. visual aids and programs). It could be possible to include these elements in sessions as they would serve as an effective framework

for managing anxiety in children and adolescents with ASD. Thus, community-based and structured sessions incorporating the above elements may have potential benefits in managing anxiety in children and adolescents with ASD, which in turn may reduce the need for tertiary services for specific programs. The main components of the treatment (Chalfant et al., 2007) Cool Kids is the recognition of anxiety feelings and physical reactions to anxiety, simplified cognitive reconstruction exercises which include recognition of ancillary and not auxiliary thoughts, dealing with self-work, each on its own (Ehrenreich-May et al., 2014, See Wood et al., 2009, Fujii et al., 2009). Building Confidence Recognition of stressful emotions and physical responses to anxiety, coping skills followed by live exposure, creating a hierarchy of fear, developing friendship skills, sessions were taught through guided discussions (Socratic questions). Initially, 16 sessions were focused on general anxiety symptoms and then the last 16 sessions focused on child relationships and on the interaction of children in school and community (social guidance) (McConachie et al., 2013).

Exploring Feelings (Feelings of anxiety) recognition and physical responses to anxiety, development of natural, social and thoughtful tools suitable for each child is also necessary. (McNally, Keehn et al., 2013). Coping Cat recognition of anxiety emotions and physical reactions to anxiety, cognitive reconstruction, anxiety management techniques, creating a hierarchy of fear, exposure, use of empowerment strategies: sessions were taught through written and visual material, specific language, sensory stimuli, and computer use (Ooi et al., 2008). The Treatment Manual - Use of CBT treatments are: recognizing emotions to themselves and others, understanding and recognizing different types of emotions, stress management techniques including relaxation training and problem solving strategies. Sessions are taught through visual clues and social stories (Reaven et al., 2012). Coping Groups include: Fighting

concerns and Facing Fears, Recognition of anxiety and body anxiety reactions, relaxation training, creating a hierarchy of fear and classified reports (Reaven et al., 2009).

Facing New Fears included elements of Coping Cat, relaxation, deep breathing. Strategies for emotional regulation, use of cognitive self-control, including a rewarding empowerment program, classified exposures, and workshops taught through worksheets, hands-on activities, video projection, and visual aids (Sofronoff et al., 2005). The child recognizes different emotions, learns relaxation techniques, develops social tools and thinking tools, and learns emotional management skills. The main elements of the treatment (Storch et al., 2013; Sung et al., 2009; Sung et al., 2011) incorporate various CBT programs including The Coping Cat Program, Exploring Feelings, and other stress management programs (White et al., 2013), the use of visual strategies (e.g. clues), role playing, social stories, and worksheets were taught through stress strategies, stress management techniques, cognitive reconstruction and problem solving strategies. Multimodal Anxiety and Social Skills Intervention Based is based on CBT principles and applied behavioral analysis (ABA), recognition of stressful feelings and physical responses to anxiety, counseling skills (e.g. relaxation training), creation of fear hierarchy, reports, development social skills including friendship development, social guidance and the development of relationships with peers (Wood et al., 2009). The baseline treatment data were reported from each study (Ung, Selles, Small, Storch, 2015).

### **3.9 Antidepressants for Treating Anxiety in Developmental Disorders**

Treating anxiety in people with developmental disorders is based on the use of a combination of interventions applied to treat anxiety in people without developmental disorders. Some more limited research has been conducted specifically in this

population. In a review chapter in a book, King, Bouras & Holt (1994), reports that there may be difficulties involved in diagnosing and treating patients with drugs, including the recording of side effects and efficacy. These patients may not be capable of self-reporting due to limitations in their ability to communicate effectively. It has been reported that for one-third with half of the patients in the community and in areas of residence for mentally handicapped people treated with psychotropic drugs, there is doubt as to whether one treatment is effective or appropriate. Also what was reviewed were the main classes of drugs (antidepressants, anxiolytics, beta-blockers and antipsychotics) used in the treatment of anxiety with people with developmental disorders. Sensitivity to drug efficacy has been observed, and drug interactions may be of particular concern. Particular attention is needed when prescribing anxiolytics because they have been shown to cause cognitive difficulties and paradoxical stimulation, mobility and withdrawal of drug inhibition in patients with developmental disorders (King, Bouras, Holt, 2007). Another review mentions extensively different types of treatment and the content of intervention that applies to patients with intellectual disability including supportive, educational, family, behavioral and cognitive therapies. Some authors emphasize the importance of individualized assessment in modifications or adaptations of interventions which are necessary for developmental disorders but state that the scientific study of these interventions is very limited (Dagnan, Boras, Holt, 2007). Flament et al. (2007) reviewed four controlled trials and a number of open-label studies demonstrating efficacy in exposure and response, a response to preventive treatment of childhood OCD (Flament, Geller, Iraq et al., 2007) also mentions a meta-analysis of use of SSRIs, but not included or specifically referred to children with co-morbidity of developmental disorders. It remains unclear how such treatments can be applied to

