

Attentional Modulation of Tilt Aftereffect Caused by Cholinergic Basal Forebrain Projections

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Abstract — Psychophysical experiments show that adaptation induced tilt aftereffect gets modulated under controlled conditions of attention. The underlying neurophysiological mechanisms are unknown. Here using a population model of primary visual cortex having detailed intrinsic and synaptic mechanisms we model orientation adaptation and the effect of attention. We report that increased attention to orientation of adapting stimulus reduces magnitude of the tilt aftereffect by modulating feedforward and intracortical synaptic efficacies. Without mechanisms for synaptic modulation, increased alertness tends to increase the magnitude of the tilt aftereffect via modulation of intrinsic membrane mechanisms. Our model is the first to relate multiple acetylcholine-induced modulations of membrane and synaptic conductances to adaptation induced aftereffects. We also report that attention to stimulus orientation opposes adaptation induced orientation plasticity, reducing the adaptation induced repulsive shift of orientation preferences.

Keywords — Attention, acetylcholine, adaptation, ionic disturbances, tilt aftereffect, orientation plasticity

1. Introduction

Adaptation to oriented visual gratings leads to tilt aftereffect, for reviews see [1, 2]. Attention modulates this perceptual aftereffect. Influence of attention has been studied using discrimination tasks between sequentially presented stimuli for adaptation [3]. Orientation or contrast discrimination tasks cause attention to be directed to either the orientation or the contrast of the gratings. Attention to orientation rather than contrast of the gratings causes the magnitude of the tilt aftereffect to reduce (see Figures 7 and 9 of [3]). The tilt aftereffect in this case is comparable to the no-task case when the subject is gazing at the adapting stimulus with low alertness; see Figure 7 of [3]. Thus it is concluded that tilt aftereffect is not sensitive to the level of alertness but is sensitive to the attended dimension, orientation or contrast.

Acetylcholine has been implicated in attention mechanisms. Voltage and calcium activated potassium channels causing spike frequency adaptation are modulated by acetylcholine leading to an increased firing rate [4]. The modulation by cholinergic basal forebrain nuclei can impact responses of primary visual cortex cells as these nuclei project to this cortical region [5]. In [6] it is discussed how acetylcholine can shift the dynamics of cortical networks such that the afferent influence dominates over the intra-cortical influence. The mechanism involves synaptic modulation via muscarinic and nicotinic receptors. Further supporting this it has been shown that high levels of acetylcholine in V1 reduce the extent of spatial integration [7]. We show here how these effects of acetylcholine on intrinsic membrane and synaptic mechanisms can explain modulations of tilt aftereffect as discussed in the above paragraph.

Tilt aftereffect is an effect of orientation adaptation observed during psychophysical experiments in awake-subjects. On the other hand, orientation plasticity is an effect of adaptation observed during electrophysiological and optical imaging experiments in anesthetized subjects [8, 9]. The relationship between tilt aftereffect and adaptation induced orientation plasticity has been discussed previously [2, 10] and in [10] it is discussed that

adaptation induced orientation plasticity opposes tilt aftereffect. Here we show that attention to the stimulus feature opposes both the tilt aftereffect and adaptation induced orientation plasticity. Preliminary results have previously been presented at [11].

2. Methods

Here we discuss the intrinsic cellular mechanisms, the primary visual cortex model and the adaptation protocol. A part of the model methods have been reported previously [12].

