Direct Observational and Biological Measurement of Reactivity to Sensory Stimuli for Use with and without Developmental Disabilities

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Emma Worthley

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Abstract

Given the inclusion of sensory reactivity as a diagnostic criterion for autism spectrum disorder (ASD) and the theorized etiological role of sensory reactivity in the development of autism, adequate sensory measures of sensory reactivity in autism, including measures extending to use in infancy, are needed. Adequate sensory measurement relies on the use of multiple methods of measurement. A scoping review of direct observational and biological measures of responses to sensory stimuli was conducted to identify plausible direct observational and biological measures of sensory reactivity for use with autistic samples. A direct observational measure of sensory reactivity was identified in the scoping review (a modified quantitative sensory testing approach) and implemented in two empirical investigations with different samples. The modified quantitative sensory testing approach was undertaken with a sample of children with and without autism (n=45, including eight autistic children) to investigate differences in tactile reactivity between children with and without autism. The modified quantitative sensory testing approach was then undertaken with a sample of typically developing children (n=34) to explore the relationship between subjective experience of tactile stimuli and behaviorally observed tactile reactivity. Through the scoping review, 111 articles reporting the use of a direct observational or biological sensory measure were identified, including 53 articles describing the use of behavioral measures of sensory reactivity, 18 articles describing the use of peripheral nervous system physiology measures of sensory reactivity, 47 articles describing the use of central nervous system physiology measures of sensory reactivity, and eight articles describing the use of circuits of sensory reactivity. The use of direct observational measure, the modified Quantitative Sensory Test (mQST), identified

differences in tactile reactivity to four tactile stimuli (light touch, pinprick, the last five seconds of the repeated von Frey, and heat), such that autistic children tended to demonstrate greater behavioral reactivity in response to these stimuli. The use of the mQST with typically developing children to interrogate the subjective experience of the mQST stimuli via self-report yielded negligible to weak correlations between subjective experience and direct observation of behavioral reactivity in response to the tactile stimuli but did, however, yield validity evidence for the use of the mQST in typically developing children. Overall, a wide variety of direct observational and biological sensory measures are available for use in autism research, with the potential to shed light on underlying mechanisms explaining differences in overt sensory behaviors.

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Chapter 1: Introduction

1.1 Overview

Assessment of sensory reactivity is important for individuals with neurodevelopmental disabilities (NDDs), particularly individuals with autism or intellectual disabilities with associated complex communication needs. Patterns of sensory reactivity (e.g., hyperresponsivity, hyporesponsivity, and sensory seeking) are included as diagnostic criteria of autism spectrum disorder (ASD) in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5;American Psychiatric Association, 2013). Individuals with intellectual disabilities are more likely to experience sensory problems and painful conditions due to co-occurring conditions (Valk & Walsh, 2008). Yet, children with intellectual disabilities are less likely than children without intellectual disabilities to be assessed and treated for pain, likely as self-report is a predominant method of pain assessment (Malviya et al., 2001). Careful consideration of sensory assessment tools that can be used across heterogeneous populations and extended to individuals with complex communication needs is needed.

1.2 Importance of Assessing Sensory Reactivity in Autism

Identifying sensory reactivity differences is essential for accurately diagnosing autism as well as exploring a potential factor in the etiology of autism. Sensory features of autism are defined as criteria for ASD in the Diagnostic and Statistical Manual of Mental Disorders, 5th ed., text-revision (DSM-5-TR) as “hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement”

(American Psychiatric Association, 2022). Differences in sensory reactivity were added to the diagnostic criteria for ASD in the DSM-5 (American Psychiatric Association, 2013) under the broader criteria of restricted, repetitive patterns of behavior.

1.2.1 Early Development

Understanding sensory reactivity differences is essential in early development, particularly in the first year of life. Sensory reactivity differences are evident as young as 12 months of age prior to the development of autism (Wolff et al., 2019). Differences in sensory reactivity during infancy have been associated with later phenotypic characteristics of autism, such as differences in social skills (Damiano-Goodwin et al., 2018; Worthley et al., 2023) and communication (Feldman et al., 2022). Importantly, beyond being associated with autistic behavioral characteristics, sensory differences during infancy have been implicated as a potential causal mechanism in the development of autism (Johnson et al., 2015). Johnson and colleagues (2015) postulate an ontogenetic adaptation framework for conceptualizing the development of autism, such that early sensory differences affect the experience of the infant and interactions with their environment that put the infant on an alternative developmental trajectory, resulting in autistic characteristics.

1.2.2 Intellectual Disability and Complex Communication Needs

The autism spectrum is widely heterogeneous, with a wide range of variability in language and cognitive levels (Georgiades et al., 2013; Munson et al., 2008). Individuals with lower cognitive levels (i.e., intellectual disability) and associated complex communication needs have historically been considered to have decreased sensitivity to pain (see Defrin et al., 2004). This ill-founded assumption, alongside the challenges of measurement approaches with individuals with complex communication needs and idiosyncratic sensory responses, results in individuals with intellectual disability being excluded from sensory assessment, resulting in inadequate pain management (Malviya et al., 2001). Not only are individuals with intellectual disability more likely not to have assessment and management of pain, but they are often altogether excluded from research. For example, autism research investigating somatosensory function often relies on self-report or motor responses and excludes participants with an IQ < 70 (see Fründt et al., 2017; Vaughan et al., 2020). Given the importance and relevance of sensory reactivity for autism, it is essential to have adequate sensory reactivity measurement tools for use across the heterogeneous autism spectrum.

1.3 Adequacy of Sensory Measures

A measurement tool's adequacy largely depends on its purpose and psychometric support for use in the intended population. Measurement tools are used for various purposes, including screening, diagnosis, assessment, and evaluation. Sensory measurement tools for use in screening and diagnosis are essential for the early identification and diagnosis of autism. Before sensory measurement tools can be recommended for use in infants and autistic children, sufficient psychometric evidence must be generated to demonstrate the adequacy of the tool. Lastly, adequate sensory measurement requires triangulation of measurement as it is well-agreed, across reviews of sensory assessments in autism and infants, that sensory assessments should include multiple types of measurement, such as pairing a caregiver-report assessment with a behavioral assessment (DuBois et al., 2017; Eeles et al., 2013; Schaaf & Lane, 2015; Yeung & Thomacos, 2020). In sum, adequate sensory measurement involves the use of multiple methods of sensory assessment, each supported by psychometric evidence for use with the intended population, aligned with the intended purpose (in this case, identify sensory differences characteristic of autism).

1.4 Current State of Affairs: Measuring Sensory Reactivity in Autism

Currently, sensory reactivity in autistic individuals is most commonly assessed using proxy-reported assessments, which measure caregiver or teacher reports of their child's behavior (Burns et al., 2017; DuBois et al., 2017; Schaaf & Lane, 2015; Yeung & Thomacos, 2020), such as the Short Sensory Profile (SSP; McIntosh et al., 1999a) and the Sensory Experiences Questionnaire (SEQ; Baranek et al., 2006). While caregiver-report questionnaires have advantages (e.g., ease of data collection), several issues need reconciliation. One issue is that there are currently no caregiver-report measures of sensory reactivity with sufficient psychometric evidence to support the recommendation of use with autistic individuals. However, the SEQ (Baranek et al., 2006), SAND (Siper et al., 2017), and BBCSS (Kolacz et al., 2018) are recommended with conditions (Gunderson et al., 2023). Another issue with caregiver-report questionnaires is that the information gathered is limited to inference-making at the behavioral unit of analysis, and inferences about sensory processing and perceptual signaling are not warranted. In other words, using proxy-report tools, we can say how the child *behaves* in response to sensory stimuli, but we cannot say anything about sensory processing or perceptual signaling.

1.5 Purpose and Research Questions

The purpose of this multi-paper dissertation study is to identify direct observational and biological types of sensory measures to inform how sensory reactivity might be measured, utilize a direct observational sensory assessment to investigate tactile reactivity differences among children with and without autism, and examine correlations between self-report and direct observation behavioral coding of a quantitative sensory measure of tactile reactivity in school-age children.

The research questions investigated were:

1. What direct observational and biological measures of sensory reactivity have been used in peer-reviewed research with young children (birth to <6 years) and individuals with complex communication needs?
2. To what extent do autistic children tend to differ in behavioral reactivity to tactile stimuli compared to children without autism?
3. To what extent does behavioral reactivity to tactile stimuli correlate with caregiver-reported tactile reactivity among children at a higher likelihood of developing autism?
4. To what extent are ratings of observed behavioral reactions to mQST stimuli correlated with self-reported experiences in typically developing school-aged children?
5. What patterns of tactile reactivity to mQST stimuli are observed among typically developing school-age children, and to what extent do patterns of tactile reactivity across mQST stimuli vary by age or sex among typically developing children?

Chapter 2: Direct Observational and Biological Measurement of Reactivity to Sensory Stimuli: A Scoping Review

2.1 Introduction

Since the addition of differences in sensory reactivity as diagnostic criteria for autism spectrum disorder (ASD) in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5, American Psychiatric Association, 2013), the need for sensory assessments with validity evidence supporting their use with autistic individuals is nigh. The use of sensory assessments in the last decade has greatly increased (DuBois et al., 2017), with proxy-report questionnaires being used as the majority assessment type (Burns et al., 2017; DuBois et al., 2017; Schaaf & Lane, 2015; Yeung & Thomacos, 2020). Most sensory assessment measures used, however, lack well-established psychometric properties, particularly for use with autistic individuals (Burns et al., 2017; Gunderson et al., 2023). Given the increased relevance and use of sensory assessments, lack of established psychometric evidence, and reliance on proxy-report measures, it is pertinent that sensory assessment in autism research and clinical application is considered in terms of direct observational and biological measurement and psychometric support.

Three main points will be discussed to set the stage for this review. First, an overview of the types of sensory measures used in autism research will be presented. Second, an additional framework to re-consider the conceptualization of sensory features of autism will be introduced. Finally, the importance of using direct observational and biological measures in sensory assessment in autism research will be argued.

2.1.1 Types of Sensory Measures Used in Autism Research

Across reviews of "sensory processing" assessments for infants (Eeles et al., 2013), autistic children (Yeung & Thomacos, 2020), and clinical assessments of "sensory features of autism" (Schaaf & Lane, 2015), sensory assessment types identified included (a) proxy report and (b) direct observation. In a review of sensory assessment approaches used with autistic adolescents and adults, five categories of assessment types were identified, including (a) self- and proxy-report questionnaires, (b) psychophysical assessment, (c) direct observational assessment, (d) qualitative interview techniques, and (e) neuroimaging, with some assessment approaches utilizing multiple measurement types (DuBois et al., 2017). Self-report, psychophysical assessment, and qualitative interview techniques will not be discussed here as they rely on self-report or motor function, and their use may not be extended across the heterogeneous autism spectrum or into infancy. Notably, sensory assessments utilizing psychophysical and neuroimaging measures were used with adult and adolescent samples but are lacking in published studies with autistic children. Without the use of biological measures (i.e., physiological and neuroimaging) to assess biological mechanisms of sensory reactivity with infants and autistic children, any inferences about sensory reactivity are limited to the level of behavior.

2.1.1.1 Proxy-Report

Proxy-report measures include any informant report, typically parents, caregivers, or teachers, such as the Sensory Experiences Questionnaire (Baranek et al., 2006) and the Sensory Profile (Dunn, 1994). Caregiver-report measures are the most common type of assessment used to measure sensory reactivity in autistic individuals (Burns et al., 2017;

DuBois et al., 2017; Schaaf & Lane, 2015; Yeung & Thomacos, 2020). Proxy-report measures have several strengths as assessment tools, including being easy to implement and collecting information about different aspects of sensory reactivity (e.g., different sensory modalities or contextual factors) in a short time (DuBois et al., 2017). Upon scrutiny of psychometric evidence supporting the use of proxy-report sensory measures with autistic individuals in a systematic review (Gunderson et al., 2023), no existing proxy-report measures adequately met the criteria for a recommendation of use with autistic samples; however, several measures, including the SEQ (Ausderau et al., 2014; Baranek et al., 2006; Lee et al., 2022; Little et al., 2011), Sensory Assessment of Neurodevelopmental Disorders (SAND; Siper et al., 2017), and the Brain-Body Center Sensory Scales (BBCSS; Kolacz et al., 2018) were recommended for use with conditions.

A few proxy-report measures of sensory reactivity in infants are used in published research, including the Sensory Rating Scale (SRS; Provost & Oetter, 1994), the Infant Toddler Sensory Profile (ITSP; Daniels & Dunn, 2000), and the SEQ (Baranek et al., 2006). The ITSP (Daniels & Dunn, 2000) was collapsed into the revised Sensory Profile-2 (SP2; Dunn, 2014), including an Infant Sensory Profile 2 (0 – 6 months) and a Toddler Sensory Profile 2, extending up to 35 months (Burns et al., 2017). Conversely, the initial SEQ (Baranek et al., 2006) extended to infants as young as 5 months of age, whereas the revised SEQ 3.0 only extends to toddlers as young as 2 years of age (Burns et al., 2017; Eeles et al., 2013; Yeung & Thomacos, 2020). Of these three proxy-report measures for infants, the use of the SEQ has the most psychometric evidence (Gunderson et al., 2023); however, the SEQ 3.0 no longer extends to infancy (see Burns et al., 2017; Eeles et al., 2013; Yeung & Thomacos, 2020). Thus, while proxy-report measures are widely used in autism research, psychometric evidence to support their use with autistic and infant populations is lacking.

2.1.1.2 Direct Behavioral Observation

Direct observational measures of sensory reactivity include a variety of techniques (e.g., measure of frequency of behavior, initiation, or sensory preference assessment) to quantify behaviors in response to sensory stimuli (DuBois et al., 2017; Eeles et al., 2013). While not as prevalent as proxy-report measures, direct observational measures are also used to assess sensory reactivity in autistic individuals (DuBois et al., 2017; Schaaf & Lane, 2015). A couple of direct observational measures of sensory reactivity in infants are used in published research, including the Test of Sensory Function in Infants (TSFI; DeGangi & Greenspan, 1989), and the Sensory Processing Assessment for Young Children (SPA; Baranek,1999).The TSFI is a norm-referenced measure for pediatric populations aged 4 to 18 months that assesses sensory defensive behaviors through evaluating tactile deep pressure, visual tactile integration, vestibular functions, and ocular motor control (DeGangi & Greenspan, 1989). The SPA is a semi-structured play-based observational tool to assess sensory response patterns (e.g., hyperreactivity, hyporeactivity) by measuring approach/avoidance, orienting, habituation, and sensory-seeking behaviors (Baranek, 1999).

2.1.1.3 Combined Proxy-Report and Direct Behavioral Observation

Direct behavioral observation and proxy-report measures may be designed to be paired or integrated into one unified assessment. For example, the observational measure, the SPA (Baranek, 1999), was designed to be used with the caregiver-report measure, the SEQ (Baranek et al., 2006). Another sensory measure for toddlers with autism, the SAND

(Siper et al., 2017), comprises caregiver-report and observational components. These combined measurement approaches have an advantage in providing information from different sources to inform the assessment.

2.1.1.4 Biological

Biological measurement approaches include physiological and neuroimaging tools. Although not necessarily included as sensory assessments, biological measures, including physiological and neuroimaging approaches, have been utilized in autism research.

2.1.1.4.1 Physiological. Physiological measures of sensory reactivity assess peripheral nervous system responses to sensory stimuli. For example, a physiological measure of a response to an auditory stimulus is to measure the change in heart rate in response to a loud, unexpected noise. Physiological measures such as electrodermal activity (EDA), heart rate (HR), and heart rate variability (HSV) have been used with autistic participants in at least 15 studies assessing physiological reactivity to sensory stimuli, including a wide range of participants from young children to adults (Lydon et al., 2016). DuBois et al. (2017) identified 18 physiological studies of sensory processing in autistic individuals; however, all studies included samples of autistic adolescents or adults. Lydon et al. (2016) found differences in physiological reactivity to sensory stimuli in nearly 80% of the studies that assessed physiological reactivity to sensory stimuli in an autistic sample. Furthermore, Lydon and colleagues found some evidence supporting an association between physiological reactivity to sensory stimuli and sensory behaviors. Physiological measures are important tools that can shed light on biological mechanisms underlying overt behavioral responses.

2.1.1.4.2 Neuroimaging. Neurophysiologic responses (i.e., physiological responses in the central nervous system) to auditory, tactile, and visual stimuli, including unimodal sensory processing and multi-sensory integration, have been measured using neuroimaging techniques (e.g., electroencephalography (EEG), magnetoencephalography (MEG), and functional Magnetic Resonance Imaging (fMRI; Marco et al., 2011). Marco et al. (2011) reviewed the literature on neurophysiologic studies of sensory processing in autism focused on unimodal sensory processing (e.g., auditory or tactile processing) and multi-sensory integration. Tactile processing was identified as a domain needing further exploration (Marco et al., 2011). However, neurophysiological measures often rely on self-report and are less often implemented with infants and very young children.

2.1.2 Sensory Constructs and Frameworks

It is also important to consider and define the sensory construct being measured in sensory assessment. There are multiple frameworks to consider sensory constructs. Two frameworks important for consideration regarding disability populations are (1) the disability category framework in the DSM-5-TR (American Psychiatric Association, 2022) and (2) the Research Domain Criteria (RDoC) framework from the National Institute of Mental Health (NIMH).

2.1.2.1 DSM-5 Disability Category Framework

From the disability category framework presented in the DSM-5-TR (American Psychiatric Association, 2022), the sensory construct of interest is ‘sensory features of autism’ and includes hyperresponsivity, hyporesponsivity, and sensory seeking. Hyperresponsivity is a heightened or exaggerated response to sensory stimuli (Baranek et al., 2006), for example, covering one’s ears upon hearing the vacuum. Hyporesponsivity is a diminished or muted response to sensory stimuli (Baranek et al., 2006), such as playing in the snow without mittens and having no adverse reaction. Sensory seeking is an unusual interest in sensory aspects of the environment (American Psychiatric Association, 2022), such as staring at spinning fans. This framework provides one way of conceptualizing the sensory features of autism.

2.1.2.2 Research Domain Criteria Framework

In addition to the categorical disability framework defined in the DSM-5-TR (American Psychiatric Association, 2022), the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) provides the potential for an additional framework to conceptualize measuring sensory responses that eschew diagnostic categories and seek to understand psychopathology in the context of basic human neurobehavioral functioning. An RDoC framework integrated with a categorical disability framework can handle issues related to heterogeneity, co-occurring diagnoses, understanding phenotypes across spectrums (including the part of the spectrum just short of meeting diagnostic criteria), and contextualizing environmental influences and developmental trajectories. The RDoC domains, however, currently need more adequate inclusion of sensory constructs, but NIMH encourages suggested additions. Harrison et al. (2019) make a compelling case for the inclusion of two classes of sensory symptoms in the RdoC matrix: (1) sensory processing (sensory sensitivity and active sensing) and (2) perceptual signaling (interoception and proprioception). These sensory constructs, sensory processing, and perceptual signaling may be essential to measure in addition to sensory constructs from the DSM-5 (i.e., hyperresponsivity, hyporesponsivity, and sensory seeking).

2.1.3 Units of Analysis

Careful consideration is also needed to clarify the sensory construct being assessed by a given measure, and the NIMH RDoC units of analysis may provide an insightful tool to clarify the sensory construct being measured. The RDoC framework outlines the following units of analysis: (a) self-report, (b) behavior, (c) physiology, and (d) circuits. Self-report as a unit of analysis will not be discussed as the focus of this review is to identify direct observation of behavior and biological measures.

2.1.3.1 Behavior

As a unit of analysis, behavior refers to both behavioral performance tasks and systematic observation of behavior. Examples of behavioral units in the RDoC include analgesia, eye blinks, hyposensitivity, repetitive behaviors, sensory arousal threshold, sensory reactivity, and visual acuity behavior, which can be assessed through measures of direct behavioral observation and coding systems.

2.1.3.2 Physiology

As a unit of analysis, physiology refers to measures of well-established indices of specific constructs (e.g., heart rate). Examples of physiological units included in the RDoC, but are not limited to, blood oxygenation level-dependent (BOLD) activation of cortical regions, breathing, EEG, fMRI, near infra-red spectroscopy (NIRS), pupillometry, and skin conductance. Physiology can be assessed using measures of physiological responses such as skin conductance response during presentation of sensory stimuli (e.g., Sensory Challenge Protocol (SCP; Miller et al., 2001)).

2.1.3.3 Circuits

As a unit of analysis, circuits refer to measures of specific circuits utilizing neuroimaging techniques or other measures validated by functional neuroimaging or animal models (e.g., somatosensory cortex). Examples of circuits (as a unit of analysis) in the RDoC include but are not limited to, ascending/descending information pathways, autonomic nervous system, sensorimotor-basal ganglia, sensorimotor-thalamus, and somatosensory cortex. Circuits can be assessed using neuroimaging techniques such as EEG during the presentation of sensory stimuli (e.g., Begum-Ali et al., 2021).

2.1.4 The Need for Direct Observational and Biological Measures

There are two primary reasons why direct observational and biological measures should be more widely used in autism research. First, given that it is well agreed that sensory assessment should optimally include multiple types of measurement, such as pairing proxy report with direct observation (DuBois et al., 2017; Eeles et al., 2013; Schaaf & Lane, 2015; Yeung & Thomacos, 2020), measures beyond proxy report, such as direct observational and biological measures, are needed. Second, direct observational and biological measures have the potential to measure constructs across different units of analysis, extending beyond the level of behavior to include physiology and circuits.

Extending inferences from sensory measures to sensory processing and perceptual functioning has the potential to shed light on underlying mechanisms that result in the sensory features of autism included as diagnostic criteria. Without such measures, we are left pondering about the level of behavior, ridden with many confounding variables such as socially learned responding, social expectations of the environment, and emotional state of the individual, to name a few, without understanding underlying mechanisms that may explain the behaviors. Direct observational and biological measures used in sensory assessment may contribute to understanding mechanisms underlying behavioral sensory reactivity in autism.

2.1.5 Purpose of the Literature Review

This scoping review aims to identify direct observational and biological measures of sensory reactivity that may be used with individuals who cannot reliably self-report, specifically young children (extending to infants) and individuals with complex communication needs. The primary research question guiding this review is: What direct observational and biological measures of sensory reactivity have been used with young children (birth to <6 years) and individuals with complex communication needs in peer-reviewed research? This includes a survey of their characteristics and key information on how sensory reactivity was measured through a direct observational or biological assessment. A scoping review approach will be taken as this review is a preliminary investigation into the potential size and scope of available observational sensory measures used in research with populations that cannot self-report (see Grant & Booth, 2009; Sutton et al., 2019). This review aims to create a menu of direct observational and biological sensory measures to encourage the field of autism research to add direct observational and biological measures to the widely used caregiver-report questionnaires in sensory assessments. Including more direct observational and biological measures in sensory assessments is essential for autism research as these measures may be able to measure sensory reactivity across different units of analysis, potentially yielding information about mechanisms underlying the sensory behaviors associated with autism.

This review is a starting point for evaluating observational measurement approaches that could be used with populations that cannot self-report.

2.2 Method

A scoping review of the peer-reviewed literature of empirical studies utilizing a direct observational or biological measure of sensory reactivity with samples of young children (birth to <6 years) or individuals with complex communication needs was conducted following guidance from the PRISMA extension for scoping reviews (PRISMA-ScR; Tricco et al., 2018).

2.2.1 Eligibility Criteria

The sources of evidence eligible for inclusion in this scoping review were peer-reviewed journal articles of empirical studies published in English, not limited by publication year. Published peer-reviewed journal articles, including an empirical study, were eligible for inclusion as the objective of this review was to identify sensory measures being used in research, with detailed methodology describing sensory measurement protocol (i.e., beyond the scope of abstracts or conference proceedings). The eligible studies were not limited by publication year as the objective of this review was to obtain a comprehensive list of direct observational and biological sensory measures, not limited to recent measurement trends.

2.2.2 Information Sources

Information sources included the following databases: APA PsycInfo, OVID Medline, CINAHL Complete, and the Web of Science Core Collection. Databases were selected to include perspectives from behavioral and social sciences, biomedical science, nursing, allied health, and a wide range of multidisciplinary work. The most recent search was executed on October 1, 2023.

2.2.3 Search

The full electronic search strategy for one database is described as an example of the search strategy executed in this scoping review. The search terms listed in Table 1 were used in the full electronic search strategy for APA PsycInfo. In Table 1, the first column denotes the two groups of search terms (sensory construct and population). The second column lists the search terms in the title, abstract, and key concepts fields. The third column lists the APA subject heading terms used in the subject headings field. The terms in the sensory construct and population rows were grouped by row in parentheses. The Boolean operation AND connected each group of terms represented by each row. The search was limited to full-text, peer-reviewed journals published in English. The search was not restricted by publication year. The search procedure executed in APA PsycInfo (2023, October 1) yielded $n_{PsycInfo} = 232$ articles. This search strategy was also implemented in OVID Medline, CINAHL Complete, and the Web of Science Core Collection, with database-specific subject headings for OVID Medline.

2.2.4 Selection of Sources of Evidence

The process for selecting sources of evidence was to compile the articles from the four database searches into Rayyan (Ouzzani et al., 2016), a title and abstract screening tool. Rayyan automatically identifies duplications, which the author then reviews and deletes. After removing the duplicates, all identified titles and abstracts were screened for inclusion. The full text of studies that could not be excluded based on the title and abstract screening were then assessed for eligibility.

2.2.4.1 Inclusion Criteria

The inclusion criteria for the selection of sources of evidence were: (a) an empirical journal article published in English in a peer-reviewed journal; (b) an article that described a study implementing the use of a direct observational or biological sensory measure, including measures of behavioral reactivity to sensory stimuli, such as the SPA (Baranek et al., 1999), physiological measures of responding to sensory stimuli, such as measuring skin conductance response to tactile stimuli, and central nervous system physiological measures of responding to sensory stimuli, such as recording auditory evoked potentials using EEG in response to tonal stimuli; (c) the direct observational or biological sensory measures described were used with young children (i.e., newborns, infants, and preschoolers; birth to <6 years) or individuals with complex communication needs. For studies that spanned a broader age range, if the age range of the study, or the mean age minus the standard deviation of age extended into the window of birth through five years of age, the study met inclusion criteria. If a study specified that the sample includes some individuals with complex communication needs, regardless of age, the study met the inclusion criteria.

2.2.4.2 Exclusion Criteria

The exclusion criteria for the selection of sources of evidence were: (a) published as a book, monograph, review paper, case study, commentary, or conference abstract; (b) an invasive procedure with the potential to expose participants to more than minimal risk; (c) sensory assessments which required participants to verbally respond, press a button, follow directions, or some other active task; (d) studies using a sensory questionnaire or caregiver-interview only; (e) studies with non-systematic observation of sensory features of sensory behaviors; (f) studies of sensory stimulation used for therapeutic purposes without a measure of sensory reactivity; (g) studies utilizing a direct observational or biological measure (e.g., fMRI) not in response to direct sensory stimuli; (h) experimental paradigms assessing higher-order sensory constructs (e.g., speech perception); (i) observational sensory measurement as a subscale on a broader measure; (j) description of sensory measure lacking details so it could not be replicated; or (k) direct observational and biological measures of sensory modalities not explicitly included in search terms (i.e., olfactory and gustatory).

