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Psychophysical correlates in children with sensory modulation disorder (SMD)

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ABSTRACT

Sensory modulation disorder (SMD), affecting ~5% of children, is characterized by sensory over or under-responsiveness to a range of stimuli in several modalities. Children with over-responsiveness (SOR) demonstrate increased aversion to certain natural stimuli that manifests as increased distress and avoidance behaviors to common stimuli, accompanied by abnormal electrodermal responses and brain evoked potentials to various stimuli. This study is the first to use quantitative sensory testing to characterize the somatosensory sub-modalities of children with SMD. Seventy eight children aged 6–10 years (44 SMD children and 34 classmate controls) were tested. A diagnosis of SMD and SMD-free using the Short Sensory Profile was ascertained by the Sensory Profile Questionnaire, both completed by participants' mothers. Sensory detection thresholds for skin warming, cooling, punctate dynamic tactile sensation, vibration and thermal pain thresholds for heat and cold were determined at several body sites. Pain and prickle intensities for pinprick and prickly stimuli and the duration and intensity of the after-sensations of prickliness and pain evoked by the prickle stimuli were assessed. Compared to the control children, SMD children showed significant cool hypoesthesia, higher pain intensity to pinprick and to prickly stimuli, and significantly more pain after-sensation to the prickly stimuli. No significant differences between groups were found in most of the sensory and pain thresholds at any tested site. These results indicate, for the first time, that children with SMD perceive more pain, and that their pain lasts longer. Our results demonstrate that SOR does not imply lowered sensory thresholds but abnormal processing suprathreshold noxious stimuli.

1. Introduction

A recent epidemiological survey indicated that approximately 5% of typically developing children in the United States demonstrate severely maladaptive responses to benign daily sensory stimuli in a manner that interferes with daily life [1]. These abnormalities, termed sensory modulation disorder (SMD), were recently acknowledged as a subtype of Sensory Processing Disorders [2–4], and the term currently refers to behaviors manifesting as over or under-responsiveness in one or more sensory modalities [2–6]. Over-responsiveness is associated with defensive behavior or withdrawal from specific daily living tasks [2–5,7,8]. Moreover, sensation and its negative characteristics may linger long after the termination of the stimulus ('after-sensation') [5]. In contrast, under-responsiveness may be associated with delayed responses to stimuli, passivity, apathy or lethargy [2–5,8].

Physiologically, under- and over-responsiveness have been recognized as separate forms of the construct of SMD [6,8] and, as such, this study concentrated on the investigation of children with over-responsiveness. Over-responsiveness characterizes 80% of referred children with SMD [9], and includes sensory experiences that are abnormally irritating, unpleasant [2–5,7,8,10] and painful [10,11]. As a result, SMD can negatively affect developmental, emotional and functional abilities [5,12,13]. These difficulties usually continue into adulthood [14], and are often accompanied by anxiety, depression and maladaptation [15].

Only a few studies have quantified the physiological correlates of SMD such as auditory cerebral event-related potentials [16], parasympathetic (i.e., cardiac vagal tone index) [17], and sympathetic (i.e., electrodermal reflex) [8] responses to sensory stimuli in several modalities. These studies have provided evidence of physiological impairments in children with SMD. However, none of these studies used psychophysical quantitative tests to determine whether the abnormalities occur at the level of detection thresholds and/or in supratheshold intensities in this population, which was the aim of the present study.

Quantitative sensory testing (QST), an approach derived from experimental psychophysics, [18] is used to test for and to characterize somatosensory hypersensitivity as well as sensory deficiencies [18,19]. As such, it offers a standardized method, which encompasses a diverse array of psychophysical procedures to assess

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the perceived intensity of a given stimulus, and thus to directly measure the individual's subjective experience [18,20], while the intensity of the stimulus is controlled by the tester [18]. Moreover, it is used to indirectly evaluate underlying sensory functioning [20] by evaluating a range of peripheral nerve system functions [21,22], as well as by revealing abnormalities related to disorders of central nervous system sensory conduction [21].

The analyses described in this paper are amongst the first to psychophysically test the nature of responses to somatosensory stimuli amongst children with SMD. SMD and control children were tested for detection thresholds of vibration and punctate dynamic light touch, thermal sensation (cool and warm) and pain (hot and cold) thresholds. In addition, responses to suprathreshold stimuli were tested through pinprick pain intensity and prickliness elicited by woolen fabrics, as well as the after-sensations of prickliness and pain produced by the prickly fabrics.

The purpose of this study was to characterize children with SMD, of the over-responsiveness type, through psychophysical quantitative somatosensory tests. Our hypothesis was that children with SMD would show significantly lower detection thresholds as well as significantly greater pain intensity ratings to the various sensory stimuli, when compared to control, SMD-free children. Furthermore, we hypothesized that the SMD group would show prolonged after-sensations.

2. Methods

2.1. Participants

Pediatric occupational therapists were contacted with a request to refer children with suspected over-responsive type of SMD to participate in the study and 76 children were referred in this manner. In order to maintain homogeneity of the study groups, the parents of the children with SMD were each asked to refer a classmate to form the control group (but no siblings of the children with SMD were invited to participate). Inclusion criteria stipulated that participants were without any known congenital malformations, complications at birth, behavioral, psychiatric or neurological diseases (including speech, vision or hearing deficits), or a family history that included such diseases. The participants were between the ages of 6 and 10 years since previous studies have found no significant differences across these ages in the sensory profile (SP) [23], and in responses to psychophysical tests [24,25].

The diagnosis of SMD for all children in the study group was made based on two measures. The first measure used to identify children with SMD was the Short Sensory Profile (SSP) [26] and children who attained a total score below 150 for this measure were included in the suspected SMD group. Thereafter, their diagnosis of SMD was verified using the full-form Sensory Profile (SP) [27]. Since the items of the SSP [26] are derived from the SP [27], the high correlation between these two measures is to be expected (and indeed, all children with suspected SMD based on the SSP [26] fulfilled the inclusion criteria based on the SP [27]), but this procedure was selected since the SSP is commonly used as a screening tool while the SP [27] is a diagnostic tool which broadens the spectrum of the child's sensory profile and which enables a deeper understanding of potential sub classifications of SMD (such as over- and under-responsivity). Children included in the SMD group were required to have scores indicative of a definite difference (behaviors reported more than others, i.e. lower scores) in all three factors of the SP [27] related to the over-responsive type of SMD (emotionally reactive, oral sensory sensitivity and sensory sensitivity).

Both forms were also completed by mothers of the children in the control group to confirm that none of them had SMD; criteria for inclusion in the control group stipulated a score above 155 for the SSP (a score that reflects typical sensory modulation) [26]. Children who fell between the cut-off scores for inclusion in the study and control groups (150–155) were excluded from the study and some of the control children were excluded for this reason. Out of 76 children with SMD and 68 control peers, 44 children with SMD (58%) and 34 control children (50%) completed the study. Reasons for drop-out from the study included technical difficulties (such as distance and compliance with the administrative requirements of the study) as well as lack of fulfillment of the inclusion and/or exclusion criteria. These sample sizes (44 and 34) enable the detection of an effect size (Cohen's d) on the order of 0.6 at a 5% level of significance with at least 80% power [28].