The V1 population model consists of regular and fast spiking orientation selective complex cells of cat layer 2/3 primary visual cortex. The single compartment cells have Na^+ and K^+ conductances for spike generation. The feedforward drive to each cell is due to excitatory postsynaptic potentials generated through 100 excitatory synapses (AMPA and NMDA [13]). Each synapse receives a Poisson spike train having a spike frequency given by $(\exp(-|\theta_s - \theta_p|/\sigma^2) * (1-f_{\text{base}}) + f_{\text{base}}) * F_{\text{max}}$, where θ_s is the stimulus orientation, θ_p is the preferred orientation of the cell, and $|\theta_s - \theta_p| = 180^\circ - |\theta_s - \theta_p|$ if $|\theta_s - \theta_p| > 90^\circ$. The tuning of the feedforward drive is determined by σ and F_{max} is the maximum pre-synaptic firing rate. Baseline stimulus is represented with a pre-synaptic firing rate of $f_{\text{base}} * F_{\text{max}}$, with f_{base} being 0.1 [14]. As our previous results [12] show more orientation plasticity at pinwheel centers as compared to within iso-orientation columns we model a local region at a pinwheel center to study attentional modulation of orientation plasticity. Excitatory cells in the local population are taken to be 160 and inhibitory cells 32. These are approximately the number of cells detected with retrograde tracing within a distance of $150\mu\text{m}$ [14]. For a pinwheel center, cells are grouped into 8 orientation groups having orientation selectivity in the range 0° - 157.5° . For model simplicity the tilt aftereffect measurements are based on the responses of the pinwheel population rather than taking into account the response of the complete orientation map. Representative cells (0° - 157.5°) at a pinwheel center receive excitatory synaptic input from the rest of the cells in the local region. The net maximal synaptic conductance from excitatory cells in an orientation group to a representative cell is determined by $g_{\text{max}} * \exp(-\theta_d^2/\sigma^2) * N_c$, where g_{max} is the maximal conductance of a single synapse, θ_d is the difference in the orientation preferences, σ is tuning bandwidth and N_c is the maximum number of cells per orientation group. Each V1 regular spiking cell contains mechanisms for L-type calcium channels, intracellular calcium buffers, calcium pumps, calcium activated potassium channels, voltage-activated potassium channels and persistent sodium channels. Fast spiking cells have a lower value for voltage-activated potassium conductance. Calcium influx, pumping mechanism and buffering are calibrated to give decay time constants of cytosolic calcium similar to experimental data [15]. Mitochondrial calcium dynamics is represented as discussed in [12]. It results in a slow recovery of accumulated cytosolic calcium. The model includes cytosolic calcium activated (voltage independent) potassium conductance, SK type, modeled as $g_{\text{KCa}}([Ca^{2+}]_i) = g_{\text{bar}} * ([Ca^{2+}]_i / ([Ca^{2+}]_i + [Ca^{2+}]_{1/2}))^4$, where $[Ca^{2+}]_i$ is the free cytosolic calcium concentration with an initial value being 50nM , g_{bar} is the maximal conductance and $[Ca^{2+}]_{1/2}$ is the half-activation Ca^{2+} concentration [15,16,17]. The hyperpolarizing current is given by $i_{\text{KCa}} = g_{\text{KCa}} * (v - E_{\text{K}})$, v is the membrane potential and E_{K} is the reverse potential. Adaptation induced extracellular ionic disturbances based increased excitability of the local neural tissue contributes to orientation plasticity [12]. For a further discussion of methods, see [12].

Cholinergic basal forebrain neurons project to primary visual cortex and acetylcholine is released during a state of high alertness and focused attention. During high alertness acetylcholine suppresses spike frequency adaptation in pyramidal cells. Spike frequency adaptation in the regular spiking cells of our model is due to voltage and calcium activated potassium conductance [4]. To reflect acetylcholine-induced suppression of spike frequency adaptation we reduce the maximal conductance of voltage and calcium activated potassium channels. The maximal conductance of voltage activated potassium conductance is reduced to $0.5\text{pS}/\mu\text{m}^2$ from $1.0\text{pS}/\mu\text{m}^2$. The maximal conductance of calcium activated potassium conductance is reduced to $150\mu\text{S}/\text{cm}^2$ from $300\mu\text{S}/\text{cm}^2$. We suggest that focused attention to stimulus orientation during the orientation discrimination tasks would require afferent activity to dominate the intra-cortical activity. This could be facilitated by a dynamical adjustment of feedforward and lateral activity [6, 7]. Acetylcholine reduces the efficacy of intracortical synapses via muscarine receptors [18]. This is represented in the model by varying the maximal conductance of intracortical AMPA and NMDA synapses between $0.002\mu\text{S}$ to $0.0009\mu\text{S}$. Acetylcholine increases the efficacy of feedforward synapse via nicotinic receptors present on these synapses [19, 20, 21]. We represent this mechanism by varying the maximal conductance of feedforward AMPA and NMDA synapses between $.0005\mu\text{S}$ to $.001\mu\text{S}$. Synaptic modulations are simultaneously applied to all representative cells in the model population irrespective of their orientation preferences.

