

Cortical Plasticity: Learning from Cortical Reorganisation

Dispatch

Jan W.H. Schnupp and Oliver Kacelnik

Neocortical circuits can undergo dynamic rearrangements, not only in response to injury, but also when new skills are acquired. But although training can lead to functional rewiring of the cortex, we are far from being able to reprogram an animal by manipulating its cortical circuitry directly.

Mammals are distinguished from other vertebrate species by their more highly developed cerebral cortex and by their larger, more complex and more versatile behavioural repertoire. The primary function of the cortex may be to mediate complex behaviours, and to facilitate adaptive changes in behaviour brought about by changes in the circumstances in which an animal lives. This notion gains support from the observation — made about a decade ago — that it is possible to induce cortical reorganisation simply by training an animal on a new task [1–5].

Primary sensory cortical areas are organised in a ‘topographic’ fashion. For example, neurons in the most lateral parts of the somatosensory cortex respond to tactile stimuli applied to the head, while more medial parts respond to stimulation of progressively more caudal parts of the body. Similarly, the sound frequency preferences of neurons in the primary auditory cortex vary systematically along a frequency axis, the orientation of which varies from species to species. Studies by Recanzone *et al.* [1,2] and by Weinberger and colleagues [3–6] demonstrated that the precise topographic organisation of these sensory fields is amenable to modification when an animal is trained to perform a specific task.

These pioneering studies used classical conditioning, with either reward or punishment, to train animals on a variety of tasks, including the detection of pure tone sounds of a particular frequency and the discrimination of tones or vibrating tactile stimuli of slightly different frequencies. When the primary somatosensory [1] or auditory [2,3,5,6] cortex of the trained animals was subsequently mapped with microelectrode recordings, it was found that the region of cortex representing the sound frequency bands stimulated in the auditory tasks, or the parts of the forepaw stimulated in the tactile task, had expanded, presumably at the cost of the representation of adjacent sound frequencies or body parts.

At about the same time, researchers became aware that changes in the topographic organisation of cortical areas can also be achieved by artificial electrical stimulation techniques, including intracortical microstimulation [7–10] (Figure 1) or stimulation of the nucleus

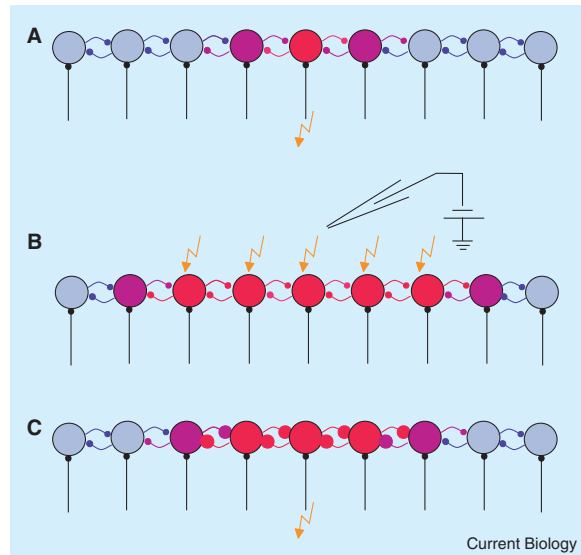


Figure 1. Likely mechanism of cortical reorganisation through intracortical microstimulation. Cortical neurons (filled circles) receive excitatory input from thalamic afferents (black) and from interconnections between neurons. (A) Thalamic afferents to primary sensory areas maintain the topographic order seen in the receptor surfaces. Stimulation of single frequency band produces a localised discharge in the thalamic afferents (lightning symbol). This causes a localised activation of cortical neurons (red), which spreads to some extent to neighbouring neurons (purple). (B) During intracortical microstimulation, electric current pulses are delivered to a patch of cortex through a stimulating electrode for several hours. This causes synchronised discharges over a relatively wide stretch of cortical neurons, leading to a strengthening of their excitatory interconnections (Hebb's rule). (C) Lateral connections between neurons subjected to intracortical microstimulation are strengthened (symbolised by thicker lines connecting these neurons). This allows a greater lateral spread of thalamic input. The cortical area activated by the input has expanded.

basalis [5,11,12]. These techniques can both lead to changes in cortical topography, in some respects resembling those seen after training in specific sensory tasks. Most notably, intracortical microstimulation and stimulation of the nucleus basalis can both increase the size of the cortical region that appears to be responsive to a particular set of stimuli. Consequently, some authors have proposed that intracortical microstimulation or nucleus basalis stimulation may serve as a useful experimental model of ‘representational plasticity’ in sensory cortex.

