Influence of Attention on Perception, Learning, Memory and Awareness

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Discussion

In this study, our ambitious goal was to understand attentional-feedback signalling and its influence on the processes of perception, learning, working memory and conscious awareness. Our experiments utilized a variety of approaches comprising psychophysics, neurophysiology, and pharmacology to answer our research questions (*Chapter I-1.2).* We can say that the top-down attentional-feedback signal carries a rich amount of information. It enables the visual system to build a stable representation of the visual scene and augments our ability to choose and segment the complex arrangement of objects and backgrounds present in the world around us. Additionally, it plays a role in the encoding, maintenance, and recall of learned information[1,2].

Source & mechanism of the attention signal

In our experiments, we saw that attentional-feedback modulation performed different functions depending on the context of the task. For example, in visual perception tasks, we saw that it helps group together discrete elements (*Chapter IV*) and enables perception of the stimuli (*Chapter VI*), whereas in tasks involving learning and memory, it facilitates efficient learning of novel objects in presence of equally perceptible distractors (*Chapter III*), and furthermore plays a role in active maintenance (*Chapter V*) of this information.

Attentional networks and areas in the cortical hierarchy

The studies by Felleman and Van Essen[3,4] reviewed the anatomical connectivity between visual areas and were instrumental in understanding the myriad of visual processing areas in the brain. For several years, the source of the attentional-feedback signal has been an area of interest in neuroscience. Our current understanding comes using neurophysiological recordings, lesion studies, and imaging techniques (fMRI, PET) in animals and healthy humans, and also from studies performed in clinical populations[5] that have deficits in attention.

Presumably, attentional-feedback signals originate in higher areas as they have access to larger receptive fields and so, are able to integrate information across the entire visual scene. Furthermore, higher visual areas have connectivity with other areas of the brain, including areas processing different sensory modalities[6] and different functions, e.g. emotion processing[7]. Most tasks activate many cortical areas, which interact and share information to fulfil task requirements. For example, areas such as the superior colliculus (SC), lateral intraparietal cortex (LIP), area MT, and frontal eye fields (FEF) are active during the maintenance of attention and shifts of attention.

Mechanisms of attentional signalling

Attention signals influence neuronal processing in a flexible and dynamic manner. In our own neurophysiological experiments *(Chapter I, IV, V*), we saw that attentional-feedback signals influenced the firing rates of neurons and altered their sensitivity for stimuli. In our behavioural experiments, attentional-feedback signals resulted in better accuracy, faster response latencies, and increased sensitivity for the stimulus (*as reported by our participants*) (*see Chapter II, III for more information*).

Attention has widespread effects throughout the cortical circuitry and it modulates firing rates in areas such as V1[8], V4[9], frontal eye fields[10] (FEF), and others[11,12]. Some studies report that attention shifts the contrast function[13-15] in area V1, but not all studies agree[16,17] (*see Chapter II*).

Neuromodulators

Over the decades of neuroscience research, many mechanisms have been proposed through which attention changes the processing of stimuli. One possible mechanism is via neuromodulatory[11] pathways. Many studies advocate that the cholinergic system (*see Chapter II, III*) plays an important role in attention[8,18,19] and feedback[20] processing. Acetylcholine has been implicated in enhancing signal-to-noise in sensory encoding[21,22]. Additionally, it is likely that attentional-feedback signals recruit neuromodulators to enable learning and memory. The 'synaptic tagging and capture' framework[23,24] suggests that learning and memory processes activate molecular machinery at synapses that are active during a task to induce plasticity. Rombouts[25] and colleagues postulated that feedback from higher to lower areas might play a role in synaptic tagging. They propose that during learning and memory tasks, attentional-feedback signals cascading down the cortical hierarchy 'tag' synapses responsible for the response selection. These tags then interact with globally released neuromodulators such as acetylcholine to determine connectivity changes.

