

BEHAVIORAL AND PHYSIOLOGICAL ENCODING OF VALUE AND VALIDITY IN THE
VISUAL CORTEX OF THE MACAQUE

by

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DEDICATION

This dissertation is dedicated to the Spirit of Truth and to my family. Without their support over the half decade, none of this would have been possible. My wife, Jenny, my son Watson, and my daughter Maddy are my inspiration and the source of my aspirations.

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ABSTRACT

Spatial attention and reward research in most humans and all animal models have inherent value and validity associated with task-relevant stimuli. To date, these variables have been investigated in isolation. Assumptions are made with the respect to the dissociability of value and validity effects on task performance and neural activity. Using a novel behavioral task, we varied value and validity within the same experiment in attempt to dissociate their effects on visual processing. Our results indicate that the assumption of dissociability between value and validity effects used to characterize attention and reward modulations is not a safe one to make. Researchers must consider complex interactions between these two variable quantities when investigating attention using incentives and while investigating incentive effects when attention is freely deployable.

CHAPTER ONE

GENERAL INTRODUCTION

Everyone knows what attention is. It is the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought. Focalization, concentration, of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others.”

–William James, *The Principles of Psychology*, 1890 –

Attention defines who we are. How we choose to apply it shapes our development and understanding. Attention is so ubiquitous and essential for daily living. Most people rarely contemplate how important attention really is, living day to day without much thought about how “taking possession of the mind” really works. James’ insights about attention in the 19th century have stood the test of time. The essence of James’ model is that attention is *intuitive*, *essential*, and *finite*.

Taking possession of the mind is a universal experience. We all know how essential it is to prioritize and direct our cognitive effort towards a select subset of the billions of bits of information that might bombard us at any given moment. In a crowded coffee shop absent of attention, I could not have a conversation with a colleague. Their message is being communicated in a sea of noisy background conversations, making decoding difficult for even the most advance signal processing algorithms.

Attention is a finite resource. If stretched to focus on multiple targets, its overall effectiveness is degraded. This is consistent with the brain having limited computational resources. Increasing attention at one location in the visual field, is thought to reduce computational power available at other locations. To optimize sensory performance, we must balance attention between locations. Those who find it difficult to focus, either chronic multi-

tasker to those who suffer from clinical disorders of attentional, like attention-deficit/hyperactivity disorder (ADHD), find quality of life degraded, often seeking interventions in the form of medications, cognitive behavioral therapy, and stimulus depleted environments. In our modern world, your sensory systems are not just overloaded, but are constantly being targeted by a variety of people and organizations. In our modern, always-on, technologically driven world, the “attention economy” has developed into an industry as communication networks link more people around the globe. Being able to direct attention externally provides new vectors to focus your perception, leading everyone from marketing executives to artificial intelligence software engineers to search for new ways to capture our attention in order to influence our behavior.

This may all seem quite harmless, but with greater and greater computational power behind optimization algorithms aimed at engagement, more of our time is surrendered by this type of attentional capture. While artificial neural nets may simply be taking advantage of our biological wetware to minimize some arbitrary cost function, the effects on human behavior are not without consequence. The lack of consideration about how attentional manipulation might impact brain’s circuitry may even raise ethical questions. While data trains algorithms, it can seem like the algorithms may be training the data generators, also known as our friends, family, neighbors, and community. Software that seeks to maximize “engagement” by any means possible has no ability to discern the unethical ways of accomplishing their computational end states, let alone leaving a trail of breadcrumbs for ethicists or programmers to decode exactly how they may have arranged themselves to do so.

These concerns are only amplified if we consider that the attentional control system interacts closely with other brain circuits that are critical for decision making, learning and memory. These mechanisms in tandem shape what we value, what we understand, and who we are. Our understanding of the behavior and physiology behind these interactions is still in its infancy. The isolation of variables in a laboratory setting is not without trade-offs, as the relationship between variables is “averaged” out, if not completely invisible. Literature to date has limited investigation into the relationships between aspects of attentional capture and those of valuation. Given the circumstances, humanity can ill-afford willful ignorance into how value influences attentional capture.

The revolution in computer science and information technology has propagated the use of engagement algorithms. This makes the competition for our attention ever the fiercer. This is not just between companies or news agencies, but also with our own volition. An understanding of our evolved representations of reward and how it interacts with attention can help define better boundaries in these mysterious places such as our brain and consciousness. The following introduction provides necessary background to provide context about why some assumptions present in valuation and attention literature need inspection. The visual system is the primary modality used in experiments to date. Visual information processing pathways are not just affected by attentional effort, but from abstract information about potential payoffs of decisions and their associated likelihoods. How validity and value information is encoded and to what level we can attribute to each observed effects on behavior and the neural activity in the extrastriate and posterior parietal cortices.

Attention

As of November 2021, there were over nine thousand published articles using the keywords ‘visual’ and ‘attention’ indexed in PubMed, a majority published in the last decade. Only about one in six contain neurophysiology, leaving any prospective investigator around 1500 papers to sort through. At a pace of one a day, it would take more than four years to review them all. At the current exponential growth rate (Carrasco, 2011), another one thousand papers would be produced during that time span. This expansion of interest appears more remarkable contrasted with the fact that in the 1970s the number of publications were near zero. Many experimental designs repeat the same basic frameworks used to study attention.

In 1980, a methodological revolution occurred providing new ways for psychologists and vision scientists to accurately quantify the effects of attention on human behavior. These novel approaches shaped (and continue to shape) the study of attention in the laboratory. Studies from Anne Treisman and Michael Posner’s laboratories demonstrated that the effects of attention on performance could be readily and accurately measured in the lab using target detection accuracy and reaction time data (Treisman and Gelade, 1980; Posner, 1980). This work complemented the recently developed “signal detection theory” framework (Green and Swets, 1974) for assessing behavioral (and later neuronal) sensitivity. By the mid-1980’s, researchers had adapted the experimental methods of Treisman and Posner for use with non-human primate observers, which in turn facilitated experimental studies of attentional modulation of cortical circuitry for the first time (Moran and Desimone, 1985; Pelli, 1985). These efforts paved the way for the characterization of attentional subclassification and identification of attention neural correlates in specific areas, primarily in the visual modality.