A recent study by Talwar and Gerstein [8], however, shows that the parallels between training-related and artificially induced cortical plasticity extend only so far. The reasoning behind their experiments was as follows. We know that extensive training in a frequency discrimination task leads to better discrimination ability and an expansion of the cortical area responsive to the frequencies used during training. If the expansion of the cortical area is indeed responsible

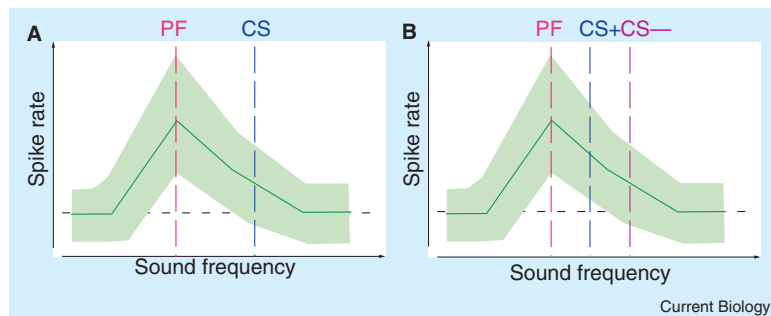


Figure 2.

Solving detection and discrimination tasks on the basis of neural responses. Tuning curves of an auditory neuron are shown schematically. The mean discharge rate of a neuron depends on the stimulus frequency (green line) and is highest for the neuron's 'preferred' frequency (PF). But neural responses are 'noisy', so the observed response may lie at some distance from the mean response rate given by the tuning curve (green shaded area). In the absence of an appropriate stimulus, the neuron's firing rate fluctuates randomly around a low resting

rate (black stippled line). (A) A 'conditioned stimulus' (CS) frequency cannot be detected reliably if the range of likely responses — intersection of blue stippled line and green shaded area — overlaps considerably with the likely background rate. The neuron can minimise this overlap by shifting its tuning curve to bring PF closer to CS. (B) To improve the discrimination of two different frequencies, CS+ and CS−, it is necessary to reduce the overlap in the range of responses to the respective stimuli. Shifting the tuning curve may do little to reduce that overlap, but increasing the slope — 'narrowing' the tuning curve — can make the responses elicited by CS+ and CS− more discriminable.

for the improved performance, then it should perhaps also be possible to achieve improved performance through intracortical microstimulation instead of training. Talwar and Gerstein's results, however, show that this is clearly not the case: training and intracortical microstimulation may both induce 'representational plasticity', but while training improves performance, intracortical microstimulation does not.

Talwar and Gerstein [8] suggest that intracortical microstimulation may fail to produce performance improvements because, unlike training stimuli, it is delivered without any 'behavioural context'. They predict that cortical plasticity induced by nucleus basalis stimulation "may also, ultimately, be behaviourally irrelevant". This explanation may well be correct, but the notion of 'behavioural context' is rather vague, making it difficult to develop testable hypotheses about how this context is manifest in the neural circuitry and how it might determine cortical information processing efficiency. It might therefore be fruitful to compare the effects of intracortical microstimulation, nucleus basalis stimulation and classical conditioning in greater detail, and to consider them in the context of the 'computational constraints' imposed by a particular task. While these techniques have in common that they can lead to a reorganisation of cortical topography, there also appear to be important differences in their effects on other neural response characteristics. Considering these differences further may provide important clues as to why some techniques are more likely to result in performance changes than others.

