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Learning without Training

Review

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Achieving high-level skills is generally considered to require intense training, which is thought to optimally engage neuronal plasticity mechanisms. Recent work, however, suggests that intensive training may not be necessary for skill learning. Skills can be effectively acquired by a complementary approach in which the learning occurs in response to mere exposure to repetitive sensory stimulation. Such training-independent sensory learning induces lasting changes in perception and goal-directed behaviour in humans, without any explicit task training. We suggest that the effectiveness of this form of learning in different sensory domains stems from the fact that the stimulation protocols used are optimized to alter synaptic transmission and efficacy. While this approach directly links behavioural research in humans with studies on cellular plasticity, other approaches show that learning can occur even in the absence of an actual stimulus. These include learning through imagery or feedback-induced cortical activation, resulting in learning without task training. All these approaches challenge our understanding of the mechanisms that mediate learning. Apparently, humans can learn under conditions thought to be impossible a few years ago. Although the underlying mechanisms are far from being understood, training-independent sensory learning opens novel possibilities for applications aimed at augmenting human cognition.

Introduction

It is an old adage that practice makes perfect, and daily experiences provide ample evidence for this wise principle. For example, intense practicing for tens of thousands of hours is required to develop the musical skills typically observed in professional musicians or to exhibit expert performance in sports. The use of non-invasive imaging techniques has enabled investigation of the impact of such intense practice and training at functional and neuroanatomical levels [1–8]. As a result, a large number of researchers in neuroscience are now examining the brain changes evoked by training and practice in order to understand the underlying learning mechanisms.

It is generally agreed that processes allowing modification of synaptic efficacy are the neural substrates for learning. Studies on synaptic plasticity use temporally specific stimulation protocols to induce long-lasting changes in synaptic transmission, but the implications of this requirement for temporally specific protocols in everyday learning remain unclear [9–13]. For example, for training- and practice-based learning to occur, sensory inputs are modified in their frequency, temporal pattern, the number of stimuli and their duration, form, size and intensity. But it is difficult to exactly quantify the changes in different input parameters that occur during training. Therefore, linking the principles of synaptic learning that induce plasticity at the cellular level to the principles at the systems level is far from straightforward.

This limitation can be overcome by what we shall refer to here as 'training-independent sensory learning'. Numerous investigations have demonstrated that human perception and behaviour can change without training, simply via exposure to sensory stimulation protocols for a few minutes to a few hours [10–20]. All these investigations have taken the approach of directly influencing human perception and behaviour by using stimulation protocols known to induce plastic changes at the cellular level [10–13,21]. The idea is to translate protocols that induce plasticity at a cellular level into sensory stimulation protocols (Figure 1).

As discussed below, recent data have suggested that even sensory stimulation may be dispensable for the induction of plasticity in perceptual processes [5,22,23]; these data challenge our understanding of plasticity and learning.

Rationales for Training-independent Sensory Learning

Persistent changes in synaptic transmission underlie plasticity and learning. From cellular studies, long-term potentiation (LTP) and long-term depression (LTD) of synaptic transmission are the leading candidates for being the relevant activity-dependent changes in synaptic connection strength [24–28]. Typically, high-frequency stimulation (10 Hz or higher) is used to induce LTP in brain slices, whereas LTD can be reliably evoked by low-frequency stimulation of around 1 Hz [27] (Figure 2A).

However, the lack of adequate input stimuli for the induction of LTP and LTD in humans has hindered direct evaluation of the impact of such protocols on human behaviour. The basic principle underlying training-independent sensory learning is to use our broad knowledge of brain plasticity to design specific stimulation protocols that allow us to change brain organization and, thus, perception and behaviour [10]. Training-independent sensory learning has the unique advantage of offering complete control of the timing and spatiotemporal allocation of the stimulation. Thus, training-independent sensory learning is not only an ideal tool for applying known protocols to humans to assess whether such protocols can affect human perception and behaviour, but also a means to systematically determine the appropriate timing for the induction of perceptual and cortical changes in humans.

In addition to LTP/LTD mechanisms, spike-timing-dependent plasticity (STDP) mechanisms have attracted much interest over the last few years. STDP assumes that there are narrow and cell-type-specific temporal windows for synaptic modification induced by the correlated spiking of pre-synaptic and post-synaptic neurons, depending on the temporal order of spiking [29–32]. The principle features of STDP are illustrated in Figure 2B [33], where the y-axis denotes the onset of spiking activity in the post-synaptic neuron. LTP effects are induced when pre-synaptic spikes are emitted before the post-synaptic neuron starts to spike, and LTD effects are induced when pre-synaptic spikes are emitted after the post-synaptic neuron starts to spike. The strength of the LTP and LTD effects depends on the proximity in time of pre-synaptic neuron activity to that of the post-synaptic neuron.

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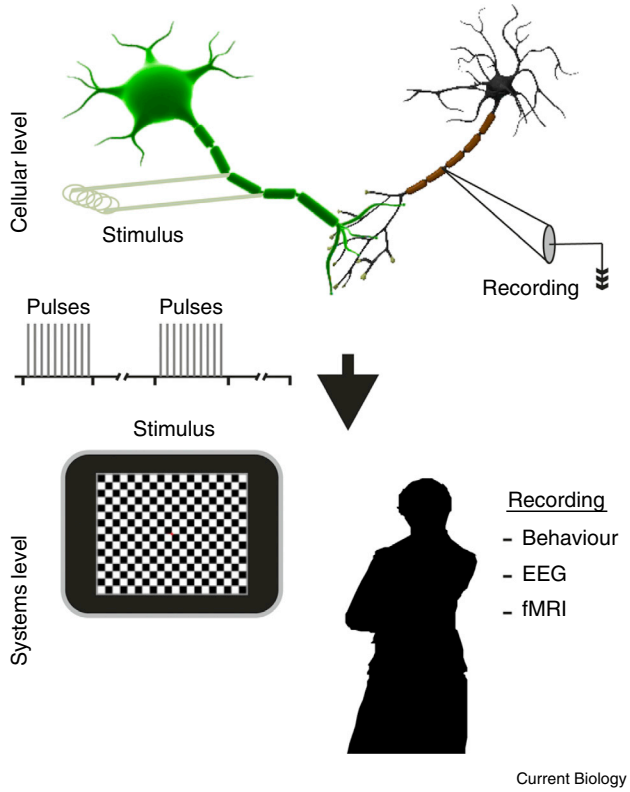

Figure 1. Idea of training-independent sensory learning.

