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Examining the neuroscience evidence for sensory-driven neuroplasticity: implications for sensory-based occupational therapy for children and adolescents.

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Examining the Neuroscience Evidence for Sensory-Driven Neuroplasticity: Implications for Sensory-Based Occupational Therapy for Children and Adolescents

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KEY WORDS
- evidence-based practice
- feedback, sensory
- neuronal plasticity
- occupational therapy
- sensation
- sensation disorders

When Ayres first presented the theory of sensory integration (SI), she grounded it in the neuroscience literature. Neuroplasticity was then, and is today, considered to be at the heart of this theory. This evidence-based review sought to critically examine the basic science literature to specifically identify evidence for the assumptions and tenets of Ayres' theory of SI. We reviewed literature between 1964 and 2005, within psychological, physiological, and biomedical areas, addressing neuroplasticity. The review focused on sensorimotor-based neuroplasticity; explored the data that addressed the links among sensory input, brain function, and behavior; and evaluated its relevance in terms of supporting or refuting the theoretical premise of occupational therapy using an SI framework (OT/SI) to treatment. Although direct application from basic science to OT/SI is not feasible, we concluded that there was a basis for the assumptions of Ayes' SI theory.

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What is the neuroscience evidence that occupational therapy using a sensory integrative framework with children and adolescents will be effective? This question was designed to investigate the basic neural and developmental science literature that might support or refute the use of occupational therapy using a sensory integration (OT/SI) frame of reference for treatment.

Statement of the Problem

Participation in daily activities in part depends on the ability to process and integrate sensory information within the body and from the environment (Ayres, 1972; Bar-Shalita, Vatine, & Parush, 2008; Bundy & Murray, 2002; Gal, Cermak, & Ben-Sasson, 2007). A significant number of children experience difficulty processing and integrating sensory information. In fact, Ahn, Miller, Milberger, and McIntosh (2004) found that 5%–15% of children in the general population of kindergarten-age children demonstrate difficulties with sensory modulation. This number is estimated to be even higher in clinical populations; 80%–90% of children with autism spectrum disorders have been identified as showing atypical sensory responsivity (Rogers & Ozonoff, 2005; Tomchek & Dunn, 2007). OT/SI is one of the most frequently requested interventions by families of children with autism spectrum disorders (Green et al., 2006; Harrington, Rosen, Garnecho, & Patrick, 2006; Mandell, Novak, & Levy, 2005). OT/SI is based on the belief that engagement in individually tailored activities, rich in the needed sensory stimuli, will improve the ability of the brain and nervous system to process sensory information, enhance the organization and integration of sensation, and, as a result, have a positive impact on the child's ability to participate in daily life activities (Ayres, 1972, 1979).

In parallel with its popularity, OT/SI is a widely criticized intervention framework (Miller, 2003; Shaw, 2002). Critics have cited insufficient direct empirical or clinical evidence to support the theoretical premise that improved processing and integration of sensory information affects function and development in positive ways. Thus, the purpose of this article is to critically examine the neuroscience literature for evidence to support or refute the potential benefit of OT/SI. In preparing this material, we focused on sensory-based neuroplasticity and explored the data in the neuroscience literature that addressed the links among sensory input, brain function, and behavior. We evaluated its relevance in terms of supporting or refuting the theoretical premise of the OT/SI framework.

Background Literature

Occupational therapy using an SI framework is a widely used intervention, primarily for children (see Ayres, 1972; Green et al., 2006; Harrington, Rosen, Garnecho, & Patrick, 2006), but also applied to the adult population (Kinnealey & Fuiek, 1999; Kinnealey, Oliver, & Wilbarger, 1995; Pfeiffer & Kinnealey, 2003). Ayres' (1972, 1979) SI theory postulated that adequate processing and integration of sensory information is an important foundation for adaptive behaviors, where *adaptive behaviors* mean actions such as play and activities of daily living. Seven basic theoretical postulates form the foundation for the SI frame of reference for treatment (Bundy & Murray, 2002; see Schaaf et al., 2009, for full listing of postulates). Several of the postulates are regarding brain behavior functions. Pertinent to the topic we examined in this review, *neuroplasticity,* defined as the nervous system's ability to change in response to environmental input and demands, is considered to be a key postulate on which OT/SI is based.

Implicit in Ayres' early work is the idea that adequate sensory processing and integration is an important foundation for occupational role performance. Ayres hypothesized that some deficits in sensory processing and integration will result in limitations in the production of adaptive behaviors and, as such, in participation. When people experience deficits in sensory processing and integration, they struggle with the performance of everyday occupations (Ayres, 1972; Bar-Shalita et al., 2008; Bundy & Murray, 2002; Gal et al., 2007). *Adaptive responses,* defined as successful interactions with the environment in response to environmental demand, can be seen as the building blocks for successful engagement and participation in occupational roles. Thus, SI/sensory processing is of concern to occupational therapists.

SI/sensory processing is the most investigated frame of reference in occupational therapy practice (Miller, 2003); most investigations of OT/SI have been clinically and behaviorally based. Although Ayres (1972) promoted SI theory as one that linked brain and behavior, the measurement tools for investigating the basic tenets of the brain–behavior link in OT/SI, as well as the impact of OT/SI on specific brain function, have only recently been realized. Thus, the scientific basis of OT/SI is currently grounded in animal research that explores the impact of environmental enrichment and single or multisensory inputs to the nervous system. As a result, this evidence-based investigation assumed a broad focus, largely outside the field of occupational therapy, and used animal and human studies (as available) that investigated the effect of sensory experiences and input on nervous system structure and function. We also examined literature that linked sensory-based interventions to the performance of skills or occupational roles. This approach carried our literature search into the examination of interventions as broad as environmental enrichment studies (e.g., rodents placed in cages with varied toys and opportunities for sensorimotor exploration; see Diamond, Rosenzweig, Bennett, Lindner, & Lyon, 1972) and as focused as tactile input to the finger tip (Ragert, Schmidt, Alternmüller, & Dinse, 2004).

Our emphasis was on the multiple reflections of neuroplasticity or changes in the brain linked to changes in environmental input or context. We examined studies focused on both developmental and reactive neuroplasticity, where *developmental neuroplasticity* refers to those changes that take place in the course of typical development and *reactive neuroplasticity* addresses changes that take place in response to biologically significant stimulus. Finally, many of the studies rely on animal behavior; the links to human behavior are assumptions and must be treated as such.

Findings

Before beginning the literature review, search terms were defined and refined to focus results on studies emphasizing sensory input as the independent variable and behavior or performance as an output. Details on the methodology underlying the search process are delineated in Arbesman and Lieberman (2010). Search terms used included variations of the following: *neuronal or neural plasticity; neuroplasticity; neural receptors; nervous system (physiology and biochemistry, pathology); intersensory processes (includes sensory integration); sense organs (physiology and biochemistry, pathology); sensory reception; sensation (physiology);*

neural coordination; psychomotor performance; perceptual motor processes; perceptual motor learning; perception; sensory integration (keyword). As noted in the Arbesman and Lieberman (2010) article, searches were refined after review of abstracts. Abstract review was based on relevance to the topic. Most articles included in this review were research based, although a few were reviews. Although the review emphasized work accomplished in the past 15 yr; some older publications (e.g., Hubel & Wiesel, 1965) were included because they are considered key in the field of neuroplasticity. Fifty-nine studies were identified to be of probable interest and relevance, and 50 were included in the final evidence table because they were deemed relevant to the question at hand. Table 1 is an abbreviated version of the original evidence table; the entire table can be viewed at www.ajot.ajotpress.net (navigate to this article, and click on "supplemental materials"). Of the 50 studies included, 9 were Level I, 27 were Level II, 12 were Level III, and there was 1 study each at Levels IV and V. The evidence table presented in this article includes a sampling of all studies. The findings are summarized in the following sections by level (Levels I–IV), including key themes that might be extended to people with problems processing and integrating sensory information. Finally, in the Discussion section, we offer some interpretations and applications of this work to occupational therapists using OT/SI.