2.2.5 Data Charting Process

Data from included studies were recorded using Qualtrics software (Qualtrics, 2023) using a coding scheme developed by the author based on the primary research question: What direct observational and biological measures of sensory reactivity are used in research with samples of young children (birth to <6 years of age) and individuals with complex communication needs? The first author completed data charting, which focused on reviewing the included studies' title, abstract, and method sections to assess the measurement procedures utilized with study participants.

2.2.6 Data Items

Variables included in data charting were primarily about the sensory measure used and the sample included in each study. Data were collected about the study, including APA citations, narrative citations, years of publication, and journals in which the study was published. Study conceptualization aspects such as the study purpose, research question about sensory measurement (if applicable), and purpose of including sensory measurement were recorded. Participant variables including sample size, average age and variance (mean ± standard deviation), age range, description of targeted participants for the study, description of any noted disability group represented in the sample, and selection of categorical participant groups (newborns, infants, preschoolers, and individuals with complex communication needs). Age groups were determined by referencing Kastner et al. (2006) and are defined as follows: newborns (birth to 1 month), infants (>1 month, <24 months), and preschoolers (2 years to <6 years). The categorical participant group, individuals with complex communication needs, was included if any of the participants in the study were described as having complex communication needs, including nonverbal and minimally verbal categories.

Sensory measure variables recorded included (a) the name of the sensory measure or a brief description of the experimental paradigm (e.g., EEG to measure auditory evoked potentials in response to repeated auditory stimuli); (b) a description of the variable being measured as a sensory reaction and how it was measured and recorded (e.g., heart rate in response to tactile stimulation measured by ECG recorded on a polygraph); (c) RDoC unit of analysis element (e.g., heart rate change); (d**)** measurement tool (e.g., electrocardiogram); (c) description of sensory stimuli; (d) a brief description of the purpose of the measure; (e) a description of the procedural implementation of the sensory measure; and (f) RDoC category of unit of analysis (i.e., behavior, physiology, or circuits). While physiology and circuit measures sometimes overlap (i.e., fMRI is measuring physiology but is also used to measure circuits), here they were categorized based on the results that were reported (i.e., changes in event-related potentials (ERP) after an auditory stimulus without specifying an RDoC circuit would be categorized as physiological whereas larger BOLD responses in the bilateral orbitofrontal cortex, striatum, pons, and cerebellum (RDoC circuits) would be categorized as circuits).

Data were also collected from the results reported in the study, including a description of any reported findings involving the direct observational or biological sensory measure and any psychometric evidence of the direct observational or biological sensory measure. Lastly, anything noteworthy for discussion, any noted strengths of the direct observational or biological sensory measure, or any noted challenges or weaknesses to the direct observational or biological sensory measure were recorded. These data items were recorded for all included studies in Qualtrics and exported as an Excel file.

2.3 Results

The search pulled in *n*=1,524 records. Records were marked as duplicates by automation tools in Rayyan (Ouzzani et al., 2016) and removed by the author. After de-duplication, *n*=1,226 records were retained. These 1,226 records were screened in a title/abstract screening that yielded *n*=338 included reports. The full-text studies for these 338 reports were retrieved and assessed for eligibility. The full-text screening for eligibility yielded *n*=111 studies included in the review. The search process results are outlined in a flow diagram in Figure 1.

2.3.1 Characteristics of Sources of Evidence

2.3.1.1 Study Level

The sources of evidence were characterized by the publication date and the discipline of the journal in which the article was published. Included sources of evidence were published between 1934 and 2023, with 2012 and 2020 being the years with the most included sources of evidence published (see Figure 2). Studies were published across a wide range of over 50 journals spanning more than 15 disciplines. The disciplines most well-represented across included studies were psychiatry (18%; e.g., Journal of Autism & Developmental Disorders), neuroscience (17%; e.g., Developmental Cognitive Neuroscience), pediatrics (17%; e.g., Developmental Medicine and Child Neurology), developmental psychology (14%; e.g., Developmental Psychobiology), and occupational therapy (8%; e.g., American Journal of Occupational Therapy). Overall, the studies included were published over a wide range of years (1934-2023) and across various disciplines (e.g., neuroscience and occupational therapy).

2.3.1.2 Participant Level

The sources of evidence were characterized by the participant groups (including newborns, infants, preschoolers, and individuals with complex communication needs) and sample size. Newborns (birth to 1 month) were included in 35% of study samples. Infants (>1 month, <24 months) were included in 48% of study samples. Preschoolers (2 years to <6 years) were included in 30% of the study samples. Individuals with complex communication needs were included in 3% of study samples (see Figure 3). Sample sizes for included studies ranged from 5 to 176, with the exception of two outliers with large sample sizes (see Figure 4). With the outliers removed, the median sample size was 40, and the interquartile range was 50.75. A majority of included studies (61%) had sample sizes greater than 30. Overall, infants were the most studied population, with a dearth of studies that included individuals with complex communication needs, and most studies did not have small sample sizes (i.e., majority of sample sizes were greater than 30).

2.3.1.2.1 Disability Groups. Studies were coded to describe the targeted participants, and disability groups were noted. Of the 111 included articles, 59% of articles were reports of studies conducted with a disability group (e.g., autism) or group with an increased likelihood of developmental delay or disability (e.g., preterm infants). Twenty studies (18%) included preterm or low birth weight infants as study participants (Anderson et al., 2001; Bart et al., 2011; Campbell-Yeo et al., 2012; Chorna et al., 2014; Cornelissen et al., 2013; Dumont et al., 2017; Ellingson, 1960; Hellerud & Storm, 2002; Lecuona et al., 2017, 2016; Lee et al., 2012; Leikos et al., 2020; Machado et al., 2023; Maimon et al., 2013; Maitre et al., 2020; Rahkonen et al., 2013; Roche-Labarbe et al., 2014; Rose et al., 1976; Vanhatalo et al., 2009; Wu et al., 2020). Twenty-seven studies (24%) included participants with autism or an elevated likelihood of developing autism. Sixteen of these studies included children with autism as study participants (Brock et al., 2012; Chang et al., 2016; de Bildt et al., 2012; De Meo-Monteil et al., 2019; Donkers et al., 2015, 2020; Espenhahn et al., 2021; Foss-Feig et al., 2012; Grzadzinski et al., 2020; Kirby et al., 2019; MacLennan et al., 2021; Mailloux et al., 2014; Rossow et al., 2021; Ruiz-Martínez et al., 2020; Siper et al., 2017; Watson et al., 2011; Woodard et al., 2012). Eight of these studies included infants or toddlers at elevated likelihood of developing autism due to various reasons, including Neurofibromatosis Type I (Begum-Ali et al., 2021), general population screening tool (Campi et al., 2022; Grzadzinski et al., 2021; Jatkar et al., 2023; Kinard et al., 2017), being a younger sibling of an older child diagnosed with autism (Damiano-Goodwin et al., 2018; Feldman et al., 2021; Riva et al., 2022), and a comparison of both community and familial samples (Baranek et al., 2018; Feldman et al., 2022). Preterm infants, children with autism, and infants/toddlers at elevated likelihood for autism were the disability/elevated likelihood for disability groups included most often.

In addition to these primary disability categories, 12 other disability categories were included among participant groups. These other disability groups included: (a) newborns with hypoxic-ischemic encephalopathy (HIE; brain injury) (Chen et al., 2002); (b) infants with Down's syndrome (Barnet et al., 1971; Chen & Fang, 2005); (c) infants with non-optimal obstetric conditions (Kittner & Lipsitt, 1976); (d) infants with pervasive developmental disorder (DeGangi et al., 2000); (e) children with "sensory" disorders, sensory processing disorder (Gavin et al., 2011; Schaaf et al., 2003) and sensory modulation disorder (Su et al., 2010); (f) children with fragile X syndrome (Baranek et al., 2002; Roberts et al., 2013); (g) children with cerebral palsy (Barney et al., 2019; Barrett & Jones, 1967); (h) children with seizure disorders (Dotto et al., 2014; Marco & Tassinari, 1981); (i) children with attention-deficit hyperactivity disorder (ADHD) (Mangeot et al., 2001); (j) children with global developmental delays (Barney et al., 2017); (k) children with myelodysplasia (cancer) (Dannenbaum & Dykes, 1984); and (l) adults with intellectual disability and communicative impairments (Symons et al., 2010). Overall, over half of the articles included a sample with a disability or elevated likelihood for disability group. While preterm infants and autism were most often represented, a wide range of disability groups were included.

2.3.1.3 Sensory Measurement Level

Each assessment method was characterized by the RDoc unit of analysis categories (e.g., physiology) and the sensory modality measured (e.g., auditory). RDoc unit of analysis categories included (a) behaviors, (b) physiology, and (c) circuits. Of the included articles, 45% included behaviors as a unit of analysis in response to sensory stimuli, 69% included physiology as a unit of analysis in response to sensory stimuli, 4% included circuits as a unit of analysis in response to sensory stimuli, with 16% of studies spanning multiple units of analysis (e.g., behaviors and physiology). Sensory modalities measured included (a) auditory, (b) tactile, (c) visual, or (d) multiple modalities. Of the sensory measures in the included articles, 50% included auditory stimuli, 58% included tactile stimuli, 43% included visual stimuli, and 30% included stimuli across multiple modalities. Overall, behaviors and physiology were more commonly measured than circuits, and each targeted sensory modality (auditory, tactile, visual) was well represented, with a small number of studies measuring across multiple units of analysis but a good proportion of sensory measurement approaches implementing sensory stimuli from more than one sensory modality.

2.3.2 Results of Individual Sources of Evidence

A variety of direct observational and biological measures of reactions to sensory stimuli were identified, primarily utilizing measures of behaviors and physiology. Table 2 charts and displays the primary characteristics of individual sources of evidence (narrative citation, targeted population, and observational sensory tool used) for all studies. The sensory measures were grouped by RDoC unit of analysis into the following categories: (a) behaviors, (b) peripheral nervous system (PNS) physiology, (c) central nervous system (CNS) physiology, and (d) circuits. Note that the RDoC does not distinguish between PNS and CNS physiology. Dividing physiology into PNS and CNS measures helped further categorize the vast physiology measures by those measuring reactivity in the brain (CNS) and the body (PNS).

2.3.2.1 Sensory Measures of Behaviors

The sensory measures of behaviors were described in terms of RDoC unit of analysis element, measurement tool, purpose (clinical or experimental), sensory stimuli, variable measured, the age range of participants, targeted participant population, and works cited in (Table 3). Among the many sensory measures of behaviors, a variety of RDoC behavioral elements were measured as a unit of analysis, including activity level, crying, disinhibition of early motor reflexes, eye blink, facial expressions, motor activity, and sensory reactivity, using behavioral observation/coding systems.

2.3.2.1.1 Sensory Reactivity. One-fourth of the studies included a measure of sensory reactivity. Sensory reactivity was most often measured through standardized clinician-administered play-based assessments (27 studies) but also measured through research-based behavioral observation/coding schemes (2 studies). Four clinician-administered observational assessments of behavior were identified, including the TSFI (DeGangi & Greenspan, 1989), Tactile Defensiveness and Discrimination Test-Revised (TDDT-R; Baranek, 2010), Sensory Processing Assessment (SPA; Baranek, 1999), and the Sensory Assessment for Developmental Disorders (SAND; Siper et al., 2017). The TSFI, a standardized tool developed to assess sensory responsiveness in infants aged 4–18 months, was used in *n*=10 studies. The TDDT-R, a standardized behavioral assessment with self-directed tactile play and experimenter-administered tactile stimulation to assess tactile defensiveness and discrimination for young children with developmental delays aged 3-12 years, was used in *n*=6 studies (half of which also used the SPA). The SPA, a play-based observational measure that assesses behavioral sensory patterns (hyper-, hypo-responsivity, and sensory seeking) across auditory, visual, and tactile modalities, was used in n=11 studies. The SAND, a standardized observational assessment paired with a caregiver interview to assess DSM-5 criteria for hypo-, hyper-responsivity, and sensory seeking for children with neurodevelopmental disorders, was used in n=3 studies. These assessments were primarily used for children with autism or at elevated likelihood for autism, but also used with children with developmental delays and typically developing controls.

2.3.2.1.2 Motor Activity, Facial Expressions, and Crying. Seventeen studies included sensory measures of motor activity, facial expressions, and/or crying as behavioral elements. These studies included a variety of infant studies, including pain in infancy, were often paired with a measure of physiology, and included the only studies with adults with complex communication needs.

2.3.2.1.2.1 Assessments of Pain Infancy. The measures of pain in infancy included four assessments: Modified Behavioral Pain Scale (MBPS; Taddio et al., 1995); Acuteness of the first cry, Burst rhythmicity, and temporal Constancy of cry intensity (ABC Scale; Bellieni et al., 2005); Behavioral Indicators of Infant Pain (BIIP; Holsti & Grunau, 2007); Premature Infant Pain-Profile (PIPP; Stevens et al., 1996); and Premature Infant Pain Profile-Revised (PIPP-R; Stevens et al., 2014). The MBPS is a tool with validity evidence supporting its use in measuring immunization pain in infants by rating facial grimacing, crying, and body movements on a pain scale from 0 (no pain) to 10 (intense pain) and was used with healthy infants to measure pain during immunizations to examine the efficacy of tactile stimulation in reducing pain (Hogan et al., 2014; Taddio et al., 2014). The ABC Scale is a tool with validity evidence supporting its use in measuring pain in newborns based on acoustic assessment of cry features (“Acuteness of the first cry, Burst rhythmicity and temporal Constancy of cry intensity") (Bellieni et al., 2005). The BIIP is a behavioral bedside assessment recording facial movements and hand actions before, during, and after a heel lance developed and validated for premature infants (Holsti et al., 2008; Holsti & Grunau, 2007). The PIPP is a seven-item, four-point scale that includes three factors (upper facial activity, physiological activity, and behavioral state) with validity evidence supporting its use to assess pain in premature infants (Stevens et al., 1996). The PIPP was revised to address feasibility and validity issues for use with extremely low gestational age infants (Stevens et al., 2014). The MBPS, ABC Scale, BIIP, PIPP, and PIPP-R were all used to measure medically necessary painful procedures in newborns and infants.

Most of these measures of pain were used to identify a group difference in responding to pain, typically an intervention group compared to a control group, but also including premature and full-term groups. The MBPS was used to investigate the efficacy of tactile stimulation on infant pain during routine painful procedures but did not detect differences between stimulation and control groups (Hogan et al., 2014; Taddio et al., 2014). The ABC Scale was sensitive to detecting differences in a sensorial saturation group, indicating less newborn pain during a heel lance (Bellieni et al., 2007). The BIIP was used to identify that early-born infants (born and tested at 28 weeks gestational age) had significantly lower BIIP scores during a heel lance than later-born infants (born and tested at 33 weeks gestational age); this difference, however, was not observed between early-born and later-born infants tested at 33 weeks (Maimon et al., 2013). The PIPP has been used to assess pain in premature and full-term healthy infants during medically necessary heel lance procedures (Campbell-Yeo et al., 2012; Eriksson et al., 2008;

Maimon et al., 2013). The PIPP-R was used with preterm infants during medically necessary venipuncture procedures (Wu et al., 2020). None of the assessments of pain were used with preschoolers, individuals with communication needs, or disability groups.

2.3.2.1.2.2 Modified Quantitative Sensory Test. Modified quantitative sensory testing (mQST) was used with adults with intellectual development and associated communication impairment (Symons et al., 2010), preschoolers with global developmental delay (Barney et al., 2017), and individuals with cerebral palsy and complex communication needs (Barney et al., 2020). The mQST protocol uses behavioral coding schemes to record behaviors associated with tactile reactivity during the application of calibrated, standardized tactile stimuli.

2.3.2.1.2.3 Other Experimental Paradigms. Various other experimental paradigms were used to measure motor activity as a behavioral element of a response to sensory stimuli, including movement, reaching, eye movements, and general behavioral activity.

2.3.2.1.3 Other Behavioral Elements. Other behavioral elements included were activity level, disinhibition of early motor reflexes, and eye blink. Activity level, as in the general movement of infants measured by a stabilimeter, was measured in response to auditory stimuli (Pratt, 1934). Disinhibition of early motor reflexes, specifically, the visual rooting reflex, was measured in individuals with autism (de Bildt et al., 2012). Spontaneous eye blinks during the presentation of visual stimuli with infants were measured as an index of central dopamine activity (Bacher & Smotherman, 2004). Overall, a variety of behavioral elements were assessed.

2.3.2.2 Sensory Measures of PNS Physiology

A variety of experimental paradigms utilizing measurement tools to assess PNS physiological responses to sensory stimuli were identified across *n*=20 articles (18% of included studies). Among the many sensory measures of PNS physiology, a variety of RDoC physiology elements were measured as a unit of analysis, including electromyography (EMG) response, eye blink reflex, galvanic skin response, heart rate change, respiration, skin conductance, and vagal tone. The sensory measures of peripheral nervous system physiology were described in terms of RDoC element, measurement tool, sensory stimuli, variable measured, the age range of participants, targeted participant population, and works cited in (Table 4).

2.3.2.2.1. Heart Rate Change. Heart rate change was the PNS physiological element most often measured in response to sensory stimuli. Seven studies measured heart rate change using ECG, biopotential electrodes, polysomnography, or the Sensory Challenge Protocol (SCP; Miller et al., 2001) in response to auditory stimuli (Anderssen et al., 1993; Brown et al., 1977; Kittner & Lipsitt, 1976; Roberts et al., 2013; Turkewitz et al., 1972), tactile stimuli (painful heel lance) (Owens & Todt, 1984), and multisensory stimuli (Schaaf et al., 2003). Three of these studies used newborn and infant populations (Kittner & Lipsitt, 1976; Owens & Todt, 1984; Rose et al., 1976).

2.3.2.2.2. Skin Conductance and Galvanic Skin Response. Skin conductance or galvanic skin response was measured as a response to sensory stimuli in five studies. The Sensory Challenge Protocol (SCP; Miller et al., 2001) was used to measure changes in skin conductance response to auditory stimuli in a sample of autistic children (Chang et al., 2012) and in response to multisensory stimuli in children with ADHD or "sensory modulation disorder" (Mangeot et al., 2001; Su et al., 2010). Additionally, galvanic skin response to routine blood sampling was measured in newborns and infants (Eriksson et al., 2008; Hellerud & Storm, 2002) .

2.3.2.2.3. Respiration. Respiration was measured as a response to auditory stimuli in three studies using polysomnography, a respiratory band, or a thermistor bead with a multichannel Grass polygraph (Anderssen et al., 1993; Mateus et al., 2018; Steinschneider, 1968). Respiration was only measured as a response to auditory stimuli. Respiration was measured in newborn and infant populations.

2.3.2.2.4. Other PNS Physiological Elements. The other measured PNS physiology elements included EMG response, vagal tone, and eye blink reflex. Vagal tone was measured in response to auditory stimuli in infants using a respiratory band (Mateus et al., 2018) and in response to multisensory stimuli in young children with "sensory processing disorder" using the SCP (Schaaf et al., 2003). EMG response was measured using EMG in newborns responding to auditory stimuli (Boyle & Hull, 1976) and responding to tactile stimuli (Cornelissen et al., 2013). Lastly, the eye blink reflex was measured using a transducer in response to auditory stimuli to assess auditory-evoked eyelid microvibration (EMV) in newborns, a reflex response indicative of brainstem function (Yamada, 1984).

2.3.2.3 Sensory Measures of CNS Physiology

Sensory measures of CNS physiology were used to assess sensory responses across $n = 44$ included articles. The RDoC physiological elements measured in the CNS included alpha, BOLD activation of cortical regions, delta, ERP, ERP components (P1, P300, P3a, N1, N2), local cerebral blood flow changes, mismatch negativity (MMN), oscillations, and theta. The tools used to measure CNS physiological responses included EEG, fMRI, neuro-MEPω EMG, and NIRS. Sensory measures of CNS physiology are described in terms of RDoC physiological element, measurement tool, sensory stimuli, variables measured, the age range of the sample, the targeted population of participants, and works cited (see Table 5).

2.3.2.3.1. Electroencephalography (EEG). A large number of studies utilizing EEG (*n*=26) across auditory, visual, tactile, and multisensory domains were included in this review. EEG was used to measure ERPs, ERP components, alpha, delta, and theta. Sixteen EEG studies measured ERP in response to sensory stimuli. Nine studies measured ERP components (N2, N1, P1, P300, or P3a). One study measured alpha, delta, and theta waves.

The most common domain assessed by EEG was auditory. Auditory evoked potentials were measured across nine studies, mostly with newborns and infants (Barnet et al., 1971; Cantiani et al., 2023; Lippé et al., 2009b; Ruusuvirta et al., 2003), including those at elevated likelihood of autism (EL-ASD; Begum-Ali, 2021). Auditory evoked potentials were also measured in autistic toddlers and preschoolers (De Meo-Monteil et al., 2019; Donkers et al., 2015, 2020; Ruiz-Martínez et al., 2020) and preschoolers with "sensory processing disorder" (Gavin et al., 2011).

Visual, tactile, and multisensory domains were also used in EEG studies. Visually evoked potentials were measured across five studies with various population groups, including typically developing infants (Ahtola et al., 2017, 2020; Lippé et al., 2007), preterm infants (Ellingson, 1960), and young children (extending to infancy) with West syndrome (Dotto et al., 2014). Somatosensory evoked potentials were measured across five studies, primarily with preterm infants (Leikos et al., 2020; Maimon et al., 2013; Vanhatalo et al., 2009) but also with typically developing infants (Meltzoff et al., 2019) and autistic preschoolers (Espenhahn et al., 2021). Lastly, four studies utilized multisensory testing paradigms to measure evoked potentials. Multisensory combinations included tactile and auditory event-related potentials in preterm infants (Maitre et al., 2020), auditory-visual event-related potentials in typically developing infants and preschoolers (Lippé et al., 2009a) and infants at elevated likelihood of autism (Riva et al., 2022), and multimodal evoked potentials across auditory, tactile, and visual stimuli in infants with Down's syndrome (Chen & Fang, 2005).

2.3.2.3.2. Near-Infrared Spectroscopy (NIRS). Next to EEG, NIRS was the measurement tool used most often to assess CNS physiological responses to sensory stimuli and was utilized across 13 studies. A variety of NIRS approaches, including functional NIRS, multichannel NIRS, and domain optical tomography (DOT), were used. NIRS was used to assess the RDoC physiological element of local cerebral blood flow changes.

NIRS was most often implemented with newborns and infants. Six studies utilizing NIRS to record responses to visual stimuli were implemented with newborns and infants (Karen et al., 2007; Kusaka et al., 2004; Watanabe et al., 2012), including explicitly awake newborns and infants (Goodwin et al., 2016; Meek et al., 1998; Taga & Asakawa, 2007). A total of five tactile NIRS studies were identified. Tactile NIRS studies were used in newborns during medically necessary painful procedures (Bartocci et al., 2006), newborns during tactile stimulation of their hand (Roche-Labarbe et al., 2014), infants during passive vibrotactile stimulation (Machado et al., 2023), and newborns and infants investigating reactivity to affective touch (Jönsson et al., 2018; Miguel et al., 2020). All three auditory NIRS studies investigated auditory-evoked cerebral blood oxygenation changes in newborns (Chen et al., 2002; Kotilahti et al., 2005; Sakatani et al., 1999). NIRS responses to tactile and visual stimuli were recorded in awake infants (Taga & Asakawa, 2007). NIRS responses to auditory, tactile, and visual stimuli were recorded in newborns (Shibata et al., 2012). NIRS was used almost entirely in typically developing newborns and infants, including awake newborns.

2.3.2.3.3. Functional Magnetic Resonance Imaging (fMRI). Three studies used fMRI to measure BOLD activation of cortical regions in response to auditory stimuli (Anderson et al., 2001; Born et al., 1998; Lee et al., 2012). fMRI was not used to measure BOLD responses to tactile, visual, or multisensory stimuli. All three fMRI studies were conducted with newborn and infant populations.

2.3.2.3.4. Electromyography (EMG). Although not included as a physiological element in RDoC, EMG was another tool used to measure a CNS response to sensory stimuli. One study used a Neuro-MEPω EMG approach to measure the RDoC physiological element, mismatch negativity (MMN), as a response to auditory stimuli in typically developing children aged 2 months to 5 years (Gupta & Bhardwaj, 2022). This approach looks at the ERP difference waveform generated by an ERP waveform elicited by a standard stimulus compared to that of a deviant stimulus.

2.3.2.4 Sensory Measures of Circuits

Sensory measures of circuits were used to assess tactile responses across $n = 7$ included articles. The RDoC circuits elements measured in the CNS included the cerebellum, orbitofrontal cortex, pons, somatosensory cortex, superior temporal sulcus, and striatum. The tools used to measure circuits included fMRI, functional near-infrared spectroscopy (fNIRS), MEG, and DOT. Circuits were only used to measure responses to tactile stimuli, not auditory, visual, or multisensory stimuli. Sensory measures of circuits are described in terms of RDoC element, measurement tool, sensory stimuli, variables measured, the age range of the sample, the targeted population of participants, and works cited (see Table 6).

2.3.2.4.1. Somatosensory Cortex. Somatosensory evoked magnetic fields were measured using MEG across four studies targeting contra- and ipsa-lateral primary (SI) and secondary (SII) somatosensory cortices and N1 cortical generators, in response to electrical stimulation on the wrist or finger taps (Lauronen et al., 2006; Nevalainen et al., 2008; Pihko et al., 2009; Rahkonen et al., 2013). These studies were conducted in various populations varying from extremely low gestational age (ELGA) infants to adults.

2.3.2.4.2. Orbitofrontal Cortex, Striatum, Pons, and Cerebellum. Connectivity networks of subcortical activation (neural correlates in response to affective touch) were measured across the orbitofrontal cortex, right ventral striatum, pons, and cerebellum using fMRI in typically developing newborns (Mariani Wigley et al., 2023).

2.3.2.4.3. Insular Cortex, Superior Temporal Sulcus, and Somatosensory Cortex. Total hemoglobin responses to affective touch using NIRS methods, specifically fNIRS or diffuse optical tomography (DOT), were identified in two studies using typically developing newborn participants. DOT was used to identify activation clusters of total hemoglobin responses in the insular cortex in response to affective touch in typically developing infants (Jönsson et al., 2018). fNIRS was used to measure local cerebral blood flow changes across the superior temporal sulcus and somatosensory region in response to affective touch in typically developing newborns (Miguel et al., 2020).

2.3.2.5 Overview of Results of Individual Sources of Evidence

The direct observational and biological measures of responses to sensory stimuli were categorized based on the following RDoC units of analysis: behaviors, physiology, and circuits. Among the 111 included articles, with some articles being multiply-counted if they used multiple measures, a measure of behaviors in response to sensory stimuli was utilized 53 times. Measures of PNS physiology in response to sensory stimuli were used 18 times. Measures of CNS physiology in response to sensory stimuli were used 47 times. Finally, measures of circuits in response to tactile stimuli were used seven times.