Much about the interaction between neuromodulators and processes such as attentional-feedback, learning, and memory is not well understood. Neuromodulators add a layer of complexity and flexibility that introduces two challenges. The first challenge is that each neuromodulator binds to many receptors, which in turn have different signalling mechanisms that affect the neuron (Table 1). Typically, the receptors are of two types: 1) ionotropic i.e. they regulate opening/closing of

System	Neuromodulator	Ionotropic receptor	Metabotropic receptor
Cholinergic	Acetylcholine	Nicotinic: nAChR	Muscarinic: mAChR (M1, M2, M3, M4, M5
Dopaminergic	Dopamine		D1, D2, D3, D4, D5
Norepinephrinergic *(noradrenergic*)	Norepinephrine (*noradrenaline)*		$\alpha_{1A\text{-}D}$, $\alpha_{2A\text{-}D}$ β_1, β_2, β_3
Serotonergic	Serotonin	5-HT_3	5-$HT_{1A,B,D\text{-}F}$, 5-$HT_{2A\text{-}C}$, 5-HT_4, 5-HT_5, 5-HT_6, 5-HT_7

Table 1: A simplified table depicting neuromodulators and their various receptors (*RBI Handbook of Receptor Classification*)[29].

ion channels present on the cell surface that affects action potentials, 2) metabotropic i.e. G-protein mediated, which when activated initiate complex signalling cascades that can trigger long-term effects on the cell such as formation or removal of synapses, synthesis or breakdown of other receptor types on the synaptic surface, and even help maintain activity for much longer[26–28] after the initial input has subsided. For example in working memory processing, the individual blocking of the *Cholinergic*, *Dopaminergic*, *Norepinephrinergic,* and *Glutamatergic* systems (*see Chapter IV for information*) all show similar effects even though they influence different signalling cascades. This leads to difficulties when attempting to assign specific functions to neuromodulators in cognitive processing. Additionally, it is likely that there are receptor subtypes that are yet to be discovered.

The second challenge is to measure the neuromodulator levels in the brain. Several techniques that have previously attempted to measure them had poor sensitivity and/or temporal resolution. This made it impossible to measure fast (< 1s) processes such as attention shifts. In *Chapter II*, we tried to use electrochemical probes to measure acetylcholine levels in awake-behaving macaque monkeys during an attention task. We encountered significant challenges that need to be resolved. In the discussion of that chapter (*Chapter II*), we highlight these challenges and offer possible solutions. It is possible that future advances in newer bio-compatible materials[30] such as PANI, PEDOT and thin film[31] enzyme based detectors may result in better sensors.

Taken together, we postulate that regardless of the task, modality, or cognitive process, attention enhances the overall 'quality' of information processed by the cortical circuitry by highlighting the information that is relevant to the subject's task.

Future research

In this dissertation, we saw attentional-feedback influenced information processing of stimuli during learning (*Chapter III*), perceptual grouping *(Chapter IV)*, working memory (*Chapter V*)*,* and conscious awareness (*Chapter VI)*, However, there is still a lot to understand and explore.

The cortical connectivity within and between areas of the cortex is quite complicated (*see Chapter I -1.1c*). The view of Hubel and Wiesel about the cortical hierarchy of areas that the visual system gradually builds up a sophisticated representation of the visual scene still largely holds true. However, over the years studies in humans and animals have shown that during a task many areas are active simultaneously. Therefore, an important question is how we distinguish between feedforward, feedback, and recurrent activity. We have gained some insight by studying response and temporal properties of neurons (see *Chapter I - 1.1e*) but many questions still remain to be addressed. Furthermore, in many tasks information is integrated across different modalities and across areas that are not activated by sensory input but other factors such as previous experience. The resolution of these complex interactions will give us a valuable insight into information processing in the brain.

Another challenge is to navigate the complexity presented by the neuromodulatory systems and their significance in information processing. Neuromodulatory systems often have a wide reach throughout the cortex with distinctive effects in different areas. Resolving this challenge would require pharmaceutical and technological developments such as creating new sensors (*see Chapter II -discussion*), drugs with target and spatial specificity, and methods to measure their effects on behaving animals.