Level I Studies

The Level I studies reviewed used a randomized controlled trial design and span from 1969 to 2004. Most of this research was done using rodents, comparing the effects of enriched conditions (ECs) and deprived or impoverished conditions (ICs) on brain function. Because the studies used random assignment to experimental group, the design was strong. However, because most of studies were on animals, human application should be done with caution. Moreover, none of the studies specifically addressed OT/SI, and as such the application of findings to clinical populations must be considered cautiously. This group of studies supports the premise that environmental enrichment alters brain structure and function in positive ways. Changes after exposure to environmental enrichment are reported in brain tissue weight, acetylcholine esterase (AChE) activity,[1] total cholinesterase (ChE) levels, dendritic branching, and number of synapses.

Dendritic branching and increased number of synapses are reflections of increased neuronal interactions and a sign of structural neuronal modification and increased complexity in neuronal interactions. Changes in dendritic branching in response to enriched environments were reported by Diamond et al. (1972), Kempermann and Gage (1999), West and Greenough (1972), and Mollgarard, Diamond, Bennett, Rosenzweig, and Lindner (1971); all of these studies used rodent models. One classic example of environmental enrichment can be found in the 1972 study conducted by Diamond and colleagues. In this investigation, earlier findings documenting the effects of environmental enrichment and impoverishment[2] on the rat cerebral cortex were expanded to look specifically at the effects of age and duration of exposure. Comparisons of cortical depth and cortical weight documented that the most drastic neuroplastic changes were evident in the EC rats at 25–55 days of age (roughly equivalent to 7–14 human yr) and that the findings were most pronounced in occipital and somesthetic cortex. However, of great interest was the finding that changes were also evident in the 60-to 90-day-old cohort (roughly equivalent to 16–24 yr in humans), most robustly in the occipital cortex.

In a second series of studies, in which data were included from animals exposed to the standard condition (see footnote 2) different effects between rearing conditions depended on the age of animals and segments of cortex studied. When comparing cortical depth to cortical weight, investigators found that active exploration was the critical component responsible for the changes in cortical depth (not visual stimulation alone).

These findings in rodents provide indirect support of at least one theoretical premise of OT/SI: Enriched environmental conditions facilitate neural changes. Of interest, the finding that active exploration is a necessary component of the brain changes described also lends support for a central premise of OT/SI: that active engagement (of the child) is needed to facilitate SI. Finally, these investigations also indicated that objects should be varied and that the period of exposure required was at least 1 hr per day over a few weeks. This finding provides some

[1]Increases in both AChE and CHe levels reflects changes in acetylcholine activity (Giovannini et al., 2001; Gold, 2003). Some investigators use the ratio of AChE to ChE because it negates the effect of tissue weight on the examination of activity changes. Acetylcholine is an excitatory neurotransmitter associated with neuromodulation and neuroplasticity, For example, an increase in acetylcholine release in the hippocampus has been documented when animals experience novelty in the environment. This increase is concurrent with improvements in cognitive performance.

[2]EC offered opportunities for exploration, exercise, play, and interaction with other animals. Play items were changed regularly. IC had small cages with solid side walls and no interaction with other animals. All animals had continual access to food and water. Standard condition was added in later studies to evaluate the magnitude of the EC effects; wire cages were used so the animals could see each other, and the cages were larger than those used for IC.

Table 1. Neuroscience Evidence That Using a Sensory-Based Approach in Occupational Therapy With Children and Adolescents Is Effective

Author/Year	Study Objectives	Level/Design/Participants	Intervention and Outcome Measures	Results	Study Limitations	Implications for Occupational Therapy
Braun et al. (2001)	The objective was to characterize the effects of motor action on organization of somatosensory cortex in normal adults.	Level III *Design* 1 group, nonrandomized *Participants* 9 men and 3 women, ages 24–43, all right handed	*Intervention* Presentation of tactile stimuli to first (D1, thumb) and fifth (D5, little finger) digits of hand, right × 2 blocks, left × 2 blocks, within a session, random application within block to D1 or D5, each finger receiving 500 stimuli. 2 sessions separated by 1 wk of time. Behavioral measure during application of input: writing without vision or rest. *Outcome Measures* • Whole head MEG for somatosensory-evoked magnetic field measurement • Motor activity measured from finger flexors and extensors • Electro-oculograms used to control for eye movement artifacts Changes in functional organization of somatosensory cortex were assessed by calculating the distance changes between representations of D1 and D5.	EMG activity greater during writing than rest; expected finding. EMG in the stimulated hand only increased during writing condition where stimuli were applied to the writing hand. MEG showed significant reduction of global field activity of somatosensory-evoked field during writing. Motor activity exerts a gating influence on the processing of somatosensory input. The distance between D1 and D5 representation grew larger during writing, and immediately became smaller during rest. Data suggest input to digits is processed separately during fine motor tasks, minimizing cross-talk. Thus, functional organization of somatosensory cortex adapts dynamically to the requirements of a specific task. The task here was highly trained (handwriting). Findings were similar for left and right hands.	Although a functional task (handwriting) was used, the situation in which it was tested was not contextually grounded. This may limit generalizability. Because this study was done on typical adults, there may be limited generalizability to children or adults with disability. Task-specific activation of cortical connectivity patterns may be reflective of how cortical networks support optimal performance.	This study provides a means to conceptualize short-term neuroplastic changes that may occur during intervention. This study examined a highly trained motor task, handwriting, and suggests that "task-dependent activation of preexisting maps might be a powerful mechanism to optimize stimulus processing." This finding suggests that development of such maps for routine activities is important for optimal stimulus processing. Perhaps improvements in routine task performance secondary to practice relates to optimal stimulus processing.
Doucet et al. (2005)	The objective was to examine the possibility that participants with blindness are more efficient at processing spectral acoustic information to solve a task.	Level II *Design* 3 groups, cohort design *Participants* Normally sighted humans ($n = 5$) • Blind participants "without bias" (could accurately localize sound	*Intervention* Stimuli were 30-ms noise bursts ranging from 2–16 kHz broadband, 2–3 kHz (low-pass), and 5–16 khz (high-band) presented at 40dBl SPL. Sound was presented binaurally; monaurally to the right ear (with left ear obstructed with a soft foam	Blind participants fell into 2 groups on the basis of bias. Group membership was not linked to etiology of blindness or presence of residual vision. Findings were robust; previously shown with psychophysiologic and PET techniques. Spectral	Small sample size and a post priori group assignment limit generalizability. The link to neuroplasticity is assumed, but there was no measure of this.	This study provides behavioral evidence of a difference in processing of sound in participants with sight and some participants without sight. It suggests that impairment of sensory input changes the way the brain processes information; changes the skill with which information and is