2.4 Discussion

The primary objective of this scoping review was to identify direct observational and biological measures of responses to sensory stimuli used in peer-reviewed research with young children (birth through age 5) and individuals with complex communication needs. This review is intended to function as a menu of direct observational and biological sensory measures that do not rely on self-report, to extend across heterogeneous populations such as autism that include individuals with complex communication needs, and extend across development into infancy.

The 111 empirical studies included in this review were categorized according to the RDoC units of analysis (behaviors, physiology, and circuits), with physiology further categorized into PNS and CNS physiology. As demonstrated in the results, the majority of sensory measures identified were used with newborn and infant populations, with a dearth of included studies for older individuals with individuals with complex communication needs (see Figure 3). This scoping review demonstrated that sensory measures of behaviors and physiology are widely used with young children.

2.4.1 Behavioral Sensory Measures

This scoping review demonstrated that sensory measures of behaviors, particularly 'sensory reactivity,' are widely used with young children. The RDoC behavioral element most often measured was 'sensory reactivity' in response various sensory domains, including auditory stimuli through researcher-developed behavioral observation/coding systems (e.g., Roberts et al., 2013), tactile stimuli using the TDDT-R (Baranek, 2010) (e.g., Donkers et al., 2015, 2020), and multisensory stimuli using the TSFI (DeGangi & Greenspan, 1989) (e.g., Feldman et al., 2021, 2022), SPA (Baranek, 1999) (e.g., Damiano-Goodwin et al., 2018), and SAND (Siper et al., 2017) (see (MacLennan et al., 2021). Both the SAND (Siper et al., 2017) and the SPA (Baranek, 1999) measure sensory reactivity in terms of DSM-5 criteria for ASD (hyperreactivity, hyporeactivity, and sensory seeking (American Psychiatric Association, 2013). Other more concrete RDoC behavioral elements such as activity level, crying, disinhibition of early motor reflexes, eye blinks, facial expressions, and motor activity were also assessed in response to sensory stimuli.

2.4.2 PNS Physiology Sensory Measures

This scoping review demonstrated that sensory measures of PNS physiology are used with newborns and infants, with a few identified instances of use with preschool-age children. Heart rate change was used as a measure of PNS physiology more often than other physiological elements and measured as a response to auditory stimuli (Brown et al., 1977; Kittner & Lipsitt, 1976; Roberts et al., 2013; Turkewitz et al., 1972), tactile stimuli (Owens & Todt, 1984), and multisensory stimuli (Schaaf et al., 2003). Other RDoC physiological elements such as eye blink reflex, EMG response, galvanic skin response, respiration, skin conductance, and vagal tone were also assessed in response to sensory stimuli. Notably, measures of PNS physiology were not identified for use as a response to auditory stimuli alone. Measures of PNS physiology were primarily used with newborns and infants. All studies identified using measures of PNS physiology with preschool-age children targeted disability groups, such as ADHD (Mangeot et al., 2001), autism (Chang et al., 2012), fragile-X syndrome (Roberts et al., 2013), "sensory modulation disorder" (Su et al., 2010), and "sensory processing disorder" (Schaaf et al., 2003). PNS physiological responses were measured in response to auditory, tactile, and multisensory stimuli but not to interrogate visual stimuli alone.

2.4.3 CNS Physiology Sensory Measures

This scoping review demonstrated that sensory measures of CNS physiology are widely used with newborns and infants. ERPs were used as a measure of CNS physiology more often than other physiological elements, and measured as a response to auditory stimuli (e.g., Lippé et al., 2009b), visual stimuli (e.g., Ahtola et al., 2017, 2020) , tactile stimuli (e.g., Espenhahn et al., 2021), and multisensory stimuli (e.g., Riva et al., 2022). Other RDoC elements of physiology measured in the CNS included alpha, BOLD activation of cortical regions, delta, ERP components (N1, N2, P1, P300, P3a), local cerebral blood flow changes, MMN, and theta.

2.4.4 Circuits Sensory Measures

Lastly, this scoping review identified only seven sensory measures of circuits. The RDoC circuits included were the somatosensory cortex, insular cortex, superior temporal sulcus, orbitofrontal cortex, striatum, pons, and cerebellum. Notable, all measures of circuits were limited to the tactile domain.

2.4.5 Relevance for Disability Groups

The sensory measures identified in this review have important implications for disability groups. This review was motivated, in part, by a pursuit of trying to understand the extent to which sensory responses may play an etiological role in the development of autism. For example, using the TDDT-R and SPA (alongside sensory proxy-report questionnaires) in a group of autistic pre-schoolers, Watson et al. (2011) claim that aberrant sensory processing may play an important role in the pathogenesis of autism and other developmental disabilities. While the claim of “aberrant sensory processing” is based on behavioral measures, inferences about sensory processing may not be warranted based on the behavioral evidence alone; however, these behavioral differences may be a signpost for investigating sensory responses at biological units of analysis (which could warrant inferences about sensory processing).

2.4.5.1 Implications for Measuring Sensory Reactivity in Autism

Sensory measurement is essential for children with autism in accessing support and services in the community, home-based services, and educational settings through disability policies such as Medicaid and Part B of the Individuals with Disabilities Education Act (IDEA, 2004). Diagnostic criteria for autism spectrum disorder include differences in sensory responsivity under the DSM-5-TR, defined explicitly as “hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment” (American Psychiatric Association, 2022). For young children with autism to access support and services in the community home-based services through Medicaid, they must be diagnosed with a disability (Chisolm et al., 2019). Similarly, for children with autism to receive special education services, they need to receive a school diagnosis of autism spectrum disorders. Diagnostic criteria, including differences in sensory responsivity, are vital for accessing care for children with autism. Having adequate measurement tools to aid in diagnosis is thus, in turn, key to accessing supports and services through disability policy requiring a diagnosis.

Beyond sensory measurement, it is also vital to adequately capture the framework conceptualizing sensory differences. The DSM-5-TR (American Psychiatric Association, 2022) conceptual framework of sensory features of autism as hyper-, hypo-responsivity, and sensory seeking may be limiting the understanding of sensory differences in autism by oversimplification. An alternative framework that eschews a priori diagnostic categories may provide a framework capable of handling the complexities of sensory reactivity. The National Institutes of Mental Health (NIMH) Research Domain Criteria (RDoC), a framework integrating basic neuroscience and behavioral research to investigate mental disorders, may be a promising future alternative (Clark et al., 2017). The RDoC framework, however, currently lacks adequate inclusion of sensory processing, but the RDoC is always open to suggested additions (Harrison et al., 2019). Harrison et al. (2019) make a compelling case for the inclusion of two classes of sensory symptoms in the RDoC matrix: (1) sensory processing (sensory sensitivity and active sensing) and (2) perceptual signaling (interoception and proprioception). While measurement tools such as the SPA (Baranek, 1999) and SAND (Siper et al., 2017) are aligned with a DSM-5 framework, experimental paradigms have the potential to measure sensory sensitivity and active sensing. A combination of measurement types may capture sensory reactivity defined in different frameworks.

2.4.6 Limitations

2.4.6.1 Generalizability

Limitations of this review include the limited parameters of scope. Related search terms such as sensory processing, sensory perception, or sensory function were not included. Measures of sensory domains such as oral and olfactory were not included. Participant groups such as those with profound intellectual impairments or motor impairments were not explicitly included and are also important groups to consider in the inclusion of measurement procedures. However, the scope of this review was already vast, necessitating the limitation of the parameters included.

Another feature of this review that limits the generalizability of findings is that the included articles were restricted to peer-reviewed research. This restriction of included materials is imbued with the file drawer problem. Namely, research that has been conducted but resulted in null findings was not included, thus adding a potential bias to the results.

2.4.6.2 Quality of Research Included

Another limitation of this review, and scoping reviews in general, is that quality indicators were not considered. A future direction could be a systematic review of a subset of observational measures evaluated with quality indicators for correlational designs (Thompson et al., 2005), a set of quality indicators with a heavy focus on methodology and measurement.

2.4.6.3 RDoC Framework

While the use of the RDoC framework to conceptualize categories of sensory measures based on units of analysis was a helpful way to categorize measurement types, there is room for improvement. First, there appears to be some overlap in physiology and circuits as units of analysis. The physiological elements included in the RDoC framework include measurement tools (e.g., EEG, fMRI, NIRS) while also including variables of measurement (e.g., ERP, BOLD activation of cortical regions, and local cerebral blood flow changes). Circuits elements included in the RDoC framework consist of brain regions (e.g., somatosensory cortex, cerebellum, pons) but do not include measurement types. Thus, the line dividing central nervous system physiology and circuits was unclear. Another obscure feature of the RDoC units of analysis is the inclusion of the behavioral element 'sensory reactivity.' Sensory reactivity is a vague behavioral element compared to other behavioral elements included in the RDoC framework, such as eye blinks or motor activity. For this review, the RDoC framework was consulted in part to anchor the conceptualization of "sensory reactivity" in more concrete terms, for example, discussing an increased level of BOLD activation of the somatosensory cortex in response to tactile stimuli, rather than discussing greater sensory reactivity.

2.4.7 Future Directions

Given the large number of articles screened and included, several systematic reviews could stem from this scoping review. One fruitful area for a systematic review would be identifying the EEG studies used to measure responses to sensory stimuli with newborns and infants. A broader systematic review could include measures of sensory responses utilizing all neuroimaging techniques, with reports of attempted and successful measurement collection. Another fruitful topic for a systematic review would be to focus on the physiological measurement tools. Lastly, a systematic review of clinician-administered direct observational assessments focusing on psychometric evidence would be helpful. Clinician-administered direct observational sensory assessments are widely reported in the literature. Still, these measures lack psychometric studies, and a systematic review could consolidate psychometric findings and identify assessments needing further psychometric investigation. Systematic reviews focused on these different measurement approaches could elucidate the quality of sensory measures.

2.4.8 Conclusion

In sum, a wide array of direct observational and biological sensory measures were identified for use in infants, toddlers, young children, and individuals with complex communication needs. In particular, 53 articles reported the use of sensory measures of behaviors, 18 articles reported the use of sensory measures of PNS physiology, 47 articles reported the use of sensory measures of CNS physiology, and seven articles reported the use of sensory measures of circuits. The autism research community could enhance autism research by borrowing sensory measures informed through an RDoC framework of behaviors, physiology, and circuits to aid in identifying sensory differences, with implications for early identification and diagnosis of autism. Perhaps most importantly, the results reporting the use of a wide array of sensory measures can help researchers think carefully about measurement tools and how they map onto constructs of interest. The results of this review can be used as a menu of sensory measures to put together a “sensory assessment dish” of complementary sensory measures more adequately capturing sensory constructs of interest than a standalone proxy-report measure that lacks validity evidence for use with autistic samples.

Chapter 3: A Natural Group Comparison of Observed Behavioral Reactivity to Tactile Stimuli Between School-Age Children with and without Autism

Estimated prevalence rates of differences in sensory reactivity among autistic samples compared to non-autistic peers is as high as 92% (Green et al., 2016). However, despite the inclusion of sensory hyper- or hyporeactivity as a diagnostic criterion for autism spectrum disorder (ASD) in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5; American Psychiatric Association, 2013) over a decade ago, no consensus on how to measure sensory reactivity in autistic individuals has been established. Sensory reactivity in autistic individuals is most commonly measured via proxy- or self-report measures (Burns et al., 2017; DuBois et al., 2017; Schaaf & Lane, 2015; Yeung & Thomacos, 2020). Direct observational measures of sensory reactivity have also been used in autism research, albeit much less frequently (DuBois et al., 2017; Marco et al., 2011). Direct observational measures have the potential to contribute to our understanding of sensory differences in autism using direct observation rather than proxy-report.

3.1.1 Limitations of Proxy-Reported Sensory Measures

There are three core issues with having a majority of sensory research in autism conducted with solely proxy-reported sensory measures. First, it is well-agreed across reviews of sensory assessments that using multiple forms of measurement is best practice in assessing sensory reactivity (DuBois et al., 2017; Eeles et al., 2013; Schaaf & Lane, 2015; Yeung & Thomacos, 2020), so reliance on proxy- and self-report measures alone is limiting. Second, none of the most commonly used proxy- and self-report measures being used have sufficient psychometric evidence to support the recommendation of their use with autistic individuals (Gunderson et al., 2023). Several proxy- and self-report measures have some psychometric evidence supporting their use and are identified as appropriate for use with conditions (Gunderson et al., 2023), including the SEQ (Ausderau et al., 2014; Baranek et al., 2006; Lee et al., 2022; Little et al., 2011), SAND (Siper et al., 2017), Brain-Body Center Sensory Scales (Kolacz et al., 2018), Sensory Perception Quotient (Tavassoli et al., 2014), and the Sensory Reactivity in Autism Spectrum (Elwin et al., 2016). Third, inferences generated from proxy- and self-report measures are limited to behavior (i.e., we can say how the child *behaves* in response to sensory stimuli). Inferences cannot be credibly extended from proxy-report measures to sensory perception, sensory function, and sensory processing.

3.1.2 Psychophysical Measurement: Quantitative Sensory Testing

Psychophysical methods can be used to go deeper than determining if there are differences in sensory behaviors and determine if there are differences in functional mechanisms underlying differences in sensory behavior (Vaughan et al., 2020). One psychophysical method, Quantitative Sensory Testing (QST), a series of psychophysical tests examining responses to a variety of calibrated thermal and mechanical stimuli, has been used in pain research to assess somatosensory function in adults and, more recently, in children (Tutelman et al., 2024). The use of QST dates back to 1966, but most research using QST has been conducted in the last decade (Tutelman et al., 2024).

The German Research Network on Neuropathic Pain developed a quantitative sensory testing (QST) protocol, including a standardized presentation of tactile stimuli testing for thermal detection and pain thresholds (including paradoxical heat sensations), mechanical detection and pain thresholds, dynamic mechanical allodynia, and pain summation (Rolke et al., 2006a, 2006b). The thermal detection threshold is the point at which a participant perceives a thermal stimulus, including cold and warm. The thermal pain threshold is the point at which the thermal stimulus becomes noxious. Paradoxical heat sensation is a sensory phenomenon in which mild cooling is perceived as a hot sensation (Vaughan et al., 2020) and indicates disturbances in Aδ-cold fiber function (Rolke et al., 2006a). The mechanical detection threshold is the point when an individual perceives a mechanical stimulus (i.e., touch, vibration), and the mechanical pain threshold is the point when mechanical stimuli (i.e., pinprick, pressure) become noxious to the participant. Mechanical detection thresholds represent Aβ-fiber function (Rolke et al., 2006a) Dynamic mechanical allodynia is pain induced by stroking movements on the skin that are typically experienced as innocuous (Koltzenburg et al., 1992) and indicates central sensitization (Rolke et al., 2006a). Temporal pain summation considered a measure of central gain of pain, is an increase in pain after repeated painful stimuli due to a wind-up process in which pain becomes integrated across repeated applications and becomes more painful at the end of the repeated application (Arendt-Nielsen et al., 2018).

The QST protocol assesses nerve fiber function across the full range of somatosensory functions (Rolke et al., 2006a). Aβ-fiber function is assessed by mechanical detection thresholds to von Frey hairs and vibration. Aδ-fiber function is assessed by cold detection threshold, mechanical pain threshold (pinprick), and paradoxical heat sensations. C-fiber function is assessed by warm detection threshold and heat pain threshold. Temporal summation is assessed using the wind-up ratio for pinprick. Thus, the QST protocol assesses Aβ-, Aδ-, and C-fiber function.

3.1.3 Quantitative Sensory Testing with Autistic Samples

The full QST battery has only been used with autistic samples in two studies. Fründt et al. (2017) and Vaughan et al. (2020) utilized the QST protocol developed by Rolke et al. (2006a) and implemented somatosensory parameters (e.g., thermal and tactile detection) with autistic adults (without intellectual disability) and healthy controls. Fründt et al. (2017) did not find group differences between somatosensory detection and pain thresholds between autistic and non-autistic participants. In contrast, Vaughan et al. (2020) identified higher thresholds for light touch detection and pain among the autistic group. The autism groups in both studies demonstrated increased variability in responding to QST parameters compared to the control groups. Both Fründt et al. (2017) and Vaughan et al. (2020) identified the presence of somatosensory features, paradoxical heat sensations, and dynamic mechanical allodynia among autistic participants but not among healthy controls, concluding that somatosensory differences in autism result from central mechanisms during sensory integration rather than peripheral dysfunction. Notably, the results from both of these studies are limited by a small sample size (each had a sample of 13 autistic adults).

In addition to the use of the full QST battery with autistic samples, several studies have used psychophysical methods to assess tactile reactivity with samples of autistic individuals. Thresholds for detecting light touch, warmth, and cool sensations were found to be similar across groups of adults with and without autism (Cascio et al., 2008). Adults with autism were found to have lower thresholds for detecting high-frequency (i.e., hypersensitive) but not low-frequency vibration (Blakemore et al., 2006); However, thresholds for detecting high and low-frequency vibration were similar across children with and without autism (Güçlü et al., 2007). The mixed findings from psychophysical methods used to assess tactile reactivity in autistic samples may reflect differences in the age of samples, methods used, or limits by small sample sizes.

3.1.3.1 Limitations to Quantitative Sensory Testing with Autistic Samples

In the assessment of heterogeneous populations such as autistic individuals, it is paramount to consider that the population includes a vast range of intellectual functioning, complex communication needs, and motor differences. It is paramount that measurement approaches used with heterogeneous populations can be used across the full range of the population. A significant limitation to utilizing the QST battery with autistic populations is that the task requires participants to report when stimuli are detected and become painful, which precludes its use among young children and individuals with significant intellectual disability and complex communication needs. For example, both Fründt et al. (2017) and Vaughan et al. (2020) excluded participants with an IQ < 70.

3.1.3.2 Quantitative Sensory Testing Modified to Accommodate Heterogeneity

A modified implementation of the QST battery was developed by Symons et al. (2010) to broaden its feasible implementation to individuals with intellectual disabilities. More specifically, the modified QST (mQST) was modified to not rely on self-report or reaction time so that it could be used with individuals with a wide range of communication skills and motor functions. The mQST has been used with various disability groups, including intellectual disability (Symons et al., 2010), pediatric developmental delay (Barney et al., 2017; Symons et al., 2022), Rett syndrome (Merbler et al., 2020), and cerebral palsy (Barney et al., 2020). Symons et al. (2010) established initial validity evidence for the use of the mQST with adults with moderate to profound intellectual impairment. Barney et al. (2017) found the mQST procedures feasible to implement with young children with global developmental delays. Although the mQST has not been used in a study explicitly investigating tactile reactivity in autism, Barney et al. (2017) included five autistic children (13% of the sample). Thus, initial validity and feasibility evidence for the use of mQST with disability groups has been established. Still, the approach has not been used with an autistic sample compared to a control group.

3.1.4 The Present Study

The primary aim of this study was to conduct a preliminary investigation of the tactile reactivity differences among school-age children with and without autism spectrum disorder (ASD). The primary hypothesis is that autistic children, on average, will show increased behavioral reactivity to tactile stimuli compared to children without autism. This study's secondary aim was to explore associations between observed tactile reactivity to mQST stimuli and caregiver-reported tactile reactivity via the Sensory Experiences Questionnaire (SEQ 3.0; Baranek et al., 2009) among the participants with a high familial likelihood of autism.

3.1.4.1 Research Questions

1. To what extent do autistic children tend to differ in behavioral reactivity to tactile stimuli compared to children without autism?
2. To what extent does behavioral reactivity to tactile stimuli correlate with caregiver-reported tactile reactivity among children at a higher likelihood of developing autism?

3.2 Method

Data in this study were collected as part of a prospective, longitudinal study of brain and behavior development in children with high and low familial autism likelihood from the Autism Center of Excellence (ACE) Network Infant Brain Imaging Study (IBIS). Participants were recruited, screened, and assessed at one of four clinical sites, including the University of North Carolina—Chapel Hill, Children's Hospital of Philadelphia, University of Washington, and Washington University. The Institutional Review Board for each study site approved study procedures. Written and informed caregiver consent was obtained for all participants.

3.2.1 Participants

Participants in this study were selected utilizing an infant siblings recruitment paradigm such that two groups of participants were recruited: (a) those with a biological, older sibling diagnosed with autism (higher familial likelihood), and (b) those with a typically developing older sibling with no immediate family history of autism or developmental disabilities (lower familial likelihood). This sampling strategy was utilized to increase the number of autistic participants in the study, as younger siblings of a child with autism are more likely to go on to be diagnosed with autism than children with no immediate family history of autism (Constantino et al., 2010; Ozonoff et al., 2011). Demographic characteristics of participants are displayed in Table 7.

3.2.1.1 Inclusion and Exclusion

Participants included school-age children with and without autism (from both high- and low-familial likelihood groups) who completed the mQST at their school-age visit. The inclusion criteria at enrollment for the high-familial autism likelihood group included infants as young as 6 months with an older biological sibling diagnosed with ASD. The proband ASD diagnosis was confirmed using the Autism Diagnostic Interview-Revised (ADI-R; Lord et al., 1994) and Social Communication Questionnaire (SCQ; Rutter et al., 2003). The inclusion criteria at enrollment for the low-familial autism likelihood group included infants as young as 6 months without any older biological siblings diagnosed with ASD. The inclusion criteria for this study included completing the diagnostic assessment and mQST at school age.

Participants were excluded if they met any of the IBIS exclusionary criteria. IBIS exclusionary criteria included: (a) evidence of a genetic syndrome or condition; (b) significant neurological or medical condition affecting physical or cognitive development; (c) significant hearing or vision impairment; (d) gestational age <36 weeks or birth weight <2,000 g; (e) exposure to neurotoxins in utero or other significant perinatal adversity; (f) contraindication for magnetic resonance imaging (MRI); (g) primary home language other than English; (h) different biological parents than older sibling with autism; (i) first-degree relative with schizophrenia, bipolar disorder, or psychosis; and (j) twins. Parent-report, including the Family Interview for Genetic Studies (Maxwell, 1992), was used to confirm exclusionary criteria.

3.2.2 Measures

The primary measure used in this study was the modified Quantitative Sensory Test (mQST; Symons et al., 2010). Secondary measures included the Autism Diagnostic Observation Scale, 2nd edition (ADOS-2; Lord et al., 2000), Autism Diagnostic Interview-Revised (ADI-R; Lord et al., 1994), and Sensory Experiences Questionnaire (SEQ 3.0; Baranek et al., 2009).

3.2.2.1 Autism Diagnostic Tools

3.2.2.1.1. Autism Diagnostic Observation Scale. The Autism Diagnostic Observation Scale, 2nd Edition (ADOS-2; Lord et al., 2000) is a semi-structured assessment that is a systematic method for directly observing social and communication behaviors through social presses in structured and unstructured play sessions. Research-reliable administrators implemented the ADOS-2 to inform ASD diagnoses for participants during their school-age visits.

3.2.2.1.2. Autism Diagnostic Interview-Revised. The Autism Diagnostic Interview-Revised (ADI-R; Lord et al., 1994) is a semi-structured, standardized caregiver interview designed to ask caregivers about behavioral features of autism. The ADI-R was administered at the school-age visit (approximately 10 years of age) to inform clinical diagnoses further.

3.2.2.2 Sensory Measurement Tools

3.2.2.2.1. Modified Quantitative Sensory Test. The modified Quantitative Sensory Test (mQST; Symons et al., 2010) is a sham-controlled sensory-testing protocol to measure behavioral reactivity to tactile stimuli that is not dependent on self-report. The mQST utilizes a stimulus-response method such that stimuli are applied at a consistent, known intensity, and participant's behavioral reactions are quantified utilizing a modified Face, Legs, Activity, Consolability and Cry (FLACC) behavioral coding system (Merkel et al., 1997). The stimuli used in the mQST were selected to align with conventional QST protocol (Rolke et al., 2006a, 2006b).

3.2.2.2.2. Sensory Experiences Questionnaire. The Sensory Experiences Questionnaire, version 3.0 (SEQ; Baranek et al., 2009), is a caregiver-report questionnaire to characterize sensory features among children ages 2 – 13 years with autism and developmental disabilities (DD). The SEQ (Version 3.0) includes 105 items across four sensory response patterns (i.e., hyporesponsiveness, hyperresponsiveness, sensory interests, repetitions and seeking behaviors, and enhanced perception). The SEQ quantifies the frequency of a child's sensory behaviors using a 5-point rating scale (1 = *Almost Never* to 5 = *Almost Always*) across 92 items. The SEQ (Version 3.0) also produces sensory modality scores (i.e., tactile, auditory, visual, gustatory/olfactory, and vestibular/proprioceptive). The SEQ tactile modality score comprised of 23 items was the only SEQ score to be used in the present analysis.

In a sample of 258 children with autism or DD, the 21-item SEQ (Version 1.0) demonstrated acceptable to good internal consistency, with a Cronbach's alpha value of $\alpha = 0.80$ for overall internal consistency (Baranek et al., 2006; Little et al., 2011). Test-retest reliability analyzed using intraclass correlation coefficients (ICC) of the SEQ (Version 1.0) with n=24 participants was found to be excellent, with ICC = .92 (Little et al., 2011). The factor structure of the SEQ (Version 3.0) was assessed using a confirmatory factor analytic model with a national sample of 1,307 autistic children aged 2 – 12 years and found to have good model fit.

3.2.3 Procedures

Data were collected through Qualtrics surveys and in-person behavioral and neuroimaging visits across the four study sites. Data collection was interrupted by the COVID-19 pandemic, resulting in 37% of the school-age visits being limited to online data collection during the pandemic. As lock-downs ended, data collection for the mQST was further limited as the mQST protocol could not be implemented until personal protective equipment (PPE; e.g., masks, MAXAIR CAPR respirators) restrictions were lifted from study sites, which only occurred for some sites. The interruption of COVID-19 resulted in a limited collection of mQSTs during the course of the study.

3.2.3.1 Modified Quantitative Sensory Test

3.2.3.1.1. Setting. The mQST was conducted in a private research space at one of the four study sites. The participant, at least one caregiver, and the mQST examiner were present for data collection. The participant sat on a chair pushed into a table with their right forearm facing up on the table, with the examiner sitting to the participant's side. The stimuli were located on a tray behind the participant and out of their sight. Two cameras filmed the protocol: one camera was set up directly across from the participant, filming their body from the tabletop up, including the arm with the stimuli application, and one camera filmed a close-up of their face. All videoed procedures included a 30-second baseline and 10-second wind-down time.

3.2.3.1.2. Stimuli. The mQST protocol consisted of six calibrated sensory stimuli (light touch, pinprick, cool, pressure, repeated Von Frey, and heat) and a sham trial. Stimuli were applied at a known, consistent intensity (not intended to be noxious) across participants. All stimuli were applied to the right volar forearm for 5 s, except the longer application of the “repeated von Frey” stimulus (30 s). All stimuli were applied to the volar forearm due to the site’s previous use in somatosensory work broadly (e.g., de Knegt et al., 2015) and ASD specifically (Cascio et al., 2008), the presence of a large muscle belly required for some stimuli (e.g., pressure, see Rolke et al., 2006a), and the ability to conduct the mQST with minimal staffing.