Protocols that can induce plasticity at a cellular level (top) are translated into sensory stimulation procedures (bottom). See text for details.

Although the significance of STDP mechanisms in network formation and in coding of temporal sequence patterns has been recognized (compare [34]), the implementation of STDP principles in sensory stimulation experiments to explore effects of STDP on human behaviour is difficult because of the problem of assigning a temporal order to sensory inputs. One recent study [35], however, used repetitive asynchronous pairing of stimuli and reported a systematic shift in the bias in face-identity perception in humans, opening up a fascinating method for influencing human perception by using predictions of STDP.

Terminology

The concept of sensory stimulation protocols to induce learning has attracted substantial interest and is currently being investigated in many laboratories as a means to drive learning and plasticity. One problem with the field is that different laboratories are using different terms to refer processes that are essentially comparable, such as 'peripheral nerve stimulation' [36], 'somatosensory stimulation' [37], 'exposure-based learning' [11,15,17], 'co-activation' [16,18,19,38], 'unattended-based learning' [21], 'repetitive sensory stimulation' [10,39,40] and 'high-frequency stimulation' [20]. The term 'co-activation' has been introduced for experiments that use a Hebbian stimulation approach [41]; in this case, the simultaneous tactile 'co-stimulation' of the skin is used to generate synchronous neural activity, which, according to Hebbian theory, is instrumental to drive plastic changes. The term 'repetitive sensory stimulation' is often used for protocols that are independent of spatial cooperativity and use frequency and temporal patterning of stimulation. Other laboratories studying training-independent sensory learning use the framework of 'tetanic' stimulation, which is commonly used in synaptic plasticity research [13,42], or use the term 'stimulus-selective response plasticity' [12]. More recently, the term 'exposure-based learning' has been introduced to contrast feedback-induced learning with that generated by training via 'exposure' to stimuli [43].

There is also some confusion about the term 'passive stimulation': in the context of repetitive sensory stimulation experiments, this term indicates that a subject is exposed to sensory stimuli without attending actively to the stimulation, whereas in the framework of task-relevant training-based perceptual learning, 'passive stimulation' is regarded as stimulation insufficient to drive learning processes. These examples indicate an obvious need for harmonization and standardization of terms used to characterize different forms of learning induction. Throughout this review we use the term 'training-independent sensory learning' for learning induced by applying synaptic plasticity protocols in human participants with the aim of changing perception and behaviour.

In the following sections, we discuss recent findings which demonstrate the feasibility and effectiveness of training-independent sensory learning approaches in the tactile, visual, and auditory domain, as well as other, distinct approaches used in attempts to alter perception with or without exposure to sensory stimuli, but without task training. In order to maintain focus, we have not covered the wide field of implicit and incidental learning in which participants learn about hidden input statistics or the field of transcranial magnetic stimulation in this review. Instead, we have referred to comprehensive reviews on these topics [44,45].

Training-independent Sensory Learning in Different Sensory Modalities

Tactile Modality

In the 'co-activation' stimulation protocol, the fingertip is repeatedly stimulated, either cutaneously or electrically, for many minutes to hours in order to induce plasticity in the corresponding primary and secondary somatosensory cortices [18,19,38]. Co-activation closely follows the idea of Hebbian learning: synchronous neural activity is generated by simultaneous tactile 'co-stimulation' of a large number of receptive fields (Figure 3A). Because of the induced plasticity, tactile perception at the stimulated skin sites is altered. Spatial tactile discrimination, 'tactile acuity', is often assessed as a simple measure of changes in tactile perception abilities. In a typical co-activation experiment, two-point discrimination thresholds are lowered, indicating improved tactile acuity, which reaches baseline levels after 24 hours [38]. This co-activation-induced improvement does not transfer to fingers of the unstimulated hand, and there is no (or only weak) transfer to the neighbouring fingers of the stimulated hand.

The relation between learning-induced changes in behaviour and individual changes in brain organization has been studied using a combination of psychophysical tests and non-invasive imaging. Neuroimaging and electric source localization by multi-channel electroencephalography (EEG) showed that co-activation led to an increase in the size of the cortical representation specific to the co-activated finger [18,19], which can be regarded as a recruitment of processing resources. The changes observed in cortical map representation were found to be linearly related to the

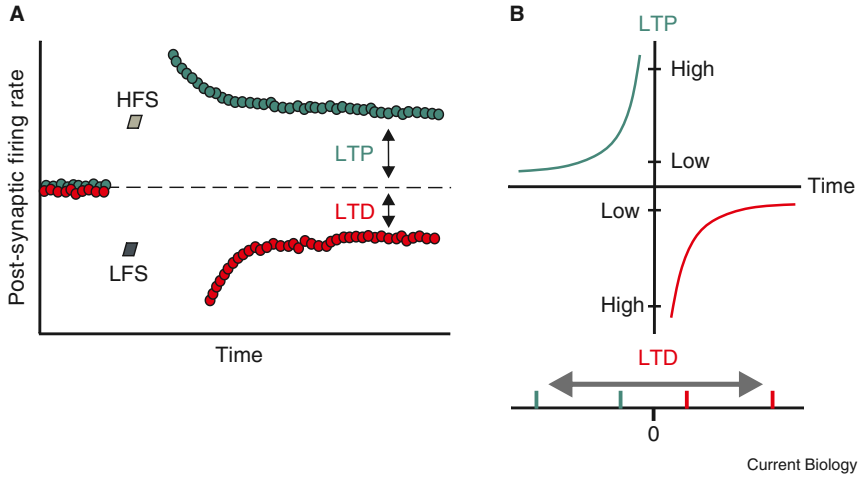

Figure 2. Principles for inducing plasticity.