2.2. Measures

2.2.1. Questionnaires

2.2.1.1. The Short Sensory Profile (SSP) questionnaire. The Short Sensory Profile (SSP) questionnaire [26] is a standardized, 38-item questionnaire derived from the Sensory Profile questionnaire (see below), used for screening children between the ages of 3 and 10 for SMD, as well as for research purposes [1,8,16,17]. The SSP enables the calculation of a score reflecting responsiveness to sensory input across all sensory modalities with the exception of pain. Using a 5-point Likert scale (1 = *always*; 2 = *frequently*; 3 = *occasionally*; 4 = *seldom*; 5 = *never*), caregivers report the frequency of behavioral responses to sensory events occurring in everyday life. The items cover responses to tactile, auditory, visual, gustatory and olfactory stimuli, movement, and body position (e.g., item #1: "The child expresses distress during grooming [e.g., haircutting, face washing, fingernail cutting]"). A total score was calculated for each participant by adding the points assigned for each item. Higher SSP scores reflect a greater number of behaviors which are within normal limits [26]. Validity of the SSP has been demonstrated using the 'known-group' procedure and factor analysis. Reliability has been measured through internal consistency (Cronbach's α values ranging from 0.70 to 0.90). Internal consistency for the SSP has been demonstrated to be high for Israeli children (Cronbach's $\alpha = 0.96$) [13].

2.2.1.2. The Sensory Profile (SP) questionnaire. The Sensory Profile (SP) questionnaire [23,27] is a 125-item questionnaire used for clinical diagnosis of SMD, by highlighting domains of atypical responses to specific daily sensory stimuli [23]. The SP questionnaire provides a detailed sensory profile of children between the ages of 3 and 10, and, in addition to responsiveness to the same sensory modalities as the SSP, assesses behavioral and emotional responses associated with sensory processing. Higher SP scores reflect a greater number of behaviors which are within normal limits. Content, discriminant and construct validity have been established [23]. High internal consistency (Cronbach's $\alpha = 0.90$) and test–retest reliability ($r = 0.89$) have been demonstrated for Israeli children. Construct validity has also been demonstrated for this population by showing statistically significant differences between Israeli children with and without SMD using the 'known-groups' procedure [29].

2.2.2. Quantitative Sensory Tests

2.2.2.1. The Fabric Prickliness Test (FPT). The Fabric Prickliness Test (FPT) quantifies the level of prickliness and pain caused by the application of prickly fabrics to the skin [30,31].

To adapt this test to children, we used three fabrics, selected based on preliminary experiments with five children (age range 6–10 years) without SMD, who graded the level of prickliness of 10 different woolen fabrics using a numerical rating scale (NRS) of 0–10 (0 = *not prickly at all*; 10 = *the prickliest fabric possible*). The three fabrics which received the highest level of consensus as eliciting minimal, moderate and maximal prickliness (Fabrics 1–3, respectively) were selected. The

least prickly, softest fabric, was of a type used to make garments meant to be worn on bare skin, whereas the prickliest fabric was of a type normally used to make garments never in contact with bare skin, (e.g., woolen coats) [30]. The FPT test consisted of 16 fabric applications: six of Fabric 2, and five each of Fabrics 1 and 3. The 16 fabrics (rectangular pieces 5×10 cm, each sewn in the middle of white cotton fabric 7×12 cm [30]), were applied to the volar surface of the non-dominant forearm, facing down (to prevent visual identification of the tested fabric). Beginning with Fabric 2, the next presentations of Fabrics 1–3 were applied sequentially in a pseudorandom order that presented each fabric type once, preceded by a fabric of a different prickliness level [30]. The investigator rapidly tapped on the fabric with digits 2–4, repeating this sequence until the child verbally indicated registering the sensation. Then the fabric was removed and the child was asked to separately rate the level of prickliness and pain the fabric evoked using the following instruments:

Prickliness intensity was rated using a mechanical sliding device that served as a visual analog scale (M-VAS) [32]. A middle slider was pulled to the right by the child revealing a red bar that indicated perceived intensity of prickliness (ranging from "not prickly at all" to "the most prickliness possible"). Turning the device over revealed a numerical scale from 0 to 10, (which was visible to the experimenter but not to the child), that corresponded to the length of the exposed red bar. This number was recorded after the application of each fabric.

Pain intensity was rated using the Faces Pain Scale [33], revised [34], which comprises schematic drawings of six faces that express increasing distress typical of individuals experiencing pain. These faces represent six levels of pain that correspond to a numerical rating scale ranging from 0 to 10 with increments of 2. The child selected the face best fitting the level of pain evoked by the fabric and the corresponding number was recorded after the application of each fabric.

Prickliness and pain 'after-sensation': After the FPT was terminated by scoring the 16th fabric, the duration of the prickliness and painfulness that continued to linger as an after-sensation was also measured. Children used the same measures to rate the intensity of the prickliness and pain, 15 s after scoring the last fabric of the FPT and repeated the ratings five times at one minute intervals thereafter.

2.2.2.2. Vibration sensation thresholds. Vibration sensation thresholds were determined by applying the Method of Limits [35], using the Vibratory Sensory Analyzer (Medoc, Ramat Yishai, Israel), by indenting the palmar aspect of the 3rd digit 2nd phalanx of the non-dominant hand with the probe at 100 Hz, increasing the amplitude at 0.2 μm/s and at a force of 40.98 g/cm^2 [24,36]. When the child perceived the vibration, he clicked a computer mouse with the contralateral hand, thereby registering the Vibration Perception Threshold (VPT) as the depth of the indentation (in μm) and resetting the probe position. Thereafter, a supraliminal vibratory stimulus (10 μm, at 100 Hz) was applied, decreasing in amplitude at 0.2 μm/s, until the sensation of vibration disappeared. Clicking the mouse signified the depth (in μm) of the Vibration Disappearance Threshold (VDT), rapidly resetting the probe position. The first trial was used for training VPT, and the VPT threshold calculation was an average of the following three trials [35,37], which were delivered at an inter-trial interval of 4 s [36]. VDT was administered and calculated in the same way [35–37].

2.2.2.3. Dynamic punctate tactile sensation thresholds. Dynamic punctate tactile sensation thresholds were determined at the pulp of the 2nd digit of the dominant hand and on the upper lip, using a series of von Frey monofilaments (Smith & Nephew Rolyan; Menomonee Falls, WI; 0.08–2943 mN). The monofilament set was calibrated to deliver its targeted bending force within a 5% standard deviation [38]. The monofilaments were selected and labeled so as to give a linear scale of perceived intensity (a logarithmic scale of applied force) ranging between 1.65 and 6.65 U (log force) (ranging from 0.008 g to 300 g/0.08 mN to 2943 mN) [38]. Starting with the filament of the lowest bending force, ascending force was applied using the Method of Limits, pressing each filament until bent [39,40] five times at a rate of ~2 Hz. The detection threshold was determined as the log force of the first monofilament producing a distinctive tactile sensation [40] in all five applications. Participants were blindfolded to prevent visual cues of the stimuli [40].

2.2.2.4. Pinprick pain. Pinprick pain was determined with three stiff filaments (Smith & Nephew Rolyan; Menomonee Falls, WI; see above), eliciting increasing levels of punctate pain, by applying a bending force of 5.46, 5.88 and 6.10 on a log force scale (29 g, 75 g and 127 g; 284.4 mN, 735.5 mN, 1245.4 mN, respectively). Preliminary experiments in seven SMD-free children (age range 6–10 years old) showed that all three filaments elicited a reasonably painful pricking sensation (pain intensity <= 6), in all tested children, when applied perpendicularly to the skin of the volar surface of the dominant forearm. While applying the filaments, children were blindfolded to prevent visual cues of the stimuli [40]. In order to rate pain intensity, the blindfold was removed after each application. Pain intensity was rated using the revised Faces Pain Scale [34]. The entire test consisted of nine applications, three of each filament, in a pseudorandom order which was identical for all children.

