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Human Neural Plasticity

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Neuroscience research in slice preparations and animal models within the last decade has shown that neural plasticity is a ubiquitous mechanism by which the brain represents and encodes its dynamic sensory world. This workshop considered how dynamic sensory representations are modified by experience, new methods for imaging those representations in human subjects, and applications of human neural plasticity to human disability.

Brain Dynamics

The brain is constantly changing. Only partially myelinated and diffusely interconnected at birth, it matures into an exquisitely complex organ, finely tuned to deal with the conditions of its evolutionary niche through many precise sensory, cognitive, and motor pathways. Through learning and memory, mediated by synaptic plasticity, the mature brain adapts to the changing contingencies in its environment; through the effects of context and attention, mediated by excitatory and inhibitory interactions of entire brain areas, it selects the most relevant environmental inputs for detailed moment-to-moment processing[1]. Animal studies have increasingly shown that sensory maps such those found in primate primary visual cortex (V1)[2] or rat barrel cortex[3] are not static representations of sensory input but rather are dynamically modulated via lateral and feedback connections that convey information to the primary sensory zones about other stimuli and about task requirements. Indeed, neurons in primary sensory areas may perform several different functions, depending on where their input is coming from. Lamme and his colleagues have argued[4] that neurons in V1 function to encode stimuli during the feedforward sweep of processing, completed by 100 ms post-stimulus, and then function to inform visual awareness in response to feedback from other cortical areas, especially frontal cortical regions, during processing that continues for several hundred milliseconds. Consistent with this theory, Vincent Di Lollo (University of British Columbia, Canada) argued that several forms of backward masking in the human visual system involve interaction in visual cortex of feedforward processing of the target with feedback processing of the previously-presented mask. Several others of us presenters echoed this dynamic modulation message for auditory, somatosensory, and cross-modality systems, using modern brain imaging and split-brain techniques. In this view, maps in the primary sensory zones should be thought of as scaffolds upon which highly dynamic representations are constructed by a convergence of top-down and bottom-up inputs from other regions of the brain.

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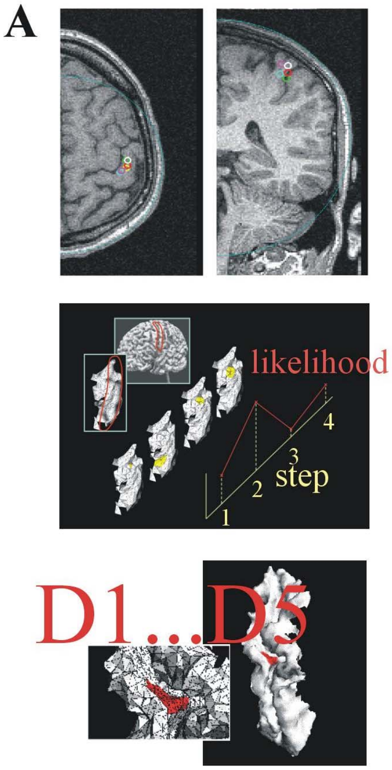
Effects of stimulus context and attention are rapid, implying tuning rather than modification of the scaffold for sensory processing. Such influences are themselves dependent on experience, which implies that while their expression may be rapid their establishment involves changes ranging from the level of synapses to sensory maps. But just how plastic *is* the scaffolding itself? Thomas Elbert (University of Konstanz, Germany) summarized some basic principles of cortical neural plasticity thus: (1) Disuse or deafferentation (via damage) leads to invasion of the unused cortical area by neurons from nearby areas; (2) Increased use leads to expansion of cortical representation; (3) Synchronous inputs lead to fusion of cortical zones representing those inputs; (4) Asynchronous inputs lead to segregation of cortical zones representing those inputs. The first principle was illustrated by evidence for cortical reorganization in humans who have been blind or deaf from birth. Josef Rauschecker (Georgetown University, USA) reported that, similarly to other animals, early visual deprivation leads to dramatic cortical reorganization in humans: occipital cortex (a visual area) of the early blind receives auditory input from inferior lobules of the parietal cortex (auditory spatial processing); there is a similar but smaller effect in the later blind. Franco Lepore (University of Montreal, Canada) showed that the blind are better at localizing sounds than are the sighted, presumably aided by additional auditory processing in occipital cortex. Robert Zatorre (McGill University, Canada) showed that the reverse happens for the early deaf: in such people the auditory cortex becomes responsive to visual input. Less dramatic experiences such as musical training can also alter sensory cortical maps, illustrating the second principle. Christo Pantev (Rotman Research



