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Effects of the Safe and Sound Protocol ™ (SSP) on Sensory Processing, Digestive Function and Selective Eating in Children and Adults with Autism: A Prospective Single-Arm Study

Effets du protocole Safe and Sound MC (PSS) sur le traitement sensoriel, la fonction digestive et l'alimentation sélective chez les enfants et les adultes ayant un trouble du spectre de l'autisme : une étude prospective à une seule branche

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Keywords

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Abstract

The purpose of the research was to evaluate the effectiveness of the Safe and Sound Protocol™ (SSP) on sensory sensitivities, digestive problems, and selective eating in individuals with autism spectrum disorder, hypothesizing a progressive decrease in symptoms at the 1-week and 4-week follow-up assessments that may be moderated by age. The effectiveness of SSP was evaluated in a prospective single-arm study, using validated caregiver reports and self-reports. Thirty-seven participants with ASD (aged 7 to 39 years) took part in the study. Auditory hypersensitivities, auditory hypo-sensitivities to voices, visual sensitivity, and digestive problems all declined at the 1-week and 4-week follow-up assessments. Tactile hypersensitivities and selective eating declined at the 4-week follow-up assessment. At the 4-week follow-up assessment, 70.3% participants showed ≥30% change in at least one domain (Cohen's d range, week-4: .22 to .50). Age moderated some effects, as adolescents showed a reduction in visual hypersensitivities and non-social tactile sensitivity. Adult participants had a decrease in tactile sensitivities at the 4-week follow-up assessment. Results support use of SSP as a promising intervention to reduce sensory sensitivities, digestive problems, and selective eating in individuals with ASD and highlight the need for controlled clinical trials in natural settings, with considerations for control conditions and testing mechanisms of effects.

Résumé

Le but de cette recherche était d'évaluer l'efficacité du protocole Safe and Sound^{MC} (PSS) sur les sensibilités sensorielles, les problèmes digestifs et l'alimentation sélective chez les personnes ayant un trouble du spectre de l'autisme (TSA) en faisant l'hypothèse d'une diminution progressive des symptômes, pouvant être modérée par l'âge, au moment des évaluations de suivi hebdomadaires des semaines 1 et 4. Trente-sept participants ayant un TSA (âgés de 7 à 39 ans) ont participé à cette étude. L'efficacité du PSS a été évaluée dans une étude prospective à une seule branche en fonction des rapports des participants ou de leurs donneurs de soins récoltés au moyen d'un instrument validé. Les hypersensibilités auditives, les hyposensibilités aux voix, la sensibilité visuelle et les problèmes digestifs avaient tous diminué au moment des évaluations de suivi des semaines 1 et 4. Les hypersensibilités tactiles et l'alimentation sélective avaient diminué 4 semaines après l'évaluation. Au suivi en semaine 4, 70.3% des participants ont démontrés des changements de ≥30% dans au moins un domaine (*d* de Cohen : .22-.50). L'âge a modéré certains effets, puisque les adolescents ont démontré une réduction des hypersensibilités visuelles et de la sensibilité tactile non sociale. Les participants adultes ont eu une diminution des sensibilités tactiles à la semaine 4. Les résultats soutiennent l'utilisation du PSS comme intervention prometteuse pour réduire les sensibilités sensorielles, les problèmes digestifs et l'alimentation sélective chez les personnes ayant un TSA et mettent de l'avant la nécessité d'essais cliniques contrôlés en milieu naturel, avec des considérations pour les conditions de contrôle et l'évaluation du mode d'action de ce protocole.

Mots-clés : trouble du spectre de l'autisme, système nerveux autonome, protocole Safe and Sound^{MC}, traitement sensoriel, théorie polyvagale

Introduction

Several sensory and gastrointestinal (GI) problems common in autism spectrum disorders (ASD) may be mediated by chronic neurobehavioural states that evolved to support response to threats but may disrupt typical brain-body functions in everyday contexts (Porges, 2005). An understanding of the neural regulation supporting these states provides a therapeutic opportunity to intervene and encourage neural regulation that supports affiliative social behaviour, sensory comfort, and GI function. One therapeutic opportunity, The Safe and Sound Protocol^{TM} (SSP), uses the acoustic features of human safety and threat cues (Kolacz et al., 2018a; Porges & Lewis, 2010) to functionally re-tune the nervous system toward safety-related function using principles from the Polyvagal Theory (Porges, 1995; 2001; 2007; Porges & Lewis, 2010). By focusing on re-tuning neurophysiological state regulation, this therapy could thereby improve clinically relevant features in individuals with autism (Porges et al., 2013; 2014).

Safety and threat responses are associated with specific bio-behavioural states that restrict the range of behaviour, socioemotional function, interoception, and sensory experience (Cannon, 1929; Craig, 2002; Critchley & Garfinkel, 2015). The Polyvagal Theory, an evolutionary neurophysiological framework (Porges, 1995; 2001; 2007), describes the organization of threat-

and safety-response systems of the brain and body in mammals that promote fight/flight and behavioural shutdown to facilitate defensive behaviours, as well as the safety-response system that promotes a calm visceral state and affiliative social engagement. The theory proposes that the phylogenetic transition to mammalian life required the ability to calm and signal cues of safety to conspecifics. This transition required neural mechanisms that linked the autonomic regulation of the heart and lungs with the neural regulation of striated muscles of the face and head (i.e., the Ventral Vagal Complex, VVC) to form an integrated Social Engagement System (Porges, 1995; 2001; 2007). The transition resulted in mammals, unlike their phylogenetic ancestors, having two areas (ventral and dorsal) within the brainstem from which vagal fibers influence the heart. When in states of safety, the myelinated vagal pathways from the VVC have an inhibitory (i.e., calming) effect on the heart and lungs providing a neurophysiological platform shifting sensory systems from defense reactivity to spontaneous social engagement and communication. During threat responses, the ventral vagus withdraws to allow for mobilization (i.e., fight-flight) or immobilization (i.e., freeze) defensive responses, sensory systems are co-opted to attend to threatening cues in the environment, and the dorsal vagus may be recruited to promote behavioural freezing and inhibit digestive processes. Difficulties with state regulation that promote a bias toward defensive responses may cause difficulty with autonomic and sensory regulation, which may be observed as auditory sensitivity, visual sensitivity, social touch/tactile sensitivity, GI processes, and food selectivity. Thus, the theory provides a possible explanation for several of the co-occurring clinical features in individuals with autism.

Evidence for Threat-Response State Challenges in ASD

Adults and children with ASD are characterized by several clinical features that may be associated with states that are biased toward defensive reactions such as hypersensitivities, GI problems, and selective eating. Studies demonstrate that autism spectrum disorders are marked by autonomic states that are sensitized toward defense reactions, exhibited by low VVC activity which can be non-invasively indexed by the amplitude of heart rate variability associated with respiration (i.e., respiratory sinus arrhythmia, or high frequency heart rate variability; Berntson et al., 1997). Respiratory sinus arrhythmia refers to an increase in heart rate during inspiration and decrease during expiration. Studies conducted with both children and adults demonstrate that, compared to age-matched controls, individuals with ASDs have lower amplitude of respiratory sinus arrhythmia (Bal et al., 2010; Bujnakova et al., 2016; Klusek et al., 2015; Lory et al., 2020; Patriquin et al., 2019; Porges et al., 2013; Thapa et al., 2019; Van Hecke et al., 2009) and the strength of the dampened VVC activity is associated with the presence and degree of sensory sensitivities and GI dysfunction, as described below.

Auditory Processing

Auditory processing deficits that have been associated with ASD often include hyperacusis and deficits orienting to speech (Dissanayake & Sigman, 2001; Rimland & Edelson, 1995; Soskey et al., 2017; Wilson et al., 2017), features that suggest a sensitivity for threat cues and dampened response to social stimuli, which may be associated with heightened chronic defensive reactions. These problems may be related to low neural tone to the middle ear muscles, which regulate the extraction of human voice from background noise (Borg & Counter, 1989). Lack of neural tone to the stapedius muscle via the facial and trigeminal cranial nerves impedes voice extraction

from background noise, limiting ability to orient to and interpret speech while potentiating high and low frequency sounds that can be aversive (Kolacz et al., 2018a; Porges & Lewis, 2010). These may compromise spontaneous social behaviour and attention (auditory hyposensitivity to voices) or increase emotional reactivity to high or low frequency sounds and broadband noise (auditory hypersensitivities). In general, controlled lab studies in which auditory stimuli are presented to participants have been inconclusive about systematic autonomic nervous system differences in listeners with ASD (Klusek et al., 2015; Lydon et al., 2016), though these patterns may be due to the lack of standardized measures, with stimuli ranging from threat response-trigger sirens, human voices, and single tones. All of these stimuli may promote different nervous system responses, promoting threat or safety responses, and their heterogeneity could give rise to the inconsistent findings reported in previous studies. However, in adolescents with ASD the intensity of self-reported hypersensitivities is correlated with greater heart rate increases in response to a noise stimulus (Keith et al., 2019).

