Cerebellum
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Sensory Integration, Sensory Processing, and Sensory Modulation Disorders: Putative Functional Neuroanatomic Underpinnings

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Abstract This paper examines conditions that have variously been called sensory integration disorder, sensory processing disorder, and sensory modulation disorder (SID/SPD/SMD). As these conditions lack readily and consistently agreed-upon operational definitions, there has been confusion as to how these disorders are conceptualized. Rather than addressing various diagnostic controversies, we will instead focus upon explaining the symptoms that are believed to characterize these disorders. First, to clarify the overall context within which to view symptoms, we summarize a paradigm of adaptation characterized by continuous sensorimotor interaction with the environment. Next, we review a dual-tiered, integrated model of brain function in order to establish neuroanatomic underpinnings with which to conceptualize the symptom presentations. Generally accepted functions of the neocortex, basal ganglia, and cerebellum are described to illustrate how interactions between these brain regions generate both adaptive and pathological symptoms and behaviors. We then examine the symptoms of SID/SPD/SMD within this interactive model and in relation to their impact upon the development of inhibitory control, working memory, academic skill development, and behavioral automation. We present likely etiologies for these symptoms, not only as they drive neurodevelopmental pathologies but also as they can be understood as variations in the development of neural networks.

Keywords Sensory integration disorder · Sensory modulation disorder · Sensory processing disorder · Basal ganglia · Cerebellum

Introduction

This paper examines the putative neuroanatomic underpinnings of conditions variously called sensory integration disorder (SID), sensory processing disorder (SPD), and sensory modulation disorder (SMD). The term "sensory integration" was originally proposed by Ayers [1, 2]. The term was introduced to identify a field of study focusing upon individuals—primarily children—who demonstrated atypical behavioral responses to sensory stimulation. This clinical condition is now referred to as SPD. SMD can be considered as a specific subtype of SPD, in which hypo and/or hyperresponsiveness to sensory stimuli is emphasized [3]. These conditions, to which we will refer to as SID/SPD/SMD hereafter, are primarily diagnosed through interviews and observational rating scales [4]; however, the diagnosis is controversial. While Regulation Disorders of Sensory Processing are included in the Diagnostic Classification of Mental Health and Developmental Disorders in Infancy and Early Childhood [5], neither SID, SPD, nor SMD is listed in the DSM-IV or ICD-9 nor were the apparently unique behavioral symptoms that define these conditions included as criteria for any DSM-IV or ICD-9 diagnosis. At the time of this paper's writing, there is continuing debate as to whether or not SPD will be included in the DSM-V.

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Thus far, the symptoms of SPD have not been variables of interest in the fields of psychiatry, neuropsychiatry, or neurology. The Handbook of Pediatric Neuropsychology makes no mention of these conditions, while the symptoms that are considered to comprise these disorders are only briefly mentioned in a short discussion of developmental dyspraxia [6]. Presently, SID/SPD/SMD only appear in the diagnostic nomenclatures of the professions that identify them, specifically, the fields of occupational and sometimes physical therapy. At the same time, the wide range of symptoms that characterize these conditions very clearly overlap with disorders diagnosed in other behaviorally defined systems. As such, while the behaviors that characterize SPD are not variables of interest within the framework of widely accepted diagnostic nomenclatures, this should not imply that the behaviors are insignificant or unimportant. Nevertheless, the validity of the constructs used to define SPD bear consideration, as do the relationships between known neuroanatomical structures and neurodynamic processes and the behaviors that characterize these conditions.

The meaning of the term "sensory" in SID/SPD/SMD needs to be clarified first. The Sensory Profile questionnaire, which is perhaps the most commonly used observational rating scale to make this diagnosis, does not operationally define "sensory processing" nor does it provide a unifying underlying neuroanatomic construct to explain it [4]. At the same time, the instrument encompasses behaviors that seem to go beyond the scope of "sensory processing," and it refers to categories or behaviors and behavioral observations that are multifactorial or multiply determined. For example, some sections of the Sensory Profile refer to auditory, visual, tactile, oral, and multisensory processing within these modalities, while others refer to sensory modulation and relate it to "endurance and tone," body position and movement, and affect and emotional responsiveness. There is a section in which emotional and social responses are rated and another that assesses presumed, predicted behavioral outcomes of sensory processing [3]. Some of the symptoms listed overlap with behaviors that are included in the diagnostic categories of the DSM.

This complex combination of factors suggests that the Sensory Profile cannot be measuring a monolithic construct or "one thing." In fact, James and colleagues recently recognized the heterogeneity of these symptom presentations and identified two subtypes of SMD characterized by externalizing and internalizing behavioral presentations, respectively [7]. Some of the symptoms listed in the Sensory Profile are vaguely defined and are observed in most children at least some of the time, which can lead to over-diagnosis of the condition. The Sensory Profile requires the identification of a group of behaviors that interfere with the child's ability to effectively participate in childhood activities in order to make the diagnosis rather than the presence or absence of a single symptom in an effort to limit false positive diagnoses.

The Sensory Profile defines aspects of sensory processing disorders within four clusters or constructs, but identifying clusters or groups of symptoms is not the same as identifying the neuroanatomic underpinnings that drive them, nor does identifying clusters or symptom groups clarify brain–behavior relationships. In this way, The Sensory Profile is akin to the DSM and ICD systems in that it represents a behaviorally defined nomenclature and not one that is neuroanatomically organized. Just as most conditions listed in the DSM are characterized by abnormalities in multiple brain regions [8], it is likely that the varying presentations of SID/SPD/SMD are characterized by anomalous functioning in multiple brain regions and mechanisms as well. Our purpose is not to criticize the Sensory Profile or any other behaviorally defined diagnostic system. Our purpose is to clarify the neuroanatomic frameworks underlying symptom presentations to facilitate communication among disciplines.

In this review, we will differentiate behaviors frequently associated with SID/SPD/SMD into several categories. We conceptualize *all behavior as inherently requiring an integration of sensory input with motor output* and we operate from a perspective strongly biased toward placing behavior in a context of *continuous sensorimotor interaction* between an individual and his/her environment [9]. Our categories will include factors involved in the perception, processing—or "noticing"—of sensory experiences, the modulation of these experiences as characterized by hyper- and hypo-sensitivities (and as observationally manifested by hyper and hypo-responsiveness), and the cognitive and behavioral symptoms that can be generated by disturbances within sensory systems. We will address these issues within the context of a neuroscientific knowledge base.

The brain's functional architecture evolved to meet the needs of interactive behavior; this evolutionary trend was strongly conserved during phylogeny. We thus do not endorse a simplified, serial information processing framework that posits: First, we perceive; then we think to organize a response; then we respond. Seminal papers by Cisek and Kalaska [9], Shadlen and Movshon [10], and Singer [11] review neurobiologic data from various disciplines and conclude that there is little evidence to support a perception–cognition–action model as a phylogenetically conserved or useful primary mode of adaptation [9–11]. Rather, we endorse a sensorimotor interaction paradigm that challenges traditional models of perception, cognition, and behavior by stressing the significant overlap and interaction between cortical and subcortical regions that

serve both consciously controlled and automatic adaptive behaviors as they occur in "real time" [12, 13]. This sensorimotor interaction paradigm also challenges the traditional views of sensory processing/sensory integration disorder for practitioners who may be biased by a perception–cognition–behavioral model.

As summarized by Cisek and Kalaska, and we agree, our perception of the world is not the result of a serial processing or reconstruction process that uses sensory data to construct an internal representation of the external world. Instead, neural processing is continuous [9]. Processing in the parietal cortex dorsal stream and reciprocally connected premotor regions is primarily concerned with pragmatic, practical representations of the opportunities for action that those objects afford or offer [14–16]. The parietal cortex focuses upon spatial information because these data are critical for specifying the parameters of ongoing and potential actions [17]. The ventral stream provides information for action selection by biasing these potential actions with information about reward value associated with the identity of objects. This behavioral biasing includes information from the reward centers of the basal ganglia and regions of the prefrontal cortex that predict reward outcomes [18]. While several potential actions are available in most situations, these potential activities are reflected over large portions of the cerebral cortex. Decision-making is not strictly localized within the prefrontal cortex, but instead it is found within the same sensorimotor circuits that are responsible for planning and executing the associated actions.

In this way, cognition is not separate from sensorimotor control [19]. The final selected action, or "decision," is the result of cortical–basal ganglia interactions. While actions lead to overt feedback from the environment, action is undertaken in interaction with predicted feedback through the cerebellum, which appropriately refines or adjusts the behavior. This model emphasizes sensorimotor interaction, or behavior in "real time" that is not easily explained through a "perception–cognition–action" model. (Unfortunately, a complete review of models based upon continuous sensorimotor interaction and affordances is beyond the scope of this paper; for a comprehensive review, see Cisek and Kalaska (9). Our manuscript focuses upon the roles of the cortex, basal ganglia, and cerebellum within this sensorimotor context and explains the symptoms of sensory processing disorders within this framework; thus, our discussion of these conditions includes a paradigm shift).