(A) Long-term potentiation (LTP) is induced using high-frequency stimulation (HFS) and leads to increases in post-synaptic firing rate. Opposed to this long-term depression (LTD) is induced using low-frequency stimulation (LFS) and leads to decreases in post-synaptic firing rate. (B) The principles underlying spike-time-dependent plasticity (STDP). If spiking in the pre-synaptic neuron occurs closely to activity of the post-synaptic neuron, LTP and LTD effects are strong. When the time difference in pre-synaptic neuron spikes and activity of the post-synaptic neuron is more, the LTP or LTD effect is weaker. LTP and LTD effects depend on whether the presynaptic neuron fires before or after the post-synaptic neuron.

degree of improvement in two-point discrimination thresholds. Accordingly, a large gain in spatial discrimination abilities was associated with large changes in cortical maps [18,19].

A similar result was obtained for changes in cortical excitability. Cellular studies have shown that increased excitability is a typical signature of effective LTP induction. In humans, so-called 'paired-pulse stimulation', the application of two stimuli in close succession, provides a reliable marker of excitability: the paired-pulse behaviour is characterized by a significant suppression of the second response at short inter-stimulus intervals. Paired-pulse suppression was reduced after co-activation, and the amount of suppression was positively correlated with the individual gain in performance [46]. Taken together, these data show that training-independent sensory learning results in selective reorganization in the primary somatosensory cortical areas. These observations also suggest the important idea that the effect size differences typically observed across individuals reflect true differences in individual brain reorganization.

To demonstrate the Hebbian nature of the co-activation protocol, the effects of co-activation were compared to those of a so-called 'single-site stimulation', where only a small 'point-like' skin area was stimulated. Stimulating the finger at a single site did not induce changes in discrimination performance or brain activity [19]. This indicates a lack of brain reorganization and suggests that it is unlikely that other tasks beyond discrimination might have benefitted from single-site stimulation. These results imply that a Hebbian 'co-activation' is crucial for the induction of plasticity effects and point to the requirement of spatial cooperative processes. Furthermore, the data emphasize that not all types of sensory stimulation can lead to perceptual changes, and that there are 'simple' forms of stimulation that remain ineffective in driving plasticity.

As outlined above, LTP and LTD are activity-dependent changes in the strength of synaptic connections which are leading candidate mechanisms of neuronal plasticity [26–28]. Therefore, we explored the efficacy of *in vitro* stimulation protocols in driving perceptual changes by applying high-frequency and low-frequency stimulation (Figure 3B). High-frequency stimulation consisted of cutaneous pulse trains applied to the tip of the right index finger with a stimulation frequency of 20 Hz. Each train consisted of 20 single pulses of 20 Hz lasting one second with an inter-train interval of five seconds. Low-frequency stimulation was applied at 1 Hz with stimulus trains consisting of 1200 pulses (Figure 3B). We found that 20 minutes of high-frequency stimulation induced a lowering of tactile discrimination thresholds, whereas low-frequency stimulation resulted in an impaired discrimination performance. Most interestingly, 24 hours after high-frequency stimulation, we found that spatial two-point discrimination thresholds were still lower than the baseline values. In contrast, 24 hours after low-frequency stimulation, the discrimination thresholds had recovered to the baseline values [20]. These results indicate that brief stimulation protocols resembling those used in cellular LTP and LTD studies can induce meaningful and persistent alterations in tactile discrimination behaviour of humans.

Cellular studies have implicated the *N*-methyl-D-aspartate (NMDA) receptor as a major player in synaptic plasticity. A possible dependency of exposure-based learning on NMDA receptor activation was directly tested in humans using memantine, a substance that blocks NMDA receptors selectively [16]. It was found that a single dose of memantine eliminated learning, both psychophysically and cortically (Figure 3C), providing strong evidence of NMDA receptor involvement in training-independent sensory learning. Importantly, this finding implied that training-independent sensory learning is a plasticity-based process, which was debatable at that time.

While many drugs block learning, a few drugs are known to enhance cortical plasticity. *In vitro* experiments have shown that alterations in synaptic efficacy can be modulated by adrenergic agents, which gate synaptic plasticity. In fact, a single dose of amphetamine [16] resulted in almost a two-fold increase in both the normally observed improvement of tactile acuity and the cortical reorganization. These findings indicate that the processes underlying repetitive stimulation are further controlled by neuromodulatory systems (compare [47] for cellular data and modelling).

In summary, the data from tactile training-independent sensory learning experiments have demonstrated the following. First, tactile perception can be bi-directionally altered by protocols that present stimuli at a pace resembling that of protocols used to induce LTP and LTD at a cellular level. Second, changes in tactile perception are paralleled by alterations in cortical maps, cortical activation and cortical excitability in the primary somatosensory cortex,