		both monaurally and binaurally; $n = 5$) • Blind participants "with bias" (localized sound presented monaurally on the side of the open ear only; $n = 5$) Groups were defined post priori on the basis of auditory testing.	plug and covered by haring protector muff); and binaurally with the contours of the ear pinna filled with acoustical paste (petroleum jelly) to equalize the circum-convolutions of the pinna. *Outcome Measure* Pointing with the dominant hand toward the perceived source of sound.	alterations negatively affected blind participants' ability to localize sound, suggesting they make better use of spectral information in the sound localization process. Authors suggested that plasticity underlies the supranormal performance of participant with blindness.		processed. If this study is generalizable to other sensory systems, it should instill some contemplation of the impact of limited sensory input on processing in other systems (i.e., avoidance of touch). We may be able to capitalize on enhanced skills and better understand skill differences.
Kempermann & Gage (1999)	The objective was to examine experience-dependent neurogenesis in the adult mouse hippocampus as modulated by Enr and Enr–WD	Level I *Design* At age of weaning (21 days), rodents were randomized to control, Enr, and Enr–WD conditions ($n = 12$/group). *Subjects* Rodents	*Intervention* Enrichment involved 1 large cage with toys, tunnels, and running wheels; periodic extra treats (fruits and crackers) provided; standard housing was 3/cage with ad lib food and water. Exposure was 68 days, withdrawal for 28 days. *Outcome Measures* • Activity and habituation to new environment • Body and brain weight, motor coordination, physical fitness, procedural learning on rotarod • Spatial learning using water maze testing, immunohistochemistry, and immunofluorescence for cell count	Sedentary mice were heavier, but their brains were not. Enr group was less active when in activity chamber, indicating better habituation. Rotarod performance was better in Enr group and improved with practice. No difference between groups on swim maze, although Enr group had faster swim times. Extension of previous work (Enr resulted in increased number of progenitor cells in hippocampus); longer exposure may preserve acute changes. WD tends to reverse changes, although this was not significant in the current study. Enr increased new neurons and cells not differentiated between neurons and astrocytes.	Animal study limits generalizability. No blinding for histology or behavioral testing could bias results.	Authors introduced the concept of *novelty* rather than simply enrichment as being important in hippocampal changes. Enr appears to increase the *potential* for neurogenesis. Authors suggest Enr findings point to the need for continuous enrichment with increasing complexity for best stimulation of hippocampal neurogenesis. They also suggest that neurogenesis may have a ceiling. Thus, although findings are intriguing, if there is a ceiling effect of neurogenesis, intervention may find a limit.
Rosenzweig & Bennett (1972)	The objective was to define environmental conditions that bring about cerebral differences (EC vs. IC); specifically, to determine whether social grouping, or	Level I *Design* 6-group randomized study with 6 experimental conditions (IC = home cage; EC = enriched condition):	*Intervention* EC exposure for 2 hr/day. Intervention phase = 30 days	Light is not essential to obtain results from EC. In the presence of light, rats showed results in the occipital cortex.	Animal study limits generalizability. Impossible to determine whether social condition will have similar findings in humans who are social beings.	This study demonstrates that the rat brain has more plasticity than previously thought and that EC affects plasticity, but certain conditions must be fulfilled

(*Continued*)

Table 1. Neuroscience Evidence That Using a Sensory-Based Approach in Occupational Therapy With Children and Adolescents Is Effective (*cont.*)

Author/Year	Study Objectives	Level/Design/Participants	Intervention and Outcome Measures	Results	Study Limitations	Implications for Occupational Therapy
	whether social grouping, or exposure to EC during light or dark, were essential components	1. IC, saline injection 2. EC, saline injection, light exposure 3. EC, saline injection, dark exposure 4. IC, methamphetamine 5. EC, light exposure, methamphetamine injection 6. EC, dark exposure, methamphetamine injection Control: IC. *Subjects* Rats	*Outcome Measures* Brain weight and chemical analysis of brain tissue, specifically ChE and ACHe activity. Calculated ACHe: CHe ratio	Brain weight in EC w/ methylphenidate was greatest (facilitated movement and play during EC in both dark and light) Social condition (EC with other rats) showed moderate change; addition of methylhenidate resulted in more dramatic change, presumably because rats were more active. Methylphenidate only did not produce an effect. All 5 groups showed significant difference from control group on ACHe:ChE ratio (a sensitive measure of effects that cancels out variable of brain weight).		to produce changes in brain weight and enzyme activity. This experiment also shows that active participation enhances plasticity. When the rats were facilitated to play either by injection of methylphenidate, prompting by the examiner, or other rats, the effects were greater. This finding supports a central premise of OT/SI: that active participation is needed to optimally facilitate brain plasticity.
Rosenzweig et al. (1969)	The objective was to study the exact nature and extent of the cerebral difference that develops between enriched experience and impoverished experience rats in the occipital cortex.	Level I *Design* Random assignment with 3 conditions: ECT, EC, and IC. *EC:* brightly lit rooms, housed in groups, provided toys, etc. *ECT:* same as EC with exposure daily (30 min) to open field environment in which pattern of barriers was changed Included blind analysis of results. *Subjects* Rats	*Intervention* EC included brightly lit rooms, housing in groups, and providing toys. ECT was the same as EC with daily exposure (30 min) to open field environment in which patterns of barriers was changed. *Outcome Measures* Dissection, weighing, and chemical analysis of brain	*EC:* Significantly greater cortical tissue weight, total AChE activity, total ChE, and cortical depth. Results occurred as clearly in adults as in young rats. *ECT vs. IC (tissue weights, cortical size):* significant differences; greatest difference in occipital cortex, least difference in somesthetic cortex. Change in AChE and ChE activity greatest in the occipital area. ChE:AChE ratio (measure of glial cell) was greatest in occipital region, although this was present in all regions.	Animal study limits generalizability. Study measures brain without providing concurrent measures of behavior; therefore, it is not possible to relate brain changes to behavioral changes. Visual experience is not a necessary component of the conditions that evoke change.	EC produced measurable brain differences in adults and young, which suggests that visual input alone is not responsible for these changes but that the sensory systems work together to produce changes. This study provided support for the idea that sensory input can shape brain activity.

				Cortical depths greatest in occipital area in EC rats.		
Stoeckel, Pollok, Schnitzler, Witte, & Seitz (2004)	The objective was to study use-dependent plasticity of human somatosensory cortex. *Study 1:* Determined differences in accuracy of localization of tactile stimuli on toes between participants who (1) used feet to accomplish simple tasks (the *F1* group); (2) used toes to accomplish everyday activities such as writing and eating (the *F2* group); and (3) control participants. *Study 2:* Determined differences in somatosensory activation patterns to tactile stimuli on toes between the 3 groups.	Level I *Design* 3 groups, randomized: • Used feet for certain actions only ($n = 10$). • Used feet extensively for everyday activities such as writing and eating ($n = 3$). • Control group; thalidomide-damaged extremities but normal hands; feet not used for any unusual actions ($n = 10$). *Participants* People with thalidomine-affected upper extremity ($n = 23$). Mean age = 39.8 (range = 39–42).	*Intervention* None *Outcome Measures* *Study 1:* Accuracy of localization of tactile stimuli on toes; examined cortical representation between groups (fMRI): • Threshold for detection of tactile stimuli on each toe determined. • Threshold monofilament was chosen to evaluate localization for all toes. *Study 2:* fMRI activation of somatosensory area during tactile stimuli	*Study 1:* Participants using their feet for everyday activities had significantly fewer errors (6%) on the tactile localization test than the comparison group ($P = .003$, 1-tailed). *Study 2:* Activation in S1 of somatosensory cortex was significantly stronger in participants who used feet for everyday activities (*p*s = .002–137).	Small experimental group size (F2 $N = 3$) limits generalizability.	fMRI evidence for cerebral reorganization is consistent with behavioral data. *Use dependent* is defined as everyday activities—this is important for occupational therapy. Use-dependent plasticity appears to depend on at least 2 principles: 1. Representation of areas of body parts used with high frequency tend to expand, and 2. Simultaneous stimulation of body parts leads to integrated, overlapping representational cortical fields. Both principles are inherent in the OT/SI approach. In addition, study provides support for OT/SI theory and practice with supporting evidence that "everyday activities" enhance neural (and behavioral) organization.
Wiesel & Hubel (1974)	The objective was to determine whether ordered sequences of orientation columns are present in very young, visually naïve monkeys.	Level II *Design* 2 groups, nonrandomized *Subjects* Macaque monkeys ($n = 6$)	*Intervention* $n = 4$ monkeys with eyes sutured shut at various times close to time of birth; 2 control participants *Outcome Measures* Recordings from Area 17 (occipital cortex)	Highly ordered sequences of orientation shifts were present and were not different from what is seen in adults, suggesting that the organization of the columns of the visual system is innately determined and NOT the result of early experience. In addition, there was deterioration of innate connections subserving binocular convergence suggesting that deprivation results in deteriorating effects.	Animal study limits generalizability.	The theory of OT/SI is built on idea that early sensory experiences shape brain development and influence learning and behavior. This study supports this foundational concept showing that although the visual system is innately organized, lack of experience (i.e., no vision) results in diminished connections. This study addresses the nature–nurture issue and shows that although the

