Window of Opportunity Remains Open for Successful Treatment of Tactile Impairment in 6- to 11-Year-Old Children with Autism Spectrum Disorder

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INTRODUCTION

Autism is the most common developmental disability in the United States and is currently estimated to affect one in 45 children [1]. Its cause remains unknown. Clinically, autism is defined by the appearance of social and language delay; unusual, repetitive behavior; and abnormal sensory responses by the age of three [2]. Developmental delay occurs on a spectrum of severity with higher functioning children developing fluent speech and more normal cognition, and lower functioning children ending with little or no language and cognitive disability [3]. Until recently, there has been no research-based early intervention that reliably improved all core symptoms of autism across the spectrum of severity, and no clear understanding of why social and language delay, abnormal behavior, and sensory abnormalities develop in children with Autism Spectrum Disorder (ASD).

A new direction for autism treatment research was opened in 2013 when abnormal sensory responses were reclassified from co-morbid symptoms of unknown etiology to core diagnostic autism symptoms. At that point, it was recognized both that abnormal responses to touch are amongst the earliest and most prevalent of abnormal sensory symptoms [4], and that the sense of touch had not been proven to be intact in autism. Qualitative research had demonstrated that children with autism are distinguished by abnormal responses to light touch and pain as well as by lack of interest in affectionate touch [5, 6], but findings had not been subjected to full diagnostic evaluation. In addition, new research in mammalian touch had demonstrated that affectionate and affiliative touch is mediated by small sensory nerves known as C-tactile fibers, the same fibers that mediate light touch and pain [7]. The clinical presentation of tactile abnormalities in children with autism was seen to fit the known signs and symptoms of loss of C-tactile fibers [8,9], and diagnostic evaluation with skin biopsy and specialized staining

[10] was called for. This year, a preliminary biopsy study reported 50% loss of C-tactile fibers in four 8- to 11-year-old children with ASD [11].

In tandem with research investigating the nature of tactile loss in autism, randomized controlled studies (RCTs) were conducted investigating the effect of a tactile stimulation protocol delivered daily by parents and weekly by trained therapists. The tactile stimulation protocol is based on Chinese medicine and is called Qigong Sensory Treatment (QST) massage for autism. The intervention is formalized in a manual with flexible procedures and has a clearly defined theory and methods. Autism is theorized to be due to tactile impairment involving the face, mouth, hands and other areas [12]. Tactile impairment in the early developmental period is proposed to explain the specific social and communication delays and abnormal behaviors characteristic of autism. Treatment uses tactile stimulation methods to normalize tactile responses by increasing circulation to the skin. The effectiveness of Chinese medical approaches to increasing skin circulation has been documented by Laser Doppler flow studies [13, 14].

Several small- and medium-sized, single-blind, RCTs evaluating the tactile stimulation protocol were carried out, culminating in a large replication study involving 103 preschool children for two years. At five months, tactile responses had normalized by 49% (Sense and Self-regulation Checklist), autistic behavior normalized by 32% (Autism Behavior Checklist), and severity of autism (Childhood Autism Rating Scale) normalized by 12% [15]. Improvements were seen across the spectrum of autism severity. Longer-term follow up indicated that further treatment resulted in further improvement [16]. Two years from beginning treatment, touch had normalized by 73%; severity of autism by 44%; and 26% of children were off the spectrum. Results support QST massage for autism being an effective treatment for tactile impairment in preschool children with autism, deliverable by parents with the support of trained staff.

The present study is part of a multi-armed, three-year study to replicate and extend research treating tactile impairment in ASD. In response to evidence that treatment of tactile impairment in preschool children with ASD decreases severity of autism, the question arose as to whether the window of opportunity for treatment remains open beyond the preschool years. For example, the window of opportunity for treating hearing impairment closes at age six, with optimum results occurring when treatment is initiated within the first 12 months [17]. And the window of opportunity for treating vision impairment closes at age one, with permanent disability resulting if vision is not corrected [18].

Here we carry out a small exploratory RCT in 35 children with ASD between the ages of 6 and 11 to measure treatment outcomes on tactile impairment. Based on effects found with younger children the present study has adequate power to detect efficacy on tactile impairment (.83), but not to detect efficacy on measures of autism. Because its design is identical with the earlier study in 103 children between the ages of 2 and 5, we compare changes in measures of autism across age groups.

The primary research question is:

1. Does the window of opportunity for successful treatment of tactile impairment remain open in children ages 6 to 11?

The secondary research questions concern whether treatment outcomes on measures of autism in 6- to 11-year-olds are comparable with those seen in 2- to 5-year-olds:

2. How do the two age groups compare with regard to outcomes on tactile impairment and severity of autism?
3. How do the two age groups compare with regard to outcomes on behavior, social, language and self-help skill development?

4. How do the two groups compare with regard to efficacy in lower- and higher-functioning children?
5. How does parent satisfaction with the intervention compare between the two groups?
6. How do parent comments about child behavior and relationships compare between the two groups? Does the qualitative data report comparable changes in children's response to affectionate touch?
7. How do cost and efficacy of this intervention compare with a more widely known intervention for autism?

MATERIALS AND METHODS

Study Design

The goal of this study was to conduct a small RCT in 35 children ages 6 to 11 with ASD to determine whether the window of opportunity for treating tactile impairment remains open after the age of six. Treatment consisted of daily parent-delivered massage for five months and weekly therapist support visits. Following completion of the RCT, the treatment group continued with daily parent massage and monthly therapist visits for the balance of a year, and the same treatment regimen was initiated in the control group. Outcomes were measured at five months and one year after starting the treatment. The pooled data in 6- to 11-year-olds (referred to below as "Study 1") was compared with similarly pooled data from a previous RCT in 103 children ages two to five (referred to below as "Study 2") [16]. Both studies were identically structured, single-blind RCTs in which the control group received the same treatment regimen upon completion of the RCT. Both studies were conducted with Institutional Review Board approval and registered with the U.S. National Institutes of Health clinical trials registry (#NCT02222662; #NCT01801696).

Participants and Recruitment

Recruitment was accomplished via distribution of brochures, emails, listserve messages, website postings, presentations, social media, TV, radio, and word of mouth. In addition, invitation letters were sent to parents of children receiving autism services from state-funded school programs in the Willamette Valley area of Oregon. Criteria for entry into the study included age of 6 to 11 years in Study 1, and age 2 to 5 years in Study 2; formal diagnosis of autism; no additional chronic disability; no psychoactive medication or pharmaceutical chelation therapy; and not receiving intensive behavioral treatment for autism. Parents agreed to give their children the daily massage treatment for the duration of the study; to follow through with all training and support visits; and not to begin additional interventions for autism during the study.

Verification and confirmation of the autism diagnosis

In both studies, children were required to have a pre-existing diagnosis of autism by formal autism evaluation as a condition of entry into the study. Prior to acceptance into the study, medical records were obtained, and the previous diagnosis of autism verified. Diagnoses were by neurodevelopmental pediatricians using DSM-IV criteria and/or instruments such as the ADI and the ADOS. Upon acceptance into the study, the autism diagnosis was confirmed using DSM-IV criteria.

Demographic Information

For children ages 6 to 11, the post-treatment average age of participants was 108.7 months. At one year the average age was 116.2 months. Boys made up 86% of the sample at one year. Lower income families were 53.8% of the participants at one year. Families of cultural minorities were 46% of the participants at one year. Ninety-seven percent of parents involved

had no previous experience with massage or Chinese medicine. Families who withdrew from the study did not have different demographics.

