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

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<td>Bach-y-Rita</td>
<td>The objective was to review work on sensory substitution.</td>
<td>Level not indicated; many studies were summarized.</td>
<td>Use of tactile vision substitution systems on motor performance of participants without sight. Vibrotactile substitution to provide meaningful information regarding postural control. Exploration between somatosensory input and environmental exploration.</td>
<td>Tactile input, once the coding of it is understood, was successfully used by people without sight to enable them to engage in activities such as perceiving a ball rolling toward them; reaching for a drink; and playing rock, paper, scissors. Postural stability could be produced with the use of a head accelerometer and vibrotactile input coding on the tongue. Study demonstrated that active exploration is required for tactile discrimination of texture and spatial temporal touch.</td>
<td>Sensory substitution paradigms are very lab oriented and generally not practical for clinical use.</td>
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<td>Bavelier et al.</td>
<td>The objective was to examine the effects of early deafness and early acquisition of American Sign Language on the organization of neural systems important in perception of visual motion (lateralization of motion processing) and visual attention (peripheral visual attention, visual orienting).</td>
<td>Level II 3 groups: deaf signers ($n = 11$); typical control participants ($n = 11$), ages 18–27; comparison group ($n = 8$) adults with hearing age 22–42, born to deaf parents (hearing signers). All were right handed.</td>
<td>Interventions 7 scans, each 4 min 16 s during which displays viewed had 12 alternating blocks of static dots and motion flow fields. Participants were asked to fixate on central point. In luminance conditions, participants monitored either static or moving blocks for increased luminance. In velocity condition, participants monitored motion blocks for abrupt changes in velocity. Outcome measures: Participants were asked how many blocks contained $\geq 3$ changes in luminosity or velocity.</td>
<td>There were no robust behavioral differences, but there was a trend for deaf signers to better detect peripheral changes and for hearing people to better detect central changes. fMRI: $\bullet$ MT–MST recruited more strongly in hearing people when the task required monitoring motion and when attention was directed centrally. $\bullet$ Greater recruitment of MT–MST in the left hemisphere in deaf and hearing signers but in right hemisphere in hearing control participants; thus, early signing modifies motion processing into a robust left-hemisphere advantage. Early deafness, not signing, leads to heightened sensitivity in posterior parietal cortex, a major center of selective attention. Deaf signers also showed greater recruitment of posterior superior temporal sulcus area, an area associated with processing of biological motion and socially relevant body signals. Findings may point to enhanced</td>
<td>Lab conditions may limit generalizability. This study will not generalize to other disruptions of sensory processing.</td>
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<td>Bennett, Diamond, Krech, &amp; Rosenzweig (1964)</td>
<td>This article is a summary of several studies examining responses of the brain to experience and the relationship of intelligent behavior in animals to brain chemistry.</td>
<td>Level II Control and 1 or 2 experimental groups of rats</td>
<td>Control (social control = SC): standard lab housing (3/cage, no special treatment) ECT: housed in groups of 10–12, provided toys, exposed daily (30 min) to open field environment in which patterns of barriers was changed; challenged “after some weeks” by mazes IC: 1 animal cage, dimly lit, quiet room, could not see or touch another animal Exposure time: 80 days</td>
<td>ECT vs. IC and SC: There was greater growth of cortex especially in visual area and to a lesser extent in somesthetic region, not reflecting increased body weight. There was increased AChE activity, with the greatest gain in visual region. Alterations were not due simply to handling. In repeat studies on “old” rats, the weight of cortex and AChE mimicked these results. Repeated in several lines of rats with some rats showing more and others less change, but all showing change.</td>
<td>Animal study limits generalizability. Classic, but older, studies mean that chemical analysis methods are dated and perhaps less accurate than optimal. No blinding for histology or behavioral testing could bias results.</td>
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<td>Bennett, Rosenzweig, Diamond, Morimoto, &amp; Hebert (1974)</td>
<td>This study investigated persistent cerebral effects of enriched vs. impoverished environmental conditions and effects of switching from EC to IC.</td>
<td>Level II 3 groups: EC throughout, EC–IC, IC throughout</td>
<td>Two studies: 1. EC: housed 12/cage; 6 toys added to environment, some new ones added each day while others were removed. Exposure to maze each day. IC: housed in separate cages in quiet, illuminated room; no handling. Exposed to EC for 30 or 80 days; then switched to IC. 2. 3 different EC conditions and 1 IC condition.</td>
<td>Cerebral effects of EC begin to dissipate when animals are removed from enriched environment, although significant differences persist. Degree of persistence varies with length of initial exposure and length of second exposure, as well as brain region studied. Findings suggest that long-term changes both behaviorally and enzymatically indicate possible effect on memory storage.</td>
<td>Classic studies cited, but the relative age of studies cited may be problematic. Animal study limits generalizability. These were “normal” nervous systems, limiting application to the central nervous system in the face of disease or dysfunction. No blinding for histology or behavioral testing could bias results.</td>
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<td>Braun et al. (2001)</td>
<td>The objective was to characterize the effects of motor action on the organization of somatosensory cortex in normal adults.</td>
<td>Level III 1 group nonrandomized participants: 9 men and 3 women, ages 24–43, all right handed</td>
<td>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.</td>
<td>Electromyographic activity was greater during writing than rest conditions—an expected finding. EMG in the stimulated hand was increased only during the writing condition in which stimuli were applied to the writing hand.</td>
<td>Although a functional task (handwriting) was used, the situation in which it was tested was not contextually grounded. This situation may limit generalizability. Because this study was done on typical adults, there may be limited generalizability to children.</td>
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2 sessions separated by 1 wk of time. Behavioral measure during application of input was 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.