people with developmental disorders (Ozsivadjian, Hollocks, Southcott, Absoud, Holmes, 2017). Tsai, Baron & Groden (2007) describe diagnostic issues and processes in psychiatric disorders, co-morbidity with autism and Asperger syndrome, and high rates of co-morbidity in various studies. The authors highlight medical and behavioral assessment and important issues such as clarifying and agreeing on behavioral problems by getting information and feedback from the family, guardians, educators and other members of the treatment group and determine at what self-reporting level the Asperger or high functional autism is able to answer. They also highlight the process for functional behavioral assessment by a psychologist or behavioral therapist. After an interdisciplinary assessment has been completed, an intervention plan involving family members, therapists, psycho-education, self-recording, cognitive therapy and demonstration of treatment responses, exposure to therapy, relaxation, cultivation of social skills and also prevention of relapse is assembled. In addition, recommendations are made for family members involved in the treatment of childhood anxiety in people with autism and It also includes types of medication and psychosocial treatment (Tsai, Baron, Groden et al., 2007) (Table 4).

INSERT TABLE 4 SOMEWHERE AROUND HERE

### **3.10 Pharmacological Interventions**

Though not directly applicable to patients with developmental disorders, a recent article publishes a review of the pharmacological treatment of childhood anxiety disorders including social anxiety, GAD, panic disorder, OCD special phobia, and PTSD (Reinblatt, Riddle, 2007; Kamimura-Nishimura et al., 2017). In the treatment of individuals in general, selective serotonin reuptake inhibitors (SSRIs) have been

reported to show efficacy in adults, but evidence for children is increasing (Murphy, Bengtson, Tan et al., 2000).

In a systematic bibliographic review of clinical trials of SSRIs of developmental disorders interventions, 3 RCTs and 10 open-label trials have been identified. The majority of these trials show improvement in general function, reduction of anxiety and reduction of repetitive behavior. The authors concluded that most side effects were moderate, but some patients had increased spontaneous mobility (Kolevzon, Mathewson, Hollander, 2006). Another review included studies that focused on the use of antipsychotics in children for a variety of disorders, including ASD and anxiety (Findling, Steiner, Weller, 2005), although they concluded that antidepressants, especially SSRIs, were not the most common used and studied. Another review covered various studies on the effects of anxiolytics, including benzodiazapines and buspirone, on the treatment of anxiety in developmental disorders (Antochi, Stavrakaki, Emery, 2003). It should be noted that the side effects of benzodiazepines may be inadequately studied and recognized in mental retardation (MR) and other developmental disorders (Kalachnik, Hanzel, Sevenich et al., 2002).

### **3.11 Special pharmacological tests**

Eight studies of pharmacological stress therapies in patients with developmental disorders were identified in the review. One of these studies was double-blind random-test testing. The remaining studies concerned individual groups and case studies and, in some cases, based on a retrospective review of patient diagrams in clinical settings. A double-blind, placebo-controlled trial in atypical antipsychotic risperidone was conducted in adults with autism and diffuse developmental disorders not otherwise specified (PDD-NOS) and anxiety consistency (McDougle, Holmes,

Carlson et al., 1998). Patients in the intervention group (n = 15) showed a significant reduction (57% of the intervention group) in anxiety and other psychiatric symptoms in the 12-week trial compared to a control group (n = 16). Anxiety has been identified using a clinically-quantized scale-ratio, called "anxiety or nervous", with no clinically significant effect. Also in the case study of 14 children and adolescents with developmental disorders treated with risperidone, 10 of the 14 patients showed a significant reduction in anxiety (Fisman, Steele, 1996). Three studies of buspirone in patients with developmental disorders and anxiety, patients showed a decrease in clinical rates of anxiety (Buitelaar, van der Gaag, van der Hoeven, 1998; Ratey, Sovner, Mikkelsen et al., 1989; Ratey, Sovner, Parks et al., 1991). 22 children aged 6-17 years old with ASD were treated for anxiety in an open-label assay of buspirone (15 = 45 mg / day) for 6 to 8 weeks. 9 children showed significant therapeutic response and 7 showed a modest response to the CGI scale. One patient showed abnormal movements (Buitelaar, van der Gaag, van der Hoeven, 1998) (Table 5).