Characterizations of Attention

William James had already noted that there are two distinct types of attention: one that is passive, reflexive, and involuntary and another that is active, sustained, and voluntary (James, 1890). Today these are usually known as *exogenous* and *endogenous* attention, respectively. Attention can be further classified into feature (or feature-based), object, and spatial attention, all three of which can be either voluntary or involuntarily. A summary of each will help in distinguishing between the elements.

Involuntary Attention. If a baseball were to break through the window while you are reading of this sentence, your attentional focus would reflexively orient towards the ball or the broken window. *Exogenous attention* is generally transient in nature. Sustaining attention on the ball requires some sort of transfer between exogenous and endogenous processes.

Research on exogenous attention has revealed that deployment to a specific location rises and decays quickly, peaking at about 100-120 milliseconds (Chica and Lupianez, 2009; Hein, Rolke, and Ulich, 2006). Involuntary attention operates in both low and high noise conditions in contrast with that of voluntary attention, which shows effects primary in high noise environments (Lu and Doshier, 2000).

Voluntary Attention. In the laboratory, voluntary attention is typically controlled experimentally using cues (Posner, 1980). For visual spatial attention, cues typically indicate the likely location where a target stimulus will eventually appear in the visual field. Allocating voluntary attention in response to a cue takes approximately 300 milliseconds and can be readily sustained for an indefinite period of time by most observers (Liu, Stevens, and Carrasco, 2007). Voluntary attention is further subdivided in to overt and covert attention. Overt attention is when

the eyes move in response to the cue to bring the attended region or object onto the fovea, while covert attention is when the eyes remain fixed in the orbit and attention is “covertly” directed to a non-foveal location in the visual field (Carrasco, 2011).

Covert attention, which is attention without looking at the attended location, is used every day in the context of driving. Gaze often remains straight ahead, while the driver continues to attend peripherally to scan for signs or threats such as approaching vehicles or wildlife without losing sight of the car ahead. In many non-human primates, including the rhesus monkeys studied here, direct eye contact is perceived as a threat. Observing other monkeys using covert attention allows monkeys to observe more dominant conspecifics without drawing undesired, aggressive threat responses.

Brain areas in the occipital, parietal, and frontal cortex exhibit enhanced responses during both endogenous and exogenous shifts of spatial attention (Brefczynski and DeYo, 1999; Beck and Kastner, 2005), with a limited understanding of specific neural substrates in common, though consensus is they are likely to have partial overlap but are ultimately independent (Peelen et al., 2004). Another distinguishing difference is exogenous attention is not mediated by feedback mechanisms from frontal and parietal areas. (Kastner and Ungerleider, 2000; Fries, et al., 2001). The transitory characteristic of exogenous attentional capture typically gives way to sustained or voluntary mechanisms after initial re-orienting (Maclean, et al., 2009). Most modern neurophysiological studies of attention have focused on endogenous, or voluntary attention. Endogenous attention can often be better controlled in the laboratory and because endogenous attention can readily be sustained for several seconds or longer, it is more amenable to fMRI, EEG and single neuron recording methods.

Receptive field sizes for foveal neurons are extremely small and have complex properties not fully understood in comparison to parafoveal or periphery neurons (Gattass, et al. 1998; Masland, 2001). Neuronal receptive fields systematically increase in size with both increasing retinal eccentricity and the number of synapses beyond the retina. Most attentional neurophysiology research has been performed in parafoveal extrastriate areas (e.g., V4, MT, LIP, etc.) in feedforward visual cortical areas, where attention modulations are most easily detectable (Gattass, et al., 2005). The comparative ease in distinguishing between response profiles between neurons in voluntary, covert, and spatial determined stimuli has led to this line of investigation in characterizing and identifying neural correlates of attention to dominate the field. Other aspects of a stimulus can be attended to such as a feature or a combination of features of an object. These elements can be attended to involuntary and voluntary depending on behavioral relevance or saliency in comparison to background noise. Further breakdown of attention has categorized attention into feature, object, and spatial based attentional facilitation.

Feature-based Attention. Attention can be directed to specific visual features, such as orientation, a direction of motion, and color (Maunsell and Treu, 2006), independent of location. In fact, this was one of the findings from the original Treisman and Gelade study – feature-based attention can operate in parallel across the visual field to efficiently select all items that share an attended feature (i.e., all red items or all L-shaped items). The enhancement of feature components throughout the visual field is useful for prioritizing behaviorally relevant stimuli distinguishable by a single feature. In visual search experiments, at least one feature distinguishes relevant stimuli from background. Targets are typically defined in advanced and

placed in an array of distractors. Increased sensitivity is achieved by enhancing representations of the attended feature and suppressing those that do not (Wolfe and Horowitz, 2004).

Feature-based attention experiments in psychophysics have demonstrated improved detection and enhancement of behavioral performance such as a reduction in reaction time (Rossi and Paradiso, 1995; Cohen and Magen, 1999; Saenz, et al., 2003). Neural correlates of feature attention have been found throughout the visual cortex via fMRI studies (Saenz, et al., 2002). Single-unit studies in V4 and MT suggest that unlike spatial attention which enhances or suppresses neural activity without changing underlying tuning properties, feature attention in these areas can shift or widen tuning curves (McAdams and Maunsell, 1999; Treue and Martinez-Trujillo, 1999). Encoding of behavioral relevance (i.e., facilitation of responses to behaviorally relevant stimuli or suppression of responses to behaviorally irrelevant stimuli) has also been observed in the parietal cortex (Assad, 2003). Feature-based attention studies are less prevalent throughout literature. In part this is because spatial attention is better understood in humans and at the behavioral level. Studies of feature-based attention are also complicated by the fact that every stimulus has both a spatial location and features, making it difficult to really study feature-based attention in the absence of spatial effects. An analogous situation exists for object attention – in short, the attribution of enhancement effects specifically to feature-based attention can be difficult in a complex visual scene that might also engage spatial and object attention circuits.

