Evaluating a Picture Schedule Reinforcement System to Improve Blood Draw Procedures for Children Diagnosed with an Autism Spectrum Disorder and Diabetes

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Abstract

In clinical settings, caregivers often report that medically related visits are often longer and more difficult for children with an Autism Spectrum Disorder (ASD). A preliminary study conducted by Dr. Robin Gabriels and Dr. John Agnew, indicated that picture schedules can reduce aberrant behaviors during a medical exam (R. Gabriels et al., 2013). The present project assessed whether a picture schedule reinforcement book can help reduce the stress experienced by children with ASD and diabetes during their routine blood draw. The Aberrant Behavior Checklist Community (ABC-C) was used to measure the subject's irritability and stereotypic behaviors. The subjects displayed reduced irritability and stereotypic behaviors during the blood draw. The subjects also had a lower cooperation scale in the treatment blood draw than in their previous baseline blood draw. The limitation of this study was the low sample size (n=2) and comparing ABC-C scores that asked parents to scores behavior for different amount of time.

Introduction:

Autistic disorder is a neurodevelopmental disorder within the broader category of Autism Spectrum Disorders (ASD) and is characterized by communication impairments, social skill impairments and restricted repetitive and stereotyped behavior (APA, 2000; WHO, 2004). ASD includes Autistic Disorder, Asperger's Syndrome, and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS)(APA, 2000; WHO, 2004). In recent years, the incidence of ASD has grown dramatically. The most recent estimates from data collected in 2008 approximate that 1 in 88 eight year old children have an ASD (CDC, 2012). This number is higher than the CDC's estimates from 2006 (1 in 111) and even higher than estimates from data collected in 2002 (1 in 156)(CDC, 2012). With the rise in ASD incidence, it is becoming increasingly important to identify effective treatment strategies for this population.

Children with ASD have unique social-communication and behavior impairments that complicate their medical care. In clinical settings, caregivers and physicians report man challenges associated with treating patients with ASD (Brachlow, Ness, McPheeters, & Gurney, 2007). Therefore, a basic premise of this study is that the addition of a picture schedule reinforcement system will help reduce stress during routine blood draw procedures as similar strategies have been used successfully with this population within the field of education (Bryan & Gast, 2000). As children with a dual diagnosis of diabetes and ASD receive regular blood draws, this specific population was sought out for the current study. If the strategy proposed in this study is successful, it could be generalized to provide primary care physicians with an approach to conduct more thorough and less challenging blood draws with their patients with

ASD. This strategy could also help decrease the time and cost of health care for children with ASD who require blood draws in a variety of medical and community settings.

Background:

Overview:

In 1943, Dr. Leo Kanner was the first to describe the condition he termed *infantile autism* (Kanner, 1943). While the diagnostic criteria have changed over the years, his description of the symptomology is still an accurate description of the population. The diagnostic definition of autism includes a widerange of problems in three core areas: social, communication, and behavior. Within clinical practice in the United States today, two valid and reliable tools used in diagnosing children with ASD are the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview (ADI), which are based upon current diagnostic criteria in the DSM-IV-TR (de Bildt et al., 2004; Lord et al., 1989; Lord, Rutter, & Le Couteur, 1994). The ADOS is a semi-structured play based assessment of the child while the ADI is a semi-structured interview with the caregiver (Lord et al., 1989; Lord et al., 1994)

While the precise etiology of ASD is still unknown, there are many hypotheses that have received a great deal of attention over the years. Some of these hypotheses have been overdramatized by the media and subsequently proven wrong (mercury exposure, vaccinations, etc.), but many more have built up momentum within the scientific community as additional data has been garnered. Influences such as genetic factors, immunological factors and prenatal exposure to serotonin have all been described as having potential influence on the development of ASD symptoms (Coutinho et al., 2007; Jyonouchi, Geng, Cushing-Ruby, &

Quraishi, 2008; Jyonouchi, Geng, Streck, & Toruner, 2011; Kane et al., 2012; Levitt, 2011; Patterson, 2009, 2011; Persico, Van de Water, & Pardo, 2012; Rossignol & Frye, 2012; Sato, 2013). It has also been proposed that preconceptional folic acid intake may reduce the risk of ASD for the child (Berry, Crider, & Yeargin-Allsopp, 2013; Schmidt et al., 2012; Surén et al., 2013). However, it is important to note that no single factor has been proven conclusively to cause or prevent ASD.

Two pharmaceuticals (risperidone and aripiprazole) are currently approved by the FDA to treat ASD symptoms effectively in the United States but many more are used off-label (Canitano & Scandurra, 2008; Chadman, 2011; Ching & Pringsheim, 2012; Farmer & Aman, 2011; Lemmon, Gregas, & Jeste, 2011; Rosenberg & Samuel, 2012; Valdovinos, Bailey, & Taylor, 2010; Wei, Huang, Qin, & Liang, 2011). While pharmaceuticals have begun to raise the quality of life for individuals with an ASD, the majority of treatments also include behavioral therapies and/or interventions. Contemporary research has shown that early intensive intervention has the most beneficial effects on individuals with ASD (Rogers, 1996). Other interventions for ASD that have proved effective are Applied Behavioral Analysis (ABA) and Equine Assisted Activities and Therapy (EAAT) (Bass, Duchowny, & Llabre, 2009; Callahan, Shukla-Mehta, Magee, & Wie, 2010; R. L. Gabriels et al., 2012; Ward, Whalon, Rusnak, Wendell, & Paschall, 2013).

The intervention being used in this study is based on research done in picture schedules with the Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH) program. Within the dental field, studies have begun to show the efficacy of using TEACCH principles in dental settings to improve dental care for individuals with ASD (Bäckman & Pilebro, 1999a, 1999b; Cuvo, Godard, Huckfeldt, & DeMattei, 2010; Lowe &

Lindemann, 1985; Pilebro & Bäckman, 2005). Additionally, other studies have begun to show how procedures specifically using picture schedule reinforcement systems are effective tools within hospital settings (Chebuhar, McCarthy, & Bosch, 2012; R. Gabriels et al., 2013).

Symptomology:

In 1943, Leo Kanner was the first to describe a group of children presenting with three common symptoms: impairments in communication, impairments in socialization, and repetitive and stereotyped behavior (Kanner, 1943). In his paper, Kanner described eleven case studies of children with “an extreme autistic aloneness” (Kanner, 1943, p. 242).

In these case studies, eight of the eleven children learned language at either a normal or delayed age while the other three never acquired verbal language (Kanner, 1943). With the children who developed language, Kanner noted that their verbal communication did not “serve to convey meaning to others” (Kanner, 1943, p. 243). In these children with language difficulties, Kanner described that while the patients had remarkable facility learning to “name” things or repeat back rhymes, poetry, the alphabet, or prayers, these pieces of language had little meaning to them (Kanner, 1943). Additionally, Kanner described language that he termed “echolalia,” when the children would repeat whatever was said to them in a “parrot-like” fashion, either immediately or later (Kanner, 1943). In one case, for example, the child would state, “Now I will give you your milk” when expressing that he wanted more milk (Kanner, 1943, p. 244). This illustrated how the child with autism would simply repeat back what they had heard when it became associated with an outcome, such as receiving more milk.

Kanner also described the most profound symptom in ASD, the social impairments. Kanner framed discussion of the social impairments around the child’s need for being alone. For example, he described how the children would ignore people in favor of toys he or she could directly control or play with. He also illustrated how the child sometimes had difficulty maintaining eye contact, and how they would sometimes view aspects of another's body as tools or discrete entities (Kanner, 1943). For example, if a child was pricked by a pin, the child would be afraid of the pin, but not the person who pricked him or her (Kanner, 1943).