(*Continued*)

Table 1. Neuroscience Evidence That Using a Sensory-Based Approach in Occupational Therapy With Children and Adolescents Is Effective (*cont.*)

Author/Year	Study Objectives	Level/Design/Participants	Intervention and Outcome Measures	Results	Study Limitations	Implications for Occupational Therapy
						visual system is guided by genetic factors, postnatal environmental influences are needed for optimal development.
You et al.(2005)	The objective was to determine whether virtual reality therapy would promote practice-dependent plasticity in a child with CP, leading to enhanced motor skills and overcoming nonuse.	Level V *Design* Case report *Participant* 8-yr-old boy with hemiparetic CP on right side	*Intervention* Single-subject study with pretesting and posttesting Intervention conducted by a therapist unaware of the research Virtual reality games that included bird-ball, conveyor, and soccer. Intervention was 60 min/day, 5 days/wk, for 4 wk. *Outcome Measures* • fMRI • Bruininks–Oseretsky Test of Motor Proficiency, item 6: touching a swinging ball • Modified Pediatric Motor Activity Log • Upper limb subtest of Fugl–Meyer assessment.	Bruininks–Oseretsky Test of Motor Proficiency score changed from 1 to 5. Pediatric Motor Activity Log increased amount of use and quality of movement. Fugl–Meyer assessment score increased from 39 to 52, showing enhanced active movement control, reflect activity, and coordination in upper extremity. fMRI showed a change in activation pattern. Preintervention activation involved bilateral primary motor and sensory cortices, sensorimotor cortex, and ipsilateral supplemental motor areas. No activation of premotor cortex postintervention showed loss of aberrant activation and primary activation of the sensorimotor cortex and contralateral primary sensory and motor cortices.	Single-subject design limits generalizability. Use of isolated items from standardized assessment tools without substantiation of their ability to stand alone; intensity of intervention precludes its reimbursement potential. However, the study suggests that using actual body movement and virtual reality feedback for knowledge of results (visual and proprioceptive feedback) in a manner that was perceived as playful and gamelike, (controlled sensory environment) can result in a combination of functional changes and neuroplasticitic changes in critical cortical regions.	These virtual reality activities targeted specific functional aspects of movement. Using actual body movement and virtual reality feedback for knowledge of results (visual and proprioceptive feedback) in a manner that was perceived as playful and gamelike, this study indicates that a controlled sensory environment can result in a combination of functional changes and neuroplasticitic changes in critical cortical regions.

Note. AChE = acetylcholinesterase; ChE = cholinesterase; CP = cerebral palsy; EC = enriched condition; ECT = enriched condition with training; EMG = electromyography; Enr = long-term stimulation (enrichment); Enr–WD = long-term stimulation and withdrawal; fMRI = functional magnetic resononance imaging; IC = impoverished condition; MEG = magnetoencephalography; PET = positron emission tomography.

basic science data that may inform investigations related to the optimal length and frequency of intervention (also known as *dosage*). No behavioral measures were included in this first series of studies; no direct inference between brain changes and behavior changes can be made.

West and Greenough (1972) worked to link neuronal changes to behavioral improvements. They exposed animals to similar complex environments and found that the length and thickening of the synaptic boutons were greater in the EC rats compared with the IC rats (see footnote 2). Rats exposed to EC were also better at performing a maze task, suggesting that changes in neuronal structure are related to behavioral improvements.

Kempermann and Gage (1999) also supported the premise that ECs can alter brain activity and structure. They studied whether experience-dependent neurogenesis in the adult mouse hippocampus is modulated by long-term stimulation; they compared this condition to long-term simulation and withdrawal. Enrichment (one large cage with toys, tunnels, and running wheels and periodic extra food treats) increased the number of new neurons and cells. However, there was not increased differentiation between neurons and astrocytes, leading investigators to conclude that enrichment may increase the potential for neurogenesis. Withdrawal of the enriched environment tended to reverse the changes noted, but this reversal did not reach significance. This study adds to Kempermann and Gage's previous work by showing that longer exposure may preserve acute changes. This work also builds on the classic studies of Diamond and colleagues (1992), providing evidence that (1) exposure to enriched environments increases cell number, neurogenesis, or the potential for neurogenesis and (2) there may be a need for continuous enrichment with increasing complexity for best stimulation of hippocampal neurogenesis.

A more contemporary study of brain–behavior relationships in humans was conducted by Lacourse, Turner, Randolph-Orr, Schandler, and Cohen (2004). These authors compared physical performance of a learned task (pushing a button in a sequence with different fingers) with mental practice and no practice, using blood-oxygen-level–dependent functional magnetic resonance imaging. Investigators examined areas of cortex and cerebellum activated and performance level. Physical performance participants practiced a sequence of button presses for 1 wk; mental practice participants practiced through motor imagery; no-practice participants did not practice. Investigators found that the physical performance group demonstrated the most improvements in behavior (121% improvement); the mental practice group demonstrated 86% improvement; and the no-practice group improved 38%. Moreover, the physical performance improvements were associated with an increase in activation of contralateral primary motor and sensory areas and the striatum along with decreased cerebellar activation. Different areas of activation change were seen in the mental practice group, suggesting different mechanisms of plasticity. The motor improvement in the physical performance group suggests that active participation, which provides somatosensory feedback, is important in motor improvement. This finding is consistent with SI theory constructs.

Additional support for the finding that active exploration, not merely seeing the stimuli, is a critical ingredient in neural changes was documented by other investigators. Examining the impact of enrichment compared with simple visual exposure, Rosenzweig and colleagues (1969) found that neuroplastic changes in the occipital cortex do not require light exposure; conversely, active exploration of the environment was crucial. In other words, the animals needed to *do* the exploration themselves; simply being exposed to the environment without exploring it was not sufficient to result in neuroplastic changes. In subsequent examination of what might be influencing the changes, investigators compared rats with increased activity level with rats that were prompted into activity by the experimenter. They found that the rats not needing to be prompted into activity in the ECs had the most profound cortical changes, although the extent of the effect varied depending on the cortical area measured (Rosenzweig & Bennett, 1972). This investigation also examined AChE and ChE activity, finding changes parallel to those for cortical depth. Investigators drew several interesting conclusions from this and previous studies. First, placing rats in a large but empty cage had no effect on cortical depth or AChE activity. However, a complex environment coupled with enhanced activity resulted in profound neuroplastic changes in the brain, both in terms of cortical structure and enzyme activity. Moreover, effects were greatest if exposure to EC took place during the rat's most active period of its circadian cycle. Thus, findings indicated that active participation or exploration was crucial; changes were most profound when animals were internally driven (rather than externally prodded) to increased interaction with the environment. This finding lends support to a central premise of the OT/SI frame of reference: that active participation by the child is needed to optimally facilitate brain plasticity.

Level I studies offer the most rigorous study design, making the findings here of great interest. The fact that all but one of the studies reflected here, and all but two reviewed for this project, were conducted on animals

makes the application to the human population somewhat tenuous. This fact can be countered by noting that there is consistency across animal models (e.g., rat, mouse, gerbil, cat), suggesting that the findings are not species specific. In broad terms, what these Level I studies point to is the importance of active exploration of complex environments for neuroplastic changes to occur in the brain; it appears to be important that engagement be ongoing rather than a single experience. Moreover, doing (physical performance) has a different effect than thinking about doing. Each of these ideas can be extrapolated, cautiously, to some of the tenets of SI theory. The sensory nature of these studies was generally broad; animals in EC conditions explored their environments, getting input through all sensory channels. In the Lacourse et al. (2004) study, human participants similarly obtained a broad range of sensory input from engagement in practice. This too is consistent with the theory of SI, as proposed by Ayres (1972). Although Ayres' original work emphasized tactile, proprioceptive, and vestibular inputs, OT/SI capitalizes on enhanced sensory opportunities in all sensory systems, consistent with that seen in these studies.

