

Use of Electroconvulsive Therapy to Treat Self-Injurious Behavior in Adults with Autism Spectrum Disorders

I. Overview:

Self-injurious behavior (SIB) is one of the strongest predictors of psychiatric hospitalization among children with Autism Spectrum Disorder (ASD) aged 5 to 21 years. While self-injury in some patients is operant-based, involuntary self-injury can be a presentation of catatonia. When psychopharmacologic interventions fail, electroconvulsive therapy (ECT) is a safe and highly effective alternative to treating catatonia and major depression. Given that catatonia may present as SIB, especially in patients with ASD, several case studies have used ECT to minimize the self-injury in treatment-resistant patients. This study will use formal measures, including the Aberrant Behavior Checklist (ABC), Repetitive Behavior Scale (RBS), and the Self-Injury Trauma (SIT) Scale to monitor the outcome of using ECT to treat SIB in patients with ASD, for whom psychotropic medication has not worked. This study will be fundamentally different from the previously published literature on the subject in that this will be a prospective study which will aim to recruit multiple participants in an open label study.

II. Specific Aims and Hypotheses:

SIB in ASD is both physically and emotionally damaging to patients. Many patients with SIB who have ASD are treatment resistant in regard to psychopharmacologic treatment. ECT has been reported as an effective treatment for SIB in ASD but only through case reports. The major aim of this research study is to provide prospective research data of the efficacy of ECT in this population.

Specific Aim 1: Clarification, verification, and characterization of the presence of SIB in ASD subjects prior to ECT, through the use of the Self Injury Trauma Scale and daily caregiver assessments of self-injurious behavior.

Specific Aim 2: To measure the efficacy of ECT on SIB by comparing clinical, physical, and psychological signs and symptoms pre and post ECT using the Self-injury Trauma Scale, Repetitive Behavior Scale-Revised, Aberrant Behavior Checklist, ASD Diagnostic Checklist, and the caregiver's daily diary card.

Hypothesis 2: ECT will be an effective treatment for SIB as measured by improvements in the Self-injury Trauma Scale, Repetitive Behavior Scale-Revised, Aberrant Behavior Checklist, and the daily diary card, kept by the caregiver. ECT will not lead to significant changes in the ASD Diagnostic Checklist.

Specific aim 3: Monitor and evaluate the side effect profile of ECT in this population of subjects.

Hypothesis 3: ECT will have no additional side effects in this population other than those seen in any psychiatric population receiving ECT.

III. Background, Rationale, and Significance of the Study:

Persons diagnosed with Autism Spectrum Disorder (ASD) are more likely to have a comorbid psychiatric disorder than their neurotypical peers.¹ As many as 11% of children with ASD in the United States have been admitted to a psychiatric hospital by the time they turn 21 years old. Moreover, self-injurious behavior (SIB) is one of the strongest predictors of psychiatric hospitalization among children with ASD aged 5 to 21 years.² Tate and Baroff define SIB as any behavior which “produces injury to the individual’s own body.”³ According to the Self-Injury Trauma Scale, SIB categories include: forceful contact with head or face; forceful contact with other body part; scratching, picking, rubbing skin; biting; eye gouging; ingestion of inedible materials; vomiting or rumination; air swallowing; and hair pulling⁴.

While self-injury can be operant-based, SIB in some patients is a presentation of catatonia.⁵ Indeed, a plethora of cases of self-injury and catatonia have been reported in the past century.⁵ Involuntary self-injury can be a form of the motor stereotypies diagnostic of catatonia.⁵ Unfortunately, the frequency of comorbidity of ASD and catatonia is unknown due to the similarities in presentation, and thus a likely underdiagnosis of catatonia in persons with autism. Shared symptoms of autism and catatonia include posturing, grimacing, negativism, motor-stereotypies, and purposeless agitation.⁶ According to the DSM-5, catatonia is not recognized as an independent class. It may occur in the context of neurodevelopmental, psychotic, bipolar, and depressive disorders. A catatonia specifier is used when there is a marked psychomotor disturbance involving at least 3 of the 12 diagnostic features of catatonia (stupor, catalepsy, waxy flexibility, mutism, negativism, posturing, mannerism, stereotypy, agitation, grimacing, echolalia, and echopraxia). The DSM-5 also recognizes catatonia due to another medical condition and unspecified catatonia, where the nature of an underlying disorder is unclear. In the literature, ASD with co-morbid catatonia has been proposed to be its own subtype of autism.⁸ Alternatively, it has been hypothesized that autism may be an early stage of catatonia.⁹ Autism Spectrum Disorders, catatonia, and some forms of SIB have been postulated to have the same neurochemical basis. GABA receptor abnormalities has been implicated in all three psychopathologies.⁷ Additionally, GABA and its subunit genes are encoded on chromosome 15q11-13, the same loci that have been implicated in catatonia and autism.¹⁰