Visual Sensitivity

Visual sensitivities are often reported in children and adults with ASD, particularly in response to bright lights (Baranek et al., 1997; Kern et al., 2001) and have been included as an additional diagnostic criterion in the latest version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychological Association, 2013). The amount of light falling on the retina is determined by pupil size, which is regulated by two antagonist iris muscles – the sphincter, which is responsible for pupil constriction and innervated mainly by the parasympathetic nervous system, and the dilator, which causes dilation and is innervated by the sympathetic system. Children with ASD demonstrate multiple atypical aspects of the pupillary light reflex (PLR) compared to typically developing children including longer reflex latency, smaller constriction amplitude, lower constriction velocity, and shorter constriction/re-dilation times (Fan et al., 2009; Daluwatte et al., 2013), all of which can contribute to the retina being exposed to greater amount of light and difficulties with efficient adjustment of pupil size to reduce light intensity in bright settings. The role of heightened threat-response states in such sensitivities is supported by findings that ASD children who have less pupillary constriction to light have faster heart rates (Daluwatte et al., 2013) and greater severity of sensory problems (Daluwatte et al., 2015).

Tactile Sensitivity

There is also evidence that individuals with ASD have amplified emotional reactivity to tactile stimulation and aversion to social touch. Caregivers report that their children with ASD react with emotional distress and active avoidance to being touched (Baranek et al., 2006; Tomchek & Dunn, 2007; Wiggins et al., 2009). However, results from experimental studies have been mixed, with increased sensitivity, decreased sensitivity, and no differences with non-ASD comparison groups reported (Mikkelsen et al., 2018; Robertson & Baron-Cohen, 2017; Rogers & Ozonoff, 2005). It is possible that this inconsistency may reflect contextual differences between the lab and home setting or biases in the sample based on sensory sensitivities (i.e., those with more sensory sensitivities may be less likely to participate in a lab study). However, observations of tactile sensitivities are common enough that they have been included as additional diagnostic criteria in the latest version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-

5; APA, 2013). Because vagal afferents are involved in regulating visceral and tactile pain thresholds (Craig, 2003; Gebhart, 2004; Kolacz & Porges, 2018; Sandkühler, 2009), heightened tactile sensitivity and aversion to social touch may be supported by the withdrawal of the Social Engagement System and heightened autonomic threat responses.

Gastrointestinal Problems

Though not included as a core criterion, ASD diagnosis is associated with a high prevalence of GI problems such as abdominal pain, constipation, diarrhea, and gastroesophageal reflux (Chaidez et al., 2014; Horvath & Perman, 2002; McElhanon et al., 2014). Digestive dysfunction can be exacerbated or maintained by the sympathetic nervous system or the dorsal vagal branch of the parasympathetic nervous system, which coordinates digestive functions across broad regions through direct innervation of the gut or interactions with the enteric nervous system (Kolacz et al., 2019; Rogers & Herman, 2012). Notably, autonomic neurostimulation has recently emerged as a promising intervention target for irritable bowel syndrome, abdominal pain, and related GI issues (Kovacic et al., 2017; Krasaelap et al., 2019; Mercante et al., 2018) and those with poor vagal regulation show the strongest treatment response (Kovacic et al., 2020), demonstrating that autonomic threat states may be a useful intervention target in this domain.

Food Selectivity

Finally, unusually strong food refusal and limited food repertoire are recurring features though not part of ASD diagnostic criteria (Cermak et al., 2010; Ledford & Gast, 2006; Sharp et al., 2013). Sensory sensitivities may contribute to food selectivity (Cermak et al., 2010; Mazurek et al., 2013; Suarez et al., 2014), with eating preferences often shaped by texture, taste, temperature, and smell (Williams et al., 2000). Food selectivity may contribute to GI problems (Mazurek et al., 2013) and cause concerns about inadequate nutrition.

Summary

When viewed in light of the integration of autonomic states with sensory experience and GI function, a reduction of threat responses and the promotion of affiliative safety-related states may be an intervention target for a range of clinical features associated with ASD.

The Safe and Sound Protocol

Theoretical Background

The importance of auditory cues to support a calm visceral state (Kolacz et al., 2018a; Porges & Lewis, 2010) suggests that an auditory intervention which targets neural regulation of the middle ear muscles may be a possible therapeutic target. The Safe and Sound Protocol (formerly the Listening Project) is an auditory intervention that presents acoustic stimulation by dynamically filtering human vocal music and amplifying the features of vocal prosody, (i.e., the expressive emotional content of speech, which is associated with auditory safety cues for the nervous system). By utilizing the acoustic channel, the intervention aims to promote feedback on the

descending pathways that control middle ear muscles, which in turn, would promote feedback, via the ventral vagal complex, to parasympathetic state control of neurophysiological state. A standard administration of the SSP consists of five daily 1-hour sessions of passive listening to the acoustic stimulation through over-the-ear headphones in a quiet room. The dynamic filtering progressively intensifies in modulation over the course the five days, increasing demands on ascending-descending feedback loops (Porges, 2014).

The Safe and Sound Protocol™ was developed to exercise the middle ear muscles (stapedius & tensor tympani) in order to improve auditory processing through the enhancement of the transmission of frequencies associated with the human voice. The middle ear muscles facilitate the extraction of human speech by inhibiting the transmission of low frequency noise (Borg & Counter, 1989). Sound from the environment travels down the external auditory canal to the eardrum, which is attached to the structures of the middle ear – the tiny bones that comprise the ossicular chain – that transmit the signal to the cochlea. The middle ear muscles, under influence of the cranial nerves, control the position of the ossicles, stiffening or loosening the eardrum (Liberman & Guinan, 1998; Zwislocki, 2002). When the eardrum is pulled tight, higher frequencies are absorbed and transmitted while low frequencies are attenuated before being passed to the inner ear (cochlea) and transmitted to the cortex via the auditory nerve (cranial nerve VIII). Complementary descending pathways from the brain regulate the middle ear muscles, determining the energy of frequencies reaching the inner ear. This pathway: a) functions as a feedback loop, with descending signals modifying the stiffness of the ossicles in response to incoming acoustic signals, and b) is functionally connected with brainstem areas that control the striated muscles of the face and head – including the middle ear muscles – and autonomic state regulation pathways (Porges, 1995; 2001; 2007). This system provides the basis of the Safe and Sound Protocol, which was developed to target these pathways.

Effects of the SSP in ASD populations

Empirical Findings

To date, the effects of the SSP in ASD populations have been examined in two laboratory studies. In the first study, the intervention improved comprehension abilities for speech on standardized measures in which speech overlapping with competing speech signals (SCAN Competing Words test) and speech overlapping with background sounds (SCAN Filtered Words test) significantly distinguished the ASD group from the comparison control group (Porges et al., 2013). Following the intervention, the ASD sample no longer significantly differed from a non-ASD comparison group. In addition, a subset of children and young adults demonstrated significant improvements in ventral vagal parasympathetic regulation as indexed by respiratory sinus arrhythmia.

In a follow up study (Porges et al., 2014), children with ASD status confirmed by diagnostic interview were recruited for a pair of randomized controlled trials. In one trial, children were randomized to five consecutive 45-minute sessions of: 1) the SSP intervention in a laboratory environment with available games and quiet activities, or 2) an identical protocol and environment but with no audio played through the headphones (headphones-only). In a parallel study, children were randomized to either take part in the SSP as described above or listen to music without dynamic filtering. In these trials, parents who were blind to study assignment reported on children's socioemotional and behavioural function before and at the 1-week follow-

up assessment. The results showed significant reductions in hearing hypersensitivities in the group assigned to the SSP compared to both the unfiltered music and headphone only conditions. In addition, children who received the SSP showed greater improvements in behavioural organization, spontaneous speech production, and listening compared to the headphones only condition as well as greater improvements in emotional control compared to unfiltered music alone.

The Present Study

To date, no studies have examined the effectiveness of SSP in the home, private clinic, or school setting, which are environments where the SSP is most likely to be administered. While laboratory studies under controlled conditions have been promising, real-world data are needed to understand the potential utility of the SSP for therapeutic use in ASD samples. In addition, there have been no prior data on long-term outcomes in response to the SSP to demonstrate delayed improvements or reduced benefits of an intervention over time, important metrics that are needed for better understanding of treatment efficacy. The primary aim of this study was to evaluate the effectiveness of the SSP on sensory sensitivities, digestive problems and selective eating at the 1-week and 4-week follow-up assessment. A secondary exploratory aim was to examine potential differential age effects in the SSP response. Because of the association of sensory sensitivities, digestive problems and selective eating with autism, recruitment for the present study was directed at individuals with a professional or suspected diagnosis of ASD (see below).

Materials and Methods

Participants

Participants were recruited in Hamburg and Berlin via e-mail, telephone, and in-person presentations at autism specialized organizations, private practices, and one autism-specialized school. Data were initially collected for clinical purposes. Adult participants provided consent to have their data used for research. Consent for minors and those who could not give independent consent were provided by caregivers. The Indiana University Institutional Review Board reviewed the methods for analysis of de-identified data and granted an official waiver that the research did not require ethical approval.

Individuals with a suspected or professionally confirmed diagnosis of ASD, who expressed interest themselves (or had a caregiver express interest) in participating in the research, were invited to a brief practice session with the SSP prior to enrolling in the study. Those who were comfortable during a brief practice session with the SSP (i.e., could tolerate listening to music through headphones), were invited to participate. The total sample consisted of 37 participants[1], 28 male and 9 female, ranging in age from 7 to 49 years (see Table 1). Thirty-three had a professionally confirmed ASD diagnosis (i.e., parent or self-report of a clinical diagnosis by an

[1] Total *n* was based on convenience, rather than formal sample size analysis, for the purpose of this preliminary study. All individuals who expressed interest and met criteria to participate were included in the study.

official ICD diagnostic clinic), two self-identified as being on the autism spectrum but were without formal diagnosis, and two were suspected to have an ASD by a parent and therapist but did not have a formal diagnosis[2]. Nine participants completed the home use version of the SSP (24%).