The sham stimulus includes holding a closed 2.0 g von Frey monofilament approximately 1 in. (2.54 cm) from the participant's arm without touching it for 5 s, consistent with the other stimuli, but without physical touch. The light touch stimulus was a 2.0 g von Frey monofilament applied to the skin by pushing the filament straight down until it bends and lifting back up, repeating five times at a rate of 1 Hz. The pinprick stimulus was applied by bringing a plastic neurological exam pin (Medipin; US Neurologicals) to the participant's forearm in a continuous motion, stopping an inch away, applying straight forward to touch the skin, and immediately pulling back, holding the pin near the arm without touching it for the remainder of the 5 s application. The cool stimulus was a room-temperature metal thermal probe (approximately 22 ºC; Tip Therm; US Neurologicals) applied by holding the cool probe flat against the participant's forearm and maintaining light contact for the entire 5 s. The pressure stimulus was applied by pushing an algometer (Wagner Instruments) into the participant's forearm at 4 lb of pressure. The repeated von Frey stimulus was a 60 g von Frey monofilament applied to the skin by pushing straight down until the filament showed a deep bend, pulling straight up, then repeating 30 times at a rate of 1 Hz. The heat stimulus was a 3 mm electronic thermal probe (WR Medical Electronics) set to 50 ºC applied with light, even contact perpendicular to the skin for a maximum of 5 s.

3.2.3.1.3. Implementation. Once the child was seated in the chair, both video cameras were turned on to record baseline behaviors for 30 s before the examiner began the sensory test. The examiner, blind to participant diagnosis, starts the sensory test by greeting the participant and telling them they will move onto the "touch test" and touch their arms with a few different touches. Each stimulus was applied to the right volar forearm, 1/3-1/2 up the forearm from the wrist (Cascio et al., 2008). Stimuli were presented in the same order for all participants: sham, light touch, pinprick, cool, pressure, repeated Von Frey, and heat. The examiner used verbal cues for each stimulus application to indicate to behavioral coders when the stimuli were applied but without signaling the stimulus type or the exact application time for participants. For each stimulus, the examiner said the number of the stimuli, starting with zero for sham to six for heat, waiting for 5 s, applying the stimulus silently, then saying "off" immediately after the application was removed. The examiner waited 10 s or longer if the participant needed a break before starting the next stimulus.

3.2.3.1.4. Behavioral Coding. Each participant's behavioral reactivity scores for each stimulus were quantified using a modified Face, Legs, Activity, Cry, Consolability (FLACC; Merkel et al., 1997) observational coding system. FLACC behavioral coders were blind to participant diagnostic information and the type of stimuli being applied. Coders scored reactivity across five behavior classes, including (a) upper facial expressions (e.g., eyebrow raise or closing eyes); (b) lower facial expressions (e.g., stretching mouth or thrusting tongue); (c) movement of the limb being touched (e.g., moving the right arm away from stimulus or flinches in that arm); (d) whole body activity (e.g., scooch chair away from examiner or postural change) and; (e) vocalizations (e.g., "that tickles" or whimper). Two repeated von Frey scores were quantified to account for the longer application length of the repeated von Frey monofilament (30 s) compared to the 5 s duration of all other stimuli: one score for the first 5 s of the repeated von Frey and a second score for the last 5 s of the repeated von Frey. The repeated von Frey application was included as a hypothesis of potential temporal summation (Rolke et al., 2006b). Behavioral reactivity was scored relative to the participant's baseline behavior. For example, if a participant had a furrowed eyebrow during most of the baseline, furrowing their eyebrow while applying a stimulus would not be scored as a reaction to the stimuli unless the intensity increased.

Scores for each behavior class for each stimulus application were rated on a 3-level rating scale (0 = *baseline or no expression; 1 = behaviors occur for less than half of the application, have neutral or positive valence of moderate intensity and short duration;* 2 = *behaviors occur for more than half of the application, involve large movements, increase in frequency or intensity, or have negative valence*). Scores across all five behavior classes were summed to create a reactivity score ranging from 0 to 10 for each stimulus.

3.2.3.1.5. Measurement Reliability. FLACC coders scoring the mQST behavioral reactivity were trained to a 90% criterion with the lead coder. Secondary coding was conducted on 22 of the 45 mQSTs collected with usable data (48%) to calculate inter-observer agreement (IOA). Two of the videos coded for IOA were consensus-coded. IOA was calculated as the percent exact agreement at the level of each behavioral category for each stimulus (e.g., light touch upper face score). IOA ranged from 62.0 to 97.5%; the average IOA was 89.5% (*SD* = 8.8%).

3.2.4 Data Analysis

Given the sample size, analyses were limited to visual exploratory analysis and tests of group differences. Participants were excluded post-data collection due to missing video footage of the mQST or examiner error during the mQST, otherwise all usable data were retained.

3.2.4.1 Data Diagnostics

The distributions of mQST and SEQ variables were explored visually through histograms and computationally through measures of skewness, and kurtosis. Skewness was interpreted according to the following categories: approximately symmetric/low skew (absolute values ranging from 0 to 0.5), moderate skew (absolute values ranging from 0.5 to 1), and highly skewed (absolute values greater than 1). The calculation of kurtosis yields an interpretation such that the kurtosis of the normal distribution is 0.

3.2.4.1.1. mQST Data. Total reactivity scores for each mQST stimulus were derived by creating total scores for application during the left arm and application during the right arm. The total scores for the left arm and right arm were summed and divided by two to create an average total reactivity score across limbs. The distributions of the averaged mQST total reactivity scores for each stimulus were examined visually via histograms and computationally via skewness and kurtosis.

The distributions of observed behavioral reactivity scores to mQST stimuli visualized in the histograms (Figure 5) illustrate positively skewed distributions for all stimuli. The skewness of reactivity scores to mQST stimuli ranged from 0.574 to 1.164, indicating that all distributions were moderately to highly positively skewed. All distributions were moderately skewed (ranging from 0.5 to 1) except for the last 5s of the repeated stimulus, which was highly skewed (>1). Table 8 displays the skewness of reactivity scores to each mQST stimulus.

The kurtosis of reactivity scores across mQST stimuli ranged from –0.91 to 1.30, indicating that all distributions were more or less mesokurtic (i.e., containing a similar number of outliers as the normal distribution). The distributions of reactivity scores to sham, pin, pressure, and heat were negative, indicating that those distributions were on the platykurtic side (i.e., producing fewer outliers than the normal distribution). The kurtosis of reactivity scores to light touch, cool, and repeated were all positive, indicating that those distributions were on the leptokurtic side (i.e., containing more outliers than the normal distribution). None of the distributions, however, had excess kurtosis. Table 8 displays the kurtosis of reactivity scores for each mQST stimulus.

As the distributions of behavioral reactivity scores for each mQST stimulus were right-tailed (see Figure 5 and Table 8), the behavioral reactivity scores for each mQST were log-transformed (with a constant of 1 added as the data contained values of 0). The distributions of log-transformed behavioral reactivity mQST scores, however, remained skewed, so the raw data was retained for data analysis via non-parametric methods.

3.2.4.1.2. SEQ Data. The SEQ 3.0 (Baranek et al., 2009) tactile sensory modality score was transformed from a raw score to an item mean score by dividing the sum of the raw scores for the 23 tactile items by the number of tactile items. The distribution of SEQ tactile reactivity scores visualized in Figure 6 illustrates a positive skew. The skewness of SEQ tactile reactivity scores was 1.21, indicating that the distribution was highly positively skewed. The kurtosis of SEQ tactile reactivity scores was .84, indicating that the distribution had more data in the tails (i.e., heavy-tailed) compared to a normal distribution. In sum, the distribution of tactile reactivity scores from the SEQ was right-skewed, indicating the need for non-parametric analytic methods.

3.2.4.2 Analytic Plan

The primary hypothesis in this study was that autistic individuals, on average, would demonstrate increased behavioral reactivity to mQST tactile stimuli compared to non-autistic individuals. Descriptive statistics (median and interquartile range), Mann-Whitney-*U* tests, and effect size estimates (Vargha & Delaney's *A*) were computed to compare behavioral reactivity to mQST stimuli between groups. As the mQST data were skewed, the median was used to measure central tendency, the interquartile range was used to measure variance, and nonparametric significant tests, such as Mann-Whitney *U* tests, were computed. Vargha & Delaney's *A* (Vargha & Delaney, 2000) was used to estimate effect size as it is a relatively straightforward effect size measure for Mann-Whitney *U* tests. Vargha & Delaney's *A* is the probability that the value from one group will be greater than the other group, ranges from 0 to 1 with 0.5 indicating that the groups are stochastically equal, so effect sizes closer to 0.5 are small and closer to 0 or 1 are large (Vargha & Delaney, 2000). Group differences in behavioral reactivity to mQST stimuli were also explored visually through box and whisker plot.

Spearman's rank order correlations were computed to investigate the secondary, exploratory aim of examining associations between observed behavioral reactivity to mQST tactile stimuli and caregiver-reported sensory reactivity via the SEQ 3.0 (Baranek et al., 2009) among the participants with a high familial likelihood of autism. These correlations were limited to participants with a high familial likelihood of autism, as SEQ scores may not be valid for typically developing participants in relation to those with an ASD family history (Wolff et al., 2019).

3.3 Results

At the school-age visit, *n*=56 participants completed the mQST and diagnostic assessments. Of these 56 participants, *n*=45 were scored for the mQST, with 18% of mQSTs collected not being scored due to missing camera footage (*n*=9) or examiner error (*n*=2). Participants include 45 children (49% female; 78% white; 87% non-Hispanic) aged 7 to 12 years (*M* = 10 years, *SD* = 1.28) who completed the mQST protocol at the school-age visit with coded data. Of the 45 participants included in the present analysis, 26 participants (58%) were in the high-familial autism likelihood group, and 19 participants (42%) were in the low-familial likelihood group, including eight autistic and 37 non-autistic children across both groups. See Table 7 for demographic data about the included participants.

3.3.1 Primary Outcome: Group Differences in Behavioral Reactions to Tactile Stimuli

The primary research question asked the extent to which autistic children differ in behavioral reactivity to mQST tactile stimuli compared to children without autism. Table 8 displays the number of participants with data for each stimulus. It also displays descriptive statistics (median and interquartile range) for reactivity scores for each mQST stimulus.

3.3.1.1 Mann-Whitney U Test Results: Group Differences to mQST Stimuli

Mann-Whitney U tests were performed to evaluate whether observed behavioral reactivity to tactile mQST stimuli differed by autism diagnostic status. Eight Mann-Whitney U tests were performed to assess group differences for the following stimuli: sham, light touch, pinprick, cool, pressure, repeated (first 5 s), repeated (last 5 s), and heat. The results indicated that autistic participants had significantly higher observed behavioral tactile reactivity scores than participants without autism for four of the stimuli: light touch, $z = 2.42$, $p = .013$; pinprick, $z = 2.48$, $p = .011$; the last 5s of the repeated Von Frey, $z = 2.29$, $p = .018$; and heat, $z = 2.62$, $p = .007$. The results indicated that there were no significant differences between observed behavioral reactivity scores of participants with and without autism to the sham stimulus, $z = 0.77$, $p = .467$, and three active stimuli: cool, $z = 1.22$, $p = .233$; pressure, $z = 1.31$, $p = .196$; and the first 5s of repeated, $z = 0.91$, $p = .376$. The results of the Mann-Whitney U tests (z-test statistics, confidence intervals, p-values) and effect size estimates computed using Vargha & Delaney's *A* are displayed in Table 8. Figure 7 shows a box and whisker plot of the behavioral reactivity scores across mQST stimuli.

3.3.2 Secondary Outcome: Associations Between Observed and Proxy-Reported Tactile Scores

The secondary research aim was to explore the extent to which observed behavioral reactivity to tactile (mQST) stimuli correlates with caregiver-reported tactile reactivity (SEQ) among children at a higher likelihood of developing autism. The study included 26 participants with a high likelihood of developing autism; of these, 21 participants had SEQ data. Of the 21 high-likelihood participants with SEQ and mQST data, 6 participants were autistic. The median SEQ tactile reactivity item mean score was 1.35, with an interquartile range of 0.48.

3.3.2.1 Spearman's Rank Order Correlations Between mQST and SEQ Scores

Spearman's rank order correlations were calculated between SEQ tactile sensory modality item mean scores and each mQST stimulus score. Negligible to weak correlations were observed between SEQ tactile sensory modality item mean scores and each mQST stimulus score: light touch, $r(19) = .07$, $p = .767$; pinprick, $r(19) = .02$, $p = .938$; cool, $r(18) = -.09$, $p = .709$; pressure, $r(18) = -.19$, $p = .431$; first 5s of repeated, $r(17) = -.13$, $p = .609$; last 5s of repeated, $r(17) = -.10$, $p = .683$; and heat, $r(16) = -.05$, $p = .855$.

3.4 Discussion

In this sample of 45 school-age children, autistic children tended to have greater behavioral reactions to four mQST tactile stimuli (light touch, pinprick, the end of the repeated von Frey, and heat) than children without autism. There were no significant group differences in behavioral reactions to the sham stimulus and three active stimuli (cool, pressure, and the beginning of the repeated von Frey). The primary hypothesis was that autistic children would tend to demonstrate more behavioral reactivity to mQST stimuli compared to non-autistic children. This primary hypothesis was supported, in part, as the sample of autistic children tended to have significantly greater behavioral reactivity scores to most of the active mQST stimuli (i.e., light touch, pinprick, the end of the repeated application, and heat). As expected, no group differences were observed in behavioral reactivity to the sham. The lack of group differences to the sham stimulus while observing group differences to some active mQST stimuli provides evidence that behavioral reactivity scored in response to the active mQST stimuli was due to reactions to the stimulus rather than the social approach or experimental setup.

Differences were observed in behavioral reactivity scores to most of the active mQST stimuli such that the group of autistic children tended to demonstrate more behavioral reactivity than children without autism. This finding could plausibly be explained by differences in nerve fiber function (Barney et al., 2017). In the conventional QST protocol, stimuli similar to light touch, pinprick, repeated application of a von Frey monofilament, and heat map on to Aβ, Aδ, and C primary afferent nerve fibers function (Rolke et al., 2006). As autistic participants, on average, were reactive to these specific mQST stimuli, it seems that peripheral sensory afferents (Aβ, Aδ, and C fibers) were transmitting tactile information centrally (Barney et al., 2017). It is plausible that differences in reacting to these stimuli in the mQST protocol among autistic children compared to children without autism warrants further investigation into nerve fiber function across Aβ, Aδ, and C primary afferent nerve fibers in autistic children.

3.4.1 Similarity of Results

While no other studies have reported results comparing reactivity to mQST stimuli between school-age children with and without autism, Barney et al. (2017) compared reactivity to mQST stimuli across young children with and without global developmental delay. Both the present study and Barney et al. (2017) identified group differences for a majority of the active mQST stimuli. Both the present study and Barney et al. (2017) found the group of children with disabilities to be significantly more reactive to light touch, pinprick, and repeated von Frey than the group of children without disabilities. Barney et al. (2017) also found significant differences in reactivity to cool and pressure between young children with and without global developmental delay. In contrast, the present study found a significant difference in reactivity to heat between school-age children with and without autism.

Although the mQST and QST are tapping different sensory constructs, they both measure responses to cold, warm, and mechanical stimuli. While no known studies report on the full QST protocol with autistic children, two studies compared reactivity to QST stimuli across adults with and without autism (Fründt et al., 2017; Vaughan et al., 2020). Fründt et al. (2017) did not identify group differences between adults with and without autism in somatosensory detection. Unlike the present study that found group differences for light touch, pinprick, repeated von Frey, and heat, Fründt et al. (2017) found no group differences in mechanical or warm detection thresholds. Vaughan et al. (2020) found that autistic adults, on average, had a significant difference in mechanical detection threshold, but not in a direction consistent with the present findings. Vaughan et al. (2020) found that autistic adults, on average, required a significantly greater force to detect light touch than the control group; however, in the present study, school-age children with autism demonstrated greater behavioral reactivity to the light touch stimulus. Any comparison between the literature on QSTs with adults and mQSTs with school-age children in the present sample is confounded simultaneously with differences in age and method.

Several studies have used psychophysical methods aligned with the QST approach for specific stimuli in autistic samples. While the present study found differences in behavioral reactivity for light touch and heat between children with and without autism, Cascio et al. (2008) found thresholds for detecting light touch, warmth, and cool sensations (all provoked by innocuous stimuli) to be similar across groups of adults with and without autism. Cascio and colleagues (2008) also found that the autism group demonstrated greater thermal pain sensitivity (i.e., cold and heat pain thresholds were lower in the autism group compared to controls). It is notable that any discrepancies in results may be due to differences in age, as the present study had a sample of children, and Cascio et al. (2008) had a sample of adults. Greater behavioral reactivity to the heat stimulus in the present study may be consistent with Cascio and colleagues (2008) finding similar warm detection thresholds across groups but that the autism group had a lower heat pain threshold if participants perceived our heat pain stimulus as noxious, warranting further investigation in C-fiber function among autistic individuals.

3.4.2 Secondary Exploratory Aim: Relationship Between Behavioral Reactivity to mQST Tactile Stimuli and SEQ Tactile Domain Score

The secondary exploratory aim of the study was to examine correlations between two different types of assessments of tactile reactivity: caregiver-reported tactile reactivity scores and observed tactile reactivity scores to the active mQST stimuli (light touch, pinprick, cool, repeated, pressure, and heat). The behavioral reactivity scores to the mQST tactile stimuli were not meaningfully associated with a caregiver-reported tactile reactivity score (i.e., negligent to weak, insignificant correlations were observed). These correlations provided evidence that no notable associations existed between caregiver-reported tactile reactivity (as measured by the SEQ tactile domain score) and observed behavioral tactile reactivity to mQST stimuli.

The negligible to weak correlations between caregiver-reported tactile reactivity and observed behavioral reactivity to mQST stimuli are not surprising. The caregiver-reported tactile reactivity score is the sum of 23 items that reflect the caregiver's perceptions of the frequency of their child's sensory behaviors across sensory response patterns: Hyper-responsivity (11 items), sensory seeking (7 items), hyporesponsivity (4 items), and enhanced perception (1 item). Examples of tactile items from the caregiver-reported SEQ include a dislike of cuddling, ignoring taps on the shoulder, craving intense firm touch, and easily finding objects by feeling (Baranek, 2009). On the other hand, the observed behavioral reactivity scores to mQST stimuli reflect the observer's quantifying the number and intensity of changes in behaviors across categories of facial expressions, movements, and vocalizations in response to tactile stimuli. While both the SEQ and mQST yield observed behavioral reactivity scores to tactile stimuli, it is not surprising that they are not correlated, given the stark differences in their scoring systems and constructs being measured.

A future direction is to further align these scoring systems and constructs by parsing apart the SEQ 3.0 tactile modality score into sensory response patterns, creating tactile-hyperresponsivity, tactile-hyporesponsive, tactile-sensory seeking, and tactile-enhanced perception scores. Furthermore, as the SEQ and mQST are on different scales, standardizing the scores prior to computing correlations would be advantageous.

3.4.3 Limitations

The sample size in this study limited generalizability in more than one way. One limitation to the generalizability of the present study findings is the small sample size, limited to only eight autistic school-aged children. Another limitation of the sample is that the participants were predominantly white, non-Hispanic, middle to upper-class families. Given these limitations of the study sample, the results cannot be extended to the general population. Similarly, given the small sample size of autistic participants, some reservation about extending study findings to individuals with autism in the general population is warranted. A third limitation of the small sample size is that statistical analyses that controlled for important confounding variables (i.e., age and sex) were not warranted. The analyses are limited to general claims about group differences in tactile reactivity in the present sample without controlling for confounding variables.

3.4.4 Conclusion

In summary, the mQST is an assessment tool that uses direct observation to measure behavioral expressions when experiencing tactile stimuli. This measurement approach is an important contribution that can be used with other sensory assessments to understand sensory differences in autistic individuals more comprehensively. This initial investigation provided evidence of tactile reactivity differences to various tactile stimuli, demonstrating that autistic children tended to have more behavioral expressions while experiencing tactile stimuli than children without autism. Future research should include larger sample sizes of autistic individuals, with sampling strategies to recruit a more representative study sample, using the mQST protocol to extend the generalizability of findings about potential differences in the behavioral expression of tactile stimuli between individuals with and without autism. The potential to have a more direct measurement of tactile reactivity with preliminary evidence that autistic children tended to display greater behavioral expressions to tactile stimuli than children without autism has important implications for understanding autism and dispelling the ill-founded view still prevalent as an example in the DSM-5-TR (American Psychiatric Association, 2022) that autistic individuals tend to have an apparent indifference to pain, heat, and cold.

Chapter 4: Evaluation of Validity Evidence for Observed Reactions to Tactile Stimuli: Consistency with Self-Report in Typically Developing School-Age Children

Assessment of sensory reactivity is essential for individuals with neurodevelopmental disabilities (NDDs), particularly individuals with autism or intellectual disabilities with associated complex communication needs. Diagnostic criteria of autism spectrum disorder (ASD) in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5, American Psychiatric Association, 2013) include patterns of sensory reactivity (e.g., hyperresponsivity, hyporesponsivity, and sensory seeking). Individuals with intellectual disabilities are more likely to experience sensory problems and painful conditions due to co-occurring conditions (Valk & Walsh, 2008). Yet, children with intellectual disabilities are less likely than children without intellectual disabilities to be assessed and treated for pain, likely as self-reporting is a predominant method of pain assessment (Malviya et al., 2001). Careful consideration of sensory assessment tools for use across heterogeneous populations and extending to individuals with complex communication needs is needed.

4.1.1 A Sensory Assessment Tool: Quantitative Sensory Testing

Quantitative sensory testing (QST) is a psychophysical method used to assess somatosensory function, which is emerging and rapidly growing in pediatric pain research (Tutelman et al., 2024). Defrin et al. (2004) developed a quantitative somatosensory testing experimental protocol to systematically measure sensitivity to noxious heat stimuli in individuals with intellectual disability (ID) to investigate the commonly held (but ill-founded) view that individuals with ID have a decreased sensitivity to pain. Heat-pain thresholds, the smallest amount of heat intensity (temperature) necessary to yield pain sensation in individuals with mild levels of ID, were established using both the method of limits (reliant on reaction time) and the method of levels (reaction time free), providing evidence that individuals with ID are more sensitive to heat-pain than individuals without ID (Defrin et al., 2004).

4.1.1.1 Method of Limits

Using the method of limits, detection and pain thresholds are measured by a gradual increase in stimuli intensity and participants indicating when the stimulus is detected or becomes painful (Fruhstorfer et al., 1976). Participants can indicate when a stimulus is felt or detected by various means, such as verbal response, pressing a button, or reversing a switch, but all depend on reaction time (Defrin et al., 2004; Defrin, et al., 2006b; Fruhstorfer et al., 1976; Lynn & Perl, 1977). Methods of measuring detection and pain thresholds dependent on reaction time, such as the method of limits, are biased by reaction time (Defrin et al., 2004; Fruhstorfer et al., 1976). Thus, groups of individuals who may have longer reaction times, such as individuals with ID, will have artificially high detection and pain thresholds due to an elongated response time (Defrin et al., 2004; Fruhstorfer et al., 1976).

4.1.1.2 Method of Levels

The method of levels is a reaction time-free measure of detection and pain thresholds. Using the method of levels, the intensity of a stimulus is increased to a predetermined target level, and participants indicate if the stimulus was detected or painful (Yarnitsky & Ochoa, 1990). Defrin et al. (2004) found significantly lower heat pain thresholds in individuals with ID compared to individuals without ID using the method of levels but not the method of limits, demonstrating the importance of using reaction-time-free measurement methods with disability populations. QST protocol, however, utilizing either the method of limits or the method of levels, traditionally relies on self-report (Defrin et al., 2004; Fruhstorfer et al., 1976; Rolke et al., 2006; Yarnitsky & Ochoa, 1990) and thus cannot be used with individuals with complex communication needs or very young children.

4.1.2 Modified Quantitative Sensory Testing

The QST approach was modified, in part, based on other assessments and measurements of pain utilizing non-verbal pain indicators Symons et al. (2010). One example of this measurement approach is the Non-Communicating Children's Pain Checklist (NCCPC; McGrath et al., 1998) which assesses pain based on six categories: body language, emotional reaction, facial expression, physiological indicators, protective reactions, and vocal expressions. One limitation of approaches to measuring non-verbal pain indicators before, during, and after a painful stimulus is that the observers are not blind to the application of the painful stimulus and thus may introduce bias into their behavioral coding of non-verbal pain indicators (Symons et al., 2010).

The QST approach was modified by adding a sham stimulus to control for potential observer bias and replacing the self-report-based method of levels or method of limits with a stimulus-response approach. This practical approach in which participants' behavior during the application of the stimuli (including sham) is behaviorally coded by observers is not dependent on reaction time or self-report (Symons et al., 2010). In the work introducing the mQST, the Facial Action Coding System (FACS; Ekman, 1978), was used to measure facial action units in response to pain and pain expression in adults with intellectual disability (Symons et al., 2010). Certain facial action units were selected by Symons et al. (2010) to measure pain and pain expression in response to mQST stimuli based on the work of Defrin et al. (2006a) and LaChapelle et al. (1999).

Subsequent research using the mQST, however, used different behavioral coding systems. The Battens Observational Scale (BOPS; Breau et al., 2010) was used to measure behavior expression in response to mQST stimuli in individuals with neuronal ceroid lipofuscinosis (Barney et al., 2015). The Pain and Discomfort Scale (PADS; Bodfish et al., 2001) was used to measure behaviors across five behavior classes (gross motor, lower face, physiology, upper face, and vocal) in response to mQST stimuli in children with global developmental delay (Barney et al., 2017; Symons et al., 2010), children with cerebral palsy (Barney et al., 2019), and individuals with Rett syndrome (Merbler et al., 2020).

While the mQST has been used with a variety of disability groups, it has not been used widely with typically developing children. Barney et al. (2017) included a sample of 20 typically developing children. However, most other studies utilizing the mQST do not have a comparison group. More work is needed to investigate tactile reactivity among typically developing individuals to establish normative reference values akin to the German Research Network Group (see Rolke et al., 2006a). Furthermore, beyond establishing normative reference values, typically developing children with the ability to self-report is an essential population for study with the mQST as tactile reactivity can be scored simultaneously and independently via (a) behavioral observation and (b) self-report. This provides an opportunity to, in part, assess the subjective experience of the mQST procedure and identify the extent to which the behavioral coding scheme quantifying observed tactile reactivity and self-reported tactile reactivity scores are correlated.

4.1.3 The Present Study

The primary aim of this study is to evaluate the extent to which the behavioral coding system used to score participant's behavioral reactions during the modified Quantitative Sensory Test (mQST) procedures correlate with subjective participant self-reports of how the mQST stimuli felt. The primary hypothesis is that the behavioral scores will be moderately to strongly correlated with self-report scores. The secondary aim is to explore patterns of tactile reactivity in typically developing school-age children (e.g., differences across sex or age).