Object-Based Attention. When target discrimination requires the combination of more than one feature, parallel processing mechanisms and feature-attention enhancements become harder to measure and characterize. Performance and reaction times are degraded as additional

target features are added, creating a requirement of conjunctive feature search, where reaction times are much slower and requires more attentional effort to maintain performance (Treisman and Gelade, 1980). Multiple features are characteristics of an object. Object-based attention is characterized differently than feature-based attention. What constitutes an object depends on the physical properties of a stimulus and how we deconstruct the visual field aligned with a behavioral goal (Baylis & Driver, 1992; Kimchi, Yeshurun, & Cohen-Savranzky, 2007; Marr, 1982).

Object shapes have been shown to create formed-derived directionality which demonstrated attentional benefit in the spatial locations inferred by object shape (Sigudarodottir, Michalak, and Sheinberg, 2014). Spatial attributes of objects have been shown to affect attentional modulation induced by involuntary or exogenous cues. In a parietal lesion study, the cost of an invalid cue was greater for targets in an uncued object for normal patients, indicating an object-based component (Egly, Driver, and Rafal, 1994).

Effects of object-based attention are difficult to parse from its feature attributes and spatial location within a visual field. Visual neuron receptive fields are retinotopic, meaning the mapping of visual input from the retina to cortical neurons. In V1, mapping is simpler than in downstream areas such as V4 and MT, where more complex “second-order” visual field representations mapping occurs, more complex still are those found in the parietal cortex (Rosa, 2002; Brewer, Wade, Wandell, 2005). The retinotopy success of the mammalian brain has influenced most investigations into visual attention towards spatial attention. Typically, a contrasting of behavior and neural activity profiles of retinotopically different but identical feature/object attributes to control for feature and object-based attention effects.

Space-based Attention. Prior to the 1980s, attention was believed to exclusively directed to location in space (Eriksen and Eriksen, 1974). Spatial attention experimental paradigms are often designed from “Posner Cueing” (Posner, 1980). In a Posner cueing paradigm, a central fixation square is presented along with a spatially orienting cue (typically an arrow pointing to the left or right visual field). The endogenous spatial cue is only partially valid (usually at 80%) meaning that part of the time the unattended field contains task detection or discrimination requirements. Responses between attended and unattended conditions are compared between invalid and valid condition sets for behavior and neuronal metrics. Utilizing the principles of this experimental framework, most inferences into attention have been derived through voluntary, covert, spatial attention.

Attention and Vision. There are many aspects of attention that continue to be debated, defined, and refined in the neuroscience and psychology literature and it is worth noting that while the focus of this work, and work throughout the field, is on visual perception and we will use visual cues to focus attention, it is clear that attention can influence perception in virtually all sensory modalities (including olfaction) and can be focused in response to cues occurring in all modalities. Posner and Peterson (1990), based on early neuroimaging studies in humans, proposed the existence of three distinct functional and anatomical networks related to attention: *alerting*, *orienting*, and *executive control*. In general, alerting is defined as a reaching a state of increased sensitivity to incoming stimuli. Orienting refers to orienting the body, sensory transducers or even attention towards an object in the visual field responsible for alerting. And executive control is the process of selecting appropriate targets for orienting when presented with multiple competing locations, features, and objects related to a goal state or that trigger alerting.

Both cortical and subcortical brain regions have been implicated in each of these three networks and include occipital to frontal lobes, and everything in between. The characterization of attention is dependent on scale and component. The separate characterizations of attention have led research into specific areas of focus. It is difficult to control for specific features and spatial locations during experiments, leading researchers to further reduce experimental design to isolate these environmental variables. This reduction of a complex system inherently risks misunderstandings and remains a reality researchers must contend with (Sigenfeld and Bar-Yam, 2019). Regardless of this risk, some findings have shown to be robust.

As noted above, 1980 was a landmark year for attention research. For the first time, researchers were able to show convincingly that “attention” was not the vague and nebulous phenomenon alluded to by James, but something that could be reliably quantified. Treisman and Gelade measured observers’ ability to detect targets appearing among non-target distractors. Posner and colleagues developed a novel cueing paradigm that control attentional targeting. Together these seminal studies showed that accuracy and reaction times are improved with the application of attention and that attention couple be reliably placed under experimental control (Treisman and Gelade, 1980; Posner, 1980; Posner and Cohen, 1984). This dissertation’s line of investigation is voluntary, covert, spatial attention.

Neurophysiology of Attention. Action potentials are metabolically expensive – Attwell and Laughlin (2001) estimated that ATP-dependent restoration of ionic gradients after action potentials dominates the brain’s metabolic demands. In primates and other vertebrates, there is growing evidence that evolution has worked to maximize the efficiency of neural encoding to reduce energy consumption, i.e., the so-called “efficient coding” hypothesis (Barlow...).

Information theoretical studies by James Stone suggests that metabolic efficiency is how the brain optimizes its complex task of information communication and less on efficient coding (Stone, 2018). Attention is another way the brain can be more efficient – attention effectively prioritizes various aspects of visual processing so that not all stimuli require full computational processing, which in turn, reduces overall energy consumption. Studies in the extrastriate cortex have shown attentional effects of neural firing rate gain and suppression for a spatially attended stimuli (Carrasco, 2011). It has also been shown that a reduction interneuronal correlations in populations of neurons correlate with performance (Cohen and Maunsell, 2009). Modeling has suggested that the reduction in these correlations help propel the signal produced by the attended feature or object within a range of neurons (Cohen and Maunsell, 2009).

Extrastriate cortex, specifically area V4, has received a lot of investigative attention in pursuit of attentional research in the visual modality. But while V4 was the first area where attentional modulation was observed in single neurons (Moran & Desimone, 1985), it is far from the only one.