To understand this point, it may be instructive to consider two different studies in which improved performance was induced by classical conditioning, but where the tasks to be learned were somewhat different. In a study by Weinberger and Bakin [5], guinea pigs were trained to associate the presentation of a particular pure tone frequency with a mild but unpleasant electric shock delivered to the paw. After a period of training, the animals learned to avoid the shock by withdrawing their paw whenever the conditioned sound frequency was presented. Subsequent electrophysiological examination indicated that neurons

originally tuned to frequencies on either side of the conditioned frequency had shifted their tuning curves toward the conditioned frequency. But the sharpness of tuning appeared to be largely unaltered [5]; the neurons also showed stronger responses on average — they fired more action potentials — when presented with the conditioned stimulus. These changes are broadly what one might expect: the shift of frequency tuning means that more cells in cortex are available to signal the presence of the conditioned stimulus, and the increased discharge rate ensures that this signal is sent loud and clear.

Compare these results with the effects of frequency discrimination training reported by Recanzone *et al.* [2]. In these studies, owl monkeys were trained to discriminate a target frequency from slightly different frequencies. For correct target detection, the animal received a food reward, but for an incorrect response (a 'false alarm') the animal was 'punished' with a timeout — testing was suspended for a short while and the animal had to wait before it would be given the opportunity to try for another reward. Recanzone *et al.* [2] also observed a shift in neural tuning curves, but unlike Weinberger and Bakin [5] they found a sharpening of frequency tuning. Again, this reported sharpening may serve a purpose: it may make responses to the conditioned target frequency more distinguishable from responses to adjacent frequencies. This may help reduce the false alarm rate (compare Figure 2), allowing the animal to maximize the food rewards it can obtain. In the detection tasks used by Weinberger and Bakin [5], the animal had no incentive to avoid false alarms, which may explain why a sharpening of neural tuning was not reported.

Talwar and Gerstein's experiments [8] involved testing the animals in a frequency discrimination task not unlike the one used by Recanzone *et al.* [2]. But their data suggest that intracortical microstimulation may have led to a broadening of frequency tuning in neurons near the microstimulation site, so in this important respect the effect of intracortical microstimulation may well be the opposite of that produced by training in a frequency discrimination task. It would be interesting to know whether intracortical microstimulation

might have any lasting effect on performance in simple detection tasks, where the sharpness of neural tuning curves is likely to be less important.

In contrast to intracortical microstimulation, nucleus basalis stimulation can have different effects on the sharpness of neural frequency tuning, depending on what type of auditory stimulation is paired with stimulation of the nucleus basalis [13]. Whether nucleus basalis stimulation will also appear to be 'ultimately behaviourally irrelevant' may well depend on how appropriate the modification of cortical response properties induced by nucleus basalis stimulation turns out to be for the particular perceptual or behavioural task under study. In principle it should be possible to use mathematical techniques like optimal observer analysis [14,15] to derive testable, quantitative predictions of how shifts, broadening or narrowing of neural tuning curves or changes in neural sensitivity, spike count or response variance are likely to influence performance in different perceptual tasks.

It may not be sufficient to consider only changes in neural response properties manifested as spike count or firing rate. Putative temporal codes must also be considered. For example, Recanzone *et al.* [2] noted that frequency discrimination training led to increased response latencies in primary auditory cortex. Given the increasing evidence that response latency may be an important coding parameter in sensory systems [16,17] these observations on response latencies may be important. In contrast, Kilgard and colleagues [13] reported that the effect of nucleus basalis stimulation on auditory response latencies is, like frequency tuning width, dependent on the type of auditory stimuli paired with nucleus basalis stimulation. The effect of intracortical microstimulation on response latencies is less clear. Dinse *et al.* [7] reported increased synchronisation of activity and increased response latencies after intracortical microstimulation in somatosensory cortex. Talwar and Gerstein [8] did not report any effects of intracortical microstimulation on response latency, but did point out they observed systematic relationships between response latency and properties of the stimulus only in the anaesthetised, not in the awake animal. That observation would appear to argue against a role of latency as a coding parameter.

Few would argue nowadays that there is not a relationship between improvement in a given perceptual learning task and cortical reorganisation, but it is increasingly clear that a deeper understanding of that relationship can be achieved only through deeper understanding of the neural coding and processing strategies employed by the sensory cortical networks under study.

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