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. This finding and other data suggest that input to the digits is processed separately during fine motor tasks, minimizing cross-talk.

Thus, functional organization of somatosensory cortex adapts dynamically to requirements of a specific task. Task in this case was highly trained task of handwriting.
Findings similar for left and right hands.

Intervention
EC, IC, or SC:
- 31 pairs (EC vs. IC = 1 pair) were started in condition at 25–55 days old (mean = 30 days).
- 18 pairs were started at 105–185 days (mean = 60 days).
- 50 pairs were started at 60–90 days (mean = 30 days).

Cortical depth and weight were greater in EC rats.
25–55 Day Cohort
EC rats showed pronounced differences in occipital cortex and somesthetic cortex.
60–90 Day Cohort
This group showed the most positive results with differences in occipital cortex significant at the .001 level.
105–185 Day Cohort
Cortical depth changes were not as marked as with the other groups. Effects of EC are similar for two 80-day groups (EC and IC) in which the age at onset differed. The caudal region of the cerebral cortex, including the occipital cortex, showed the greatest effects.

The second series of studies in which they included SC data showed different effects depending

Animal study limits generalizability. Studies demonstrate improvements in cortical weight and depth, but the changes are not related to behavioral or learning improvements.
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<td>Doucet et al. (2005)</td>
<td>The objective was to examine the possibility that participants with blindness are more efficient at processing spectral acoustic information to solve a task.</td>
<td>Level II Design 3 groups, cohort design Participants Normally sighted humans ((n = 5)) - Blind participants “without bias” (could accurately localize sound 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.</td>
<td>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 40dB SPL. Sound was presented binaurally, monaurally to the right ear (with left ear obstructed with a soft foam plug and covered by hearing 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.</td>
<td>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 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.</td>
<td>Small sample size and a post priori group assignment limit generalizability. The link to neuroplasticity is assumed, but there was no measure of this.</td>
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<td>Gómez-Pinilla, Ying, Roy, Molteni, &amp; Edgerton (2002)</td>
<td>The objective was to examine the possibility that exercise induces an integrated response of brain-derived neurotrophic factor and its receptor that may result in synaptic modification or adaptation.</td>
<td>Level II Nonrandom assignment to voluntary exercise or sedentary groups Exposed to 3 or 7 days running Rat model</td>
<td>Outcome Measures Total and mRNA for brain-derived neurotrophic factor and its receptor, protein in soleus muscle and lumbar cord</td>
<td>Voluntary exercise increased expression of molecules associated with brain-derived neurotrophic factor action on synaptic function and neurite growth in lumbar cord and soleus muscle. Paralysis (botox) resulted in reduced brain-derived neurotrophic factor in cord and muscle, although there was some mediation of this effect in the cord by exercise.</td>
<td>Animal study limits generalizability. No blinding for histology or behavioral testing could bias results.</td>
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<td>Guest &amp; Spence (2003)</td>
<td>This was a series of studies designed to move prior work with abrasive textures into the realm of “ecologically appropriate” textures of pilled fabrics. In addition, the authors examined hypothesis that attention is distributed between Level III Humans, 1 group Experiment 2: All stimuli were presented bimodally. Identification was of rough–smooth for both stimuli. Specific stimuli were identified for each participant to be within 60%–90% correct on the age of animals and segments of cortex studied. Active exploration is the critical component responsible for the changes in cortical depth (not visual stimulation).</td>
<td>Experiment 1: 4 textures of pilling fabric; participants determined which of pair was “roughester” using touch, vision, or both. Each approach occurred in different session. Pairs were randomized within sessions. 40 trials occurred for each stimulus pair with</td>
<td>Experiment 1: Neither individual system dominated. Bimodal enhancement was not consistently found. Experiment 2: No evidence of consistent bias was found toward bimodal intervals.</td>
<td>Small sample sizes with lack of control group, lab setting, and use of typical adults limit generalizability.</td>
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vision and touch during many texture-based tasks. 80% accuracy range, $n = 10$. Participants not naïve to experimental protocol as they were for Experiments 1 and 2.

Experiment 2: Same overall design, but 1 stimulus was presented unimodally (touch paired with vision; touch paired with vision–touch) ($n = 15$).

Outcome Measures
Correct/incorrect identification

All participants first practiced the task by squeezing a ball at 40% maximum force with their right hand while visual feedback was provided about the amount of force.

Next, the task was divided into 13-min parts with 10-min breaks in between to minimize the effects of fatigue and loss of attention. Participants were instructed to squeeze the ball as hard as needed to match the force shown on the screen. Force was measured using a sphygmomanometer bulb connected to a blood pressure transducer that translated air compression into an analog signal that was digitized. A continuous-force trajectory channel was calculated.

Event-related potentials were recorded via EEG using an electrocap with 64 channels. There were 4 main event-related potential measures: Microstate 1 was attributed to visual target processing; Microstate 2 is related to movement execution, Microstate 3 appears during the release phase, ends after movement execution, and reflects feedback processing or visuomotor integration. Microstate 4 was attributed to changes in general attention, but was small, and authors did not consider it further.

Experiment 3: Study of attention found that visual and tactile inputs act as independent sources of information and both contribute to discrimination process. Thus, vision and touch interact but do not show integration. These multiple sources of input appear potentially redundant.