2.2.2.5. Thermal sensations and pain detection thresholds. Thermal sensations and pain detection thresholds were tested with the Thermal Sensory Analyzer (TSA-2001) (Medoc, Ramat Yishai, Israel). A Peltier thermode (30×30 mm) was secured with a Velcro© elastic band at the tested site, and kept in contact with the skin for the entire duration of the test to minimize tactile or pressure stimulation [22]. Starting from an adaptation temperature of 32 °C [21,22], warm, cool, heat and cold stimuli were applied at the forehead (as a non lateralized body site), thenar eminence (of the non-dominant hand as a standard body site), and calf (same side; as a poorly sensory innervated body site) to determine the thermal detection and pain thresholds. The child's feedback was registered when the child clicked a handheld computer mouse.

Warm and cool detection thresholds (thermesthesia) were assessed with the Method of Levels [19,22,41]. Warm detection threshold (WDT) and cool detection threshold (CDT) were determined using a computerized program that followed a sequence of heating or cooling ramps that depended on feedback from the tested child or the experimenter: When no feedback was provided by the child, the experimenter keyed in a signal indicating an absence of response. For CDT and WDT the rate of temperature change was 1 °C/s [21,22,24]. Stimuli were presented at an initial ramp of 3 °C (i.e., 35 °C for WDT and 29 °C for CDT), with the thermode returning to the adaptation temperature of 32 °C immediately thereafter. For WDT, stimuli continued to be increased by ramps of 3 °C until the tested child indicated detecting a change from the starting baseline temperature. Additional stimuli were then presented to identify the detection threshold at a higher resolution. To this end, the ramp temperature was halved for each successive stimulus, with the direction changing according to the child's response, increasing the temperature when no feedback was provided or decreasing it when the child indicated that he felt the stimulus. The test was completed when the last stimulus was 0.1 °C from the previous stimulus. The detection threshold (WDT) was calculated by the computerized apparatus as the average of the last two trials — the one that was detected and the one that was not. The opposite procedure was used to determine the CDT. Random dummy stimuli were also used [22].

Heat (HPT) and cold (CPT) pain thresholds (thermalgesia) were assessed using the Method of Limits [22,42]. These stimuli were trains of heating or cooling at a rate of 1.5 °C/s [24,43], each starting from the baseline temperature of 32 °C [22,24]. As soon as the stimulus was

perceived to be painful, the child interrupted the train by feedback, resetting the probe temperature to the baseline at a rate of 10 °C/s [24]. This sequence was repeated three more times, at 10–15 s intervals [22,24,43]. The first stimulus was used for training the child, and the average of the last three trials was used to determine the HPT. The same procedure, but with cold stimuli, was used to determine the CPT. The interval between measures of the HPT and CPT was five minutes.

2.3. Procedure

The experimental protocol was approved by the Ethics Review Board of Reuth Medical Center, Tel Aviv, Israel. Written informed parental consent was obtained after the procedures had been fully explained to parents, and children verbal assent was obtained before the testing session began.

Parents of participating children received a letter explaining the purpose of the study and its procedures, an informed consent form, the SSP questionnaire and a detailed socio-demographic and health caregiver questionnaire, in a return-addressed and stamped envelope. Mothers were asked to be the responders since they have been found to report atypical behaviors more accurately than fathers [44,45]. Based on the returned SSP questionnaires, initial group placement was determined [26]. Thereafter a psychophysical testing session that did not exceed one hour was carried out at the Reuth Medical Center Outpatient Clinic, in a quiet room, with the child sitting in a comfortable recliner. Standardized instructions were delivered via computer presentations and training trials were performed prior to every test. Tests followed a standard protocol, presented in a randomized order to avoid sequence effects and to balance out possible influences of fatigue and attention span. All children were tested by the same investigator (T.B-S.) who was blinded as to the group placement of the tested child. All participants were requested to have no analgesics for 24 h prior to the testing session. While the child was tested, mothers completed the SP questionnaire. Based on the scores of the SP questionnaire [23,27], children assigned to the SMD group were ascertained as having an over-responsive profile. Parents were not reimbursed for time and travel costs but received the test report and were offered a free consultation session with an occupational therapist specializing in treating children with SMD.

2.4. Data analysis

Statistical analysis was performed using SAS v9.1 (SAS Institute Cary NC. USA). Categorical variables are presented as a count and percentage and compared with a chi-squared test or Fisher's exact test. Continuous variables are summarized by a mean and standard deviation and compared with a two-tailed independent samples *t*-test. Pearson's correlation coefficient between SSP and SP scores was calculated. Group means are plotted with standard errors of the mean (SEM). Each of the Quantitative Sensory Test scores (or their change from baseline) was modeled as dependant variables using a repeated measures analysis of variance model (RMA; using PROC MIXED in SAS). For each model fixed-effect parameters (such as gender, fabric type, time) depending on the data were entered into the model with interactions where appropriate. Risk of SMD was evaluated using logistic regression modeling (using PROC GENMOD in SAS in the case of repeated measurements or PROC LOGISTIC otherwise). No adjustment for multiple testing was done in this preliminary study.

3. Results

No significant group differences were found in parental demographic and socioeconomic variables, such as marital status, ethnic origin, occupation and education (data not shown). No significant difference was found in the average age between the study groups (Table 1). We found a higher percentage of boys in the SMD group, whereas boys and girls were similarly distributed in the control group (Table 1). This is in keeping with evidence from the literature that a larger percentage of boys are both referred and diagnosed with developmental disorders [46–49]. To control for potential confounding effects, we adjusted the statistical models for gender.

3.1. Group placement

Statistically significant differences were found between the SMD and control groups in the SSP mean scores [127.1 (SD = 22.82) and 171.3 (SD = 10.44), respectively, $t_{74} = 9.68$, $p < 0.0001$; effect size = 2.42] and the SP scores [428.5 (SD = 62.29) and 556.7 (SD = 33.94), respectively, $t_{73} = 10.61$, $p < 0.0001$; effect size = 2.25]. Statistically significant differences were also found for the three SP Factor scores: [Factors 2; 4 and 7: ($t = -8.63$, $p < 0.0001$); ($t = -7.18$, $p < 0.0001$); ($t = -5.12$, $p < 0.0001$) respectively].

Due to the fact that this study specifically aimed to investigate the somatosensory system, 14 items from the SP questionnaire [27] which assess the frequency of over-responsiveness to tactile stimuli were selected. The average scores of these items were significantly lower in the SMD group, compared to the control group 46.86 (SD = 10.43), 65.10 (SD = 3.70), respectively; $t_{73} = 9.57$, $p < 0.0001$), indicating that children with SMD had abnormal processing of tactile stimuli. This further supported the rationale for comparing the responses of SMD and control children using the following somatosensory psychophysical tests.

3.2. Quantitative Sensory Tests

3.2.1. The Fabric Prickliness Test (FPT)

Prickliness and pain intensity were evaluated using two repeated measures analysis of variance models (RMA) as a function of group (SMD/control), gender, fabric type (least painful, moderately painful, most painful) and the fabric type*group interaction).