A subgroup of patients with both ASD and self-injurious behavior have been found to be “treatment-resistant”. In these individuals neither behavioral interventions nor psychotropic medications have been found to be effective in controlling the SIB. Electroconvulsive therapy (ECT) is highly effective at treating catatonia and severe depression. In life-threatening catatonia, ECT is considered a first-line treatment due to its speed and efficacy in treating the life-threatening emergency. ECT has been shown to have an efficacy of at least 80% in the resolution of catatonia among patients who have been treatment-resistant, with higher rates of efficacy shown for the resolution of primary catatonic symptoms.^{11,12} Because self-injurious behavior can be a presentation of catatonia, several case-studies have been published that show the efficacy of using ECT to minimize or resolve SIB in children and young adults with ASD.^{13,14,15,16,17} However, all studies to date have been retrospective in nature and there were few formal outcome measures.¹⁸

Significance

This study will use formal measures, including the Aberrant Behavior Checklist (ABC), Repetitive Behavior Scale (RBS), and the Self-Injury Trauma (SIT) Scale to monitor the outcome of using ECT to treat SIB in patients with ASD, for whom psychotropic medication has not worked. This study will be fundamentally different from the previously published literature on the subject in that this will be a prospective study which will aim to recruit multiple participants in an open label study rather than the previously reported case studies.^{13,14,15,16,17}

IV. Research Methods and Procedures

Inclusion and exclusion criteria

For this study, all adult individuals presenting to EVMS Psychiatry and Behavioral Sciences will be considered for this clinical treatment study if they have a documented ASD diagnosis by a psychiatrist or psychologist. Participants (N=20) must be over the age of 18, and must have an LAR who can consent to medical treatment and attend all appointments with the participant. Only the participant's LAR may consent to treatment (no participants in this study will be permitted to self-consent). Those individuals considered wards of the state will be considered for the study as long as they meet all inclusion/exclusion criteria and are able to follow through with all steps of the protocol (e.g., guardianship, consent, transportation, etc.). Additionally, the participant must have a present history of self-injurious behavior (SIB) that significantly impacts their quality of life, for which they have tried and failed at least four other treatment methods in the past. SIB is any behavior "which produces injury to the individual's own body." (Tate and Baroff, 1966). All subjects must be medically cleared per the clinical ECT protocol already in place, which includes obtaining an EKG, Chest X-Ray (CXR), Complete Metabolic Panel (CMP), and Complete Blood Count (CBC). Subjects must also obtain a head CT scan. All studies must be less than 6 months old. Additionally, subjects must receive a full clinical psychiatric evaluation with the principal investigators: Dr. Shriti Patel, MD to evaluate for appropriateness for and response to ECT and Dr. Maria Urbano, MD to evaluate for ASD symptoms in subjects prior to, during, and at follow-up.

Study Design

This study design is single subject design over multiple participants. Any patient who is enrolled for ECT with a diagnosis of ASD and SIB that meets inclusion and exclusion criteria will be entered into the study if their guardian/subject provides consent/assent. All ECT procedures will be performed at the SNGH outpatient surgical suite.

Procedure

After the individual has been screened and is determined to meet the inclusion and exclusion criteria they will be scheduled for two pre-treatment appointments and sent a consent form to review ahead of time. As part of the inclusion and exclusion criteria, the participant must have an appointment with their primary care provider or a hospital internist to complete a physical exam and required tests (EKG, CXR, CMP, CBC, and head CT scan). At the first pre-treatment appointment (Visit 1), the participant and their legal guardian will go over the consent form with the investigator. In addition to the consent form, to be signed by the legal guardian, the

participant will receive an assent of the cognitively impaired. After giving consent, the legal guardian will be given a Sentara release of medical information form so that investigators will have access to the ECT-performing physician's medical notes. The guardian or other caregiver will then fill out the ASD Diagnostic Checklist, Repetitive Behavior Scale- Revised, and the Aberrant Behavior Checklist. The physician will complete the Self-Injury Trauma Scale, which documents the number, type, and severity of unhealed self-injury traumas. At the end of the Visit 1, the guardian/ caregiver will receive a Subject Diary Card to record the number of self-injury episodes per day, the number of aggressive episodes per day, and the perceived severity of episodes that day. The Diary Card also has space to record the medication taken by the participant every day.