The Safe and Sound Protocol™ Intervention

The SSP was administered either in the presence of a therapist (at a private practice clinic or a private room in the participants' school) or at home by the child's caregivers with therapists' remote supervision. All recommended guidelines for administrators (i.e., completion of the SSP certification/training program) and environment (i.e., relaxed and safe space) were followed. Intervention location was selected by the participants, based on proximity to the clinic. Two participants in the clinic group completed three sessions of SSP in the clinic and two sessions of SSP in the home. In all cases, the SSP was administered for 1 hour per day, for five consecutive days. All study participants used a standardized music player with preloaded music tracks for each day of the intervention. The music players were outfitted with high fidelity semi-open over-the-ear headphones with a 53mm diameter speaker with a frequency response of 15 Hz – 28 kHz. Before the listening session, participants were shown how to adjust the volume before listening sessions and instructed to set the volume to a comfortable level.

During sessions provided in clinic or school, therapists were present to provide gentle motivation and non-verbal responses to participants via gestures and mimicry. The private practice room was approximately 22 square metres and outfitted with a sitting area, table, and a soft floor play area. Participants were invited to bring a favourite toy or activity tool with them, if these items were not provided in the clinic or school. Provided items included colouring opportunities, puzzles, quiet games, tactile sensory tools, clay, cards and space to move. Caregivers generally stayed in an adjacent waiting area during listening sessions but were allowed to be present during listening sessions if deemed necessary to make for participant comfortable. Sessions in the school were conducted in private rooms that included chairs, couches, and quiet games. In some instances, these rooms were not available and sessions took place in the child's typical classroom environment.

Participants who took part in the study at home received the SSP player by mail and an instructional video was provided online. Prior to beginning the SSP, one of the study authors scheduled a video conference call with the participant or, if the participant was 18 or younger, the participant and a caregiver. During the call, the researcher demonstrated the use of the device, observed the participant as they practiced playing the music, and gave feedback on appropriate activities to do during the listening sessions. Examples of appropriate concurrent activities included colouring, building with blocks, and quiet games without screens (e.g., board games). Computer or mobile phone use, reading, and dancing during listening was discouraged.

[2] Individuals who self-identified as having ASD (n = 2; ages 8, 38 years), or were suspected as having ASD (n = 2; ages 13, 19 years), were included in study, given the overlap in clinical characteristics and sensory sensitivities with those with a professional diagnosis.

Brain-Body Center Sensory Scales

Participants or their guardians completed the Brain-Body Center Sensory Scales (BBCSS; Porges, 2012), a 50-item questionnaire to assess auditory hypersensitivity, auditory hyposensitivity to voices, visual hypersensitivity, tactile hypersensitivity, social touch aversion, digestive problems, and selective eating. Item responses are on a 4-point Likert type scale (1 = almost always, 4 = almost never) and include a "not applicable/ not sure" option that is not scored. Subscale scores are calculated by taking the mean of valid item responses (i.e., excluding the "not applicable/not sure" responses). The psychometric properties, reliability, and validity of the parent/caregiver version of the scale has been documented in children and adults with fragile X syndrome and ASD (Kolacz et al., 2018b). The ingestion subscale was not included in this analysis due extensive missing values (>50% "not applicable/ not sure" responses for each item) and little variability in subscale values (i.e., floor effect).

English-to-German translation of the BBCSS was conducted using a back-translation method. First, two native German speakers with English fluency conducted a forward translation. Both translators were therapists who work directly with clients with ASD and their families in Germany. To test fidelity, the resulting German translation was then back translated to English by a native English/German-fluent researcher not involved in the study. The English source and target text were grammatically and semantically equivalent, with text meaning being preserved during the translation.

BBCSS forms for participants age 18 or younger were completed by caregivers. Participants who were 19 years or older and living independently completed the self-assessment. For the two adult participants with verbal abilities that were too low, the forms were completed by the caregiver. The questionnaires were completed prior to the SSP, 1-week after the last day of the SSP, and 4-weeks after the last day of SSP. For those participating at a clinic or school, the questionnaires were provided on paper forms. For home use clients, questionnaires were sent by email and participants either submitted their responses by electronic or traditional mail.

Analysis

Data analysis was conducted in R 3.6 (R Core Team, 2019) using linear mixed models with the lme4 package (Bates et al., 2015). Mixed effects were used as the modeling strategy because of their ability to incorporate all available data, even in the presence of some missing values. Interaction terms with the time parameters were added to assess the effects of baseline features on the time effect. Parametric bootstrapped samples with 10,000 draws were used to calculate 95% confidence intervals for predicted values (Davison & Hinkley, 1997).

Standardized effect sizes were calculated to examine effect magnitude in order to inform power analysis and sample size planning for future studies. Effect sizes of the changes from baseline were defined as the standardized mean difference using Cohen's d method for paired samples (Cohen, 1988). In this formalization, the effect size is the difference in means of the groups divided by the standard deviation of baseline assessment. Standard deviation of the baseline was chosen as the denominator due to its conceptual importance as the reference sample by which changes are assessed and its robustness to bias introduced by correlations between assessments (Cumming, 2012; 2013).

Results

Descriptive Statistics

Descriptive statistics of continuous variables are presented in Table 1. Twenty-seven percent of participants were non-verbal, 27% partly verbal, and 46% had age-appropriate language ability. All participants were willing to communicate with intervention staff at least non-verbally through gestures and facial expressions. Sixty-two percent of participants had limited or lack of age-appropriate self-care ability. Age, language and self-care abilities were not significantly related to any BBCSS subscale.

Table 1

Continuous Variable Descriptive Statistics

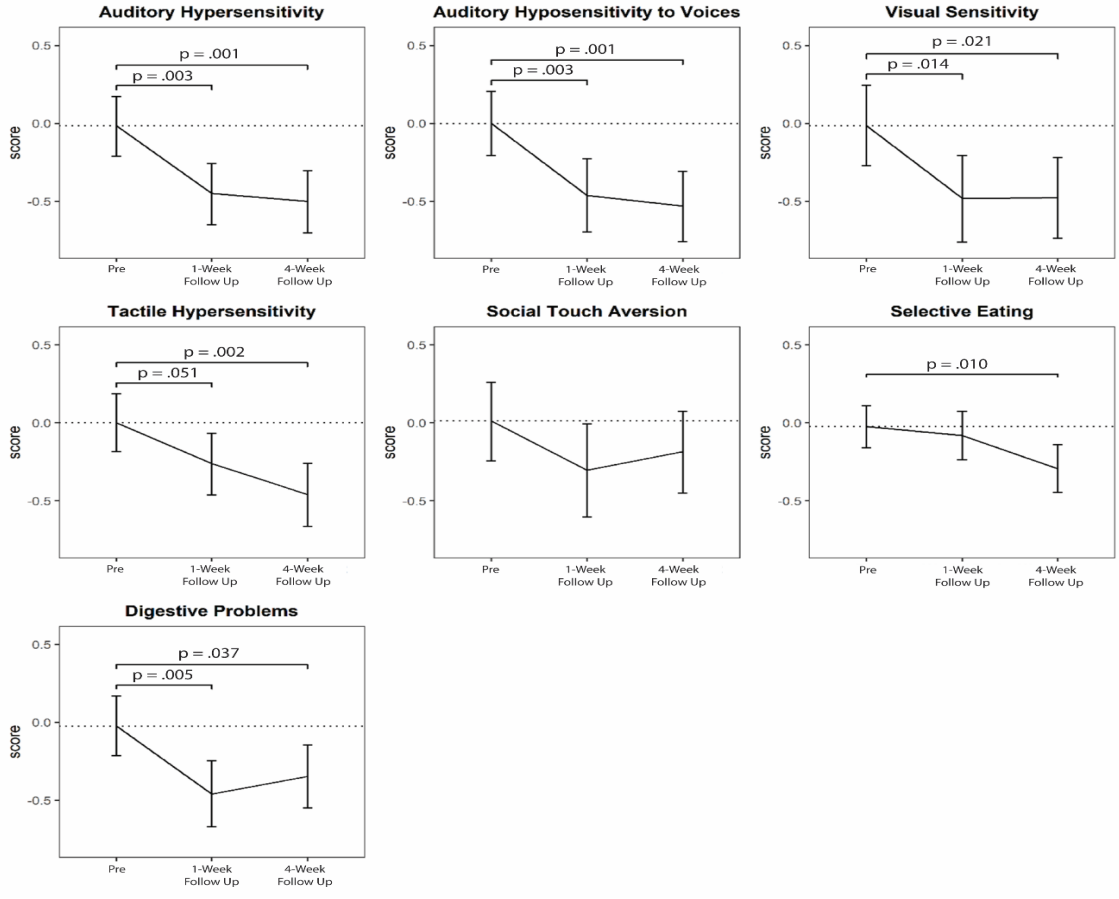
Variable	Time	n	Mean	SD	Median	Min	Max
Age (years)		37	16.43	10.71	14.00	7.00	49.00
Auditory Hypersensitivity	Pre	36	2.43	0.70	2.31	1.17	3.89
	1-Week Post	35	2.12	0.71	2.00	1.00	3.88
	4-Week Post	34	2.09	0.78	2.07	1.00	3.75
Auditory Hyposensitivity to Voices	Pre	37	2.21	0.67	2.40	1.00	3.40
	1-Week Post	31	1.95	0.59	1.80	1.00	3.00
	4-Week Post	33	1.88	0.64	1.75	1.00	3.25
Visual Sensitivity	Pre	33	2.26	0.67	2.00	1.00	3.70
	1-Week Post	30	1.95	0.65	1.95	1.00	3.17
	4-Week Post	32	1.94	0.72	1.90	1.00	4.00
Tactile Hypersensitivity	Pre	36	2.19	0.84	2.21	1.00	4.00
	1-Week Post	33	2.00	0.78	2.00	1.00	3.57
	4-Week Post	31	1.83	0.76	1.60	1.00	3.56
Social Touch Aversion	Pre	30	1.81	0.75	1.58	1.00	3.33
	1-Week Post	23	1.64	0.62	1.50	1.00	3.00
	4-Week Post	29	1.69	0.85	1.33	1.00	4.00
Digestive Problems	Pre	34	1.83	0.74	1.71	1.00	3.67
	1-Week Post	30	1.53	0.61	1.42	1.00	3.00
	4-Week Post	31	1.58	0.73	1.25	1.00	3.50
Selective Eating	Pre	36	2.37	0.88	2.33	1.00	4.00
	1-Week Post	31	2.45	0.91	2.40	1.00	4.00
	4-Week Post	31	2.18	0.86	2.17	1.00	3.50