Level II Studies

Level II studies are those that compare at least two groups but in which randomization of subject to group has not been used. Examples of Level II studies include cohort and case–control designs. Of the Level II studies reviewed, 9 used human participants, 2 used nonhuman primate participants, and 16 used other animals (primarily rodent models, with some mammal models). The studies reviewed spanned from 1964 to 2005 and provide evidence that supports neuroplasticity in the central nervous system in response to sensory input. A variety of models and designs was used, including exposing animals to ECs, the results of altered or enhanced sensory input (e.g., training to enhance auditory or tactile discrimination skills; Bangert & Altenmüller, 2003; Mercado, Bao, Orduña, Gluck, & Merzenich, 2001; Zhang, Bao, & Merzenich, 2001), and the effects of sensory alterations (caused by congenital or induced lesions such as blindness and deafness) on brain processing and functions (Doucet et al., 2005; Hubel & Wiesel, 1965; Stryker & Sherk, 1975).

For the sake of brevity, the animal data are broadly summarized here. In numerous studies, strong support that sensory input (altered or enhanced) changes the way the nervous system processes information was provided (Bennett, Diamond, Krech, & Rosenzweig, 1964; Gordon & Stryker, 1996; Moses, Martin, Houck, Ilmoniemi, & Tesche, 2005; Recanzone, Schreiner, & Merzenich, 1993). The mechanisms for these changes included increased dendritic branching (Volkmar & Greenough, 1972), histological changes (in cell structure and function; Volkmar & Greenough, 1972), anatomical changes (in sensory and motor maps or reorganization of brain areas), changes in cellular activation patterns (Bennett et al., 1964; Recanzone et al., 1993), and, most recently, through upregulation of genes (increasing gene expression) associated with neuroplasticity by means of brain-derived neurotrophic factor (BDNF; Gómez-Pinilla, Ying, Roy, Molteni, & Edgerton, 2002).[3]

As was the case for Level I studies, results from Level II animal studies are shown most consistently in response to ECs (opportunities for sensory, motor activity, and social interaction; Bennett, Rosenzweig, Diamond, Morimoto, & Hebert, 1974; Brown et al., 2003; Kempermann, Kuhn, & Gage, 1998) and in the visual and auditory systems (Moses et al., 2005; Recanzone et al., 1993). Neuroplastic changes are also documented in the somatosensory cortex but less consistently (Merzenich, Recanzone, Jenkins, & Grajski, 1990; Wu, van Gelderen, Hanakawa, Yaseen, & Cohen, 2005). The documented changes may not be global (i.e., in the entire nervous system) but rather specific to precise areas of the central nervous system—the hippocampus being one of these areas (Kempermann et al., 1998).

These same concepts are supported in the human studies, but the data are not as strong because of limitations in studying human brain tissue and processing (Bach-y-Rita, 2004; Mercado et al., 2001). The human studies do, however, demonstrate that (1) the auditory system demonstrates plasticity both in its processing (activation patterns) and cortical representation in response to auditory input (Bangert & Altenmüller, 2003; Doucet et al., 2005; Moses et al., 2005); (2) the brain processes stimuli differently because of either training (piano playing) or ECs (Röeder, Rösler, & Neville, 2000); and (3) processing of sensory stimuli is dynamic and flexible; that is, the sensory systems used during a task are flexible and dependent on the task presented (Russo, Nicol, Zecker, Hayes, & Kraus, 2005). Additional human studies (Doucet et al., 2005; Sober & Sabes, 2005) demonstrated plasticity in human sensory systems. For example, participants who have blindness demonstrate auditory system reorganization such that they become more efficient at processing auditory cues

[3]BDNF is a brain protein and neurotrophic factor. It can promote increased neuronal survival as well as the growth of new neurons, and it has been found in areas linked to learning and memory.

(Doucet et al., 2005). Sober and Sabes (2005) demonstrated that the use of sensory cues was dynamic, flexible, and dependent on availability; participants could readily shift their degree of reliance on vision or proprioception, depending on what was available during a reaching task.

Level II studies reinforced outcomes related to EC identified in Level I studies and provided some interesting information about human sensory processing. They suggested that deficits in one sensory modality result in alterations in how the brain processes information in other modalities and that a typical nervous system can flexibly rely on the sensory information available within the environment to complete a task. This last point offers some support for the SI theory assumption that a successful environmental interaction promotes processing and integration of sensory information. In this case, success depended on the participant's ability to blend visual and proprioceptive strategies. Both studies used adults as participants; mature nervous systems may process information differently from developing nervous systems.

Levels III, IV, and V

Studies at Levels III, IV, and V are characterized as single-group, nonrandomized (III); single-subject design, case series (IV); or case reports/expert opinion (V). Those reviewed here spanned 1967 to 2005 and included many human studies, as well as studies on monkeys, kittens, and rats. Early studies of visual cortex in animal models demonstrated that the sensory systems had an innate and predetermined organization but that this organization was dependent on sensory input and experience for full expression of function (Wiesel & Hubel, 1965, 1974). Lesions resulted in reactive morphological and physiological changes in sensory systems, suggesting that the brain reorganizes when deprived of specific sensory input. This finding was supported behaviorally in the Doucet et al. (2005) study described previously. Studies such as that of Hubel and Wiesel (1965) also showed that there were critical periods for development and restoration of function after lesion and that function did not necessarily return after a period of deprivation or lesion. Thus, there appear to be limits to degree of plasticity in organization and function.

Reactive neuroplasticity, documented behaviorally by Sober and Sabes (2005) and described earlier, was identified in the organization of human somatosensory cortex (Schaefer, Heinze, & Rotte, 2005; Wu et al., 2005). This region of the brain was shown to adapt dynamically to requirements of a specific task; sensory input during a task resulted in changes in tactile discrimination ability. For instance, using magnetoencephalography (MEG)[4] as an outcome measure, Schaefer et al. (2005) found more distant and distinct somatosensory cortical finger representation when Digits 1 and 5 were stimulated during a fine motor/cognitive task than when participants were "at rest." The plasticity was highly task dependent and dynamic in that changes were shown *during* task performance. These investigators concluded that changes to the somatosensory cortex are dynamic and task specific. Moreover, the fact that changes were greater during tasks that required cognitive processing suggested that dynamic plasticity can be facilitated by activation of frontal and prefrontal cortex.

The integration of visual and auditory sensory input was investigated by Moses and colleagues (2005), also using MEG. These investigators presented paired visual and auditory stimuli and noted activation in expected brain regions. Subsequently, presentation of a visual stimulus alone resulted in specific MEG responses in the auditory cortex. These investigators interpreted this finding as "associative neural plasticity" (p. 787). The demonstration in this study that the presentation of sensory information from one modality can produce brain activity in the primary cortex of another sensory modality suggested that the processing of sensation from different modalities is linked when the sensations are paired. Because our world is not one of single-channel sensory inputs, pairing of sensation is the rule, not the exception. This rule is a foundation of OT/SI; sensations are intended to be meaningfully paired such that input in one sensory modality can be used to influence processing in another modality. Because the Moses et al. (2005) study was specific to the auditory and visual systems, application to other sensory systems must be done cautiously.

Also of interest in these studies was the degree of coding engaged in by the brain. *Coding* refers to the process of programming activity in brain regions needed to produce the desired response. Less coding is needed for simple tasks, and the brain appears to allocate only the resources needed for the task. Examining coding of texture within the tactile and visual systems, Guest and Spence (2003) demonstrated that participants used both vision and touch in accomplishment of a task only if the task specifically required it. Integration of both sensory modalities did not take place when tasks were very

[4]MEG is a highly sensitive imaging technique measuring the magnetic fields produced by the brain's electrical activity.

simple, suggesting that multi-SI may depend on task difficulty or complexity.