Diagnostic Presentations

Parents frequently describe their children as exhibiting various symptoms associated with SID/SPD/SMD. Hypo- and/or hypersensitivity (responsiveness) to sensory stimulation is estimated to occur in 5% of children within the general population, while it is found in 40% to 80% of children with developmental disorders, and it is typically disabling in terms of a child's ability to accomplish practical, daily activities and age-appropriate learning tasks [20]. Despite an exhaustive review of the literature, we were unable to find operational definitions that clearly and consistently separate the categories of SID/SPD/SMD. Instead we find that these terms are frequently and unfortunately used interchangeably [21]. The Interdisciplinary Counsel of Developmental and Learning Disorders has categorized SMD into three subtypes: sensory overresponsivity, sensory underresponsivity, and sensory seeking/craving. A recent study by James and colleagues did not support the existence of these three particular behaviorally defined subtypes [7]. However, this type of attempt at categorization can remain helpful in providing a clinically useful nosology for the subtyping of SMD. The DSM nosological system for identifying psychiatric disorders and this way of subtyping SMD both remain behaviorally defined rather than anatomically organized approaches. They allow us to describe what we see, while they do not allow us to understand why what we see is occurring.

Rarely does SID/SPD/SMD appear alone. While Reynolds and Lane reported three cases in which the subjects presumably presented with SPD who did not technically meet the criteria for any DSM diagnosis, it is not clear as to whether or not these subjects presented with other behavioral and/or cognitive symptoms. This seems unlikely since, by definition, people diagnosed with SPD experience some deficit in adjustment [22]. It is common to find SID/SPD/SMD "diagnosed" in children with co-morbid conditions. The tactile and other sensory perceptual hyper- and hyposensitivities that are often a feature of SID/SPD/SMD, for example, are observed in children with autism spectrum disorders (ASD) and are often associated with increased stereotyped behaviors in that population [23]. They are also observed in ADHD populations and within this group are associated with increased levels of hyperactivity [24]. Sensory-perceptual hypersensitivities have been reported with comparable frequency in children with autism and with global developmental delays [25, 26]. They have been reported with increased frequency in children who demonstrate sleep problems, behavioral problems, and other neurodevelopmental conditions, such as developmental coordination disorder, which is very frequently co-morbid with cognitive and emotional regulation problems, including the so-called cerebellar cognitive affective syndrome [27–32]. Symptoms of SMD also occur frequently with cerebral palsy [27]. When young, school-aged children present for clinical evaluation and are assigned a formal

DSM-type diagnosis, a previous diagnosis of SID/SPD/SMD is frequently observed in the child's history.

While these findings imply that the neurobiologic mechanisms underlying SID/SPD/SMD and ADHD, autism, and other diagnosable neurodevelopmental disorders are shared, the manner in which the symptoms of SID/SPD/SMD are organized within the Sensory Profile lacks a coherent neuroanatomic explanation [25, 26]. In her classic work, *Sensory Integration and the Child*, Jean Ayers concludes that the symptoms reflected in SID "are the end products of inefficient and irregular sensory processing in the brain (page 54)." She does not, however, address the significance of specific brain–behavior relationships, including the possible interactive roles of the neocortex, the basal ganglia, and cerebellum [1]. Instead the theory of SID is based upon a pyramid of sensory, cognitive, and behavioral systems that places tactile, vestibular, and proprioceptive systems at the base, above which are the distal senses of vision and audition, while the complex sensorimotor, cognitive, and behavioral systems are found at the highest levels [27]. While this model might make intuitive sense, the brain–behavior relationships inherent in this view of the brain's organization have not been established [1]. Accordingly, while the symptoms that comprise the criteria for SID/SPD/SMD are common and real, the conditions lack clear operational definitions and they are poorly understood from an anatomic point of view.

Sensory hypersensitivities have been identified through behavioral observation and in some psychophysiological studies, but the results of studies that have focused on evaluating sensory thresholds have been inconsistent [22, 33]. Certain work has focused on electrodermal reactivity in an effort to make inferences about the levels of activity within the sympathetic nervous system [34–38]; however, this work does not speak to the myriad brain regions that can contribute to activity within the peripheral nervous system. Investigations that focus on the role of the RAS in regulating the peripheral nervous system appear to be in their infancy [39]. Studies of ASD have attempted to explore the neural underpinnings of abnormal sensory processing within the auditory, tactile, and visual modalities with techniques such as electroencephalography, magnetoencephalography, and functional magnetic resonance imaging (fMRI). However, the results of these studies of unimodal sensory processing and multi-sensory integration in ASD have been highly inconsistent and contradictory [40].

We believe that the relevant symptoms of SID/SPD/SMD can be readily classified within a neuroscientific knowledge base if we examine the brain–behavior relationships that should theoretically underlie the symptoms and disorders. Because the various symptoms associated with SID/SPD/SMD are related to movement and perception, we see them as necessarily tied to neurodevelopment and learning in pediatric patient populations. As movement and perception are fairly well understood by the neurosciences, a putative functional neuroanatomy for the symptoms associated with these conditions can be inferentially developed. We believe that all of these symptoms can be understood and parsimoniously explained within an integrated model of brain function, which is characterized by dynamic interactions between the neocortex, the basal ganglia, and the cerebellum. Therefore, we will begin with a very basic model of brain function and adaptation, and we will build from there.

A Dual-Tiered Model of Brain Functioning and Adaptation

The purpose of an organism is to survive. Survival is achieved through interaction with the environment. Interactions are based upon movement, perception, and mental representations that essentially comprise ideas and plans or are the outcomes of them. Much of what we do—perhaps 95% of an adult's activity or behavior—is routine or automatic [41, 42]. These are things we do spontaneously, "without thinking," simply because they need to be done. At times, however, while we are executing routine behaviors, something about the context or demand characteristics of the environment changes that precludes our routine responses being adaptive. In such moments, we need to recruit conscious, cognitive control and effort in order to change our behavior. With conscious, cognitive control, we may modify and refine what we are doing or we may select a different activity that will be more effective [43]. This system, in which episodes of automatic behavior alternate with the recruitment of higher-order control, essentially comprises a dual-tiered model of adaptation. Engaging in automatic behaviors recruits an interaction of brain structures that run on the basis of *acquired or learned associations*. These brain regions include the motor cortices, the basal ganglia, and the cerebellum [44–46]. Changing or modifying behaviors and learning new behaviors involves the interaction of different brain structures and regions, including the prefrontal cortex, the SMA, and subcortical structures, as will be described in subsequent sections of this paper [45, 46].

The brain serves adaptation by conserving resources. Developing effective behaviors to meet the challenges presented by novel or new situations initially requires effortful cognitive control. The more a behavior is practiced, the less cognitive effort its performance requires and the more automatically it can be generated. Automating frequently occurring behaviors allows the brain to conserve energy, while it simultaneously frees up the conscious cognitive control system to manage or "problem-solve" the

next experience of novelty. The brain functions according to this principle of novelty-routinization [47–49]. It essentially takes that which is novel and makes it familiar. This model of brain functioning requires interactions between the neocortex, the basal ganglia, and the cerebellum. These interactive processes are at a premium in child development specifically because the pediatric population, by definition, is in the process of acquiring adaptive skills to use to interact effectively with the environment. Child development proceeds according to the increasing control a child can exercise over the motor system [50, 51]. This process requires efficient sensorimotor interaction and development and it proceeds in a predictable way. Motor activity supervenes initially, when mental activity or action is less prominent. During the toddler years, both factors are coincident. In school-aged children, these factors begin to coexist, while gradually mental action subordinates motor activity as automaticity is achieved [52, 53].

The Neocortex

The posterior regions of the neocortex are exquisite sensory processors and the anterior neocortical regions are elegant motor programmers. Accordingly, the human being can perceive the world and develop and execute specialized motor programs like no other species. This higher-order and flexible range of adaptation generates enormous, complex behavioral possibilities so that the individual is almost constantly confronted with the need to select that to which to attend and the behavior in which to engage. In other words, the price we pay for our highly developed neocortex and its associated advanced cognitive and behavioral possibilities is the demand to contend with the overwhelming selection problem it generates [54, 55]. However, this "selection problem" is not unique to humans and it existed well before the significant expansion of the neocortex [56]. All animals, and specifically vertebrates, are confronted with *sensory perceptions and motor responses* that require behavioral choices and decisions to be made in the service of the best interest of the organism as a whole. Interactions between the cortex, which primarily functions according to principles of excitation, and the basal ganglia, which is a massive inhibitory system, represent the vertebrate solution to this selection problem [54, 57]. Balancing excitatory with inhibitory processes allows appropriate *perceptual* and *action* selections to be made.

The Basal Ganglia

The basal ganglia serve multiple roles, among which are several functions critically important to this discussion: They provide a *selection mechanism* for attention and motor activity [58] and they play a central role in "binding" or "chunking" (learning) new motor sequences and programs that are retained in the cortex [44, 59–62]. Aspects of this role have been considered by some to be analogous to the role of the hippocampus within the medial temporal lobe (MTL) memory system. Just as the MTL memory system binds sensory-perceptual experience, the basal ganglia bind motor sequences [44, 63, 64]. The basal ganglia also play a role in instrumental learning and, specifically, in selection processes related to behavioral choice, decision-making, and timing [65–68]. Aspects of basal ganglia functioning represent an underpinning to frontal lobe functions, which in general concern the temporal organization of behavior [66, 69].