Response to SSP

Intra-class correlation coefficients (ICCs) of the repeated measures BBCSS subscales ranged from .37 to .82, indicating that there was substantial correlation between time points. To account for these within-individual correlations, the mixed effects models included a random intercept for each individual. Figure 1 depicts the model-implied estimates and 95% confidence intervals for each of the outcome variables, standardized and centred at the pre-assessment time point. Auditory hypersensitivities, auditory hypo-sensitivities to voices, visual sensitivity, and digestive problems all declined at the 1-week and 4-week follow-up assessments, in relation to the pre-assessment. Tactile hypersensitivities and selective eating showed a significant decline only at the 4-week follow-up assessment. There was no significant change in social touch aversion. Effects sizes comparing raw baseline and the subscale scores at the 4-week follow-up assessment were calculated using Cohen's d (Figure 2). Effects were strongest for auditory hypersensitivity, auditory hyposensitivity to voices, visual sensitivity, and tactile hypersensitivity (range: .45–.50) and smaller for digestive problems and selective eating.

Figure 1

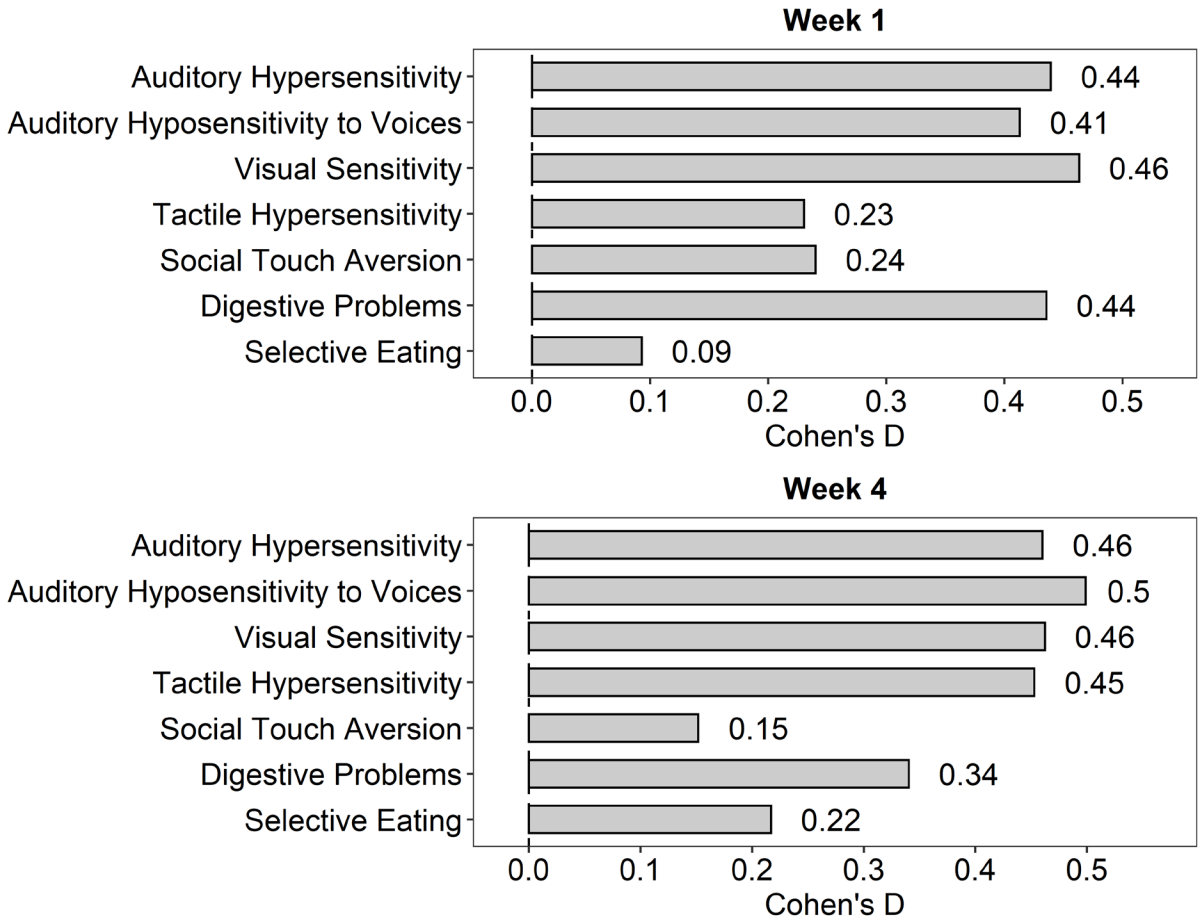
Predicted values and 95% confidence intervals for measured variables before, and at the 1-week and 4-week follow up assessments.



Note. Estimates are from mixed effects models with random subject intercepts. Variables are standardized and centered at the baseline assessment. Significance markers (*) represent model parameters that had 95% confidence intervals that did not include 0.

Figure 2

Effect sizes for changes in the 1-week and 4-week follow-up assessments.



Note. Effect sizes were calculated using the absolute value of Cohen's d (Cohen, 1998).

To examine individual treatment responses across all outcome domains, percent improvement in each domain was calculated for all outcomes from baseline to the 4-week follow-up assessment. The calculations indicated that 70.3% of participants (26 out of 37) had a 30% or more decrease in at least one domain and 43.2% of participants (16) had a 30% decrease in two or more domains.

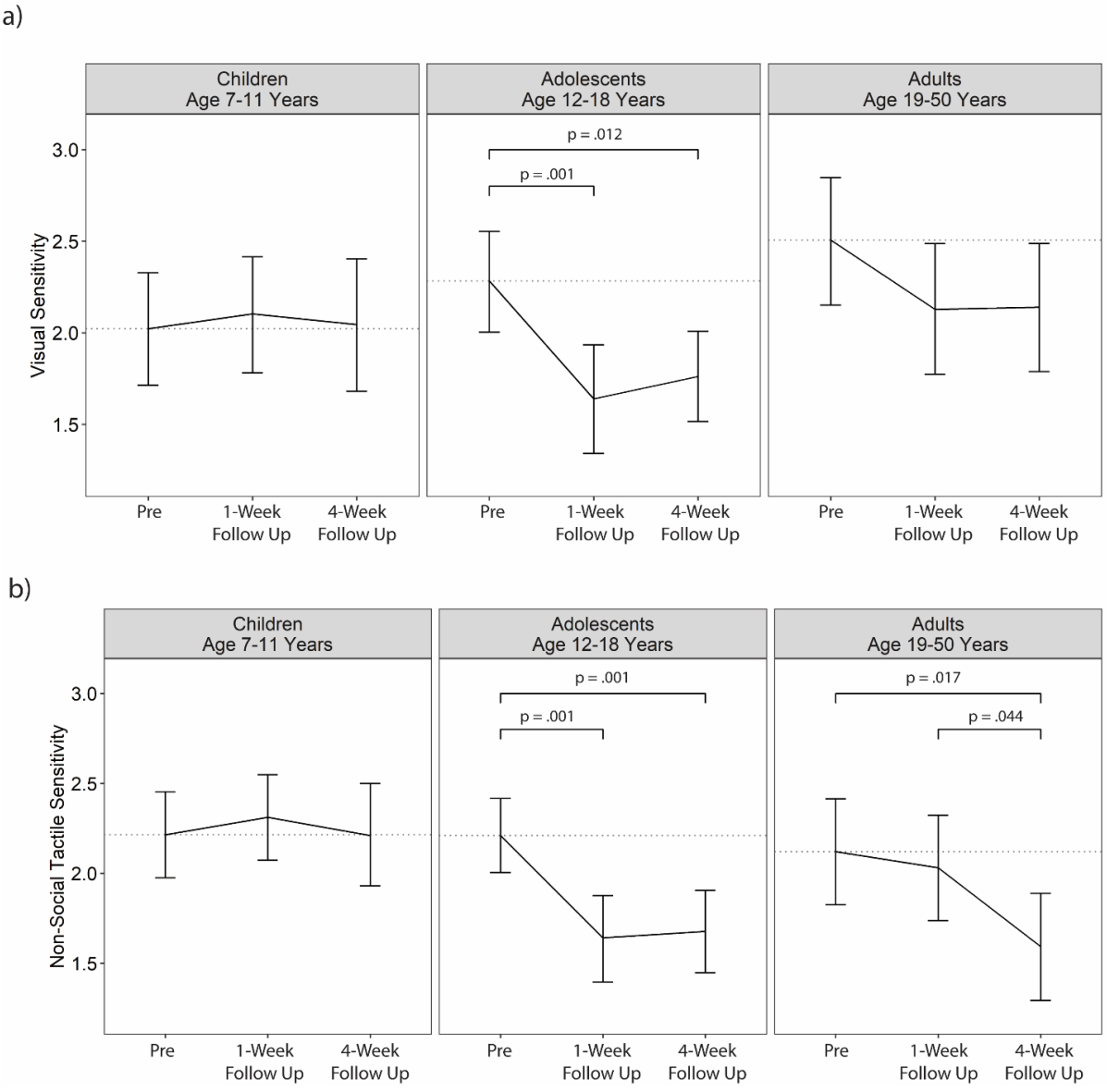
Predicting Time Effect From Baseline Features