3.2.1.1. Prickliness intensity. Both the SMD and control groups associated significantly increasing prickliness levels with the three fabric types (Fig. 1a) as depicted by the significant effect of fabric type [$F(2, 74) = 34.60$; $p < .0001$]. This indicated that the selected fabrics enabled discrete grading of the intensity of prickliness in the FPT. Children with SMD did not differ significantly from control children in the level of prickliness elicited by the three fabrics as neither the group effect [$F(1,74) = 2.02$, $p = 0.16$] nor the interaction term [$F(2,74) = 1.15$; $p = 0.32$] were found to be statistically significant. Thus, we conclude that children with SMD do not have prickle hyperesthesia when stimulated with prickly fabrics.

3.2.1.2. Pain intensity. Likewise, the three woolen fabrics elicited discretely increasing levels of pain in both groups [interaction term: $F(2,74) = 23.56$, $p < 0.0001$; Fig. 1b]. This confirmed that the FPT is a valid measure for testing pain levels produced by woolen fabrics.

Children with SMD significantly differed from control children in the level of pain elicited by the application of the fabrics [group effect: [$F(1,74) = 9.99$, $p = 0.0023$; Fig. 1b], but no significant group by fabric type interaction was found [$F(2,74) = 1.20$, $p = 0.31$]. Irrespective of

Table 1
Age and gender comparison between the SMD and control groups.

		Group	*n*	Statistic	Value	Test
Age		SMD	44	Mean	7.50	$t_{76} = -0.77$; $p = 0.44$
				SD	1.20	
		Control	34	Mean	7.75	
				SD	1.33	
Gender	Boys	SMD	33	%	64.7	$\chi^2 = 4.12$; $p = 0.04$
	($N = 51$)	Control	18	%	35.2	
	Girls	SMD	11	%	40.7	
	($N = 27$)	Control	16	%	59.2	

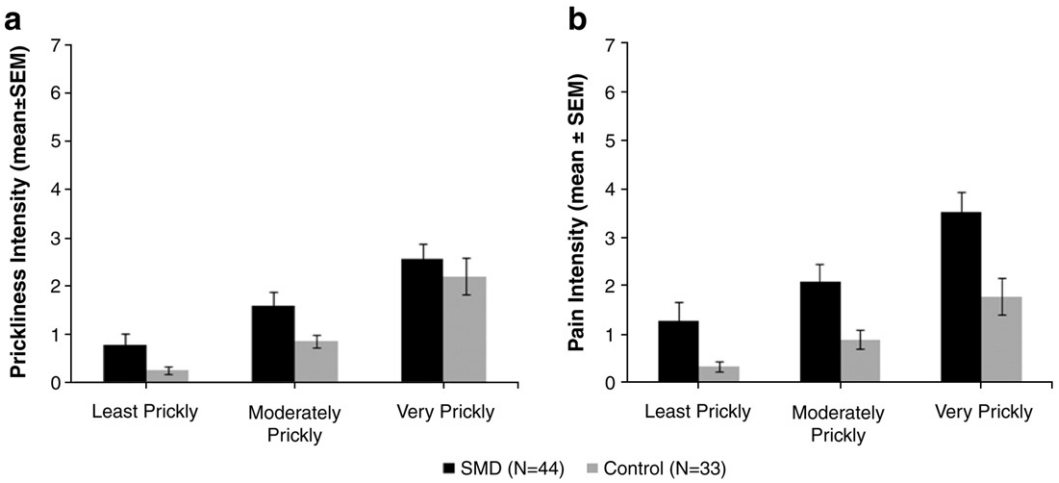

Fig. 1. Prickliness (a) and pain (b) intensity VAS scores [mean (±SEM)], in SMD and control children for each of the three fabric types.

fabric type, children with SMD reported significantly higher pain levels in response to application of the woolen fabrics than control children.

3.2.1.3. Correlation between pain and prickliness. Pain was modeled as a function of prickliness, group, gender and the group*prickliness interaction. A significant group*prickliness interaction [RMA, $F(1,74)=19.3$; $p<0.0001$] indicated that the slope (i.e., the correlation between pain and prickliness) in the SMD group was significantly higher than that of control children, irrespective of fabric type (0.94 and 0.43, respectively).

3.2.1.4. After-sensation of prickliness and pain. The change from baseline (15 s) after sensation prickliness and pain scores were modeled with an RMA model as a function of group, gender, time-after-fabric-application and the group*time-after-fabric-application interaction. No significant differences between the groups were found in the after-sensation of prickliness [group effect: $F(1,77.7)=0.08$, $p=0.78$; Fig. 2a]. However, Fig. 2b shows that, while the after-sensation of pain in control children disappeared over 5 min after the last fabric application, children with SMD expressed lingering pain. A statistically significant difference between the SMD and control groups was found in the intensity of the after-sensation of pain [$F(1,78.6)=4.64$, $p=0.034$; Fig. 2b]. This difference did not vary over fabric applications, since the time-after-fabric-application*group interaction was not significant [$F(1.77.6)=0$, $p=0.98$; Fig. 2b].

No significant gender differences were found in any of the models above (data not shown).

3.2.2. Vibration sensation thresholds

No statistically significant differences were found between groups in the vibration perception threshold (VPT) or the vibration disappearance threshold (VDT) of a 0.5″ disk applied to the palmar aspect of the third digit at a vibration frequency of 100 Hz (Table 2).

3.2.3. Dynamic punctate tactile sensation threshold

No statistically significant differences were found between the groups in the detection threshold of light touch applied repetitively with a von Frey monofilament, regardless of the tested body site (Table 2).

3.2.4. Pinprick pain

Pinprick pain was modeled as a function of group, filament bending force, gender and the interaction between filament bending force and group.

Statistically significant differences were found between the monofilament bending force irrespective of group [$F(2,74.5)=48.63$, $p<0.0001$], but no significant interactions were found between filament bending force and group [$F(2,74.5)=0.71$, $p=0.49$]. This indicated that the three filaments selected for this test enabled discrete grading of increasing levels of pain [Fig. 3] in both groups in a similar manner.

Next, we found statistically significant differences between groups, for the same monofilament, with higher pain scores reported by the SMD group [$F(1,76)=11.94$, $p=0.0009$]. No significant gender differences were observed [$F(1,76)=0.8$, $p=0.37$]. Thus, we conclude that children with SMD rate pain intensity higher than control children, when stimulated with painful prickly stimuli.

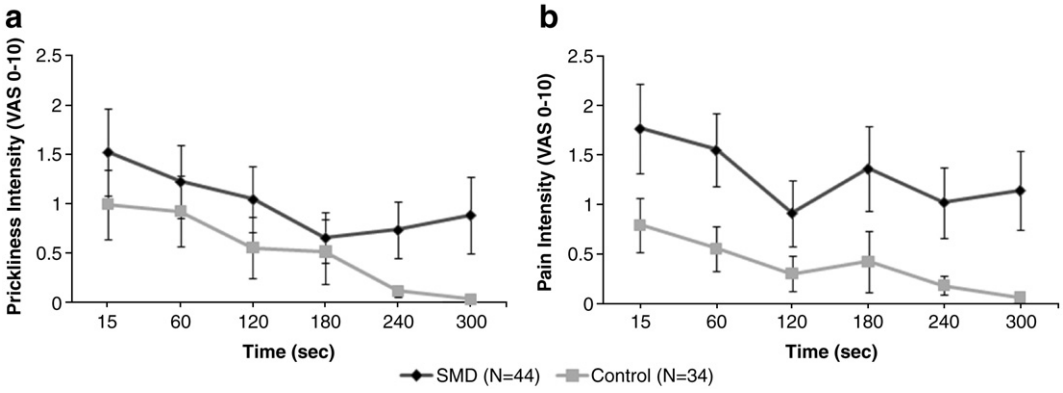

Fig. 2. Plots of the mean (±SEM) intensity of the after-sensations of prickliness (a) and pain (b) over five minutes, beginning 15 s after the last fabric application.