For preschool children, the post-treatment average age of participants was 57.7 months. At one year the average age was 64.1 months. Boys made up 90% of the sample at 12. Lower income families were 33% of the participants at one year. Families of cultural minorities were 28% of the participants at one year. Eighty percent of parents involved had no previous experience with massage or Chinese medicine. Families who withdrew from the study did not have different demographics.

Study Completion Data

Thirty-three of the 35 children entering Study 1 completed the five-month RCT, including 17 in the treatment group and 16 in the control group. Twelve of the children in the control condition went on to receive treatment and assessment post treatment. Thirteen of the children in the original treatment condition underwent follow-up testing at one year.

Eighty-four of the 103 children entering Study 2 completed the five-month RCT, including 42 in each group. Thirty-three of the children in the control condition went on to receive treatment and assessment post treatment. A total of 67 children remained in the study through follow-up testing at one year [16].

Randomization Procedures

For both studies children and their families from each geographical area who met study criteria were randomly assigned into either the treatment or control group condition based on age in months to reduce bias on developmental measures. A random number generator was used. Pairs of siblings were assigned into the same group by necessity.

QST Massage Protocol

The QST massage protocol is a whole-body protocol that takes about 15 minutes to complete and is usually done at bedtime. It is formalized in a parent training manual with flexible constraints [19]. The parent is taught not to avoid areas that are uncomfortable but instead to adjust the techniques to the child's responses, within the comfort zone of the child. Over the course of treatment, tactile responses undergo predictable change from hyposensitive to hypersensitive to normosensitive. The protocol requires adjustment of manual technique with each transition. The protocol utilizes touch to sequentially stimulate social and self-regulatory activity, first by stimulating awareness and receptivity to massage, then by stimulating eye contact and smile, and finally by stimulating deep relaxation with touch.

The protocol has 12 parts that follow the acupuncture channels down the front and back of the body. Massage is carried out towards the hands and feet in the direction of capillary blood flow. Both patting and pressure are used according to the child's response. Generally, a quicker, lighter, patting technique is used to begin with, especially in areas of hyposensitivity. In areas where the child withdraws from touch or is ticklish, slower pressing techniques are used. Additional options are available when neither patting nor pressure resolves discomfort. For a summary of the massage movements, go to http://qsti.org/wp-content/uploads/2014/06/12MovementsAutism.pdf.

Therapists providing the parent training and support program benefitted from a 60-hour training. Seven therapists participated in Study 1; 19 therapists participated in the Study 2. Parent training unfolded with a group training followed by weekly one-on-one support. At each visit, therapists inquired about fidelity with daily massage, provided ongoing support and training, and gave children a massage treatment.

There are four periods when parents are at risk for discontinuing the program. These include: (1) upon initiating the program and not knowing how to deal with children's resistance to massage; (2) during the transition period when the sensory system switches from hyposensitive to hypersensitive and massage techniques must be modified; (3) the transition period when touch has sufficiently normalized for the child to experience a sense of self and to move into the autonomy phase of development (this phase must be recognized for what it is and parenting techniques modified); and (4) the period after which the child has come to relax and enjoy the massage, progress is no longer dramatic, and daily massage can fall off the priority list. Therapists were instructed to watch for these at-risk periods and provide the necessary support.

Measures

The following measures were used to evaluate baseline five-month and one-year outcomes.

1. *Childhood Autism Rating Scale, 2nd Edition, Standard Version* (CARS) [20]. The CARS is a widely used rating scale for the diagnosis of autism and a stable measure of autism severity. The CARS rates children on 15 core components of autism, and yields a composite score ranging from non-autistic to mildly, moderately, or severely autistic. Studies indicate that the CARS demonstrates high concordance with clinical diagnosis by DSM-IV criteria [21]. Independent psychometric support for the CARS reports high criterion-related validity, interrater and test-retest reliability, and internal consistency. A score of 25.5 serves as the cutoff for a diagnosis of autism on the mild end of the autism spectrum; 30 to 36 is scored as moderate; 37 and higher is scored as severe [20]. A decrease in score represents a decrease in severity of autism. The pretreatment median score of 39 was used as the criteria in the analyses to determine effects on language development by level of severity. The CARS was administered by qualified professional examiners who were blind to group assignment.

2. *Preschool Language Scale, 5th Edition* (PLS-5) [22]. The PLS-5 is a measure of global language skills and standardized subscales evaluating relative ability in receptive and expressive language. Internal consistency (split-half reliability) ranges from .91 to .93 for the subscale scores and .95 for the total score. Independent psychometric support for the PLS indicates high criterion-related validity, interrater and test–retest reliability [23]; and that it is a valid measure of language in children with ASD [24]. An increase in score represents high language skills. The PLS-5 was administered by experienced professional examiners who were blind to group assignment.

3. *Vineland Adaptive Behavior Scales, 2nd Edition* (Vineland-II) [25]. The Vineland-II is a validated parent interview that assesses socialization, communication, motor skills, and daily living skills. Cronbach's alpha is .97 for the composite scale and ranges from .83 to .95 for the domains. The Vineland parent interview was conducted by experienced professional examiners who were blind to group assignment. An increase in score represents an increase in development.

4. *Autism Behavior Checklist* (ABC) [26]. The ABC is a validated measure of autism and a component of the Autism Screening Instrument for Educational Planning. The ABC is a sensitive measure of change in response to classroom interventions. It measures behaviors typical of autism in multiple domains: sensory, relating, body and object use, language, social and self-help. Crohbach's alpha is 0.89. The mean value for typically developing children is reported at 17.81 [27]. A decrease in scores represents a reduction in autistic behavior. The Autism Behavior Checklist was filled out by parents.

5. *Sense and Self-Regulation Checklist* (SSC) [28]. The SSC is a validated parent/caregiver measure of abnormal sensory responses and self-regulatory delays in children with autism. It is used as a clinical and research outcomes measure that is capable of discriminating peripheral

impairment of the sense of touch and validating severity of tactile impairment with simultaneous evaluation of delay of early touch-dependent self-regulation milestones. Cronbach's alpha is 0.83. SSC scores clearly differentiate between children with ASD and typical development; mean scores are 39.6 (SD 10.6) and 18.4 (SD 9.5), respectively. Mean oral/tactile scores for ASD and typical children are 29.2 (SD 7.9) and 14.5 (SD 7.2), respectively. Mean self-regulatory difficulty scores for ASD and typical children are 56.8 (SD 14.1) and 25.8 (SD 11.3), respectively. The overall SSC mean scores for ASD and typical children are 89.5 (SD 21.4) and 38.4 (SD 18.0), respectively. A decrease in scores represents a decrease in sensory abnormalities and self-regulatory difficulties. The SSC was filled out by parents.

6. *Beach Center Family-Professional Partnership Scale* [29]. The partnership scale is a validated tool that assesses satisfaction with services received. This scale is designed for use as a research tool. Cronbach's alpha is 0.93. Parents completed the partnership scale at post-testing.

7. *Fidelity and Social Validation Testing.* Therapists monitored parent fidelity with massage procedures by testing parents at weeks one, two, and 12, as well as at one year. The principal investigator monitored therapist fidelity with the parent training and support program. For the first year of treatment, parents completed a daily log recording fidelity with daily massage, reasons for missing the massage, and problems or concerns. In addition, parents completed surveys at five months and one year consisting of a series of open-ended questions exploring their reactions to treatment and outcomes. See Table 1 for survey questions.