4.1.3.1 Research Questions

1. To what extent are ratings of observed behavioral reactions to mQST stimuli correlated with self-reported experiences in typically developing school-aged children?
2. What pattern of tactile reactivity to mQST stimuli is observed among typically developing school-age children, and to what extent do patterns of tactile reactivity across mQST stimuli vary by age or sex among typically developing children?

4.2 Method

Data analyzed in this study were collected as part of a prospective, observational study in typically developing school-age children. This study was motivated by and utilized a subset of data from a previous study (Byiers et al., 2021). Byiers and colleagues aimed to evaluate developmental patterns of behavioral reactivity among typically developing children and adults in response to mQST stimuli to serve as a normative sample for behavioral reactivity among disability groups. The present study focused on tactile reactivity among typically developing children aged 6 – 12 years, as measured by behavioral coding and self-report in response to mQST stimuli.

4.2.1 Participants

4.2.1.1 Inclusion and Exclusion

Inclusion criteria included typical development, defined by the lack of diagnosed genetic, neurologic, metabolic, endocrine, or cardiac/respiratory disorders (according to parental report), and age 6 to 12 years. Exclusion criteria included (a) diagnosed genetic, neurologic, metabolic, endocrine, and cardiac/respiratory disorders identified based on parent reports; (b) primary language other than English; or (c) diagnosed with sensory differences such as deaf/hard of hearing.

4.2.1.2 Sampling Procedures

Participants in this analysis were recruited through two studies conducted by the same principal investigator. Recruitment procedures for both studies utilized convenience sampling (e.g., emailing staff from Gillette Children's Specialty Healthcare, the Masonic Institute for the Developing Brain (MIDB)), and recruitment tools such as the Institute for Child Development participant pool. Participants were self-selected into the study by responding to recruitment materials.

Data were collected at Gillette Children's Specialty Healthcare and the Center for Neurobehavioral Development (CNBD). Written and informed caregiver consent was obtained for all participants. Written assent was obtained for all children above 8 years of age. For children younger than 8 years, verbal assent was sought whenever possible. Participants were monitored for behavioral signs of nonverbal dissent (e.g., crying).

Participants were provided a $25 gift card for participating in the study. The Institutional Review Board approved the study procedures.

4.2.1.3 Sample Size, Power, and Precision

The intended sample size for this analysis is n=40. An a priori power analysis indicated that a sample size of 38 would be required to determine whether a correlation coefficient differs from zero, with a Type I error rate of $\alpha = 0.05$, 90% power, and an expected correlation of $r = .50$. This expected correlation was based on a preliminary investigation with a sample size of $n = 13$ children, aged 5 – 12 years (Byiers et al., 2021). A subgroup of participants (n=15) from Byiers et al. (2021), children between the ages of 6 and 12 years, were included in the present analysis. A recruitment strategy to recruit 15 – 30 more participants was executed.

4.2.2 Measures

The primary measure used in this analysis was behavioral reactivity to the modified Quantitative Sensory Test (mQST; Symons et al., 2010). The mQST is a sham-controlled sensory-testing protocol to measure behavioral reactivity to tactile stimuli without requiring a verbal or motor response for use with individuals with intellectual disabilities. The mQST utilizes a stimulus-response method such that stimuli are applied at a consistent, known intensity, and participant's behavioral reactions are quantified utilizing a modified Face, Legs, Consolability and Cry (FLACC) behavioral coding system (Merkel et al., 1997). The stimuli used in the mQST were selected to align with conventional mQST protocol (Rolke et al., 2006a).

4.2.3 Procedures

The procedure described below was the same across data collection in Byiers et al. (2021) and the present study.

4.2.3.1 Data Collection

4.2.3.1.1 Setting. The participant, at least one caregiver, the mQST examiner, and a second researcher recording a video were present for data collection in a private research space. The participant sat on a chair, with their legs on the ground or a footrest and a tray covering their lap. The examiner sat at the participant's side. The stimuli were placed on a tray behind the participant and out of their sight. Two cameras recorded the protocol: one camera was set up directly across from the participant, filming their entire body, and another researcher held a second camera and recorded a close-up of the participant's face. All video recordings of the mQST protocol included a 30-second baseline and 10-second wind-down time before and after the mQST.

4.2.3.1.2 Stimuli. The mQST protocol consisted of six calibrated sensory stimuli (light touch, pinprick, cool, pressure, repeated Von Frey, and heat) and a sham. Stimuli were kept at a known, consistent intensity (not intended to be noxious). All stimuli were applied to the back of each calf for 5 s, except the more extended application of the "repeated von Frey" stimulus (30 s).

The sham stimulus included holding a closed 2.0 g von Frey monofilament approximately 1in (2.54 cm). from the participant's leg without touching it for 5 s, consistent with the other stimuli but without physical touch. The light touch stimulus was a 2.0 g von Frey monofilament applied to the skin by pushing the filament straight down until it bends and lifting it back up, repeating five times at a rate of 1 Hz. The pinprick stimulus, a plastic neurological exam pin (Medipin; US Neurologicals), was applied by bringing the “pin” to the participant’s calf in a continuous motion, stopping approximately 1 in. (2.54 cm) away, applying straight forward to touch the skin, and immediately pulling back, holding the pin near the arm without touching it for the remainder of the 5 s application. The cool stimulus was a room-temperature metal thermal probe (approximately 22 ºC; Tip Therm; US Neurologicals) applied by holding the cool probe flat against the participant’s calf and maintaining light contact for 5 s. The pressure stimulus, an algometer (Wagner Instruments), was applied by pushing the algometer into the participant’s calf at 4 lb. of pressure. The repeated von Frey stimulus was a 60 g von Frey monofilament applied to the skin by pushing straight down until the filament showed a deep bend, pulling straight up, then repeating 30 times at a rate of 1 Hz. The heat stimulus, a 3-mm electronic thermal probe (WR Medical Electronics), set to 50 ºC, was applied perpendicular to the skin with light, even contact for 5 s.

4.2.3.1.3 Implementation. Once the child was seated in the chair, both video cameras were turned on to capture 30 s of baseline before the examiner began the sensory test. The examiner started the sensory test by greeting the participant and telling them they would begin the “touch test” and that they would touch their legs with a few different touches. Each stimulus was applied to both calves. Stimuli were presented in the following order: sham, light touch, pinprick, cool, pressure, repeated Von Frey, and heat. The examiner used verbal cues for each stimulus application to indicate to behavioral coders when the stimuli were applied but without signaling the stimulus type or the exact application time for participants. For each stimulus, the examiner said a letter assigned to that stimulus, waited 5 s, applied the stimulus silently, and then said “off” immediately after the application was removed. The examiner waited 10 s (or longer if the participant needed a break) before starting the next stimulus application.

4.2.3.1.4 Self-Report. To evaluate participants' subjective response to the mQST, they were asked to rate their discomfort using a 0 to 10 visual analog scale, a numerical rating scale with a corresponding faces scale, after each stimulus application during the mQST, with 0 being no discomfort and 10 being the most discomfort. To ensure that participants understood the rating scale, the ability of young children to self-report using the scale was evaluated by asking them to rate how they would feel in hypothetical scenarios (e.g., "How would you feel if you fell and skinned your knee?"). Participant data was excluded if they provided illogical responses to the hypothetical scenario or demonstrated a lack of understanding of the rating scale throughout the mQST (e.g., responding 0 to all stimuli).

4.2.3.1.4 Behavioral Coding. Each participant's behavioral reactivity scores for each stimulus were quantified using a modified Face, Legs, Activity, Cry, Consolability (FLACC; Merkel et al., 1997) observational coding system. FLACC behavioral coders were blind to the type of stimuli being applied. Coders scored reactivity across five behavior classes, including (a) upper facial expressions (e.g., eyebrow raise or closing eyes; (b) lower facial expressions (e.g., stretching mouth or thrusting tongue); (c) movement of the limb being touched (e.g., moving limb away from stimulus or flinches in the limb being touched); (d) whole body activity (e.g., scooch chair away from examiner or postural change) and; (e) vocalizations (e.g., "that tickles" or whimper). To account for the longer application length of the repeated von Frey monofilament (30 s), compared to the 5 s duration of all other stimuli, two repeated von Frey scores were quantified: one score for the first 5 s of the repeated von Frey and a second score for the last 5 s of the repeated von Frey. This was done as a hypothesis of potential temporal summation (Rolke et al., 2006b). Behavioral reactivity was scored relative to the participant's baseline behavior. For example, if a participant had a furrowed eyebrow during most of the baseline, furrowing their eyebrow while applying a stimulus would not be scored as a reaction to the stimuli unless the intensity increased.

Scores for each behavior class for each stimulus application were rated on a 3-level rating scale (0 = *baseline or no expression; 1 = behaviors occur for less than half of the application, have neutral or positive valence of moderate intensity and short duration;* 2 = *behaviors occur for more than half of the application, involve large movements, increase in frequency or intensity, or have negative valence*). Scores across all five behavior classes were summed to create a reactivity score ranging from 0 – 10 for each limb for each stimulus. For terminated applications, a maximum score of 10 was applied (e.g., the participant started crying during pinprick; their score for the repeated stimulus for the left leg was 10). When a stimulus was terminated prior to the application of the second leg or the participant said they didn't want to try the stimulus on the second leg, the application to the second leg was considered not attempted and scored as NA. When an entire mQST test was terminated, any subsequent stimuli were not attempted and were scored as NA (e.g., the participant started crying after repeated terminating the test, so the subsequent heat stimulus was not applied and was scored as NA). Reactivity scores were averaged across the left and right limbs for each stimulus to derive stimuli-specific reactivity scores for each participant. For example, if a participant had a reactivity score of 6 during the heat application on the left leg and a reactivity score of 4 on the right leg, then their heat reactivity score would be 5.

4.2.3.1.5 Measurement Reliability. FLACC coders scoring the mQST behavioral reactivity were trained with the lead coder to a 90% criterion. Secondary coding was conducted on 29% of mQSTs collected to calculate inter-observer agreement (IOA). IOA was calculated as the percent exact agreement at the level of each behavioral category for each stimulus (e.g., light touch upper face score). IOA ranged from 81.11 to 97.50%; the average IOA was 88.82% (*SD* = 6.56%).

4.2.4 Data Analysis

4.2.4.1 Data Diagnostics

Participants were excluded after data collection if (a) their videos were not able to be coded (i.e., due to missing video footage, implementation errors, or technical difficulties), or (b) their self-report data seemed inaccurate (i.e., the range of an individual's self-report scores is less than 2). Exploratory data analysis was conducted to identify data distributions (i.e., histograms and Shapiro-Wilk tests). As data were collected as part of two studies, differences between variables (e.g., mQST stimuli reactivity scores) were assessed using Mann-Whitney U tests across studies to rule out study as a confounding variable.

4.2.4.2 Analytic Plan

The primary hypothesis in this study was that the behaviorally coded tactile reactivity during the mQST will be moderately to strongly correlated with self-report tactile reactivity during the mQST. Correlations between self-report and behavioral reactivity scores for each mQST stimulus was investigated using Spearman's rank correlation coefficient. The secondary aim of this study was to explore patterns in how typically developing children react to mQST stimuli and the extent to which this varies by biological variables (i.e., sex assigned at birth and age). Patterns in mQST reactivity were explored through descriptive statistics (i.e., medians and interquartile range) and visually through a box and whisker plot. Significant differences between reactivity to active stimuli (i.e., light touch, pinprick, cool, pressure, repeated von Frey, and heat) compared to the initial sham stimulus were investigated using Wilcoxon signed-rank tests.

4.3 Results

4.3.1 Descriptive Statistics

The sample included 34 children between 6 and 12 years of age (*M* = 8 years, *SD* = 2 years). The sample comprised 35% female, 62% male, and 3% non-binary participants. In the included sample, 94% of the participants were white, 3% Asian, and 3% did not provide racial data. In the included sample, 97% of the participants were not Hispanic or Latino, and 3% did not offer ethnic data.

4.3.2 Data Missing or Excluded After Collection

Self-report data were excluded after collection if (a) videos were not able to be coded or (b) participants had inaccurate self-report scores (i.e., reported the same number for all stimuli). Self-report data from four participants were excluded after data collection due to ratings for all stimuli reported as 0 or 1. Additionally, one participant was missing self-report data as they were not asked to self-report.

Figure 8 depicts the flow of the sample size for mQST behavioral scores for each stimulus. Thirty-four participants underwent the mQST protocol. Three participants had some missing data due to technical difficulties, including missing body camera video and missing heat probe stimulus. Three participants had some stimuli only applied to one leg due to requesting not to have the examiner apply the stimulus to the second leg. One participant terminated the entire test due to their response to the pinprick stimulus, two other participants terminated the repeated stimulus, and one participant met termination criteria between the repeated and heat stimulus.

4.3.3. Data Distributions

The distributions of modified FLACC scores for each mQST stimulus were examined visually via histograms and computationally via Shapiro-Wilk normality tests. The histograms of FLACC scores for each mQST stimulus display right-tailed distributions (see Figure 9). According to Shapiro-Wilk tests, the distribution of FLACC scores for each mQST stimulus departed significantly from normality: Initial sham ($W = .82$, $p < .001$), randomized sham ($W = .79$, $p < .001$), light touch ($W = .90$, $p = .007$), pinprick ($W = .84$, $p < .001$), cool ($W = .88$, $p = .004$), pressure ($W = .86$, $p = .001$), beginning of repeated von Frey ($W = .88$, $p = .004$), end of repeated von Frey ($W = .73$, $p = < .001$), and heat ($W = .83$, $p = .001$). The histograms and Shapiro-Wilk tests of the distribution of FLACC scores for each mQST stimulus indicate that non-parametric tests should be used.

The distributions of self-report scores for each mQST stimulus were examined visually via histograms and computationally via Shapiro-Wilk normality tests. The histograms of self-report scores for each mQST stimulus showed that the distributions for light touch, pinprick, cool, and pressure were right-tailed and that the distributions for repeated and heat were normal (see Figure 10). According to Shapiro-Wilk tests, the distributions of self-report scores for most mQST stimuli were significantly non-normal: light touch ($W = .78$, $p < .001$), pinprick ($W = .83$, $p < .001$), cool ($W = .89$, $p = .006$), and pressure ($W = .91$, $p = .022$). The Shapiro-Wilk tests of distributions of self-report scores for mQST stimuli, however, did not show evidence of non-normality for two mQST stimuli: repeated von Frey ($W = .95$, $p = .199$) and heat (W=.94, $p = .180$). The histograms and Shapiro-Wilk tests of the distribution of self-report scores for each stimulus indicate that non-parametric tests should be used as self-report scores for most stimuli are not normally distributed.

4.3.4. Comparisons Between Two Periods of Data Collection

Data in this study were collected in two distinct periods of data collection with different study personnel and locations. Mann-Whitney U tests were used to determine the extent to which FLACC scores to mQST stimuli differed based on the data collection period. There was not a significant difference in FLACC scores for the following stimuli: Initial sham ($z = .41$, $p = .696$), light touch ($z = 0.14$, $p = .897$), pinprick ($z = 0.92$, $p = .366$), cool (z =0 .50, $p = .632$), pressure ($z = 0.57$, $p = .581$), beginning of repeated von Frey (z = – 0.44, p = .672), end of repeated von Frey (z = – 0.10, p = .932), and heat ($z = 0.64$, $p = 0.534$). There was a significant difference in FLACC scores for the randomized sham ($z = 2.80$, $p = .004$). Comparisons of differences in FLACC scores to mQST stimuli between data collected in 2019 and 2024 using Mann-Whitney U tests provide evidence for significant differences for the randomized sham but no other stimuli.

4.3.5. Correlations Between Behavioral and Self-Report Scores

The primary aim of this study was to investigate the extent to which self-report scores and scores yielded from direct observation of behavior in response to mQST stimuli were correlated. Spearman's rank correlation was used to describe the relationship between self-report and behavioral scores in response to mQST stimuli. Results from the Spearman's rank correlations identified negligible to weak relations between self-report and behavioral scores in response to mQST stimuli for individual stimuli: Light touch, $r(28) = .19$, $p = .306$; Pinprick, $r(28) = .27$, $p = .165$; Cool, $r(27) = -.01$, $p = .943$; Pressure, $r(27) = -.02$, $p = .897$; Repeated von Frey, $r(26) = .24$, $p = 0.214$; or Heat, $r(24) = 0.34$, $p = .100$. Overall, there were negligible to weak correlations between self-report and behavioral scores in response to mQST for all stimuli.

4.3.6 Patterns in mQST Behavioral Responses

The secondary aim of this study was to investigate patterns of behavioral reactivity in response to mQST stimuli and explore the extent to which biological variables (i.e., age and sex assigned at birth) explain these differences. Descriptive statistics (median and interquartile range), Wilcoxon Signed-Rank Tests, and a box and whisker plot were used to examine differences between the initial sham stimulus and the other mQST stimulus (i.e., randomized sham, light touch, pinprick, cool, pressure, repeated von Frey, and heat). Boxplots of FLACC scores of behavioral reactivity to mQST stimuli are displayed in Figure 11.

The Wilcoxon Signed-Rank Tests indicated that FLACC scores for initial sham stimulus were statistically lower than FLACC scores for the active mQST stimuli: Light touch ($z = -2.78$, $p = .005$), pinprick ($z = -3.50$, $p < .001$), cool ($z = -2.95$, $p = .003$), pressure ($z = -2.19$, $p = .028$), the first 5 s of the repeated von Frey ($z = -4.27$, $p < .001$), the last 5 s of the repeated von Frey ($z = -4.21$, $p < .001$), and heat ($z = -2.96$, $p = .003$). The FLACC scores for reactivity to the randomized sham were not significantly different from the initial sham ($z = 0.22$, $p = .826$). The Wilcoxon Signed-Rank tests indicate that participants had greater behavioral reactivity to active mQST stimuli than the initial sham stimulus and did not have greater behavioral reactivity to a randomized sham than the initial sham (see Table 9).

4.3.6.1 Sex Differences in Behavioral Reactivity to mQST Stimuli

Mann-Whitney U tests, with effect size estimates using Vargha & Delayney's *A* (Vargha & Delaney, 2000), were used to examine sex differences between female and male children (sex assigned at birth) behavioral responsivity to mQST stimuli. Nine Mann-Whitney U tests were performed to evaluate group differences for the following stimuli: initial sham, randomized sham, light touch, pinprick, cool, pressure, repeated (first 5 s), repeated (last 5 s), and heat. The results indicated that there were no significant differences between the observed behavioral reactivity scores of female participants compared to male participants: Initial sham, $z = 1.49$, $p = .143$; randomized sham, $z = 1.23$, $p = .234$; light touch, $z = 1.63$, $p = .107$; pinprick, $z = – 0.59$, $p = .569$; cool, $z = 0.24$, $p = .833$; pressure, $z = – 0.36$, $p = .733$; the first 5 s of repeated von Frey, $z = 1.67$, $p = .100$. the last 5 s of the repeated von Frey, $z = 0.88$, $p = .393$; and heat, $z = – 0.80$, $p = .435$. There were medium effect sizes (albeit insignificant) for sex differences in response to light touch and the first 5 s of the repeated von Frey application. Table 10 displays descriptive statistics (median, IQR), the results of the Mann-Whitney U tests (*z*-test statistics, *p*-values), and effect size estimates computed using Vargha & Delaney's A.

4.3.6.2 Age Differences in Behavioral Reactivity to mQST Stimuli

The distribution of participant age followed a right-tailed distribution (see Figure 12), with 6-year-olds being the most well-represented in the dataset. Spearman's rank correlations were computed between participant age and each mQST stimulus score to examine any relationship between age and tactile reactivity. There were weak to moderate, significant correlations between the age of the participants and behavioral reactivity to several stimuli (pinprick, $r(32) = -0.35$, $p = 0.042$; pressure, $r(31) = -.40$, $p = .020$; last 5 s of repeated von Frey, $r(31) = .42$, $p = .016$; and heat, $r(30) = -.41$, $p = .028$. The negative correlations between age and four mQST stimuli (pinprick, pressure, last 5s of the repeated von Frey, and heat) indicate that older participants exhibited less behavioral reactivity to these stimuli than younger participants. Results from the Spearman's rank correlations identified weak relations between age and behavioral scores in response to mQST stimuli for the following stimuli: Initial sham, $r(32) = -0.26$, $p = .156$; randomized sham, $r(19) = -0.22$, $p = .341$; light touch, $r(32) = -0.12$, $p = .496$; cool, $r(31) = -0.25$, $p = .155$; and the last 5 s of repeated von Frey, $r(30) = -0.25$, $p = 0.161$.

4.4 Discussion

The objective of this study was to investigate the relationship between tactile reactivity scores generated by self-report compared to scores generated by direct behavioral observation in response to tactile stimuli presented in the mQST protocol. This study specifically focused on testing this relation in a sample of typically developing children between 6 – 12 years of age as this population can reliably self-report, and previous preliminary work (see Byiers et al., 2021) found greater behavioral reactivity among children compared to adults. So, in sum, the sample was selected because this age group of children was suspected to demonstrate behavioral reactivity to tactile stimuli (as opposed to adolescents and adults who may mask reactions, following social norms and learned behaviors) and to be able to report about it. Substantial associations between self-report tactile reactivity scores and tactile reactivity scores yielded from direct behavioral observation in response to mQST stimuli in a sample of typically developing children were not found, evidenced by negligible to small correlation coefficients (*r*'s < .35).

The secondary aim of this study was to explore patterns in behavioral reactivity to mQST stimuli in typically developing children, including any effect of biological variables (i.e., sex assigned at birth and age). Differences in behavioral reactivity to active stimuli (i.e., light touch, pinprick, cool, pressure, repeated von Frey, and heat) and the randomized sham compared to the initial sham trial were investigated to explore patterns in behavioral reactivity to mQST stimuli in typically developing children. Behavioral reactivity scores for all active mQST stimuli were significantly greater than the initial sham stimulus in this sample of typically developing children (*z*'s > 2, *p*'s < .03). Behavioral reactivity scores for the randomized sham were comparable to behavioral reactivity scores for the initial stimulus. This finding that there is significantly greater behavioral reactivity to active stimuli compared to sham stimuli, but not between the initial and randomized sham stimuli replicates findings from Symons et al. (2010), adding to the validity evidence for the mQST protocol and extending validity evidence to a population of typically developing children.

In addition to looking at differences in behavioral reactivity between active mQST stimuli and sham stimuli, sex differences in behavioral reactivity to mQST stimuli were investigated. The results did not identify significant differences in sex assigned at birth and behavioral reactivity to mQST stimuli in this sample of typically developing children (*z*'s < 1.7, p's > .1). There were, however, medium effect sizes for sex differences in response to light touch and the first 5 s of the repeated von Frey. While repeated von Frey was included as a test of temporal summation, the first 5 s to repeated von Frey and light touch are similar stimuli in that they are both applied using von Frey monofilaments applied at a frequency of 1 Hz for 5 s. The light touch stimulus is a 2.0 g von Frey monofilament, and the repeated stimulus is a 60 g von Frey monofilament. Sex differences between these two stimuli may indicate differences in responding to dynamic stimuli, but inferences cannot be made about differences in mechanical detection threshold or mechanical pain threshold.

The last explorative investigation in this study was to examine relations between the age of participants and behavioral reactivity across mQST stimuli. The distribution of the age of participants was skewed such that the data contained more younger participants than older participants. Negative correlations were found between the age of the participants and behavioral reactivity to pinprick, pressure, the first 5 s of the repeated von Frey, and heat, such that older children tended to demonstrate less behavioral reactivity to mQST stimuli. This relation was expected to be observed as older children are more likely to have learned and abide by social norms, which may include suppressing reactivity to sensory stimuli.

4.4.1 Plausible Explanations for the Lack of Relations Between Self-Report and Behavioral Reactivity Scores

The plausible explanations for the lack of relationship between self-reported and observed behavioral scores to mQST stimuli are manifold. First, it is conceivable that young children are unreliable self-reporters. The study included many 6-year-olds (32% of the sample) who may have provided less reliable self-report data. Unreliable self-report data may have masked any potential relations between self-report and behavioral scores. Second, it is plausible that the self-report data was unproblematic, and a scale of self-reported “bothersomeness” does not correspond to a scale of pain behaviors. A third point to consider is that the mQST stimulus protocol was designed to include innocuous stimuli. Among the mQST stimuli, the highest correlations between self-report and behavioral scores were observed for two of the more noxious stimuli (pinprick and heat). Although the measure of pain behavior was modified to accommodate innocuous stimuli, measuring responses to innocuous stimuli is challenging. Yet, this may not be an issue, as individuals are expected, overall, to have low FLACC scores in response to mQST stimuli, but the observation of high FLACC scores may be indicative of allodynia. However, further consideration of behavioral measures of reactivity to innocuous stimuli is warranted.

A fourth point to consider is that the experimental setting of the mQST protocol may be biasing tactile reactions. The experimental procedure asks children to sit in a chair and primes them to expect an examiner to touch their limbs with different objects. The social expectation of abiding by another’s requests may dampen behavioral reactions. For example, individuals may be less inclined to move their limb away from the object, knowing the expectation is to let different objects touch their leg. Some behavioral pain or tactile reactions may be more affected by social expectations than others. Furthermore, this artificial lab setting may dampen tactile reactions compared to those observed in natural settings. For example, the light touch stimulus may not be bothersome in a lab setting, knowing that an examiner is applying a tickly object. In contrast, behavioral reactions to tickly stimuli in the natural environment may invoke a greater behavioral reaction. This issue highlights essential concerns for comparisons across disability and age groups as following social expectations varies with intellectual development and age. Thus, one concern is that the mQST protocol may be biased by social expectations and artificial settings, which would be unequivocally differentiated across disability groups, age groups, and sex.

A final point to consider is the issue of measurement error. In the mQST protocol, stimuli are applied once at one point in time. Taking repeated measures of the same stimuli applied to the same participants and averaging the scores may minimize the issue of measurement error. This approach has been taken with the traditional QST approach (Rolke et al., 2006b). Repeated measures, however, come at the cost of feasibility and ethical considerations.

4.4.2 Future Directions

Given the present findings, some next steps can be taken to contextualize the results. One step is to use statistical modeling to explicate the effects of age and sex assigned at birth on the relations between self-report and behavioral scores in response to mQST stimuli. Another step is to investigate the reliability of self-report scores, particularly the effect of younger reporters on the reliability of self-reporting. Third, self-report data were also collected on (a) whether or not participants felt the stimulus, (b) whether or not the stimulus was perceived as painful, and (c) a description of what the stimuli felt like. These data have the potential to elucidate the experience of the mQST stimuli for participants and inform the mQST protocol. The categorical self-report data recording whether or not the stimulus was painful could be examined to contextualize whether potential sex differences in response to dynamic stimuli (light touch and repeated von Frey) suggest possible differences in mechanical detection thresholds or mechanical pain thresholds. The qualitative data describing how stimuli felt to participants can elucidate the experience of the mQST stimuli for participants and inform the mQST protocol.

