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Indexing sensory plasticity: Evidence for distinct Predictive Coding and Hebbian learning mechanisms in the cerebral cortex

M.J. Spriggs [a,c,*,1], R.L. Sumner [a,1], R.L. McMillan [b], R.J. Moran [d,e], I.J. Kirk [a,c], S.D. Muthukumaraswamy [b]

[a] School of Psychology, The University of Auckland, New Zealand
[b] School of Pharmacy, The University of Auckland, New Zealand
[c] Brain Research New Zealand, New Zealand
[d] Department Engineering Mathematics, University of Bristol, BS8 1TH, UK
[e] Department of Neuroimaging, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK

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ABSTRACT

The Roving Mismatch Negativity (MMN), and Visual LTP paradigms are widely used as independent measures of sensory plasticity. However, the paradigms are built upon fundamentally different (and seemingly opposing) models of perceptual learning; namely, Predictive Coding (MMN) and Hebbian plasticity (LTP). The aim of the current study was to compare the generative mechanisms of the MMN and visual LTP, therefore assessing whether Predictive Coding and Hebbian mechanisms co-occur in the brain. Forty participants were presented with both paradigms during EEG recording. Consistent with Predictive Coding and Hebbian predictions, Dynamic Causal Modelling revealed that the generation of the MMN modulates forward and backward connections in the underlying network, while visual LTP only modulates forward connections. These results suggest that both Predictive Coding and Hebbian mechanisms are utilized by the brain under different task demands. This therefore indicates that both tasks provide unique insight into plasticity mechanisms, which has important implications for future studies of aberrant plasticity in clinical populations.

Introduction

Perceptual learning relies on the structural and functional modification of neural networks in response to external stimulation (Fahle, 2004). This experience-dependent neuroplasticity within the sensory systems provides an opportunity to non-invasively study the mechanisms underlying neuroplasticity throughout the brain. However, different external demands (e.g., task demands) may elicit different encoding mechanisms (Koch and Poggio, 1999) and to date, the differences between such mechanisms have not been characterized.

A rapidly growing focus of neuroimaging research has been that of Bayesian models of perceptual learning. Such models propose that the brain is equipped with a generative model, which is built upon prior expectations extracted from sensory data and provides a mapping of (hidden) cause to (sensory) consequence (Friston, 2005; Knill and Pouget, 2004). The Predictive Coding model proposes that prediction errors are used to adjust the generative model until divergence is minimized; allowing for an accurate model of the cause of incoming information (Bastos et al., 2012; Friston, 2005; Garrido et al., 2009a; Huang and Rao, 2011). The reduction of prediction error is dependent on the passing of top down predictions and bottom up prediction errors through hierarchical, reciprocally connected networks. Neurocomputational modelling of prediction errors suggests that top-down predictions are expressed through N-methyl--D-aspartate (NMDAR) and γ-aminobutyric acid receptor (GABAR) receptor pathways, while bottom up prediction errors rely on fast feedback via α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPAR) receptors (Corlett et al., 2016). Under the Predictive Coding framework, experience-dependent plasticity corresponds to the reciprocal updating of internal models of the environment through these pathways.

The most studied empirical example of Predictive Coding in the brain is the Mismatch Negativity (MMN). The MMN is a large, negative, frontocentral electrophysiological component induced by a surprising or 'deviant' tone following a sequence of predictable or 'standard' tones (Garrido et al., 2009a). The widely used 'Roving MMN' paradigm

* Corresponding author. School of Psychology, University of Auckland, Private Bag 92019, Auckland, 1142, New Zealand.
E-mail address: mspr827@aucklanduni.ac.nz (M.J. Spriggs).
[1] M.J.S and R.L.S contributed equally to this work.

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involves the presentation of trains of tones of the same frequency, where the first (deviant) tone in each train induces the MMN response, and this subsequently returns to a standard response over successive presentations. Under the predictive coding framework, the MMN represents a failure to predict bottom-up sensory input and, consequently to suppress prediction error (Friston, 2005; Garrido et al., 2009a). In support of this, previous studies have demonstrated that the MMN is generated by modulations in intrinsic auditory cortex (A1) connectivity, as well as reciprocal message passing within a fronto-temporal network (Auksztulewicz and Friston, 2015; Garrido et al., 2008; Garrido et al., 2007; Moran et al., 2014; Schmidt et al., 2013). This suppression of prediction error corresponds to perceptual inference (Auksztulewicz and Friston, 2016; Garrido et al., 2009b). The MMN paradigm has been used to demonstrate disrupted perceptual inference in clinical populations (Boly et al., 2011; Dima et al., 2010) and under pharmacological intervention (Rosch et al., 2017; Schmidt et al., 2013; Timmermann et al., 2017).

While Predictive Coding has become a dominant framework for understanding perceptual learning and inference, it is not the only model for experience dependent plasticity in the neocortex. Hebbian learning provides an alternative framework, within which learning is dependent on increases in synaptic efficacy between the neurons in a network (Hebb, 1949; Lynch, 2004). The most widely studied form of Hebbian plasticity is Long Term Potentiation (LTP). LTP refers to an activity dependent increase in synaptic connectivity following repeated neuronal co-activation; the most common type is dependent on an influx of Ca^{2+} through NMDARs leading to long term alterations in cell structure and function (Abraham and Williams, 2003; Bliss and Lømo, 1973; Cooke and Bliss, 2006; Teyler and DiScenna, 1987). Importantly, LTP conforms to many Hebbian characteristics such as input-specificity, co-activation and associativity (Hebb, 1949). As such, Hebbian LTP is regarded as the most likely neuronal mechanism underlying memory formation.