Kanner described some of the stereotyped and repetitive behavior found in autism in this report as well. For example he stated, "Once blocks, beads, and sticks have been put together in a certain way, they are always regrouped in exactly the same way, even though there was no definite design" (Kanner, 1943, p. 245). Here Kanner described the need for sameness and structure common in patients with ASD (Kanner, 1943). While Kanner did not describe the repetitive behaviors such as hand flapping, or body rocking he did state that the patients would sometime "exercise power over their own bodies by rolling and other rhythmic movements" (Kanner, 1943, p. 246). He also described some of the sensory issues common in ASD such as loud noises or moving objects bringing "minor panic" or anxiety (Kanner, 1943). Thus, in 1943 Kanner accurately described the condition we still term autism with many of the hallmark symptoms still associated with the disorder.

Diagnostic Tools:

Two common tests used for diagnosis of ASD in the United States are the ADI and the ADOS. These tools are standardized, semistructured interviews for parents or children, respectively, which aim to identify if the child has the symptoms outlined in the DSM-IV-TR diagnostic criteria, and the severity these symptoms (de Bildt et al., 2004; Le Couteur, Haden, Hammal, & McConachie, 2008). The ADI, or ADI-R (Autism Diagnostic Interview- Revised) is an "investigator-based interview for caregivers" (Lord et al., 1994, p. 660), while the ADOS is an "assessment of social interaction, communication, play, and imaginative use of materials for individuals suspected of having autism spectrum disorders" (Lord et al., 2000). Both of these tests have been found to have good validity and reliability (de Bildt et al., 2004). They have also been found to have lower specificity for low-functioning individuals, but the ADI-R may also have lower sensitivity for high-functioning individuals (de Bildt et al., 2004; Le Couteur et al., 2008). Using these tools, it is somewhat likely to diagnose a low-functioning individual with autism when that diagnosis may not be accurate. Using just the ADI-R, it is also more likely to miss the diagnosis of high-functioning individuals with autism. When the ADI-R and ADOS are used in combination with each other and other tools, the diagnosis of the individual becomes much more accurate (de Bildt et al., 2004).

Etiology:

Kanner described Autism in 1943, and its cause has been debated ever since. With the dramatic rise in ASD prevalence throughout the world, researchers have proposed various environmental factors that could be affecting this rising rate. One such widely reported hypothesis proposed by Wakefield in 1998 suggested that the measles, mumps and rubella (MMR) vaccination was correlated with the development of autistic symptoms in several children (Wakefield et al., 1998). After publication, this study gained publicity and created a great of deal of discussion and controversy. In addition, there was worry among clinicians that participation in vaccination programs would drop due to fear of autism (Taylor et al., 1999).

Subsequently, research concluded that the rising rates of ASD diagnoses did not match up with the rise in vaccination rates and that MMR vaccinations do not cause ASD symptoms (Chez, Chin, & Hung, 2004; D'Souza & Todd, 2003; Fombonne, 2008; Hviid, Stellfeld, Wohlfahrt, & Melbye, 2003; Peltola et al., 1998; Price et al., 2010; Taylor et al., 2002; Taylor et al., 1999). It was later proposed that thimerosal, a preservative used in the MMR vaccine containing mercury, may affect development of ASD symptoms. Some studies have illustrated that this is not the case, while others have pointed out that thimerosal has been almost entirely removed from MMR vaccinations but the prevalence of ASD is still increasing (Chez et al., 2004; Fombonne, 2008; Hviid et al., 2003; Price et al., 2010). Additionally, it appeared that there were significant conflicts of interest in Wakefield's initial study as well as lack ethic committee approval, causing the initial publisher, *The Lancet* to fully retract the paper from "the public record" in 2010 (Lancet, 2010). It therefore appears that the correlation between age of the child when parents first notice autistic symptoms and age of receiving the MMR vaccination is what led to the highly popularized and incorrect findings (Taylor et al., 2002; Taylor et al., 1999).

Genetics:

Recently the CDC observed that approximately 1 in 88 children in the United States have an ASD (CDC, 2012). Various sibling studies have observed significantly higher rates of ASD in siblings of affected children than the population at large. (Risch et al., 1999; Szatmari et al., 2007). Even with the wide range of findings from these studies, the data thus indicate that there is likely a genetic component or risk factor involved in ASD. Twin studies have also shown a concordance rate between 60% and 92%, further supporting the likelihood of a genetic influence (Szatmari et al., 2007). However, some empirical studies estimate that only 6-15% of ASD cases are due to genetic syndromes (Rossignol & Frye, 2012). Therefore, while genetics likely plays a role in ASD, it is probable that there are other factors at play in most ASD cases.

Various researchers all seem to agree that ASD is not caused by a single gene, but that is all that researchers seem to agree upon. For example much of the research identifying specific loci as the source of the disorder has not been replicated in follow up studies (Risch et al., 1999; Rossignol & Frye, 2012; Szatmari et al., 2007). Copy Number Variants (CNVs) have been implicated as possible risk factors for ASD as well as alterations in chromosome regions 1p, 2q, 7q and 17q (Szatmari et al., 2007). Currently, it is widely felt that specific changes in chromosome region 7q are among the most common genetic risk factors for ASD (Risch et al., 1999; Szatmari et al., 2007).

However, the many loci identified also have diverse functions. Some studies have implicated genes encoding immune function (Patterson, 2009, 2011; Persico et al., 2012), while some studies have implicated genes encoding serotonin metabolism and neurotransmission, (Coutinho et al., 2007) and others have implicated genes encoding neurexins and neuroligins (Szatmari et al., 2007). Neurexins are proteins which induce postsynaptic differentiation in glutamatergic neurons while neuroligins are proteins which induce presynaptic differentiation in glutamatergic neurons (Szatmari et al., 2007). All of these genes appear to be risk factors for ASD to some degree. As these genes appear to have the same effect behaviorally, some researchers have suggested that a common pathway may exist on the molecular level to affect the behavior of the patients (Jyonouchi et al., 2011).

Immune System:

Another factor that appears linked to ASD is dysregulation within the immune system. For instance, one literature review found that of 437 publications describing the link between immune dysregulation or inflammation and ASD, 416 or 95% of these articles supported the association (Rossignol & Frye, 2012). Studies have also increasingly shown an association between genes encoding microglial and astrocyte activation with cytokine up-regulation in the central nervous system (CNS) and cerebral spinal fluid (CSF) in patients with ASD (Patterson, 2009; Rossignol & Frye, 2012). Other studies have reported abnormal growth factors, the presence of autoantibodies in brain tissue, and abnormal biomarkers of immune function in the CNS or CSF in patients with ASD (Rossignol & Frye, 2012).

From a clinical standpoint, the connection between the immune system and ASD is feasible, as patients with ASD often have co-morbid conditions such as gastrointestinal symptoms or other immunodysregulations (Gondalia et al., 2012; Ibrahim, Voigt, Katusic, Weaver, & Barbaresi, 2009; Jyonouchi et al., 2008; Jyonouchi et al., 2011; Maenner et al., 2012; Mazurek et al., 2013). Additionally, recurrent infections are sometimes accompanied by exacerbations in ASD symptoms in some patients (Jyonouchi et al., 2008; Jyonouchi et al., 2011). However, given the large interconnection between the immune system and neurodevelopment, some researchers question whether these abnormal immune functions are symptoms or causes of ASD (Persico et al., 2012).