To test moderating effects, interactions with age group were added to mixed effects models. Age group significantly moderated the time effect of visual hypersensitivity and non-social tactile sensitivity (Figure 3a). The age groups were not significantly different at baseline but showed different trajectories over the observation period. The reduction in visual hypersensitivities was only significant for adolescents (age 12–18 years), with the reduction upheld at the 4-week

follow-up assessment. Likewise, there were no significant difference between age groups at baseline. Adolescents had a significant reduction in non-social tactile sensitivity at the 1-week follow-up assessment that was maintained at the 4-week follow-up assessment (Figure 3b). Adult participants (age 19 and older) had a decrease in non-social tactile sensitivities at the 4-week follow-up assessment only.

Figure 3

Age moderation of the change from baseline to the 1-week and 4-week follow-up assessments for visual sensitivity and non-social tactile sensitivity (predicted means and 95% confidence intervals).



Results of Statistical Analysis After Removal of the Four Participants Without a Formal Diagnosis of ASD

Acknowledging that self-identification or suspicion of autism does not always agree with a professional diagnosis, results were re-analyzed with exclusion of participants with suspected ASD, yielding a reduced $n = 33$ (see Figures 4 and 5 in the Supplemental Section following the References). The results were almost identical to the full sample, except that in the smaller sample, significance for the 1 week/4 week comparison in the interaction for age and non-social tactile sensitivity in adults was lost, a minor secondary outcome (compare Figure 3b, panel 3 in the text with Figure 5b, panel 3 in the Supplemental Section). This provides justification for describing the study sample of 37 participants as "autistic".

Discussion

To our knowledge, this is the first study to assess the short and longer-term effects of the Safe and Sound Protocol™ (SSP) in home, therapy, and school administration settings. The results supported the hypotheses by demonstrating that the short-term effects of the SSP persisted to the 4-week follow-up assessment, with additional effects that were detected at the 4-week follow-up assessment only. Regarding the exploratory aim, adolescents and adults had some of the strongest effects in response to the intervention, though all age groups showed improvements.

As assessed by the BBCSS, participants demonstrated decreased auditory hyper- and hypo-sensitivities, visual hypersensitivities, non-social tactile sensitivities, and digestive problems at the 1-week follow-up assessment, compared to baseline, with effects persisting at the 4-week follow-up assessment. At the 4-week follow-up assessment, there were delayed effects of decrease in selective eating and tactile hypersensitivities. There were no effects of SSP on social touch aversion.

Regarding auditory processing, this study replicated previous findings showing that a 5-day course of the SSP improved auditory processing in studies that included randomization and lab-based standardized assessments. The effect size of the caregiver- and self-reported improvement in auditory hyposensitivity to voices in the present sample was similar to the effect size of improvement in spoken speech processing using a standardized lab-based evaluation in a previous study (Porges et al., 2013). This effect also replicates the improvement in parent-reported listening previously reported with randomization to filtered music and headphones only condition (Porges et al., 2014). The reduction of auditory hypersensitivities also replicates the findings of Porges et al., (2014) which showed that the SSP filtered music improved auditory hypersensitivities compared with both non-filtered music and a headphones only condition. However, this is the first study to suggest that effect may be maintained 4-weeks after intervention.

The present study included five domains which had not previously been examined: tactile sensitivity, social touch aversion, visual hypersensitivities, GI function, and selective eating. Of these, visual hypersensitivities, tactile hypersensitivities, and digestive problems all decreased at the 1-week follow-up assessment and significant improvements were retained at the 4-week follow-up assessment. Selective eating and tactile hypersensitivities declined at the 4-week follow-up assessment, suggesting the possibility of delayed reorganization of eating behaviour

that may be related to the decrease in tactile hypersensitivities. It is hypothesized that tactile hypersensitivities may cause restricted eating (Cermak et al., 2010; Mazurek et al., 2013; Suarez et al., 2014) and thus it is possible that changes in selective eating may follow reductions in tactile hypersensitivities with some delay as individuals begin to recognize that certain tactile features of food no longer trigger the discomfort they had before.

Effect sizes at the 4-week follow-up assessment were most robust in auditory domains, visual sensitivity, and tactile hypersensitivity. This indicates that these domains may be most responsive to the SSP intervention, though substantial effects were also observed for digestive problems and selective eating. Cohen's d provides an important criterion for assessing strength of effects in relation to sample variability. However, assessments using clinical cut offs are needed in future studies to better determine the clinical significance of such decreases.

Age moderated the effects of the SSP intervention for non-social tactile sensitivities and visual sensitivities. Adolescents and adults decreased in non-social tactile sensitivities over the course of the study while children (11 years and younger) did not. Adolescents, in particular, also reported a more immediate and substantial decrease in visual sensitivities at the 1-week follow-up assessment. Given these preliminary data, there may be added benefits of the SSP for adolescents and adults, though most domains that showed decrease did not have interactions with age.

Limitations

First, constraints on study size did not permit a comparison group; thus, interpretation is based on a single-group design. These findings are thus preliminary, and a future replication should include a randomized control trial in the settings in which the SSP is typically administered. Notably, however, the auditory problem decreases in this study are consistent with Porges et al. (2014), a randomized controlled study that included unfiltered music and headphones-only conditions for comparison. Including two comparison groups in the design of the Porges et al. (2014) study reduced the Hawthorne effect (i.e., participants may change their behaviour (or evaluation) in response to their awareness of being observed (McCarney et al., 2007); however, the current study was not able to address this potential confound in a single-group design. Additionally, the reduction in sensitivities in the current study may be due to a learning effect whereby familiarity with the intervention resulted in improvement (Rogers et al, 1998; Rosler et al., 1999), which is another issue that was addressed in the design of the Porges et al. (2014) study, but not in the current single-group design. Both of these limitations could be addressed in the design of a future clinical trial.

Second, study participants were permitted to receive other interventions or medication during the course of the research, which may have introduced additional variability into the results. Stopping all medication use and other therapies during the SSP is not recommended, and thus this design preserves ecological validity for how the SSP is administered in real-world settings. However, future studies are needed to document how medication and additional therapy modalities interact with the SSP.

Third, the outcomes in the study were tracked using self- and parent-reports and future studies should include objective measures, especially given the inherent bias when the majority of participants required assistance to completing the questionnaires (for adults with limited verbal

or self-care ability) or caregivers who completed the questionnaires based on their observations of the participant. Individuals who were completing questionnaires, or assisting with questionnaire completion, were not blind to assessment session (e.g., baseline, 1-week, 4-week follow-up assessment). While this measurement method can introduce bias, it can increase the representativeness of the sample and reduce missing data due to experimental testing of sensory sensitivities causing distress and non-compliance, especially in those with most severe problems. Future studies should include objective measures that can be compared to self- and other reporters to better determine how each method contributes to results, especially in adults with ASD. Additional outcome measures, such as those evaluating movement and social engagement behaviours, would also allow for a broader perspective on the effects of the intervention and how they may be connected with a decrease in sensory sensitivities.

Fourth, recruitment procedures for the study yielded a referral or treatment-based sample, thereby introducing potential bias in the representation of individuals with ASD. Individuals with ASD (confirmed or suspected) were selected as the clinical population for this study given the widely recognized symptomatology of hypersensitivity. However, given that there are varying degrees of autism spectrum disorder, symptom severity should likewise be assessed in future studies both as predictive and outcome measures, as these could influence the effectiveness of the SSP. Future studies could not only recruit individuals from additional sources who represent a fuller range in the spectrum of ASD (such as the general population), but also recruit individuals with difficulty in behaviour/state regulation, regardless of diagnosis, for which the SSP may be effective.

Fifth, variations in the type of SSP stimuli or schedule for administration may be considered for future studies. Although most of the participants in the current study enjoyed the music selection in the SSP, had a positive attitude towards the daily sessions and did not request any breaks (informal approximation of 70%), other participants required frequent breaks throughout the daily sessions. Future SSP design may consider including a non-lyrical music option or a variety of other music playlists for the participants to choose (including music in their preferred language, as the SSP music playlist in the current study used English-lyrics).