The most fundamental anatomical scheme of cortical–basal ganglia connections is characterized by two connectional profiles. In the direct pathway, projections originate from the cortex, which projects to the striatum, from the striatum to the globus pallidus interna (GPi), and from there to the thalamus, which sends its projections back to the cortex where the circuit originated. The indirect pathway is characterized by circuits that originate in the cortex, which again projects to the striatum, but from there the circuit projects to the external segment of the globus pallidus (GPe). The GPe then projects to the subthalamic nucleus (STN) which projects to the GPi. The activity within the direct pathway selects a perception or a behavior by releasing GPi inhibition on the thalamus, which activates a specific region of the cortex. Activity within the indirect pathway results in increasing pallidal inhibition on the thalamus, therefore suppressing cortical activity. There is also a hyperdirect pathway that originates in the frontal cortex and projects directly to the STN. Activity within this pathway quickly inhibits behavior.

Five frontal–striatal (basal ganglia) circuits were initially identified, comprising the motor, oculomotor, dorsolateral prefrontal, lateral orbitofrontal, and anterior cingulate circuits [70]. Two prototypical posterior, sensory processing circuits were subsequently identified and described as consisting of temporal–basal ganglia and parietal–basal ganglia circuits [71]. All of these circuitries have been functionally characterized as fundamental underpinnings in solving the selection problem and in influencing instrumental learning and adaptation [65, 72, 73]. These circuits were initially described as highly segregated, with each circuit subserving a discrete functional behavior [74, 75]. Each circuit follows the connectional pattern of the direct and indirect pathways. While all circuits operate as parallel processes, it makes both intuitive and logical sense that discrete, specific behaviors are a manifestation of the segregated operations of this pattern of parallel circuitry activation. This explains how attention (sensory processing

selections) and action/behavioral selection become highly focused and maintained. Segregated circuitry supports specific, focused attention selection and behavioral activation. Developing appropriate responses to events in "real life" requires us to continually update and change responses and requires us to learn to adjust behaviors "on line" as new data (novel sensory information) from either the external or internal "environments" become available [9, 76]. In short, adaptation requires ongoing *sensorimotor* interaction with the environment.

Responding with smoothly executed, goal-directed behaviors requires interaction and coordination between the limbic/emotional/motivational and the cognitive, sensory, and motor circuitries. Unfortunately, parallel and segregated processing of functional information through the identified cortical–basal ganglia circuits does not adequately explain how this occurs. In fact, this pattern of segregated circuitries interferes with our understanding of how information flows between circuits for the adaptive purpose of generating new, or changing previously learned, behaviors or actions. Addressing this issue is critical if we are to understand sensorimotor integration as a function that serves general adaptation. In an important step, Humphries and Prescott have provided a comprehensive review of various integrative roles that the ventral striatum in particular play in adaptive behavior based on coordinating spatial navigation, reward evaluation, and behavioral strategy [62]. In the pediatric population, learning new behaviors is essential to the process of neurodevelopment. Therefore, the issue of how cortico-basal ganglia circuits interact is critical to operationally defining, conceptualizing, and applying an over-arching concept such as "SID" and will be discussed in a later section which concerns the integrative networks of the basal ganglia [77].

The Basal Ganglia as an Interface Between Neocortical and Lower-Level Systems

Cortico-basal ganglia circuits and their associated functions provide the anatomic underpinning for the vertebrate brain's solution to the "selection problem." This makes sense from a phylogenetic perspective [54]. Evolution has demonstrated the cortex's progressive involvement in processing thalamic sensory information projected to the striatum of tetrapods [78]. In amphibians, sensory inputs originate from the dorsal thalamus, while in reptiles they originate from the ventral area of the olfactory cortex. In mammals—especially in primates, which have the most specialized systems of sensory information processing and movement—a parallel expansion of the neocortex and basal ganglia occurred. Mammalian striatal inputs arrive from the neocortex, which is the largest and presumably most important sensory region of the brain [79]. Ascending the phylogenetic scale in this manner allows us to see that the striatum invariably receives more and more highly processed and specialized sensory input. Mammals always direct output from the basal ganglia back to the thalamus and, from there, back to cortex, which allows segregated, parallel circuits to be maintained. From a functional perspective, this circuitry allows *perceptions and behaviors to be activated.*

Reiner asserts, "You cannot have a vertebrate brain without a basal ganglia" [57]. The evolutionary trend also reveals that the basal ganglia serve as a "relay station" interface between both cortical and lower-level brain regions and systems, which are additionally modulated by basal ganglia–subcortical "loops." Certain thalamic neurons project back upon the striatum (as is also the case in lower-level vertebrates). Many of these thalamic projections originate in brainstem sensorimotor structures [80]. These regions of origin include the superior and inferior colliculi, the pedunculopontine nucleus, and various pontine and medullary nuclei [81–83]. The output structures of the basal ganglia (globus pallidus interna and substantia nigra pars reticulata) also project back to these brainstem nuclei. Subcortical connectional profiles have been referred to as colliculo-thalamo-basal ganglia-collicular and tecto-thalamo-basal ganglia-tectal loops.

Therefore, the functional connections between the basal ganglia and brainstem structures were developed before the neocortex emerged, with connectional profiles that feature the basic direct–indirect pathway circuit plan [56]. The selection problem existed in the early phases of evolution, well before the neocortex had developed significantly [84]. For instance, it has never been adaptive or practical to look (or to perceive and process) at two distant, unrelated objects simultaneously or to react in two different ways. One would not want to dedicate energetic resources to both, approaching and avoiding the same stimulus simultaneously. The basal ganglia have provided—and continue to provide—a mechanism to prioritize in such circumstances in consideration of the vertebrate organism's context, so decisions can be made that are in its best interests. There may be situations that demand quick decisions and require brainstem systems to act before the basal ganglia "disinhibit" a behavior by interacting with the cortex. In these circumstances, a useful response might be initiated while the circuits between basal ganglia and cortex continue to process information to enable the organism to learn how to respond more effectively in comparable circumstances in the future [84–87]. This type of process would obviously contribute to sensorimotor learning, which will also be addressed in a subsequent section of this paper.

Just as structures in the brainstem connect with the basal ganglia, the basal ganglia and the cerebellum are recipro-

cally connected [88–90]. The STN projects to sensorimotor, associative, and limbic regions of the dentate nucleus of the cerebellum. The dentate nucleus of the cerebellum projects back to the striatum; at the same time it projects back to the cerebral cortex. The co-evolution of the basal ganglia with subcortical sensorimotor structures established the basic looped circuitry or architecture onto which the neocortex was later grafted [56]. The relevance of this connectional architecture will be discussed in a subsequent section on the conditions of SID/SPD/SMD.

The Cerebellum

While the cerebellum can be described in terms of numerous structural divisions, for our limited clinical purposes, we will refer to the cerebellum's regions in terms that coincide with its commonly accepted functional divisions. These include the vestibulocerebellum, the spinocerebellum, and the cerebrocerebellum [91]. As its name might imply, the vestibulocerebellum is involved in making postural adjustments to vestibular stimulation. This region of the cerebellum is believed to be fully operational at the time of birth [53]. The spinocerebellum is responsible for maintaining muscle tone, for coordinating the muscles involved in balance, for changes in posture, and for adapting motor programs for varying conditions, including walking and running. The cerebrocerebellum plays critical roles in learning new sensorimotor skills and in the modulation of non-motor, sensory, cognitive, and affective processing [92–95].

Therefore, as is true for the basal ganglia, the cerebellum is not a monolithic structure. Rather the cerebellum consists of multiple regions and can be described as playing a number of roles that are not easily described according to one functional principle [96, 97]. It is a multipurpose neural mechanism that modulates the quality of motor and non-motor functions, including the control of sensory data acquisition [98, 99]. In this review, we emphasize the role of the cerebellum in regulating the rate, rhythm, and force of sensation and behavior. These functions are critical to the establishment of automatic, procedural learning that is an essential requirement for sensorimotor adaptation in this dual-tiered model of functioning [99–103]. The functional processes of the cerebellum underlie the automation of all behavior, whether related to motor control or to the cognitive activity of the prefrontal cortex [104]. However, the modulation of sensory processing input is fundamental to these processes [96, 99, 105–107]. In this way, the cerebellum serves as a critical node in a dual-tiered model of cognition that adapts to the environment through alternating episodes of automatic behavior and conscious cognitive control as situations develop or unfold.