Halder et al. (2005) examined movement repetition and practice in 10 healthy adults, using a nonskilled task (power grip using vision to control force). Electroencephalogram measurements indicated different changes in neural activity at each stage of the motor task (preparation, movement execution, and feedback integration). The researchers concluded that, in a motor task, distinct mechanisms of plasticity occur during specific stages of information processing and, with practice, motor variability decreases. This finding suggests a role for sensory feedback mechanisms in various stages of motor task execution, an example of sensory–motor integration. Moreover, using single-case design, You et al. (2005) noted that training, either actual or using virtual reality, resulted in reorganization of cortical regions that were associated with changes in performance, again suggesting a role for feedback, either actual sensory feedback or virtual feedback.

Together, the findings here suggest that neuroplasticity is dynamic and that the sensory systems interact such that pairing influences processing. Sensory strategies used are typically task and experience specific, and sensory processing strategies can be linked to stage of motor performance. Globally, these findings support the tenets of SI theory as proposed by Ayres (1972).

Discussion

This review provides direct and robust support for neuroplasticity in many brain regions in response to ECs or direct sensory input, which can be enhanced during motor activity. Findings indicated that changes in neuronal function and structure, and in some studies changes in behavioral indexes, were linked to these neural modifications. Many of the investigations reviewed here were conducted on animals; those on humans typically used adults; both of these facts limit the application of the findings to OT/SI.

Nonetheless, many interesting parallels can be drawn between these basic science studies and Ayres' (1972) SI theory. First, several of the studies reviewed described experimental manipulations that paralleled individual SI theory premises. First, the classic studies of environmental enrichment (e.g., Bennett et al., 1974, 1996; Diamond et al., 1972; Rosenzweig & Bennett 1972; Rosenzweig et al., 1969) provided early evidence that neuroplasticity is possible and that the environment has an impact on neural structure and function. This finding has tremendous implications for occupational therapy in general and OT/SI specifically. Occupational therapists, using multiple intervention frames of reference, work to facilitate successful participation in life activities. More specific to OT/SI, successful participation in life activities is supported through the provision of an enriched environment. Using OT/SI, the "enriched environment" is designed to match expectation for performance with the client's skills and offer the "just-right challenge" to promote processing and integration of sensory information. In this respect, OT/SI differs from the foundational work on neuroplasticity, in that the *enrichment* is specific to the individual's needs and thus neuroplastic changes may be individually driven; however, this application warrants investigation.

Building on these classic studies, investigations of specific sensory interventions reported on in this review documented changes in central nervous system function, organization, and structure after sensory manipulations. A few key points are particularly relevant to OT/SI:

- The sensory environment and environmental opportunities or affordances generally affect brain structure and function (e.g., Bennett et al., 1974; Diamond et al., 1972; Kempermann & Gage, 1999; West & Greenough, 1972).
- Noted changes are often, although not invariably, documented in behavior and in brain structure and function (e.g., Halder et al., 2005; Russo et al., 2005; You et al., 2005).
- All regions of the brain do not show the same response to either specific sensory activation or enriched environments (e.g., Mercado et al., 2001).
- Changes can be task specific, making it important to be focused in terms of outcome measures (e.g., Halder et al., 2005; Recanzone et al., 1993).
- Changes are highly dynamic and seen very quickly (e.g., Pantev et al., 2003).
- Changes can be long lasting, depending on the person and the environment (e.g., Stoeckel et al., 2004).
- Some sensory systems have "critical periods" when processing changes may be easier to document or times when processing centers are more readily influenced by sensory input (e.g., Bavelier et al., 2001; Zhang et al., 2001).
- Documentation supporting interaction among sensory systems exists; stimulus pairing may be an effective intervention tool. However, it is used as needed; if the task is simple, only one sensory modality may be needed, and integration of modalities does not occur (e.g., Guest & Spence, 2003; Hodzic, Veit, Karim, Erb, & Godde, 2004; Moses et al., 2005; Sober & Sabes, 2005).
- It is important to consider the cognitive demands associated with a given task because these appear to have

an effect on motor output and sensory processing (e.g., Braun et al., 2001; Kourtzi, Betts, Sarkheil, & Welchman, 2005).
- Rich sensory input, contextualized in meaningful activity, facilitates neuroplasticity and thus growth, development, and behavior (e.g., Gómez-Pinilla et al., 2002).

There is little question that the nervous system is plastic and that sensory input is an important mediator of this plasticity. Motor activity and interest in task also appear to be important contributors, and active engagement is seen to enhance the effects. Moreover, these studies indicated that neuroplastic changes were developmental, dynamic (reactive), and task specific. In this regard, these data provide indirect support for the use of OT/SI, which is built on the premise that active engagement in meaningful, sensorimotor activities at the just-right challenge and in a playful or meaningful context has a positive impact (by means of neuroplasticity) on processing in the nervous system (Ayres, 1972). Beyond this support, the studies reviewed inform us that multi-SI may be task specific or dependent on task complexity. This finding warrants consideration in the provision of OT/SI.

Applied to OT/SI, the message is that tasks intended to tap into more than a single sensory processing system must do so naturally if integration is to be seen. For instance, if we are hoping to integrate proprioceptive and visual inputs, then swinging on a trapeze over a bolster and targeting a pile of pillows as the drop point has the potential to be integrative; this activity combines proprioceptive (muscle contraction involved in hanging on and flexing the trunk to clear the bolster), vestibular (swinging and linear movement), and visual (identification of the target) inputs in a natural and highly motivating manner. Conversely, passive input (e.g., passive spinning, passively applied touch) would appear not to create the same affordance for integration.

In looking to address the specific question posed for our investigation (i.e., What is the neuroscience evidence that using a sensory-based approach in occupational therapy with children and adolescents will be effective?), the studies examining environmental enrichment provide the closest match to OT/SI because they offer the participant (animal or human) control over activity, novelty, and challenge; a "playful" environment; and more lifelike context (Bennett et al., 1964; Rosenzweig & Bennett, 1972). In addition, several of the specific principles of OT/SI are at least indirectly supported. For example, OT/SI purports that intervention is best delivered in a child-directed, playful manner that allows for flexible adaptations to achievable challenges, rather than teaching to a specific task. This idea is supported in the human data demonstrating that brain processing of sensory input is flexible and dynamic and that the greatest changes come when interaction with the environment is not forced but rather self-initiated (vanPraag, Kempermann, & Gage, 1999).

Another principle of the SI frame of reference that is supported is the notion that enriched sensorimotor experience enhances the brain's processing of information and provides a foundation for learning. This principle is demonstrated in studies showing that ECs (sensory, motor, and problem-solving opportunities) produce neuroplastic changes in areas of the brain related to learning and memory—for instance, the hippocampus—that were concurrent with behavioral improvements in learning (Kempermann & Gage, 1999), thus supporting Ayres' (1972) original notion that sensorimotor activity provides a foundation for learning.

Authors' Note

This review of neuroplasticity literature is necessarily limited. The entire body of this literature is vast, expanding across many decades and professional areas. This project was initiated in 2005; as such, the review includes materials felt to reflect the literature up to that date. Since the conclusion of this review, additional research has been published that continues to add support to the conclusions reached in this investigation. Reflecting on these publications goes beyond the intent of this article. This is an area of growing interest, likely to continue to scaffold support for the effectiveness of sensorimotor–based interventions on improving task and role performance. It is time occupational therapists joined this movement fully, adding their collective voices to this body of neuroscience knowledge and providing the scientific evidence needed to better understand the effectiveness of OT/SI. ▲

References

Ahn, R. R., Miller, L. J., Milberger, S., & McIntosh, D. N. (2004). Prevalence of parents' perceptions of sensory processing disorders among kindergarten children. *American Journal of Occupational Therapy, 58,* 287–293.

Arbesman, M., & Lieberman, D. (2010). Methodology for the systematic reviews of occupational therapy for children and adolescents with difficulty processing and integrating sensory information. *American Journal of Occupational Therapy, 64,* 368–374.

Ayres, A. J. (1972). *Sensory integration and learning disorders.* Los Angeles: Western Psychological Association.

Ayres, A. J. (1979). *Sensory integration and the child.* Los Angeles: Western Psychological Association.

*Bach-y-Rita, P. (2004). Is it possible to restore function with two percent surviving neural tissue? *Journal of Integrative Neuroscience, 3*(1), 3–6.