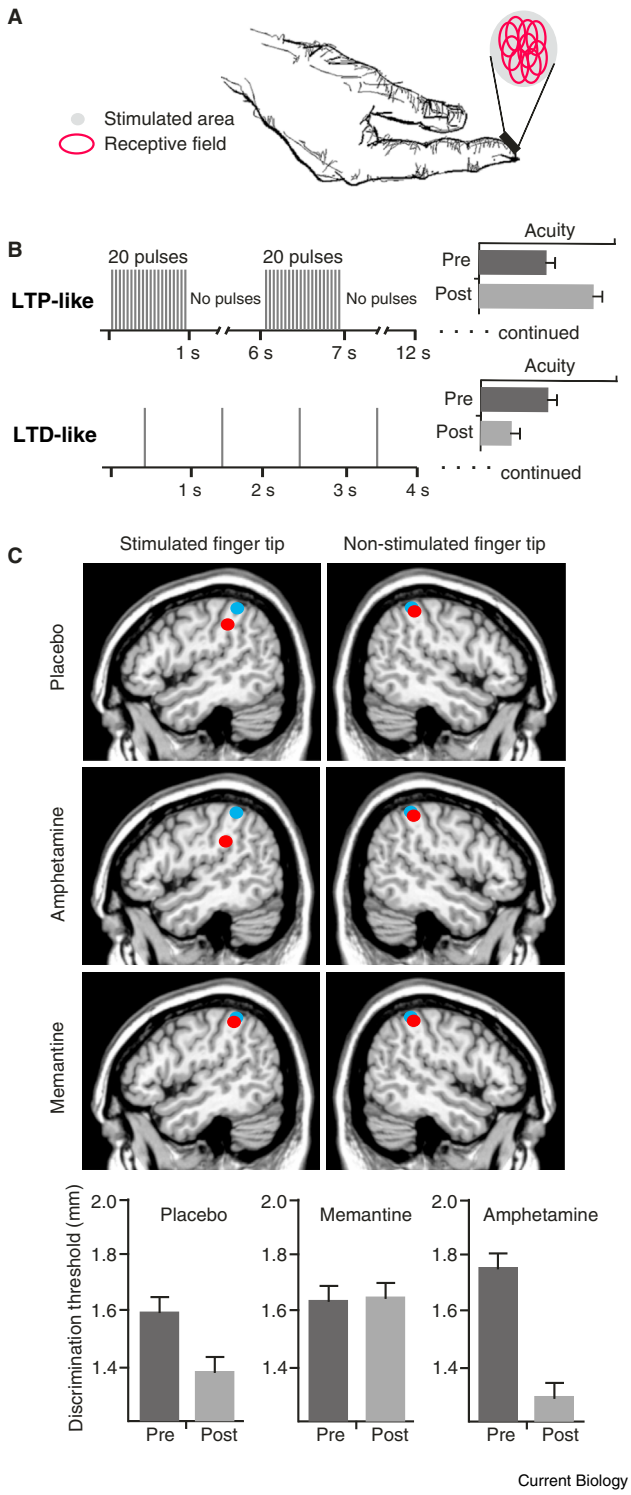

Figure 3. Training-independent sensory learning in the tactile modality.

(A) Schematic representation of a stimulation device placed on the top of an index finger. The red circles denote the different receptive fields that were stimulated in the area underneath the stimulation patch. (B) Depiction of LTP- and LTD-like stimulation protocols, together with their effects on tactile two-point discrimination threshold. Acuity thresholds are lowered after LTP-like stimulation, but increased after LTD-like stimulation. (C) Results of pharmacological manipulation using memantine (NMDA-R blocker) and amphetamine on tactile-discrimination performance, together with changes in the cortical representation of the stimulated finger in somatosensory cortex [16].

which points to a susceptibility of early cortical processing stages. Third, cortical changes correlate with the individual change in perception, suggesting a causal role of cortical changes in mediating perception. And fourth, perceptual and cortical changes depend on NMDA receptor activation and can be potentiated by application of amphetamine, indicating involvement of neuromodulatory systems.

Visual Modality

In contrast to the numerous studies that have been done on training-independent sensory learning in the tactile domain, fewer studies have looked at training-independent sensory learning in the visual domain. Animal studies provided the first evidence that the visual cortex (V1) undergoes plastic changes following pure exposure: repeated presentations of grating stimuli with a single orientation resulted in a persistent enhancement of responses evoked by these stimuli [48]. Conversely, perceptual learning has been shown to induce LTP in the visual cortex of rats, and to enhance cortical excitability in humans [49,50]. A study on humans found that visual sensory stimulation with checkerboard patterns at 9 Hz for a few minutes resulted in changes in early processing in the visual cortex, as indicated by an amplitude enhancement of the N1 event-related potential (ERP) component of the visual evoked potential [51]. Similarly, a functional magnetic resonance imaging (fMRI) study found an increase in hemodynamic responses in the extrastriate visual cortex after brief periods of 9 Hz checkerboard stimulation [42]. While these data show that visual cortical processing is modifiable, direct evidence for the induction of perceptual changes by LTP-like protocols has been lacking. Interestingly, however, a recent paper [52] suggested that perceptual learning has many features that are typical of LTP, such as the requirement of a minimal number of trials or the hindrance of learning by the interleaved presentation of more than one stimulus type.

Beste *et al.* [11] modified visual stimulation protocols that had been shown to be effective at the cellular level to modify visual perception in humans. In this study, we used a paradigm that resembles a change-detection task [53], in which two bars that were either darker or brighter than the background were presented to subjects who had to report luminance changes was employed (Figure 4A). Four different types of change were possible in this task: on the left or right side of a fixation cross, changes could be made to either the luminance or the orientation of a single bar; both the luminance and orientation of one bar (luminance-orientation unilateral, LOU); or the luminance and orientation of the two bars (luminance-orientation bilateral, LOB). In the last condition, the occurrence of the change in orientation induced a highly salient apparent motion; the simultaneous change in luminance is much less salient and difficult to detect.

To increase the rate of detection of the luminance change, stimuli with varying luminance were used in an LTP-like protocol consisting of intermittent high-frequency stimulation (Figure 4B). In the re-test, participants exhibited an elevated detection performance that was of high spatial selectivity. Changes occurred only on the side of stimulation, and did not transfer to the non-stimulated hemifield. Even slight changes ($\sim 3^{\circ}$) in the spatial position of stimuli presented during the exposure-based learning and testing within a visual hemifield reduced the amount of learning [15]. A similar pattern was observed in animal studies, where changes in the stimulus orientation of about 5° led to significantly lower

effects of learning [12,48,50]. Furthermore, the degree of improvement depends on the duration of the LTP-like stimulation [15], indicating a gradually developing plasticity. These effects were surprisingly stable for at least 10 days, depending on the saliency of the distracter. The exposure-based learning was less effective if the distracter was very salient [11]. Similar effects have been found in animal studies that examined stimulus-specific response potentiation [12,48].