ASD becomes apparent very early in the life of patients, therefore researchers have looked to prenatal development for causes of this disorder. Some have argued that maternal immune activity is one of the primary risk factors for ASD (Patterson, 2011). For example, Ciaranello and Ciaranello stated, "the principal non-genetic cause of autism is prenatal viral infection"(Ciaranello & Ciaranello, 1995). Studies supporting this hypothesis have shown that prenatal exposure to rubella or cytomegalovirus is associated with an increased risk for ASD (Patterson, 2009). In an animal model examining how a human influenza infection in pregnant mice can affect their children, it was found that the young mice displayed behavioral abnormalities such as deficits in social interaction, prepulse inhibition and open field and novel object exploration (Patterson, 2009). These behaviors are thought to be associated with ASD symptoms in humans. Additionally, brain abnormalities in these mice were also found in the hippocampus and cortex. These abnormalities included a spatial restriction deficit in Purkinje cells, a neuropathology thought to be common in autism (Patterson, 2009). These mice also experienced transcription alterations and abnormalities in serotonin production in the cerebellum, implicating an epigenetic influence (Patterson, 2009).

High-fat, and specifically high omega-6 intake, has been shown to have numerous deleterious effects, including activation of pro-inflammatory responses (Ramsden et al., 2011; Shankar et al., 2012). It is therefore possible that the increased prevalence of ASD may be associated with the rise in pro-inflammatory diets in mothers. However, so many factors affect prenatal neurodevelopment that further research is required to make this connection.

Other Hypotheses:

Serotonin has also recently been investigated as to its effect on ASD occurrence (Coutinho et al., 2007; Croen, Grether, Yoshida, Odouli, & Hendrick, 2011; Kane et al., 2012;

Levitt, 2011; Sato, 2013). Evidence has arisen that neurotransmitters, such as serotonin, glutamate and GABA, may impact neurodevelopment during the first trimester in humans (Levitt, 2011). Serotonin is thought to have an effect on neuronal migration, axonal guidance and determining the trajectory of thalamocortical pathways (Kane et al., 2012). The use of selective serotonin reuptake inhibitors, especially during the first trimester, may be a risk factor for ASD (Croen et al., 2011). However, Croen et al. have noted that depression alone can also increase risk for poor developmental outcomes and therefore the findings of this study should be interpreted cautiously (Croen et al., 2011).

Further support for this hypothesis has come from genetic studies. The HTR5A gene alone was found to be a significant risk factor for the development of ASD symptoms (Coutinho et al., 2007). In this study, a three-locus model of a synergistic effect between ITGB3 and SLC6A4 with an additive effect of HTR5A, was additionally identified as a contributing risk factor for ASD (Coutinho et al., 2007). HTR5A is a serotonin receptor gene, SLC6A4 is a serotonin transporter gene and ITGB3 encodes the integrin β3 subunit (Coutinho et al., 2007). This study thus implicated a possible link between serotonin metabolism and serotonin transportation with ASD.

One large population-based study has recently described a connection between early pregnancy folic acid supplement use and a decreased risk for ASD in the child (Berry et al., 2013; Schmidt et al., 2012; Surén et al., 2013). The study found 4-week early pregnancy usage of 400 µg or more per day decreased the risk of the child being later diagnosed with ASD (Berry et al., 2013; Surén et al., 2013). This study suggested that the critical exposure interval for this effect was between 4 weeks and 8 weeks after the start of pregnancy (Surén et al., 2013).

Women taking folic acid in the critical exposure interval were more likely to have a college education, have a planned pregnancy and to be nonsmokers (Surén et al., 2013). While this may have affected the child's risk for ASD, it was noted that mothers taking fish oil supplements had a similar profile, but did not see the reduction in ASD risk (Surén et al., 2013).

Therapies and Interventions:

ASD is a complex disorder and thus the therapies for this disorder are vast. Risperidone and Aripiprazole are the two pharmaceutical agents currently approved by the FDA to treat ASD symptoms. While these pharmaceuticals have been shown to have a beneficial effect for some patients, most interventions for individuals with ASD include or are primarily focused on behavioral therapies.

Risperidone and Aripiprazole, are both considered atypical antipsychotics. Risperidone has been shown to reduce many aberrant behaviors in children with ASD as well as improved social responsiveness (Canitano & Scandurra, 2008; Nagaraj, Singhi, & Malhi, 2006; Wei et al., 2011). However, it has also been shown that a large side-effect of taking Risperidone is increased appetite and weight gain (Nagaraj et al., 2006; Ratzoni et al., 2002). Aripiprazole has also been shown to decrease aberrant behaviors in children with ASD and in some others with other developmental disorder, with side-effects that include sleepiness and weight gain (Ching & Pringsheim, 2012; Farmer & Aman, 2011; Marcus et al., 2009; Owen et al., 2009; Valicenti-McDermott & Demb, 2006).

Behavioral based therapies ASD include programs such as early intensive interventions, TEACCH and EAAT. However, TEACCH and EAAT are often used for children over six years old, after early interventions are no longer possible (Bass et al., 2009; "Training and Education of Autistic and Related Communication Handicapped Children (TEACCH)," 2013). While these therapies are very effective, the most effective treatment for individuals with ASD has been shown to be early intensive intervention (Francis, 2005; Rogers, 1996; Rogers & Vismara, 2008). In early intensive interventions at ages 2-4 years, the patients experienced the greatest improvement when the intervention included at least 15 hours of treatment per week and the child to adult ratio was 1:2 or more (Rogers, 1996). However, despite the variety of early intensive interventions, most of the treatments examined in one review reported significant acceleration in developmental rates, significant IQ gains, significant language gains, improved social behavior and decreased ASD symptoms in patients after treatment (Rogers, 1996). Additionally, studies have shown that children who began intervention between 2 and 4 years of age benefited more than older children entering the same program (Rogers, 1996).

It has also been shown that those who do not go through an early intensive intervention, but go through another behavioral intervention such as TEACCH later in life, have improved ASD symptomology and experience structural changes in white matter tracts such as the uncinate fasciculus (Keel, Mesibov, & Woods, 1997; Mesibov & Shea, 2010; Panerai et al., 2009; Pardini et al., 2012; Tsang, Shek, Lam, Tang, & Cheung, 2007). Thus, while patients entering therapy when they are older may not receive all the benefits seen in early intensive interventions, significant improvements can still be made. The TEACCH program uses the visual learning strengths common in those with an ASD as well as their attention to detail and routine in order to effectively help individuals with ASD learn various adaptive skills (Mesibov & Shea, 2010). The TEACCH approach to educating children with ASD addresses the certain difficulties inherent in the population such as poor organization or sequencing, sensory processing, and social-communication skills. The TEACCH approach assumes that these deficits are directly linked to the difficult behaviors observed in this autism population and thus are the areas of focus in TEACCH based therapies (Cox & Schopler, 1993). TEACCH has been shown to effectively improve adaptive behaviors in the patients and even to decrease depressive symptoms in the caregivers of children with ASD (Mesibov & Shea, 2010).

Another intervention that has begun to show beneficial results to those with ASD is EAAT. One type of EAAT is therapeutic horseback riding. Patients who received therapeutic horseback riding have been shown to have improvement in their inattention and distractibility, improved social responsiveness and improved social motivation (Bass et al., 2009). Therapeutic horseback riding has also been shown to improve irritability, lethargy, stereotypic behavior, hyperactivity and expressive language skills when compared to a control group made up of children on the waitlist for this program (R. L. Gabriels et al., 2012). One recent study has shown that participants in a therapeutic horseback riding program saw significant gains in social interaction and a significant decrease in ASD symptomology. However, these results were not maintained without further therapeutic horseback riding (Ward et al., 2013).