INSERT TABLE 5 SOMEWHERE AROUND HERE

A study of 6 adults with MR showed a decrease in aggression and anxiety (Ratey, Sovner, Parks et al., 1991). Nine of the 14 patients with ASD, anxiety and aggressive and self-traumatic behavior responded positively to a control group (Ratey, Sovner, Mikkelsen et al., 1989). The effectiveness of antidepressants has been studied in 3 studies. Two studies searched for the effect of SSRI citalopram on children and adolescents with ASD and anxiety (Namerow, Thomas, Bostic et al., 2003; Couturier, Nicolson, 2002). A retrospective study looked at 17 patients with 4-15 years of age who were treated with an open-label citalopram test (5-40 mg) for an average of 7

months 10 (59%) were judged to have improved significantly or significantly in targeted symptoms, especially anxiety and aggression, using the Clinical Global Impression Scale. Four patients showed significant side effects including insomnia and teak stimulation. (Couturier, Nicolson, 2002). The second presented a retrospective review of charts of 15 children and adolescents with high functioning autism, including Asperger, autism and PDD-NOS treated with citalopram. Anxiety symptoms were significantly improved in 66% of patients. Five patients, or 33% reported moderate side effects (Namerow, Thomas, Bostic et al., 2003) including headaches, narcosis, aggression, shaking and dyskinesia of the lips. A third study looked at 26 patients with ASD were treated with an open-label trial of SNRI mirtazapine (7.4-45 mg / day) for 150 days. 9 patients (34.6%) were judged to be significantly improved or significantly improved in the Clinical Global Impression Scale of anxiety and various other symptoms including anxiety, self-injury, sensitivity, hyperactivity, depression and insomnia; some patients experienced small side effects such as increased appetite, sensitivity and transient suppression (Posey, Guenin, Kohn et al., 2001). Another case report examines the use of fluvoxamine in a patient with autism and co-morbidity OCD (McDougle, Price, Goodman, 1990) showing a decrease in OCD symptoms and overall improvement in rates in Clinical Global Impression.

### **3.12 Assumptions for Special Populations**

Professionals should take precautions when treating certain anxiety populations, including patients with significant dependence, obstructive chronic lung disease (COPD) or other respiratory illness, pregnant or older patients. Benzodiazepines are generally considered unsafe for use in pregnancy and in substance-dependent patients. In these populations, the combined treatment of SSRI with CBT therapy is preferable.

If benzodiazepines are necessary, it is important to start at a lower dose, higher fluid density, and design for short-term use only.

#### **4. Discussion**

The aim of this review is the investigation of approaches and treatments of anxiety of individuals with ASD world wide in a comparative review. Literature review, of the period 1980s until 2017, on interventions gave 137 research and studies, published articles, and links that propose several approaches from different point of views (e.g. psychologist, medical doctor, teacher). The issue of treatment of anxiety in people with ASD is interdisciplinary field. Professionals in the field see the issue from its different aspects and propose interventions and approaches that vary from pharmacological to social skills, cognitive behavioral approaches etc.

In order individualized interventions to be designed multifaceted, assessment should be implemented. Approaches should be selected according to individual characteristics as well as to cause of anxiety. Thus a combination of techniques and approaches would be more appropriate to be tried than one single approach. CBT seem to have longer lasting results, however, it can not be applied in each person in the spectrum since it demands a level of semantic pragmatic development (it depends on factors like e.g. vocabulary, IQ) (Danial, Wood, 2013). Psychoeducation and Coordination of Care Are the First Steps of Treatment. Educating youth and families about anxiety symptoms is an important first step. Other points include delineating specific and measurable treatment outcomes (eg, decreased avoidance of feared stimuli, more responsive to psychosocial interventions when anxious, sleeping in own

room every night). Coordinating the treatment plan with parents and care providers (e.g., therapists, school staff) is recommended to track progress.