Remarkably, the opposite effect — a decrease in the detectability of the luminance change — was found when protocols resembling an LTD-pace were used [11]. However, the detection of luminance in these change-detection tasks is complicated because of the concomitant change in orientation. Therefore, an alternative intervention strategy was required to increase the detectability of the luminance change indirectly, and this was achieved by decreasing the saliency of the orientation change via stimulation using an LTD-pace, in which stimuli are presented at a time pace that is used in electrical stimulation to induce long-term depression effects. The data showed that the modulatory effects of LTP- and LTD-pace stimulation also depend on the feature used during stimulation. Although the temporal structure of the stimulation and the neural mechanisms involved in these two types of stimulation are identical, the outcomes can be opposing. This suggests that contrasting learning mechanisms may yield an equivalent behavioural outcome.

To sum up, the results we have described show the following regarding training-independent sensory-learning-induced changes in visual processing [15]. First, stimulations using an LTP- or an LTD-pace modulates perception bi-directionally. Second, the effectiveness and stability of training-independent sensory learning effects depend on the saliency of competing stimuli. Third, the degree of training-independent sensory learning changes increases gradually with the duration of the stimulation. Fourth, contrasting learning mechanisms (LTP-pace versus LTD-pace) may have an equivalent behavioural outcome. And fifth, the effects of visual training-independent sensory learning are spatially very selective.

The fact that changes in visual processing are confined to the spatial positions targeted during stimulation and are not generalized across the visual field may be taken as evidence that attentional processes themselves are not affected by exposure-based learning, as attentional modulation tends to generalize across visual fields [54,55]. To explain the effects observed in the change-detection task, we suggested that changes occur at a perceptual level, which, in turn, affects subsequent attentional selection processes. Many lines of evidence [56] have indicated that attention emerges at several points between the input and the response, and that objects in the visual field compete for limited processing capacity and control of behaviour [57]. This competition is largely determined by the saliency of stimuli [56]. In the context of training-independent sensory learning effects, attentional processes may emerge as a function of the perceptual evaluation that is determined by stimulus attributes. Therefore, it is possible that training-independent sensory learning changes perceptual sensitivities, which subsequently affect attentional selection processes and lead to better behavioural performance in the task.

Neurophysiological data obtained using ERPs and reflecting attentional processes [58] underscore this assumption.

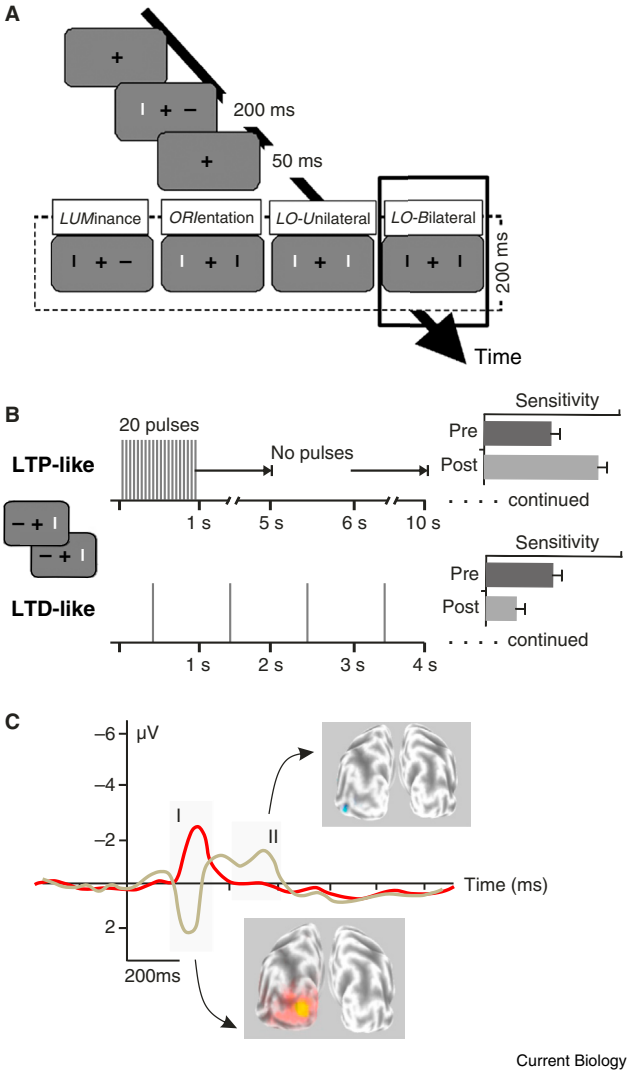

Figure 4. Training-independent sensory learning in the visual modality. (A) Schematic overview of the task used to examine LTP- and LTD-like exposure-based perceptual learning in the visual domain [11]. (B) Overview of the visual LTP- and LTD-like learning protocols, which can increase or decrease visual sensitivity, respectively. (C) Electrophysiological effects of LTP-like visual stimulation on attentional selection. Prior to stimulation, attention is allocated to the distracter (positive deflection), whereas after successful LTP-like learning, attention is allocated to the target (negative deflection). These processes occur in the extrastriate visual areas [15]. Attentional reallocation processes mediated by areas located downwards from the ventral processing stream are not evident after LTP-like stimulation.

These ERPs can be used to trace the time course of the spatial allocation of attention towards the target and the distracter (Figure 4C). Before exposure-based learning, ERPs show that attention is initially allocated to the distracter and is only subsequently allocated to the target. After successful training-independent sensory learning, attention is directly allocated to the target stimulus and distraction no longer occurs. These changes induced by exposure-based learning were attributed to the modulation of the extrastriate visual areas [15], which are core structures in the selection of visual stimuli [57,59]. These results reveal further key properties of training-independent sensory learning in the visual

domain: attentional allocation processes may be altered on the basis of the changes in perceptual sensitivities; and training-independent sensory learning alters the perceptual sensitivity of neuronal networks that represent the stimulus in the extrastriate visual areas.