Use of Picture Schedules in Medical Settings:

A variety of challenges have been documented regarding medical procedures and the ASD population. Thus the present study and former studies have examined how to improve medical care for individuals with ASD. In order to decrease cost and anxiety, the TEACCH practice of using picture schedules in education has recently been adapted for use in various medical settings. Picture schedules are common tools used in educational, community and home settings and have been shown to decrease anxiety, decrease problem behaviors and increase compliance with the task at hand (Chebuhar et al., 2012). However, very little research has been done using picture schedules in medical settings (Chebuhar et al., 2012).

Various studies have illustrated the need for a strategy such as a picture schedule. For example some studies looking into the cost of health care for children with and without ASD and suggest that costs are significantly higher for children with ASD (Flanders et al., 2013; Hudson, 2006). A national health care sample revealed that children with autism spent significantly more time with the physician during visits (31.9 minutes) compared to a general population of children without ASD, depression or an intellectual disability (15.8 minutes) (Liptak, Stuart, & Auinger, 2006). Another study showed that medical specialists and primary care providers tended to demonstrate outdated beliefs about autism (Liptak, Orlando, et al., 2006). Additionally children with ASD have been shown to visit physicians more (8.0 vs. 2.5 visits annually) and have more medication prescribed annually (21.8 vs. 5.9) than children with mental retardation, indicating the high amount of contact children with ASD have with health care settings (Liptak, Stuart, et al., 2006).

Several studies aimed at improving healthcare management and cooperation for children with ASD have been done within the dental field, many using picture schedules to increase compliance. One study evaluated the effectiveness of preparing children with ASD for a dental exam using a picture book illustrating a dental visit to children with autism ages 3.3 to 6 years (Bäckman & Pilebro, 1999b). This picture book contained photographs of dental exam items and the steps that would be involved in the upcoming dental visit. Cooperation with procedures was “superior” for those in the treatment group exposed to the picture book in comparison to those in the control group who were not shown the picture book (Bäckman & Pilebro, 1999b).

Another study examined using priming videos and still photos to teach five children ages 3-5 years with PDD-NOS or autism compliance with dental exams (Cuvo et al., 2010). Results indicated that children were able to complete steps of the dental exam when distracting stimuli were present and reinforcement was used. Children were also able to maintain compliance for up to one month after the end of training (Cuvo et al., 2010). However, as a package of training components was used, no individual component's efficacy could be assessed.

Needle phobia for an 18-year old diagnosed with Type 2 diabetes, autism and mental retardation was also assessed in a particular case study (Shabani & Fisher, 2006). This case study found success in gradually increasing the young man's exposure to the fear-evoking stimulus and reinforcing the desired behaviors. The participant's mother was able to successfully obtain daily blood samples post-intervention (Shabani & Fisher, 2006).

Another study expanded the use of the visual pedagogy and evaluated the effectiveness of employing this technique for 12 months on improving oral hygiene/tooth brushing behaviors in 14 children with autism ages 5 to 13 years (Pilebro & Bäckman, 2005). Clinical examinations of the child's teeth were made prior to the introduction of the visual pedagogy and then again after 8 and 12 months of treatment. This treatment included usage of photos describing steps for brushing teeth. Prior to the study, parents reported having difficulty helping their child maintain good oral hygiene, whereas most parents found this to be easier after the study. All children had visible plaque reduction after 12 months of the study (Bäckman & Pilebro, 1999b; Pilebro & Bäckman, 2005).

The challenges of conducting an adequate dental exam and maintaining safe dentist-patient interactions were addressed in a study by Lowe and Lindeman in 1985. They did this through using a modeling reinforcement system during dental exams with 20 patients with ASD and 20 non-autistic matched controls (ages 3 to 30 years) (Lowe & Lindemann, 1985). Thorough and successful completion of exams was quantified and the behavior management treatment strategies were used with both population groups. Following the introduction of this approach, “successful exams” were obtained in 85% of the participants with autism on their first appointment. “Successful exams” were obtained in 90% of the non-autistic participants on their first appointment (Lowe & Lindemann, 1985).

Methods:

Participants:

This study attempted to recruit eighteen existing patients from the Barbara Davis Center for Diabetes between the ages of 3 and 17 diagnosed with ASD and either Type I or Type II diabetes. These individuals previously agreed to be contacted for research purposes including, but not limited to the proposed study. Caregivers of these potential subjects were screened over the phone and asked about the child's irritable and stereotypic behaviors during routine blood draws using the ABC-C. If the child's score was 11 points or higher on this checklist, then they were invited to participate in the study. The incentive offered to parents to participate in the study was a free nonverbal IQ test with a corresponding report.

Two participants, subjects A and B, who were age 14 and 10, respectively, participated in the study. Both subjects had previously been diagnosed with an Autistic Disorder or Asperger's Disorder. Additionally, subjects A and B were rated by their caregivers as either having "Poor Cooperation" or being "Completely Uncooperative" with their previous blood draw on a 4-point scale of cooperation.

Measures:

Primary caregivers were asked to complete child behavior questionnaires. The primary caregiver is defined as the adult living with the child who is most familiar with the participant's behavior. The same caregiver completed all forms for each participant.

Leiter International Performance Test-Revised (Leiter-R):

The Leiter-R is a reliable and valid measure of non-verbal intelligence for ages 2 years to 20 years, 11 months (Roid & L.J., 1997). This measure of nonverbal problem-solving and learning is commonly used to assess IQ in children with ASD or other language-impairments, as it does not require verbal instructions or responses for administration or extensive fine motor skills. However, it can also be used to assess the nonverbal cognitive abilities of children who have fluent language. The Brief IQ version of this test was chosen to limit the assessment demands of the child and because the correlation between the Leiter-R Brief IQ score and the Full Scale IQ scores of the WISC-III is reported as 0.85 (Roid & Miller, 1997). The Leiter-R was administered to all subjects participating in this study.

Social Communication Questionnaire (SCQ):

The SCQ, formerly known as the *Autism Screening Questionnaire*, is a parent-caregiver completed measure that assesses the presence of behaviors common to an autism spectrum disorder (Rutter, Bailey, & Lord, 2003). The SCQ is a 40-item survey that is based on the Autism Diagnostic Interview-Revised (ADI-R). One study has shown that the SCQ has an 82% sensitivity and 88% specificity (Johnson et al., 2011). The SCQ is thus a good diagnostic tool for detecting ASD. Though the risk of false positives is present when using the SCQ, this questionnaire was used solely to confirm an already diagnosed condition. The SCQ was completed by the primary caregiver during the screening.