Data Collection

Pre- and post-intervention data collection was conducted within a one month window both prior to beginning of treatment and after the 20 week intervention for children in both the treatment and control conditions. One year from pre-intervention data collection also occurred for children

initially assigned to the treatment condition. Parents completed an online set of surveys and background questionnaires that included the Sense and Self-Regulation Checklist and the Autism Behavior Checklist. The Vineland-II, CARS, and PLS-5 were administered in the home by trained, blind-to-condition professionals. Treatment fidelity was monitored throughout the 20 week intervention by assigned therapists.

Table 1. Parent post-treatment questions.

Post-Test	Question
5 months	What has the massage done for you and your child?
5 months	What changes have you seen in your child since beginning the massage?
1 year	Do you see any differences in your relationship with your child, comparing the first half of last year to the second half?
1 year	What differences, if any, did you notice about your child's development from the first half of last year to the last six months?

Data Analysis

Multiple sets of analyses were conducted. The first set were used to determine whether the window of opportunity for treating abnormal tactile response closes after age six. Initial analyses were conducted to detect any potential attrition bias in the older group using 2-way ANOVA and MANOVA on pre-assessment outcome measures. This was followed with analyses to confirm equivalence of treatment and control groups on pre-assessment outcome measures using 2-way ANOVA and MANOVA. Descriptive and paired t-tests on outcome measures were conducted for both treatment and control groups. Main treatment effects were tested using 2-way repeated measure ANOVAs.

Testing whether treatment outcomes in the older group were independent of language ability was conducted first by conducting Wilcoxon Signed Rank Tests on pre-post measures. This was followed by 2-way repeated measures ANOVA.

A second set of analyses were conducted to determine whether the magnitude of change in 6- to 11-year-olds was comparable to 2- to 5-year-olds. Pooled data from the two studies were subjected to within subject Repeated Measures ANOVA, Mann-Whitney Tests, and TOST equivalence testing.

Finally, maintenance of effects to one year follow-up was analyzed using within subjects Repeated Measures ANOVA.

RESULTS

Sample Size Justification and Power Analysis

A power analysis to determine sample size for the older children study was conducted using published results for children under six receiving the QST intervention. The primary outcome used was the total score from the Sensory and Self-Regulation Checklist. Based on the results from the younger children study, a total sample size of 42 with $p < .05$, yields a power of .90 on the SSC, but lower power on other measures of autism and development. With assumed attrition at 10%, an initial sample of 46 was thought to be required to obtain adequate power. Our sample did not meet this criterion. Using the same a-priori criteria, our final sample size of 33 was sufficient to obtain a power of .83.

Potential Attrition Bias

Participants in the control and treatment conditions for the older children withdrew at a proportional rate: one from each group. Two-way MANOVA indicated no differences between completers and non-completers on outcome measures at pre-assessment. F values ranges from .007 to 3.13 with associated p. values ranging from .934 to .086. Similar results were found for the younger children.

Equivalence of Treatment and Control Groups

Older children in the treatment and control conditions did not differ on outcome measures or age. Two-way ANOVA and MANOVA indicate no differences between groups on outcome measures and age. F values ranged from .008 to 2.35 with associated p. values ranging from .928 to .136. Treatment and control groups had equivalent scores on all outcome measures. Similar results were found for the younger children.

Pre-assessment to Post-assessment Changes

Table 2 displays descriptive pre- and post-outcomes for both treatment and control groups of older children. Paired t-test results are also shown. Treatment group participants experienced significant improvement on all measures except severity of autism. Control group participants experienced significant improvements in behavior, living skills, social skills and language. The magnitude of changes found in the younger children are presented for initial comparisons.

Intervention Effects on Main and Secondary Outcomes

Main and secondary outcomes include abnormal oral-tactile response, self-regulatory difficulties, behavior, severity of autism, social and living skills and language. Table 3 presents results from the 2-way repeated measures ANOVA and MANOVA analyses for the older children. A significant treatment effect (time by group interaction) was found for Abnormal Tactile Response with a large effect size. A similar significant treatment effect with large effect size was found for self-regulatory difficulties. Time by group interactions failed to reach significance for behavior, severity of autism or language. Effect sizes were in the medium range for behavior, medium-small for language and small for severity of autism. No overall treatment effect (time by group interaction) was found for general development, though multi-variate and post-hoc univariate effects sizes were all in the medium range.

Table 2. Pre-assessment to post-assessment results for the QST Massage.

	Pre-Post	Treatment Group (*n* = 17)					Control Group (*n* = 16)				
Measures **Primary Outcome**	mean difference 2-5 year olds	Pre Mean (SD)	Post Mean (SD)	Diff	*t*	*p*	Pre Mean (SD)	Post Mean (SD)	Diff	*t*	*p*
Tactile/Oral Abnormalities	-7.2	27.2 (8.3)	19.9 (8.5)	-7.3	-4.65	<.000	26.8 (7.6)	24.4 (9.2)	-2.6	-1.88	.080
Secondary Outcomes											
Self-Regulatory Difficulties	-12.5	53.7 (14.4)	42.1 (13.9)	-11.6	-5.46	<.000	52.0 (13.0)	47.9 (9.1)	-4.1	-1.90	.078
Behavior (ABC)	-20.9	81.5 (26.1)	58.1 (28.9)	-23.4	-4.87	<.000	82.3 (23.3)	69.6 (21.5)	-12.7	-	
Severity of Autism (CARS)	-1.5	39.7 (6.3)	38.8 (6.9)	-0.9	-1.47	.161	38.6 (6.2)	38.0 (6.0)	-0.6	-	
Daily Living Skills	+8.4	70.8 (44.7)	81.7 (46.4)	10.9	3.72	.002	75.1 (35.1)	80.8 (34.4)	5.7		
Social Skills	+9.5	61.5 (36.0)	68.5 (41.4)	7.0	2.61	.019	79.1 (82.5)	82.5 (29.6)	3.4		
Language (PLS-5)	+8.2	78.8	81.7	2.9	2.19	.044	86.1	91.5	5.4		

Note: SD = standard deviation; Diff = the change from pre to post score; ABC = Autism Behavior Checklist; CARS = Childhood Autism Rating Scale; PLS-5 = Preschool Language Scale, 5th edition.

Table 3. Children ages 6 to 11 treatment effects for QST Massage.

Variable	Group Main Between Subject Intervention Effects			
	F	*(degrees of freedom)*	*p*	η_p^2
		Univariate Analysis		
Primary Outcome				
Abnormal Oral-Tactile Response	5.79	(1,31)	.022	.157
Secondary Outcomes				
Self-Regulatory Difficulties	5.96	(1,31)	.021	.161
Behavior (ABC)	2.25	(1,31)	.144	.068
Severity of Autism (CARS)	0.16	(1,31)	.691	.005
Language	0.95	(1,31)	.337	.030
Multivariate Analyses				
General Development	1.28	(2,30)	.294	.078
Social Skills	1.26	(1,31)	.271	.039
Living Skills	2.29	(1,31)	.141	.069

Note: ABC = Autism Behavior Checklist; CARS = Childhood Autism Rating Scale.

Results would indicate that a window of opportunity to treat tactile abnormalities remains open in children ages 6 to 11. Resultant improvements in self-regulation are also evident. While the magnitude of change on other variables is comparable between preschool and elementary

school aged children, Study 1 with older children appears under powered to detect group by time interaction effects.