A fourth step could be reconsidering the measurement and analysis of the repeated von Frey, a proxy for a test of potential temporal summation. Participant behavioral reactivity to the repeated von Frey was measured as behavioral reactivity for the first 5 s of the application, compared to the last 5 s. The German Research on Neuropathic Pain QST protocol uses pinprick as a test of temporal summation represented by the wind-up ratio, calculated by dividing the mean rating of applying a series of 10 repetitive pinprick stimuli by the mean rating of applying a single pinprick (Rolke et al., 2006b). Perhaps more analogous ways exist to compute a wind-up ratio using the mQST protocol, which can be explored in future work.

Lastly, patterns of behavioral reactivity to mQST stimuli in typically developing children were investigated by a) looking at differences between behavioral reactivity to active stimuli and the sham stimuli, b) exploring sex differences, and c) investigating a potential effect of age, yet, patterns of self-report to mQST stimuli were not explored in this same manner. It may be fruitful to investigate these patterns of self-report scores to contextualize the relations (or lack thereof) between self-report and behavioral observations in response to mQST stimuli.

4.4.3 Conclusion

In conclusion, evidence of moderate associations between self-reported and observed behavioral scores in response to mQST stimuli was not found in a sample of typically developing children. It was observed that typically developing children exhibited greater behavioral reactivity to all active mQST stimuli compared to the sham stimulus, providing validity evidence for using the mQST protocol in typically developing children. While no significant effects of sex assigned at birth were observed, medium effect sizes in behavioral reactivity to mechanical stimuli (i.e., light touch and the first 5 s of repeated von Frey) were evident, such that children assigned female at birth were more reactive to mechanical stimuli than children assigned male at birth. Additionally, age was associated with reactivity to pinprick, pressure, the first 5 s of repeated von Frey, and heat, such that younger children exhibited greater reactivity to these stimuli than older children. While some validity evidence for the use of the mQST in typically developing children was identified, further work is needed to understand participants' subjective experience during the application of mQST stimuli and how subjective experience relates to the behavioral coding scheme used to measure behavioral reactions to mQST stimuli.

Chapter 5: Conclusion

A multi-paper dissertation was conducted to investigate direct observational and biological measures of reactivity to sensory stimuli, interrogate tactile reactivity differences between school-age children with and without autism, and explore relations between subjective experience and direct observation of reactivity to tactile stimuli. This work was motivated by (a) the inclusion of sensory reactivity as diagnostic criteria for autism spectrum disorders in the DSM-5 (American Psychiatric Association, 2013), (b) a potential etiological role of sensory reactivity in the development of autism (Johnson et al., 2015), (c) the preponderance of proxy-report sensory measures lacking psychometric support for the recommendation of use with autistic samples, without conditions (Gunderson et al., 2023) to identify measures that can be used across heterogeneous populations extending to individuals with complex communication needs as to include historically excluded populations from research.

The scoping review paper of direct observational and biological measures of responses to stimuli ranging from behaviors, physiology, and circuits provides a menu of sensory measures for research groups to consider when designing their research protocol. A multi-method approach to sensory assessment is recommended, and the oft-used proxy report measures are supplemented with direct observational and biological measures.

One of the direct observational measures of tactile reactivity identified in the scoping review, the mQST (Symons et al., 2010), was subsequently used to interrogate tactile reactivity differences to mQST stimuli (i.e., light touch, pinprick, cool, pressure, repeated von Frey, and heat) between school-age-children with and without autism. Statistically significant differences with medium to large effect sizes were found in behavioral reactions to light touch, pinprick, the last 5 s of repeated von Frey, and heat, such that autistic children tended to exhibit greater behavioral reactivity than children without autism. A tendency among autistic participants to have greater behavioral expressions in response to tactile stimuli, including heat, provides preliminary evidence that autistic children respond to tactile stimuli, including potentially painful stimuli, more than children without autism, contrary to the example included in the DSM-5 of autistic individuals displaying “apparent indifference to pain, heat, and cold” (American Psychiatric Association, 2022).

The use of the mQST in a sample of typically developing children was then interrogated to provide evidence that the subjective experience of the mQST was related to the behavioral reactivity scores yielded from the coding scheme. While evidence indicated negligible to weak relations between subjective experience of mQST stimuli and behavioral scores, validity evidence was generated for the use of the mQST in typically developing controls, in addition to some potential gender and sex differences in behavioral reactivity to mQST stimuli. While no statistically significant differences in behavioral reactivity to mQST between children assigned female at birth compared to children assigned male at birth were identified, medium effect sizes were found for sex differences in responses to mechanical stimuli (i.e., light touch and the first 5 s of repeated von Frey) such that children assigned female at birth were more responsive to mechanical stimuli than children assigned male at birth. There were effects of age identified for behavioral responsivity scores to light touch, pinprick, the last 5 s of repeated von Frey, and heat, such that younger children tended to have greater behavioral reactivity to these stimuli compared to older children.

Taken together, there is a wide variety of direct observational and biological measures of sensory reactivity that are not dependent on self-report that may be suitable for use with autistic individuals and other neurodevelopmental disabilities. Direct observational and biological measures have the potential to assess sensory reactivity in autism to identify underlying mechanisms in the peripheral and central nervous system that explain sensory reactive behaviors. The mQST is a direct observational measure that quantifies pain behaviors in response to standardized tactile stimuli to assess nerve fiber function. Preliminary evidence using the mQST with autistic children suggests autistic children tend to have greater behavioral reactions to a variety of mQST stimuli compared to children without autism. As the mQST stimuli were selected based on conventional QST stimuli (Rolke et al., 2006a), and as the conventional mQST stimuli were selected to assess differences in Aβ-, Aδ-, and C-afferent nerve fiber function, differences in behavioral reactivity warrants further investigation into afferent sensory nerve fiber function with autistic children. Further work with the mQST provided initial validity evidence for the mQST for use with school-age children, as typically developing children reacted more to active stimuli than the sham. Overall, the mQST is a direct observational measure that measures behavioral expression to tactile stimuli and could yield information to contribute to understanding sensory reactivity in autism; however, further psychometric work is warranted.

5.1 Limitations

The limitations weighing the most heavily on this multi-paper dissertation are as follows. The scoping review of direct observational and biological sensory measures was limited in the search scope as infants, toddlers, and young children were better represented in the search terms than individuals with complex communication needs. There may be additional measures used with individuals with complex communication needs that were not identified in the search. The two empirical studies were limited by sample size. In the empirical study investigating tactile reactivity differences in children with and without autism, only eight autistic children were included. The sample was underpowered in the empirical study examining the relationship between subjective self-report of tactile stimuli and tactile reactivity scores yielded from direct behavioral observation. A power analysis identified a sample of 38 participants to look at correlations between self-report and behavioral scores. While 34 participants were included, there was an overabundance of six-year-olds in the data (32% of the sample) and a lack of female participants (36 %).

5.2 Discussion

The broad menu of direct observational and biological measures identified in the scoping review may serve as a source for researchers in designing study protocols. The measures identified cover a wide range of behavioral and physiological elements as responses to sensory stimuli across auditory, tactile, visual, and multisensory domains, with some measures of circuits in response to affective touch. Of the direct observational and biological measures identified in the scoping review, the mQST was the only measure used in populations with complex communication needs. In contrast, the remaining measures were used with newborns, infants, and young children. The mQST was demonstrated to identify tactile reactivity differences in a sample of autistic school-age children compared to children without autism. The use of the mQST was also extended to a sample of typically developing children and yielded validity evidence of the use of the mQST with a typically developing sample, yet did not provide evidence that the subjective self-experience of the mQST tactile stimuli was related to observed behavioral reactivity. The mQST and other direct observational and biological measures of responses to sensory stimuli have the potential to deepen our understanding of underlying mechanisms of sensory reactivity.

5.3 Recommendations

Direct observational and biological sensory measures should be included in research more often, ideally triangulating measurement approaches. As the oft-used proxy-report measures are limited to making inferences about the behaviors of individuals, direct observational and biological measures may shed light on underlying mechanisms. In measuring constructs within widely heterogeneous populations, it is critical to select measures appropriate for the entire population rather than excluding groups of participants (i.e., those who cannot self-report). Measurement of sensory reactivity in autism can also be enriched by considering broader frameworks for considering sensory reactivity beyond the sensory features of autism outlined in the categorical disability framework of the DSM-5 (i.e., hyperresponsivity, hyporesponsivity, and sensory seeking) and also considering sensory reactivity in terms of sensory sensitivity and perceptual signaling (Harrison et al., 2019). Additionally, preliminary evidence demonstrated that a group of autistic children had greater behavioral reactivity to heat, and potentially noxious stimuli. Further work to demonstrate that individuals with autism are not indifferent to pain, heat, or cold (contrary to the DSM-5) example is warranted. All this to say, more psychometric work across the board is needed to support the recommendation of use for any particular sensory measure with any specific population, particularly heterogeneous populations with idiosyncratic behavioral expressions and challenges with verbal reporting.

5.4 Conclusion

The broad menu of direct observational and biological measures identified in the scoping review may serve as a source for researchers in designing study protocol. The measures identified cover a wide range of behavioral and physiological elements as responses to sensory stimuli across auditory, tactile, visual, and multisensory domains, with some measures of circuits in response to affective touch. Of the direct observational and biological measures identified in the scoping review, the mQST was the only measure used in populations with complex communication needs whereas the rest of the identified measures were used with newborns, infants, and young children. The mQST was demonstrated to identify tactile reactivity differences in a sample of autistic school-age children compared to children without autism, providing some evidence that autistic children may not be indifferent to pain and heat. The use of the mQST was also extended to a sample of typically developing children and yielded validity evidence of the use of the mQST with a typically developing sample, yet did not provide evidence that the subjective self-experience of the mQST tactile stimuli was related to observed behavioral reactivity. The mQST and other direct observational and biological measures of responses to sensory stimuli have the potential to contribute to our understanding of sensory reactivity across different groups, including individuals with autism.

Tables

Table 1 *Search Terms*

Variable	Title, abstract, and key concepts	Subject headings
Sensory construct	"sensory responsiveness" OR "sensory responsivity" OR "sensory reactivity" OR "sensory feature" OR "sensory features" OR "sensory sensitivity" OR "sensory sensitivities" OR "sensory profile" OR "sensory profiles" OR "sensory behavior" OR "sensory behaviors" OR "tactile reactivity" OR "tactile stimulation" OR "auditory reactivity" OR "auditory stimulation" OR "visual reactivity" OR "visual stimulation"	"tactual stimulation" OR "auditory stimulation" OR "visual stimulation"
Population	babies OR baby* OR infanc* OR infant* OR toddler* OR preschool* OR "early childhood" OR "early development" OR "infant development" OR "early childhood development" OR "early autism" OR "complex communication needs" OR nonverbal OR "minimally verbal"	"infant development" OR "childhood development" OR "communication barriers"

Table 2 *Results of Individual Sources of Evidence (n=111)*

Narrative Citation	Participants	Observational Measurement Tool Used
Ahtola et al. (2017)	normally developing infants	Electroencephalography (EEG)
Ahtola et al. (2020)	typically developing infants	EEG
Anderson et al. (2001)	healthy term and preterm infants	functional Magnetic Resonance Imaging (fMRI)
Anderssen et al. (1993)	healthy infants	polysomnography (including EEG and physiological parameters)
Bacher & Smotherman (2004)	infants	behaviorally coded blinking
Baranek et al. (2002)	boys with full-mutation FXS	Tactile Defensiveness and Discrimination Test-Revised (TDDT-R; Baranek, 2010; Baranek & Berkson, 1994)
Baranek et al. (2018)	infants at elevated risk of autism	Sensory Processing Assessment (SPA; Baranek, 1999)
Barnet et al. (1971)	normal and Down's syndrome infants	EEG
Barney et al. (2017)	global developmental delays	modified quantitative sensory test (mQST)
Barney et al. (2020)	CP, complex communication needs	mQST
Barrett & Jones (1967)	hemiplegic children with CP	Sensory Story
Bart et al. (2011)	late preterm infants and term infants	Test of Sensory Function in Infants (TSFI; DeGangi & Greenspan, 1989)
Bartocci et al. (2006)	newborn infants	Near Infrared Spectroscopy (NIRS)
Begum-Ali et al. (2021)	Neurofibromatosis Type 1 infants	EEG
Bellieni et al. (2007)	neonates	ABC Scale (Bellieni et al., 2005)
Bench & Wilson (1976)	clinically normal infants	behaviorally coded movements
Born et al. (1998)	children	fMRI
Botha et al., (2022)	typically developing infants	TSFI (DeGangi & Greenspan, 1989)
Boyle & Hull (1976)	newborn infants	Electromyography (EMG)
Brock et al. (2012)	children with autism	SPA (Baranek, 1999); TDDT-R (Baranek, 2010)

Narrative Citation	Participants	Observational Measurement Tool Used
Brown et al. (1977)	infants	Beckman biopotential (chest) and miniature electrodes (eye)
Campbell-Yeo et al. (2012)	stable preterm twins	Premature Infant Pain Profile (PIPP; Stevens et al., 1996)
Campi et al. (2022)	children at elevated likelihood of ASD	SPA (Baranek, 1999)
Cantiani et al. (2023)	infants	EEG
Chang et al. (2012)	children with ASD and controls	Sensory Challenge Protocol (SCP; Miller et al., 2001)
Chen & Fang (2005)	infants with DS and controls	EEG
Chen et al. (2002)	newborns, elevated likelihood of ASD	NIRS
Chorna et al. (2014)	preterm infants	TSFI (DeGangi & Greenspan, 1989)
Cornelissen et al. (2013)	preterm and term infants	EMG
Damiano-Goodwin et al. (2018)	children, elevated likelihood of ASD	SPA (Baranek, 1999)
Dannenbaum & Dykes (1984)	myelodysplastic children	observation of behavioral response to electrical stimulation
de Bildt et al. (2012)	individuals with ASD and/or ID	behavioral observation of visual rooting reflex
De Meo-Monteil et al. (2019)	toddlers, autism and megalencephaly	EEG
DeGangi et al. (2000)	Infants, regulatory disorder or PDD	TSFI (DeGangi & Greenspan, 1989)
Donkers et al. (2015)	children with autism and controls	EEG; SPA (Baranek, 1999); TDDT-R (Baranek, 2010)
Donkers et al., (2020)	Children with ASD, DD, and TD	EEG; SPA (Baranek, 1999); TDDT-R (Baranek, 2010)
Dotto et al. (2014)	children with West syndrome (WS)	EEG
Dumont et al. (2017)	preterm neonates	behaviorally coded movements
Ellingson (1960)	full-term and preterm infants	EEG
Eriksson et al. (2008)	healthy full-term infants	PIPP (Stevens et al., 1996)
Espenhahn et al. (2021)	children with autism and controls	EEG

Narrative Citation	Participants	Observational Measurement Tool Used
Feldman et al. (2021)	infants at familial likelihood of ASD	SPA (Baranek, 1999); TSFI (DeGangi & Greenspan, 1989)
Feldman et al. (2022)	infants at familial likelihood of ASD	SPA (Baranek, 1999); TSFI (DeGangi & Greenspan, 1989)
Foss-Feig et al. (2012)	children with ASD	TDDT-R (Baranek, 2010; Baranek & Berkson, 1994)
Freund-Azaria et al. (2023)	infants	TSFI (DeGangi & Greenspan, 1989)
Gavin et al. (2011)	children with SPD and controls	EEG
Goodwin et al. (2016)	healthy, alert, upright infants	functional near-infrared spectroscopy (fNIRS)
Grzadzinski et al. (2020)	children at elevated likelihood of ASD	SPA (Baranek, 1999, 2007, 2013)
Grzadzinski et al. (2021)*	children at elevated likelihood of ASD	SPA (Baranek, 1999, 2007, 2013)
Gupta & Bhardwaj (2022)	healthy infants and young children	EMG
Hellerud & Storm (2002)	preterm and term infants	electrodes measuring skin conductance activity (SCA)
Hogan et al. (2014)	healthy infants	Modified Behavioral Pain Scale (MBPS; Taddio et al. (1995)
Hyde et al. (2010)	healthy full-term 3-month-old infants	EEG
Jatkar et al. (2023)*	toddlers at elevated likelihood of ASD	SPA (Baranek, 1999, 2007, 2013)
Jönsson et al. (2018)	healthy infants	diffuse optical tomography (DOT)
Karen et al. (2007)	term neonates	NIRS
Kinard et al. (2017)	high risk of ASD	SPA (Baranek, 1999, 2007, 2013)
Kirby et al. (2019)	children with ASD or DD	SPA (Baranek, 1999); TDDT-R (Baranek, 2010)
Kittner & Lipsitt (1976)	newborns with obstetric conditions	Electrocardiogram (EKG)
Kotilahti et al. (2005)	healthy full-term newborn infants	NIRS; EEG; EMG
Kusaka et al. (2004)	infants	multichannel near-infrared spectroscopy (MNIRS)
Kushnerenko et al. (2001)	full-term neonates	EEG
Lauronen et al. (2006)	healthy full-term newborns	MEG

Narrative Citation	Participants	Observational Measurement Tool Used
Lecuona et al. (2016)	low birth weight premature infants	TSFI (Degangi & Greenspan, 1993)
Lecuona et al. (2017)*	premature infants	TSFI (Degangi & Greenspan, 1993)
Lee et al. (2012)	preterm and term infants	fMRI
Leikos et al. (2020)	preterm infants	EEG
Lippé et al. (2007)	infants and children	EEG
Lippé et al. (2009a)	infants and children	EEG
Lippé et al. (2009b)	infants and children	EEG
Machado et al. (2023)	full-term and pre-term infants	fNIRS; TSFI (DeGangi & Greenspan, 1993)
MacLennan et al. (2021)	children with autism	Sensory Assessment for Neurodevelopmental Differences (SAND; Siper et al., 2017)
Mailloux et al. (2014)	young children: ASD, LD, and controls	Postrotary nystagmus (PRN) test
Maimon et al. (2013)	preterm infants	EEG; Behavioral Indicators of Infant Pain (BIPP; Holsti & Grunau, 2007)
Maitre et al. (2020)	preterm and full-term infants	EEG
Mangeot et al. (2001)	children with ADHD and controls	SCP (McIntosh et al. 1999)
Mariani Wigley et al. (2023)	infants	fMRI
Mateus et al. (2018)	healthy full-term infants	ECG; respiratory band
Mateus et al. (2021)	infants	fNIRS
Meek et al. (1998)	infants	NIRS
Meltzoff et al. (2019)	8-week-old infants	EEG
Miguel et al. (2020)	twelve-month-old infants	NIRS
Nevalainen et al. (2008)	healthy full-term newborns	MEG
Owens & Todt (1984)	infants in the second full day of life	ECG; observations of audiotapes
Pihko et al. (2009)	healthy volunteers	MEG

Narrative Citation	Participants	Observational Measurement Tool Used
Pratt (1934)	newborn infants	stabilimeter
Rahkonen et al. (2013)	preterm infants	MEG
Riva et al. (2022)	infants at elevated likelihood of ASD	EEG
Roberts et al. (2013)	young boys with FXS and controls	telemetry; coded behavioral responses
Roche-Labarbe et al. (2014)	preterm neonates	fNIRS
Rose et al. (1976)	premature and full-term infants	ECG; behavioral coding
Rossow et al. (2021)	preschool-aged children with ASD	SAND (Siper et al., 2017)
Ruiz-Martínez et al. (2020)	children with ASD and control children	EEG
Ruusuvirta et al. (2003)	healthy newborn infants	EEG
Sakatani et al. (1999)	newborns	NIRS
Schaaf et al. (2003)	children with SPD and controls	SCP (Miller et al., 2001)
Shibata et al. (2012)	healthy newborns	NIRS
Siper et al. (2017)	children with ASD and controls	SAND (Siper et al., 2017)
Steinschneider (1968)	term neonates	thermistor bead
Su et al. (2010)	children with SMD and controls	SCP (McIntosh et al., 1999; Miller et al., 1999)
Symons et al. (2010)	nonverbal adults with ID	quantitative sensory protocols (see Rolke et al., 2006)
Taddio et al. (2014)	infants undergoing vaccination	MBPS (Taddio et al., 1995)
Taga & Asakawa (2007)	young infants	near-infrared optical topography (NIR-OT)
Taga et al., (2003)	newborn infants	NIR-OT
Turkewitz et al. (1972)	female infants	researcher designed chamber; autonomic, behavioral responses
Vanhatalo et al. (2009)	extremely low birth weight infants	EEG

Narrative Citation	Participants	Observational Measurement Tool Used
Watanabe et al. (2012)	full-term healthy 6-month old infants	NIRS
Watson et al. (2011)	children with ASD or DD	SPA (Baranek, 1999); TDDT-R (Baranek, 2010)
Woodard et al. (2012)	children with ASD and controls	Lifeshirt (Vivometrics, Inc.); behavioral 5-point rating scale
Wu et al. (2020)	preterm infants needing venipuncture	Premature Infant Pain Profile-Revised (PIPP-R; Stevens et al., 2014)
Yamada (1984)	preterm and full-term newborns	auditory-evoked eyelid microvibration (AMV)

Note. CP = Cerebral Palsy; ASD = Autism Spectrum Disorder; DS = Down's syndrome; PDD = Pervasive Developmental Disorder; SPD = Sensory Processing Disorder; DD = Developmental Disorder; LD = Learning Disabilities; FXS = Fragile X Syndrome; SMD = Sensory Modulation Disorder; ID = Intellectual Disability.
* = same sample and measure as reported in prior included report.

Table 3 *Measures of Behaviors in Response to Sensory Stimuli*

RDoc element	Tool	Purpose	Stimuli	Variable measured	Age range	Pop.	Cited in
Auditory							
Activity Level	Stabilimeter	Exp.	Repeated auditory stimuli	General activity	2 – 11 days	Newborns	(Pratt, 1934)
Motor Activity	Behavioral Observation/ Coding Systems	Exp.	Tonal mixtures	Eye movements; Finger movements	1 – 50 weeks	Newborns; Infants	(Anderssen et al., 1993; Bench & Wilson, 1976; Brown et al., 1977; Turkewitz et al., 1972)
Sensory reactivity	Researcher-developed behavioral Observation/ Coding Systems	Exp.	Alarm clock (5 s)	Behavioral reactivity (none, mild, moderate, or severe)	1 – 11 years	FXS	(**Roberts et al., 2013**)
Tactile							
Crying	ABC Scale (Bellieni et al., 2005)	Clinical	Heel prick (pain)	Features of crying (pitch, constancy, rhythmicity)	n.s.	Newborns	(Bellieni et al., 2007)

RDoc element	Tool	Purpose	Stimuli	Variable measured	Age range	Pop.	Cited in
Crying	Behavioral Observation/ Coding Systems	Clinical	Heel lance (pain) and non-invasive tactile stimulation	Percentage of time crying	2 days	Newborns	(**Owens & Todt, 1984**)
Crying/ Facial Expressions/ Motor Activity	Modified Behavioral Pain Scale (MBPS; Taddio et al., 1995)	Clinical	Immunizations (pain)	Facial grimacing, crying, body movements	1 – 12 months	Infants	(Hogan et al., 2014; Taddio et al., 2014)
Facial Expressions	**Premature Infant Pain Profile (PIPP; Stevens et al., 1996, 2014)**	Clinical	Heel lance (pain); venipuncture (pain); caregiver touch (tactile stimulation)	Facial pain response; Facial expressions	3 – 28 days	Newborns; Preterm	(Campbell-Yeo et al., 2012; Eriksson et al., 2008; Wu et al., 2020)
Facial Expressions/ Motor Activity	Behavioral Indicators of Infant Pain (BIIP; Holsti & Grunau, 2007)	Clinical	Heel lance (pain)	Sleep/wake state, facial movement, hand actions	n.s.	Newborns	(**Maimon et al., 2013**)
Facial Expressions/ Motor Activity	modified Quantitative Sensory Test (mQST; Symons et al., 2010)	Exp.	Light touch, pin prick, cold, deep pressure, repeated von Frey, heat	PADS (vocal, upper face, lower face, gross motor); FACS (facial activity)	3 – 67 years	CP; GDD; ID	(Barney et al., 2017, 2019; Symons et al., 2010)

RDoc element	Tool	Purpose	Stimuli	Variable measured	Age range	Pop.	Cited in
Motor Activity	Sensory Story (Barrett & Jones, 1967)	Exp.	Story with tactile stimuli (soft, smooth, bumpy, hard, dry, wet, hot, cold)	Reached for, accepted, or refused object	19 – 60 months	CP	(Barrett & Jones, 1967)
Motor Activity	Behavioral Observation/ Coding Systems	Exp.	Vibrotactile stimulation	Body movements (habituation or startle response)	9 months	Infants	(Dumont et al., 2017; **Rose et al., 1976**)
Sensory Reactivity	Tactile Defensiveness and Discrimination Test-Revised (TDDT-R; Baranek et al., 1998)	Clinical	Structured self-directed and experimenter-administered touch stimuli	Tactile responsiveness; Defensiveness, discrimination	2 – 12 years	ASD; DD; FXS; TD	(Baranek et al., 2002; Brock et al., 2012; **Donkers et al., 2015, 2020**; Foss-Feig et al., 2012; Kirby et al., 2019)
				Visual			
Disinhibition of early motor relflexes	Behavioral Observation/ Coding Systems	Exp.	Oscillating wand	Visual rooting reflex	3 – 20 years	ASD + ID	(de Bildt et al., 2012)

RDoc element	Tool	Purpose	Stimuli	Variable measured	Age range	Pop.	Cited in
Eye blink	Behavioral Observation/ Coding Systems	Exp.	Stuffed animals	Spontaneous eye blinking	10 – 12 weeks	Infants	(Bacher & Smotherman, 2004)

Multisensory

RDoc element	Tool	Purpose	Stimuli	Variable measured	Age range	Pop.	Cited in
Sensory Reactivity	Test of Sensory Function in Infants (TSFI; DeGangi & Greenspan, 1989)	Clinical	Visual-tactile integration; Standardized clinician administered tool with 24-items	Tactile deep pressure, adaptive motor function, visual-tactile integration, ocular-motor control, vestibular stimulation	4 – 24 months	EL-ASD; Premature infants; TD	(Bart et al., 2011; Botha et al., 2022; Chorna et al., 2014; DeGangi et al., 2000; Feldman et al., 2021, 2022; Freund-Azaria et al., 2023; Lecuona et al., 2017; Lecuona et al., 2016; **Machado et al., 2023**)

RDoc element	Tool	Purpose	Stimuli	Variable measured	Age range	Pop.	Cited in
Sensory Reactivity	Sensory Processing Assessment for Young Children (SPA; Baranek, 1999)	Clinical	Auditory, tactile, and visual stimuli; Semi-structured, play-based observation with a series of novel toys affording sensory experiences	Hyporeactivity, Hyporeactivity, Sensory Seeking Behaviors; Approach, Avoidance, Habituation, Orientation, Defensiveness	1 – 12 years	ASD; DD; EL-ASD	(Baranek et al., 2018; Brock et al., 2012; Campi et al., 2022; **Damiano-Goodwin et al., 2018**; **Donkers et al., 2015, 2020**; Feldman et al., 2021, 2022; Grzadzinski et al., 2020, 2021; Jatkar et al., 2023; Kinard et al., 2017; Kirby et al., 2019; Watson et al., 2011)
Sensory Reactivity	Sensory Assessment for Neuro-developmental Disorders (SAND; Siper et al., 2017)	Clinical	Auditory, tactile, and visual; Clinician-administred observation (15 sensory toys, 5 per domain) and caregiver interview	Total sensory score; DSM-5 criteria scores (Hypo-, hyper-, and seeking); Sensory domain scores (auditory, visual, tactile)	2 – 6 years	ASD; TD	(MacLennan et al., 2021; Rossow et al., 2021; Siper et al., 2017)

RDoc element	Tool	Purpose	Stimuli	Variable measured	Age range	Pop.	Cited in
Sensory Reactivity	Researcher-developed behavioral Observation/ Coding Systems	Exp.	Auditory, visual, and tactile; Sensory presentations of 22 stimuli	Behavioral responsivity; Hyporesponsivity, Moderate reactivity; Hyperreactivity	2 – 3 years	ASD; TD	(**Woodard et al., 2012**)

Note. ; Exp. = Experimental; ABC = Acuteness of the first cry, Burst rhythmicity and temporal Constancy of cry intensity (Bellieni et al., 2005); FACS = Facial Action Coding System (Ekman, 1978); PADS = Pain and Discomfort Scale (Bodfish et al., 2001); ASD = autism spectrum disorder. CP = cerebral palsy; DD = developmental disabilities; EL-ASD = elevated likelihood of autism; FXS = fragile X syndrome; GDD = global developmental delay; n.s. = not specified; TD = typically developing; Bolded measures and citations indicate the use of multiple-methods of sensory measurement (e.g., Machado et al. (2023) used measures of behaviors and physiology).