The adaptation protocol involves presentation of an adapting stimulus orientation (112.5°) for 30 seconds. Test stimulus having an orientation of 135.0° is presented for 1 second before and after adaptation. Spike

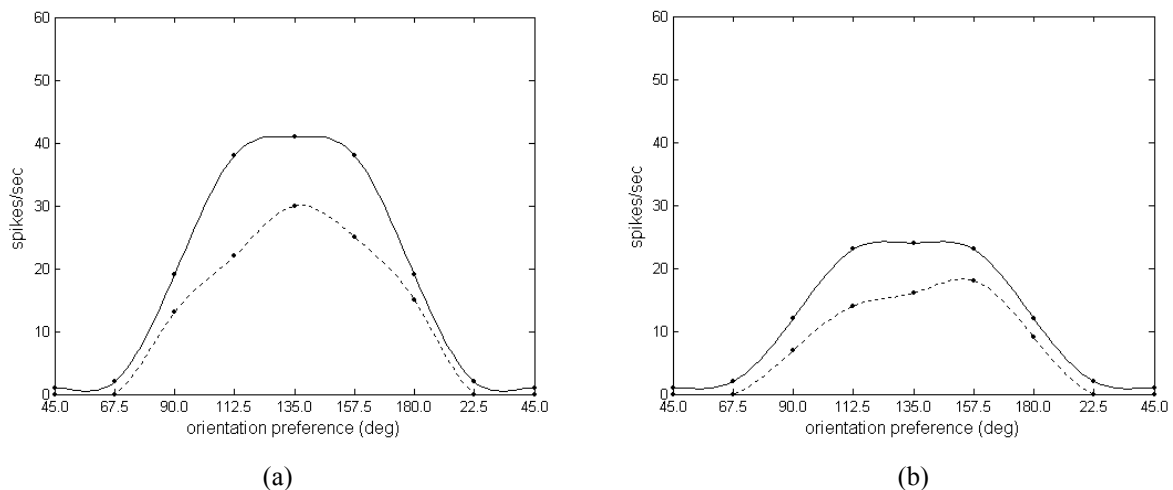


Figure 1. Acetylcholine induced modulation of feedforward synapses reduces magnitude of tilt aftereffect in the right figure. Both figures show pre (bold) and post adaptation (dashed) population response curves for a 135.0° test stimulus and a 112.5° adapting stimulus.

responses of cells representing all orientation groups are used to generate pre and post adaptation population response curves. These population response curves determine the perceived stimulus orientation before and after adaptation. For this we use the population vector method, see [10] for a discussion on different methods. Each cell contributes a two-dimensional vector with orientation equal to twice its orientation preference and length equal to its firing rate. Summation of these vectors results in a population vector having an orientation twice the perceived orientation. Tilt aftereffect is the difference between the pre and post adaptation perceived stimulus orientations. Here we determine modulations of cellular mechanisms that either decrease or increase the tilt aftereffect magnitude. As discussed in [22] we do not focus on fitting the model parameters to replicate the exact aftereffect magnitude determined from psychophysical experiments. Eight test orientations, 0° - 157.5° , are presented for 1s each to determine the orientation tuning curves and preferred orientations before and after adaptation. Orientation plasticity i.e. adaptation induced shift in orientation preference, is measured in cells having an orientation preference of 135.0° [12]. V1 cells are simulated using Neuron 5.8 and data analysis is done using Matlab.