In a study [35] that attempted to link STDP to high-level human perceptual learning, the repeated asynchronous presentation of faces resulted in a systematic bias in face-identity perception. It was assumed that, during pairing, the successively presented face images evoke temporally offset volleys of synaptic activity. Thus, two volleys of excitatory postsynaptic potentials (EPSPs) can be assumed to reach a face-responsive neuron immediately before and immediately after the neuron starts firing. After pairings of EPSPs and spikes that fall within the permissive window for STDP, the synapses carrying input from the first stimulus (face A) will be strengthened, and the synapses conveying input from the second stimulus (face B) will be weakened, which changes synaptic weights and renders the network more sensitive to face A input and less sensitive to face B input. Accordingly, the training-independent sensory learning approach is able to incorporate predictions obtained from the STDP mechanisms for altering human behaviour. Further studies are needed to obtain more insights on how human behaviour can be altered using STDP protocols.

Auditory Modality

Recent data have provided evidence that training-independent sensory learning is also effective for the auditory domain. Using an intermittent, high-frequency protocol consisting of auditory stimuli (band-pass-filtered frozen noise with lower cut-off frequency 2 kHz; upper cut-off frequency 11 kHz, applied at trains of 10 bursts of 960 ms duration delivered at a rate of one per five seconds) was effective in driving cross-modal plasticity in patients with hemianopia [60]. In an earlier report [13], high-frequency, repetitive, auditory stimulation (two minutes of tone pips presented 13 times per second) was used to determine whether induction of a long-lasting increase of the human auditory evoked potential (AEP) was possible. After high-frequency stimulation, the N1 component of the AEP was significantly enhanced for more than one hour.

In other studies, passive listening of sounds has been shown to improve their discriminability [61], and learning was further enhanced by combining an auditory frequency-discrimination task with additional exposure to acoustic stimuli that roughly matched the sounds from the material used for practicing [62]. However, these effects were not discussed in the context of stimulus timing, and how far they fit into the training-independent sensory learning framework remains unclear.

Similarities and Dissimilarities of Exposure-based Learning across Modalities

The data discussed above show that training-independent sensory learning is effective for the tactile, visual and auditory modalities. Sensory stimulation protocols with an almost identical temporal structure have been found to induce changes in tactile, visual, or auditory perception, providing a strong argument that the training-independent sensory learning approach uses principles of plasticity that are ubiquitous across all modalities.

There are, however, differences in the application and outcome of training-independent sensory learning across the distinct modalities. For example, in tactile experiments, stimuli were delivered either cutaneously or by electrical stimulation of the finger nerves, the latter being a highly unspecific form of stimulation. In contrast, in visual experiments [11], the stimuli were highly specific (small bars of light characterized by a defined orientation). Furthermore, the results of the experiments differed, in that in the tactile experiments, although the effect was specific to the stimulated finger, it generalized to a surprisingly broad range of abilities, including sensorimotor performance [10,21]. In the visual domain, the training-independent sensory learning effects were found to be highly task and stimulus specific. Finally, the tactile effects typically returned to the baseline after one or two days, whereas the visual effects persisted for at least 10 days. It is tempting to speculate that differences in the type of stimulation contribute to the differences in the outcome of training-independent sensory learning; however, it is also possible that modality-specific properties may constrain the outcome of plasticity. Further experiments are needed to clarify the possibilties.

Earlier Evidence against Learning through Mere Exposure

Attention is known to play an essential role in perceptual learning and experience-related plasticity. Many studies have shown that learning depends on whether subjects focus their attention on specific features, supporting the hypothesis that the learning of a feature requires subjects to be aware of, and focus their attention on, the stimulus feature (compare [63]). Close inspection of the literature revealed that much of the apparent evidence for a role of attention in perceptual learning has been presented as evidence against passive learning, in the sense of learning following pure exposure [14]. Some reports have explicitly stated that prolonged and 'passive' stimulation is not sufficient to drive plastic changes. Studies of auditory learning have revealed that the pairing of sensory stimulation with electrical stimulation of the nucleus basalis results in rapid and selective reorganization of cortical maps [64]; however, control experiments revealed that sensory stimulation alone, without the electrical stimulation of the nucleus basalis, was ineffective. Similarly, passive exposure to tactile stimulation in monkeys performing an auditory-discrimination task had no effect on tactile-discrimination abilities [65].

How do these observations fit into the framework of training-independent sensory learning. First, the role of attention in perceptual learning is apparently less clear, as was thought previously [14,63,66]. Second, a simple explanation for the apparent discrepancies is that, during training-independent sensory learning, an average of many thousand stimuli is applied. This is a much stronger stimulation in terms of stimulus number per time compared to that received by the monkeys (500 to 700 per day) during the so-called passive discrimination training [65]. Furthermore, experiments performed using single-site stimulation [19,20], as described above, found that small-field or single-site stimulation had no effects on the discrimination abilities or on cortical processing. Accordingly, to be effective, a sensory stimulation must have strong spatial (co-activation) and/or temporal (high frequency) features.

To provide a general framework that explains the remarkable effectiveness of the passive sensory stimulation applied during training-independent sensory learning, it has been suggested that the response to a sensory stimulation has

to pass a 'learning threshold' [14]. Under conventional task-training conditions, factors such as reinforcement, motivation and attention combine to drive learning beyond this threshold. An alternative approach to crossing this threshold involves 'optimization' of the sensory stimulation. Such optimization can be achieved by factors such as high-frequency or burst-like stimulation, as well as heavy schedules of stimulation (a large number of sensory stimuli); these factors boost responses to sensory stimuli that are normally insufficient to drive learning past this threshold. According to this framework, therefore, application of canonical plasticity protocols serves the purpose of optimization, and consequently, short episodes of sensory stimulation can induce persistent changes in perception and behaviour.

Neural Substrates of Training-independent Sensory Learning

The available data on tactile and visual training-independent sensory learning suggest that, as a result of learning, early sensory areas are modulated. Many features of processing in the primary (SI) and secondary somatosensory cortices (SII) are modified during tactile-training-independent sensory learning [16,18,19,46,67,68]. In contrast, in visual training-independent sensory learning, processing is altered in the extrastriate visual areas [15] (though effects in the primary visual cortex, V1, are still possible, as this has been little investigated to date). Changes in the primary sensory areas have long been implicated in perceptual-training-based learning, though this has not been without debate [2,69,70]. Although training-independent sensory learning is based on the assumption that protocols in which stimuli are presented at a similar pace to the stimulation procedures that induce LTP and LTD lead to plasticity that affect perception and behaviour directly, the cellular bases of the effects remain to be elucidated.