The second pre-treatment appointment (Visit 2) will consist of a complete psychiatric evaluation with review of all medical evaluations. The subject must receive medical clearance as defined by Sentara Norfolk General Hospital to undergo ECT treatment. The first Diary Card will be collected at this time, and a second Diary Card will be given.

After receiving medical clearance, or "low risk" to undergo ECT, participants (accompanied by their guardians/ caregiver) will begin to receive ECT treatments. They will receive ECT 3 times a week for 4 weeks, for a total of 12 treatments (Visits 3- 14). All ECT treatments will take place in the Outpatient Surgery and Diagnostic Unit of Sentara Norfolk General, and will be performed by Dr. Shriti Patel or Dr. Justin Petri. All subjects will receive bilateral "brief" ECT, based on the potential risk that self-injurious behavior holds. Participants will be placed under general anesthesia (Etomidate) and after it is determined that the anesthesia is in effect they will be given a primary muscle relaxant (Succinylcholine). Patients will receive one bag of IV NS fluids. An anesthesiologist or nurse anesthetist will hyperventilate the patient to lower their seizure threshold. Two electrodes will be placed bi-temporally. An electric current will pass through the electrodes to the brain through a process of conduction. During initial treatment (Visit 3), the total amount of energy will be titrated until a short seizure is produced, which is called seizure threshold. During subsequent visits (Visits 4-14), the settings will be adjusted to a total energy of 2.5 x seizure threshold, as determined by the ECT provider. Electrical activity in the brain, including seizure quality, duration, and post-ictal suppression of seizure, will be determined by electroencephalogram (EEG). Throughout the procedure, the provider will be monitoring blood pressure, heart rate, and oxygen saturation. While asleep, the participant will be given oxygen through an oxygen mask and a bite block will be placed to protect the teeth and tongue during stimulation. Following the procedure, the patient will recover in the Post Anesthesia Care Unit.

Throughout the course of the treatment, guardians/ caregiver will continue filling out the Diary Card. Once treatment begins, guardians/ caregiver will be asked to also include any side effects of the treatment noted by themselves or the participant. Guardians/ caregiver will turn in and receive new Diary Cards at Visit 3, Visit 6, Visit 9, and Visit 12. After Visit 14, patients will begin to receive maintenance ECT as prescribed by the ECT physician.

After acute ECT treatment is complete, patients and their guardians/ caregiver will return to EVMS Department of Psychiatry and Behavioral Sciences for post-treatment appointments (Visits 15-18). At these post-treatment appointment guardians/ caregiver will complete the ASD

Diagnostic Checklist, Repetitive Behavior Scale- Revised, and the Aberrant Behavior Checklist. The physician will complete a second Self-Injury Trauma Scale. At this time the Diary Card will be collected and subjects will receive Diary Cards for 1 month. Visits 15-18 will occur at 1 month, 2 months, 6 months, and 12 months post – acute ECT treatment. See the next page for a timeline summary of visits.

		Appointment Type	To-Do	Diary Card
Week 1	Visit 1	Pre- ECT Appointment	Consent and Assent forms, Release of Medical Information, ADC, RBS-R, ABC, Self-Injury Trauma Scale	Receive Diary Card 1
Week 2	Visit 2	Pre- ECT Appointment	Psychiatric Evaluation, Medical Clearance	Return DC 1, Receive DC 2
Week 3	Visit 3	ECT	Determine Seizure Threshold	Return DC 2; Receive DC 3
	Visit 4	ECT	Treatment	
	Visit 5	ECT	Treatment	
Week 4	Visit 6	ECT	Treatment	Return DC 3; Receive DC 4
	Visit 7	ECT	Treatment	
	Visit 8	ECT	Treatment	
Week 5	Visit 9	ECT	Treatment	Return DC 4; Receive DC 5
	Visit 10	ECT	Treatment	
	Visit 11	ECT	Treatment	
Week 6	Visit 12	ECT	Treatment	Return DC 5; Receive DC 6
	Visit 13	ECT	Treatment	
	Visit 14	ECT	Treatment	
Week 7	Visit 15	Post- ECT visit	ADC, RBS-R, ABC, Self-Injury Trauma Scale	Return DC 6; Receive DC 7, 8, 9, 10
Week 11	Visit 16	Post- ECT visit	ADC, RBS-R, ABC, Self-Injury Trauma Scale	Return DC 7, 8, 9, 10
6 Months	Visit 17	Follow-up visit	ADC, RBS-R, ABC, Self-Injury Trauma Scale	
12 Months	Visit 18	Follow-up visit	ADC, RBS-R, ABC, Self-Injury Trauma Scale	