Controlled repetition of the same movement leads to rapid cortical plasticity within 30 min. The finding that there are differential repetition effects (EEG changes) on each stage of the task (preparation, movement execution, and feedback integration) suggests that "partly distinct neural mechanisms of cortical plasticity operate on different stages of information processing" (during motor learning; p. 2276).

Movement variability decreased significantly over trials, indicating that the motor system optimizes behavior by increasing consistency, despite constant effort. Effects of repetition were observed at multiple stages and did not correlate, suggesting that motor learning occurs in stages. For example, there appears to be a consolidation period in promoting repetition-induced plasticity (this means that the brain has distinct stages of neural processing during motor learning; 1 stage is consolidation that has a specific neural correlate).

There was a change in activity (temporal decoupling) between visual and motor processing with practice, suggesting a decreased dependence on visual information as movement automation progresses.

It is suggested that changes in the extent of lateral inhibition mediated by $\gamma$-aminobutyric acid underlie plasticity in motor areas and may be the physiological correlate of the pattern observed here.

The sample size was small and a 1-group design. Participants were all young, so findings cannot be generalized to other age groups.
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| Hodzic, Veit, Karim, Erb, & Godde (2004) | This study investigated alterations in cortical topography and task specificity of learning in a protocol that used passive tactile co-activation without attention to stimuli. | Level III 1 group 11 right-handed adults Pretest–posttest design | Intervention: Conducted premapping fMRI, co-activation procedure, postmapping  
Outcome Measures: fMRI mapping of somatosensory (SI and SII) representation of right index finger (compared with left or control)  
Co-activation: Tactile input was applied to the finger tip to co-activate all receptive fields within area. Applied with varying interstimulus interval to prevent habituation over the 3-hr application.  
Spatial discrimination: Grating orientation task featured 8 domes with gratings cut in the surface rubbed on finger tip, randomly orienting grooves to parallel or orthogonal to axis of finger tip. Outcome was discrimination threshold based on width of bars and grooves.  
Temporal discrimination: Vibrotactile stimuli were played via speakers attached to the computer and applied to the finger tip. Participants were given 500 ms. Two-alternative forced-choice paradigms were used to determine whether the frequency of test stimulus was higher or lower than reference stimulus. | After passive co-activation, the grating orientation task discrimination was improved. Improvement was strongly correlated with reorganization in contralateral SI. Reorganization also seen in SII, but not linked to improved grating orientation task. Findings suggest that SI has a predominant role in processing and discrimination.  
Temporal discrimination did not improve; in some participants, it worsened. Findings may be linked to the drive of the brain to create the most behaviorally useful representation of sensation, which in this case may have been spatial. Alternatively, increased spatial responsiveness may have been accompanied by prolonged duration of response, thus impairing temporal discrimination. | The study lacked a control group, although each subject had a control finger. Lab setting limits generalizability. |
| Kempermann & Gage (1999) | The objective was to examine how experience-dependent neurogenesis in adult mouse hippocampus is modulated by long-term stimulation (Enr) and long-term simulation and withdrawal (Enr–WD). | Level I  At age of weaning (21 days), mice were randomized to control, Enr, and Enr–WD conditions; n = 12/group.  
Enrichment involved 1 large cage with toys, tunnels, and running wheels; periodic extra treats (fruits and crackers) were provided. Standard housing was 3/cage with ad lib food and water. Exposure was 68 days, withdrawal for 28 days. | Sedentary mice were heavier but their brains were not.  
The Enr mice were less active when in activity chamber, indicating better habituation.  
Rotarod performance was better in Enr mice and improved with practice. No difference was observed between groups on swim maze, although Enr mice had faster swim times. | Animal study limits generalizability. No blinding for histology or behavioral testing could bias results. |
Outcome Measures
Overall 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

Previous work had shown Enr resulted in increased number of progenitor cells in hippocampus. This study showed that longer exposure may preserve acute changes. Withdrawal tends to reverse changes, although this was not significant in the current study. Enr did increase new neurons and cells not differentiated between neurons and astrocytes. Thus, Enr might increase the potential for neurogenesis.

Introduced the concept of novelty rather than simply enrichment as being important in hippocampal changes.

68-day exposure led to more cells differentiating into neurons: a threefold increase in labeled neurons in 20-mo-old mice and a more than twofold increase in 8-mo-old mice compared with littermates living under standard laboratory conditions. Astrocytes not affected.

Enriched environment: Social interaction (13 mice/cage), exploratory options (toys, rearrangeable tunnels, activity wheel), food treats (cheese, crackers, fruit) in addition to food and water ad libitum

Standard environment: Food, water ad libitum, 3 animals/cage

All animals exposed to environment for 40 days when 5 from each group were sacrificed for the study. Others stayed in the environment for an additional 28 days for behavioral water maze testing; sacrificed at age of 20 mo.

Water maze testing: 2×/day for 10 days.

Immunohistochemistry, phenotype analysis, and stereology of granule cells conducted.