Comparison of Results between Preschool and Older Children

Data from Study 1 and Study 2 are pooled to compare change over time in the main and secondary outcome variables. Results for both pre-/post-testing for all children receiving treatment as well as intact pre, five-month, and one-year post-testing assessments are compared. A total of 75 children ages 2 to 5 received the treatment either in the original treatment group or after completing their control condition. A total of 67 of these children also were assessed at one year. A total of 29 children ages 6 to 11 received the treatment either in the original treatment group or after completing their control condition. A total of 13 of these children also were assessed at one year.

Pre to post change scores during treatment for older and younger kids were compared using the Mann-Whitney test. There were no significant differences in the pre-post change scores on any of the outcomes of interest. Z-scores ranged from -.124 to -1.885 with associated p-values ranging from .901 to .059 (ABC).

Results from the repeated measures ANOVA for pre-post and one year assessments are shown in Table 4. Overall significant positive differences were found for all outcomes for both groups. In all cases except the CARS for 6- to 11-year-olds, there was a significant change from pre-to post-treatment. For 2- to 5-year-olds significant improvements from post to one year were also seen on the CARS, Living Skills, and Socialization. For 6- to 11-year-olds significant improvements from post to one year were seen in Abnormal Tactile Response, the CARS, Self-Regulation, Socialization, Living Skills, and Language. Both groups experienced significant improvements on all measures from pre-treatment to one year assessments. For example, the one

year results for children ages 6 to 11 on tactile abnormalities represent a mean 84.9% normalization in scores. That is the decrease from 28.5 to 16.6 is an 84.9% change toward the score of 14.5 of typically developing children. By one year over half the children (53.8%) had attained a score of 14.5 or lower on tactile abnormalities. Two- to five-year-olds achieved a 56.9% mean normalization at one year and 23.9% of children achieved a score of 14.5% or lower. Both 6- to 11-year-olds and 2- to 5-year-olds achieved about a 50% mean normalization at one year in the area of self-regulatory difficulties, with 14.9% of 2-6 year olds and 7.7% of 6-11 year olds achieving a score of 25.8 or lower. Six- to 11-year-olds achieved a mean normalization of 51.2% on the ABC, with 7.7% of children reaching a normal score of 17.8 or lower at one year. Two- to five-year-olds achieved a 34.7% mean normalization on the ABC with 8.9% of children reaching the normal score of 17.8 or lower at one year. On the CARS, 6- to 11-year-olds achieved a 21.4% mean normalization, though none of the children reached the cut off score of 25.5 at one year. Two- to 5-year-olds achieved a mean normalization of 26.8% at one year and 11.9% of children scored 25.5 or lower at one year.

Table 4. One-year follow-up outcomes by age group.

Pre-Post-One Year Outcomes	1-Pre Mean (SD)	2-Post Mean (SD)	3- 1 Year Mean (SD)	F (2,65) F(2,11)	p	η^2	Tukey's HSD
Abnormal Tactile Response: 2-5 year olds	34.7 (4.3)	26.4 (7.6)	25.4 (8.5)	25.8	<.000	.625	1>2,3
Abnormal Tactile Response: 6-11 year olds	28.5 (7.1)	20.4 (9.9)	16.6 (10.2)	15.1	<.000	.733	1>2,3 2>3
Childhood Autism Rating Scale: 2-5 year olds	40.4 (7.4)	39.0 (7.7)	37.0 (8.4)	8.2	.001	.362	1>2,3 2>3
Pre-Post-One Year Outcomes	1-Pre Mean (SD)	2-Post Mean (SD)	3- 1 Year Mean (SD)	F (2,65) F(2,11)	p	η^2	Tukey's HSD
Childhood Autism Rating Scale: 6-11 year olds	39.5 (6.4)	38.6 (7.2)	36.5 (7.2)	12.7	.001	.696	1>3 2>3
Autism Behavior Checklist: 2-5 year olds	89.0 (24.2)	74.1 (29.8)	70.0 (28.6)	7.8	.002	.334	1>2,3
Autism Behavior Checklist: 6-11 year olds	86.8 (24.4)	58.4 (28.8)	51.4 (28.5)	15.0	.001	.731	1>2,3
Self-Regulation: 2-5 year olds	61.2 (12.1)	49.4 (12.9)	47.6 (14.4)	19.4	<.000	.556	1>2,3
Self-Regulation: 6-11 year olds	55.0 (14.6)	40.9 (14.0)	35.8 (15.6)	23.1	<.000	.808	1>2,3 2>3
Vineland Socialization: 2-5 year olds	35.9 (15.6)	41.9 (14.7)	51.1 (24.5)	17.8	<.000	.551	1<2,3 2<3

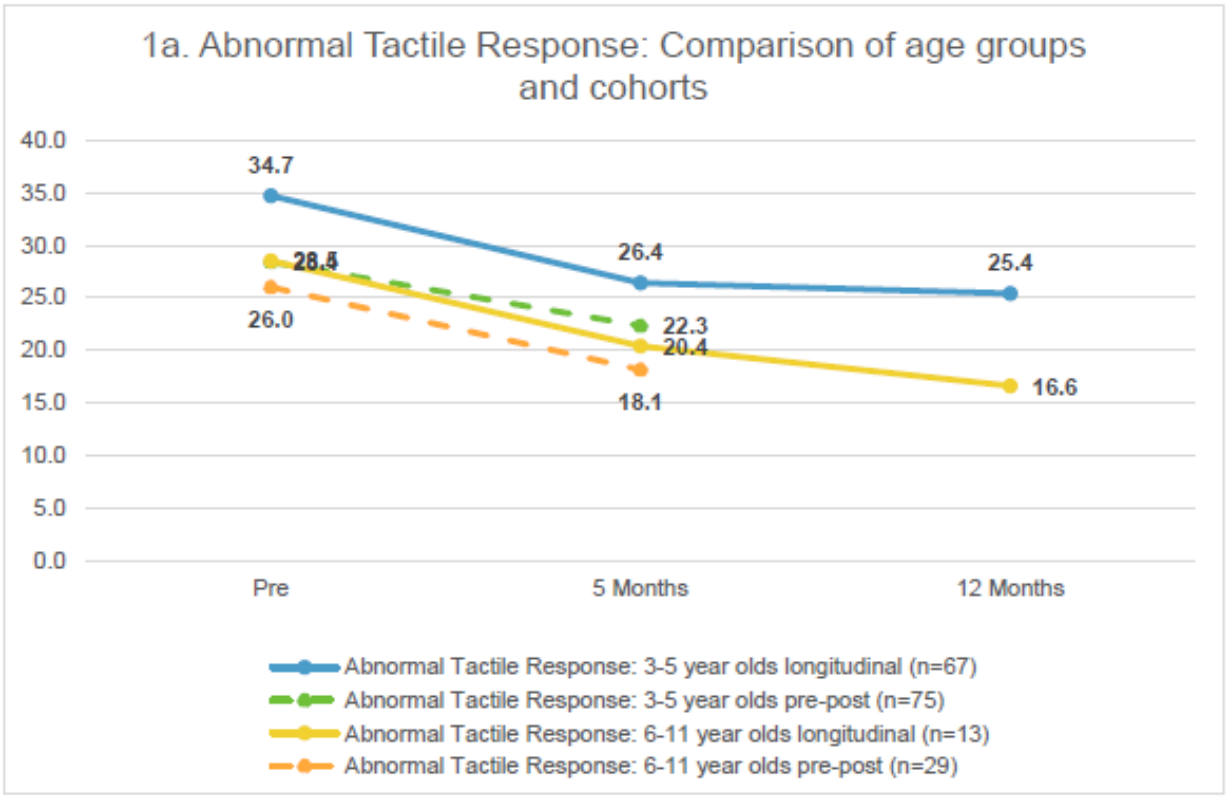
Vineland Socialization: 6-11 year olds	69.4 (36.2)	78.5 (41.3)	87.6 (44.1)	12.5	.001	.695	1<2,3 2<3
PLS-Total: 2-5 year olds	49.6 (20.5)	56.8 (22.6)	60.5 (28.2)	18.2	<.000	.557	1<2,3
PLS Total: 6-11 year olds	89.5 (39.9)	93.9 (41.6)	98.2 (39.8)	11.1	.002	.669	1<2,3 2<3
Vineland Daily Living Skills: 2-5 year olds	32.3 (19.7)	39.9 (19.2)	49.4 (31.2)	24.7	<.000	.630	1<2,3 2<3
Vineland Daily Living Skills: 6-11 year olds	78.5 (47.2)	91.8 (46.9)	99.6 (51.1)	9.9	.003	.642	1<2,3 2<3