In addition to these cortical areas, attention modulation has been detected in superior colliculus, an ancient and highly conserved subcortical structure implicated in orienting responses in general, and, in primates specifically, eye movements (Kraulis, 2014), and the thalamus. fMRI studies have shown a multitude of areas with BOLD differences when comparing attention and unattended states. In their entirety, attentional research has implicated a complex interaction between subcortical and cortical visual processing structures. However, neurophysiology investigations into subcortical structures of primates and humans are difficult and risky. It has been hard to identify and verify neural correlates.

Attention research has utilized mammalian animal models to significant effect. However, most studies in this require an incentive to induce an attentional state within an experimental paradigm. Does this confound those results? Are the attention effects induced from valuation mechanisms separable from the effect from incentives themselves?

Valuation

Like attention, we all have an intuitive idea of what it means for something to be of high or low “value.” At some level, we all understand that many decisions consider the potential gains and losses associated with outcomes. Through either experience or observation, we develop an ability to assign value to objects and actions. The natural environment is not static, and neither are we. Changes to object and action values may be due to our own biological or psychology needs (i.e., internal state changes). Dirty water is not appealing when satiated but may become highly desirable when thirsty. The brain has evolved to encode value and to use value to inform decision making. Anticipatory outcomes are compared to actual outcomes to generate prediction errors, which are in turn through to be used to update value representations (Gold and Shadlen, 1999) and behavior strategies (Sutton and Barto, 2005). Perceptual cues can inform us about context, such as a sense of probability of outcome, which can change how stimuli are processed. These elements are involved in a decision-making cycle where environmental stimuli are used to make decisions based on encoded anticipatory choice outcomes with feedback updating representations.

Valuation in the Visual Modality

In a landmark study in 1999 (see figure 1), Paul Glimcher and Michael Platt performed an experiment to test key principles of economic decision theory. They showed two visually identical objects to non-human primate observers under stochastic reward conditions, indicating which object was of higher value through iterative experience. Observers were required to saccade to one of the objects and were rewarded stochastically after the saccade. At the same time Glimcher and Platt recorded neural activity in parietal area LIP. The

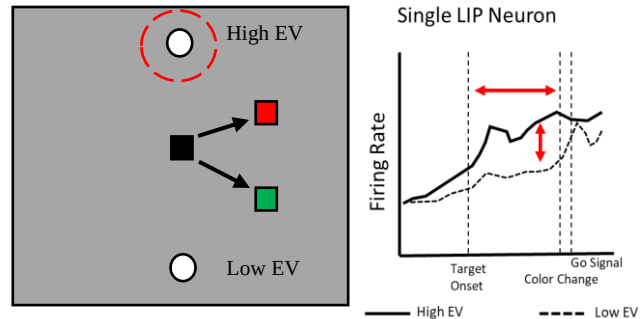


Figure 1: Expected Value Modulations to LIP Neural Activity. A central fixation square begins the experiment, and two identical stimuli appear, one location is associated with a large reward, the other with a low reward. The color of the central cue instructs the monkey which location to saccade towards. When the fixation square disappears, and a saccade is made to the cued location. In interleaved blocks, the expected value (EV) the locations were reversed. Inset shows neural responses to the stimulus inside the RF in the blocks when the stimulus was high EV and low EV Adopted

report described both forced choice and free choice paradigms. What they observed has sparked the creation of a new sub-discipline of neuroscience: *neuroeconomics*. They found that many LIP neurons were sensitive to nominal expected value (EV) of the stimuli in their RF. That is, when the same stimulus was associated with either a high or low EV, the visual response of the cell was modulated, even though the visual stimulation conditions were identical in the high and low value conditions. When the animals could choose freely, the choices observers make, and neural activity were correlated with the relative amount of gain that the animal can expect from each response. Lastly, LIP neurons showed modulated responses to the gain expected prior to the

initiation of a saccade, needed for observers to realize the reward as part of the task. (Platt and Glimcher, 1999).

The field of neuroeconomics attempts to connecting concepts from classical economic theory to neural circuits. As we saw was the case for attention, neuroeconomic studies over the last 20 years have revealed a wide range of brain regions sensitive to reward value, many of which also show attentional modulation. Mirroring the explosive growth in attentional research, the field has seen an exponential increase in the number of neuroeconomics papers over the past 20 years. The primary tools used to elicit economic behavior reside in experimental economics and experimental game theory. These concepts are too rich to explain in this short section of this introduction but have their intellectual origins from economic observations recorded human history and include great minds such as John Von Neuman and other mathematicians in developing these theories. The relevance to this thesis topic is not so much as how experiments were conducted, but on where and how they affect regions of the brain.

In a series of fMRI studies that presented stimulus values for appetitive food items, BOLD signal differences were detected in the ventromedial prefrontal cortex (vmPFC), the dorsal later prefrontal cortex (dlPFC), and subcortical structures such as the ventral striatum and posterior cingulate cortex. (Grabenhorst et al, 2010; Kable and Glimcher 2007). It is unsurprising that the bulk of evidence of valuation and decision making comes from the frontal cortex, long established as the center for executive control functions. Frontal areas such as FEF, and *supplementary eye field* (SEF) are implicated in visual processing, especially with respect to attention as covered in the previous section. SEF has been shown to modulate its activity during a *metacognition* task about choices made but before reward delivery (Middlebrooks and

Sommer, 2012). The anatomical connections of the PFC, OFC, ACC, and striatum indicate they interact and work together during action valuation.

While the strongest signals related to valuation appear in frontal cortex, the anatomical and functional connections between frontal and parietal and other visual areas have been well documented (Sporns, 2003). The network hubs, like frontal cortex, are sources of reward-related modulation observed in earlier sensory areas.

Several *calcium imaging* studies of mouse V1 have

indicated that stimuli

associated with reward had enhanced neural representation. (Henscke, et al, 2020; Monk, et al,

2020).