**Anxiety Can Be Treated With Modified CBT Techniques.** Preliminary data suggest that modified CBT (MCBT) is an efficacious treatment of children and adolescents with high-functioning ASD and DSM-5 anxiety disorders. MCBT can be administered individually or in a group and often includes parental involvement. CBT in TD youth involves many components, including affective education, cognitive restructuring, reducing avoidance behaviors, relaxation, modeling, and exposure to the feared stimuli (with response prevention). Some youth with high-functioning ASD can understand basic cognitive concepts of CBT and therefore may be responsive to both the cognitive and the behavioral elements of MCBT. In ASD, special CBT adaptations are needed to facilitate understanding of cognitive and emotional concepts. These include the use of visual supports and concrete language, the use of written materials and lists, opportunities for repetition and practice, incorporating special interests, video modeling, and more active parent engagement in therapy. Behavioral therapy with exposure may be particularly useful for youth who have language and cognitive difficulties, thereby precluding participation in the cognitive components of treatment (Vasa et al., 2014; Vasa, Mazurek, 2015). Some families may have limited access to mental health professionals with expertise in ASD and MCBT protocols, in which case medications may be an option. Sometimes, a child may be resistant or severely anxious during therapy (e.g., exposure to a feared stimulus results in severe tantrums). In these situations, parents and clinicians must decide together whether medication should be tried to facilitate engagement in therapy.

Certain medications can be considered for the treatment of anxiety. Medications could potentially be considered for the treatment of anxiety in youth with ASD. These medications have not been rigorously studied in youth with ASD, the doses are based on data in TD children and adolescents. The recommendations, however, are to start medications at low doses and titrate slowly with close monitoring (eg, monthly office visits) of both benefits and adverse effects. Most important, we recommend that primary care providers have a low threshold for seeking consultation from a developmental/behavioral pediatrician or child psychiatrist when prescribing psychotropic medications. Consultation could be requested either before starting the medication or during the titration process, especially if higher doses are used. Mental health professionals can assist pediatricians with titration and safety monitoring, and help tease out the complex developmental, psychosocial, and medical issues that can affect treatment outcomes. If medications are ineffective or poorly tolerated, gradual discontinuation is recommended. Liquid preparations are available for slower titration or if pills cannot be swallowed. Medications with efficacy in TD children can be tried for anxiety in ASD. Robust evidence supports the efficacy of selective serotonin reuptake inhibitors (SSRIs) for the treatment of anxiety disorders (separation anxiety, generalized anxiety, and social phobia) in TD youth. Indeed, SSRIs are the most effective pharmacologic treatments for anxiety disorders in TD youth, although benefits may not be seen for several weeks after treatment initiation. SSRIs are frequently prescribed in youth with ASD; yet, there is a lack of double-blind placebo-controlled trials supporting their efficacy for anxiety in this population. Data from SSRI trials in youth with ASD report high rates of behavioral activation, which is expressed as increased activity level, impulsivity, insomnia, or disinhibition without manic symptoms. This behavioral activation typically occurs at the beginning of SSRI

treatment or with dose increasement and resolves with reducing the dose or discontinuing the medication. Other prescribing considerations include a family history of bipolar disorder, drug interactions, and the black box warning of suicidal ideation. Given these factors, certain SSRIs are preferred over others. In summary, SSRIs should be prescribed cautiously in youth with ASD, with close monitoring (Moree, Davis, 2010; Modell, Rider, Menchetti, 1997; Murphy et al., 2017; Nadeau, 2011). Medications can be used to treat specific anxiety-associated symptoms based on evidence in ASD as well as expert clinical consensus. Several studies discuss the management of sleep disturbance in youth with anxiety and ASD. Insomnia secondary to anxiety can be treated initially with melatonin, and if ineffective, there is preliminary evidence indicating that clonidine, a short-acting  $\alpha$ -agonist, may help with insomnia. Although no data are available, low-dose trazodone can also be considered. Antihistamines with anticholinergic effects (eg, diphenhydramine) should be avoided for chronic sleep difficulties due to the potential for delirium and constipation. Referral to a sleep specialist should be considered as necessary if these interventions are ineffective. Some children with anxiety may exhibit significant physiologic arousal symptoms including increased heart rate, blood pressure, sweating, and muscle tension. Although no data are available,  $\alpha$ -agonists and propranolol could be considered to reduce such physiologic symptoms (Kolevzon, Mathewson, Hollander, 2006). Anxiety can also result in behavioral dysregulation, which can be characterized by irritability, aggression, property destruction, and self-injury.  $\alpha$ -Agonists (clonidine, guanfacine, guanfacine extended release), which improve symptoms of attention-deficit/hyperactivity disorder in youth with ASD, may potentially reduce some of these behaviors. The ATN pathway for the treatment of accompanying irritability and problem behaviors can also be followed to manage

these behaviors. Youth with ASD frequently experience situational anxiety such as during family events, holiday time, blood draws, and other medical procedures. There are no data on pharmacologic treatments for situational anxiety. Short-acting benzodiazepines (e.g., lorazepam) or a  $\beta$ -blocker (eg, propranolol) can be considered temporarily with close attention to sedation, cognitive impairment, and behavioral activation. If anxiety is extremely impairing or is not responding to interventions children with complex presentations or partial or no response to medications should be referred to an ASD mental health clinician (eg, a child psychiatrist, developmental pediatrician, psychologist, and others). If the child's anxiety triggers self-injury and/orelopement, treating clinicians should initiate appropriate interventions to keep the child safe. Appropriate intervention may include a referral to an inpatient or partial hospitalization program.