Animal study limits generalizability. The underlying mechanism remains to be delineated and could not be derived from this study. The relationship to neurogenesis of astrocytes needs further exploration because although they did not appear to be equally affected by the environmental experience, a chance remains that the neuronal outcome was related to an effect on glia. The possible influence of glutamate is of interest, but it was not elucidated in this study. The extent to which the actual activities influencing spatial learning might have contributed to the noted behavioral improvements in water maze activity is undefined by this study.
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<td>Kujala et al. (2003)</td>
<td>MMN is an index of permanent auditory cortical representation of native-language speech sounds. When a new type of communication system is acquired (such as Morse coding skills), new representations must be formed. This study aimed to examine the development of the cortical memory traces for the Morse-coded acoustic language units in relation to existing memory traces for native-language speech sounds (plasticity) using MEG.</td>
<td>Level III 1 group, nonrandomized Convenience sample: 7 participants from Finnish navy Ages 19–23 Right handed Native speakers of Finnish Setting Laboratory</td>
<td>Experiment 1: Low-salience stimuli (difficult to distinguish from background) Experiment 2: High-salience stimuli fMRI of V1, V2, VP, V4 (early retinotopic visual areas), and lateral occipital complex Outcome Measures fMRI: Responses were evoked when participants detected trained novel shapes vs. nontrained shapes. Responses occurred when salience of target shapes was altered in distinctiveness. Behavioral (right/wrong) responses were tracked.</td>
<td>Initially, the MMN to Morse-coded syllables was stronger in the hemisphere opposite the 1 dominant for the MMN native-language speech sounds (4 participants were left-hemisphere dominant, and 3 were right-hemisphere dominant). After the 3-mo training period, the pattern reversed, and the MMN for Morse code became lateralized to the hemisphere that was predominant for the speech sound MMN. This study provides neurophysiologic evidence that “new memory traces” and brain reorganization occur in response to auditory sensory stimuli.</td>
<td>Small, nonrandomized sample limits generalizability.</td>
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<td>Lacourse, Turner, Randolph-Orr, Schandler, &amp; Cohen (2004)</td>
<td>The objective was to determine whether physical performance of a learned task (pushing a button in a sequence with different fingers) differs from mental practice in terms of areas of cortex and cerebellum activated and performance level.</td>
<td>Level I Participants randomly assigned to 3 groups: physical performance, mental practice, or no practice 39 boys, 21 girls; mean age = 23.3 (standard deviation = 5 yr).</td>
<td>Sequential button-press task with right hand during 2 test sessions and daily practice. 2 different sequences practiced. Movement activation was measured by BOLD fMRI. Movement performance was measured by counting the number of completed sequences</td>
<td>Physical performance demonstrated the most improvements in behavior (121% improvement). Mental practice demonstrated 86% improvement. No practice improved 38% for Sequence A (similar but smaller improvements for Sequence B).</td>
<td>Possible design limitation in that both physical performance and mental practice were performed as rapidly as possible during practice, whereas the task was visually paced at 2 Hz during the test sessions. Control of rate may have created a secondary confounding effect by varying the spatiotemporal requirements of the task.</td>
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IV = practice group, test (pre or post), and sequence (A or B)Brain activation and movement sequence performance

and errors during repetitive 30-s epochs of the button-press task.

and errors during repetitive 30-s epochs of the button-press task.

Physical performance improvements were associated with an increase in contralateral primary motor and sensory areas. Mental practice activated similar areas but also activated other brain areas, suggesting that somewhat different mechanisms may be at play with physical performance vs. mental practice.

Mercado, Bao, Orduna, Gluck, & Merzenich (2001)

This study determined whether pairing basal forebrain stimulation with the presentation of complex sound resulted in spectrotemporal response sensitivity and selectivity changes in rat auditory cortex.

Level II

Single groups in 2 separate studies were both compared with nontreated rats (n = 10). All animals received electrical stimulation of the nucleus basalis.

Intervention

Experiment 1 (n = 2):
Stimulation paired with sound upshift train

Experiment 2 (n = 4):
Stimulation paired with upshift and no stimulation paired with downshift sound trains, random presentation of paired and unpaired

Background white noise:
Studies delivered e-stim randomly every 8–40 s, 400–500/day, for 10–20 days.

Outcome Measures
Multiple-unit or single-unit extracellular recordings from right auditory cortex (ipsilateral to site of stimulation)

Previous studies demonstrated pairing basal forebrain (nucleus basalis) stimulation with short-duration, pure-tone sounds mediated experience-induced changes in auditory cortical responses. This study adds to an understanding of auditory cortex plasticity. The auditory cortex regions responsive to sounds were larger, magnitude of response was greater, and number of neurons responding selectively was greater with paired stimulation. These findings were identified in mature rats, indicating continued plasticity even in the mature brain.

Moses, Martin, Houck, Ilmoniemi, & Tesche (2005)

This study used MEG to investigate the spatial and temporal properties of associative plasticity during “magnetocerebral” conditioning.

Level III

1 group, nonrandom assignment

Convenience sample of 4 men and 4 women ages 24–31, no known pathology

Intervention
Participants were exposed to various experimental conditions.

Outcome Measures
MEG activity was recorded during a habituation phase, delay conditioning training, extinction, and trace conditioning. CS was an achromatic square; CS+ included a diagonal or vertical striped pattern and the CS− had a checkerboard pattern. Unconditioned stimulus was 100 ms binaural white noise. Stimuli within each phase were randomized.

After pairing auditory and visual stimuli, auditory activation was found with a visual stimulus even in the absence of auditory input. Activation was found in and near Heschl’s gyrus. These findings support other findings using fMRI and PET scans and are similar to paired and unpaired findings using somatosensory and auditory inputs.

MEG may be useful in understanding the dynamics of conditioned response across multiple sensory modalities. Pairing visual and auditory input results in activation of regions of
### Supplemental Table 1. Neuroscience Evidence That Using a Sensory-Based Approach in Occupational Therapy With Children and Adolescents Is Effective (cont.)