LTP has been primarily studied in laboratory animals using direct neuronal electrical stimulation (Bliss and Lømo, 1973; Figurov et al., 1996; Harris et al., 1984; Kirkwood and Bear, 1994; Teyler and DiScenna, 1987). However, following the demonstration of visually-induced enhancements in the neural activation of rodents (Heynen and Bear, 2001), Teyler et al. (2005) presented one of the first electroencephalography (EEG) paradigms for measuring LTP-*like* mechanisms noninvasively in humans. High frequency (~9 Hz) visual stimulation was used to induce an enhancement of the visually evoked potential (VEP) to later low frequency (~1 Hz) presentations of the same stimulus. Subsequent human and rodent studies have demonstrated that this visually-induced enhancement conforms to many of the Hebbian characteristics seen in rodent LTP such as longevity, NMDAR dependence (Clapp et al., 2006) and input specificity (McNair et al., 2006; Ross et al., 2008). Furthermore, this paradigm has been used to demonstrate modulated plasticity in healthy, and clinical populations (Çavuş et al., 2012; Normann et al., 2007; Smallwood et al., 2015; Spriggs et al., 2017). Together, this body of human and rodent studies indicates that this visually induced enhancement represents the induction of an Hebbian LTP-*like* form of neuroplasticity (Clapp et al., 2012; Kirk et al., 2010).

While potentiation of the VEP has been well characterized, modulations to the underlying network remain largely unexplored. Both EEG source localization and functional magnetic resonance imaging (fMRI) have localized the LTP-*like* enhancement to extrastriate visual cortex (Clapp et al., 2005; Teyler et al., 2005). From extrastriate visual cortex, the ventral and dorsal visual streams extend to the medial temporal lobe and parietal lobe respectively (Felleman and Van Essen, 1991; Grill-Spector and Malach, 2004). Experience-dependent plasticity within these networks is understood to underlie visual perceptual learning (Fahle, 2004; Kourtzi and DiCarlo, 2006), with changes occurring at some of the earliest levels of cortical processing (Cooke and Bear, 2014; Kourtzi and DiCarlo, 2006). The ventral visual stream is understood to support object recognition, and is closely intertwined with medial temporal memory networks (Desimone et al., 1985; Felleman and Van Essen, 1991; Grill-Spector and Malach, 2004; Kourtzi and DiCarlo, 2006). As such, one can speculate that LTP-induction will enhance connectivity within this ventral visual network.

As illustrated above, both Predictive Coding and Hebbian mechanisms have been independently implicated in perceptual learning and the Roving MMN and visual LTP paradigms were designed to index these models respectively. However, the two models are built upon fundamentally different assumptions of how perceptual learning is encoded in the brain; primarily, while Predictive Coding is dependent on updating an internal, generative model, Hebbian learning is not. The coexistence of Predictive Coding and Hebbian mechanisms has been explored in models of cortical responses such as the Free Energy Principle (Friston, 2005, 2009, 2010). Under the Free Energy Principle, Predictive Coding and Hebbian mechanisms are used to define the hidden states and causes of an internal generative model respectively (Bastos et al., 2012; Friston, 2010). However, it may be possible that Hebbian processes can occur independent of a generative model, and that the brain may employ different encoding mechanisms for different tasks (Koch and Poggio, 1999). As such, the aim of the current study was to compare the mechanisms underlying the generation of the MMN using the Roving MMN paradigm, and the potentiated VEP using the visual LTP paradigm. It was hypothesized that the paradigms would induce different changes within the underlying neural network. Specifically, as the primary difference between Hebbian and Predictive Coding models is dependence on a generative model, it was hypothesized that the paradigms would differ in their modulation of top-down connectivity.

Materials and methods

Participants

44 male and female participants volunteered for the study (age range: 19–33, 33 female and 7 male; the imbalance in gender split is due to overlap of participants with another study). Four participants were excluded from the final analysis due to insufficient data quality, leaving a final sample of 40. Participants were required to have no history of neurological conditions or concussion, and normal or corrected to normal vision. This study was approved by the University of Auckland Human Participants Ethics Committee. Participants provided informed written consent prior to participation.

Equipment

EEG data were collected using 64 channel Acticap Ag/AgCl active shielded electrodes and Brain Products MRPlus amplifiers recorded in Brain Vision Recorder (Brain Products GmbH, Germany) with a 1000 Hz sampling rate, and 0.1 μV resolution. FCz was used as an online reference, AFz as ground. Electrode impedance was maintained below 25 kΩ.

Stimuli were displayed on an ASUS VG248QE computer monitor with a screen resolution of 1920 × 1080 and 144 Hz refresh rate. TTL pulses generated through the parallel port of the display computer provided synchronisation of stimulus events with EEG acquisition.

Tasks

All participants were presented with both the MMN and LTP tasks. To avoid carry-over effects, the presentation order was such that for 25% of participants the MMN task preceded the LTP task, for 25% it followed the LTP task, and for 50% it took place during the rest period of the LTP task.

Mismatch negativity

EEG was recorded continuously while participants engaged in a roving auditory oddball task used to probe the mismatch negativity in response to unattended stimuli (Fig. 1i; Garrido et al., 2008). The task was written and run in MATLAB using the Cogent toolbox (www.vislab.ucl.ac.uk/cogent.php).

The stimuli consisted of trains of one to 11 identical sinusoidal tones.