Table 2
Comparison of vibration and punctate thresholds between the SMD and control groups.

Test	Stimulated body site	Variable	Group	Mean	SEM	*t*	*p*
Vibration (100Hz)	Digit #3	Vibration perception threshold (μm)	SMD	1.21	0.11	0.92	0.34
			Control	1.03	0.15		
		Vibration disappearance threshold (μm)	SMD	1.70	0.18	−0.18	0.86
			Control	1.75	0.20		
Repetitive tactile stimulation (von Frey filaments)	Digit #2	Light touch detection threshold (log force)	SMD	2.33	0.10	0.11	0.91
			Control	2.31	0.12		
	Upper lip		SMD	2.03	0.09	0.47	0.64
			Control	1.97	0.11		

3.2.5. Thermal sensations and pain detection thresholds

Groups were compared for thermal thresholds (CDT; WDT; CPT and HPT) with each threshold modeled separately with a RMA model, as a function of body site, gender and the interaction between body site and group.

3.2.5.1. Cool detection threshold (CDT). Children in the SMD group were significantly less sensitive than children in the control group to cooling of the skin, irrespective of the stimulated body site [($F(1,72)=9.52$, $p=0.0029$; Fig. 4]. Both groups reacted in the same manner at the different body sites, as no significant interaction between body site and group was found [$F(2,68.7)=1.21$, $p=0.30$)]. The overall difference between body sites was significant [$F(2,68.7)=12.93$, $p<0.0001$]. Thus, we conclude that children with SMD have hypoesthesia to cool stimuli.

3.2.5.2. Warm detection threshold (WDT). No significant differences were found between groups for warm detection threshold [$F(1,76.9)=1.7$, $p=0.20$); Fig. 4]. The overall difference between body sites (irrespective of group) was significant [$F(2,74.2)=37.93$; ,$p<0.0001$]. Nevertheless, both groups reacted in the same manner at the different body sites, as no significant interaction between body site and group was found [$F(2,74.2)=0.46$; $p=0.6332$)].

3.2.5.3. Thermal pain thresholds (CPT; HPT). Significant differences were found between the three body sites, irrespective of group [CPT: $F(2,70.1)=4.95$, $p=0.0097$; HPT: $F(2,71.9)=8.18$, $p=0.0006$]. However, no significant differences were found between groups, both for the cold and hot pain thresholds [CPT: $F(1,78.1)=0.25$, $p=0.62$; HPT: $F(1,76.6)=0.78$, $p=0.38$, respectively]. Thus, we conclude that children with SMD do not differ from control children in thermal pain thresholds.

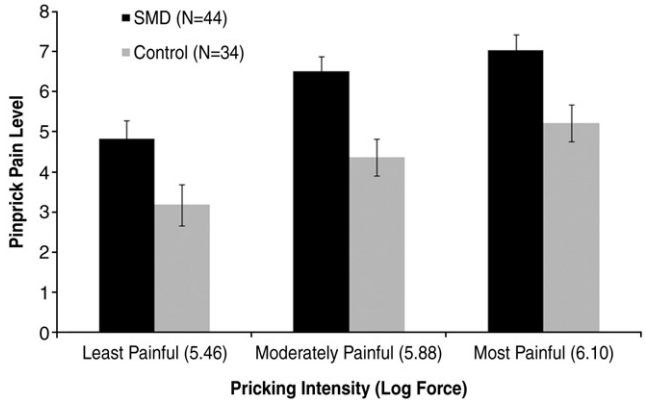

Fig. 3. Mean pinprick pain intensity (±SEM) per group determined by *The Faces Pain Scale (Revised)*.

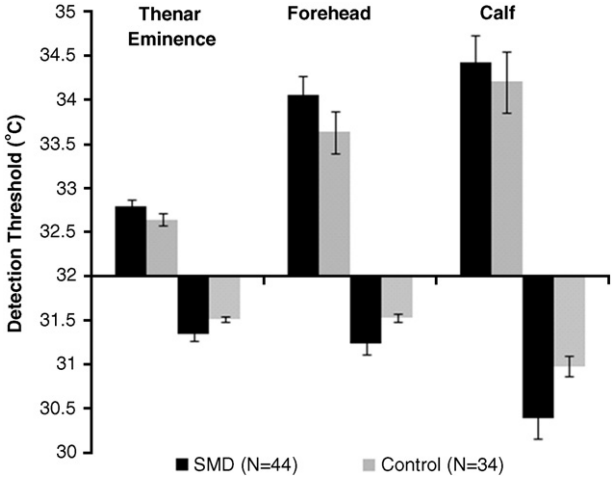

Fig. 4. The average (±SEM) Cool Detection Threshold (CDT) and Warm Detection Threshold (WDT) (in °C) at which control and SMD children detected the appearance of cooling or warming sensations in the three stimulated body sites.

3.3. Predictive ability of the sensory tests to identify children with SMD

In order to assess the ability of the sensory tests to predict SMD, logistic regression models (employing PROC GENMOD in SAS) were applied as a preliminary evaluation. The FPT and pinprick scores were evaluated, as was the fabric type by score interaction and the filament bending force by score interaction. For cases where the interaction was found to be significant, separate logistic models were applied to estimate the odds ratios of the respective score associated with a certain fabric type or filament bending force. Using a similar approach, cool and warm detection thresholds, and cold and hot pain thresholds, were modeled with the interaction of body site by score. No adjustment was made for gender in these evaluations, since gender was not found to be a significant variable in any of the comparisons and models mentioned above.

3.3.1. The Fabric Prickliness Test (FPT)

We tested whether reported levels of prickliness (Model 1) and/or pain (Model 2) elicited by the fabrics increased the likelihood of being diagnosed with SMD. While no statistically significant association was found between the levels of prickliness and SMD diagnosis (Model 1, Table 3), a significant association was observed between pain levels and SMD status (Model 2, Table 3). For every unit increase in the level of pain produced by the prickly fabrics, the risk of having SMD was increased by 27% (Table 3). Thus, reported levels of pain, but not of prickliness, predicted having SMD.

Model 2 shows that there is a statistically significant difference in association of pain levels with SMD between the fabric types (Model 2, Table 3), and thus three separate models were analyzed, one for each fabric type. The odds ratio of having SMD when the prickliest fabric was applied was the smallest of the three (Models 2a–c, Table 3).

3.3.2. Pinprick

A statistically significant association was observed between the level of pain evoked by pinprick and SMD as determined by the SSP scores (Model 3, Table 3). This association was modified slightly by the filament bending force, since the interaction term was significant ($p=0.008$). We found that with each unit increase in the pain scores there is a 30% increase in the risk of being classified as having SMD (Model 3, Table 3). Since the interaction between filament bending force and group was significant, we applied separate logistic regression

Table 3
Association between risk of having SMD and sensory tests to innocuous and noxious stimuli in children.