Bangert, M., & Altenmüller, E. O. (2003). Mapping perception to action in piano practice: A longitudinal DC-EEG study. *BMC Neuroscience, 4,* 26. doi:10.1186/1471-2202-4-26

Bar-Shalita, T., Vatine, J. J., & Parush, S. (2008). Sensory modulation disorder: A risk factor for participation in daily life activities. *Developmental Medicine and Child Neurology, 50,* 932–937. doi:10.1111/j.1469-8749.2008.03095.x

*Bavelier, D., Brozinsky, C., Tomann, A., Mitchell, T., Neville, H., & Liu, G. (2001). Impact of early deafness and early exposure to sign language on the cerebral organization for motion processing. *Journal of Neuroscience, 21,* 8931–8942.

*Bennett, E. L., Diamond, M. C., Krech, D., & Rosenzweig, M. R. (1964). Chemical and anatomical plasticity of brain: Changes in brain through experience, demanded by learning theories, are found in experiments with rats. *Science, 146,* 610–619.

Bennett, E. L., Diamond, M. C., Krech, D., & Rosenzweig, M. R. (1996). Chemical and anatomical plasticity of brain. *Journal of Neuropsychiatry and Clinical Neurosciences, 8,* 459–470.

*Bennett, E. L., Rosenzweig, M. R., Diamond, M. C., Morimoto, H., & Hebert, M. (1974). Effects of successive environments on brain measures. *Physiology and Behavior, 12,* 621–631. doi:10.1016/0031-9384(74)90212-1

*Braun, C., Heinz, U., Schweizer, R., Wiech, K., Birbaumer, N., & Topka, H. (2001). Dynamic organization of the somatosensory cortex induced by motor activity. *Brain, 124,* 2259–2267. doi:10.1093/brain/124.11.2259

Brown, J., Cooper-Kuhn, C. M., Kempermann, G., Van Praag, H., Winkler, J., Gage, F. H., et al. (2003). Enriched environment and physical activity stimulate hippocampal but not olfactory bulb neurogenesis. *European Journal of Neuroscience, 17,* 2042–2046. doi:10.1046/j.1460-9568.2003.02647.x

Bundy, A. C., & Murray, E. A. (2002). Sensory integration: A. Jean Ayres' theory revisited. In A. C. Bundy, S. J. Lane, & E. A. Murray (Eds.), *Sensory integration theory and practice* (2nd ed., pp. 3–34). Los Angeles: Western Psychological Association.

*Diamond, M. C., Rosenzweig, M. R., Bennett, E. L., Lindner, B., & Lyon, L. (1972). Effects of environmental enrichment and impoverishment on rat cerebral cortex. *Journal of Neurobiology, 3,* 47–64. doi:10.1002/neu.480030105

*Doucet, M. E., Guillemot, J. P., Lassonde, M., Gagné, J. P., LeClerc, C., & Lepore, F. (2005). Blind subjects process auditory spectral cues more efficiently than sighted individuals. *Experimental Brain Research, 160,* 194–202. doi:10.1007/s00221-004-2000-4

*indicates studies that were systematically reviewed for this article and are listed in the evidence table available at www.ajot.ajotpress.net.

Gal, E., Cermak, S. A., & Ben-Sasson, A. (2007). Sensory processing disorders in children with autism: Nature, assessment, and intervention. In R. Gabriels & D. Hill (Eds.), *Growing with autism: Working with school-age children and adolescents* (pp. 95–123). New York: Guilford.

Giovannini, M. G., Rakovska, A., Benton, R. S., Pazzagli, M., Bianchi, L., & Pepeu, G. (2001). Effects of novelty and habituation on acetylcholine, GABA, and glutamate release from the frontal cortex and hippocampus of freely moving rats. *Neuroscience, 106,* 43–53. doi:10.1016/S0306-4522(01)00266-4

Gold, P. E. (2003). Acetylcholine modulation of neural systems involved in learning and memory. *Neurobiology of Learning and Memory, 80,* 194–210. doi:10.1016/j.nlm.2003.07.003

*Gómez-Pinilla, F., Ying, Z., Roy, R. R., Molteni, R., & Edgerton, V. R. (2002). Voluntary exercise induces a BDNF–mediated mechanism that promotes neuroplasticity. *Journal of Neurophysiology, 88,* 2187–2195. doi:10.1152/jn.00152.2002

Gordon, J. A., & Stryker, M. P. (1996). Experience-dependent plasticity of binocular responses in the primary visual cortex of the mouse. *Journal of Neuroscience, 16,* 3274–3286.

Green, V. A., Pituch, K. A., Itchon, J., Choi, A., O'Reilly, M., & Sigafoos, J. (2006). Internet survey of treatments used by parents of children with autism. *Research in Developmental Disabilities, 27,* 70–84. doi:10.1016/j.ridd.2004.12.002

*Guest, S., & Spence, C. (2003). What role does multisensory integration play in the visuotactile perception of texture? *International Journal of Psychophysiology, 50,* 63–80. doi:10.1016/S0167-8760(03)00125-9

*Halder, P., Sterr, A., Brem, S., Bucher, K., Kollias, S., & Brandeis, D. (2005). Electrophysiological evidence for cortical plasticity with movement repetition. *European Journal of Neuroscience, 21,* 2271–2277. doi:10.1111/j.1460-9568.2005.04045.x

Harrington, J. W., Rosen, L., Garnecho, A., & Patrick, P. A. (2006). Parental perceptions and use of complementary and alternative medicine practices for children with autistic spectrum disorders in private practice. *Journal of Developmental and Behavioral Pediatrics, 27*(Suppl.), S156–S161. doi:10.1097/00004703-200604002-00014

*Hodzic, A., Veit, R., Karim, A. A., Erb, M., & Godde, B. (2004). Improvement and decline in tactile discrimination behavior after cortical plasticity induced by passive tactile coactivation. *Journal of Neuroscience, 24,* 442–446. doi:10.1523/JNEUROSCI.3731-03.2004

Hubel, D. H., & Wiesel, T. N. (1965). Binocular interaction in striate cortex of kittens reared with artificial squint. *Journal of Neurophysiology, 28*(6), 1041–1059. doi:10.1007/BF00348878

*Kempermann, G., & Gage, F. H. (1999). Experience-dependent regulation of adult hippocampal neurogenesis: Effects of long-term stimulation and stimulus withdrawal. *Hippocampus, 9,* 321–332. doi:10.1002/(SICI)1098-1063(1999)9:3<321::AID-HIPO11>3.0.CO;2-C

*Kempermann, G., Kuhn, H. G., & Gage, F. H. (1998). Experience-induced neurogenesis in the senescent dentate gyrus. *Journal of Neuroscience, 18,* 3206–3212.

Kinnealey, M., & Fuiek, M. (1999). The relationship between sensory defensiveness, anxiety, depression, and perception of pain in adults. *Occupational Therapy International, 6,* 195–206. doi:10.1002/oti.97

Kinnealey, M., Oliver, B., & Wilbarger, P. (1995). A phenomenological study of sensory defensiveness in adults. *American Journal of Occupational Therapy, 49,* 444–451.

*Kourtzi, Z., Betts, L. R., Sarkheil, P., & Welchman, A. E. (2005). Distributed neural plasticity for shape learning in the human visual cortex. *PLoS Biology, 3,* e204. doi: 10.1371/journal.pbio.0030204

*Kujala, A., Huotilainen, M., Uther, M., Shtyrov, Y., Monto, S., Ilmoniemi, R. J., et al. (2003). Plastic cortical changes induced by learning to communicate with non-speech sounds. *NeuroReport, 14,* 1683–1687.

*Lacourse, M. G., Turner, J. A., Randolph-Orr, E., Schandler, S. L., & Cohen, M. J. (2004). Cerebral and cerebellar sensorimotor plasticity following motor imagery-based mental practice of a sequential movement. *Journal of Rehabilitation Research and Development, 41,* 505–524. doi: 10.1682/JRRD.2004.04.0505

Mandell, D. S., Novak, M. M., & Levy, S. (2005). *Frequency and correlates of treatment use among a community sample of children with autism.* San Diego, CA: International Meeting for Autism Research.