Cerebro-Cerebellar Circuitry, Working Memory, and the Construction of Cerebellar Control Models

The connectional profile of cerebro-cerebellar circuitry is well known. This prototypical circuitry originates in the neocortex (although projections originate from other brain regions as well). Segregated projections from prefrontal, frontal, parietal, and superior temporal regions synapse within similarly segregated regions of the pontine nuclei in the brainstem, which then project this information to specific, topographically organized zones of the cerebellar cortex [108–111]. Through the Purkinje cells of the cerebellar cortex, output is projected to one of four specialized deep cerebellar nuclei—dentate, emboliform and globose (interpositus), or fastigial. These nuclei project to the thalamus, which then connects to the region of the cerebral cortex from which the initial projection originated. The cerebellum uses information it receives from the parietal and temporal lobes, from cortical association areas, from motor cortices, from paralimbic regions that mediate emotional and motivational responses, and from reticular, hypothalamic, and vestibular systems. This facilitates the efficiency with which these systems function, so a homeostatic response appropriate to the situational context can be generated [112–116]. Therefore, the cerebellum is in a position to influence a wide range of functional processes, including the reticular system, the limbic system, sensory systems, as well as cognition and motor behavior. Cerebellar circuitry represents an important underpinning to the symptoms of SID/SPD/SMD.

Cerebellar Control Models

This circuitry allows the cerebellum to "know" what the cortex wants to do. It provides for an information exchange that essentially makes it possible for the cerebellum to *copy* the content of cortical working memory. This copy contributes to the cerebellum's construction of an internal "model" of that activity's requirements. The model includes all of the sensory and motor information that have been features of and are absolutely necessary for the performance of the activity. It then predicts or anticipates the consequences of motor activities. This sensorimotor "program" is referred to as a forward model [117]. This anticipation/prediction is critical and essential to adaptation because *direct cortical sensory feedback processes operate too slowly* for us to generate effective responses in "real time" [118]. Since adaptation involves continual sensorimotor interaction with the environment, this functional architecture is at a premium for survival.

The cerebellum learns from repeated experience. It constructs, through a learning process, an internal model

that contains all of the dynamic processes necessary to perform a movement or behavior. It reproduces and adjusts these dynamics every time the behavior is repeated, refining the model [117, 119]. This model allows the brain to perform the activity precisely, without the need to refer to direct sensory feedback from the moving body parts. In this way, we are able to move very skillfully after repeated practice. This is the manner in which the cerebellum plays its critical role in the initial learning of procedural skills [120].

The acquisition of a behavior results in the generation of an inverse model. This is essentially an automation of the behavior, which is no longer under the control of any conscious awareness or "executive function" guidance. The cerebellum plays this critical role in acquiring and adjusting procedures and sensory experiences all the time, in all situations, so that we may generate the most economical and appropriate behaviors across similar contexts [17, 118]. In short, the neocortex connects to the cerebellum and tells it "what" needs to be done. However, "how" it is to be done in the best or most efficient way depends upon the specific area of the cerebellum to which this afferent information projects at the other end of the "loop," where all the necessary parameters are elaborated outside of conscious awareness, within the cerebellum [98]. This allows the brain to store the most efficient representation of the behavior [121]. Early cerebellar abnormalities will result in neurodevelopmental problems. They may affect sensorimotor and/or cognitive aspects of learning since learning requires considerable information to be integrated in order to construct and refine the appropriate "models" that allow it to occur. Given the cerebellum's significance, it is important to review its infrastructure in order to understand how it performs its operations.

Infrastructure of the Cerebellum—Structural Layers, Inputs, and Output

The cerebellum is composed of three layers: the granular layer, the Purkinje cell layer, and the molecular layer. It receives two major sources of input: the mossy fiber system and the climbing fiber system. Various regions of the cerebral cortex send segregated projections to the pons. The pons maintains these segregated projections and sends mossy fibers to the granule cells within the granule layer through the appropriate segregated region of cerebellar cortex. These afferent fibers then form the parallel fibers, which project to the molecular layer and synapse with Purkinje cell dendrites. The Purkinje cell comprises the only output, or efferent, neuron in the cerebellum, and its output is exclusively inhibitory on the deep cerebellar nuclei [122, 123].

Deep Cerebellar Nuclei: Important and Unique Properties

The phylogenetically oldest region of the cerebellum, the vestibulocerebellum, projects its output through the vestibular system rather than through the cerebellar nuclei. However, the fastigial nucleus, globus and emboliform nuclei (interpositus), and dentate nuclei, which have evolved more recently, possess unique, intrinsic features that are not shared by the vestibular system. While these deep cerebellar nuclei receive very considerable inhibitory input from Purkinje neurons, the phylogenetically newer, deep cerebellar nuclei are also spontaneously active. That is, they generate action potentials *even without excitation* [124]. Similarly, these nuclei, and particularly the dentate, are involved myriad functional networks that include projections to thalamic nuclei, sensorimotor and associative cortices, the striatum, and the hypothalamus [125]. Therefore, it can be understood that the cerebellar nuclei occupy a strategic position from which they can potentially influence nearly all sensation and behavior. Since the deep cerebellar nuclei project to the cerebral cortex via the thalamus and influence sensorimotor (and non-motor) behavior, it might be predicted that different disturbances of Purkinje cell output upon deep cerebellar nuclei would manifest in either overly excited or overly inhibited neuronal messages being sent to the cortex via the feedback limb of cerebro-cerebellar circuitry [116, 126]. This neuronal information would theoretically have a profound effect on the experience of sensation, the ability to acquire age-appropriate sensorimotor programs, on cognition, and on the experience and expression of emotion [127]. Tavano and Borgatti have also provided evidence for the link between cognition, emotion, and language in cerebellar malformations [128]. Disturbances in sensation, sensorimotor abnormalities, cognition, and problems in emotional reactivity are often described as primary disturbances in children diagnosed with developmental disorders, including SID/SPD/SMD [27].

Cerebellar Interneurons

Within the granular layer, Golgi cells (cerebellar interneurons that are excited by parallel fibers) exert feedback modulation on the transmission of information from the mossy fibers [129]. This inhibits the granule cell, which inhibits the granule cell excitation of Purkinje cells, which then indirectly inhibits the output of Purkinje cells. Stellate cells (projecting to the Purkinje cell body) and basket cells (cerebellar interneurons that project to Purkinje cell dendrites) are also excited by parallel fibers within the molecular layer, while these interneurons modulate Purkinje

cell excitability and its inhibitory output as well [130]. This places the interneurons of the cerebellum in a critical position to modulate and direct the flow of afferent information through a very delicate, intricate, and subtle interplay of excitation and inhibition on Purkinje cell output. These subtle interactions are governed by adrenergic fibers projected to the cerebellar cortex from brainstem nuclei. The raphe nuclei project serotonin to the granular and molecular layers; the locus coeruleus sends noradrenergic fibers to all three layers of the cerebellum. The inhibitory output of the Purkinje cells is gabaergic and acts upon the excitation of the deep cerebellar nuclei. Given the putatively accepted roles of noradrenergic and serotonergic activity, a role for these neurotransmitters in the modulation of sensory experience (hypo- and/or hypersensitivity to sensory stimulation) can easily be envisioned at the level of the cerebellum. However, a review of neurotransmitter dynamics is beyond the scope of this paper.

The Climbing Fiber System

The second source of Purkinje cell input and modulation originates in the climbing fiber system. The inferior olivary nucleus, which is the origin of the climbing fiber system, is also organized in an orderly, somatotopic way, from all regions of the nervous system [98, 131, 132]. Climbing fibers project to several Purkinje cells, but each Purkinje cell receives afferent information from only one parallel fiber to facilitate this "fine tuning." The Purkinje cells represent the "pivotal neurons" that refine the "rate, rhythm, and force" of behavior by inhibiting the output of the deep cerebellar nuclei [133]. This system plays a significant role in refining "error" signals and allows appropriate Purkinje output to refine the behavior in question every time it is repeated. Inferior olivary nucleus connections with the deep cerebellar nuclei have also been documented [134] and it is proposed that these connections comprise additional circuitry that modulates the activity of deep cerebellar nuclei and in this way changes the quality of the information that is relayed back to the cerebral cortex [135].

The processes and mechanisms that affect Purkinje cell and deep cerebellar nuclei output are the basis for appropriate sensorimotor learning and sensory modulation. Fronto-olivocerebellar pathways have also been identified [136]. It has been proposed that these frontocerebellar connections are involved in switching from voluntary to completely automatized behaviors during skill learning while they also provide automatic sensorimotor surveillance during the performance of actions or sequences of actions in an increasingly precise and accurate manner.

Operationalizing SPD/SMD

The symptoms of these conditions can readily be understood within the context of basal ganglia and cerebellar functions. One important symptom concerns the fact that certain children diagnosed with SPD seem to "notice" too many stimuli. Sensory stimuli appear much too easily perceived and cannot be ignored by the individual. This issue can be understood as a manifestation of anomalous functioning within the basal ganglia. The basal ganglia, which are a largely dopaminergic gating system, serve as the interface between the cortical and lower-level brain systems. As described above, the basal ganglia select objects for neocortical attention by releasing inhibition on the thalamus, which allows the appropriate region of the cortex to become active. Within the higher-level cortical system, this can include visual, auditory, and tactile sensory stimuli. Within lower-level systems, the basal ganglia provide inhibition over orienting responses, including those responses mediated by the superior and inferior colliculi.