Table 1 *Measures of Peripheral Nervous System Physiological Responses to Sensory Stimuli*

RDoc Element	Tool	Stimuli	Variable Measured	Age Range	Pop.	Cited in
			Auditory			
EMG Response	EMG	Single pure tone (100 db)	EMG potential	1 – 10 days	Newborns	(Boyle & Hull, 1976)
Eye Blink Reflex	Transducer	1,000 Hx, 10 s tone	Auditory-evoked eyelid microvibration (EMV); Reflex responses; Brainstem function	Not specified	Newborns	(Yamada, 1984)
Heart Rate Change	ECG	Auditory habituation (85 dB); Tonal mixtures	Heart-rate response (autonomic); Cardiac activity	1 – 3 days	Newborns	(Kittner & Lipsitt, 1976; Turkewitz et al., 1972)
Heart Rate Change	Biopotential electrodes (chest); miniature electrodes (eye); Dynograph	Complex sound (75 dB) repeated 8 times	Cardiac activity and conjugate eye movements (orienting behavior)	6 – 9 weeks	Infants	(Brown et al., 1977)
Heart Rate Change	ECG	Alarm clock (sudden, loud, unexpected stimulus)	Interbeat interval (arousal, index of	1 – 11 years	FXS, TD	**(Roberts et al., 2013)**

			parasympathetic tone)			
Respiration	Thermistor bead and multichannel Grass polygraph	Four tones of increasing intensity	Respiration (average peak and return log time)	2 – 5 days	Newborns	(Steinschneider, 1968)
Respiration/ Heart Rate Change	Polysomnograph	White noise bursts at 80 dB	Apnea (passive defense response)	2 – 13 months	Infants	**(Anderssen et al., 1993)**
Skin Conductance	Electrodes	SCP auditory stimuli (siren at 78 dB, standard tone at 84 dB)	Changes in skin conductance response (sympathetic nervous system)	5 – 12 years	ASD, TD	(Chang et al., 2012)
Vagal tone/ Respiration	ECG; Respiratory band	Click-like tones at two intensities (higher, lower)	Respiratory sinus arrhythmia (RSA); Baseline and vagal tone change; Indices of vagal regulation	1 – 12 months	Infants	(Mateus et al., 2018)
			Tactile			
EMG Response	EMG	Heel lance, von frey hair	Flexion withdrawal reflex activity	0 – 14 days	Newborns; PT, FT	(Cornelissen et al., 2013)

Heart Rate Change	ECG	Heel lance and non-invasive tactile stimulation	Changes in heart rate and crying	1 – 3 days	Newborns	(Owens & Todt, 1984)
Galvanic Skin Response	Beckman GSR electrodes	Routine blood sampling (pain), caregiver's touch	Galvanic skin response compared to PIPP	3 – 5 days	Newborns	(Eriksson et al., 2008)
Skin Conductance	Beckman electrodes	Heel prick/ immunizations	Skin conductance activity (waves per second)	1 day – 3 months	Newborns, Infants	(Hellerud & Storm, 2002)

Multisensory

Skin Conductance	Electrodes	SCP (auditory, tactile, visual, olfactory, vestibular)	Electrodermal response; magnitude of largest peak	5 – 13 years	ADHD; SMD; TD	(Mangeot et al., 2001; Su et al., 2010)
Vagal tone/ Heart Rate	ECG	SCP (auditory, visual, tactile, olfactory, vestibular)	Cardiac vagal tone index (marker of PNS activity)	4 – 8 years	SPD	(Schaaf et al., 2003)

Note. Pop. = population; ECG = electrocardiography; EMG = electromyography; GSR = galvanic skin response; SCP = Sensory Challenge Protocol (Miller et al., 2001); ADHD = attention deficit hyperactivity disorder; ASD = autism spectrum disorder; FXS = fragile X syndrome; FT = full-term; PT = preterm; SMD = sensory modulation disorder; SPD = sensory processing disorder; TD = typical development;

Table 2 *Measures of Central Nervous System Physiological Response to Sensory Stimuli*

RDoC element	Tool	Stimuli	Variable measures	Age range	Pop.	Citations
Auditory						
BOLD activation of cortical regions	fMRI	Frequency modulated pure tone	BOLD signal parallel to superior temporal gyrus; cortical activation	1– 14 days	PT, FT	(Anderson et al., 2001)
BOLD activation of cortical regions	fMRI	Flickering/ flashing light	BOLD signal change in occipital area; occipital lobe activation	3 days – 48 months	TD	(Born et al., 1998; Lee et al., 2012)
ERP	EEG	Broadband noises	Cortical auditory evoked potentials (CAEP)	1 month – 5 years	TD	(Lippé, et al., 2009b)
ERP	EEG	Rapid Auditory Processing	Average auditory event related potentials	8 days – 6 months	DS, TD	(Barnet et al., 1971; Cantiani et al., 2023)
ERP; Oscillations	EEG	Complex tones; Serial presentation of tones	Auditory ERPs; Low-level stimulus detection and registration, mismatch response; Global field power (GFP)	2 days – 48 months	ASD, TD	(De Meo-Monteil et al., 2019; Kushnerenko et al., 2001; Ruusuvirta et al., 2003))
ERP Components (P300, N2)	EEG	Sensory Registration Paradigm	Peak-to-peak amplitude and latency for N200 and P300 components	5 – 10 years	SPD, TD	Gavin et al. (2011)

RDoC element	Tool	Stimuli	Variable measures	Age range	Pop.	Citations
ERP Components (P1, N2, P3a); MMN	EEG	Oddball paradigms with deviant sounds	ERP; Repetition suppression, change detection, auditory discrimination; Mismatch negativity (MMN); Grand average waveforms	1 day – 12 years	ASD, EL-ASD, TD	(Begum-Ali et al., 2021; Donkers et al., 2015, 2020; Ruiz-Martínez et al., 2020)
MMN	Neuro-MEPω EMG	Oddball paradigm	Latencies and amplitudes of MMN	2 mo. – 5 years	TD	(Gupta & Bhardwaj, 2022)
Local cerebral blood flow changes	NIRS	Popular piano music; Sinusoidal tones in stimulus train	Auditory evoked cerebral blood oxygenation (CBO) changes; Hemodynamic response	1 day – 3 days	HIE; TD	(Chen et al., 2002; Kotilahti et al., 2005; Sakatani et al., 1999)
Visual						
Alpha	EEG	Video of moving shapes (muted)	Frontal alpha asymmetry	18 months	ASD, TD	(Damiano-Goodwin et al., 2018)
ERP	EEG	Complex visual stimuli	Cortical responses to orientation reversal, global form, and global motion	27 days – 5 years	TD	(Ahtola et al., 2017, 2020; Lippé et al., 2007)
ERP	EEG	Flashes of light, varying intensities	Evoked potentials from occipital electrodes	0 – 5 days	PT, FT	(Ellingson, 1960)

RDoC element	Tool	Stimuli	Variable measures	Age range	Pop.	Citations
ERP	EEG	Phase-reversal sine wave gratings	Grating visual acuity; Sweep visually evoked potentials technique	6 – 108 months	WS	(Dotto et al., 2014)
Local cerebral blood flow changes	NIRS	Checkerboard patterns, unpatterned screen, flashing lights, lights	Changes in concentration of oxy- and deoxyhemologin	1 day – 8 months	TD	(Goodwin et al., 2016; Karen et al., 2007; Kusaka et al., 2004; Meek et al., 1998; Taga et al., 2003; Watanabe et al., 2012)
Tactile						
Alpha, Delta, Theta	EEG	Pain (heel lance)	EEG power; Right-left frontal asymmetry	Not specified	PT infants	(Maimon et al., 2013)
ERP	EEG	Body rep. paradigm	Somatosensory evoked waveforms	52 – 64 days	TD	(Meltzoff et al., 2019)
ERP	EEG	Suprathreshold stimulation	Somatosensory evoked potentials to mechanical stimuli	4 – 6 years	ASD, TD	(Espenhahn et al., 2021)
ERP	EEG	Tactile stimulation of hand (palm) and foot (sole)	Somatosensory evoked potentials	Birth – 40 days	PT; ELBW	(Leikos et al., 2020; Vanhatalo et al., 2009)

RDoC element	Tool	Stimuli	Variable measures	Age range	Pop.	Citations
ERP	EEG	Heel tapping	Extreme somatosensory evoked potentials; Clinical use for predicting seizures	2 – 12 years	Varied disabilities and seizures; TD	(Marco & Tassinari, 1981)
Local cerebral blood flow changes	NIRS	*G*entle stroking (toothbrush); vibrotactile stimulus; venipuncture	Changes in concentration of oxy- and deoxyhemoglobin over somatosensory cortices; Cerebral metabolic rate of oxygen consumption (rCMRO2)	1 day – 12 months	FT, PT; TD	(Bartocci et al., 2006; Jönsson et al., 2018; Machado et al., 2023; Roche-Labarbe et al., 2014)
			Multisensory			
ERP	EEG	*Tactile/Auditory* Light touch and /ga/ syllable	Multisensory neural response interactions; Topographic clustering; Multisensory integration	1 – 3 days	PT, FT	(Maitre et al., 2020)
ERP; ERP Components (N2)	EEG	*Auditory/Visual* McGurk Paradigm; Uni- and bi-modal stimuli	Audio-visual event related potentials; Audio-visual integration; Auditory evoked potentials; Multisensory integration	3 – 13 months	EL-ASD; TD	(Hyde et al., 2010; Riva et al., 2022)
ERP	EEG	*Auditory, Visual* Pattern reversal and broadband noises	Complexity of EEG signal for auditory compared to visual stimuli; Comparing multiple sensory domains	27 days – 5 years	TD	(Lippé et al., 2009a)

RDoC element	Tool	Stimuli	Variable measures	Age range	Pop.	Citations
ERP Components (N1, N2)	EEG	*Auditory, Tactile, Visual* Clicking sound; LED goggles; Current on wrist	multimodal evoked potentials; brainstem auditory evoked potentials, visual evoked potentials, and short-latency somatosensory evoked potentials; Comparing multiple sensory domains	6 – 18 months	DS, TD	(Chen & Fang, 2005)
Local cerebral blood flow changes	NIRS	*Auditory, Tactile, Visual* Music, speech, pink noise, vibration, flashing light	cortical hemodynamic changes; broad cortical activation (parietal, temporal, occipital); Primary sensory area	2 – 9 days	TD	(Shibata et al., 2012)
Local cerebral blood flow changes	NIRS	*Auditory, Visual* Checkerboard pattern reversal and speech sounds	changes in oxygenated and deoxygenated hemoglobin bilateral temporal cortex (NIR OT); multimodal perception	2 – 4 months	TD	(Taga & Asakawa, 2007)

Note. Pop. = population; BOLD = blood oxygenation level-dependent; ERP = event-related potentials; MMN = mismatch negativity; EEG = electroencephalography; fMRI = functional magnetic resonance imaging; Neuro-MEPω EMG = electromyography and EP Digital Neurophysiological System software (M/S Neurosoft Ltd, Ianovo, Russia); NIRS = near-infrared spectroscopy; ASD = autism spectrum disorder; DS = Down's syndrome; ELBW = extremely low birthweight; EL-ASD = elevated likelihood for autism spectrum disorder; FT = full-term; HIE = hypoxic-ischemic encephalopathy; PT = preterm; SPD = sensory processing disorder; TD = typical development; WS = West syndrome.

Table 3 *Measures of Circuits in Response to Tactile Stimuli*

RDoC elements	Tool	Stimuli	Variables measured	Age range	Pop.	Citations
BOLD activation of cortical regions; Orbiotofrontal cortex, Striatum, Pons, Cerebellum	fMRI	Soft brush strokes (child asleep)	Neural correlates of affective touch; Subcortical activation; connectivity neworks; orbitofrontal cortex, right ventral striatum, bilateral inferior striatum, pons, cerebellum	11 – 40 days	TD	(Mariani Wigley et al., 2023)
Somatosensory cortex	MEG	Electrical stimulation of wrist; Taps on fingers	Somatosensory evoked magnetic fields (SEFs); Somatosensory cortex activation (contra- and ipsilateral primary (SI) and secondary (SII) somatosensory cortices; N1 cortical generators	1 day – 57 years	Non-verbal adults, ELGA, TD	(Lauronen et al., 2006; Nevalainen et al., 2008; Pihko et al., 2009; Rahkonen et al., 2013)
Local cerebral blood flow changes; Insular cortex; Somatosensory cortex; Superior Temporal Sulcus	DOT, fNIRS	Affective touch	Total hemoglobin responses in the left hemisphere (activation cluster in temporal cortex (centered in middle temporal gyrus), and insular cortex); superior temporal sulcus, left somatosensory region (discriminatory), and right temporal region (affective touch)	46 days – 17 months	TD	(Jönsson et al., 2018; Miguel et al., 2020)

Note. fMRI = functional Magnetic Resonance Imaging; MEG = magnetoencephalography; DOT = Diffuse Optical Tomography; fNIRS = functional near-infrared spectroscopy; TD = typical development; ELGA = extremely low gestational age.

Table 4 *Participant Demographic Characteristics for n=45 IBIS Participants with mQST Data*

Characteristic	Autistic Group (*n*=8)		Non-autistic Group (*n*=37)	
	n	%	*n*	%
Sex				
Female	3	37.5%	19	51.4%
Male	5	62.5%	18	48.6%
Race				
Asian	1	12.5%	1	2.7%
Multiracial	0	0.0%	4	10.8%
White	6	75.0%	29	78.4%
Not answered	1	12.5%	3	8.1%
Ethnicity				
Hispanic	0	0.0%	2	5.4%
Non-Hispanic	7	87.5%	32	86.5%
Not answered	1	12.5%	3	8.1%
Income				
<50,000	1	12.5%	10	27.0%
50,000 – 100,000	5	62.5%	12	32.4%
100,000 – 150,000	1	12.5%	7	18.9%
>150,000	0	0.0%	4	10.8%
Not answered	1	12.5%	4	10.8%

Note. Sex is sex assigned at birth.

Table 5 *Descriptive Statistics and Results for Mann-Whitney U Tests of Group Differences in Tactile Reactivity Scores*

				Autistic Group		*Nonautistic Group*					
Stimulus	*n*	*Skewness*	*Kurtosis*	*Median*	*IQR*	*Median*	*IQR*	*z*	*CI*	*p*	*A*
Sham	45	0.87	-0.11	1.5	1.50	1.0	2.0	0.77	–1, 1	.467	.42 (small)
Light touch	44	0.98	0.55	4.5	3.75	1.0	3.0	2.42	0, 5	.013	.25 (large)
Pin	44	0.68	-0.91	3.5	3.00	1.0	3.0	2.48	1, 4	.011	.25 (large)
Cool	44	0.87	0.46	2.5	3.25	1.5	2.0	1.22	0, 3	.233	.38 (small)
Pressure	44	0.72	-0.44	4.0	3.50	2.0	2.5	1.31	–1, 4	.196	.37 (small)
Repeated 1	41	0.99	0.17	2.0	2.25	1.0	3.0	0.91	–1, 2	.376	.31 (medium)
Repeated 2	41	1.16	1.30	4.0	0.75	2.0	3.0	2.29	0, 3	.018	.19 (large)
Heat	36	0.57	-0.88	5.0	2.00	1.0	3.0	2.62	1, 5	.007	.32 (medium)

Note. Tactile reactivity scores are the observed behavioral reactivity scores to modified Quantitative Sensory Testing (mQST; Symons et al., 2010) stimuli and range from 0 to 10. IQR = Interquartile Range. The *z*-test statistic, confidence interval (CI), and *p*-values are from the Mann-Whitney U tests. Effect size was estimated using Vargha & Delaney's *A*.

Table 6 *Wilcoxon Signed-Rank Tests Examining Differences Between mQST Sham and Active Stimuli*

mQST Stimulus	*Median*	*IQR*	*z*	*df*	*p*
Sham (initial)	0.50	1.00			
Sham (randomized)	0.50	1.50	0.22	20	0.826
Light touch	1.25	2.00	–2.78	33	.005
Pin	1.00	3.38	–3.50	33	< .001
Cool	1.00	1.50	–2.95	32	.003
Pressure	1.00	1.00	–2.19	32	.028
Repeated Von Frey (first 5s)	2.00	1.50	–4.27	31	< .001
Repeated Von Frey (last 5s)	2.00	2.00	–4.21	31	< .001
Heat	1.00	2.00	–2.96	29	.003

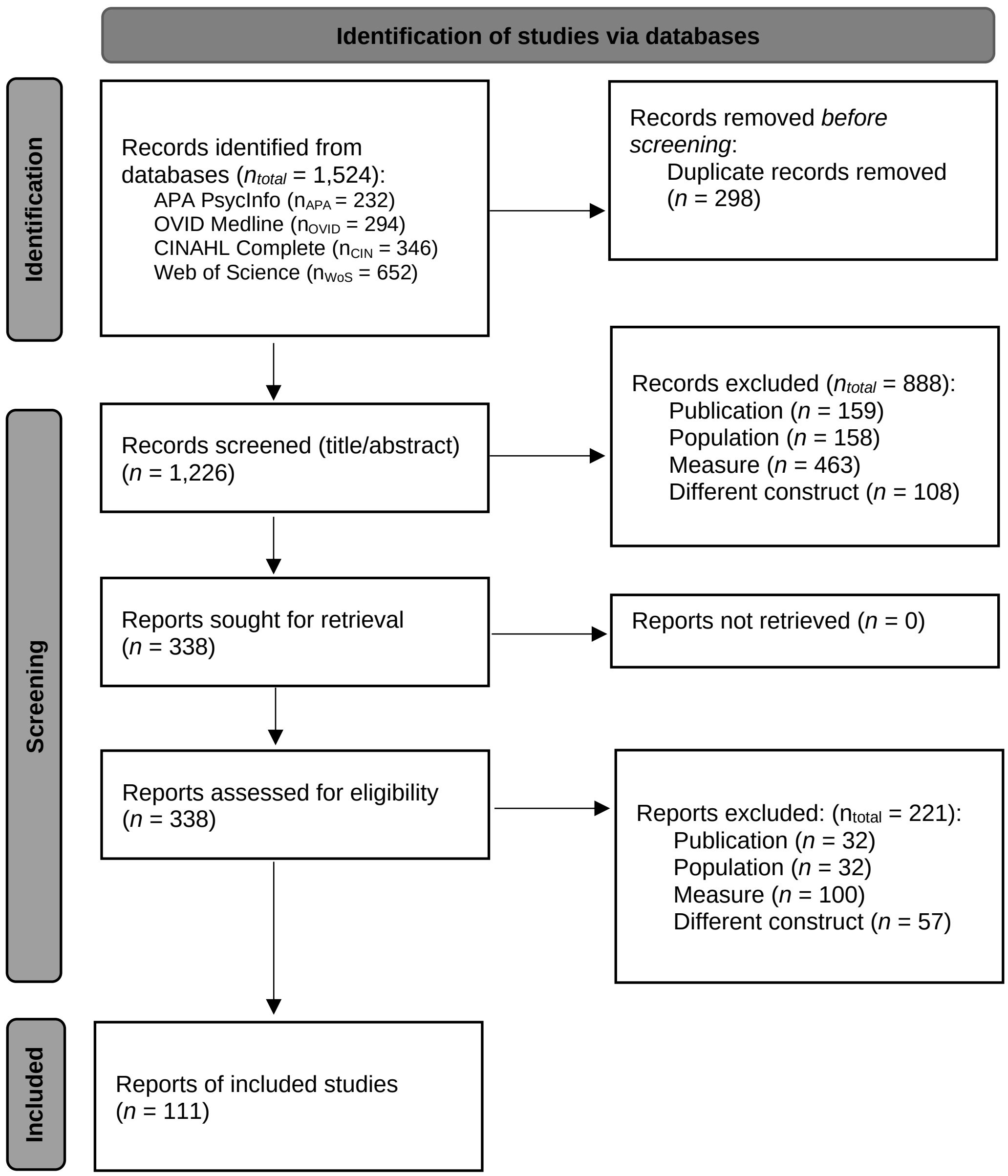
Table 7 *Mann-Whitney U Tests Examining Sex Differences in Behavioral Reactivity to mQST Stimuli*

mQST Stimulus	Female (*n*=12)			Male (*n*=21)			*z*	*p*	*A*
	n	*Median*	*IQR*	*n*	*Median*	*IQR*			
Sham (initial)	12	0.75	1.13	21	0.50	0.50	1.49	.143	0.65 (small)
Sham (randomized)	7	1.00	2.25	13	0.50	1.00	1.23	.234	0.50 (negligible)
Light touch	12	2.00	1.75	21	0.50	1.50	1.63	.107	0.68 (medium)
Pin	12	0.75	3.50	21	1.00	2.50	–0.59	.569	0.44 (negligible)
Cool	12	1.25	1.50	20	1.00	1.13	0.24	.833	0.50 (negligible
Pressure	12	1.00	1.13	20	1.25	1.38	–0.36	.733	0.44 (negligible)
Repeated Von Frey (first 5s)	11	2.50	0.50	20	1.25	2.13	1.67	.100	0.68 (medium)
Repeated Von Frey (last 5s)	11	3.00	2.00	20	1.50	1.63	0.88	.393	0.60 (small)
Heat	10	1.00	1.50	18	1.25	3.63	–0.80	.435	0.43 (negligible)

Note. The effect size estimate used was Vargha & Delayney's *A*.

Figures

Figure 1 *Flow Diagram of Scoping Review Retrieval and Screening Process*



Note. The framework for this flow diagram was developed by Page et al. (2021).