Cooperation Scale:

The primary caregiver rated the child's of level of cooperation with the subject's previous blood draw administration at the Barbara Davis Center both during the phone screen as part of the screening and at the informed consent. The caregiver and researcher also independently rated the child's level of cooperation immediately following the blood draw administration. This scale was modified from a shorter version used to assess cooperation in dental exams (Forsberg, Quick-Nilsson, Gustavson, & Jagell, 1985). (See Cooperation Scale below)

HOW COOPERATIVE WAS THE CHILD DURING TODAY'S PHYSICAL EXAM?
0 = No problems with cooperation
1 = Minor problems with cooperation: child shows mild behavior problems and/or anxiety symptoms
2 = Poor cooperation: Child's behavior problems and/or anxiety symptoms requires that the medical staff have to spend extra time and effort to manage the child and complete the exam
3 = Completely uncooperative: Exam is not possible due to child's behavior problems and/or anxiety symptoms

Aberrant Behavior Checklist-Community:

The Aberrant Behavior Checklist-Community (ABC-C) is a 58-item symptom checklist for assessing behavior problems in people with developmental disabilities (Aman, Burrow, & Wolford, 1995). The ABC-C yields five distinct factors: Irritability, Hyperactivity, Lethargy, Stereotypy, and Inappropriate Speech. This test was originally developed for use with individuals with mental retardation, but has since become a common tool used within ASD populations as well (Brinkley et al., 2007; Hill, Powlitch, & Furniss, 2008). The ABC-C has also been shown to have good interrater and test-retest reliability (Aman, Singh, Stewart, & Field, 1985; Aman, Singh, & Turbott, 1987).

Only the Irritability and Stereotypy factor scores were used in this project to assess the presence of behaviors such as aggression, self-injury, tantrums, screaming, and repetitive, nonfunctional body movements (see appendix II). The caregiver completed the baseline measure for the ABC-C based upon the four weeks of the subject's behavior leading up to the study. This was compared to the ABC-C score given by the caregiver during the blood draw procedure. The researcher also completed the ABC-C based upon the subject's behavior during the blood draw.

Procedure:

Screening:

After approval from the Institutional Review Board, those diagnosed with both an ASD and either type I or type II diabetes were called by the undergraduate investigator. Caregivers interested in the study were provided a brief summary of the study over the phone and asked several questions specific to study inclusion and exclusion criteria (see Appendix III). schedule intervention.

Informed Consent:

Participants who met initial study criteria were scheduled for a screening visit at the hospital clinic prior to the subject's blood draw. Participants' DSM-IV diagnosis of autism or Asperger's was confirmed using information from the Social Communication Questionnaire (SCQ) (Rutter et al., 2003). Participants' nonverbal intelligence was evaluated using the Leiter-R Brief IQ (Roid & Miller, 1997). Participants with standard Leiter-R scores less than 40 would have been excluded due to concerns that such individuals might not understand the visual. The subject's baseline ABC-C score was ascertained from the parents based on the previous four weeks of behavior. Subject cooperation in the previous blood draw was also ascertained from the cooperation scale completed by the caregiver. The subject and caregiver were also asked questions pertaining to their child's exposure to visual schedules and demographic information using the Child and Caregiver Information Form. Nonverbal IQ was then measured administering a Leiter-R IQ test.

Intervention:

Subjects A and B both went through their routine blood draws after the initial screening. A physical examination accompanied the blood draw. Before the blood draw, the subject briefly waited in the waiting room before going into a room accompanied by one or two nurses, the researcher and the caregiver. The BDC nurses, who were trained to run blood draws and had agreed to take part in this procedure, administered the blood draw while the researcher presented the picture schedule reinforcement system to the subject.

The picture schedule reinforcement system consisted of a picture schedule booklet (see appendix I) accompanied by a reinforcement of dried apple treat rewards. The nutritionist at the BDC recommended that a quarter cup of dried apples would be ideal so that the subject did not require an insulin injection following the treatment. The 8 ½" x 11" picture booklet contained a total of 6 laminated color photos of the object being used in the exam or a task designed as a distraction tool. Plastic baggies were placed behind each page to hold the reward. Pictures were distinct color-prints of each small step of the physical exam visit without irrelevant details. Simple and concrete descriptions were written above each picture to describe what the child was expected to do in the exam (sit on table, put on armband, etc.). After each step, the subject received a portion of reward. During the blood draw, caregivers and the researcher rated the participants using the ABC-C and the cooperation scale. After the blood draw the parents were asked in an exit interview what they thought was beneficial in the procedure and what could be changed for future studies.

The steps outlined in the booklet were:

1. Time for Blood Test
2. Rest on Table
3. Put Arm Band On
4. Clean Skin and Hold Still
5. Count Faces
6. All Done with Blood Test!

Results:

Blood draw procedures were done to completion in both subjects with no adverse reactions or effects (see figure 1 for demographics). Subjects A and B were both male and four years apart in age. These subjects had very different levels of functionality as represented by their SCQ and Nonverbal IQ score. The cutoff SCQ score for ASD is 15. The ABC-C is scored by adding up the individual scores from each behavior on the questionnaire (see appendix II). The cooperation scale is a scale from 0 to 3. The higher the score, the less cooperative the subject was with the procedure.

Characteristic	Subject A	Subject B
Age	14	10
Gender	Male	Male
Leiter-R IQ Score	71	137
SCQ	27	15
Caregiver ABC-C Baseline	26	19
Caregiver ABC-C Blood draw	0	1
Researcher ABC-C Blood draw	7	0
Caregiver Cooperation Scale Previous Blood Draw	2.5	1
Caregiver Cooperation Scale Present Blood Draw	1	0
Researcher Cooperation Scale Present Blood Draw	1	0

Figure 1-
Summary of collected data

Subject A had the blood draw procedure done immediately following the screening process. For this subject, the caregiver reported that getting the needle into the subject's arm was the aspect of the blood draw procedure that was most difficult, and why the last blood draw attempted with the subject was not able to be completed at the Barbara Davis Center. This blood draw was accomplished very rapidly by the two nurses administering the blood draw. After the procedure the caregiver stated in the exit interview that the booklet was “very helpful” for the subject. Of note, the subject initially requested pineapples rather than apples for a reward. The subject also held each piece of dried apple in his hand to “save for later.” Subject A saw a large decrease in his ABC-C score between baseline conditions and the present blood draw (see figure 3). He also saw a decrease in his cooperation scale score from the previous blood draw to the present blood draw. (see figure 5).

Subject B was screened before the physical examination. The blood draw was administered following completion of the physical exam. For this subject only one nurse was present. The subject maintained attention towards the picture schedule booklet throughout most of the procedure and smiled most times he received the reward. This subject was given a baggie containing a piece of a dried apple. After the procedure, in the exit interview the caregiver commented that the booklet was helpful and that “he really seemed to enjoy the bags of dried apples.” She also stated that the pictures were “pretty boring”, that maybe a word search could have been used instead of the counting faces task. She also stated that quarters could potentially be a good reward to replace the dried apples. Subject B saw a large decrease in his ABC-C score between baseline conditions and the present blood draw as scored by the caregiver (see figure 4). He also saw a small difference between his cooperation scale scores from the previous blood draw to the present blood draw as scored by the caregiver (see figure 6).