3. Results and Discussion

3.1 Increased attention to the orientation of the adapting stimulus reduces the magnitude of tilt aftereffect

Figure 1(a) shows the pre and post adaptation population response curves when the feedforward maximal synaptic conductance is $0.0005 \mu\text{S}$ and the model does not have intra-cortical contributions. The tilt aftereffect measured using the population vector method from Figure 1(a) is 3.56° (see Methods). Acetylcholine increases the efficacy of feedforward synapses via nicotinic receptors (see methods). This is represented by changing the feedforward maximal synaptic conductance to $0.001 \mu\text{S}$ for each of the representative cells (0° - 157.5°). The pre and post adaptation population response curves are depicted in Figure 1(b). Tilt aftereffect measured from these population response curves is 1.86° . This shows that acetylcholine induced modulation of feedforward synapses cause reduction in tilt aftereffect.

Figure 2(a) shows the pre and post adaptation population response curves when the excitatory intra-cortical maximal synaptic conductance is $0.002 \mu\text{S}$. The tilt aftereffect as measured from these population response curves is very high, 8.16° . Acetylcholine reduces the efficacy of intra-cortical synaptic conductance via muscarinic receptors (see methods). With maximal intra-cortical excitatory synaptic conductance reduced to $0.0009 \mu\text{S}$ the tilt aftereffect reduces to a 0.85° . This is measured from the pre and post adaptation population response curves of Figure 2(b). Figure 3(a) shows a gradual decrease in tilt aftereffect as the feedforward synaptic efficacy increases. A similar effect is observed as the intra-cortical efficacy reduces in Figure 3(b).

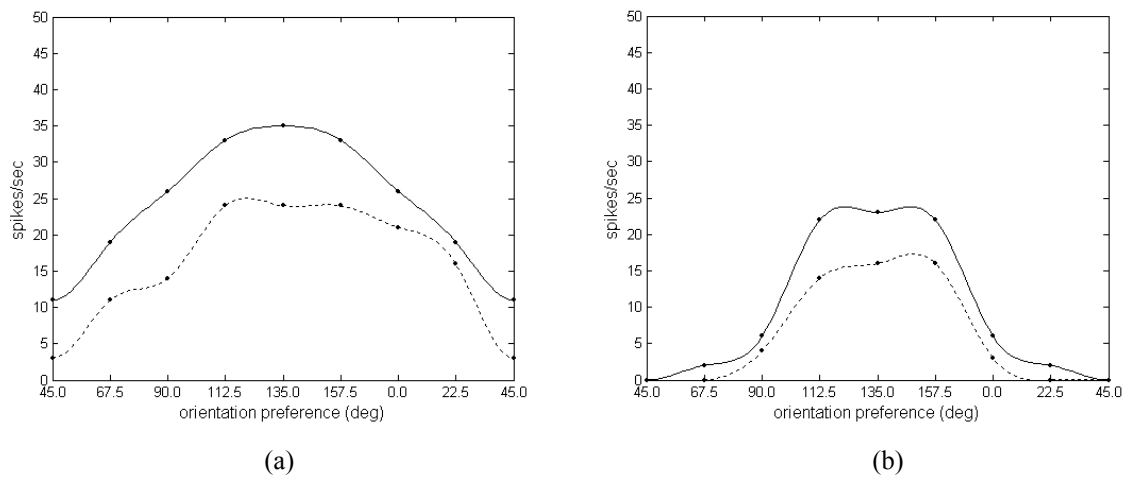


Figure 2. Acetylcholine induced modulation of intra-cortical synapses reduces magnitude of tilt aftereffect. The excitatory intra-cortical maximal synaptic conductance is 0.002μ and $0.0009 \mu S$ for (a) and (b), respectively. Both figures show pre (bold) and post adaptation (dashed) population response curves for a 135.0° test stimulus and a 112.5° adapting stimulus.