In conclusion approaches for the treatment of anxiety need to be tailor made to individual characteristics. A Combination of techniques is more suitable for individual cases than one single approach. Periodical assessment and reset of techniques might be necessary in individual cases. The identification of anxiety's cause would contribute to the design of suitable approaches. Further research and updating of information on interventions is important to continue since inclusion of individuals with ASD and anxiety symptoms can increase.

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Table 1

*Psychosocial and combined therapies applied to the management of anxiety in patients with developmental disorders*

Study	Description	Patients	Findings	Comments
Davis et al., 2007	Type of study: Single case study CBT, exposure therapy for water and heights phobia	7- year old M with developmental delays and severe behavior problems	Reduced symptoms of fear and avoidance	
Suveg et al., 2006	Type of study: Single case study Modified CBT	8 year-old F with cognitive delay, social phobia, selective mutism, and GAD	Significant reduction of anxiety, GAD and mutism symptoms	
Reaven and Hepburn, 2006	Type of study: Single case study Modified CBT	7 year-old F with Asperger and OCD	Reduction of most OCD symptoms	Parents involved in therapy. Patient's literal style accommodated. Visual aids and social stories used
Lemmon and Mizes, 2002	Type of study: Case report Exposure therapy	Patient with MR and PTSD from sexual assaults	Reduced PTSD symptoms	Used imaginal and in vivo exposure with simplification of concepts
Lindsay et al., 1989	Type of study: Four treatment groups control group Relaxation therapies	50 Patients with moderate and severe MR	Significant reduction of anxiety and physiological arousal in treatment groups compared to controls	Behavioral relaxation technique is simpler and may be easier to understand that relaxation based on internal awareness

Hoelzley, 1991	Type of study: Case study Music therapy with wind instruments	Child with pervasive developmental disorder, reduction in fear, anxiety, and avoidance	Reduced fear, anxiety, and avoidance and improved cognitive skills	Authors conclude effects may be due to reciprocal inhibition
Ellis et al., 2006	Type of study: Two children Graded exposure to tolerance of skin care products	2 children with autism	Increased tolerance of skin care products	Used modeling and social attention
Lindsay et al., 1994	Cue control relaxation	Adults with severe MR	Reduced anxiety over several sessions	
Lindsay et al. 1989	Comparison of different relaxation treatments for anxiety	Adults with moderate and severe MR	Behavioral relaxation more effective than abbreviated progressive relation	

(Davis, Saeed, Antonacci, 2008)

CBT: Cognitive Behavior Therapy

GAD: Generalized Anxiety Disorder

OCD: Obsessive Compulsive Disorder

MR: Mentally Retarded

PTSD: Post-traumatic stress Disorder

Table 2  
*Practical Clinical Guidelines*

1. Anxiety disorders are common in patients with developmental disorders but are often not diagnosed.
2. Use of well-balanced, valid, credible evaluations. Use of ratings specially designed

for patients with developmental disorders.
3. Use of multiple, cross-referenced information sources.
4. Evidence, elements of efficacy of treatment in reducing anxiety symptoms along with risk for side effects when prescribing drugs.
5. Psychosocial treatment, but mainly that few studies exist that apply the therapies to patients with anxiety and developmental disorders. Adaptations and modifications to standard or well thought-out approaches may be necessary.
6. Use of multi-therapy and group intervention.

(Davis, Saeed, Antonacci, 2008).

Table 3  
*Psychopharmacological Therapy Studies for Children and Adolescents Anxiety with ASD*