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<td>Nakahara et al. (2004)</td>
<td>In light of studies that show that exposure of kittens or rat pups to a modulated tonal stimuli during an early postnatal period resulted in expansion of the representation of the exposed sound frequency in auditory cortex (A1), the purpose of this study was to clarify how the cortical representation of the dynamic aspects of complex sound are specifically shaped by the spectrotemporal patterns of auditory input during development.</td>
<td>Level II 2 groups nonrandomized Litters of 9–12-day-old rat pups Stimuli consisted of 2 sets of tone sequences with distinct temporal orders. Recordings taken from A1 and frequency/intensity response areas were reconstructed in detail to create cortical maps. Detailed maps were obtained from groups of ≥5 experimental and control rats at each postnatal benchmark age.</td>
<td>MEG data were averaged and filtered. Regions of interest were identified for each MEG, corresponding to regions around Heschl’s gyrus. Peak response amplitudes for CS+ and CS– were compared for trace and delay conditioning. Peak amplitude and latency of response were compared for paired CS+ and unpaired CS– in the left hemisphere. Position and orientation of regions of interest in paired CS+ and unpaired CS– were compared. Pupil diameter after delay and trance sessions was documented to verify that the stimulus parameters produced autonomic responses.</td>
<td>Exposure to specific complex acoustic stimulus in the early postnatal critical period resulted in large-scale remodeling of the A1 neuronal response selectivity. The tonotopic organization of A1 was changed so that responses to specific sound stimuli were elaborated and wakened to the representations of others. An unresponsive zone emerged between the cortical zones of representation of the hypothetically competitive low- and high-tone stimulus sequences. Neurons responded more reliably to the elements of these complex input sequences when they were delivered in the order that was applied in the exposure protocol. Changes endured into adulthood without significant change (even though sound stimuli were terminated at end of critical period).</td>
<td>Animal study limits generalizability. The study was not randomized.</td>
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Pantev et al. (2003) The objective was to examine the effects of music-induced cortical plasticity, specifically (1) effects of short-term laboratory training involving learning to perceive virtual instead of spectral pitch, (2) cross-modal plasticity when lips of trumpet players are stimulated at the same time as a trumpet tone, and (3) automatic encoding and discrimination of pitch contours and internal info are specifically enhanced in musicians compared with nonmusicians.

Level III
1 or 2 groups; nonrandomized:
- Group 1: 10 nonmusicians
- Group 2: 10 musicians (trumpeters), 3 women and 7 men age 26 (± 2.9), and 9 nonmusicians (3 women and 6 men age 25 ± 3.9).
- Group 3: Neural coding of melody—is it affected by training?
  12 musicians (8 women) and 12 nonmusicians (9 women) matched in age (20–40).

Musicians and nonmusicians learning short melody tones
Tactile and auditory stimuli were presented separately and together (bimodal).
Sequence of note melodies: Intervals were changed from trial to trial. Interval condition and standard stimuli condition consisted of the same 5-note melody. Magnetic MMN field was used to investigate the neural mechanisms for the automatic encoding of melodic features. Control stimulus was frequency deviation to single tone.

Plasticity can be induced through relatively short-term training. All participants demonstrated a sudden switch from spectral to virtual mode of pitch perception, indicating higher synchronization of the cortical networks. Plastic reorganization processes occurred.

Multimodal interaction was more pronounced in the musicians \( (p = .012) \) and significantly larger on the left \( (p = .037) \). Cross-modal musical training leads to remarkable modifications in cross-modal processing because of the behaviorally relevant somatosensory and auditory modalities and the increased use of these modalities during training.

In general, the magnetic MMN field was significantly larger in musicians than in nonmusicians (ANOVA \( p < .01 \) for both contour and interval conditions. Performance of musicians was better than that of nonmusicians. Findings support the hypothesis that musical experience leads to specific changes in the neural mechanisms for processing abstract melodic information and that long-term musical training enhances the processing of pitch between notes of melody.

Sample size was small. No measures of brain morphologic changes are associated with behavioral changes observed.

Ptito, Moesgaard, Gjeddel, & Kupers (2005) The objective was to examine the cerebral correlates of cross-modal plasticity using sensory substitution (where information acquired with 1 sensory modality is used to accomplish a task that is normally subserved by another sensory modality). Tactile stimuli were substituted on tongue for vision in congenitally blind and sighted blindfolded control participants.

Level II
2 groups: Congenitally blind \( (n = 6; \text{mean age} = 38; \text{all men}) \) and sighted blindfold \( (n = 5; \text{mean age} = 29; \text{2 men and 3 women}) \).

Behavioral training occurred over 7 consecutive days.
Participants learned to use the tongue display unit to detect the orientation of a Snellen pattern applied to the tongue. Laboratory setting with examiner
Outcome Measure
Cerebral blood flow in visual cortex area before and after training via positron emission tomography

After training, participants with blindness activated large areas of the occipital, parieto occipital, and occipitotemporal cortices, whereas control participants showed no activation of visual cortex. Control participants showed a significant deactivation of the visual cortex during orientation task, before and after training, possibly suggesting increased activity in somatosensory cortex to perform a tactile-based orientation task.