Failure to appropriately gate or select stimuli would result in poorly focused attention, which would manifest in "noticing" too many stimuli. Basal ganglia and dopaminergic disturbances are observed in a variety of neurodevelopmental disorders and can result from a variety of etiologies [137]. An anomalous structure or neurochemical function of the basal ganglia results in disinhibition over lower and/or higher level sensory and motor systems. Aspects of conditions such as ADHD, Tourette's syndrome, addictions, schizophrenia, and Parkinson's disease are understood in this way [138–140]. The basal ganglia play an important role in the sensory gating of information into motor "what" and "when" [141–143]. Similarly, a variety of sensory processing abnormalities have been observed in cerebral palsy [27]. In this regard, insult or injury to the cerebral cortex, as is observed in cerebral palsy, would weaken the neural signals projected through the direct, indirect, and/or subthalamic pathways of the basal ganglia, preventing appropriate inhibition of perceptual processing systems [39].

These dynamics are critical to understanding SPD/SMD. Basal ganglia dysfunction can impair perceptual selection and therefore sensory processing because it leads higher- and lower-level sensory inputs to act competitively and independently instead of cooperatively. Inputs that should not be noticed or acted upon become undue distractions because the basal ganglia do not "gate" properly. For example, if brainstem systems such as the superior and inferior colliculi are disinhibited by the basal ganglia, as described above, the individual will be vulnerable to the competing and distracting influences of extraneous auditory and visual stimuli. This distractibility will be observed as a readiness to respond or a hypersensitivity to stimuli within

those sensory modalities. Stimuli that go unnoticed or are held at bay by the majority of individuals with intact selection mechanisms will capture the attention of the individual with a dysfunctional selection mechanism because the processes by which selection occurs are disturbed. As a result, he or she will "select" too much and be bothered by the types of auditory, visual, and tactile stimuli listed in the Sensory Profile. In other words, aspects of SPD/SMD can be conceptualized as arising from the basal ganglia's failures to guide the brain's solution of the selection problem. These types of behaviors are consistent with the recent findings of James and colleagues, who described a subtype of SMD characterized by hyperactivity, impulsivity, externalizing behaviors, impaired cognitive and social functioning, and sensory seeking behavior [7].

James and colleagues' findings are relevant for interpreting sensory seeking behavior and impaired cognitive control in general. Children with sensory processing disorders are often described as exhibiting "sensory seeking" behaviors. These children are into everything. They are observed as constantly touching objects and sometimes even people (generating the impression that they are insensitive to social cues), and in these ways their behavior can be quite disruptive. However, the term "sensory seeking," which evolved from the original sensory integration formulation proposed by Ayres, has become a highly controversial concept. Describing this behavior as sensory seeking implies that the child in question does not experience enough sensation and therefore actively seeks sensory stimulation as a compensation for a certain type of deficit in touch processing. While this clinically intuitive interpretation attributes a purpose to the behavioral observation, this explanation lacks a scientific foundation. An accepted neurobiologic mechanism has not been proposed to explain this type of sensory seeking.

Within the context of an interactive sensorimotor model of behavior, these behaviors are not sensory seeking. We were literally born to move. These behaviors are more effectively anatomically explained as the result of disinhibition or insufficient inhibitory influence from the topographically organized Gpi over the thalamus [144]. This failure in inhibition has the effect of activating posterior sensory and anterior motor cortices and results in behavior that is more accurately described as "stimulus-bound" than "sensory seeking" in nature. Numerous experimental and computational models of behavior support framing "sensory seeking" behavior in this way [39, 145, 146]. The interpretation we offer assists in explaining certain co-morbid behavioral observations seen in ADHD, ASD, SPD, and even other neurodevelopmental disorders by implying shared, parsimonious neurodynamic mechanisms. This behavior was observed and described by Lhermitte [147]. People with damage to the frontal lobes were observed performing familiar actions with everyday objects. Patients would use cutlery despite the absence of food; they would touch and start to use whatever object was placed before them. The behavior of these patients was *reactive and independent of appropriate context*. This behavior is very similar to what sensory integration theory describes as "sensory seeking." The behavior constitutes a failure in response inhibition, which is a critically important function of frontal–basal ganglia interactions in developing children. It represents a disturbance in gating mechanisms of the frontal–striatal–pallidal–thalamic–cortical modulatory loop of interaction that forms an essential underpinning of cognitive control.

Cognitive Control

Whether these touching and utilization behaviors are interpreted as disturbances in sensory processing or as a manifestation of disinhibition is not a trivial, semantic issue. These viewpoints do not simply represent opposite sides of the same coin. Instead the interpretation one chooses for the genesis of these behaviors has significant implications for development. Within the vertebrate brain, inhibition, attention, and working memory work together to "guide" purposive, self-directed behavior [51, 139]. Interpreting stimulus-bound behavior as sensory seeking fails to recognize the importance of inhibitory capacities in development. An ability to not respond in the immediate circumstance serves as a central prerequisite for the development of metacognitive executive function, cognitive control, and, ultimately, self-control [50]. Inhibition provides the platform of time between a stimulus and a response that allows the opportunity to think. In young children, this includes thinking about appropriate *context*, if only as might be needed in the moment. However, this ability develops into working memory [50, 148, 149]. This ability allows for the child to proactively prepare for even just the *predictable future* while eventually developing more complex goal setting and planning.

Young pre-school aged children and even infants may be capable of demonstrating primitive inhibition and working memory on various developmental tasks within the laboratory or experimental setting [150, 151]. However, children do not rely upon this type of metacognitive capacity to proactively drive behavior; young children do not function on the basis of a weaker or "watered down" version of working memory. In fact, children can be notoriously tied to the present. Young children demonstrate *reactive* as opposed to *proactive context* processing in making behavioral choices [146]. However, in normally developing children, reactive processing is *context appropriate*.

These are critically important issues in explaining sensory seeking behaviors. According to Chatham and colleagues,

reactive context processing is characterized by a tendency to react to events as they occur, but this includes *retrieving information from memory as needed for the moment* [146]. In terms of neuroanatomic underpinnings, this processing requires an interplay between hippocampal and frontal systems that shifts over the course of development [146, 152, 153]. Therefore, appropriate behavioral control in young pre-school children (3.5 years of age) is dependent upon the integrity of prefrontal–hippocampal interactions; the prefrontal contribution keeps context-dependent knowledge temporarily on line; the hippocampal contribution recalls the knowledge within appropriate context. Therefore, in young, normally developing children, prefrontal system–hippocampal interactions are essential for behavior appropriate to the current context, in the here-and-now. The so-called "sensory seeking" behaviors, by definition, are contextually inappropriate. Children engaging in these behaviors are not behaving according to appropriate situational context. This implies profound disturbances within prefrontal system–hippocampal interactions that have never been systematically determined, described, identified, or even investigated in children with sensory processing disorders.

As children approach the age of 8 years, there is a dynamic switch from reactive towards proactive behavioral control mechanisms, during which normally developing children begin to develop metacognitive strategies that allow them to rely upon proactive behavioral control [154].This essentially comprises the forerunner of working memory that allows for future goal setting, planning, and appropriate behavioral execution. While our understanding of the mechanisms governing this shift (towards increasing self-control) remains in its infancy, we can readily hypothesize that failures in reactive control, in the absence of proactive control mechanisms (essentially inhibition and context assignment), largely explain children's difficulties in cognitive/behavioral shifting, inferential reasoning about the context/meaning of the thoughts of other people, and thinking outside the moment of the here-and-now. In this regard, Morton and Munakata [145] have proposed a very parsimonious account in which *advances in inhibitory control are inexorably and intrinsically linked to advances in active memory capacities and working memory functions* (page 263). In our opinion, this provides a contemporary and direct link between what has been labeled and construed as "sensory seeking behavior" and the development of self-directed, adaptive, executive or metacognitive behavior.

The Cerebellum and SPD/SMD

The cerebellum is implicated in the "force" with which sensory stimuli are experienced. For example, fMRI data have suggested that odor concentration and sniff volume are inversely proportional [155]. The stronger the odor concentration, the smaller the amplitude or volume of the sniff. The cerebellum receives olfactory sensory information concerning odor concentration in order to modulate or regulate the force of the sniff, which in turn modulates subsequent olfactory input [156]. Abnormalities within the architecture of the cerebro-cerebellar system might be expected to play a significant role in sensory hypo- and hypersensitivities and responsiveness [74]. The information processed through the cerebellum could vary in the sense modality involved since the cerebellum has reciprocal projections with nearly every sensory system [116, 157]. Similarly, the cerebellum has been described as specifically involved in monitoring and adjusting the acquisition of most of the sensory data on which the rest of the nervous system depends [99]. Therefore, the cerebellum should be considered as very strongly implicated in aspects of the symptom presentation of SID/SPD/SMD.

The cerebellum receives projections from nearly all cortical and brainstem regions. After changing the *quality* of that information, the cerebellum returns it to its source of origin [108, 158]. The cerebellum is divided into specialized "zones" of information processing [98, 111, 159, 160]. The specificity of the neuroanatomic connections *between* the cerebellum and the spinal cord, the brainstem, the basal ganglia, and the cerebral hemispheres facilitates the topographic organization of sensory, cognitive–associative, emotional, and motor functions *within* the cerebellum. Different regions of the cerebellum manage information from different domains, which means that impairment in specialized zones of cerebellar processing would produce specific, differential effects on sensation, associative cognitive functions, affective, and motor behavior, depending upon the focal region of involvement.