Measures

Self-Injury Trauma Scale (SIT) allows differentiation and quantification of self-injury. In conjunction with a complete medical assessment, the physician records location of injury, type of injury, number of injuries, and an estimate of severity. Given these findings a Number Index, Severity Index, and Estimate of Current Risk can be calculated. The scale has been shown to have high interrater reliability.⁴

ASD Diagnostic Checklist (ADC) was designed after the ADOS, ADI-R, and DSM-V criteria for autism. It is a 25 item instrument, completed by the caregiver, used to assess, (1) qualitative impairment in social interaction, (2) difficulties in communication, and (3) restricted, repetitive, and stereotyped patterns of behavior. It is a tool that will be used as verification that the subject qualifies for an ASD diagnosis in addition to providing the density of ASD symptoms present specific to each patient..

Repetitive Behavior Scale-Revised (RBS-R) is a 43 item instrument completed by caregivers that is rated on a four-point Likert scale ranging from “behavior does not occur” to “behavior occurs and is a severe problem”. The revised scale is specifically intended to assess the variety of RRBs in individuals with ASDs. It is grouped into 5 subscales: 1) stereotyped behavior, 2) self-injurious behavior, 3) compulsive behavior, 4) ritualistic/sameness behavior and 5) restricted behavior. Cronbach’s alpha ranged from 0.78 for the restricted interest subscale to 0.91 for the ritualistic/sameness behavior subscale.¹⁹

Aberrant Behavior Checklist (ABC), is useful for evaluating inappropriate and maladaptive behavior. It is normed from childhood to adulthood and has 58 items rated on a Likert scale. Separate factor analyses result in five-factor subscales: 1) Irritability, Agitation, Crying; 2) Lethargy, Social Withdrawal; 3) Stereotypic Behavior; 4) Hyperactivity, Noncompliance; and 5) Inappropriate Speech^{20,21}. The ABC has had confirmatory and exploratory factor analyses in 1893 children evaluated as part of the Autism Treatment Network which supported the convergent and divergent validity of the ABC as a measure of behavior problems in ASD.²² In practice, the ABC has the option to be completed by a parent, teacher, supervisor, or other guardian/ caregiver. In this study, the ABC will be completed only by a guardian/LAR/ caregiver or by the participant.

Human Subjects Protection

Data collection will be in accordance with an IRB approved protocol. This research project involves the collection of psychological data under the direction of the principal investigator Dr. Shriti Patel, MD. All tests and measures have been widely and safely used with diverse populations. All written research material will be kept in a locked file cabinet in a locked room, and will be identified only with numerical codes (rather than name) to protect confidentiality. Data containing a link between the participants’ numerical code and their names will be accessed via password entry only. Data will be reported as group data and will not be identifiable as individual responses.

Risks to the Subject

Electroconvulsive Therapy (ECT), like any other medical or surgical procedure, involves a certain amount of risk. Careful medical evaluation of each case will be completed to ensure that

there are no overriding medical contraindications to the treatment. Fatalities are extremely rare, but may occur due to heart problems or a prolonged seizure. Risk of mortality is 1 in 10,000-80,000. Cardiovascular complications such as cardiac arrest, arrhythmias, ischemia, hypertension, and hypotension are rare but may occur. Prolonged seizures or status epilepticus are two other rare possible sources of morbidity. Complications, although infrequent, may include fractures and/or dislocations or adverse reactions to intravenous medications. Oral or dental trauma may occur as a result of the seizure. In some patients with bipolar disorder, manic symptoms may emerge or worsen with ECT.