Small sample size and lack of randomization limit the study.
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<tr>
<td>Recanzone, Schreiner, &amp; Merzenich (1993)</td>
<td>This study is similar to study reported by Nakahara, Zhang, &amp; Merzenich (2004). Adult owl monkeys were used. The objective was to determine whether the tonotopic organization of the primary auditory cortex is altered as a result of training on an auditory frequency discrimination task.</td>
<td>Level II Group design 10 adult owl monkeys—5 trained, 5 not trained</td>
<td>5 monkeys were trained to detect a difference in the frequency of sequentially presented pairs of tones. Stimuli were delivered at pseudorandomized intervals.</td>
<td>The auditory frequency discrimination abilities of the 5 trained monkeys improved progressively with training. Improvements occurred in relatively short and steep phase (large improvements early on) followed by a longer period with smaller gains. Largest gains were in the initial 5 sessions.</td>
<td>Animal study limits generalizability. Study was not randomized.</td>
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<tr>
<td>Renier et al. (2005)</td>
<td>The objective was to investigate the neural substrates of depth perception when a device substituting vision with audition was used. Using PET, the authors examined whether 2-dimensional or 3-dimensional perception with sensory substitution device recruited similar brain areas as in vision.</td>
<td>Level III 1 group, nonrandomized 9 male volunteers (mean age = 29.4 ± 12 yr)</td>
<td>A training session was held to learn the system to locate and estimate the distance of an object. <strong>Outcome Measures</strong> PET scan</td>
<td>Activation in visual association areas during both the target search task and the depth perception task were found. The findings suggest that some brain areas of the visual cortex are relatively multimodal and may be recruited for depth perception by means of senses other than vision. The study supports brain plasticity in response to sensory based training.</td>
<td>No control group and no long-term testing limit generalizability.</td>
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<tr>
<td>Röder, Rösler, &amp; Neville (2000)</td>
<td>The objective was to determine whether blind people process language differently than sighted people.</td>
<td>Level II 2 groups 11 in each group; matched in age, gender, handedness, and education 6 men and 5 women congenitally blind (mean age = 35; range = 25–48). Mean age of sighted people = 35; range = 23–48.</td>
<td>Event-related potentials (N400) In language context, the N400 effect is a centroparietal-distributed negative wave that is sensitive to semantic and lexical processes.</td>
<td>N400 distribution was different in blind vs. sighted people, and the effect started earlier in blind people. N400 had a left-lateralized frontocentral scalp distribution in the sighted participants but a symmetric and broad topography in the blind participants.</td>
<td>Study was not randomized. Because this was a human study, findings are highly applicable.</td>
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<tr>
<td>Rosenzweig &amp; Bennett (1972)</td>
<td>The objective was to define environmental conditions that bring about cerebral differences (EC vs. IC), specifically to determine whether social grouping, or</td>
<td>Level I 6-group randomized study of rats IC = home cage; EC = enriched condition.</td>
<td><strong>Intervention</strong> 6 experimental conditions and 1 control group: 1. IC, saline injection 2. EC, saline injection, light exposure</td>
<td>Light is not needed to obtain results from EC, but rats in the light condition showed results in occipital cortex. The most significant increase in brain weight in EC was in rats</td>
<td>Animal study limits generalizability. Impossible to determine whether similar findings will be shown in social conditions with humans who are social beings.</td>
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exposure to EC during light or dark, were essential components.

Rosenzweig et al. (1969) The objective was to study the exact nature and extent of the differences in rat cortical structure and function when animals were exposed to enriched experiences and impoverished experiences.

Level I
- 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
- Blind analysis of results

Intervention
Training using perceptual auditory training software: Hearobics.

Setting: Laboratory

Dissection, weighing, and chemical analysis of brain

Rats exposed to EC developed significantly greater cortical tissue weight, total AChE activity, total ChE, and cortical depth. Results occurred as clearly in adult rats as in young rats.

Visual experience is not a necessary component of the conditions that evoke change.

Tissue weights and cortical size = significant differences between ECT and IC, with greatest difference in occipital cortex and the least for somesthetic cortex.

AChE activity greatest change (decrease) was in the occipital area.

ChE activity greatest change was in the occipital area.

ChE:AChE ratio (measure of glial cell) was greatest in the occipital region, although present in all regions. Cortical depths were greatest in occipital area in EC rats.

Animal study limits generalizability. Measures were only of brain, and the authors did not provide concurrent measures of behavior, so it is not possible to relate brain changes to behavioral changes.

Russo, Nicol, Zecker, Hayes, & Kraus (2005) The objective was to determine whether auditory training targeted to remediate perceptually

Level II
- 9 experimental participants diagnosed with a language-based learning problem

Intervention
Training using perceptual auditory training software: Hearobics.

Setting: Laboratory

Transient response did not demonstrate plasticity.

Sustained response increased significantly in the trained participants.

Lack of randomization is a concern. The authors did not test beyond 3 mo postraining; there is no way to know whether the findings persist long term.
Supplemental Table 1. Neuroscience Evidence That Using a Sensory-Based Approach in Occupational Therapy With Children and Adolescents Is Effective (cont.)

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<td>Schaefer, Heinze, &amp; Rotte (2005)</td>
<td>The objective was to test the hypothesis of top-down influence on frontal areas of the primary sensory cortex; that is, testing the hypothesis that prefrontal-cortical sensory gating is responsible for tactile maps in SI of the fingers during an activity.</td>
<td>Level III 1 group, 3 task conditions (Tower of Hanoi, control, rest) during imaging  ( N = 10 ) male volunteers ages 18–30, healthy.</td>
<td>MEG imaging of cortical representation of stimulated fingers (digits 1 and 5) during the 3 task conditions</td>
<td>Cortical areas of D1 and D5 were more distant during a task that required cognitive function (Tower of Hanoi) than the same motor task not requiring cognitive function. Authors concluded that frontal or prefrontal regions can facilitate neuronal responsiveness in the primary sensory cortex, depending on the task demand. Differences were seen between the digits, and future studies will be needed to examine other digits. Authors also suggested that this “short-term” neuroplasticity indicates that somatopic representations can be altered dynamically and in a task-specific manner.</td>
<td>Earlier reported findings of other investigators were not supported, and the current study did not explain these differences. Subject pool was small and not well described.</td>
</tr>
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Schapiro & Vukovich (1970) | The objective was to assess the effects of environmental stimulation on the development of rat cortical pyramidal cell | Level I Randomized selection of rats for experimental and control groups | Stimulation 3–5×/day from day of birth to Day 16. Stimulation = handling, stroking, shaking on a mechanical shaker. | Increased number of spines per micrometer in 8-day-old animals and increased number of neurons at 8–16 days | Animal study limits generalizability. In the absence of behavioral measures, it is not impossible to correlate... |
This study investigated the weighting of visual and proprioceptive feedback on production of motor response. In both studies, participants had visual feedback from reaching arm that disappeared once arm began to move.