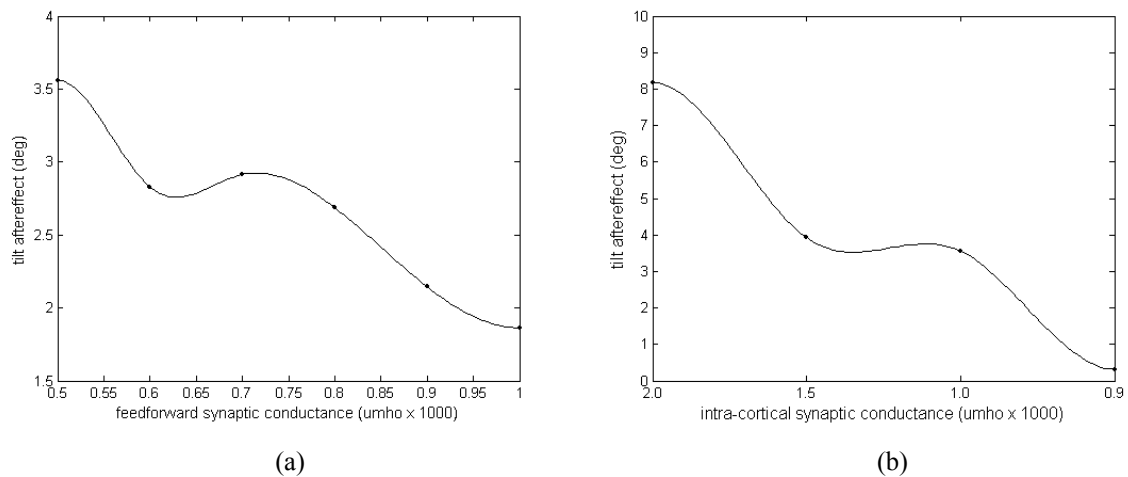


Figure 3. Reduction in tilt aftereffect (a) as the maximal feedforward synaptic conductance increases and (b) as the maximal intra-cortical synaptic conductance decreases over a range.

We have shown above two different acetylcholine dependent mechanisms to reduce tilt aftereffect. We propose these are applicable during a state of increased attention to the orientation of the adapting stimulus. But increased feedforward drive to all of the V1 cells in the local population could also cause the intra-cortical excitatory drive to increase. This could counteract the reduction in tilt aftereffect obtained above via the nicotinic mechanism. We suggest that the possible increase in intra-cortical drive is prevented by the muscarinic mechanism shown above.

There could be possibly an increase in the intra-cortical inhibitory drive due to an increased efficacy of excitatory feedforward synapses to inhibitory inter-neurons (nicotinic mechanism). There could also be a reduced intra-cortical inhibitory drive, which could be due to a reduced efficacy of intra-cortical inhibitory synapses (muscarinic mechanism). We do not model these mechanisms but assume that the changes in the inhibitory drive would be in manner that maintains a balance between excitation and inhibition [14].

A non-uniform suppression of the population response curve causes the perceived stimulus orientation to shift away from the adapting orientation leading to the repulsive tilt aftereffect. Figure 4(a) shows adaptation-induced disparity between the left and right flanks of the population response curve of Figure 1(a). The horizontal axis denotes the difference of the preferred orientations from the test orientation (135.0°) at which the