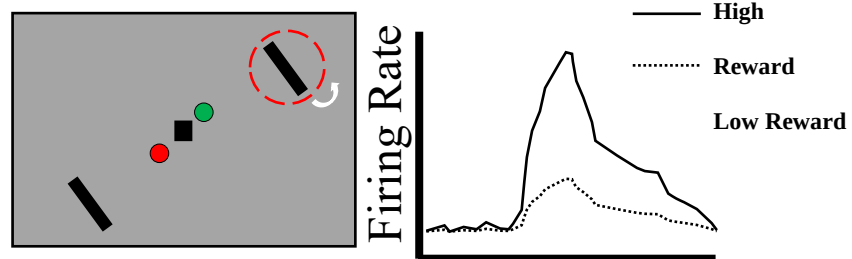


Figure 2: Reward Modulations to V4 Neural Activity. A central fixation square begins the experiment, and two identical stimuli appear. Animal observers eye gaze remain on the fixation square and response when the orientation of one of the bars changes. Color cues are presented at central fixation to indicate reward values associated with each stimulus. Figure modified from Baruni, Lau, and Saltzman, 2015.

In primates' activity in area V4 has been shown to be modulated by reward magnitude (Baruni, Lau, and Saltzman, 2016; Shapcott, et al, 2020). Further down the ventral processing stream, stimulus and reward associations have been observed in IT, (Spriegler and Mishkin, 1981), and lesions in the medial forebrain of Rhesus monkeys lead to impaired object reward associations (Easton and Gaffan, 2001). In the dorsal processing stream, MT recordings suggest evidence of reward modulation when compared with punishment (Murty, et al, 2017; Steel, et al, 2019).

Most of the investigations of reward modulation in posterior cortical areas center around the posterior parietal cortex. fMRI and neurophysiological studies have demonstrated modulated neural activity in this area with the representation of task-reward associations (Wisniewski, et al, 2015), reward-value based gain control (Louie, Gratton, and Glimcher, 2011), correlations with desirability of action (Dorris and Glimcher, 2004), social target value (Klein, O. Deaner, and Platt, 2008), and in humans, value-based modulations has been shown in the parietal area in conjunction with the frontal cortex (Serences, 2018).

The interaction between the visual system and reward structures is not entirely clear. There is substantial evidence of the parietal cortex's encoding of a visual saliency map, incorporating visual sensory information with goal-state information from the frontal cortex (Gilbert and Li, 2013; Itti and Koch, 2000; Leathers and Olson, 2012; Goldberg, et al, 2006). Action value as predictable by a reward cue is a factor in the construction a saliency map during the duration of task. Reward modulations in this instance resemble those of attention, with similar gain and suppression effects found throughout both the ventral and dorsal streams, in the parietal cortex, and frontal areas such as FEF and SEF.

Attention and Value Interactions

Attention and valuation share anatomical connections, network hub areas, and even use similar neuromodulators (Pessoa, 2015). Anatomical connections between known attention and valuation areas. An example is the prefrontal cortex (PFC), an executive control of attention (Rossi, Pessoa, Desimone, & Ungerleider, 2009) and an area known for its response to value, the orbitofrontal cortex (OFC). (Barbas & Pandya, 1989). The cingulate cortex, also with

connections to PFC, has demonstrated correlation with stimulus value (Rushworth & Behrens, 2008).

Network hubs (i.e., brain regions that are highly interconnected with other areas, such as

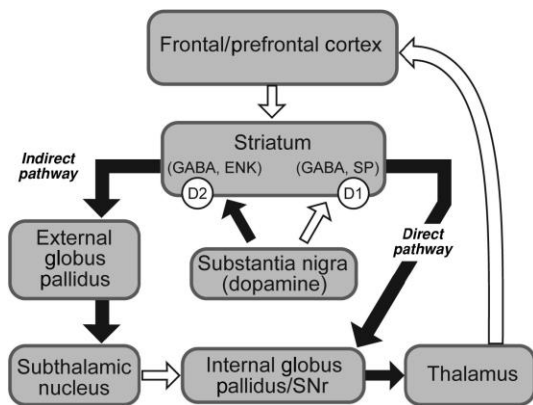


Figure 3: Frontal/Prefrontal-subcortical reward pathways. Adopted from Lichter, 2013.

the dorsal-medial prefrontal cortex) are involved in all kinds of neural processes including attention, working memory and valuation. (Cassaday, Nelson, & Pezze, 2014, Rushworth & Behrens, 2008). These anatomical connections along with hub regions modulate other areas across the brain. For example, an MRI study of human observers were asked to do a response-conflict task

(Kinnison, Padmala, Choi, & Pessoa, 2012). BOLD responses showed significant cortical and subcortical area activity during the task. They then categorized the activity into two separate networks, an attentional network, and a value network. The value network comprised OFC, anterior insular, medial prefrontal cortex (mPFC), posterior cingulate cortex (PCC), frontal eye field (FEF), caudate, putamen, nucleus accumbens, and midbrain. Through these findings they suggested the mechanism in which reward affects attention: reward cue enhances the activity of the value network and through coupling, engagement of the fronto-parietal attentional regions increases, and this enhancement improves the efficiency of visual processing (Kinnison et al., 2012). It remains unclear which component of neural activity creates perceptual benefit from reward and attention. (Noudoost & Moore, 2011).

With respect to neuromodulators, studies indicate that dopamine (DA) can modulate the efficacy of excitatory responses in way that is optimized for DA level whereas the synaptic efficacy declines outside of this amount (Noudoost & Moore, 2011). Studies have established that PFC DA effects attention by modulating the signals in sensory cortical areas. In a simultaneous recording of V4 and FEF neurons, D1R-mediated FEF activity was manipulated by injecting a D1 antagonist into sites within FEF. V4 neurons with similar spatial receptive fields as corresponding FEF manipulated neurons, the visual stimulus inside the RF was chosen more often as a saccade target. It was also observed that during passive fixation, the gain of visual signals showed an enhanced magnitude of response, a more selective stimulus orientation tuning and a more coherent response profile, all similar effects of covert attention in the extrastriate cortex. Manipulation of D2R yielded no enhancement of response yet did show preference to target selection. These dissociable effects of DA point to the separate roles of DA in decision making and attention gain modulation (Noudoost & Moore, 2011). PFC is also involved with working memory, showing sustained, persistent activity. Studies have shown D1Rs can modulate this persistent activity, making clarity between attention executive control and working memory linked in PFC (Gao, Krimer, & Goldman-Rakic, 2012).