A step in this direction has been made by studies of the training-independent sensory learning mechanisms in animal models, with the aim to obtain insight into changes in synaptic modifications. As the effects of training-independent sensory learning unfold very quickly (within less than an hour), it is unclear whether they involve structural changes as seen in training-induced plasticity (compare [7]). Remarkably, visual training-independent sensory learning exerts long-term effects that last at least 10 days [11]. Interestingly, for task-relevant, training-based learning it has been shown that, within the first few weeks of visual stimulation, there are increases both in activation in the V1 subregion of the trained visual field quadrant and in task performance. But while performance saturated, brain activation in the corresponding areas decreased to baseline levels [6].

These findings indicate that there might be distinct temporal phases in which the long-term maintenance of perceptual alterations is coded in cortical regions beyond the primary areas. This observation can be explained by the two-stage model [71,72], according to which plastic changes first develop transiently in early sensory areas, but are then transferred to higher cortical areas, thereby stabilizing the long-term learning effects. Further experiments are needed to clarify whether training-independent sensory learning-induced changes can be accounted for using such a two-stage model.

Applications of Training-independent Sensory Learning

A new field of 'augmenting cognition' is developing in which neuroplasticity mechanisms are employed to drive targeted improvement of cognition, behaviour and perception [73]. Sensory stimulation approaches such as training-independent sensory learning appear to be prime candidates for influencing human perceptual and cognitive abilities. While research using training-independent sensory learning is still in its infancy and its neurobiological foundations are not fully understood, the properties of training-independent sensory learning, such as the high stability of the plastic changes and its ease of application, render training-independent sensory learning a promising tool in the targeted intervention aimed at improving perception, behaviour, and cognition.

Neuroplasticity-based rehabilitation after brain injury and stroke uses task-specific training and massed practice to drive brain reorganization and improve sensorimotor functions [74,75]. As many patients have restricted mobility, however, the development of additional and alternative approaches that may supplement, enhance or even replace conventional training procedures would be of advantage. Therefore, the feasibility of repetitive sensory stimulation approaches is being increasingly explored [10,21,36,37,76]. Available data suggest that application of training-independent sensory learning to patients with brain injury provides a surprisingly effective way to ameliorate perceptual and behavioural impairments [36,37,77–80]. The particular advantage of training-independent sensory learning is its passive nature, which does not require the active participation or attention of subjects. Therefore, training-independent sensory learning approaches can be applied in parallel with other techniques, which makes this intervention very easy to implement and more acceptable to the individual.

The same rationale holds true for the treatment of age-related impairments, although an appreciation of the urgent need of treatment of age-related degradation compared to that of impairments after brain injury is less apparent. Nonetheless, given the dramatic changes in the age structure of industrialised societies, substantial efforts are currently being undertaken to improve cognition and sensorimotor performance of the elderly by training, exercising, and practicing [81]. Some recent studies on elderly individuals showed improvement in tactile and sensorimotor performances [82,83] and stabilized recovery, over repeated applications of training-independent sensory learning [40,83]. These data suggest that training-independent sensory learning is also effective in aged populations characterized by severe impairments of perception and sensorimotor behaviour.

Other Training-independent Sensory Learning Approaches

The previous sections dealt with training-independent sensory learning approaches in different modalities. Common to all these approaches is the use of sensory stimulation at a pace that resembles the stimulation procedures used to induce LTP or LTD effects at a cellular level. This procedure contrasts with the classical task-relevant learning scenario, in which subjects are exposed to sensory stimuli that have to be attended to and are relevant to the task to be learned [71]. Training-independent sensory learning approaches, by contrast, are entirely independent of the task and can operate without the subjects paying attention to the stimuli required to drive plasticity.

In recent years, other approaches to training-independent sensory learning have been introduced, which do not explicitly rely upon LTP and LTD analogies. These approaches also do not require attention, or even, in the extreme form,

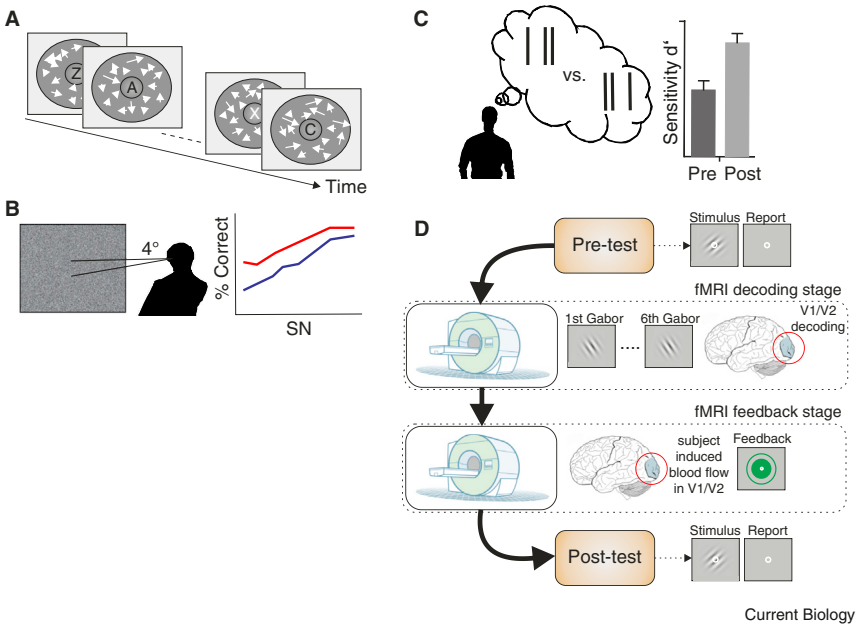

Figure 5. Other approaches for training-independent sensory learning.