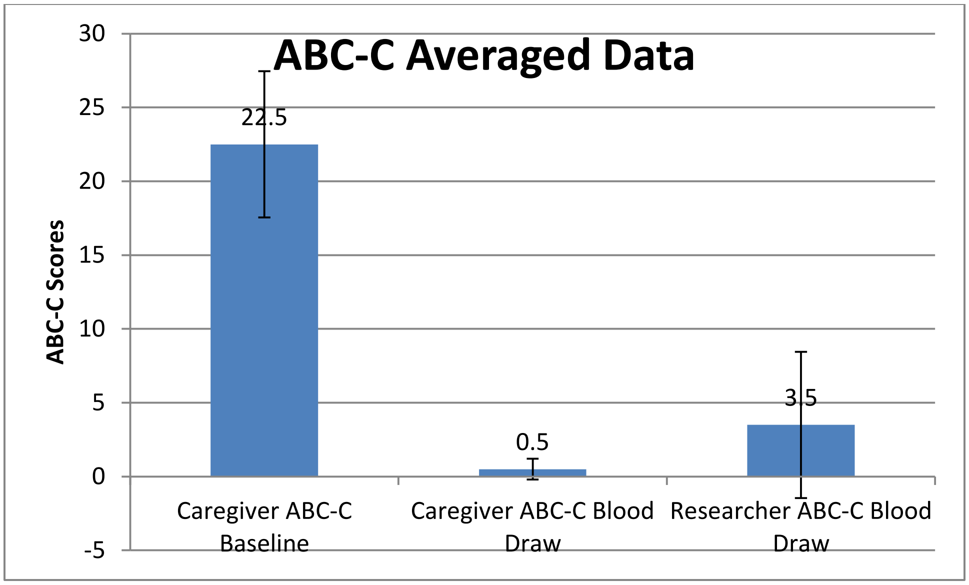

Figure 2-
Average ABC-C Scores

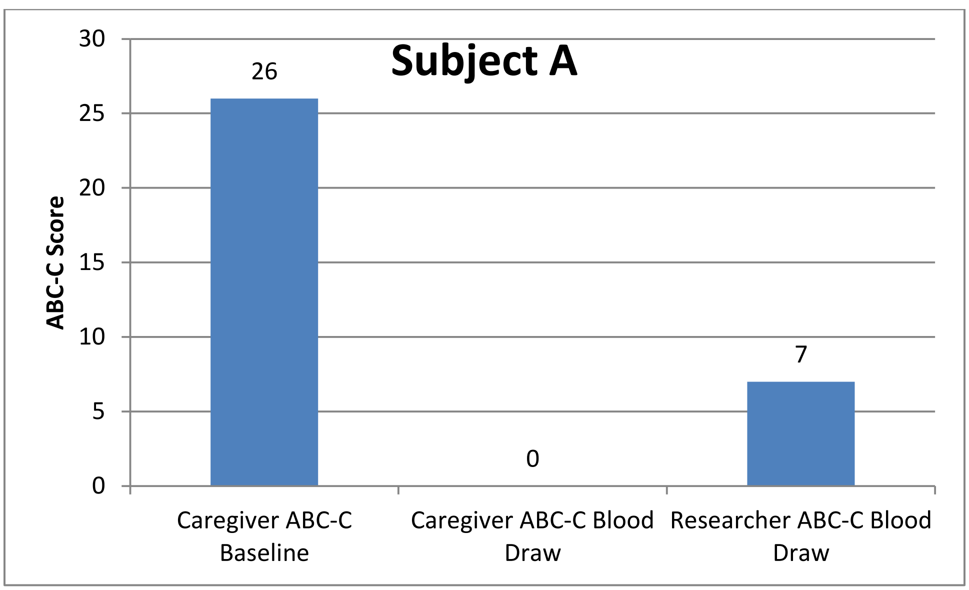

Figure 3-
Subject A ABC-C data

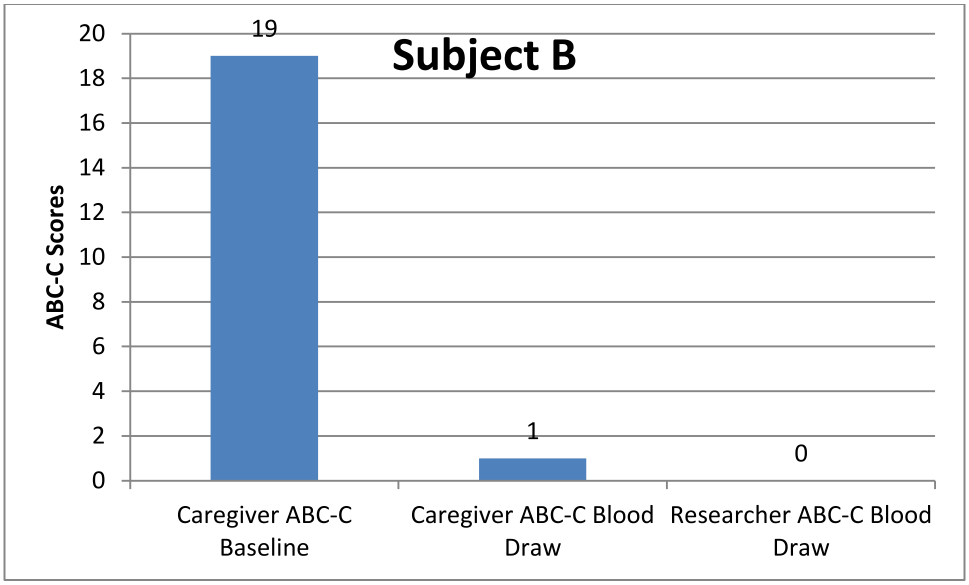

Figure 4 –
ABC-C Data comparing baseline and blood draw scores

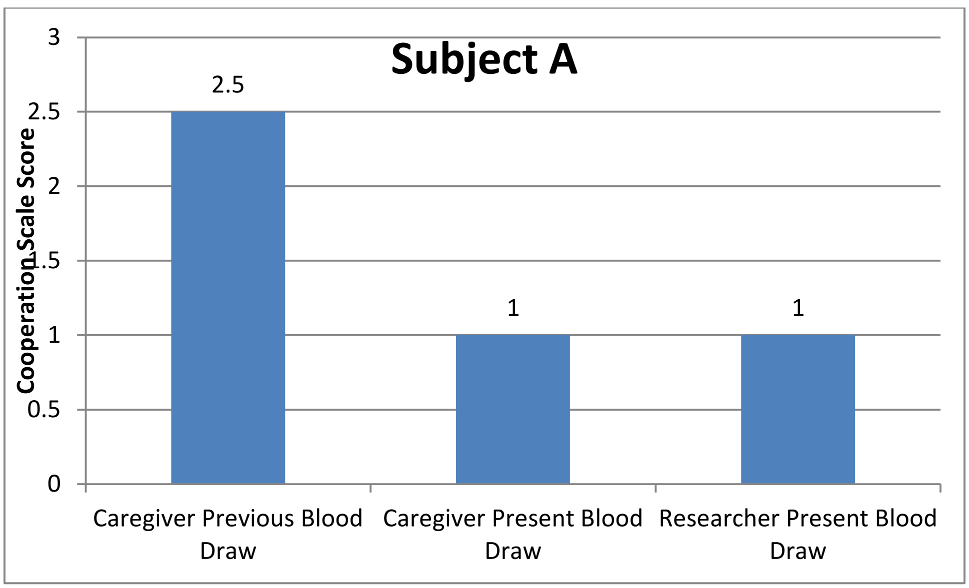

Figure 5 –
Subject A Cooperation Scale Data

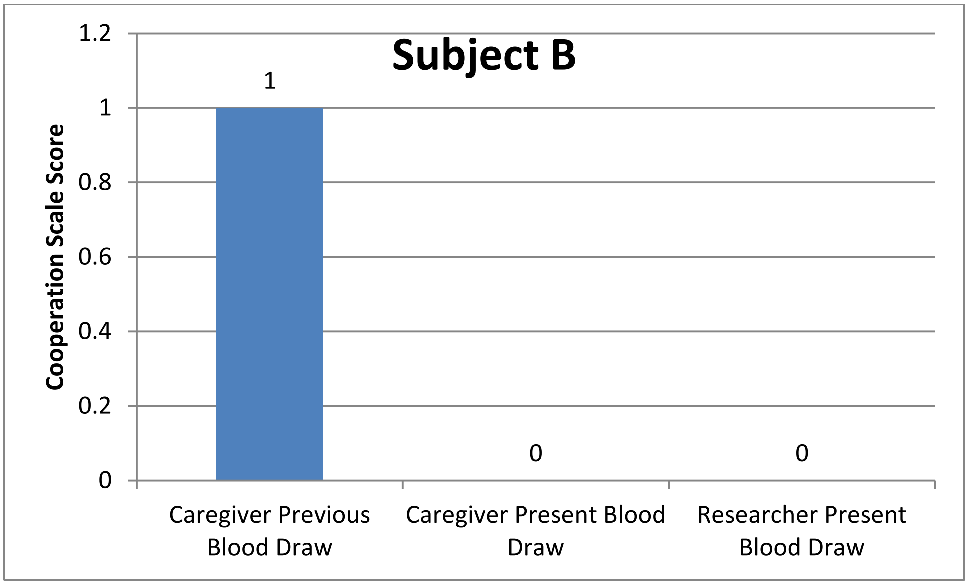

Figure 6-
Subject B Cooperation Scale data

There was found to be significant decrease in ABC-C scores between the caregiver baseline and treatment scores using a standard t-test (p=.007). This decrease indicated that overall aberrant behavior severity was lower during the blood draw than in baseline conditions (see figure 2). Additionally, the caregiver ABC-C score did not differ significantly from the researcher ABC-C score (p=.27). While there was no significant difference between the previous blood draw cooperation score and the treatment cooperation score, there appeared to be a trend toward a decrease in the score (more cooperative) from baseline to treatment conditions (see figures 5 and 6).

Discussion:

Both subjects had successful blood draws and both appeared to benefit from the use of picture schedules. Subjects A and B also had lower cooperation scores (were more cooperative) at this blood draw when compared against the caregiver's memory of their previous blood draw at the Barbara Davis Center. A significant reduction from the baseline ABC-C scores to the treatment was also noted. Hence, the picture schedule reinforcement system's marriage of TEACCH picture schedules and ABA positive reinforcement may have benefited these subjects. This strategy therefore shows promise as both caregivers reported that the picture schedule reinforcement system was helpful.

In this study, the subjects' functionality was wide. In both the SCQ, and the Leiter-R, the subjects' scores were wide (see table 1). The cutoff score for ASD when using the SCQ is 15, while the maximum score a subject can receive on this questionnaire is 40. Subject B scored a 15 on this measure, while subject A scored a 27. Higher scores on the SCQ are associated with lower social communication skills, which can be a symptom of ASD (Johnson et al., 2011). Additionally, subject A scored a 71 on the Leiter-R nonverbal IQ test while subject B scored a 137. The population average for the Leiter-R is approximately 100 with a standard deviation of 15 (Roid, 1997). When taken together these scores illustrate the difference in functionality between the two subjects. It therefore appears that the picture schedule reinforcement system may be able to aid individuals with varied severities of ASD. From clinical observations, it appeared that while both subjects benefited, different aspects of the picture schedule reinforcement system were beneficial to different subjects.

For example, subject A was not able to complete the blood draw attempted before the present study due to irritability. However, this blood draw was able to be accomplished with no adverse reactions. Subject A largely did not utilize the picture schedule booklet until the nurses were finding the vein to insert the needle. At this point in the procedure, he participated in the "counting faces" task in the booklet as opposed to engaging in conversation with the nurses. As his caregiver stated that this was the most difficult part of the blood draw for the subject in the last attempted blood draw. It appeared that this strategy may have played a part in easing the administration of the procedure for this individual.

While the distraction task was helpful for subject A, he did not appear to pay much attention to the picture schedule during the remaining portion of the procedure. One possible reason for this was the subject's lack of interest in the dried apple reward. Subject A, once presented with the piece of dried apple requested pineapple instead of apples. As the subject also did not eat the apple until coaxed to do so by one of the nurses, it appears that this system of rewards was ineffectual. A way to improve this in future studies would be to have the caregiver bring in the preferred treat for the individual.