Model	Variable	Level	Odds ratio	95% CI lower, upper	*p* values
1	FPT-prickliness		1.11	0.94, 1.32	0.18
2	FPT-pain		1.27	1.07, 1.51	0.002
2a	Pain by fabric	Least painful	1.77	0.97, 3.23	0.06
2b		Moderately painful	1.52	1.08, 2.15	0.02
2c		Most painful	1.33	1.08, 1.64	0.007
3	Pinprick-pain		1.30	1.07, 1.57	0.002
3a	Pinprick-pain by	5.46 (log force)	1.23	1.03, 1.45	0.02
3b	filament	5.88 (log force)	1.38	1.14, 1.69	0.001
3c		6.10 (log force)	1.30	1.08, 1.57	0.006
4	Cool-detection		0.44	0.26, 0.74	0.001
4a	Cool-detection by Body Site	Thenar eminence	0.15	0.02, 1.09	0.06
4b		Forehead	0.58	0.33, 1.01	0.055
4c		Calf	0.26	0.06, 1.08	0.06
5	Warm-detection		1.15	0.9, 1.47	0.21
6	Cold-pain		0.99	0.94, 1.04	0.57
7	Hot-pain		0.98	0.88, 1.10	0.73

models for each filament bending force, calculating the odds ratio (Models 3a–c, Table 3). The moderately painful filament, having a bending force of 5.88 on the log force scale, was the most predictive test stimulus with a 38% increase in risk of having SMD.

3.3.3. Thermal detection thresholds

A significant association was found between SSP scores and the CDT for being classified as having SMD (Model 4, Table 3). The implication of this result is that the odds of having SMD are reduced by 54% with every one degree (°C) temperature increase in the CDT. In addition, Model 4 demonstrated that there is a significant difference between body sites ($p = 0.0039$), and thus three separate models were analyzed, one for each body site. However, none of these estimates was significant (Models 4a–c, Table 3).

No significant association was found between SMD and WDT scores (Model 5, Table 3). These results indicate that the association between having SMD (as reflected in the SSP scores) and thermal detection thresholds existed only for detection of coolness (CDT) but not of warmth (WDT).

3.3.4. Thermal pain thresholds

Models 6 and 7 revealed no statistically significant associations between thermal pain thresholds and the risk for having SMD (CPT: $p = 0.73$, Model 6; HPT: $p = 0.57$, Model 7, Table 3).

We conclude that increased pain levels evoked by woolen fabrics and pinprick, as well as decreased cool detection thresholds, are predictive of having SMD in children (Table 4).

Table 4
Summary of the main observations made amongst children with SMD.

Sensory tests and questionnaires	Stimulated site	Variable	Results[a]
Punctate light touch (von Frey filaments applied at 2 Hz)	Finger	Touch detection threshold	SMD = CON
	Face		SMD = CON
Vibrating disk (100 Hz)	Finger	Vibration detection threshold	SMD = CON
Repetitive tapping a prickly fabric against the skin	Forearm	Prickliness	SMD = CON
		Prickliness after-sensation	SMD = CON
		Pain	**SMD > CON**
		Pain after-sensation	**SMD > CON**
Pinprick	Forearm	Pain	**SMD > CON**
Warm	Hand	Detection threshold	SMD = CON
	Face		
	Leg		
Cool	Hand	Detection threshold	**SMD < CON**
	Face		
	Leg		
Hot	Hand	Pain detection threshold	SMD = CON
	Face		
	Leg		
Cold	Hand	Pain detection threshold	SMD = CON
	Face		
	Leg		
SP questionnaire	Face	Frequency of abnormal responses to 14 daily tactile stimuli	**SMD > CON**
	Hands		
	Feet		

>: denotes that children with SMD were significantly more sensitive or reported more pain than control children.
<: denotes that children with SMD were statistically significant less sensitive or reported less pain than control children.
=: no statistically significant difference between the groups was found.
[a] **Bold font**: comparisons yielding a statistically significant difference between the groups.

4. Discussion

The present study is the first to systematically test somatosensory thresholds and suprathresholds of children with sensory modulation disorder (SMD), using psychophysical methods. Thresholds of punctate light touch, vibration, thermal detection and pain were assessed, and suprathresholds were investigated by assessing responses to prickliness and pain intensity as well as the duration of the after-sensations to these stimuli. Our data demonstrated that, with the exception of cool detection thresholds, no threshold differences were found between children with SMD and controls. In general, this trend towards normoesthetic somatosensory thresholds is compatible with previous reports that found no abnormal tactile discriminability in children with SMD [50].

Our finding of cool hypoesthesia in children with SMD suggests that a high stimulus intensity (i.e. colder stimuli) was required for stimulus detection than that required in typically developing children. Several studies from other realms of investigation have shown that isolated cold stimulation has a higher diagnostic sensitivity than warm stimulation [51–53]. Our single finding of cool threshold differences amongst children with SMD may suggest that SMD is associated with abnormal processing of input evoked by cool stimuli in the thalamus, since lesions to the thalamic Ventral caudal nucleus (Vc), not including Ventral medial posterior nucleus (VMpo), are sufficient to produce cold hypoesthesia and central pain in post stroke patients [54]. More research is needed to investigate this sub-modality amongst children with SMD.

The finding of no group differences between the control and SMD groups in reported prickliness in response to the applications of the woolen fabrics may not be altogether surprising. This may be explained based on the different natures of the questions asked of the children. While the questions related to rating the prickliness intensity of the stimuli may be viewed as considering “discriminatory” aspects of the stimuli (such as more–less, strong–weak etc), the questions assessing the pain invoked by these stimuli address more affective elements of the experience. This finding of no discriminatory differences but significant affective differences in the responses to stimuli is again in accordance with reports that children with SMD do not have difficulties in sensory discrimination per se [50]. This is supported by the findings of the logistic regression analyses.

With regard to suprathreshold noxious stimuli, children diagnosed with SMD reported higher levels of pain than those reported by typically developing children in response to both pinprick (von Frey monofilaments) and prickly fabrics. Pinprick is widely used to assess the nociceptive system [55,56]. In animal models, it has been demonstrated that application of woolen (prickly) fabrics to the rat glabrous skin

activated firing in Aδ- and polymodal C-fibers carrying mechanical nociceptors [31]. In humans, higher pain ratings were associated with application of fabrics that evoke more prickle sensation [30,31]. Our results suggest that children with over-responsiveness to sensory stimuli might have a more vigilant nociceptive system. It is noteworthy that, while control children in the present study ranked the two fabrics of the lower levels of prickliness as almost not painful at all, children with SMD already assigned significantly higher levels of pain from the less prickly fabrics. Likewise, children with SMD associated higher levels of pain with the pinprick stimuli than children without SMD.

While it may be assumed that the responses of children with SMD to certain sensory stimuli would become more extreme as stimuli becomes more intense, our findings suggest that this is not the case; it appears that children with SMD show greater aversive responses in comparison to typically developing children even in response to seemingly less intense stimuli. Indeed, this appears to be one of the definitive features of SMD, that these individuals demonstrate increased aversion to non-aversive sensory stimuli [2–9] while not necessarily having "more aversive" responses than typically developing individuals to extremely aversive stimuli. When examining the histograms, it is clear that the difference in the affective responses between the SMD and typically developing children decreases as the aversive nature of the stimulus increases. Moreover, further support for this interpretation is provided by the logistic regression which revealed the smallest odds ratio for having SMD when the prickliest of the three fabrics was applied.

Despite clinical reports of symptoms described by individuals with SMD, the phenomenon of after-sensation has not been investigated in this population. We found that the increased sensation of pain to the prickly fabrics lingered for at least 5 min after the termination of the test. Pain after-sensation is a characteristic symptom of certain types of neuropathic pain [57]. Prolonged firing of spinal ascending nociceptive neurons, which outlasts stimulus duration, has been recorded in a number of species using several preparations of neuropathic pain, and is one of the hallmarks of 'central sensitization' [58]. This study lends empirical support for a commonly described, symptom of SMD that has not been investigated as of yet.