Headache, mild muscle soreness, or nausea sometimes occurs, but these are infrequent and usually respond to symptomatic management. As the treatments progress, short term memory impairment (anterograde and retrograde) may gradually occur. This is usually transitory and should return to baseline within weeks to months after completing treatments. There are occasional residual areas of memory impairment, but this is not common. Inadvertent release of PHI is a potential risk to the subject.

Protection against Risks

Information concerning the potential side effects of ECT will be discussed with the subject/legal guardian/ caregiver so that the subject has sufficient understanding. All subjects and guardians/ caregiver will be given information on how to contact the co-investigators should they have any questions or problems concerning ECT side effects. All interviews and questionnaires have been widely and safely used with diverse populations. All questionnaires and written research materials will be kept in a locked file room. All information will be identified only with numerical codes (rather than identifying information such as a name). To protect against risks, all subjects must be medically cleared per the clinical ECT protocol already in place, which includes obtaining an EKG, Chest X-Ray (CXR), Complete Metabolic Panel (CMP), and Complete Blood Count (CBC). Subjects must also obtain a head CT scan. These tests will help determine if a subject is at an increased risk for an adverse effect. Patients with preexisting cardiac illness, compromised pulmonary status, a history of brain insult or medical complications after earlier courses of anesthesia are likely to be at an increased risk, but will not be excluded from the study as none of these complications are absolute contraindications. The treatment team will be capable of managing the major classes of cardiovascular complications, including cardiac arrest, arrhythmias, ischemia, hypertension, and hypotension. To protect against prolonged seizures, the first treatment will determine the seizure threshold of the patient and following treatments the patient will receive the lowest affective dose. The team will be capable of dealing with instances of prolonged apnea, prolonged or tardive seizures, and status epilepticus. Participants will be monitored on an electroencephalogram (EEG) during the procedure. Vital signs will be continually monitored before, during and after each ECT procedure, and patients will only leave the recovery area once the vital signs are stable. Muscle relaxants are administered to protect the subject from fractures or dislocations. A mouth guard will be placed in the participant's mouth prior to induction of the seizure to protect against oral/dental trauma. At every treatment patients and their caregivers will be questioned by the psychiatrist to determine that ECT treatment is not exacerbating any psychological symptoms, such as mania. Given the nature of the risks, all

subjects must have tried and failed at least four alternative treatments for their self-injurious behavior before being considered for this study.

Data and Safety Monitoring Plan

Research Staff Training

Each member of the research staff is required to complete and pass all EVMS IRB required courses in human subject protection before they are permitted to conduct research. These courses emphasize essential issues of patient confidentiality and informed consent procedures. The senior investigators also instruct and supervise staff on appropriate research conduct and monitor the staff's ongoing activities to ensure adherence to the guidelines.

Data Management

Data are collected exclusively for the purpose of research. All procedures will be conducted in compliance with HIPAA. Patients provide information through interviews (e.g., clinical assessments, medication side effect assessments), through medical examination (e.g., lab values), and by guardian/ caregiver -performed questionnaires. All data obtained from the patient are coded with a study identification number (not the patient's social security number) and maintained in paper form in a Case Report Form booklet. The Case Report Forms are stored in a locked file cabinet and kept in a locked research office. The data will also be entered and stored in a computerized database on computers that are password protected. Dr. Patel and the project manager maintain the master list that matches the patient's name with the study identification number. This list is secured in paper form in a locked file cabinet and in a computer file on a computer that is password-protected; both are kept in a locked research office. The informed consent that includes the patient's name is secured in a separate file in a locked file cabinet in a locked research office. Any identifying information on the test measures will be blacked out and replaced with the participant's assigned subject number. The investigators monitor and verify that informed consent is obtained before *any* data collection activities, and that all data are coded and maintained with the proper study identification number.

Reporting of Serious Adverse Events

Drs. Maria Urbano and Shriti Patel will evaluate side effects, laboratory examination, EKG and physical examination data. They will assess the relationship of all serious adverse ECT side effects to the administration of treatments. All SAEs will be reported immediately (i.e., when investigator or members of investigational staff becomes aware of SAE) to the IRB. The immediate reports will be followed by detailed written reports within 72 hours to the IRB. Assessment of the relationship of the SAE to the study ECT treatments will be made using the following categories: Not Related, Doubtful, Possible, Probable and Very Likely. Subject information on the SAE report will include the patient's study identification number and not their name, personal identification number or address. All initial SAE reports will report the outcome of the SAE (e.g., recovered without sequelae, recovered with sequelae, not yet recovered, death).