(A) Depiction of a task used to induce task-irrelevant learning. The arrows represent the velocity of the coherent motion of the random dot pattern [84]. (B) Effects of rewards unrelated to a task trigger perceptual learning [88]. (C) Visual learning induced by mental imagery. The mere imagery of stimuli, without actual exposure to these stimuli, induced increases in the sensitivity to discriminate the bars [23]. (D) Illustration of an fMRI biofeedback procedure used to induce learning without visual stimulation [5].

sensory stimuli. 'Task-irrelevant learning' [84], which is also based on exposure to stimuli, occurs in the absence of conscious awareness of the stimuli used for learning, under conditions in which the irrelevant stimuli are consistently presented during the performance of a task based on other types of stimuli [63,66,85]. In a typical experimental setup (Figure 5A), subjects are presented with moving dot patterns of varying coherence, which are task irrelevant, whereas the relevant task is to identify letters shown at the centre of the display [84]. A small fraction of dots moves in the same direction, whereas the other dots move in varying directions. The fraction of coherent motion is so small that subjects are unable to detect it. However, after 'training' to report the letters (task-irrelevant training), subjects are able to discriminate the motion of dots. These results indicate that a conscious effort in the sense of explicit training and attentional allocation [86] is not necessary to induce learning [69]. Task-irrelevant learning has also been demonstrated to occur in the auditory domain. The perception of single-formant transitions was improved to the same extent after exposure to a stimulus to which the subjects did not pay any attention as that observed after explicit training; however, the unattended exposure was paired with an auditory-discrimination task [87].

Task-irrelevant learning has been explained by suggesting that the internal reinforcement signals triggered by task processing or rewards result in learning of the irrelevant features [85]. A recent study by Seitz *et al.* [88] showed (Figure 5B) that even rewards unrelated to a task can trigger perceptual learning. Taken together, these data suggest that reinforcement signals for and exposure to a specific feature are not necessary for perceptual learning of that feature.

A completely different approach to influencing human sensorimotor performance is based on the application of noise stimuli. In general, addition of noise can improve the reliable transfer of information, a phenomenon known as stochastic resonance (compare [89,90]). This idea has been applied to improve sensorimotor performance in humans. For example, applying mechanical or electrical noise stimulation to the skin of the hands or feet was shown to improve perception of vibrations and tactile stimuli in diabetes patients with moderate-to-severe neuropathy [91], to lower the touch thresholds for the hands of elderly subjects [92], and to improve foot sway parameters in young and elderly subjects [93,94]. These findings suggest that stochastic resonance is effective in influencing human perception and behaviour. The difference between training-independent sensory learning and stochastic resonance is that stochastic resonance affects thresholds by enhancing inputs that are otherwise sub-threshold, whereas training-independent sensory learning alters the modes of neural processing via selective changes in synaptic efficacy and connections.

Video game playing can be regarded as, in a sense, intermediate between 'training-induced learning' and 'learning without training'. The seemingly numerous beneficial effects observed in action video game players have spurred a controversial discussion. There is an agreement that playing action video games enhances many basic perceptual capabilities, as well as attentional selection functions [95–102]. Conceivably, these beneficial effects are achieved by not directly training for particular tasks; instead, the effects can be assumed to effectively unfold because players are exposed to an almost unique combination of factors that are all crucial to the facilitation of learning, including high attentional demand, reward, motivation, high-frequency stimulation, and display of rapid sequences.

Learning without Sensory Stimulation

To induce task-irrelevant learning, stimuli are presented, although they are not relevant for the task itself. Recent studies have demonstrated that perceptual learning is even possible without the presentation of stimuli (Figure 5C). Instead, training is performed using only imaginary stimuli [22]: subjects were asked to imagine the inner part of a bisection stimulus as being offset either to the left or to the right while only the two outer lines were presented; after this form of 'training', the performance of subjects improved, as typically observed with real bisection stimuli. Imagery training has similarly been shown to improve motion-direction discrimination [23]. Such studies imply that the neural processes underlying perceptual learning, which are usually assumed to be primarily dependent on

stimulus processing, can be equally based on mentally generated signals, without any actual exposure to stimulation [103].

Shibata *et al.* [5] went a step further by completely removing sensory stimulation (Figure 5D). These authors showed that visual plasticity and learning could be induced by neurofeedback alone, without any stimulus presentation. In this study, first the subjects' discrimination performance on Gabor stimuli was assessed, and then the functional MRI data, obtained while subjects discriminated Gabor patterns, were decoded. Next, the subjects were instructed to "somehow regulate activity in posterior brain areas" (p. 1413) when the subjects were still within the scanner. Thus, the decoded brain activation pattern was implemented into a feedback procedure. When the subject-induced activation pattern matched that evoked by the stimuli, a feedback was provided. Subsequently, the orientation-discrimination performance of the subjects was improved [5]. These results show that brain activity can be regulated intrinsically and enhanced to induce learning without any direct training by using a stimulus.

Summary

Here we have reviewed novel approaches to inducing plasticity and learning that do not require explicit task training. We have primarily focused on the training-independent sensory learning approach in which sensory stimulation protocols consistent with the temporal requirements needed to induce synaptic plasticity are applied to drive persistent changes in human perception and behaviour; this approach links synaptic plasticity research to human behaviour and learning. This approach can be used not only to evaluate the functional relevance of timing-specific synaptic plasticity protocols in improving human behaviour, but also to introduce and test novel timing conditions in terms of their ability to drive human learning, which have not been studied at the cellular level, so far. However, how effective is the training-independent sensory learning approach in modulating more complex behavioural and cognitive tasks remains an open question. In addition to training-independent sensory learning, several other novel experimental approaches have been shown to effectively induce perceptual learning without any sensory stimulation. Apparently, humans can learn under conditions in which learning was thought to be impossible a few years ago. In fact, these new approaches pose severe challenges regarding our understanding of learning mechanisms. Although the mechanisms underlying training-independent sensory learning are far from understood, the current application of this approach to augment cognition and behaviour is straightforward and many attempts of its use in therapy such as in rehabilitation and as an intervention are underway. Future research is needed to understand the neurobiological basis of the various forms of 'learning without training'. Further, it remains to be seen how far is it possible to subsume the many forms of perceptual learning discussed in this review into a unified model of learning.

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