Additional research is needed to determine whether the sensory abnormalities observed in children with SMD result from chronically sensitized mechanical nociceptors and/or abnormal processing in the CNS of sensory input. Unlike sensory nerve action potentials, the QST explores the status of somatosensory afferents, (small caliber and large myelinated fibers), all the way between cutaneous receptor to central nerve system structures without providing clues as to the precise locus of dysfunction along the channels [18,52]. However, in line with recent findings [16,59], the following arguments favor CNS mechanisms as underlying SMD.

The sensations of both prickliness and pain that co-occur in response to prickly stimuli [60,61] result from activation of mechanical nociceptors on Aδ-, and C-fibers [31]. If SMD results in part from sensitization of these receptors, one would expect children with SMD to report significantly higher levels of prickliness than the control group, in addition to increased pain levels. Thus, the lack of difference between the groups in the reported levels of prickliness supports our conclusion that SMD is caused in part by abnormal CNS processing of nociceptive input.

Since SMD is associated with abnormalities in additional modalities to cutaneous sensibility [2–8,16,17] the most likely explanation for the increased pain to the pinprick and the prickly fabrics, and the pain after-sensation, is an abnormally higher gain of activation of CNS pain pathways by the afferent input these stimuli elicited in nociceptive afferents. It is possible that this abnormality is caused by chronically sensitized pain pathways in the CNS [58], perhaps caused by constitutively lower inhibitions, abnormal regulation of descending controls [59,62], or abnormal processing of painful stimuli in structures that attribute an affective negative value to afferent inputs [63]. If validated in future experiments, (e.g., using brain imaging), this could explain why stimuli in other modalities are perceived by children with SMD as aversive.

The results of this study reveal that, from a psychophysical perspective, children with SMD have abnormalities in suprathreshold noxious tactile sensations, but not at the detection threshold level (with the exception of cool stimuli). This conclusion is in line with maternal behavioral reports (based on the SP and SSP questionnaires) that children with SMD show a higher frequency of increased aversive responses to suprathreshold tactile stimuli as compared to control children. Arguably, most daily encounters with such stimuli are at suprathreshold intensities. Our findings support the suggestion that children with SMD suffer from abnormal sensory processing at the CNS level.

5. Conclusions

This is the first psychophysical profile to characterize the sensory abnormalities of children with SMD. It demonstrates that children with over-responsiveness form of SMD do not show overly sensitive detection ability, but rather express increased sensitivity to painful stimuli, suggesting a CNS involvement. This might explain the observable behavioral responses (e.g. defensive, withdrawal behaviors) seen in children with over-responsiveness form of SMD.

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References

[1] Ahn RR, Miller LJ, Milberger S, McIntosh DN. Prevalence of parents' perceptions of sensory processing disorders among kindergarten children. Am J Occup Ther 2004;58:287–93.
[2] Interdisciplinary Council on Developmental and Learning Disorders (ICDL. Regulatory sensory processing disorder access 1. Diagnostic Manual for Infancy and Early Childhood (ICDL–DMIC). Bethesda, MD: Interdisciplinary Council on Developmental and Learning Disorders; 2005. p. 73–112.
[3] PDM Task Force. Psychodynamic diagnostic manual. Silver Spring, MD: Alliance of Psychoanalytic Organizations, 2006, IEC200 Series.
[4] Zero to Three. Diagnostic classification of mental health and developmental disorders of infancy and early childhood, revised. (DC:0–3R). Arlington, VA: National Center for Clinical Infant Programs; 2005. p. 28–9.
[5] Miller LJ, Anzalone ME, Lane SJ, Cermak SA, Osten ET. Concept evolution in sensory integration: a proposed nosology for diagnosis. Am J Occup Ther 2007;61:135–40.
[6] Reynolds S, Lane S. Diagnostic validity of sensory over responsivity: a review of the literature and case reports. J Autism Dev Disord 2008;38:516–29.
[7] Kinnealey M, Oliver B, Wilbarger P. A phenomenological study of sensory defensiveness in adults. Am J Occup Ther 1995;49:444–51.
[8] McIntosh DN, Miller LJ, Shyu V, Hagerman RJ. Sensory modulation disruption, electrodermal response and functional behaviors. Dev Med Child Neurol 1999;41:608–14.
[9] Schaaf RC. Parasympathetic nervous system functions in children with sensory modulation dysfunction: a preliminary study. Bell & Howell information and learning; 2001. p. 1–70.
[10] Fisher AG, Dunn W. Tactile defensiveness: historical perspectives, new research — a theory grows. Sens Integr Spec Interest Sect Newsl 1983;6:1–2.
[11] Reeves GD. From neuron to behavior: regulation, arousal, and attention as important substrates for the process of sensory integration. In: Roley SS, Blanche EI, Schaaf RC, editors. Understanding the nature of sensory integration with diverse populations. USA: Therapy Skill Builders; 2001. p. 89–108.
[12] Ayres AJ. Sensory integration and learning disorders. Los Angeles: Western Psychological Services; 1972.
[13] Bar- Shalita T, Vatine JJ, Parush S. Sensory modulation disorder: a risk factor for participation in daily life activities. Dev Med Child Neurol 2008;50:932–7.
[14] Brown C, Tollefson N, Dunn W, Cromwell R, Filon D. The adult sensory profile: measuring patterns of sensory processing. Am J Occup Ther 2001;55:72–82.
[15] Kinnealey M, Fuick M. The relationship between sensory defensiveness, anxiety, depression, and perception of pain in adults. Occup Ther Int 1999;6:195–206.
[16] Davis P, Galvin WJ. Validating the diagnosis of SMD using EEG technology. Am J Occup Ther 2007;16:176–89.