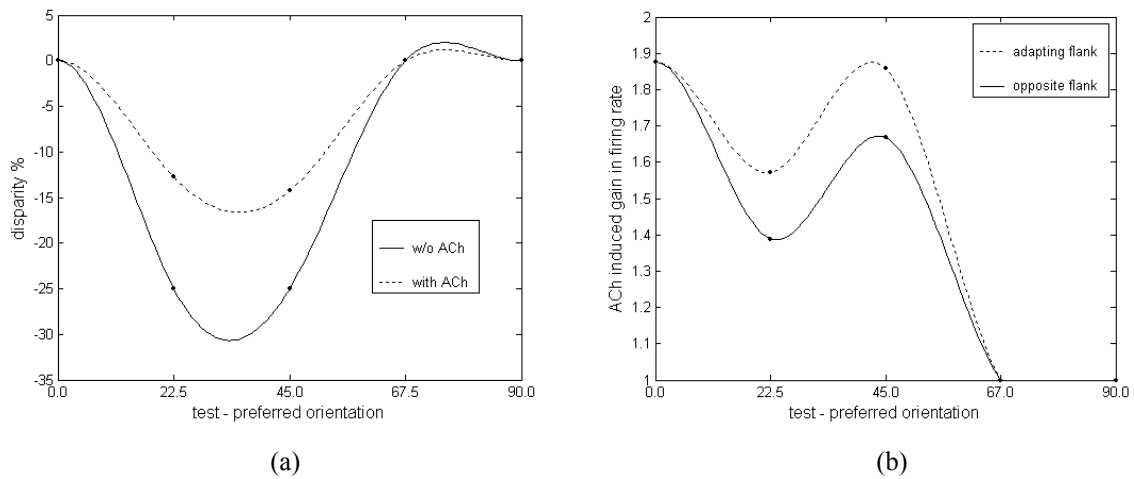


Figure 4. (a) Acetylcholine induced reduction in disparity between the adapting and opposite flanks of the population response curve. (b) Acetylcholine induced gain in spiking activity.

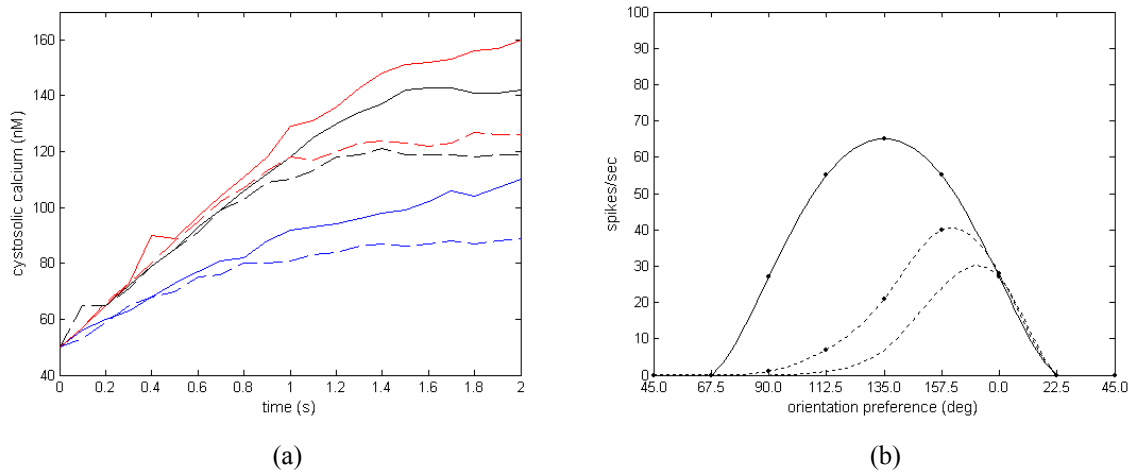


Figure 5. (a) Increased alertness to adapting stimulus causes a larger accumulation of intracellular calcium and (b) a larger suppression of responses on the adapting flank of the population response curve.

disparity is measured. For example, -25% disparity at 22.5° denotes that the spike response of (135.0° - 22.5°) 112.5° cells is 25% lower than (135.0°+ 22.5°) 157.5° cells. As shown in Figure 4(a) acetylcholine reduces the disparity between the flanks. This causes the tilt aftereffect to reduce. To further understand how this disparity is reduced we plot acetylcholine induced gain in spiking activity for all cells, Figure 4(b). Here also the horizontal axis denotes the difference of the preferred orientations from the test orientation (135.0°), at which the gain is measured. We observe that gain is more for cells on adapting flank as compared to the opposite flank. This shows how effect of acetylcholine can be cell specific.