While reward can affect selective attention, the underlying neural mechanisms and circuit-level organization of this interaction remain unclear. Selective attention modulations visual processing and in turn modulates perception (Shore, Spence, and Klein, 2001). It is not entirely clear how reward affects perception and decision making directly. The basal ganglia (BG) have shown an essential role in choice behavior (Bogacz, 2007). In a meta-analysis of decision-making areas, brain activity was increased in the bilateral pre-supplementary motor area

(pre-SMA), bilateral anterior insula, the right putamen, the right opercular supramarginal area (pFop), and the left middle frontal gyrus (MFG) showed significant activity in most studies.

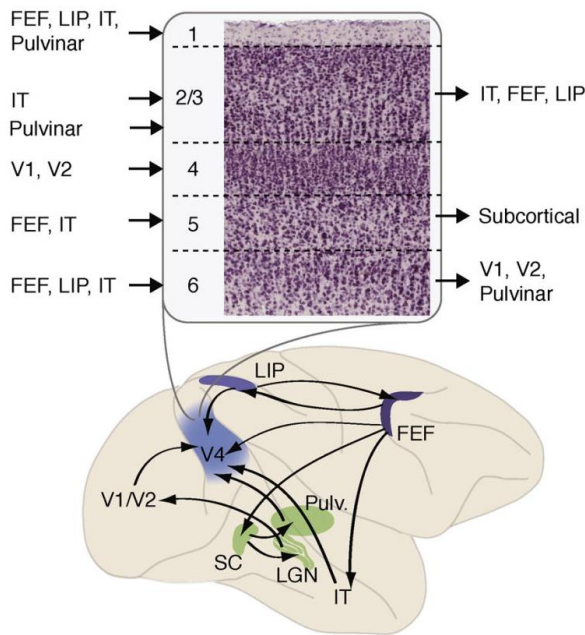


Figure 4. Routes for attentional signals to V4 and LIP. Corticocortical feedback projections from FEF, LIP, IT synapse in superficial and deep layers. Pulvinar projections synapse to V4. Feedforward input from visual areas synapse at layer four in V4 with layers 2 and 3 projecting to IT. FEF projects to subcortical structures such as SC and striatum in addition to V4 and LIP. SC projects to the pulvinar and LGN. Figure adopted from Noudoost, et al., 2011.

(Keuken et al., 2014). They also explored the regions which showed the highest differential activity to rewarding in contrast to not rewarding choice behavior. They found that the bilateral striatum, right substantia nigra, and the left insula were the most differential activity. Diedrich and Busemayer (2006) proposed that decision making in the presence of reward information comprises two stages: in the first stage, the sensory information is processed with no influence of reward. Next, in the second stage, reward information affects the process and biases the perceptual choice towards the more rewarding option. Other studies have

proposed that reward information explicitly modulates the sensory processing like selective attention, causing perceptual bias in decision making (Liston & Stone, 2008; Voss et al., 2008). These studies rely heavily on modeling between choice behavior and reaction times. Neural correlates of reward modulation in sensory areas have not had much investigation.

The exploitation of external cues to contextualize the environment and facilitate decision making underlies the processes of learning. Action outcomes associated with decisions or choices made facilitate learning. However, the sensory system does not provide the perfect information, therefore inference based on context is often required during decision making under natural conditions. The stochastic nature of the environment can create challenges to learning, especially in ambiguity. The assignment of meaning to sensory cues therefore is important to survival and thus evolutionary success. It should be no surprise that neural mechanisms have developed to contextualize and assign meaning to these sensory stimuli. The deployment of attention to decipher the proper meaning of broad sensory information to exploit other environment details facilitates this abstract meaning assignment. The enhancement of auditory perception helps distinguish sounds of leaves and when combined with sensations of wind can reduce uncertainty of a threat and thus the actions likely selected by the bird will be different than when a predator is identified.

In the above case of the bird, how much of these mechanisms are innately present and how many are designed to be modulated for nuance understanding and long-term learning of the environment is still a subject with much investigation required. The general trend of the evolutionary hierarchy culminates at humans with a large frontal lobe compared to every species on earth, attributed to our ability to learn and create simulations for potential actions, selecting one, and perceiving and incorporating the environmental feedback of that action. This process leads toward confidence in expected outcomes of a set of actions given an environment. In this way, stimulus detection or discrimination is followed by a degree of confidence and certainty of

choice. (Grimaldi, Lau, & Basso, 2015; Kepecs, Uchida, Zariwala, & Mainen, 2008). How this process is completed by the brain is a mystery.

Neural correlates of *saliency* and decision making have been found in areas such as LIP, FEF, SC, and caudate nucleus of the basal ganglia. (Platt and Glimcher, 1999; Gold and Shadlen, 2000; Scherberger and Anderson, 2007; Ding and Gold, 2010). Working memory and long-term memory are also systems that interact with reward and attention and play a role in the ability to ascertain saliency and select from a set of action-outcome prediction pairs. Patients with amnesia have a reduction in volume of their prefrontal cortex and thalamus. Other patients with lesions in the anterior prefrontal cortex show reduced confidence in the decisions they make (Del Cu, et al, 2009). These findings are support in *transcranial magnetic stimulation* (TMS) studies of the prefrontal cortex increased uncertainty in decision-making but maintained perceptual discrimination ability (Rounis, et al, 2010). It is well established that decisions are highly affected by expected reward from an action. The ventral striatum has been found to show increased activity when observers reported confidences in their choice of actions. It has been established that the ventral striatum is involved with reward processing, with activity levels fluctuating with reward outcomes (Hebert et al, 2016).

These findings create a complex interaction between subcortical and cortical brain areas. In modeling of these interactions, a suggested role of dopamine signals not only reflect reward *prediction error* but also confidence of perceptual accuracy (Notomoto, et al, 2017) suggesting a role for dopamine during the decision process itself, not just decision evaluation. Non-human primate studies often require the initiation by animal observers to begin a task. Animals routinely opt-out when they reach *satiation*, boredom, are distracted or are irritated. An increase in activity

of the pulvinar for correct and incorrect has been showed when compared to trials in which the animal observers opted out. When the pulvinar was inhibited using a *GABA* agent, animals were more likely to opt-out of task initiation more often. (Li, et al, 2012).