Evaluating ability to co-regulate during the SSP may also inform variations in the type of SSP stimuli or schedule for administration. For example, in the current study, participants with lower verbal capacities overall were easier to co-regulate during the SSP, while participants who were more verbal needed more active support to find activities to regulate within the setting during the sessions. If the participants who needed frequent breaks felt over-stimulated by the SSP (or had difficulty co-regulating), scheduling specific breaks during the daily listening or dividing the duration of the entire SSP over more than 5 days (if needed) may improve the effectiveness of the intervention.

Finally, noting that individuals who were not able to tolerate wearing headphones and/or listening to music through headphones (i.e., those individuals with extreme sensory or auditory sensitivity) were excluded from the study, evaluating the effectiveness of administering the intervention in a closed room or using ear pods may expand the range of individuals who may benefit from the SSP.

Conclusions

The results in this study present the first available evidence that the Safe and Sound Protocol (SSP) applied in a real-world home, school, or therapeutic setting may have long term benefits for auditory hypersensitivities, listening, tactile sensitivities, digestive problems, and selective eating in children and adults with ASD. Importantly, the SSP is based on a theoretical foundation and method that is distinct from other sound therapies, and the effects described here cannot be generalized to any other type sound of therapy (e.g., the Tomatis Method).

Demonstrating that the SSP can be effectively administered outside of a clinic setting allows for potential increased availability of the SSP by families/individuals without access to a local SSP provider or who have limited schedule/transportation availability. Additionally, administering the SSP in environments that are already safe and familiar to the individual (such as school or possibly in the home) may further increase the effectiveness of the SSP by helping the individual maintain state regulation during SSP administration through familiar environmental cues.

These findings suggest a possible therapeutic benefit of the SSP for multiple sensory, digestive, and eating behaviour problems that require further evaluation in clinical trials. Given the research is preliminary, the data are promising for potential use, but further testing is required. Thus, practitioners would need to make practice decisions about the data with extreme caution and acknowledgment of the limited evidence that the study provides. If practitioners choose to implement this approach clinically, they need to carefully document treatment content, client responses to the treatment, and changes in client functioning from start to end of treatment, particularly with respect to those issues listed in the Limitations.

Practitioners should consider incorporating the SSP within an integrated treatment model, as the SSP is not designed as a standalone intervention. As part of an integrated treatment strategy, SSP functionally may calm the neurobehavioural state and enable the client to be more accessible to treatments.

Key Messages From This Study

People with Disabilities: The Safe and Sound Protocol™, a listening intervention, has been shown to help people with autism spectrum disorders by reducing hearing sensitivities, digestive problems and selective eating. However, more research studies need to be done to look more closely at the effects and how long the effects last.

Professionals: Reducing sensory sensitivities, digestive problems, and selective eating in individuals with autism spectrum disorder via the Safe and Sound Protocol™ may improve clinical outcomes, but further research is needed.

Messages clés de cette étude

Personnes ayant une incapacité : Il a été démontré que le protocole Safe and Sound^{MC}, une intervention d'écoute, peut aider les personnes ayant un TSA en réduisant les sensibilités auditives, les problèmes digestifs et l'alimentation sélective. Cependant, d'autres études de recherche doivent être menées pour examiner de plus près ses effets et leur durée.

Professionnels : La réduction des sensibilités sensorielles, des problèmes digestifs et de l'alimentation sélective chez les personnes ayant un TSA via le protocole Safe and Sound^{MC} peut améliorer les résultats cliniques. Des recherches supplémentaires sont toutefois nécessaires.

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References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (DSM-5). https://doi.org/10.1176/appi.books.9780890425787

Bal, E., Harden, E., Lamb, D., Van Hecke, A. V., Denver, J. W., & Porges, S. W. (2010). Emotion recognition in children with autism spectrum disorders: Relations to eye gaze and autonomic state. *Journal of Autism and Developmental Disorders*, *40*(3), 358–370. https://doi.org/10.1007/s10803-009-0884-3

Baranek, G. T., Foster, L. G., & Berkson, G. (1997). Tactile defensiveness and stereotyped behaviors. *The American Journal of Occupational Therapy: Official Publication of the American Occupational Therapy Association*, *51*(2), 91–95. https://doi.org/10.5014/ajot.51.2.91

Baranek, G. T., David, F. J., Poe, M. D., Stone, W. L., & Watson, L. R. (2006). Sensory Experiences Questionnaire: discriminating sensory features in young children with autism, developmental delays, and typical development. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *47*(6), 591–601. https://doi.org/10.1111/j.1469-7610.2005.01546.x

Bates, D., Maechler, M., Bolker, B., & Walker, S. (2015). Fitting linear mixed-effects models using lme4. *Journal of Statistical Software, 67(1),* 1-48. https://doi.org/10.18637/jss.v067.i01

Berntson, G. G., Bigger, J. T., Jr, Eckberg, D. L., Grossman, P., Kaufmann, P. G., Malik, M., Nagaraja, H. N., Porges, S. W., Saul, J. P., Stone, P. H., & van der Molen, M. W. (1997). Heart rate variability: origins, methods, and interpretive caveats. *Psychophysiology, 34*(6), 623–648. https://doi.org/10.1111/j.1469-8986.1997.tb02140.x

Borg, E., & Counter, S. A. (1989). The middle-ear muscles. *Scientific American*, *261*(2), 74–80. https://doi.org/10.1038/scientificamerican0889-74

Bujnakova, I., Ondrejka, I., Mestanik, M., Visnovcova, Z., Mestanikova, A., Hrtanek, I., Fleskova, D., Calkovska, A., & Tonhajzerova, I. (2016). Autism spectrum disorder is associated with autonomic underarousal. *Physiological Research*, *65*(Suppl 5), S673–S682. https://doi.org/10.33549/physiolres.933528

Cannon, W. B. (1929). Organization for physiological homeostasis. *Physiological Reviews*, *9*(3), 399–431. https://doi.org/10.1152/physrev.1929.9.3.399

Cermak, S. A., Curtin, C., & Bandini, L. G. (2010). Food selectivity and sensory sensitivity in children with autism spectrum disorders. *Journal of the American Dietetic Association*, *110*(2), 238–246. https://doi.org/10.1016/j.jada.2009.10.032

Chaidez, V., Hansen, R. L., & Hertz-Picciotto, I. (2014). Gastrointestinal problems in children with autism, developmental delays or typical development. *Journal of Autism and Developmental Disorders*, *44*(5), 1117–1127. https://doi.org/10.1007/s10803-013-1973-x

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Erlbaum. https://doi.org/10.4324/9780203771587

Craig, A. D. (2002). How do you feel? Interoception: the sense of the physiological condition of the body. *Nature Reviews. Neuroscience*, *3*(8), 655–666. https://doi.org/10.1038/nrn894

Craig, A. D. (2003). A new view of pain as a homeostatic emotion. *Trends in Neurosciences*, *26*(6), 303–307. https://doi.org/10.1016/s0166-2236(03)00123-1

Critchley, H. D., & Garfinkel, S. N. (2015). Interactions between visceral afferent signaling and stimulus processing. *Frontiers In Neuroscience*, *9*, 286. https://doi.org/10.3389/fnins.2015.00286

Cumming, G. (2012). *Understanding the new statistics: Effect sizes, confidence intervals, and meta-analysis*. Routledge. https://doi.org/10.4324/9780203807002

Cumming, G. (2013). Cohen's d needs to be readily interpretable: Comment on Shieh (2013). *Behavior Research Methods*, *45*(4), 968–971. https://doi.org/10.3758/s13428-013-0392-4

Daluwatte, C., Miles, J. H., Christ, S. E., Beversdorf, D. Q., Takahashi, T. N., & Yao, G. (2013). Atypical pupillary light reflex and heart rate variability in children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *43*(8), 1910–1925. https://doi.org/10.1007/s10803-012-1741-3

Daluwatte, C., Miles, J. H., Sun, J., & Yao, G. (2015). Association between pupillary light reflex and sensory behaviors in children with autism spectrum disorders. *Research in Developmental Disabilities*, *37*, 209–215. https://doi.org/10.1016/j.ridd.2014.11.019

Davison, A.C., & Hinkley, D.V. (1997) *Bootstrap methods and their application*. Cambridge University Press. https://doi.org/10.1017/CBO9780511802843

Dissanayake, C., & Sigman, M. (2001). Attachment and emotional responsiveness in children with autism. In L. M. Glidden (Ed.), *International review of research in mental retardation: Autism* (Vol. 23, pp. 239–266). Academic Press.