As we have implied, any imbalance between Purkinje cell and cerebellar interneuron interactions would significantly affect inhibitory/excitatory influence over deep cerebellar nuclei, which would in turn affect the functions in question. Elimination of Golgi cells, for example, abolishes GABA and disrupts inhibitory Purkinje cell output [161]. This results in the excessive activation of the dentate nucleus and severely disrupts movement. Therefore, if this occurs in a motor region, we propose that a similar mechanism taking place in a sensory region would result in comparable sensory disturbance disrupting the experience of sensation.

Both basket and stellate cells receive excitatory input from parallel fibers and inhibitory input from other interneurons [162]. Jorntell and colleagues thus proposed that interneurons can provide either global inhibition or a more localized inhibition that can "prune" a specific excitatory response. Oldfield, Marty, and Stell have also demonstrated that single interneurons can "toggle" Purkinje

cell output [163]. Therefore, we can envision that the activity of cerebellar interneurons represents an important underpinning of hyper- and hyposensitivities, while these differences in experiential sensitivity can be conceptualized along a metric dimension, as proposed by Schmahmann and colleagues [164].

Within the cerebellar motor system, this concept is illustrated by dysmetria. A patient with dysmetria who reaches for an object displays movements that are erratic in amplitude. The person reaches past the object or does not reach far enough to touch it. This is conceived as "overshooting" and "undershooting" the target. It can also be seen as movement with either hypermetric and hypometric components. It is, in essence, a disruption in the quality of the movement. Hypo- and hypersensitivities can be conceptualized within these dimensions as well. Hypersensitivity to sensation—a response to the stimulus with too much amplitude—is conceived as "overshooting." Hyposensitivity to sensation—a response to the stimulus with not enough amplitude—is conceived as "undershooting."

This principle of over- and under-reaction can be applied to responses within systems governing sensation, cognition, and emotion [164, 165]. The amplitude or force of information from each domain that is processed through the cerebellum contains the potential to be experienced or expressed with a *hypermetric* and *hypometric*/*hypotonic* valence. At the neuronal level, this is perhaps best exemplified by the fact that Purkinje cells, the only source of cerebellar output (that projects to the deep cerebellar nuclei before projecting back to thalamus and cortex), are entirely inhibitory [131]. Excessive inhibition results in hypometric behavior; insufficient inhibition is manifested by hypermetric behavior. Schmahmann and colleagues have described a variety of pediatric cases featuring documented, structural cerebellar pathology that presented with hypo- or hypersensitivities in addition to cognitive and affective pathology [164]. These pediatric cases included children with cerebellar agenesis. The patients' symptoms included changes in responsivity to touch/tactile sensations, pain, sound, and food textures; exaggerated emotional responsiveness; a lack of emotional reactivity; and emotional expressions of excessive duration that were exaggerated relative to the situations that evoked them [166, 167]. These children would fulfill behaviorally defined criteria for a diagnosis of SPD/SMD according to the Sensory Profile.

Basal Ganglia and Cerebellar Interactions

The basal ganglia serve function beyond facilitating selection processes for higher and lower level aspects of sensory and motor systems. As indicated above, there are reciprocal connections from the STN—a primary inhibitory nucleus of the basal ganglia—to sensorimotor, associative, and limbic regions of the cerebellum. The cerebellum projects back to neocortex and to the striatum, which is the basal ganglia's primary source of sensory input [89, 168]. Circuitries between the basal ganglia and cerebellum have potentially profound implications for understanding the symptom picture of SMD.

Stimulation within the STN of the basal ganglia inhibits or "stops" behavior and, in this way, is implicated in perceptual and activity selection processes and impulse control [169, 170]. Basal ganglia-cerebellar and cerebro-cerebellar circuitry may interact cooperatively, competitively, or independently. Problematic interactions may generate hypo- and hypersensitivities that characterize SPD/SMD. While STN impairment results in inhibitory failures that lead a child to notice, be attracted to, or be distracted or bothered by stimuli to which he/she would ordinarily habituate, the cerebellum mediates the force of sensory input and motor output. Insufficient activity of the STN–cerebellar projection system, however, could lead to *increased dentate nucleus activity or an over-excited cortical sensory region* which would intensify and dysregulate sensation and behavior. Increased STN activity would generate the opposite effect. In this way, a direct link between aberrant selection capacity and both hypo- and hyperresponsiveness to sensory stimuli can be established. The Sensory Profile is replete with items that reflect hypermetric and hypometric dimensions of experience in all of the various sensory modalities [171].

The Roles of the Cortex, the Basal Ganglia, and the Cerebellum in "SID"

SID, as currently conceptualized, remains problematic because it lacks a consistent operational definition and, more importantly, its symptoms lack a coherent neuroanatomical explanation. Nevertheless, as a putative neuroanatomy of SMD and SPD can be ascertained, an anatomic conceptual framework for certain other symptoms of SID can also be established that is consistent with a dual-tiered, integrated model of brain function. These symptoms concern movement, for which "sensorimotor integration" is essential. Developing an operational definition of SID is a challenge by virtue of its nomenclature. For example, we were "born to move." Movement and perception are characterized by a bi-directional relationship that is inexorably inseparable [172]. Sometimes we move to perceive; sometimes we perceive to move. As stated by Dewey (1896), "what we have is a circuit…the motor response determines the stimulus, just as truly as sensory stimulus

determines movement" (page 363) [173]. While we sometimes move to perceive, and sometimes perceive to move, such movement is context dependent in the normally developing child. Every behavior in which we engage requires a process of "sensorimotor integration," which occurs at multiple levels within the brain [174, 175].

For example, parietal, temporal, and occipital regions of the cerebral cortex "integrate" visual, auditory, and contextual sensory information [176, 177]. Damage to different combinations of these brain regions often results in the symptoms of apperceptive and associative agnosias in adult patient populations [178]. As reviewed by Heilman and Rothi, aspects of movement formulas or time–space motor representations to which they refer as *praxicons* are stored within parietal cortices [141, 179]. When these praxicons are disconnected from motor areas, apraxic behaviors are generated. Therefore, parietal–motor regions interact to generate behaviors that are also fundamental types of "sensorimotor integration" as clearly implied in the "behavior in real-time model" we have chosen as foundational for this paper. Aspects of developmental coordination disorder and developmental dyspraxia have been hypothesized in this way [6]. In fact, sensorimotor abnormalities mediated by cerebellar abnormalities have been documented in a range of psychiatric disorders [180]. In learning new behaviors/motor sequences, the striatum also clearly integrates "sensorimotor" information with the behavior's reward value [181]. This additionally implicates frontal–striatal interactions which will be further discussed below.

Krienen and Buckner recently identified four separate frontal–cerebellar circuits through fMRI imaging [110]. These circuits were identified as the MOT (motor) circuit, DLPFC (dorsolateral prefrontal cortex) circuit, MPFC (medial prefrontal cortex) circuit, and APFC (anterior prefrontal cortex) circuit. All circuits were characterized by dissociable, segregated, and reciprocal projections within specific regions of the cerebellum. Of particular interest are the findings that two posterior regions of the lateral cerebellum (regions that are characterized by secondary sensorimotor functions of the cerebellum) also projected to lateral parietal and temporal lobe regions. These projection systems are significant for at least three reasons. First, these connectional profiles support our original neuroanatomic framework for this manuscript, which specified that the functional architecture of the human brain evolved to serve the needs of interactive behavior in "real time." These networks provide the underpinning to establish specific parameters of ongoing and potential actions. Second, the finding of cerebellar connectivity is especially important with respect to establishing sensorimotor automaticity through the development of forward and inverse models since children diagnosed with sensory integration disorder frequently exhibit deficits in automating behavior [1]. Third, children with sensory integration and/or sensory processing disorders are often characterized as exhibiting "visuo-motor integration" deficits. Anomalies in functioning within this recently identified circuitry profile have implications for a "visual theory" of sensory processing aberration, particularly since the parietal lobes (which assist in visually guided movement) and the superior temporal sulcus (which is involved in the detection of movement) are essential to the above-described network. Voogd and colleagues have subsequently identified and reviewed the anatomic components of the "visuomotor cerebellum" in humans and primates [182]. Similarly, Davis, Pitchford, and Limback have recently documented the relationships between visual processing, fine manual control, and the interrelation between cognitive and motor skills in normally developing children between the ages of 4 to 11 years [183]. This remains an issue for further investigation in understanding visuomotor control in SID and the disorders in which it occurs co-morbidly.

In learning new behaviors/motor sequences, the striatum clearly integrates "sensorimotor" information with the behavior's reward value [181]. This additionally implicates frontal–striatal interactions. As described above, the segregated, parallel connectional pattern of the cerebro–striatal–pallidal–thalamo–cortical circuitry profile explains how attentional and action/behavioral selections can be sustained or maintained. However, adults and children live in a constantly changing environment in which attention and behavior must be continually changed and adapted. This type of adjustment requires an understanding of how information flows between circuits to serve the adaptive purpose of generating new or changing previously learned behaviors or actions. As we have noted previously, parallel and segregated processing of functional information through identified cortical–basal ganglia circuits simply does not address this issue. Once again, this reflects our behavioral bias towards a paradigm that reflects "real–time," sensorimotor interaction with the environment, in which "sensorimotor integration" is essential. In our view, deficits in "sensory integration" or "sensory processing" must be evident in these processes of adaptation.