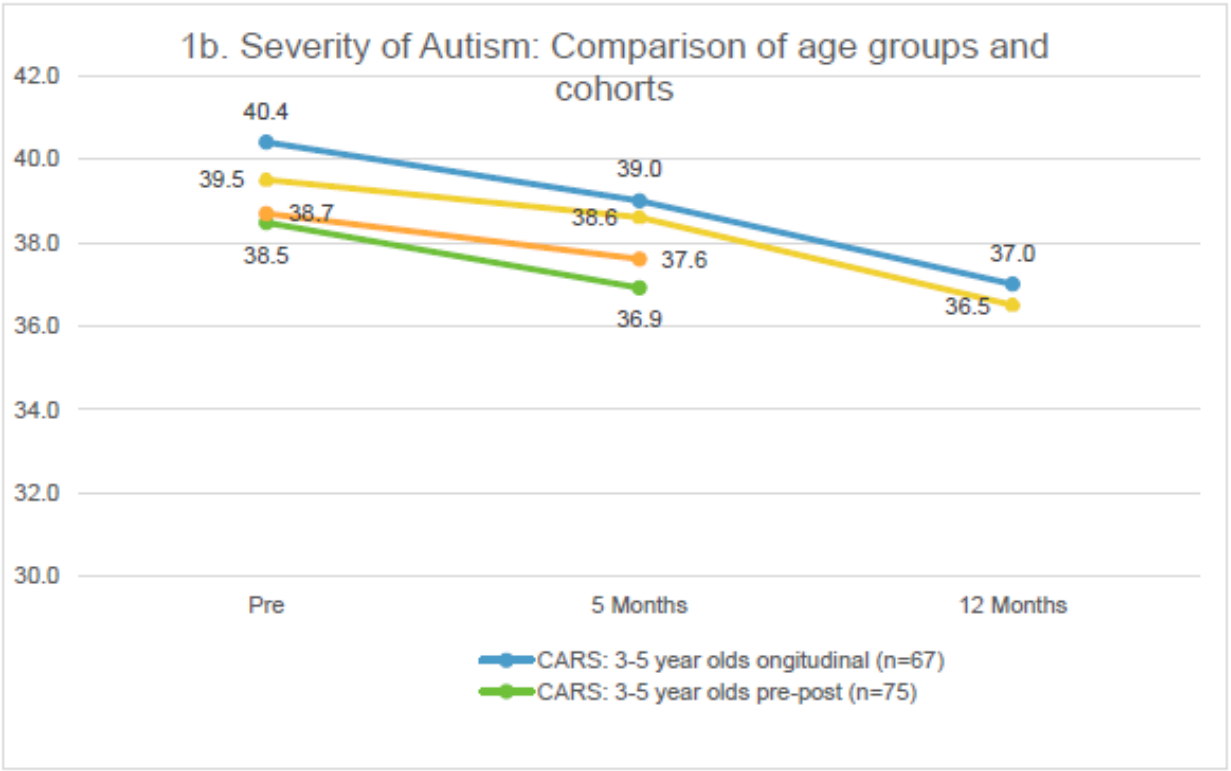
Based on effect size estimates and Tukey's HSD, children ages 6 to 11 benefit as much or more from the treatment than do younger children, though results are very comparable. The small sample size in the older children and unequal sample sizes pose challenges in using equivalence testing techniques reliably to determine whether results are truly equivalent. Recent research by statisticians indicates that while in practice, the Confidence Interval approach is superior to the common student's t-test with large samples, the student's t-test is actually superior to the CI approach with small samples and/or samples with large variances, given both tend to inflate the denominator in the t-statistic [30]. As a result, most of the differences fall into the indeterminate range, with 95% confidence intervals not fully inside or outside the range of equivalence.

These patterns of improvement can be seen in Figures 1 to 3 below. Both pre-post and pre-post-one-year cohorts are graphed. As can be seen in Figures 1a and 1b, the slopes of the lines are similar for both age groups as well as for cohorts for improvements in abnormal tactile

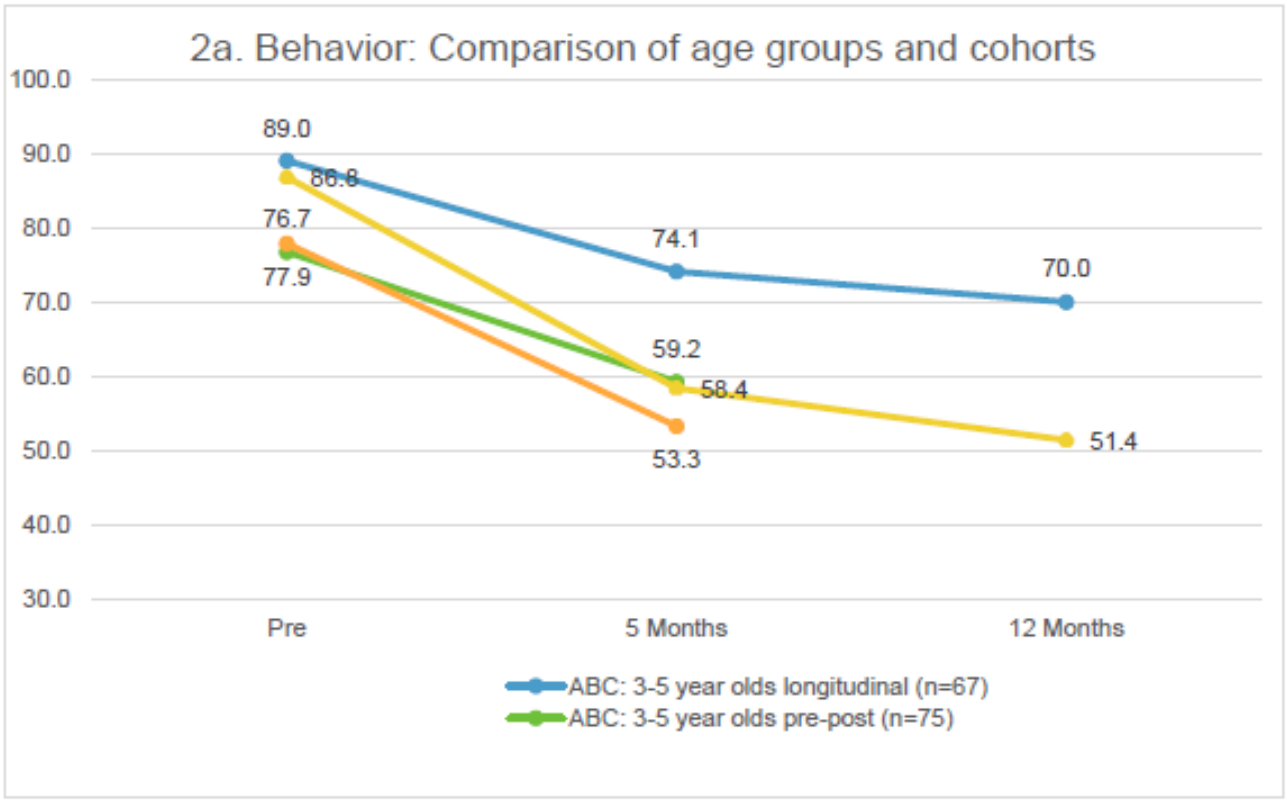
response and severity of autism. This is also the case for improvements in behavior and self-regulation, though the pre-treatment mean scores vary. The slopes of the lines are also similar for socialization, living skills, and language, though again the pre-treatment scores vary.