The environment changes over time. These changes create uncertainty within any agent conducting actions during a dynamic state. In a study two major types of uncertainty, expected uncertainty and unexpected uncertainty were compared. Researchers suggested that *Acetylcholine* signals associated with expected while *norepinephrine* signals were associated with unexpected uncertainty (Yu and Dayan, 2005). Acetylcholine has been implicated in increased attention application (Noudoost and Moore, 2011), suggesting attention interactions within the processes of analyzing uncertainty from environmental cues. Studies in rodents have proposed sensory processing may be modulated by PFC and the ascending cholinergic projections (Sarter, et al, 2005).

Distinguishing between Validity and Value Effects

Attention is an essential component of naturally occurring goal-directed behavior. Spatial attention creates a spatially restricted or focused region of enhanced or suppressed responses to sensory stimuli. Feature-based visual attention serves as a selection mechanism that enhances processing of specific behaviorally relevant visual scene features, regardless of spatial location. Attention is thought to filter and prioritize incoming sensory signals by synthesizing internal, topographical representations of visual salience in the physical environment (Bisley, et al, 2001; Falkner, Suresh, and Goldberg, 2010).

Information represented in the salience map can be used to choose from a set of actions directed at different visual field location; importantly, each action (e.g., saccading or initiating a

reach to the location) has a corresponding expected value, that is, expected reward associated with the choosing that action. Expected value coding is distributed throughout the brain, including parts of visual cortex (Goldberg, et al, 2006; Anderson, 2016).

Pathologies of the attentional control and valuation circuits are associated with a host of cognitive disorders: attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), Schizophrenia, anxiety, and depression (Chun, Golomb, and Turk-Brown, 2011). To date it has been difficult to find clear neural pathologies associated with these disorders (APA, 2013); and improved understanding of the functional networks underlying attentional control and action value encoding that includes their interactions, would be a major step towards improving diagnostics and therapeutics for these conditions. In addition to these known pathologies, the *attention economy* has led to heavy investment in big data analysis regarding engagement and choices. Optimization algorithms have been generated to maximize engagement and profit for these actors with little acknowledgement or concern to the effect it has on our attention and valuation systems.

The visual system in primates is well developed and highly conserved in a few areas, early processing areas among them (Brewer, et al, 2002). Attention and expected value research in these areas has occurred the last twenty plus years, but a gap in knowledge surrounding their interaction. At both the behavioral and physiological level, modulation of sensory processing by attention and expected value are remarkably similar and can be easily confused. Since the seminal work of Posner (1980) and Treisman (1980), it has been well accepted that spatial attention can reduce reaction time and increase accuracy on detection and discrimination tasks in humans and animals.

More recently, it has become clear that reaction times and accuracy are similarly modulated when targets have high value or are associated with large probability of reward (Krajbich and Rangel, 2011). This leads to a potential confound – when studies of expected value find that high value targets are associated with faster reaction times or increased performance, is the observed behavioral enhancement caused by the reward conditions? Or is it because high value targets happen to draw our attention, making the proximal source of enhancement attentional modulation? This confound is significant in behavioral studies, which have demonstrated that both attention and expected value are correlated with increased behavioral accuracy, saccade precision, pupil size; (McCoy and Theeuwes, 2018; Gallivan, et al, 2018) and in neurophysiological studies of single neurons, where attention and expected value changes have both been reported to result in similar patterns of firing rate modulation, decreased noise correlations, and changes in local field potential (LFP) power. In fact, based solely on neurophysiological observations of increased firing rates in visual and frontal cortical areas whether stimuli driving responses are attended or have high expected value (Moore and Zirnsak, 2017; Surgrue, Corrado, and Newsome, 2004).

In the laboratory, behavior is often motivated by asking observers to perform carefully designed (and often esoteric) tasks in return for rewards. Rewards can take many forms – in studies of human observers, rewards are often monetary, but can also be more abstract (e.g., points in a competitive setting). In animal studies, rewards are more typically delivered as desirable foods or fluids. In animal studies, behavioral training depends on rewards. This means that even in studies of non-reward systems (e.g., attention), rewards are used to incentivize stable performance over time and between observers. As noted above, this potentially confounds the

effects of the dependent variable (e.g., attention) and reward expectation. To give a concrete example, consider a classical Posner cueing experiment, where observers are cued to attend to either the left or right side of a display and the cue is 75% valid (that is, when the cue indicates a target on the right, the probability the target will appear on the right is 75%, so on 25% of trials the target will appear on the left). In the traditional “attentional” framework, a cue to the right directs spatial attention to the right side of the display. However, if we consider the task in a “value” framework, the expected value associated with the right side of the display is 75% of the reward size, while the location on the left has an expected value of 25% of the reward size. This is because expected value of each choice (left or right) is the product of the reward size and the probability of the target appearing at each location. The two sides of the screen, therefore, are associated with different attentional states (attend-in vs attend-out) and different expected value.

With a few exceptions (Munneke, et al, 2015; Bucker and Theeuwes, 2016), traditional attentional paradigms do not effectively distinguish between attentional facilitation and the effects of changing value. The same is also true for traditional neuroeconomic studies of value coding, where value coding is potentially confounded with the effects of attention, as attention may be automatically deployed to high value targets. To date, researchers have ignored possible confounds, focusing on either attention or reward modulation, but not interactions between the two. Full dissociation of these two essential modulatory processes is challenging, particularly in the case of animal studies, where it is always necessary to use rewards to maintain consistent performance, but the effect of reward is often not fully considered if reward processing is not being explicitly studied. While recent published reports have recognized this problem, to date

there has been limited progress in the field addressing it, particularly in the context of neurophysiology.