SID and the Basal Ganglia

The divisions of the frontal cortex are associated with specific functions. The basal ganglia process cognitive, limbic, motivational, and motor information projected from specialized regions of the frontal cortices in parallel and segregated functional streams. Because adapting to a changing environmental landscape requires ongoing updating and learning, these systems have to be coordinated in

order to generate and execute appropriate goal-directed behaviors. An informational flow *between* circuits is needed if previously learned actions are to be adapted and new behaviors are to be developed [184, 185].

There appear to be four integrative networks across basal ganglia circuits [184]. First, while cortico–striatal pathways are primarily characterized by focal, circumscribed, and topographically organized projections, there is some overlap between terminal fields from these different functional regions. There are specific regions where focal projections from cognitive and reward-related prefrontal areas converge. Cortical cognitive and motor control areas also converge at specific regions within the srtiatum [184, 186]. Second, although the globus pallidus interna is also topographically organized according to functional domains, information integration through the pallidum occurs by convergence at the borders between functional domains. In addition, within the external segment of the globus pallidus, projection fibers extend well into other functional domains besides through the domain border areas [76]. Third, a striato–nigro–striatal projection system has been identified. This midbrain, substantia nigra system includes reciprocal connections with cognitive, limbic/motivational, and motor regions of the striatum, which establishes a mechanism for the integration of motivation and cognition to influence motor decision-making processes in response to environmental cues. Fourth, the thalamo–cortical pathway is not a simple "relay station" for thalamus to activate cortex. Instead the thalamus has additional, non-reciprocal connections that project to nearly all cortical layers besides those parallel and segregated regions from which the cortico–striatal–thalamo–cortico loop originated.

Therefore, cognitive/associative, motivational/reward, sensory, and motor control functions are not discretely, distinctly, or completely segregated within the cortico–striatal–thalamic networks. In addition to the traditionally recognized parallel and segregated circuits, specific integrative networks function in concert with parallel circuitry. This allows behaviors to be focused, maintained, modified and changed and allows new behaviors to be learned so that the organism can act in its own best interest. This clearly represents an aspect of "sensory integration" while additionally implicating the thalamus in integrating information between different cortical regions. As summarized by Jog and Aur, "the basal ganglia (BG) appear to be well suited for taking large quantities of functionally important information including context, cognition, and sensory input, and performing an integrative function to provide a particular motor output" (page 213) [187]. Disturbances within this circuitry can be construed as underlying the procedural and instrumental (reward-based) learning difficulties that are so characteristic of children with neurodevelopmental disorders [188–190].

SID and the Cerebellum

The integrated model of brain functioning described in this paper identifies the cerebellum as another primary contributor to "sensory integration." Therefore, the overarching term "sensory integration" has face validity only when it is operationally defined relative to a specific context. The entire brain functions within a principle of "sensory" and "sensorimotor integration" so that SID as a monolithic term quickly becomes meaningless. It can be best described in terms of putative neuroanatomic underpinnings, dependent upon the symptoms under consideration.

In this regard, the early maturing vestibulocerebellum should provide a well-integrated and stable platform for early sensorimotor development. Perhaps this is classically apparent in the VOR, which would support the proprioceptive feedback necessary for the asymmetrical tonic neck reflex and the symmetrical tonic reflex, which would allow for the initial stages of infant movement [39]. These reflex head and eye movements eventually support balance and gait during the course of development and later support eye–hand coordination [191]. Early disturbances in this system could easily disrupt initial sensorimotor learning, delaying sensorimotor development. In addition, the accessory neural pathway that links the vestibulocerebellum with reticular areas in the brainstem could theoretically influence the regulation of the peripheral nervous system. While disturbances could disrupt the sympathetic division, excessive noradrenergic activity could presumably disrupt the pattern of excitation–inhibition within the cerebellar cortex, thus contributing to sensory hyperresponsiveness, manifested by exaggerated responses to sensory stimulation. Similarly, because of projections to the anterior regions of the vermis, this could be associated with outcomes such as anxiety, panic, and emotional dysregulation as reported by Schmahmann [127, 164]. Also, since the vestibulocerebellum projects through the vestibular nuclei, one might speculate that relatively common conditions such as chronic otitis media might easily affect this system; this actually corresponds with the learning disturbances so frequently observed in neurodevelopmental disorders associated with chronic ear infection, including an association with reading disabilities.

The vermal regions of the spinocerebellum receive vestibular input, while paravermal zones receive spinal afferents that include proprioceptive and cutaneous stimulation. This cerebellar region, when noradrenergically overstimulated, would theoretically contribute to cutaneous hypersensitivity manifested and observed through "tactile defensiveness." Similarly, diminished Purkinjie cell Gabaergic output has been documented in autism, along with vermal and paravermal pathology [192]. This could underlie the hyperresponsiveness to various sensory stimuli, as well as the tactile defensiveness which is frequently

observed in that condition. Numerous behaviors of this type are listed in the Sensory Profile.

Similarly, the spinocerebellar division is responsible for maintaining muscle tone and the synergistic muscles involved in balance, postural adaptation, and executing routine motor programs such as in the developmental motor sequences of crawling and walking. Involvement of these cerebellar regions is consistent with the recently reported finding of impaired stance control in children with SMD [193]. Volumetric differences within the vermal and paravermal regions within this cerebellar area have also been associated with the symptoms of ADHD, the severity of the condition, and its therapeutic outcome [194]. These findings assist in explaining aspects of the overlap between the symptoms of ADHD and sensory processing disorders on the basis of a shared neuroanatomic underpinning. These cerebellar regions have been associated with the development of dyslexia as well [195]. It has repeatedly been noted that children with a certain subtype of dyslexia exhibit balance difficulties as compared to normal controls [196]. Difficulties with balance are often associated with other motor problems that affect the achievement of motor milestones, manifested by delays in sitting up, crawling, and walking. These factors are often associated with problems in fine motor control, including delayed control over speech musculature; this can generate misarticulations which can in turn contribute to deficits in the precise timing required for phonological processing and can result in problems acquiring sound–symbol correspondences [197]. Lonnemann and colleagues have recently demonstrated a similar relationship between balance and the development of arithmetic skills in 8- to 10-year-old children [198]. Poor balance was associated with poor arithmetic computation, and the authors interpreted the findings in terms of cerebellar involvement in arithmetic tasks. Paravermal regions of the spinocerebellum coordinate appendicular movements and appear to be involved in regulating the speed, intensity, direction, transitions, and general coordination of skilled actions [91]. Numerous behavioral/movement items listed in the Sensory Profile are consistent with disturbance within this cerebellar region.

The cerebellum is critical for coding and integrating the sensory and temporal information necessary for motor control and for acquiring new procedural skills that are at a premium for sensorimotor adaptation in a constantly changing, unpredictable environment [100]. The cerebellum assists in the acquisition and development of automatic behaviors by developing and refining forward and inverse models. As the forward model or behavior is consciously repeated or practiced, it becomes overlearned and automatic, operating outside of conscious control or awareness. At this point, it is referred to as the inverse model [117, 199]. By developing these models, the cerebellum synchronizes perception and action between the distributed brain areas that are involved in myriad sensorimotor tasks. In the performance of tasks such as drawing and handwriting, there is not only an activation of the premotor cortex but also a consistent recruitment or "coupling" between the cerebellum and the contralateral posterior parietal cortex [200, 201]. Similarly, the cerebellum and motor cortex are reciprocally connected and are simultaneously activated in the performance of sensorimotor tasks [120, 160, 202]. Disturbances in this network further assist in explaining the visuo-motor precision deficits frequently observed in sensory integration disorders as well as in other neurodevelopmental conditions ranging from ADHD to ASD to DCD.

Sensory processing and integration are inherent in cerebellar model development. The cerebellum plays a significant role in regulating the proprioceptive feedback required during successful motor execution, in "integrating" sensory inputs appropriately, and in predicting the consequences or outcomes of a motor/sensorimotor activity. The Sensory Profile is replete with motor observations that can be attributable to abnormalities within cerebellar circuitries. Difficulties learning and automating motor behaviors, for example, might result from abnormalities within posterior sensorimotor regions of the cerebrocerebellum and/or its afferent or efferent connections to the cerebral cortex that would preclude these behaviors becoming automated or successfully applied across contexts. Similarly, disturbances in sensorimotor reinforcement learning that recruits the cerebellum could easily be the result of abnormal limbic system input. For example, it has been documented that amygdala conditioning modulates sensory input into the cerebellum and affects cerebellar learning processes [203].

Discussion

We have described a dual-tiered model of brain function that requires interactions between the neocortex, the basal ganglia, and the cerebellum. Each brain region makes a characteristic and unique contribution to sensation and perception, cognition, emotion and affect, and motor adaptation. Understanding this neuroanatomic framework enhances our appreciation for variations in normal development and adaptation as well as in a variety of pathologies [8, 204]. We believe that symptoms of SID/SPD/SMD are best understood when they are conceptualized within the neuroanatomic model of integrated and interactive brain functioning that we have described.