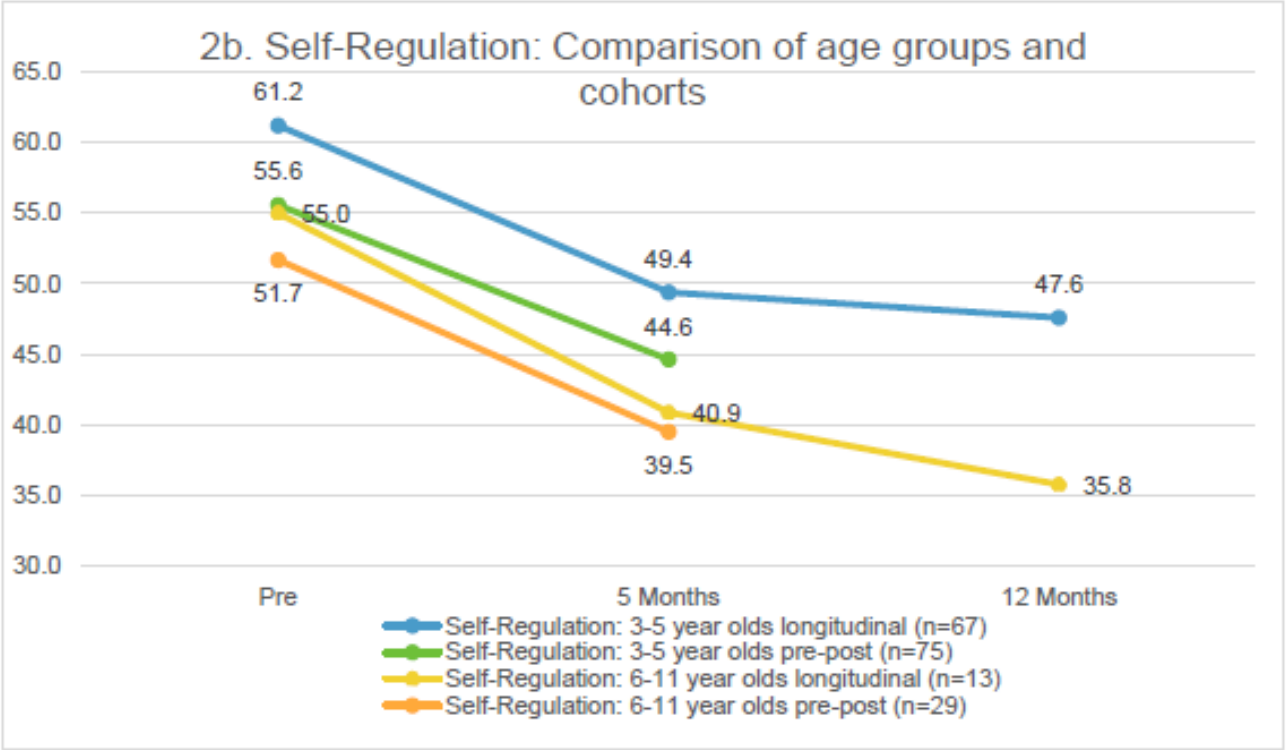
Figures 1a and 1b. Abnormal Tactile Response and Severity of Autism: Comparison of age groups and cohorts.