**Level II**

There was a single group for each study, using control and experimental trials. Stimulation was passive. Unable to determine whether changes noted continue after stimulation.

Sober & Sabes (2005)

Experiment 1 ($n = 7$): 2 conditions of reach, 1 to a visual target, the other to a proprioceptive target identified as position of the left index finger (which had been passively positioned). 8 reaches to each of 6 targets, each with visual shift, to total 144 reaches.

Experiment 2 ($n = 10$): Investigation of information content of visual feedback; visual feedback representing arm and joint configuration or just location of fingertip. All reaches to visual target.

Not outcome measures; rather, results:

- **Experiment 1**: Brain weights, sensory feedback to minimize adverse effects of transforming arm position to reach target.
- **Experiment 2**: When feedback represents only fingertip position, movement is driven by proprioception; when feedback is whole arm, vision and proprioception contribute equally. Suggestion that this means that key difference between 2 conditions is information about configuration of joints.

During movement toward target, same sensory signals can be given different weightings at different stages of reach planning or at same stage of planning for different tasks. Thus, sensory integration for reach planning is dynamic and driven by task demands.

Integration of sensory information is determined not only entirely by features of sensory input but also by the computations required for task execution.

Experimental conditions are difficult to link to typical environments.
## Supplemental Table 1. Neuroscience Evidence That Using a Sensory-Based Approach in Occupational Therapy With Children and Adolescents Is Effective (cont.)

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<td>Stoeckel, Pollok, Schnitzler,</td>
<td>The objective was to study use-dependent plasticity of human somatosensory cortex.</td>
<td>Level I</td>
<td>Not an intervention study</td>
<td>Study 1: Participants using their feet for everyday activities had significantly fewer errors (6%) on the tactile localization test than the comparison group (1-tailed ( p = .003 )). Study 2: Activation in Study 1 of somatosensory cortex was significantly stronger in F2 participants (participants who used feet for everyday activities; ( p = .002–137 )).</td>
<td>Small experimental group size (F2: ( n = 3 )) may limit generalizability.</td>
</tr>
<tr>
<td>Write, &amp; Seitz (2004)</td>
<td>Study 1 was to determine any differences in accuracy of localization of tactile stimuli on toes between participants who (1) used feet to accomplish simple tasks, (2) used toes to accomplish everyday activities such as writing and eating, and (3) control participants. Study 2 was to determine any differences in somatosensory activation patterns to tactile stimuli on toes between the 3 groups.</td>
<td>3 groups randomized 23 thalidomide-affected participants with malformed upper extremities Mean age = 39.8 yr (range = 39–42). Setting Clinic-type environment</td>
<td>3 groups: 1. Used feet for certain actions only ((n = 10)) (F1). 2. Used feet extensively for everyday activities such as writing and eating ((n = 3)) (F2). 3. Control group: thalidomide-damaged extremities but normal hands; feet not used for any unusual actions ((n = 10)).</td>
<td>2 studies: 1. Tested accuracy of localization of tactile stimuli on toes; examined cortical representation between groups. • Threshold for detection of tactile stimuli on each toe determined • Threshold monofilament was chosen to evaluate localization for all toes. 2. Determined differences in activation of somatosensory area during tactile stimuli.</td>
<td></td>
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<td>vanPraag, Kempermann, &amp; Gage (1999)</td>
<td>This study separated aspects of enrichment to look at socialization, larger housing, physical activity, and forced activity-related learning in promoting hippocampal neurogenesis.</td>
<td>Level II 5 groups, ( n = 14 )/group; mice.</td>
<td>Cell proliferation increased in mice housed with unrestricted access to running wheel. Both runners and enriched mice showed increased survival of progeny neural cells. Researchers were able to rule out additional food or treats or social groupings in promotion of neurogenesis, although enriched showed better survival of new cells and potential long-term effects.</td>
<td>Groups: • Control subjects • Learners (daily training in water maze) • Swimmers (placed in water without specific task) • Runners (in cage with wheel) • Enriched (14 mice/cage, access to environmental toys). Outcome measures: Progenitor cell proliferation and survival of progeny.</td>
<td>Animal study limits generalizability.</td>
</tr>
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</table>

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### Volkmar & Greenough (1972)

The objective was to examine the differences in higher-order dendritic branching in visual cortical cells in young rats reared in 3 different environments.

**Level II**
- Enriched environment, standard environment, impoverished environment
- Animals ages 22–25 days

**Intervention**
- **EE:** 12/cage, wood, metal, and plastic toys changed daily, 30 min “free play” daily in another environment.
- **IE:** standard cages.
- **SE:** pairs in standard cages.