In consideration of this model and the brain systems it implicates, it is no surprise that the symptoms of SPD occur

as often as 80% of the time in children who are diagnosed with developmental disorders. Abnormal structure and/or function of the basal ganglia and the cerebellum are frequently identified in developmental disorders, while both of these brain regions are implicated in sensorimotor and procedural learning as well, on which the mastery of reading, spelling, and arithmetic all depend [195, 197, 205–207]. The basal ganglia play a significant role in "chunking" together new behavioral sequences, while the cerebellum assists in automation by allowing the brain to retain the most efficient representation of behavior in order to generalize its execution across settings [17, 208, 209]. To the extent that certain focal regions of the basal ganglia and cerebellum might be disturbed—structurally or functionally—the acquisition of activities mediated by those regions would also be affected.

As sensory–perceptual abnormalities are manifestations of disturbances within the interactions of the neocortex, basal ganglia, and cerebellum, we would predict they would coexist with deficits in motor functioning, in cognitive and communication deficits, and in abnormalities in social functioning. This is because sensory processing anomalies are subtle indicators of deficits in broadly defined "executive control." They are likely to be evident earlier than more sophisticated executive control can be measured in a developing brain, which may explain why SID/SPD/SMD is "diagnosed" early in children who later are diagnosed with more conventionally measurable, diagnosable conditions. Development of working memory functions depends upon inhibitory control. In the absence of inhibitory capacity to sustain focused attention, thought-guided behavior is precluded. Deficits in cognitive abilities, affective control, academic skill sets, and even communication and social competencies would all be predicted based upon the regions and extent of pathology within brain systems that mediate selection and regulation. In this regard, early detection of hypo- and/or hypersensitivities and responsiveness could lead to the development of treatment approaches that enhance adaptation in a variety of functional domains.

SID/SPD/SMD very seldom occurs by itself. It is almost always observed within the context of other known conditions. This makes good diagnostic sense since these other conditions are characterized by clusters of "sensory processing" symptoms that interfere with a child's ability to participate in age-appropriate activities. Therefore, almost by definition, there must be behavioral, cognitive, and/or affective abnormalities associated with SID/SPD/SMD that would overlap with other established diagnostic conditions. This is exemplified in the DSM diagnosis of developmental coordination disorder, which is frequently accompanied by other regulatory problems, including the cerebellar cognitive affective syndrome, which comprises a wide range of cognitive and affective symptoms, as well as disturbances in sensory modulation [31, 210–212]. This co-morbidity occurs because the symptoms share aspects of the same neurobiologic networks and mechanisms.

We believe that disturbances in "sensory processing" can occur as a result of abnormal structure and/or neurochemistry within the basal ganglia and/or the cerebellum. This appears to be a logical hypothesis since these subcortical brain regions mature much earlier than the neocortex, while the symptoms of SID/SPD/SMD are apparent early in childhood, thus implying some degree of subcortical abnormality. Symptoms can be associated with a variety of etiologies, which is why the symptoms are so common among developing children. For example, even relatively slight elevations in perinatal bilirubin levels can generate brain abnormalities, particularly within the basal ganglia [213]. BINDS, or bilirubin-induced neurotoxic disorders, are often associated with the development of cognitive deficits, including problems with attention that reflect disturbance within basal ganglia gating mechanisms [214, 215]. Based upon the neuroanatomic position and function of the basal ganglia, disturbances in the gating of sensory perceptions might be predicted as well [216].

Similarly, prematurity and low birth weight are clear "at risk" factors for developmental disorders [217–220]. While prematurity can be associated with abnormalities in many brain regions, cerebellar abnormalities have been demonstrated with reasonable consistency [221–223]. Even relatively mild birth prematurity, defined within the range of 37 to 38 weeks of gestation, has been associated with structural brain abnormalities that contribute to the occurrence of developmental learning disorders [224]. These brain abnormalities can be focal to cerebellar brain regions, each of which develops at different rates, prenatally and postnatally [225–227]. To the extent that the cerebellum is involved, the symptoms of SID/SPD/SMD might easily be present. The cerebellum adjusts sensation, motor activity, emotional responsiveness, and associative cognition within a hypometric–hypermetric continuum. It functions to "smooth out" performance in all domains of functioning and to modify behavior according to context. Because this process takes place outside of conscious cognitive control or awareness, the range of functional processes that can be affected can be difficult to manage.

Finally, it is also theoretically possible that the symptoms of SID/SPD/SMD are transient in a wide range of cases, depending upon the maturity level of various brain regions. The development of the human brain follows a complex trajectory of age-specific neuroanatomic changes. The dual-tiered model of brain functioning presented in this paper is dependent upon the establishment and development of brain networks. Pathologies featuring focal brain

abnormalities or disturbances in specific brain regions can generate many of the symptoms that have been described within this paper. However, the emerging area of investigation that applies the techniques of network analysis to the developing brain has recently demonstrated that, at each stage in normal neurodevelopment, age-specific skill sets correlate with age-specific distributed brain networks, which develop in a predictable way [228]. Even slightly delayed maturation or maturity within a specific network region could contribute to a presentation of early-onset symptoms that spontaneously remit, perhaps simply reflecting a wider range of variation in neurodevelopmental maturation.

We have presented our argument because the diagnosis of SID/SPD/SMD remains controversial. A coherent neuroanatomy of this condition has not yet been identified. The field of occupational therapy, which often makes the diagnosis, has attempted to explain aspects of the condition but has as of yet been unable to place SID/SPD/SMD within the context of an accepted, integrated functional anatomy. We have attempted to provide such a framework. We have supported our inferences and conclusions with information from a clinical and neuroscientific knowledge base. We hope that our proposal will be subject to rigorous scientific investigation. In this regard, a useful initial step would be to include symptoms of SID/SPD/SMD as a variable of interest when investigating recognized developmental disorders. The frequent co-morbidity of these symptoms with established disorders should be considered and behavioral research should be coupled with neuroimaging studies that can identify the functional networks involved in these clinical presentations, a technique which has been useful in identifying the brain networks involved in AD(H)D and other conditions.

The ultimate "answers" that allow "sensory processing" disturbances to be better understood will not come from any single field, nor should we expect any single neuroanatomic explanation. Neurology primarily focuses on identifying/treating symptoms generated by recognized disease processes; neuropsychiatry emphasizes an understanding of the biochemical processes that underlie DSM-defined behavioral pathologies; neuropsychology often employs "tests" that have limited ecological validity and that emphasize cortical functioning while measuring static, rather than dynamic, networks of brain–behavior relationships; neuropsychological assessment does not employ assessment procedures that allow for an interpretation of how an individual learns to benefit from interacting with the environment through a process of sensorimotor adaptation; the fields of occupational and physical therapy administer motor and sensory testing and training programs without necessarily focusing upon establishing the neuroanatomic underpinnings of the conditions or treatment. Presently, because none of these fields collaboratively integrate their respective knowledge bases, the symptoms discussed in this paper often "fall between the cracks" of these various professional domains.

While the solutions offered to the symptoms discussed in this paper remain incomplete, the multiple solutions that likely exist can only be identified and understood through the greater understanding that inter-professional collaboration will confer. We view this as an opportunity to unify what has been seen as disparate elements of behavior in different fields of practice and study. With a common language and shared theoretical understanding upon which to base our discussion and work, it is our hope that a better understanding of normal and abnormal development can be facilitated and that developmental problems can be identified and treated earlier and more effectively. Ultimately, members of different professions can and should work together to enhance the outcomes of the children that we serve.

Summary

This paper examined the controversy of conditions variously referred to as sensory integration disorder, sensory processing disorder, and sensory modulation disorder. A dual-tiered anatomical model of adaptation was presented while emphasizing a continuous sensorimotor interaction between a person and his/her environment. The symptoms of these conditions were explained as manifestations of anomalous functioning within interactions between the neocortex, basal ganglia, and cerebellum. Disturbances in sensory selections were interpreted as a result of either abnormal structure or function of cortico–basal ganglia–subcortical circuitry. Disturbances in the "force" with which sensation is experienced were considered as a manifestation of anomalous operations within the cerebellar system. The term "sensory integration" always needs to be operationally defined. Disturbances in praxis can be the manifestation of dysfunctional frontal–parietal interactions. Disturbances in instrumental sequence learning and procedural learning can be the result of cortical–striatal and/or cerebro-cerebellar interactions, which can generate deficits in the automation of various sensorimotor and academic skill sets. Therefore, a firm neuroanatomic underpinning for the symptoms of the conditions of SID/SPD/SMD was hypothesized based upon principles of well-documented brain–behavior relationships and established neuroscientific evidence. Comorbidities occur because different currently well-accepted and recognized diagnostic conditions share the same neurobiologic mechanisms and neural networks that generate the symptoms of SID/SPD/SMD. This represents a scientifically testable model that calls for translational research between clinical professions and a unification of nomenclatures and

terminologies so that we can better understand and serve the patients we evaluate and treat.

Conflicts of Interest The authors have no conflicts of interest associated with this manuscript.

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