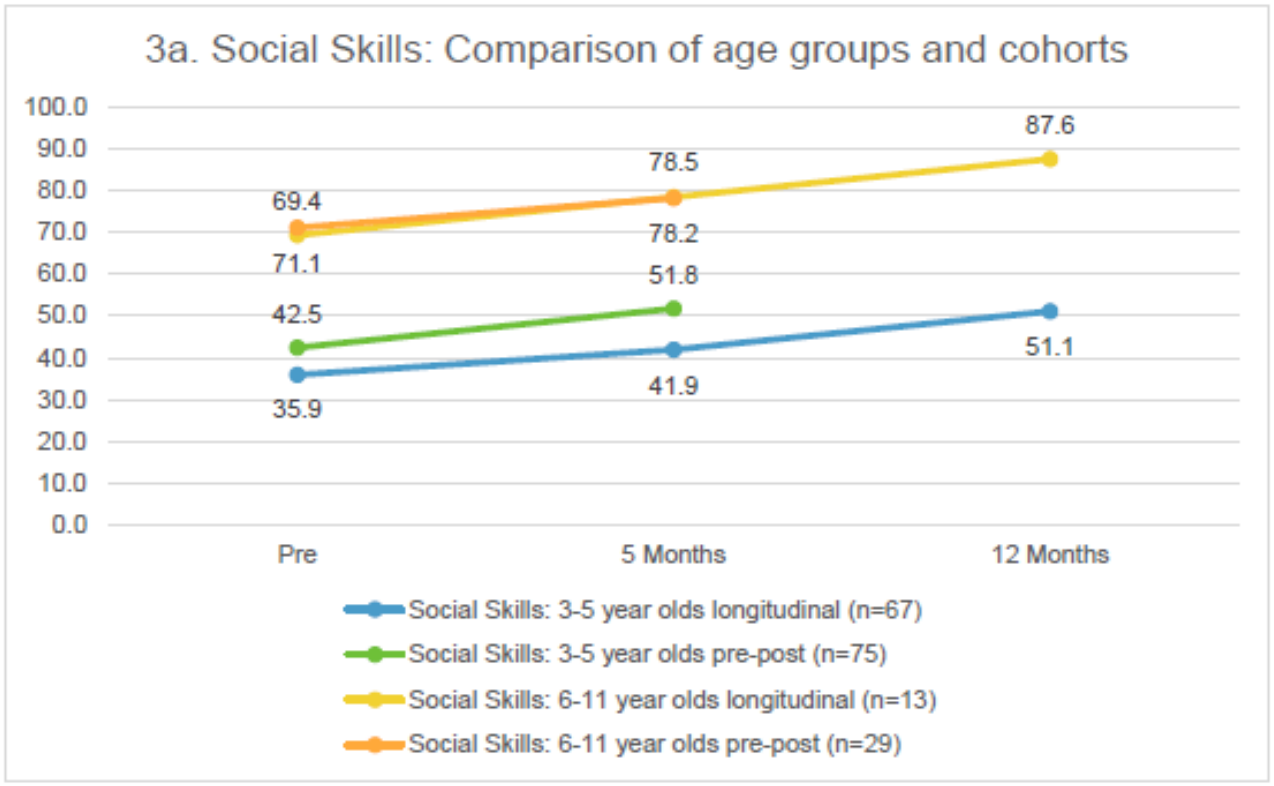


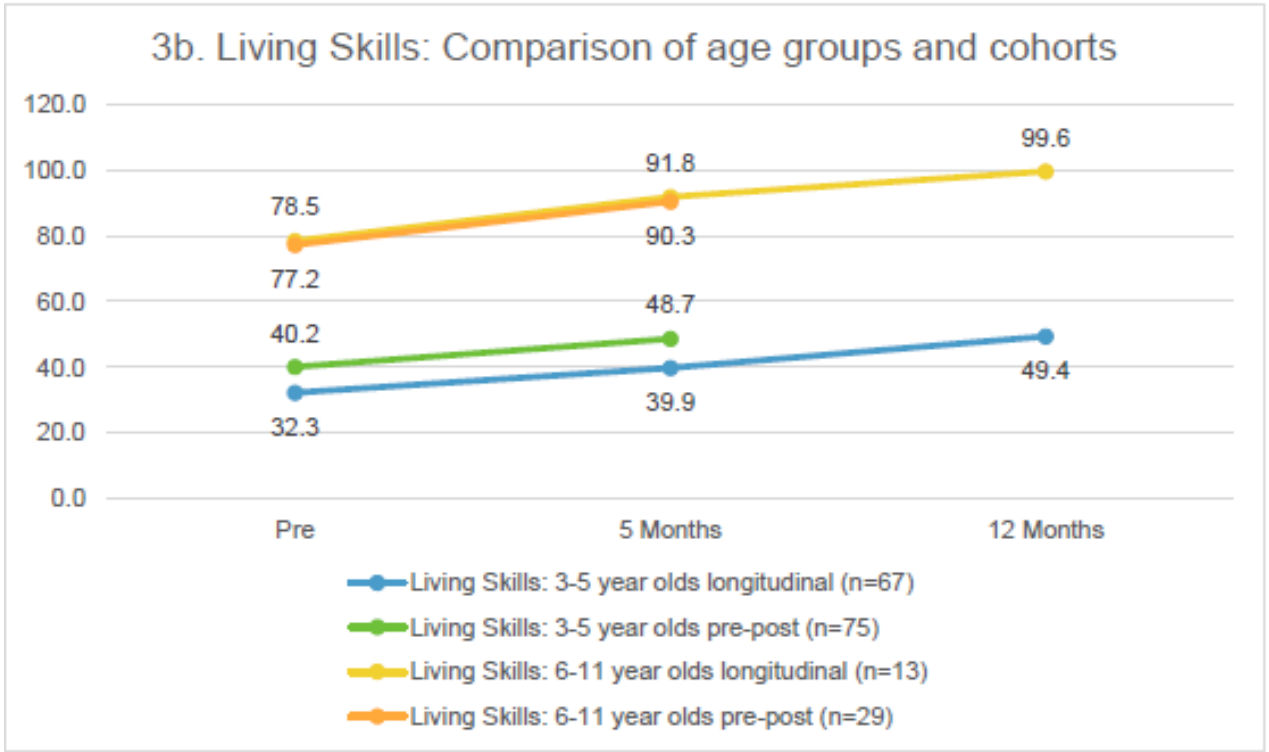
Figures 2a and 2b. Behavior and Self-regulation: Comparison of age groups and cohorts.

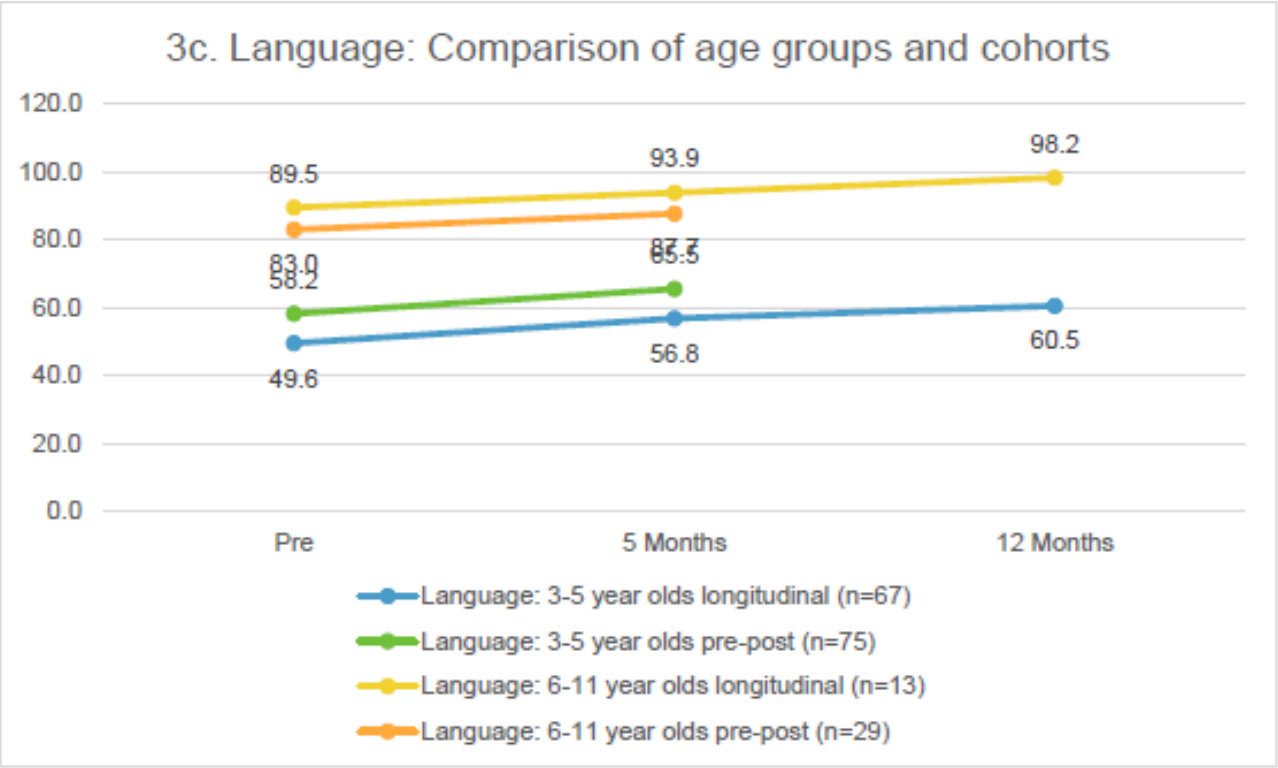




Figures 3a, 3b, and 3c. Social Skills, Living Skills and Language: Comparison of age groups and cohorts.







Effectiveness of Treatment by Severity of Autism

To test whether the effectiveness of the treatment was independent of language (based on the PLS-5), children receiving the treatment were split into two groups: high and lower language skills. Wilcoxon signed ranks tests were performed on pre and post scores for the subgroups for both younger and older children. For younger children, both high and low language skills groups made significant gains. Z-scores ranged from 2.785 to 4.933 with associated p values ranging from .005 to <.000. For older children both high and low language skills groups made significant gains (except for high language kids on the CARS). Z scores ranged from 1.602 (CARS) to 3.412 with associated p values of .109 (CARS) to .001. Generally, treatment effects were independent of language ability.

To determine whether these changes were comparable in older and younger children, Mann-Whitney tests were performed on pre to post change scores for the subgroups. For the

older group, no significant differences in change scores were found between children with higher and lower language abilities on any of the outcome variables of interest (Z values ranged from -.088 to -.983 with associated p. values from .949 and .331). Similar results were found for younger children as well. There were no significant differences found between children with higher and lower language abilities on any of the outcome variables of interest (Z values ranged from -.409 to -1.129 with associated p. values from .683 and .076). Both older and younger children experienced significant improvements regardless of language ability.