Study	Study N Age (years) Anxiety diagnose sb Study design Medicati on Study duration Outcome measures Resultsa	N	Age (years)	Study design	Medication	Study duration	Outcome measuresc	Results	Adverse events (n)	Drop outs (n)
Buitelaar et al. (1998)	Diagnose s not specified Open label Buspiron e (15 – 45 mg/day, M = 29.3 mg/day) 6–8 weeks; 2–12 month	22	6–17 Diagnoses not specified	Open label	Buspirone (15 – 45 mg/day, M = 29.3 mg/day)	6–8 weeks; 2–12 month follow up	CGI (unblind)	41 % had a marked response and 32 % had a moderate response	Sedation (2), mild agitation (2), nausea (1), abnormal involuntary movements (1)	Lack of response (1)
Couturier and Nicolson (2002)	17	4– 15	Diagnoses not specified	Chart review	Citalopram (5–40 mg/day, M = 19.7 mg)	M = 7.4 months, range 1–15 months	CGI (unblind)	59 % showed improvement		Agitation (2), tics (1), insomnia (1)
Martin	18	7–	GAD,	Open	Fluvoxami	10	CGI-I	Group did	Akathisia,	Behavior

et al. (2003)		18	SAD, SoP, OCD, school phobia, and panic/somatic symptoms	label	ne (37.5 – 175 mg/day, M = 66.7 mg/day)	weeks	(unblind) C-YBOCS SCARED-P	not improve as a whole. Females were more likely to respond compared to males (100 vs. 29 %)	agitation, behavioral activation (9), sleep problems (9), headaches (6), change in appetite (4), abdominal discomfort (3), rhinitis (2)	al activation (3)
Namerow et al. (2003)	15	6–16	Rigidity, stereotypes, repetitive behaviors, preoccupations with routines	Chart review	Citalopram (5–40 mg/day, M = 16.9 mg)	M = 219 days (SD = 167 days)	CGI-I CGI-S (unblind)	66 % had improvement in anxiety symptoms	Headaches, sedation, aggression, agitation, and lip dyskinesia (5)	Side effects (2), lack of efficacy (2)
Chalfant et al. (2007)	47	8–13	Not reported	Cognitive behavioral studies SoP (20) GAD (14) SAD (8) SP (3) PD (2)	RCT	Group CBT versus WL	12 weeks	ADIS-C/P RCMAS-C SCAS-C/P	71.4 % in the CBT group were diagnosis free versus 0 % in the WL group. CBT group had fewer anxiety symptoms as per SCAS parent (d = 4.11) and child (d = 2.74) report	Parent work schedules (2), relocation (1), treatment ineffective (1)
McNally et al. (2013)	22	8–14	55 %	GAD (18) SAD (8) SoP (15) SP (15) OCD (2)	RCT	Individual CBT versus WL control	16 weeks; 2 month follow up	ADIS-P SCAS-C/P	58 % in CBT group were diagnosis free versus 0 % in WL group. CBT group had reduction in SCAS-P scores (d = 1.17) but not SCAS-C scores	None reported
Reaven et al. (2009)	33	8–14	81 %	GAD (22) SAD (6) SoP (5)	CT	Group CBT versus WL	12 weeks	SCAREDC/P KSADS-PL	CBT group had a reduction in SCAREDC-P total (d = 0.88) and subscale	busy schedules and family crisis (2)

									scores (GAD, SAD, social, school, panic scores). No reduction as per SCARED-C	
Reaven et al. (2012)	50	7–14	84 %	GAD SoP SAD SP	RCT	Group CBT versus TAU	12 weeks; 3 and 6 month follow up	ADIS-P CGI-I (blind) CGI-S SCAREDC/ P	As per CGI-I, 50 % in CBT group responded versus 8.7 % in WL group (d = 1.03) As per CGI-S, reduction in anxiety severity seen across all disorders (d = 0.66– 0.87) As per ADIS-P, significant reduction in GAD. As per SCARED C/P, reduction in scores at 3 and 6 months	3 in the treatment group due to unspecifi ed reason
Sofronoff et al. (2005)	71	10–12	Not reported	GAD, SAD, SoP, SP, Panic/ Agora phobia and OCD sympt oms	RCT	Individ ual CBT versus parent/ child sessions versus WL	6 weeks	SCAS-P SWQ-P	Both treatment groups showed a decrease in SCAS-P (individual : d = 0.48; family: d = 1.29) versus WL as well as a decrease in SAD, GAD, OCD, and SoP symptoms	2 in the treatment and 3 in the WL group for unspecifi ed reasons
Storch et al. (2013)	45	7–11	84 %	SoP (18) GAD (14) SAD	RCT	Individ ual CBT versus TAU	16 weeks; 3 month follow up	ADIS-C/P CGI-I (blind) CGI-S (blind)	38 % in CBT group were diagnosis free versus	7 in the treatment group: distance from