Fan, X., Miles, J. H., Takahashi, N., & Yao, G. (2009). Abnormal transient pupillary light reflex in individuals with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *39*(11), 1499–1508. https://doi.org/10.1007/s10803-009-0767-7

Gebhart, G. F. (2004). Descending modulation of pain. *Neuroscience and Biobehavioral Reviews*, *27*(8), 729–737. https://doi.org/10.1016/j.neubiorev.2003.11.008

Horvath, K., & Perman, J. A. (2002). Autism and gastrointestinal symptoms. *Current Gastroenterology Reports*, *4*(3), 251–258. https://doi.org/10.1007/s11894-002-0071-6

Keith, J. M., Jamieson, J. P., & Bennetto, L. (2019). The influence of noise on autonomic arousal and cognitive performance in adolescents with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *49*(1), 113–126. https://doi.org/10.1007/s10803-018-3685-8

Kern, J. K., Miller, V. S., Cauller, P. L., Kendall, P. R., Mehta, P. J., & Dodd, M. (2001). Effectiveness of N,N-dimethylglycine in autism and pervasive developmental disorder. *Journal of Child Neurology*, *16*(3), 169–173. https://doi.org/10.1177/088307380101600303

Klusek, J., Roberts, J. E., & Losh, M. (2015). Cardiac autonomic regulation in autism and Fragile X syndrome: A review. *Psychological Bulletin*, *141*(1), 141–175. https://doi.org/10.1037/a0038237

Kolacz, J., Kovacic, K. K., & Porges, S. W. (2019). Traumatic stress and the autonomic brain-gut connection in development: Polyvagal Theory as an integrative framework for psychosocial and gastrointestinal pathology. *Developmental Psychobiology*, *61*(5), 796–809. https://doi.org/10.1002/dev.21852

Kolacz, J., Lewis, G. F., & Porges, S. W. (2018a). The integration of vocal communication and biobehavioral state regulation in mammals: A polyvagal hypothesis. In S. M. Brudzynski (Ed.), *Handbook of ultrasonic vocalization: A window into the emotional brain* (pp. 23–34). Elsevier Academic Press. https://doi.org/10.1016/B978-0-12-809600-0.00003-2

Kolacz, J., & Porges, S. W. (2018). Chronic diffuse pain and functional gastrointestinal disorders after traumatic stress: Pathophysiology through a Polyvagal Perspective. *Frontiers In Medicine*, *5*, 145. https://doi.org/10.3389/fmed.2018.00145

Kolacz, J., Raspa, M., Heilman, K. J., & Porges, S. W. (2018b). Evaluating sensory processing in fragile X syndrome: Psychometric analysis of the Brain Body Center Sensory Scales (BBCSS). *Journal of Autism and Developmental Disorders*, *48*(6), 2187–2202. https://doi.org/10.1007/s10803-018-3491-3

Kovacic, K., Hainsworth, K., Sood, M., Chelimsky, G., Unteutsch, R., Nugent, M., Simpson, P., & Miranda, A. (2017). Neurostimulation for abdominal pain-related functional gastrointestinal disorders in adolescents: A randomised, double-blind, sham-controlled trial. *The Lancet. Gastroenterology & Hepatology*, *2*(10), 727–737. https://doi.org/10.1016/S2468-1253(17)30253-4

Kovacic, K., Kolacz, J., Lewis, G. F., & Porges, S. W. (2020). Impaired vagal efficiency predicts auricular neurostimulation response in adolescent functional abdominal pain disorders. *The American Journal of Gastroenterology*, *115*(9), 1534–1538. https://doi.org/10.14309/ajg.0000000000000753

Krasaelap, A., Sood, M. R., Li, B. U. K., Unteutsch, R., Yan, K., Nugent, M., Simpson, P., & Kovacic, K. (2020). Efficacy of auricular neurostimulation in adolescents with irritable bowel syndrome in a randomized, double-blind trial. *Clinical Gastroenterology and Hepatology: The Official Clinical Practice Journal of the American Gastroenterological Association*, *18*(9), 1987–1994.e2. https://doi.org/10.1016/j.cgh.2019.10.012

Ledford, J. R., & Gast, D. L. (2006). Feeding problems in children with autism spectrum disorders: A review. *Focus on Autism and Other Developmental Disabilities*, *21*(3), 153–166. https://doi.org/10.1177/10883576060210030401

Liberman, M. C., & Guinan, J. J., Jr (1998). Feedback control of the auditory periphery: Anti-masking effects of middle ear muscles vs. olivocochlear efferents. *Journal of Communication Disorders*, *31*(6), 471–553. https://doi.org/10.1016/s0021-9924(98)00019-7

Lory, C., Kadlaskar, G., McNally Keehn, R., Francis, A. L., & Keehn, B. (2020). Brief Report: Reduced heart rate variability in children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *50*(11), 4183–4190. https://doi.org/10.1007/s10803-020-04458-8

Lydon, S., Healy, O., Reed, P., Mulhern, T., Hughes, B. M., & Goodwin, M. S. (2016). A systematic review of physiological reactivity to stimuli in autism. *Developmental Neurorehabilitation*, *19*(6), 335–355. https://doi.org/10.3109/17518423.2014.971975

Mazurek, M. O., Vasa, R. A., Kalb, L. G., Kanne, S. M., Rosenberg, D., Keefer, A., Murray, D. S., Freedman, B., & Lowery, L. A. (2013). Anxiety, sensory over-responsivity, and gastrointestinal problems in children with autism spectrum disorders. *Journal of Abnormal Child Psychology*, *41*(1), 165–176. https://doi.org/10.1007/s10802-012-9668-x

McCarney, R., Warner, J., Iliffe, S., Van Haselen, R., Griffin, M., & Fisher, P. (2007). The Hawthorne effect: A randomised, controlled trial. *BMC Medical Research Methodology*, *7*(1), 30. https://doi.org/10.1186/1471-2288-7-30

McElhanon, B. O., McCracken, C., Karpen, S., & Sharp, W. G. (2014). Gastrointestinal symptoms in autism spectrum disorder: A meta-analysis. *Pediatrics*, *133*(5), 872–883. https://doi.org/10.1542/peds.2013-3995

Mercante, B., Ginatempo, F., Manca, A., Melis, F., Enrico, P., & Deriu, F. (2018). Anatomo-physiologic basis for auricular stimulation. *Medical Acupuncture*, *30*(3), 141–150. https://doi.org/10.1089/acu.2017.1254

Mikkelsen, M., Wodka, E. L., Mostofsky, S. H., & Puts, N. A. J. (2018). Autism spectrum disorder in the scope of tactile processing. *Developmental Cognitive Neuroscience*, *29*, 140–150. https://doi.org/10.1016/j.dcn.2016.12.005

Patriquin, M. A., Hartwig, E. M., Friedman, B. H., Porges, S. W., & Scarpa, A. (2019). Autonomic response in autism spectrum disorder: Relationship to social and cognitive functioning. *Biological Psychology*, *145*, 185–197. https://doi.org/10.1016/j.biopsycho.2019.05.004

Porges, S. W. (1995). Orienting in a defensive world: Mammalian modifications of our evolutionary heritage. A Polyvagal Theory. *Psychophysiology*, *32*(4), 301–318. https://doi.org/10.1111/j.1469-8986.1995.tb01213.x

Porges, S. W. (2001). The polyvagal theory: Phylogenetic substrates of a social nervous system. *International Journal of Psychophysiology: Official Journal of the International Organization of Psychophysiology*, *42*(2), 123–146. https://doi.org/10.1016/s0167-8760(01)00162-3

Porges, S. W. (2005). The vagus: A mediator of behavioral and physiologic features associated with autism. In M.L. Bauman & T.L. Kemper (Eds.), *The Neurobiology of Autism* (pp. 65–78), Johns Hopkins University Press.

Porges, S. W. (2007). The polyvagal perspective. *Biological Psychology*, *74*(2), 116–143. https://doi.org/10.1016/j.biopsycho.2006.06.009

Porges, S. W. (2012). *The Brain-Body Center Sensory Scales (BBCSS)*. The Brain-Body Center. University of Illinois at Chicago.

Porges, S. W., Bazhenova, O. V., Bal, E., Carlson, N., Sorokin, Y., Heilman, K. J., Cook, E. H., & Lewis, G. F. (2014). Reducing auditory hypersensitivities in autistic spectrum disorder: Preliminary findings evaluating the listening project protocol. *Frontiers In Pediatrics*, *2*, 80. https://doi.org/10.3389/fped.2014.00080

Porges, S. W., & Lewis, G. F. (2010). The polyvagal hypothesis: Common mechanisms mediating autonomic regulation, vocalizations and listening. In S. M. Brudzynski (Ed.), *Handbook of ultrasonic vocalization: A window into the emotional brain* (pp. 23–34). Elsevier Academic Press. https://doi.org/10.1016/B978-0-12-809600-0.00003-2

Porges, S. W., Macellaio, M., Stanfill, S. D., McCue, K., Lewis, G. F., Harden, E. R., Handelman, M., Denver, J., Bazhenova, O. V., & Heilman, K. J. (2013). Respiratory sinus arrhythmia and auditory processing in autism: Modifiable deficits of an integrated social engagement system? *International Journal of Psychophysiology: Official Journal of the International Organization of Psychophysiology*, *88*(3), 261–270. https://doi.org/10.1016/j.ijpsycho.2012.11.009

Porges, S. W., Bazhenova, O. V., Bal, E., Carlson, N., Sorokin, Y., Heilman, K. J., Cook, E. H., & Lewis, G. F. (2014). Reducing auditory hypersensitivities in autistic spectrum disorder: Preliminary findings evaluating the listening project protocol. *Frontiers in Pediatrics*, *2*, 80. https://doi.org/10.3389/fped.2014.00080

R Core Team (2019). *R: A language and environment for statistical computing.* R Foundation for Statistical Computing. https://www.R-project.org/

Rimland, B., & Edelson, S. M. (1995). Brief report: A pilot study of auditory integration training in autism. *Journal of Autism and Developmental Disorders*, *25*(1), 61–70. https://doi.org/10.1007/BF02178168