Advances in technologies such as high-field fMRI[32–34] have allowed us to view the processing of signals in layers and cortical columns[35] of large areas of the cortex simultaneously. Optogenetic[36] methods allow us to control firing of neurons in awake-behaving animals using light. Although optogenetic tools have shown promise already, their implementation in non-human primate models such as *rhesus macaques*' is still under development[37]. Another new tool are DREADDS[38,39] (Designer Receptor Exclusively Activated by Designer Drugs), pharmaco-genetic substances that can also help us gain insight into the effect of neuromodulators on neuronal signalling. In parallel to the above technologies, many efforts are being made to refine and expand electrophysiological techniques such as implementing high-density neural electrode arrays (1000+ electrodes)[40] and wireless implantable sensors[41] ("neural dust"). The above advancements can help us gain a deeper insight into information processing by the cortex.

Conclusion

Taken together, it can be inferred that attention is an integral part of our conscious experience. It is likely an emergent phenomenon arising from dynamic interactions in distributed networks and is the psychological manifestation of neuronal processes such as feedforward-feedback signalling and neuromodulatory effects. Functionally, attention acts as a gatekeeper, linking signals from input pathways and those that are generated internally to help us effectively interact with the environment (Fig. 1).

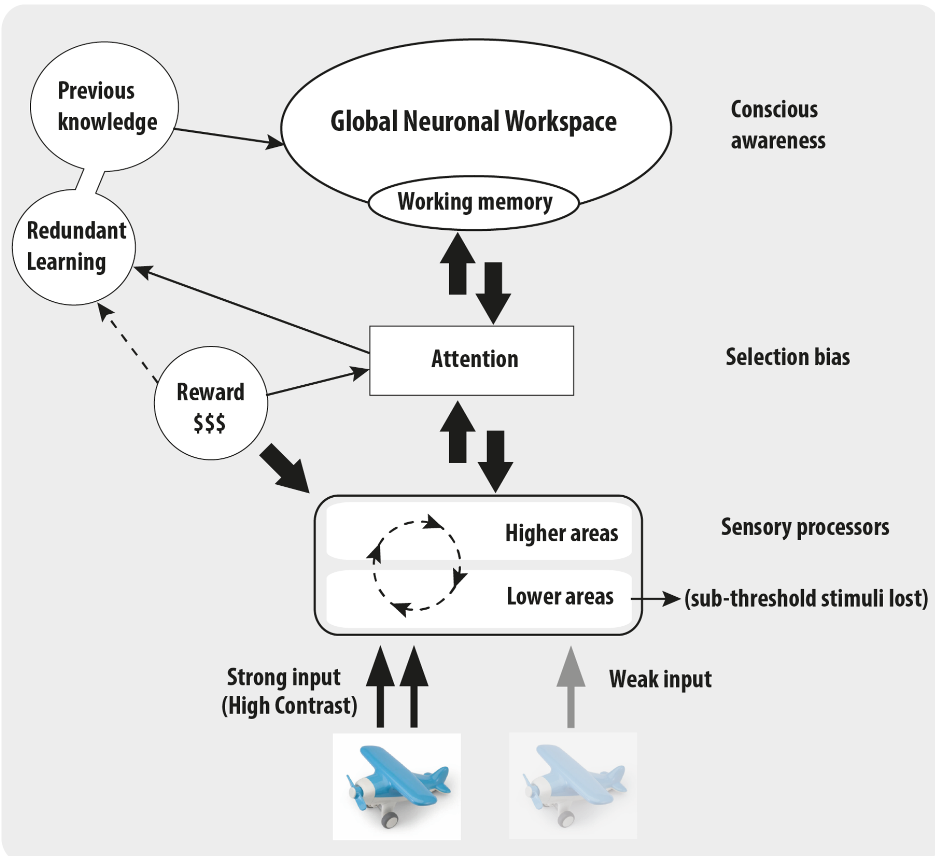

Figure 1: A speculative illustration of the role of attention and its influence in cortical processing based on key findings of this dissertation.
*(Perceptual learning processes/effects not shown.)

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