3.2 Without mechanisms for synaptic modulation, increased alertness tends to increase the magnitude of tilt aftereffect

We observe in data of [3] that tilt aftereffect is larger during a state of higher alertness as compared to a state of low alertness (no discrimination task). Compare data for first 60 trials, full line curve and the dashed line curve, of Figure 8 in [3]. We observe from Figure 9 of [3] that tilt aftereffect during the first 20 trials is similar for attention to stimulus contrast or orientation. As adaptation progresses the tilt aftereffect for attention to stimulus orientation reduces. We suggest that this happens because acetylcholine induced synaptic modulation

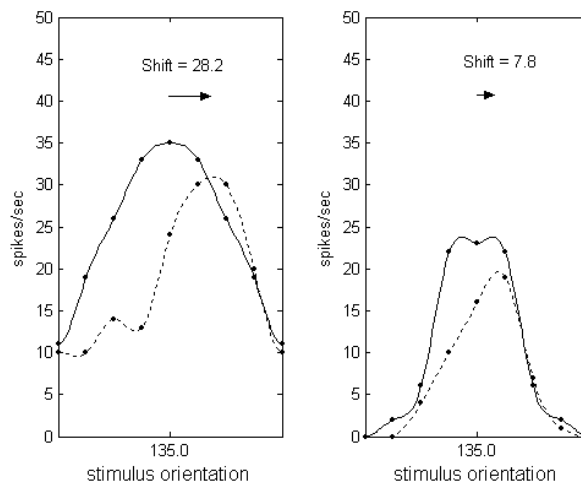


Figure 6. Attention to stimulus orientation opposes orientation plasticity. The right figure shows a reduced adaptation induces repulsive shift of orientation preference.

mechanisms that reduce tilt aftereffect take some time to become effective (see section 3.1). So, without mechanisms for synaptic modulation, increased alertness tends to increase the magnitude of tilt aftereffect.

Adaptation induced intracellular ionic disturbances lead to a larger hyperpolarization in cells having orientation preferences near the adapting orientation [12]. As can be seen in Figure 1(a), the post adaptation population response curve gets more suppressed at its left flank i.e. the flank towards the adapting orientation, 112.5° . During a state of high alertness acetylcholine reduces spike frequency adaptation (see methods). This causes a higher accumulation of free cytoplasmic calcium. Data for three cells having orientation preferences as 112.5° (red), 90.0° (black) and 67.5° (blue) is shown in Figure 5(a). Compare full line curves with dashed line curves.

In Figure 5(b) the two dashed curves show adaptation-induced suppression of responses on the left flank of the population response curve. The curve with lower spike responses is due to higher intracellular ionic disturbances during a state of high alertness. Higher suppression on the left flank could increase the disparity between the adapting (45.0° to 135.0°) and opposite (135.0° to 45.0°) flanks, leading to a larger tilt aftereffect.

3.3 Increased attention to stimulus orientation opposes orientation plasticity

Adaptation leads to suppression on the flank of the orientation-tuning curve that is near the adapting orientation. For cells at a pinwheel center adaptation can even lead to facilitation of responses on the opposite flank. This leads to a repulsive shift in orientation preferences [8, 9, 12]. The suppression and facilitation on the opposite flanks is respectively due to the reduced and increased intra-cortical amplification [12]. We report here that attention modulates adaptation induced orientation plasticity. Figure 6 shows a case with a large (28.2°) adaptation induced shift in orientation preference. The adapting orientation is 112.5° and the preferred orientation is 135.0° . The orientation preference shift reduces by 20.4° when a reduction in the intra-cortical synaptic efficacy is applied (muscarinic mechanism). It reduces by only 0.23° when an increase in the feedforward synaptic efficacy is applied (nicotinic mechanism).

Acetylcholine as it corrects orientation perception by reducing tilt aftereffect also reduces adaptation induced repulsive shift of orientation preferences. Attention to stimulus orientation thus opposes both adaptation induced perceptual aftereffect and orientation plasticity. Perceptual learning in V1 has been studied using repetitive orientation identification tasks [23]. A future extension of our work could possibly help to explain how perceptual learning modulates orientation tuning of V1 cells.

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