In comparison, subject B seemed to enjoy and use a greater deal of the picture schedule. Subject B may have paid more attention to the picture schedule due to his higher functionality, but the subject also seemed to enjoy the rewards more. One of the differences between the administrations of these two procedures was that subject B was given the baggie containing the dried apple treat while subject A was only given the dried apple treat. For subject B, the baggie had to be removed via Velcro from the back of a page of the booklet. By the end of the procedure, the subject smiled every time he heard the sound of the Velcro pieces being torn apart and saw the researcher taking the bag being taken off the booklet. Subject B did not particularly seem to like dried apples, but he did enjoy receiving the bag. One possibility is that the subject simply liked plastic bags or Velcro. Another possibility is that as the sound of the Velcro became associated with receiving a reward, the subject connected rewards with the sound.

A major limitation of this study was the small sample size (n=2). Due to the small sample size, this study does not provide strong evidence to support this picture schedule reinforcement system as a strategy for use with those with a dual diagnosis of ASD and diabetes. While the literature supports the use of picture schedule for use within dental and medical settings, this study illustrates that it is possible that the same tool may be helpful for individuals with ASD in adverse procedures such as blood draws (Bäckman & Pilebro, 1999b; Chebuhar et al., 2012; Cuvo et al., 2010; R. Gabriels et al., 2013). This study illustrates that further research should be done to examine the utility of this strategy or other similar strategies aimed at aiding those with an ASD go through difficult, invasive, or even common medical procedures.

The most important addition to any future study would be a larger sample size. One possible way to increase the sample size would be to broaden the inclusion criteria to include any individuals with ASD who receive regular blood draws. The population with both ASD and diabetes is small, but the population with ASD who have received blood draws is a great deal larger. Also, as this study found it very hard to incentivize individuals to be a part of this study, it would be advisable to offer something akin to monetary reimbursement for the time spent in this study. As costly as standardized testing for individuals with ASD is, offering free testing does not seem to be a good enough incentive to recruit the numbers originally desired in this study. By increasing the sample size, future studies could increase the power of the study and allow the researchers to examine this approach more thoroughly.

A potential addition to future studies would be the inclusion of treats or rewards brought by parents for the expressed purpose of the picture schedule reinforcement system. This could potentially give subjects more motivation to comply with the picture schedule and the blood draw as a whole. In this study, the picture schedule gave the subjects a structure and task to follow, but the reward was meant to increase the motivation of the subjects to accomplish each step of the task. As the subjects did not have their ideal reward for this procedure, a way to increase compliance with the picture schedule, and thus decrease anxiety in patients, would be to increase the reward's value to the subject.

Future studies could also potentially use different picture schedule books to see exactly what variables affect participation among the subjects. The pictures within the book could be altered to include different subject genders, location, lighting, etc. to examine whether these variables affect the utility of the booklet. As time with health care individuals can be costly, another variable that would be useful to examine in future studies would be the amount of time the procedure takes. This could examine to what degree this approach could reduce time, and therefore the health care costs for individuals with ASD.

Another limitation to this study is the manner in which the ABC-C was used to measure irritable and stereotypic behaviors of the subjects. The baseline measure asked caregivers to rate the severity of irritable and stereotypic behaviors over the previous four weeks leading up to the blood draws. The treatment ABC-C measure asked parents to rate the severity of the same behaviors through the course of the blood draw. Thus the comparison is between ABC-C scores rating four weeks of behavior to a procedure that generally takes less than a half hour. According to previous study done by Gabriels et al. the average decrease in the ABC-C irritability and stereotopy subscore was 10.2 for the group using the picture schedule and 1.1 for the control group (R. Gabriels et al., 2013). The observed decrease seen in the present study was much larger, indicating the importance of comparing ABC-C scores taken from similar time lengths.