**Outcome Measure**
- Investigation of dendritic branching in 4 types of cortical cells.

**Profound differences in all 4 cell types.**

**Substantially greater higher-order dendritic branching in enriched environment condition than in impoverished environment condition.**

**Differences between SC and IC were less clear but still apparent.**

Data suggest that regulation of neuronal growth is through “use” related to the environment in which the animal is reared.

Animal study limits generalizability.

### West & Greenough (1972)

The objective was to examine whether rats reared in groups in complex environments have longer postsynaptic regions in the occipital lobe.

**Level I**
- 2-group randomized design matched for body weight
- Animals ages 0–40 days

**Intervention**
- **EC:** reared in groups with toys and play time; n = 12.
- **IC:** cage reared in isolation, n = 12.

**Measure**—after 35 days, rats were given 5 trials/day on a maze.

**Outcome Measures**
- Electron microscope used to analyze synaptic size in visual cortex. Synaptic bouton diameter and length of the postsynaptic thickening were analyzed.
- 23–51 synapses/animal were measured.

**EC group performed significantly better on the maze.**

**The length of the postsynaptic opaque region was significantly greater for the EC animals.**

There was a tendency for Type 1 synaptic boutons to be larger in EC animals, but it was not significant.

Animal study limits generalizability.

### 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.
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| Wu, van Gelderen, Hanakawa, Yaseen, & Cohen (2005) | The objective was to examine effects of somatosensory stimulation (by means of direct stimulation of nerve) on brain activation/excitability in the primary motor cortex, somatosensory cortex, and dorsal premotor cortex to determine whether this is a mechanism of neuroplasticity. | Level II 1 group, nonrandomized (n = 19) under 3 experimental conditions: (1) electrical stimulation of median nerve; (2) electrical stimulation of skin over deltoid; (3) no stimulation. Setting = laboratory | Intervention 2-hr electrical stimulation applied to median nerve at the wrist, to skin over deltoid, and no stimulation.  
Outcome Measures  
- fMRI  
- BOLD  
- Perfusion images of primary motor cortex, somatosensory cortex, and dorsal premotor cortex. | Brain activation is measured by the number of voxels activated.  
fMRI: There was an increase in number of voxels activated in primary motor cortex, somatosensory cortex, and dorsal premotor cortex after median nerve stimulation activated by performance of thumb movements for up to 60 min.  
Results suggest that median nerve stimulation can lead to an expansion of the thumb representation in somatosensory cortex—a form of plasticity that may underlie the influence of somatosensory stimulation on motor cortex function. | No control group and passive input limit generalizability.  
No behavioral measures included, so the reader is unable to determine whether brain changes are related to behavioral change.  
A strength is that the number of voxels activated was comparable across sessions using either fMRI, BOLD, or perfusion. |
| You et al. (2005)          | The objective was to determine whether virtual reality therapy would promote practice-dependent plasticity in a child with cerebral palsy, leading to enhanced motor skills and overcoming nonuse. | Level V Case report Single-subject study with pre- and posttesting Intervention conducted by therapist unaware of research. Participant 8-yr-old boy with hemiparetic cerebral palsy on right side | Intervention Virtual reality games that included bird-ball, conveyor, and soccer Intervention was 60 min/day, 5 day/wk, over 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 showed increased amount of use and quality of movement. Fugl-Meyer assessment score improved from 39 to 52, showing enhanced active movement control, reflect activity, and coordination in the upper extremity.  
fMRI showed a change in activation pattern such that preintervention activation involved bilateral primary motor and sensory cortices, sensorimotor cortex, and ipsilateral supplemental motor areas with no activation of the 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; use of isolated items from standardized assessment tools without substantiation of their ability to stand alone and intensity of intervention precludes its reimbursement potential.  
However, 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 game like (controlled sensory environment) can result in a combination of functional changes and neuroplastic changes in critical cortical regions. |
The objective was to examine structural and functional development of auditory cortex as modified by early environmental and learning experiences. Experimental and control conditions

Adult rats and rat pups were used to map primary auditory cortex.

Intervention

Experience exposure for pups and dams involved placement in sound-shielded and calibrated chamber for 10–16 hr/day, postnatal days 9–28 and exposure to a 25-ms monotone at 60–70 dB, at 6 pulses/s, with 1-s intervals. Tone frequency included 4 kHz and 19 kHz.

Outcome Measure

Auditory mapping in adults and immature rats

In adults, monotone presentation did not induce organizational changes. Changes in the organization of rat pup cortex appeared as both tone frequency-dependent effects (which argues for the important role of sound environment in early development) and tone frequency-independent effects (general degradation of tonotopic organization and response selectivity suggests that tonotopic development requires temporally patterned input). Differences exist between these findings and those in other sensory systems. Investigators concluded "acoustic environments are very important and potentially crucial in instructively defining the basic functional organization and processing capabilities of the auditory cortex" (p. 1128).

Laboratory situations and animal study limit generalizability.

Note.

AChE = acetylcholinesterase; ANOVA = analysis of variance; BOLD fMRI = blood-oxygen-level-dependent functional magnetic resonance imaging; ChE = cholinesterase; CS = conditioning stimulus; EC = enriched condition; ECT = enriched control with training; EE = enriched environment; EEG = electroencephalogram; EMG = electromyography; fMRI = functional magnetic resonance imaging; IC = impoverished condition; IE = impoverished environment; MEG = magnetoencephalography; MMN = mismatch negativity; MT–MST = medial temporal–medial temporal superior area, motion selective area; PET = positron emission tomography; SC = social control; SE = standard environment; SI = sensory integration; SII = secondary sensory cortex.

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