*Mercado, E., Bao, S., Orduña, I., Gluck, M. A., & Merzenich, M. M. (2001). Basal forebrain stimulation changes cortical sensitivities to complex sound. *Neuroreport, 12,* 2283–2287. doi:10.1097/00001756-200107200-00047

Merzenich, M. M., Recanzone, G. H., Jenkins, W. M., & Grajski, K. A. (1990). Adaptive mechanisms in cortical networks underlying cortical contributions to learning and nondeclarative memory. *Cold Spring Harbor Symposia on Quantitative Biology, 55,* 873–887.

Miller, L. J. (2003). Empirical evidence related to therapies for sensory processing impairments. *NASP Communique, 31,* 34–37.

Mollgarard, K., Diamond, M. C., Bennett, E. L., Rosenzweig, M. R., & Lindner, B. (1971). Quantitative synaptic changes with differential experience in rat brain. *Journal of Neuroscience,* 113–128.

*Moses, S. N., Martin, T., Houck, J. M., Ilmoniemi, R. J., & Tesche, C. D. (2005). The C50m response: Conditioned magnetocerebral activity recorded from the human brain. *NeuroImage, 27,* 778–788. doi:10.1016/j.neuroimage.2005.05.017

*Nakahara, H., Zhang, L. I., & Merzenich, M. M. (2004). Specialization of primary auditory cortex processing by sound exposure in the "critical period." *Proceedings of the National Academy of Sciences of the United States of America, 101,* 7170–7174.

*Pantev, C., Ross, B., Fujioka, T., Trainer, L. J., Schulte, M., & Shulz, M. (2003). Music and learning induced cortical plasticity. *Annals of the New York Academy of Science, 999,* 438–450.

Pfeiffer, B., & Kinnealey, M. (2003). Treatment of sensory defensiveness in adults. *Occupational Therapy International, 10,* 175–184. doi:10.1002/oti.184

*Ptito, M., Moesgaard, S. M., Gjedde1, A., & Kupers, R. (2005). Crossmodal plasticity revealed by electrotactile stimulation of the tongue in the congenitally blind. *Brain, 128,* 606–614.

Ragert, P., Schmidt, A., Altenmüller, E., & Dinse, H. R. (2004). Superior tactile performance and learning in professional pianists: Evidence for meta-plasticity in musicians. *European Journal of Neuroscience, 19,* 473–478. doi:10.1111/j.0953-816X.2003.03142.x

*Recanzone, G. H., Schreiner, C. E., & Merzenich, M. M. (1993). Plasticity in the frequency representation of primary auditory cortex following discrimination training in adult owl monkeys. *Journal of Neuroscience, 13,* 87–103.

*Renier, L., Collignon, O., Poirier, C., Tranduy, D., Vanlierde, A., Bol, A., et al. (2005). Crossmodal activation of visual cortex during depth perception using auditory substitution of vision. *NeuroImage, 26,* 573–580.

*Röder, B., Rösler, F., & Neville, H. J. (2000). Event-related potentials during auditory language processing in congenitally blind and sighted people. *Neuropsychologia, 38,* 1482–1502. doi:10.1016/S0028-3932(00)00057-9

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

*Rosenzweig, M. R., & Bennett, E. L. (1972). Cerebral changes in rats exposed individually to an enriched environment. *Journal of Comparative and Physiological Psychology, 80,* 304–313. doi:10.1037/h0032978

*Rosenzweig, M. R., Bennett, E. L., Diamond, M. C., Wu, S.-Y., Slagle, R. W., & Saffran, E. (1969). Influences of environmental complexity and visual stimulation on development of occipital cortex in rat. *Brain Research, 14,* 427–445. doi:10.1016/0006-8993(69)90120-6

*Russo, N. M., Nicol, T. G., Zecker, S. G., Hayes, E. A., & Kraus, N. (2005). Auditory training improves neural timing in the human brainstem. *Behavioural Brain Research, 156,* 95–103. doi:10.1016/j.bbr.2004.05.012

Schaaf, R. C., Schoen, S. A., Smith Roley, S., Lane, S. J., Koomar, J. A., & May-Benson, T. A. (2009). A frame of reference for sensory integration. In P. Kramer & J. Hinojosa (Eds.), *Frames of reference for pediatric occupational therapy* (3rd ed., pp. 99–186). Philadelphia: Lippincott Williams & Wilkins.

*Schaefer, M., Heinze, H. J., & Rotte, M. (2005). Task-relevant modulation of primary somatosensory cortex suggests a prefrontal-cortical sensory gating system. *NeuroImage, 27,* 130–135doi:10.1016/j.neuroimage.2005.04.005

*Schapiro, S., & Vukovich, K. (1970). Early experience effects upon cortical dendrites: A proposed model for development. *Science, 167,* 292–294.

Shaw, S. R. (2002). A school psychologist investigates sensory integration therapies: Promise, possibility and the art of placebo. *Autism Today.* Retrieved November 25, 2009, from www.autismtoday.com/articles/School_Psychologist_Investigates_Sensory_Integration.htm

*Sober, S. J., & Sabes, P. N. (2005). Flexible strategies for sensory integration during motor planning. *Nature Neuroscience, 8,* 490–497.

*Stoeckel, M. C., Pollok, B., Schnitzler, A., Witte, O. W., & Seitz, R. J. (2004). Use-dependent cortical plasticity in thalidomide-induced upper extremity dysplasia: Evidence from somaesthesia and neuroimaging. *Experimental Brain Research, 156,* 333–341. doi:10.1007/s00221-003-1794-9

Stryker, M. P., & Sherk, H. (1975). Modification of cortical orientation selectivity in the cat by restricted visual experience: A reexamination. *Science, 190,* 904–906. doi:10.1126/science.1188372

Tomchek, S. D., & Dunn, W. (2007). Sensory processing in children with and without autism: A comparative study using the Short Sensory Profile. *American Journal of Occupational Therapy, 61,* 190–200.

*vanPraag, H., Kempermann, G., & Gage, F. H. (1999). Running increases cell proliferation and neurogenesis in the adult mouse dentate gyrus. *Nature Neuroscience, 2,* 266–270.

*Volkmar, F. R., & Greenough, W. T. (1972). Rearing complexity affects branching of dendrites in the visual cortex of the rat. *Science, 176,* 1445–1447. doi:10.1126/science.176.4042.1445

*West, R. W., & Greenough, W. T. (1972). Effect of environmental complexity on cortical synapses of rats: Preliminary results. *Behavioral Biology, 7,* 279–284. doi:10.1016/S0091-6773(72)80207-4

Wiesel, T. N., & Hubel, D. H. (1965). Extent of recovery from the effects of visual deprivation in kittens. *Journal of Neurophysiology, 28,* 1060–1072.

*Wiesel, T. N., & Hubel, D. H. (1974). Ordered arrangement of orientation columns in monkeys lacking visual experience. *Journal of Comparative Neurology, 158,* 307–318. doi:10.1002/cne.901580306

*Wu, C. W., van Gelderen, P., Hanakawa, T., Yaseen, Z., & Cohen, L. G. (2005). Enduring representational plasticity after somatosensory stimulation. *NeuroImage, 27,* 872–884. doi:10.1016/j.neuroimage.2005.05.055

*You, S. H., Jang, S. H., Kim, Y. H., Kwon, Y. H., Barrow, I., & Hallett, M. (2005). Cortical reorganization induced by virtual reality therapy in a child with hemiparetic cerebral palsy. *Developmental Medicine and Child Neurology, 47,* 628–635. doi:10.1017/S0012162205001234

*Zhang, L. I., Bao, S., & Merzenich, M. M. (2001). Persistent and specific influences of early acoustic environments on primary auditory cortex. *Nature Neuroscience, 4,* 1123–1130. doi:10.1038/nn745