[17] Schaaf RC, Miller LJ, Seawell D, O'Keefe S. Children with disturbances in sensory processing: a pilot study examining the role of parasympathetic nervous system. Am J Occup Ther 2003;57:442–9.
[18] Hansson P, Baconga M, Bouhassira D. Usefulness and limitations of quantitative sensory testing: clinical and research application in neuropathic pain states. Pain 2007;129:256–9.
[19] Dyck PJ, Zimmerman I, Gillen DA, Johnson D, Karnes JL, O'Brien PC. Cool, warm, and heat-pain detection thresholds: testing methods and inferences about anatomic distribution of receptors. Neurology 1993;43:1500–8.
[20] McGrath PA, Brown SC. Quantitative sensory testing in children: practical considerations for research and clinical practice. Pain 2006;123:1–2.
[21] Bartlett G, Stewart JD, Tamblyn R, Abrahamowicz M. Normal distributions of thermal and vibration sensory thresholds. Muscle Nerve 1998;21:367–74.
[22] Hagander LG, Midani HA, Kuskowski MA, Parry GJG. Quantitative sensory testing: effect of site and skin temperature on thermal thresholds. Neurophysiol Clin 2000;111: 17–22.
[23] Dunn W. Sensory profile user manual. San Antonio, TX: The Psychological Corporation; 1999.
[24] Meier PM, Berda CB, Dicanzio J, Zurakowski D, Sethna NF. Quantitative assessment of cutaneous thermal and vibration sensation and thermal pain detection thresholds in healthy children and adolescents. Muscle Nerve 2001;24:1339–45.
[25] Thibault A, Forget R, Lambert J. Evaluation of cutaneous and proprioceptive sensation in children: a reliability study. Dev Med Child Neurol 1994;36:796–812.
[26] McIntosh D, Miller LJ, Shyu V, Dunn W. Overview of the Short Sensory Profile (SSP). In: Dunn W, editor. Sensory profile user manual. San Antonio, TX: The Psychological Corporation; 1999. p. 59–74.
[27] Dunn W. The sensory profile: caregivers' questionnaire. San Antonio, TX: The Psychological Corporation; 1999.
[28] Cohen J. Statistical power analysis for the behavioral sciences. NJ: Hillsdale, Erlbaum; 1988.
[29] Tal-Saban M, Yochman A, Parush S. Validity and reliability of the Sensory Profile in an Israeli population of children aged 3–6 years old. Isr J Occupat Ther 2002;11: H33–48.
[30] Cervero F, Meyer RA, Campbell JN. A psychophysical study of secondary hyperalgesia: evidence for increased pain to input from nociceptors. Pain 1994;58:21–8.
[31] Garnsworthy PK, Gully RC, Kenins P, Mayfield RJ, Westerman RA. Identification of the physical stimulus and the neural basis of fabric evoked prickle. J Neurol 1988;59:1083–97.
[32] Price DD, Bush FM, Long S, Harkins SW. A comparison of pain characteristics of mechanical visual analogue and simple numerical rating scales. Pain 1994;56:217–26.
[33] Bieri D, Reeve RA, Champion GD, Addicoat L, Ziegler JB. The faces pain scale for self -assessment of the severity of pain experienced by children: development, initial validation, and preliminary investigation for ratio scale properties. Pain 1990;41:139–50.
[34] Hicks CL, von Baeyer CL, Spafford PA, Korlaar IV, Goodenough B. The faces pain scale- revised: toward a common metric in pediatric pain measurement. Pain 2001;93:173–83.
[35] Goldberg JM, Lindblom U. Standardized method of determining vibratory perception thresholds for diagnosis and screening in neurological investigation. J Neurol Neurosurg Psychiatry 1979;42:793–803.
[36] Hagander LG, Midani HA, Kuskowski MA, Parry GJG. Quantitative sensory testing: effect of site and pressure on vibration thresholds. Neurophysiol Clin 2000;111:1066–9.
[37] Hilz MJ, Axelrod FB, Hermann K, Haertl U, Duetsch M, Neundorfer B. Normative values of vibratory perception in 530 children, juveniles and adults aged 3–79 years. J Neurol Sci 1998;159:219–25.
[38] Voerman VF, van Egmond J, Crul BJP. Elevated detection thresholds for mechanical stimuli in chronic pain patients: support for central mechanism. Arch Phys Med Rehabil 2000;81:430–5.
[39] Baumgartner U, Magerl W, Klein T, Hopf HC, Treede RD. Neurogenic hyperalgesia versus painful hypoalgesia: two distinct mechanism of neuropathic pain. Pain 2002;96: 141–51.
[40] Keizer D, van Wijhe M, Post WJ, Uges DRA, Wierda JMKH. Assessment of the clinical relevance of quantitative sensory testing with Von Frey monofilaments in patients with allodynia and neuropathic pain. A pilot study. Eur J Anaesthesiol 2007;24:658–63.
[41] Yarnitsky D, Sprecher E. Thermal testing: normative data and repeatability for various test algorithms. J Neurol Sci 1994;125:39–45.
[42] Yarnitsky D, Sprecher E, Zaslansky R, Hemli JA. Heat pain thresholds: normative data and repeatability. Pain 1995;60:329–32.
[43] Harrison JLK, Davis KD. Cold -evoked pain varies with skin type and cooling rate: a psychophysical study in humans. Pain 1999;83:123–35.
[44] Koniak-Griffin D, Verrzemnieks I. The relationship between parental ratings of child behaviors, interaction, and home environment. Matern Child Nurs J 1995;23:44–56.
[45] Schaughency EA, Lahey BB. Mothers' and fathers' perceptions of child deviance: roles of child behavior, parental depression, and marital satisfaction. J Consult Clin Psychol 1985;53:718–23.
[46] Biederman J, Mike E, Faraone SV, Braaten E, Doyle A, Spencer T, et al. Influence of gender on attention deficit hyperactivity disorder in children referred to a psychiatric clinic. Am J Psychiatry 2002;159:36–42.
[47] Bröring T, Rommelse N, Sergeant J, Scherder E. Sex differences in tactile defensiveness in chilren with ADHD and their siblings. Dev Med Child Neurol 2008;50:129–33.
[48] Parush S, Sohmer H, Steinberg A, Kaitz M. Somatosensory functioning in children with attention deficit hyperactivity disorder. Dev Med Child Neurol 1997;39:464–8.
[49] Turner G, Webb T, Wake S, Robinson H. Prevalence of the fragile X syndrome. Am J Med Genet 1996;64:196–7.
[50] Case-Smith J. The effects of tactile defensiveness and tactile discrimination on in hand manipulation. Am J Occup Ther 1991;45:811–8.
[51] Claus D, Hiltz MJ, Hummer I, Neundorfer B. Methods of measurement of thermal thresholds. Acta Neurol Scand 1987;76:288–96.
[52] Verdugo R, Ochoa JL. Quantitative somatosensory thermotest. A key method for functional evaluation of small calibre afferent channels. Brain 1992;115:893–913.
[53] Zeigler D, Mayer P, Wiefels K, Gries FA. Assessment of small and large fiber function in long-term type 1 (insuline-dependent) diabetic patients with and without painful neuropathy. Pain 1988;34:1.
[54] Kim JH, Greenspan JD, Coghill RC, Ohara S, Lenz FA. Lesions limited to the human thalamic principal somatosensory nucleus (Ventral Caudal) are associated with loss of cold sensations and central pain. J Neurosci 2007;27:4995–5005.
[55] Keizer D, van Wijhe M, Post WJ, Wierda JMKH. Quantifying allodyniain patients suffering from unilateral neuropathic pain using von Frey monofilaments. Clin J Pain 2007;23:85–90.
[56] Neddermeyer TJ, Fluhr K, Lotsch J. Principle components analysis of pain thresholds to thermal, electrical and mechanical stimuli suggests a predominant common source of variance. Pain 2008;138:286–91.
[57] Lindblom U. Analysis of abnormal touch pain and temperature sensation in patients. In: Boivie J, Hansson P, Lindblom U, editors. Touch temperature and pain in health and disease: mechanisms and assessment progress, vol. 3. Seattle WA: IASP press; 1994. p. 63–84.
[58] D'Mello R, Dickenson AH. Spinal cord mechanisms of pain. Br J Anaesth 2008;101:8–16.
[59] Parush S, Sohmer H, Steinberg A, Kaitz M. Somatosensory function in boys with ADHD and tactile defensiveness. Physiol Behav 2007;90:553–8.
[60] Campbell JN, LaMotte RH. Latency to detection of first pain. Brain Res 1983;266:203–8.
[61] Sinclair D. Mechanisms of cutaneous sensation. Oxford: Oxford University Press; 1981.
[62] Zeilhofer HU. Loss of glycinergic and GABAergic inhibition in chronic pain-contributions of inflammation and microglia. Int Immunopharmacol 2008;8:182–7.
[63] Price DD. Central neural mechanisms that interrelate sensory and affective dimensions of pain. Mol Interv 2002;2:392–400. http://intl-molinterv.aspetjournals.org.