				(9) OCD (4)				PARS MASC-P CBCL RCMAS-C	5 % in TAU group; reduction in anxiety in CBT group as per all clinician- rated measures ( $d = 0.84-1.06$ ). Gains maintained at 3 months	clinic (2) and without any specified reason (5)
Sung et al. (2011)	70	9-16	0 %	GAD, SAD, SoP, OCD, panic/ AG, and injury symptoms	RCT	Group CBT versus social recreational program	16 weeks; 3 and 6 month follow up	CGI-S (blind) SCAS-C	Both groups had reduction in anxiety severity, and SCASC total anxiety and generalized anxiety symptoms after treatment and at 6 months	6 due to lack of interest, schedule conflicts, preference for other services, medication changes for other psychiatric conditions
White et al. (2013)	30	12-17	87 %	SoP (23) GAD (19) SP (16) OCD (4) SAD (1) PD (1) PTSD (1)	RCT	Individual and group CBT/ social skills intervention versus WL	14 weeks; 3 month follow up	CGI-I (blind) CASI-Anx PARS	No significant reduction in anxiety in the treatment group on the CASI- Anxiety and PARS	2 in treatment group; decrease in teasing and social anxiety (1), increased selfharm, and recurring suicidal behavior (1); 3 in the WL group due to unspecified reason
Wood et al. (2009)	40	7-11	48 %	SoP (35) SAD (24) GAD (19) OCD (17) PTSD	RCT	Individual CBT versus WL	16 weeks; 3 month follow up	ADIS-C/P MASC-C/P CGI-I (blind)	64.3 % in CBT group were diagnosis free versus 9.1 % in the WL group. CBT group	1 in the treatment group and 2 in the CBT for unspecified reasons

				(1)					had decrease in MASC-P versus WL (d = 1.23) but not MASC-C	
Edelson et al. (1999)	12	4–13	Not reported	Diagnosis not specified	Alternative treatment studies CT	Deep pressure versus placebo	6 weeks (twice a week)	CPRS derived anxiety scales	Treatment group had significant reduction in tension and marginal reduction in anxiety	Separation anxiety (1), refusal to participate in galvanic skin response (1)
Jarusiewicz (2002)	24	4–13	Not reported	Diagnosis not specified	CT	Neurofeedback versus WL	6–8 months	Parent interview	Treatment group had reduction in anxiety	Family factors (7), illness (1)

Vasa et al., 2014

a All studies included participants with various ASD subtypes including autistic disorder, Asperger’s syndrome, and pervasive developmental disorder not otherwise specified. All studies except Buitelaar et al. (1998) included participants with comorbid intellectual disability

b OCD: Obsessive compulsive disorder, GAD: Generalized anxiety disorder, SAD: Separation anxiety disorder, SoP: Social Phobia

c CGI: Clinical Global Impressions scale, CGI-I: Clinical Global Impressions scale—Improvement, CGI-S: Clinical Global Impressions scale—Severity, C-YBOCS: Children’s Yale-Brown

Obsessive Compulsive Scale, SCARED-P: Screen for Child Anxiety and Related Emotional Disorders, parent report

a In all studies, various autism spectrum disorder diagnoses were included, i.e., autistic disorder, Asperger’s syndrome, and pervasive developmental disorder not otherwise specified

b RCT refers to randomized controlled trial. CT refers to non-randomized controlled trial

c GAD: Generalized anxiety disorder, SAD: separation anxiety disorder, SoP: social phobia, SP: specific phobia, OCD: obsessive compulsive disorder, PD: panic disorder, PTSD: posttraumatic stress disorder, AG: agoraphobia

d WL: Waitlist, TAU: Treatment as usual

e ADIS C/P: Anxiety Disorders Interview Schedule, RCMAS: Revised Children’s Manifest Anxiety Scale, SCAS: Spence Children’s Anxiety Scale, CPRS: Conners Parent Rating Scale, CGIS: Clinical Global Impressions scale-Severity, CGI-I: Clinical Global Impressions scale-Improvement, CASI-Anx: Child and Adolescent Symptom Inventory-4 ASD Anxiety Scale, CATS:

Children’s Automatic Thoughts Scale, K-SADS-PL: Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime version

f Results report % that are diagnosis free of their primary anxiety disorder

Table 4.