Parent Satisfaction and Parent Survey Data

Parents in both studies were surveyed as to their satisfaction. Parents were asked to respond to items from the Beach Center Family-Professional Partnership Survey. Based on a five-point scale with 5 being very satisfied, parents of children ages 2 to 5 responded with a mean rating of 4.89. Parents of children ages 6 to 11 responded with a mean rating of 4.87. There was no difference between groups.

Qualitative Data on Bonding and Response to Touch

Parents in both studies were surveyed with the post-treatment questions in Table 1. Table 5 lists examples of parent comments about changes in the child and changes in relationships in the older group. Silva et al [16] includes examples of parent comments about changes in the child and changes in relationships in the preschool group. Themes that emerged in both groups were improved bonding, increased eye contact, and calmer behavior.

Table 5. Parent comments about changes in child behavior and changes in relationships in children ages 6 to 11

Changes in Child Behavior	Changes in Relationships
More sounds and less anxious. Focuses a lot more	The massage relaxes my child and we bond
The massage has helped him be more calm and his behavior skills increased	He lets us touch him more and makes a little more eye contact with us
Better eye contact and vocalization. He is more calm and regulated. He has become more engaged	It promotes a sense of closeness that no other therapy we have done provides. This closeness allows me to better understand my child and bridges the much needed bond between us
Less aggression, more focus. More language, listens better. More open to new ideas. Follows directions better. More independent, better self care. Better at self soothing	Gave us an opportunity to function better as a family
He speaks more	We are closer. He spends more time with us as a family. We play Uno together
Helped him calm and move through transitions better. Decreased tactile reactivity and increased ability to accept physical affection	Greater bonding and relationship satisfaction for family members. Benefits for the whole family
He can sit and relax now. He communicates more	Brought our family closer
He can joke, tell us his feelings and will talk to us without being prompted	He has helped out with chores because he wants to
Better overall behavior at home. Definitely more peaceful and confident. Self esteem has improved	It has helped soothe and relax him and has enabled us to have more moments with him where we touch
He speaks in more complete sentences, he is doing better with his comprehension and vocabulary	It has made our bond stronger
Melt-downs less extreme, shorter, and less frequent. Verbal complexity raised and self-reflection ability raised	A wonderful opportunity to connect with and understand my child better
My son is showing more empathy, is seeking ways to help out our family	We have done a lot of therapies but we had to push for them. He loves being massaged. He seeks it out. He also likes giving the massage
He seems more relaxed. He enjoys it and uses more words.	We feel closer to him
His language has exploded. He is talking in full sentences, using the words “I” and “me”. When we go out in public It has helped us so much - he no longer takes off running	Massage creates a bond between us that helps the child and parent to calm down. He is playing with other kids and calling them by name

Her tantrums/meltdowns have almost completely disappeared. She is using verbal communication and clearly asking for what she needs. She is expressing her emotions verbally as well	She is actively seeking relationships with other children
It has helped him calm down and be more open to communication with us. He is also more open to other people. He hasn't been as obsessive since the treatment started.	He loves hanging out and talking with us. He tries harder to make friends
Increased eye contact, vocabulary. More affectionate	Made us closer and more in-tune with each other
Making jokes and using his imagination. Social and language skills definitely improving	Massage makes a nice time for calming and bonding before sleep.
He can communicate his needs more clearly. He has done massage on me and his mom	This has brought us closer physically and emotionally
His spent the night at a friend's house for the first time. He is making eye contact like crazy	It's a profound experience that allows parents to bond with their child in a way they haven't been able to and gives them an active role in treating the symptoms of autism.

Cost-efficacy Comparison

Previously, we compared professional and parent hours per week for implementation, efficacy on core autism symptoms, and areas where efficacy is limited for QST Massage, with a widely known intervention for autism, early intensive behavioral intervention [16]. For the comparison, we used hours per week required for implementation as our measure of cost in order to avoid confusion with regional variations in cost. Cost efficacy ratios were substantially better in QST Massage for Autism.

Fidelity

Therapists in both studies assessed parents on the 12 massage movements after the first, second and twelfth week of treatment. Fidelity with massage procedures was adequate and comparable between both groups. Fidelity with daily massage was best in the first five months of both studies, when parent support visits occurred weekly. It tended to drop when the frequency of parent support visits dropped to once a month.

Adverse Effects

No adverse effects were reported in the older child RCT. In the younger child RCT, one parent with severe wartime PTSD found that he was unable to give the massage due to excessive anxiety triggered by his child's resistance to touch. Once he stopped giving the massage, he experienced no further anxiety relative to the massage.

Discussion

The findings of this study indicate that the window of opportunity for treating tactile impairment in children with ASD remains open between the ages of 6 and 11. The exercise of comparing treatment outcomes in 2- to 5-year olds with 6- to 11-year-olds showed that treatment is similarly effective in both groups at five months and at one year. The downward trends in mean outcomes for touch, overall severity of autism, and behavioral difficulties are parallel between the two groups, as are the improving trends in social, language, and self-help skills. For both groups, the pace of improvement approaches the pace of normal development, and represents a significant change from the previous pattern of developmental delay.

In the younger group, non-verbal and minimally verbal children made progress on measures of language. In the older group, non-verbal and minimally verbal children also made progress on measures of language. As such, we did not see the effect of a closing window of opportunity for learning language in children who were non-verbal. However, the small number of children in the older group who were nonverbal made it difficult to draw firm conclusions on this issue.

Parents reported that the massage helped to build a stronger bond and improved the experience of touch and relationship. Children sought out touch and affection from their parents, and parents felt closer and more connected. Child-to-parent attachment difficulties are described

in the autism literature [31], and the profound degree to which they impact the parenting experience is illustrated in the parent comments and the very high parent satisfaction rate (95%) reported. Attachment theory has had difficulty in accounting for attachment difficulties in autism because they exist despite evidence of normal parent-to-child bond and sensitivity [32]. The data suggests that normal attachment requires normal child sensitivity to touch and that remediation of tactile impairment improves child-to-parent bonding.

Recovery of normal touch responses and improved closeness and bonding was consistent with a process involving normalization of the sense of touch. It was encouraging that 100% recovery of touch was possible in some children at one year. Previously published two-year data for younger children indicated that continued improvement is possible when treatment is continued for a second year, and that children with more severe tactile impairment initially require longer treatment for full recovery [16].

Although from a developmental standpoint it is evident that tactile impairment should be treated as early as possible, as with hearing or vision impairment, there are many school-aged children who do not receive treatment in the preschool years. It is good to have a treatment option for them, particularly in the area of behavioral self-regulation. School-aged children with autism have high rates of challenging behavior that is difficult to manage and hampers academic achievement [33, 34]. As with preschool children, treatment of school-aged children addressed the sensory cause of challenging behavior and normalized behavioral self-regulation.

CONCLUSIONS

This study provides evidence that the window of opportunity for treatment of tactile impairment in children with ASD remains open until at least age 11. Compared with preschool children, treatment of tactile impairment in elementary school aged children yielded similar improvement

of social, language, and behavioral abnormalities in autism, and similar decreases in sensory problems and autism severity. Treatment was effective in lower and higher functioning groups across the age range studied.

CONFLICTS OF INTEREST

The author declare that there is no conflict of interest regarding the publication of this paper.

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