Figure 2 *Year of Publication of Included Studies*

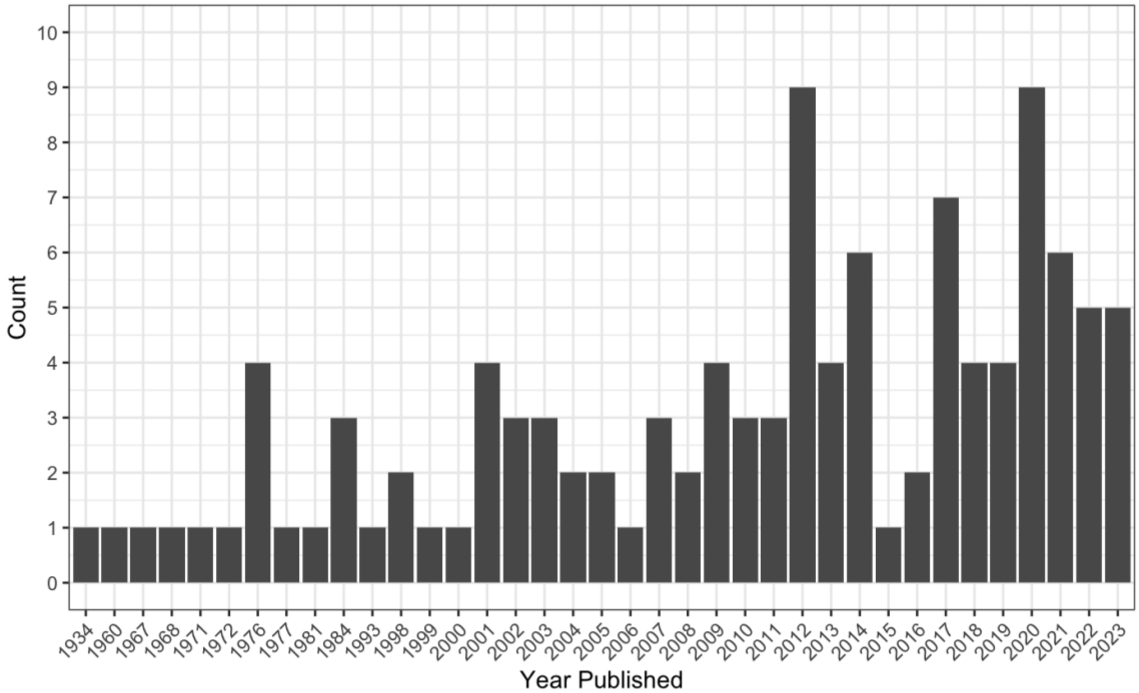
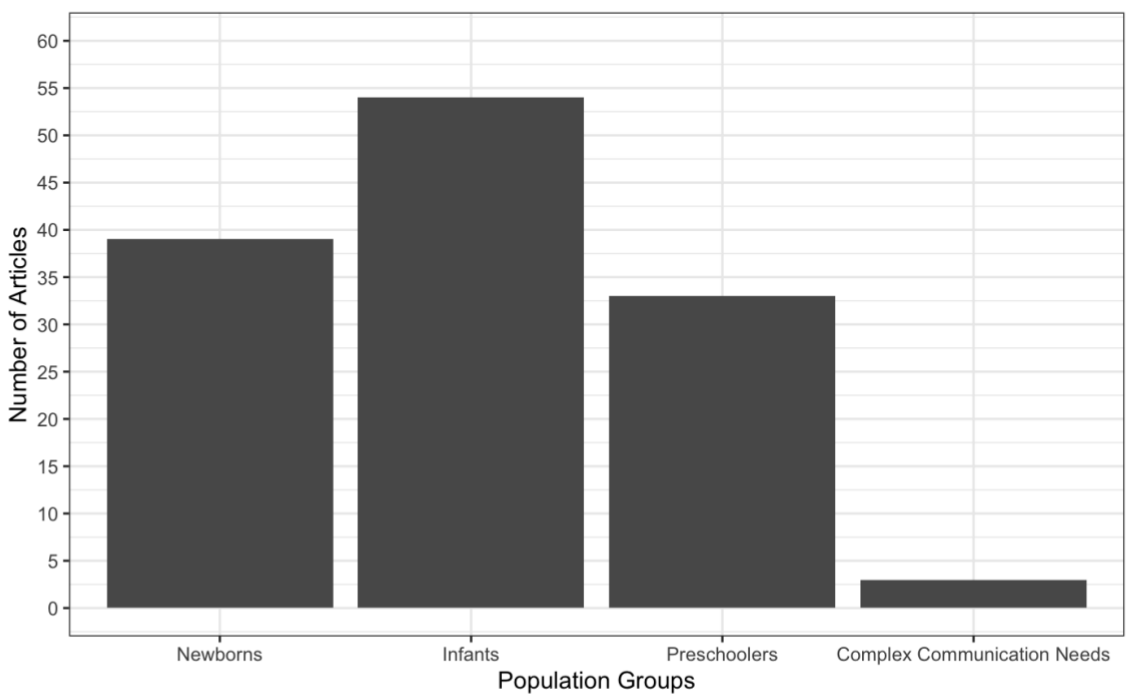
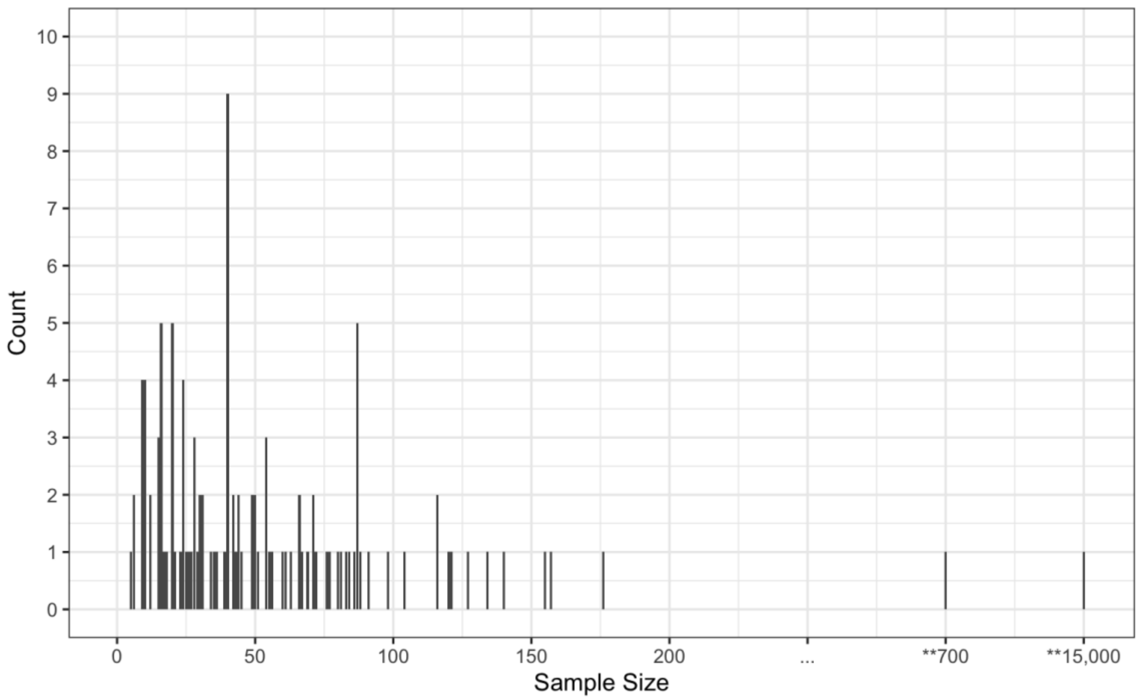


Figure 3 *Participant Groups Across (n=111) Included Studies*



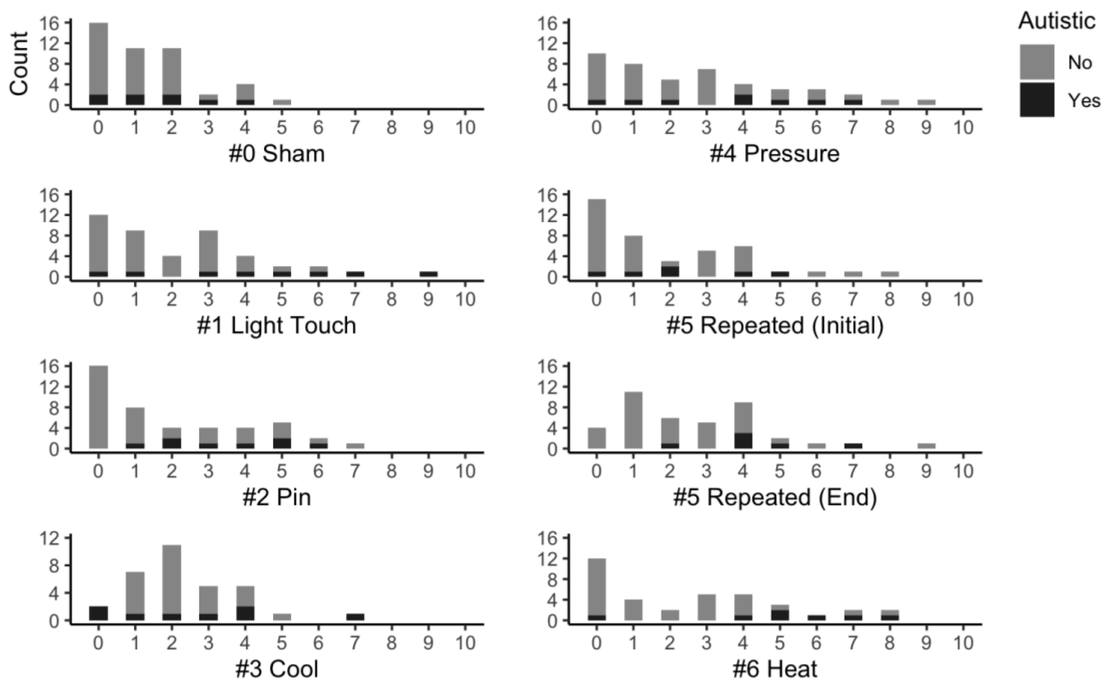
Note. Articles reporting on multiple groups were counted multiple times.

Figure 4 *Sample Sizes Across Included Articles (n=111)*



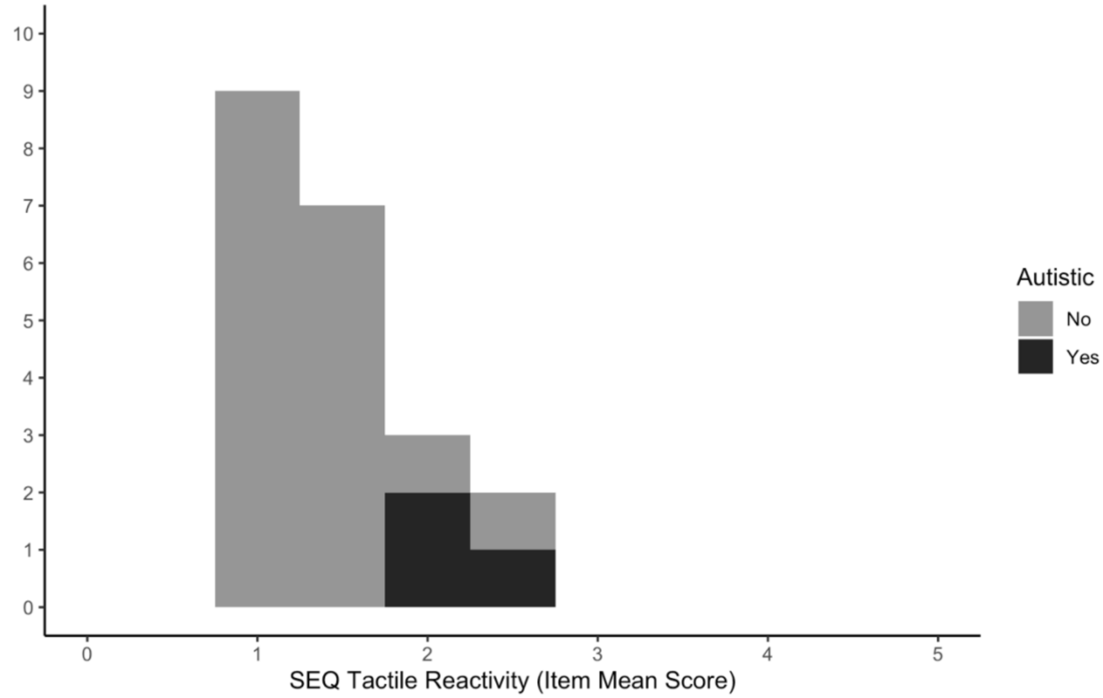
Note. The x-axis ranges from 0 to 200, breaks, and then indicates the sample size for 700 and 15,000.

Figure 5 *Distribution of Observed Behavioral Reactivity Scores to Tactile Stimuli*



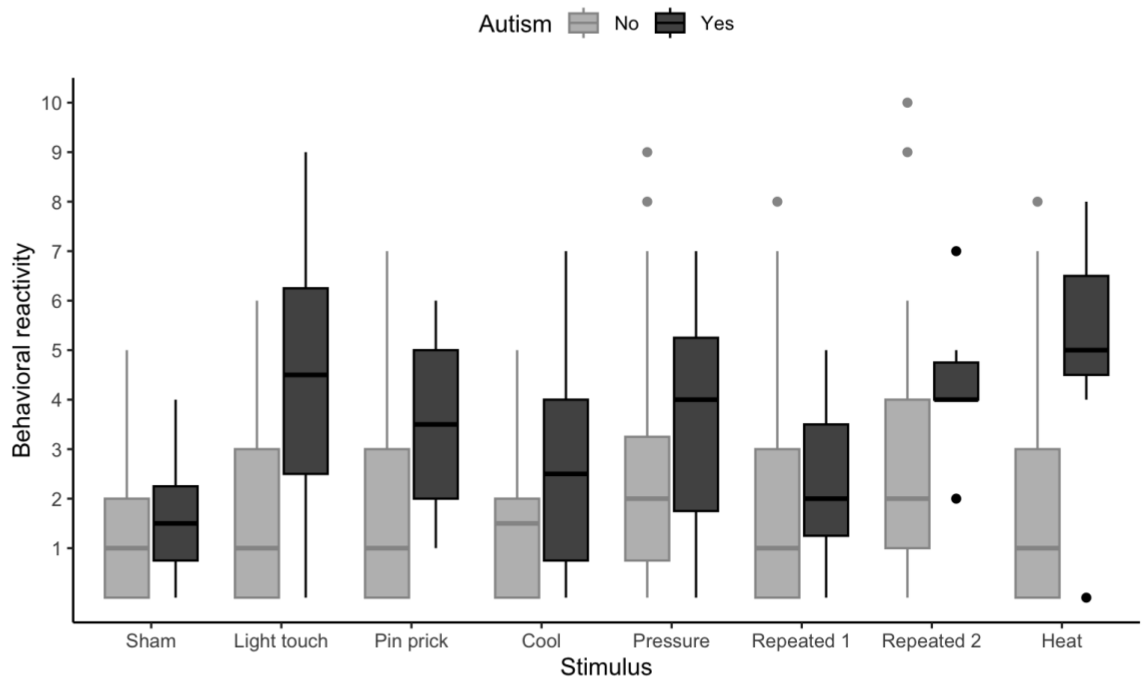
Note. The *x*-axis displays observed behavioral reactivity scores for each modified quantitative sensory test (mQST) stimulus (including sham). The *y*-axis displays the number of participants with each behavioral reactivity score. Gray indicates participants without autism (n=37), and black indicates participants with autism (n=8). The fifth stimulus, repeated Von Frey, is displayed twice: #5 Repeated (Initial) displays behavioral reactivity for the first 5 s, and #5 Repeated (End) displays behavioral reactivity for the last 5 s of the repeated application.

Figure 6 *Stacked Histogram Displaying Distributions of Caregiver-Reported Tactile Reactivity Scores*



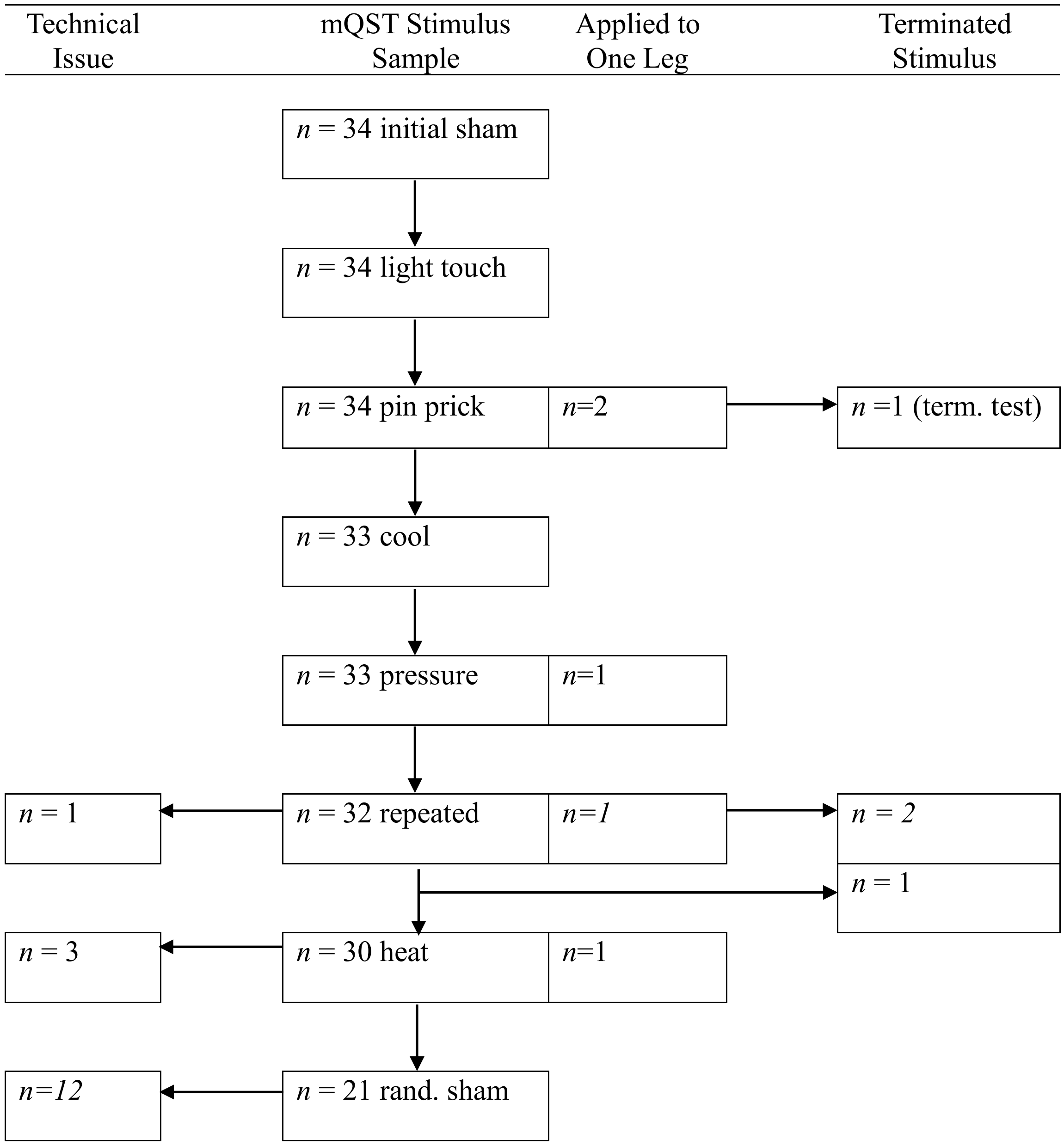
Note. The item mean score for the tactile reactivity sensory modality score on the Sensory Experiences Questionnaire 3.0 (SEQ; Baranek et al., 2009) was plotted with the binwidth set to 0.5. Gray indicates participants without autism and black indicates participants with autism.

Figure 7 *Box and Whisker Plot Displaying Group Differences in Behavioral Reactivity*



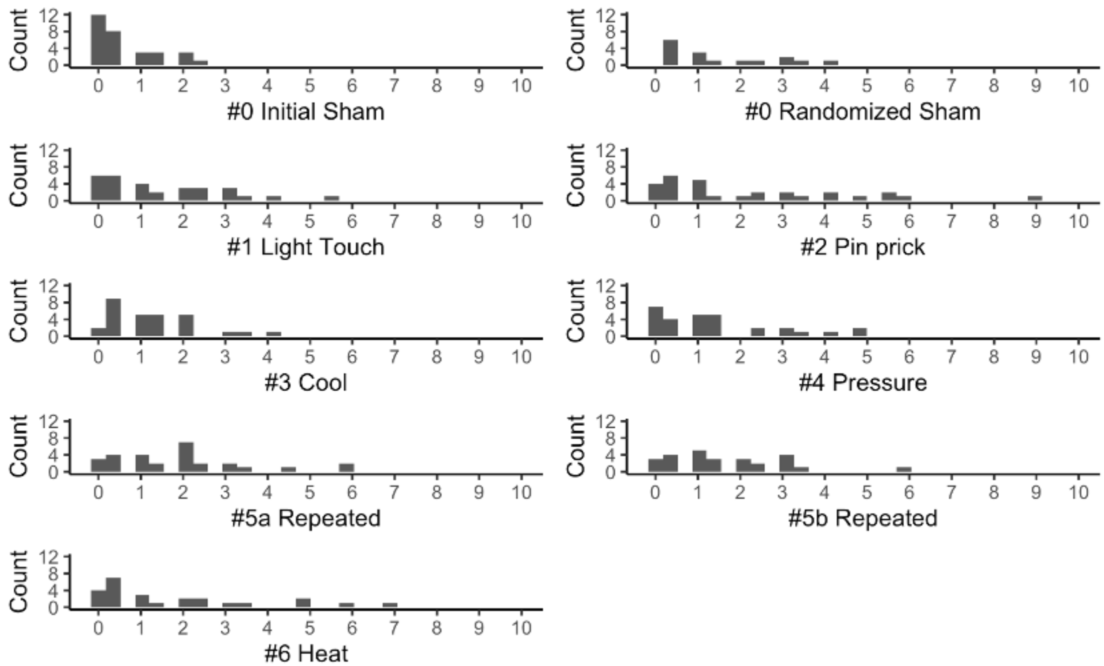
Note. The *x*-axis displays modified Quantitative Sensory Testing (mQST; Symons et al., 2010) stimuli. The *y*-axis displays behavioral reactivity to mQST stimuli across participants with (*n*=8; dark gray/black) and without (*n*=37; light gray) autism. Repeated 1 indicates the first 5 s, and Repeated 2 indicates the last 5 s of the repeated von Frey application.

Figure 8 *mQST Sample Size Progression in Typically Developing Children*



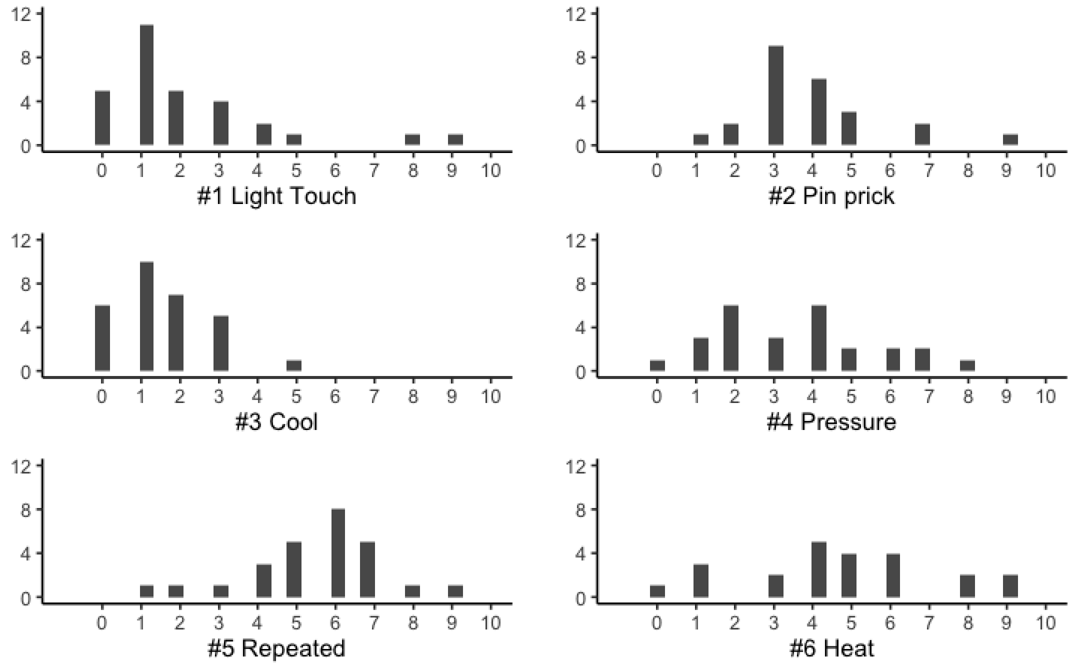
Note. Technical issues included missing face camera video, the heat probe not working, and adding the randomized sham after data collection began. The mQST stimulus sample indicates how many participants were scored for the particular stimulus. Applied to one leg indicates participants who were scored, but only based on application to one leg because the participant requested not to have the stimulus applied to the second leg. Terminated stimulus indicates participants who met termination criteria. Term. test indicates the participant terminated the entire test and was not included in subsequent stimuli applications. Rand. sham was a randomized sham that took place at different points in the protocol for each participant.

Figure 9 *Distributions of FLACC Scores for mQST Stimuli in Typically Developing Children*



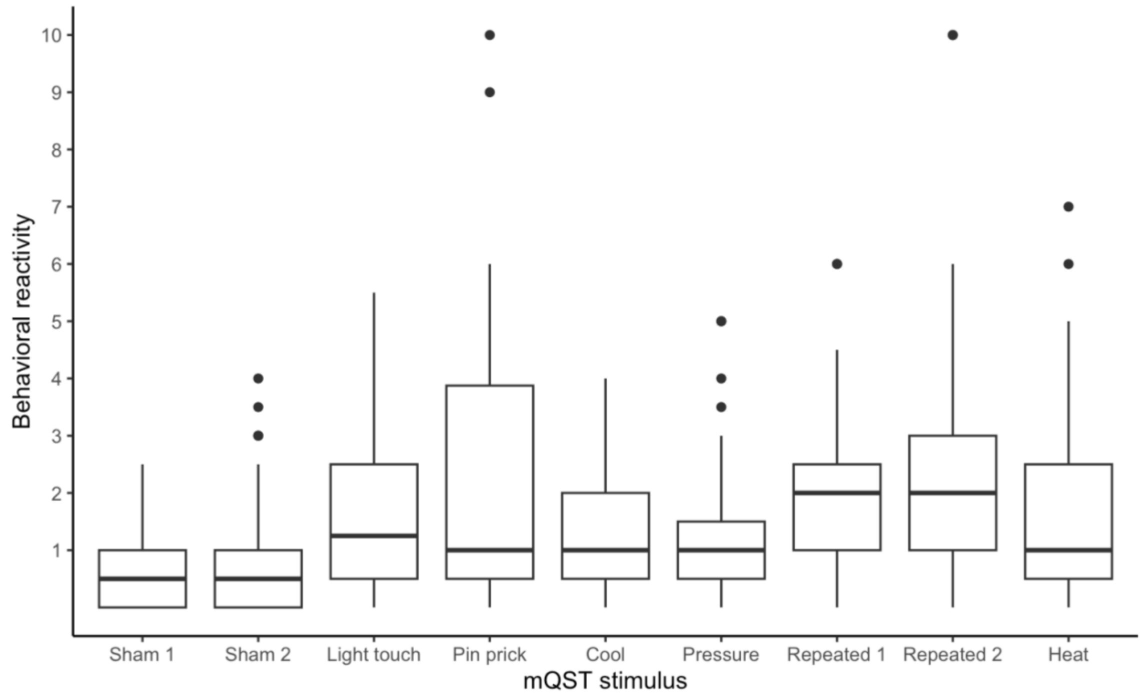
Note. FLACC = Face, Legs, Activity, Cry, Consolability (Merkel et al., 1997); mQST = modified Quantitative Sensory Test (Symons et al., 2010); '#5a Repeated' = First 5s of repeated von Frey application; '#5b Repeated' = Last 5s of repeated von Frey application.

Figure 10 *Distributions of Self-Report Scores for mQST Stimuli*



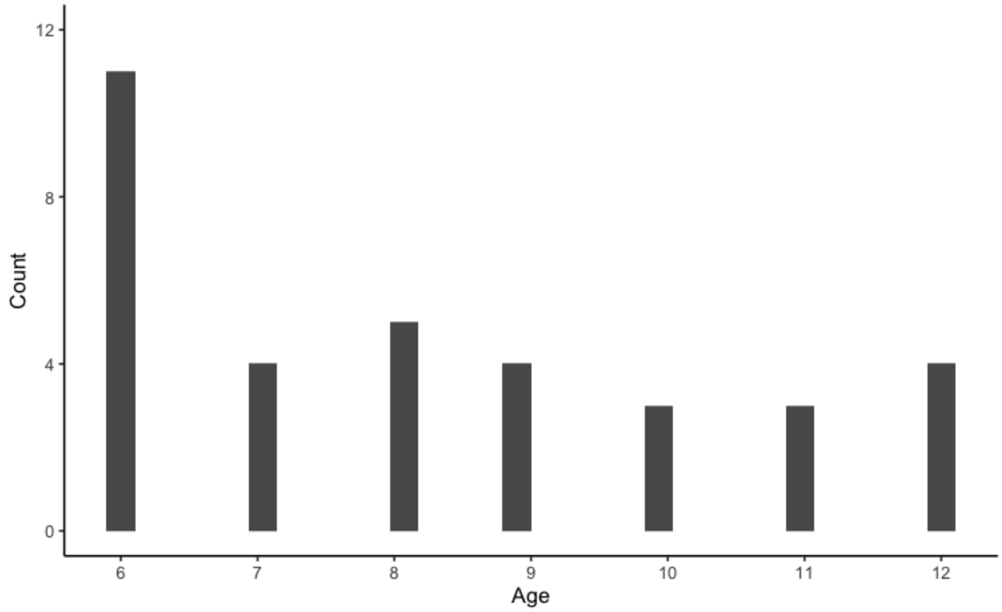
Note. mQST = modified Quantitative Sensory Test (Symons et al., 2010).

Figure 11 *Boxplot of FLACC Behavioral Reactivity Scores to mQST Stimuli (n=34)*



Note. FLACC = Face, Legs, Activity, Cry, Consolability (Merkel et al., 1997); mQST = modified Quantitative Sensory Test (Symons et al., 2010); Sham 1 = initial sham; Sham 2 = randomized sham; Repeated 1 = First 5s of repeated von Frey application; Repeated 2 = Last 5s of repeated von Frey application.

Figure 12 *Histogram of Age Distribution of Typically Developing Participants (n=34)*



Note. Age is displayed by year.

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