Therefore, a control blood draw would also be beneficial for any future study examining the effects of picture schedule reinforcement systems in medical procedures. In this study, the baseline scores were based entirely off of caregiver reports depending upon the caregiver's memory of the child's behavior over the previous four weeks and of the child's cooperation with their previous blood draw. In future studies, a way to eliminate this would be to include two blood draws, a control blood draw and a treatment blood draw. By randomizing the subjects to either receive the control or treatment blood draw first, the researchers would be able to minimize further bias from the subjects.

Thus a possible future study design would be as follows: Subjects recruited would be: children between the ages of 3 and 17, diagnosed by a research reliable psychologist with an ASD, have received a blood draw within the past 2 years, and planning on receiving a blood draw as part of their routine medical care. Monetary compensation would be given to subjects for participation as well as a summary of the tests provided. The subjects could be screened using the same screening procedure used in the present study, possibly adding an additional diagnostic tool such as the ADOS to further confirm the diagnosis of the subjects. Subjects could additionally be kept blind to the aims of the study to reduce bias. After the subject has been screened they could be randomized into one of two groups. The subjects should be randomized based upon their ABC-C scores to ensure that the more irritable subjects are not concentrated in a single group. Subjects should also ideally be stratified by age and ASD symptom severity as measured by the SCQ, ADOS, or another tool. A matched subject design could also be employed, matching subjects to others with the same comorbid conditions, to minimize the potential confound of comorbid diseases.

Both groups would go through two blood draws separated by at least six months. The first group would receive the picture schedule reinforcement system at the first blood draw and go through blood draw without the system in the second blood draw. The second group would go through the first blood draw without the system and use the system on the second blood draw. During each blood draw procedure, the caregiver and an independent rater blind to the aims of the study would rate the child on the ABC-C and cooperation scale. Additional scales monitoring the behavior of the subject could also be used here. The independent raters could also measure the time the procedure takes, as it could help illustrate the effectiveness of the system. Ideally, having two independent raters who have been trained to be consistent in the ABC-C and cooperation scales would be best. In this way, each rater would be assigned to rate either just the blood draws using the picture schedule reinforcement system, or the blood draws not using the system. Therefore, the rater's blindness to the aims of the study would be maintained. The subject's blood draw without the system would thus act as a control group. In this way, the effectiveness of the picture schedule reinforcement system could be measured using behavioral measures and time in a double-blinded control group study. As the literature does not appear to have any studies examining the efficacy of picture schedules using blinded control group studies, a study such as this could be enormously beneficial to the ASD community.

This study could also be repeated to examine other variables with potentially profound effects on the blood draw procedure. Comparing blood draws using the picture schedule reinforcement system could be compared to blood draws using a picture schedule with no reward. The number of nurses tending to the subject could also be altered to examine how important this variable is.

Communication impairment is one of the three primary symptoms of (APA, 2000; WHO, 2004). Given this, it appears that visual instructions are sometimes incorporated better than verbal or written instructions (Bryan, 2000). Picture schedules, such as the one used in this study, are becoming increasingly understood as useful tools for individuals with ASD (Bäckman, 1999; Bryan, 2000; Chebuhar, 2012; Pilebro, 2005).

Overall this study provides useful circumstantial data supporting the use of a picture schedule reinforcement systems for blood draw procedures with individuals with ASD and diabetes. The study was limited by the sample size and confounds within the ABC-C data collection. Within education and the medical field it is becoming increasingly important to examine novel tools to aid individuals with ASD. While there is not enough power in this study to support picture schedule reinforcement systems, it illustrates that this strategy could have profound benefits for individuals with a dual diagnosis of ASD and diabetes or any individual with ASD who goes through blood draws.

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Appendix

Table of Contents

Children's Hospital Colorado

Picture-Schedule Reinforcement Book for Blood Draws

Developed by
Robin Gabriels, Psy.D
MaryAnn Morrow, RN

Time for Blood Test

1

2

3

4

5

1

Rest on Table

2

3

4

5

2

Put Arm Band On

3

4

5

3

Clean Skin and Hold Still

4

5

4

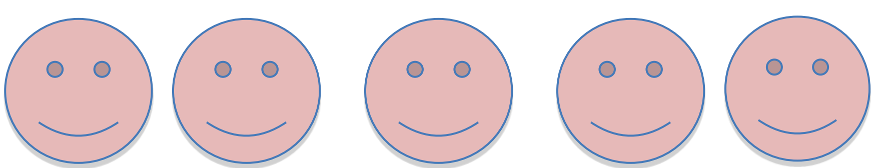
Count Faces

(Give Reward)

(Give Reward)

(Give Reward)

(Give Reward)



(Give Reward)

(Give Reward)

5

All Done with Blood Test!

Get Big Prize

Aberrant Behavior Checklist – Irritability/Stereotypy Items

I. Please rate the child's behavior during the blood draw. For each item, decide whether the behavior is a problem and circle the appropriate number.

0= not at all a problem | 1=the behavior is a problem but slight in degree
2= the problem is moderately serious | 3=the problem is severe in degree

02. Injures self on purpose	0	1	2	3
04. Aggressive to other children or adults (verbally or physically)	0	1	2	3
06. Meaningless, recurring body movements	0	1	2	3
08. Screams inappropriately	0	1	2	3
10. Temper tantrums/outbursts	0	1	2	3
11. Stereotyped behavior; abnormal, repetitive movements	0	1	2	3
14. Irritability and whiny	0	1	2	3
17. Odd, bizarre in behavior	0	1	2	3
19. Yells at inappropriate times	0	1	2	3
25. Depressed mood	0	1	2	3
27. Moves or rolls head back and fort repetitively	0	1	2	3
29. Demands must met immediately	0	1	2	3
34. Cries over minor annoyances and hurts	0	1	2	3
35. Repetitive hand, body, head movements	0	1	2	3
36. Mood changes quickly	0	1	2	3
41. Cries and screams inappropriately	0	1	2	3
45. Waves or shakes the extremities repeatedly	0	1	2	3
47. Stamps feet or bangs objects or slams doors	0	1	2	3
49. Rocks body back and forth repeatedly	0	1	2	3
50. Deliberately hurts himself/herself	0	1	2	3
52. Does physical violence to self	0	1	2	3
57. Has temper outbursts or tantrums when he/she does not get own way	0	1	2	3

modified form

Phone Screen Questions

Participant Information

I. **Circle the item that best applies to how cooperative your child is typically during blood draws.**

0 = No problems with cooperation

1 = Minor problems with cooperation: child shows mild behavior problems and/or anxiety symptoms

2 = Poor cooperation: Child's behavior problems and/or anxiety symptoms requires that the medical staff have to spend extra time and effort to manage the child and complete the blood draw

3 = Completely uncooperative: Blood draw is not possible due to child's behavior problems and/or anxiety symptoms

Comments:____

____

II. **List any aspects of a blood draw that your child is compliant with.**

____

____

III. **List the aspects of a blood draw that are the most difficult for your child.**

____

____

IV. **List any sensitivities (e.g., sights, sounds, etc.) your child has that we should know about.**

____

____

V. **List any special interests or treats your child finds motivating.**

____

____