If SAE is ongoing, then a final follow-up report will be submitted to applicable regulatory authorities (e.g., IRB, FDA).

V. References

1. Leyfer OT. Comorbid Psychiatric Disorders in Children with Autism: Interview Deve. 2014
2. Mandell. Psychiatric Hospitalization Among Children with Autism Spectrum Disord. 2014
3. Tate BG; Baroff GS. Aversive control of self-injurious behavior in a psychotic boy. *Behav Res Ther.* 1966;4(4):281-7.
4. Iwata BA; Pace GM; Kissel RC; Nau PA; Farber JM. The Self-Injury Trauma (SIT) Scale: a method for quantifying surface tissue damage caused by self-injurious behavior. *J Appl Behav Anal.* 1990;23(1):99-110.
5. Wachtel LE; Dhossche DM. Self-injury in autism as an alternate sign of catatonia: implications for electroconvulsive therapy. *Med Hypotheses.* 2010;75(1):111-4.
6. Dhossche DM; Reti IM; Wachtel LE. Catatonia and autism: a historical review, with implications for electroconvulsive therapy. *J ect.* 2009;25(1):19-22
7. Dhossche DM; Carroll BT; Carroll TD. Is there a common neuronal basis for autism and catatonia? *Int Rev Neurobiol.* 2006;72:151-64
8. Ghaziuddin M; Quinlan P; Ghaziuddin N. Catatonia in autism: a distinct subtype? *J Intellect Disabil Res.* 2005;49(Pt 1):102-5.
9. Dhossche DM. Autism as early expression of catatonia. *Med Sci Monit.* 2004;10(3):Ra31-9.
10. Chagnon YC. Shared susceptibility region on chromosome 15 between autism and catatonia. *Int Rev Neurobiol.* 2006;72:165-78.
11. Hawkins JM; Archer KJ; Strakowski SM; Keck PE. Somatic treatment of catatonia. *Int J Psychiatry Med.* 1995;25(4):345-69.
12. Rohland BM; Carroll BT; Jacoby RG. ECT in the treatment of the catatonic syndrome. *J Affect Disord.* 1993;29(4):255-61.

13. Haq AU; Ghaziuddin N. Maintenance electroconvulsive therapy for aggression and self-injurious behavior in two adolescents with autism and catatonia. *J Neuropsychiatry Clin Neurosci.* 2014;26(1):64-72.
14. Wachtel LE; Contrucci-Kuhn SA; Griffin M; Thompson A; Dhossche DM; Reti IM. ECT for self-injury in an autistic boy. *Eur Child Adolesc Psychiatry.* 2009;18(7):458-63.
15. Wachtel LE; Griffin M; Reti IM. Electroconvulsive therapy in a man with autism experiencing severe depression, catatonia, and self-injury. *J ect.* 2010;26(1):70-3.
16. Wachtel LE; Schuldt S; Ghaziuddin N; Shorter E. The potential role of electroconvulsive therapy in the 'Iron Triangle' of pediatric catatonia, autism, and psychosis. *Acta Psychiatr Scand.* 2013;128(5):408-9.
17. Zaw FK; Bates GD; Murali V; Bentham P. Catatonia, autism, and ECT. *Dev Med Child Neurol.* 1999;41(12):843-5.
18. Dejong H; Bunton P; Hare DJ. A Systematic Review of Interventions Used to Treat Catatonic Symptoms in People with Autistic Spectrum Disorders. *J Autism Dev Disord.* 2014
19. Lam KSL, Aman MG. The Repetitive Behavior Scale-Revised: independent validation in individuals with autism spectrum disorders. *J Autism Dev Disord.* 2007. **37**(5): p. 855–866.
20. Aman MG, Singh NN, Stewart AW, Field CJ. The aberrant behavior checklist: a behavior rating scale for the assessment of treatment effects. *Am J Ment Defic.* 1985. **89**(5): p. 485–491.
21. Aman MG, Kasper W, Manos G, et al. Line-item analysis of the Aberrant Behavior Checklist: results from two studies of aripiprazole in the treatment of irritability associated with autistic disorder. *J Child Adolesc Psychopharmacol.* 2010. **20**(5): p. 415–422.
22. Kaat AJ, Lecavalier L, Aman MG. Validity of the Aberrant Behavior Checklist in Children with Autism Spectrum Disorder. *J Autism Dev Disord.* 2013.