*Overview of approaches to address anxiety in people with developmental disorders*

Study	Design	Description	Comments
Franklin M.E, March	Comprehensive Review of treatment	Describes the use of exposure and	Expertise in CBT in treating pediatric

J.S., Garcia A, et al, 2007	of OCD in children without DDs	response prevention as part of CBT as most well-supported along with SSRI, but cautions that children may have only partial responses to	OCD may be limited in many communities
Tsai et al. 2007	General review of treatment literature for children with anxiety disorders	Recommends involving family members, lists questions for therapists, reviews types of psychosocial and medication therapies that may be applicable	
Reinblatt and Riddle, 2007	Pharmacological Review of pharmacological management of childhood anxiety disorders	Summarizes pharmacological treatment of pediatric anxiety disorders, especially OCD, including multiple outcome measures, effect sizes for several SSRIs and tricyclic antidepressants and side effects	Did not include studies of children with DDs and anxiety.
Kolevzon et al. 2005	Review of the use of SSRI's in autism	Systematic literature review of clinical trials of SSRIs in treatment of DDs. Identified 3 RCTs	Concluded that most side effects were mild, but some patients had increased agitation

		and 10 open-label trials. Majority found improvements in global functioning and reductions in anxiety and repetitive behavior	
Findling et al. 2005	Reviews use of antipsychotics in children	Review of studies examining use of antipsychotics in pediatric patients for a variety of disorders, including PDDs and anxiety	Cautioned against overuse of antipsychotics in children when there is little or no research evidence in support of their use
Antochi et al. 2003	Review of pharmacological treatments in patients with dual diagnosis of DD and psychiatric disorders	Review based on comprehensive literature search of and PsychInfo for clinical trials in DDs from 1975 to 2001. Found that antidepressants, especially SSRI, were most commonly studied. Reviews several studies on the effects of anxiolytics, including benzodiazapines and buspirone, in treatment of anxiety. Concluded that	Also covers mood stabilizers, antipsychotics, and several other medications studied in DDs. Provides clinical guidelines, recommendations for future research, and tables listing specific studies

		benzodiazapines should only be used for maximum of 3 weeks, but that anxiolytics may cause agitation, aggression, and paradoxical excitement.	
Kalachnik et al., 2002	Review of side effects of benzodiazepine in patients with MR	Side effects may be underrecognized in patients with MR and occurred in 13% of patients in studies reviewed	
Murphy et al. 2007	Design Description Comments Review of SSRI trials for anxiety disorders in children and adults	SSRIs have generally demonstrated efficacy in adults and evidence is increasing in childhood anxiety discusses developmental differences that should be considered	

(Davis, Saeed, Antonacci, 2008)

OCD: Obsessive Compulsive Disorder

DD: Developmental Disorders

CBT: Cognitive Behavior Therapy

SSRI: Selective serotonin reuptake inhibitor

RCT: Randomized Controlled Trial

PDD: Pervasive Developmental Disorders

MR: Mentally Retarded

Table 5

*Drug studies for anxiety in patients with developmental disorders*

Published studies	Design	Description	Patients	(Comments)
Namerow et al. [Namerow LB, Thomas P, Bostic JQ, et al, 2003]	Single group— unblinded chart review	Citalopram (SSRI) Ave 16.9 mg over ave 218.68 days, Anxiety Sxs improved in 66%	15 children and adolescents ages 6–16 with Asperger's, autism, or PDD NOS	Used clinical global impression (CGI) as outcome, 75% improved mood, 33% mild side effects
Couturier and Nicolson, 2002	Retrospective single group	Citalopram, mean 7.4 months	17 patients, Ages 4–15 years with PDDs and aggression, anxiety, stereotypies and preoccupations	
Posey et al. 2001	Open label, single group	Mirtazapine, mean 30.3 mg	26 patients ages 3.8–23.5. with autism, Asperger's, Rett's and PDD NOS, 20 with comorbid MR	Used CGI and aberrant behavior checklist
	Open label, single group Buspirone, 6–8 weeks 22 patients ages 6–17 with pervasive developmental disorder and symptoms of anxiety and irritability Buitelaar et al.			

McDougle et al. 1990	Double-blind, placebocontrolled	12 trial of risperidone, significant (P<0.001) reduction in anxiety or nervousness, 8 or 14 (57%) in treatment group classified as responders	31 Adults, mean age 28.1, with autism or PDD NOS	Used Y_BOCS rating scale
Fisman and Steele, 1996	Series of case studies	Use of risperidone in PDDs	14 children ages 9–17, 10/14 showed marked reductions in anxiety	
McDougle et al., 1990	Case report	Fluvoxamine	Comorbid autistic disorder and OCD	
Ratey et al., 1989	Single group	Buspirone 9 of 14 responded	14 DD patients with anxiety	Used clinician ratings on CGI scale

SSRI: Selective serotonin reuptake inhibitor

CGI: Clinical Global Impressions scale

PDD NOS: Pervasive Developmental Disorders Not Otherwise Specified

PDD: Pervasive Developmental Disorders

Y-BOCS: Yale-Brown Obsessive Compulsive Scale\_

OCD: Obsessive Compulsive Disorder