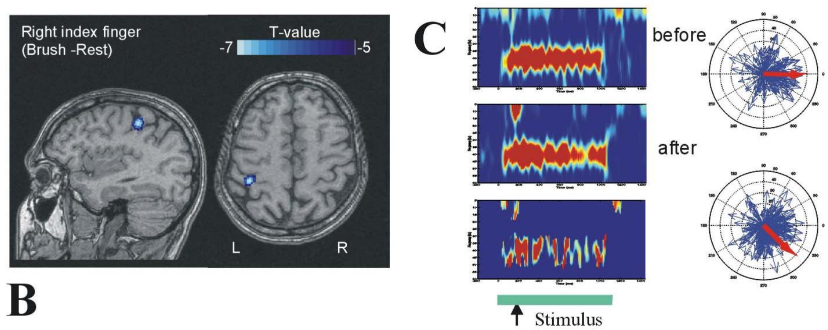


Figure 1. **A** (C. Braun). Top: Minimum residual variance dipole fits for digits of the right hand (MRI left hemisphere). Middle: Reconstructed area 3b shows four maximum likelihood fits for the 5th digit, the second of which is accepted. Bottom: Maximum likelihood fits for five digits showing extent of somatotopic map. The D1-D5 distance is sensitive to task context. **B** (D. Cheyne): Focal desynchronization in somatosensory cortex produced by brushing of the index finger of the right hand and detected by Synthetic Aperture Magnetometry. This activation is detected by spatial filtering of the continuous MEG record and is not time locked to a single stimulus. **C** (L. Roberts and D. Bosnyak). Left panels show EEG spectrum (5-60 Hz, 100 ms sliding sine/cosine window, bivariate r^2) before (top) and after (middle) 15 sessions of training at pitch discrimination using 40 Hz amplitude modulated pure tones of 1 sec duration (data from one subject). The third spectral plot (bottom) shows a bivariate r^2 of the before/after difference, revealing an augmented transient response (P2 component, 5-12 Hz, upper part of image) and a phasic, temporally patchy modulation of 40 Hz activity commencing about 30 ms after stimulus onset (lower part of image). Monte Carlo simulations indicate that r^2 shown in light blue to red are significant ($p<.01$). 40-Hz responses have been localized to Heschel's gyrus and reflect activity in the tonotopic map of primary auditory cortex. Right panels show sine/cosine plots (each vector a single trial) before (upper) and after (lower) training, at the time point indicated by the black arrow. For this subject the r^2 difference is reflected by a phase advance (red arrows, resultants) distributed in bursts throughout the stimulus period.

Institute and University of Toronto, Canada) showed that learning of melodies contained in missing fundamentals (virtual pitch) alters the response of the primary auditory cortex to the melodic stimuli. Laurel Trainor (McMaster University, Canada) and Larry Roberts (McMaster University, Canada) reported differences between the brain responses of musicians and nonmusicians to musical stimuli that correlated with effects of early training (before ten years of age)[5]; the brain responses of musicians resemble those induced by extensive training of adults on specific pitch discriminations. William Gaetz (McMaster University, Canada) talked about evidence gathered by the McMaster group for fusion/segregation of digit representations by multiple digit frequency discrimination, nicely illustrating the third and fourth principles.

New Methods

New techniques for the noninvasive measurement of sensory maps are extending the domain of research in human neural plasticity. Christoph Braun (University of Tuebingen, Germany) described morphometric studies in which somatotopy is represented for individual subjects by determining maximum likelihood fits of magnetic field patterns evoked by finger stimulation on the reconstructed surface of cortical area 3b. This method, illustrated in Figure 1A, permits a noninvasive measurement of the cortical distance between representations of the digits so that the dynamics of somatotopic maps can be studied under different task conditions. Braun used this technique to show that somatotopic representations are not statically fixed but are dynamically modulated by task requirements. Homuncular organization of the digits is segregated when subjects are required to detect the direction of motion of a tactile stimulus at a single digit compared to when they are required to detect the direction of motion of the same stimuli across the fingers. A different method, Synthetic Aperture Magnetometry (SAM), depicts areas of brain activation through the use of beamformers which can detect sources in unaveraged data by removing spatially correlated background activity[6]. Douglas Cheyne (CTF Systems and Simon Fraser University, Canada) presented SAM images processed from MEG data which revealed MRI-coregistered focal activations in somatosensory cortex produced by passive stroking of the fingers. Figure 1B illustrates the precise, high quality images obtained with this technique. Larry Roberts (McMaster University, Canada) and Daniel Bosnyak (McMaster University, Canada) described a different approach to measuring sensory representations. They use 40-Hz amplitude-modulated tones differing in carrier frequency in their studies of pitch discrimination in human subjects.

Combined with suitable signal processing, this approach separates components of the auditory evoked potential (or magnetic field) whose cortical sources are known to differ based on MEG studies. This method is illustrated for a single subject in Figure 1C, where the low frequency response (5-12 Hz) represents distributed neural activity incorporating the parabelt regions of the auditory cortex, whereas the 40 Hz activation is focused principally in Heschel's gyrus where the tonotopic map of primary auditory cortex is found. Discrimination training produces a patchy modulation of the tonotopic map that can be expressed in the number of neurons firing (amplitude) as well as in their temporal response properties (phase). Terence Picton (Rotman Research Institute and University of Toronto, Canada) described how distortion products generated by presenting multimodal stimuli amplitude-modulated at different repetition rates can identify neural sites where information converges within the cortical processing stream. All of these new methods enhance noninvasive measurement of the dynamic properties of the human brain and allow visualization of how these dynamic properties vary with experience and task conditions.

Neurorehabilitation Medicine

Augmented ability on a spared modality when a different modality is deprived, such as better sound localization in the early blind, is one example of the possible benefits of neural plasticity, albeit unintentional. An example of intentional benefit is the emerging field of neurorehabilitation medicine. In line with his principles of neural plasticity, Thomas Elbert presented evidence that primary auditory and somatosensory cortical fields can be dramatically affected by operant and instrumental conditioning. He demonstrated successful behavioral therapy for focal hand dystonia in musicians[7] (overuse causes inability to precisely control finger movements), and discussed its potential for extension to the notoriously difficult syndromes of phantom limb pain in amputees and tinnitus (ringing in the ears). His therapeutic approach has been based on Constraint-Induced therapy, developed originally by Edward Taub, in which highly-motivated patients are forced to use an impaired system intensively. It has been successful in relieving stroke-induced conditions like hemiplegia[8] (paralysis of one side of body) and aphasia (impaired speech) when there exists some residual function. Possibilities for neurorehabilitation, as well as implications of neural plasticity for pedagogy, proved to be especially popular at a 2-hour plus public forum that was organized by Harold Weinberg (Simon Fraser University, Canada) as part of the workshop. Attended by nearly 200 people, the lively and rewarding forum discussion was a poignant reminder to the scientists from the workshop of the real faces behind the brain images purchased with their research dollars.

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