Robertson, C. E., & Baron-Cohen, S. (2017). Sensory perception in autism. *Nature Reviews. Neuroscience*, *18*(11), 671–684. https://doi.org/10.1038/nrn.2017.112

Rogers, R. C., & Hermann, G. E. (2012). Brainstem control of the gastric function. In L. J. Johnson, F. K. Ghirshan, J. D. Kaunitz, J. L. Merchant, H. M. Said, J. D. Wood (Eds.) *Physiology of the Gastrointestinal Tract* (5th ed., pp. 861–891). Academic Press. https://doi.org/10.1016/B978-0-12-382026-6.00031-2

Rogers, S. J., & Ozonoff, S. (2005). Annotation: What do we know about sensory dysfunction in autism? A critical review of the empirical evidence. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 46*(12), 1255–1268. https://doi.org/10.1111/j.1469-7610.2005.01431.x

Rogers, S. L., Farlow, M. R., Doody, R. S., Mohs, R., & Friedhoff, L. T. (1998). A 24-week, double-blind, placebo-controlled trial of donepezil in patients with Alzheimer's disease. Donepezil Study Group. *Neurology*, *50*(1), 136–145. https://doi.org/10.1212/wnl.50.1.136

Rösler, M., Anand, R., Cicin-Sain, A., Gauthier, S., Agid, Y., Dal-Bianco, P., Stähelin, H. B., Hartman, R., & Gharabawi, M. (1999). Efficacy and safety of rivastigmine in patients with Alzheimer's disease: international randomised controlled trial. *BMJ (Clinical research ed.)*, *318*(7184), 633–638. https://doi.org/10.1136/bmj.318.7184.633

Sandkühler, J. (2009). Models and mechanisms of hyperalgesia and allodynia. *Physiological Reviews*, *89*(2), 707–758. https://doi.org/10.1152/physrev.00025.2008

Sharp, W. G., Berry, R. C., McCracken, C., Nuhu, N. N., Marvel, E., Saulnier, C. A., Klin, A., Jones, W., & Jaquess, D. L. (2013). Feeding problems and nutrient intake in children with autism spectrum disorders: A meta-analysis and comprehensive review of the literature. *Journal of Autism and Developmental Disorders*, *43*(9), 2159–2173. https://doi.org/10.1007/s10803-013-1771-5

Soskey, L. N., Allen, P. D., & Bennetto, L. (2017). Auditory spatial attention to speech and complex non-speech sounds in children with autism spectrum disorder. *Autism Research: Official Journal of the International Society for Autism Research*, *10*(8), 1405–1416. https://doi.org/10.1002/aur.1790

Suarez, M. A., Nelson, N. W., & Curtis, A. B. (2014). Longitudinal follow-up of factors associated with food selectivity in children with autism spectrum disorders. *Autism: The International Journal of Research and Practice*, *18*(8), 924–932. https://doi.org/10.1177/1362361313499457

Thapa, R., Alvares, G. A., Zaidi, T. A., Thomas, E. E., Hickie, I. B., Park, S. H., & Guastella, A. J. (2019). Reduced heart rate variability in adults with autism spectrum disorder. *Autism Research: Official Journal of the International Society for Autism Research*, *12*(6), 922–930. https://doi.org/10.1002/aur.2104

Tomchek, S. D., & Dunn, W. (2007). Sensory processing in children with and without autism: a comparative study using the short sensory profile. *The American Journal of Occupational Therapy: Official Publication of the American Occupational Therapy Association*, *61*(2), 190–200. https://doi.org/10.5014/ajot.61.2.190

Vaughan Van Hecke, A., Lebow, J., Bal, E., Lamb, D., Harden, E., Kramer, A., Denver, J., Bazhenova, O., & Porges, S. W. (2009). Electroencephalogram and heart rate regulation to familiar and unfamiliar people in children with autism spectrum disorders. *Child Development*, *80*(4), 1118–1133. https://doi.org/10.1111/j.1467-8624.2009.01320.x

Wiggins, L. D., Robins, D. L., Bakeman, R., & Adamson, L. B. (2009). Brief report: Sensory abnormalities as distinguishing symptoms of autism spectrum disorders in young children. *Journal of Autism and Developmental Disorders*, *39*(7), 1087–1091. https://doi.org/10.1007/s10803-009-0711-x

Williams, P. G., Dalrymple, N., & Neal, J. (2000). Eating habits of children with autism. *Pediatric Nursing*, *26*(3), 259–264.

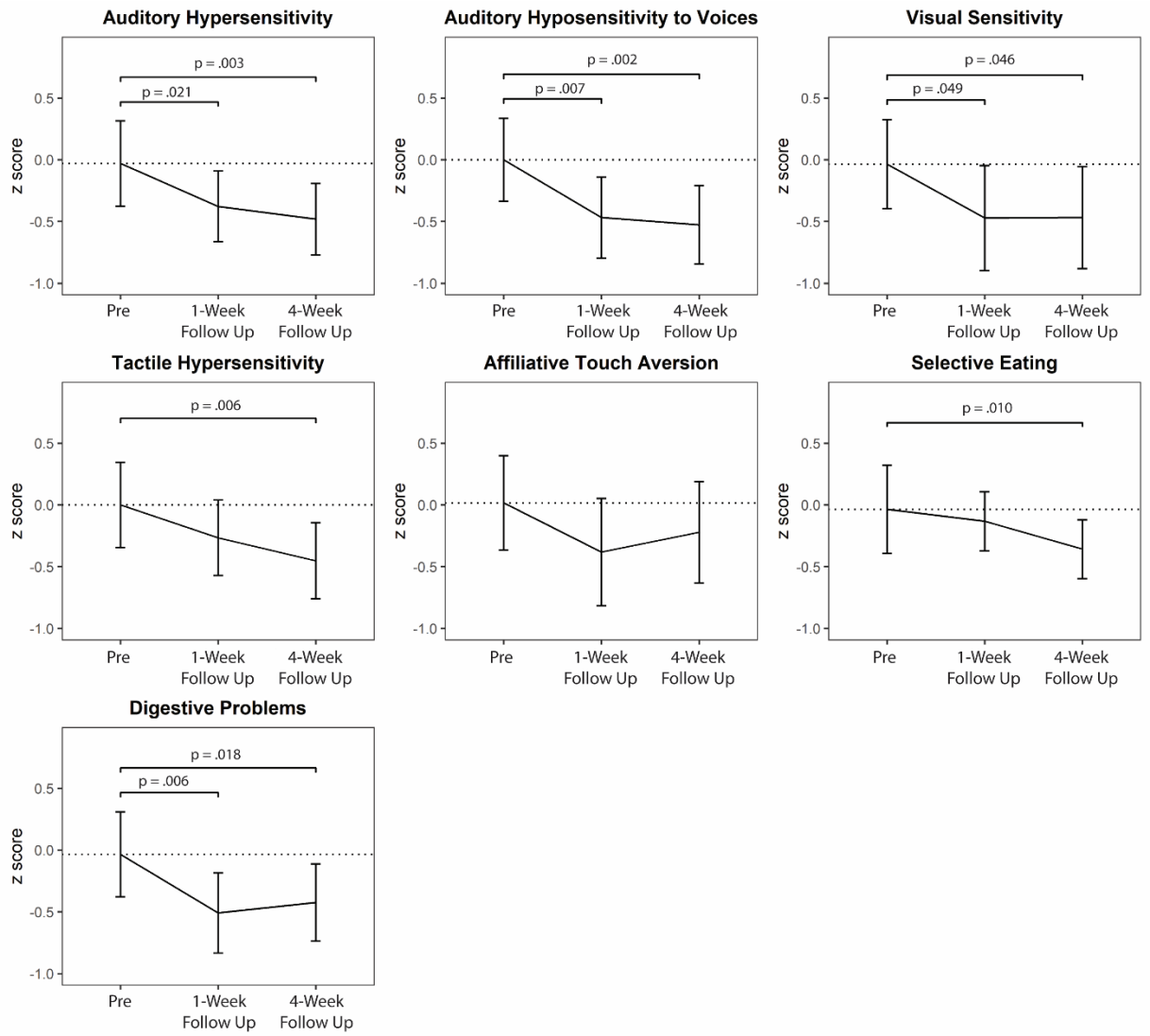
Wilson, U. S., Sadler, K. M., Hancock, K. E., Guinan, J. J., Jr, & Lichtenhan, J. T. (2017). Efferent inhibition strength is a physiological correlate of hyperacusis in children with autism spectrum disorder. *Journal of Neurophysiology*, *118*(2), 1164–1172. https://doi.org/10.1152/jn.00142.2017

Zwislocki, J. J. (2002). Auditory system: Peripheral nonlinearity and central additivity, as revealed in the human stapedius-muscle reflex. *Proceedings of the National Academy of Sciences of the United States of America*, *99*(22), 14601–14606. https://doi.org/10.1073/pnas.222543199

Supplemental Section

Figure 4

Predicted values and 95% confidence intervals for measured variables before, and at the 1-week and 4-week follow up assessments, only for those participants with a formal diagnosis (n=33).



Note. Estimates are from mixed effects models with random subject intercepts. Variables are standardized and centered at the baseline assessment. Significance markers (*) represent model parameters that had 95% confidence intervals that did not include 0.

Figure 5

Age moderation of the change from baseline to the 1-week and 4-week follow-up assessments for visual sensitivity and non-social tactile sensitivity (predicted means and 95% confidence intervals), only for those participants with a formal diagnosis (n=33).