As discussed above, the first published report of attentional modulation of single neurons was Desimone and Moran's (1985) study of area V4 neurons in behaving primates. They described the attentionally-driven changes in the "selectivity" of V4 neurons. In their experiment, two stimuli were presented in the RF of a single neuron – one "good" stimulus and one "bad" stimulus (corresponding to green and red stimuli in Figure 5, respectively) – the good stimulus, presented in isolation, elicited activity, while the bad stimulus did not. In one experiment, the bad stimuli were associated with rewards, while the good stimuli were not; both appeared simultaneously in the receptive field. The interpretation at the time was that this modulation corresponded to attentional modulation – that is, attention towards one stimulus suppressed the response to the other. The assumption is that attentional deployment was on the reward producing stimuli and neural activity of the cell when presented with both stimuli, shut down activity. When the reward linked stimuli was placed

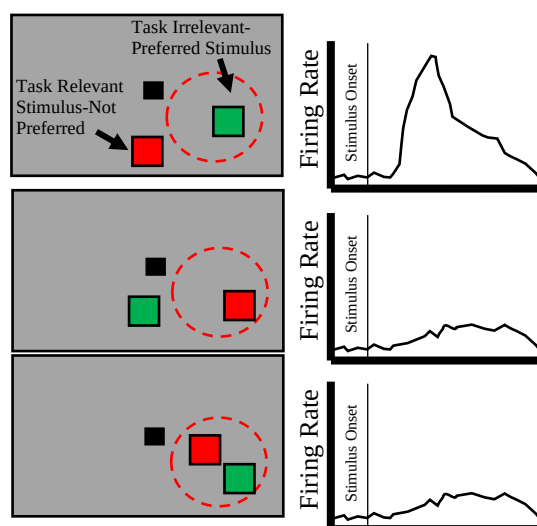


Figure 5: Gating of Sensory Information. Neural activity was recording from V4 neurons with a preferred (change in firing rates) and non-preferred stimulus in the receptive field. When the non-preferred stimulus was linked to task-relevance or reward linked, the activity when the preferred stimulus was present did not occur. This effect was eliminated when the preferred stimulus was task relevant when both stimuli occupied the receptive field. Figure modified from Moran and Desimone, 1985.

outside of the cell's receptive field, the neuron again showed activity present as it did when identifying higher activity (Desimone and Moran, 1985).

Posner cueing relies on spatial validity to compare attended and unattended responses. The incentive structure is designed to apply attention towards the spatial cue because it has a higher probability of target appearance. This has an inherent expected value to that location. In stochastic reward experiments, a stimulus has an associated expected value with attention freely deployable. The relationship between value of a reward and the validity of a spatial cue is not understood. To date, no study was found to independent change variables in the same experiment. This begs the question for how dissociable and attributable observed effects between validity and value information are?

Hypothesis

Value and validity effects on behavior and neural activity are not dissociable.

Definitions

Validity. There Validity is defined by the correctness of the spatial cue. For example, in a Posner cueing paradigm, the cue that suggests target appearance on one side of the visual field is only 80% valid, meaning 20% of the time the target appears on the other side. Spatial attention is quantified by comparing behavior and neural activity between the two locations. Two validities will be used, 90% and 70%, categorized as high and low validity, respectively.

Value. Value is defined as the potential reward delivered when a task is performed correctly. The reward delivered is not stochastically varied as in expected value experiments but

is cued as an absolute reward value. Two reward values will be used, categorized as high and low, with high rewards at three times the volume of that of low rewards.

Dissociability Tests

Statistical Independence. Independence between two variables X and Y with marginal probability density $f(x)$ and $f(y)$ and a joint probability density function $f(x, y)$ is defined by the identity: $\frac{f(x,y)}{f(x)f(y)} = 1$. Each variable combination will undergo an examination for independence and all evidence considered in determining whether to reject or fail to reject the hypothesis.

Condition Sets. Validity and value in previous experiments have been limited to a single element in at least one of the variables. At least two elements are required to test the dissociability. Experimental design and anatomical considerations require the distinction between cued and uncued hemifields. Specific conditions are the product of value, validity, and spatial hemifield defined as: value= {High, Low}, validity= {High, Low}, hemifield= {Cued, Uncued}.

Cartesian Product of Effects. Comparing the differences between a single variable in condition sets will allow for a range of tests into statistical independence (i.e., Cued – Uncued observations between combinations of value and validity). This sets up three cartesian product tables:

Modulations in Cued-Uncued Conditions		
Value/Validity	V (High Validity)	v (Low Validity)
R (High value)	RV	Rv
r (Low Value)	rV	rV

Modulations in High-Low Value Conditions		
Validity/Hemifield	C (Cued)	U (Uncued)
V (High Validity)	VC	VU
v (Low Validity)	vC	vU

Modulations in High-Low Validity Conditions		
Validity/Hemifield	C (Cued)	U (Uncued)
R (High Value)	RC	RU
r (Low Value)	rC	rU

Coupled Systems. Attention and reward systems are considered coupled throughout literature asserting that the inputs of value affect the outputs of selective attention. This is not the assumption made when investigating value representation in the visual cortex (or attention), where validity or value are assumed separable when assigning responsibility of effects measured by behavior and neural activity in both the extrastriate and parietal cortices. If value and validity effects are not dissociable in these areas, that does not mean they are not separable elsewhere in

other brain areas. Dissociability may be a matter of the scales (i.e., neurotransmitters, electrophysiology, BOLD, choice behavior, reaction times, etc.) along the line of investigation.

Biological Considerations. Representations of value and validity information have not been shown to represent precise variable step changes when manipulating variables in response profiles. (Kahneman and Tversky, 1979; Platt and Glimcher, 1999, Baruni, Lau, and Saltzman, 2015). Variables will be treated as categoricals when conducting hypothesis testing.

Potential Outcomes. If value and validity were dissociable, evidence when varying validity and value in contrasting between cued and uncued hemifields would show a product of effect between each state of the system as defined by statistical independence. In contrasting the difference in value and validity responses themselves, within each hemifield condition, the varying of a value or validity metric should not change responses. The following cartoons illustrate expected observations if value and validity are dissociable:

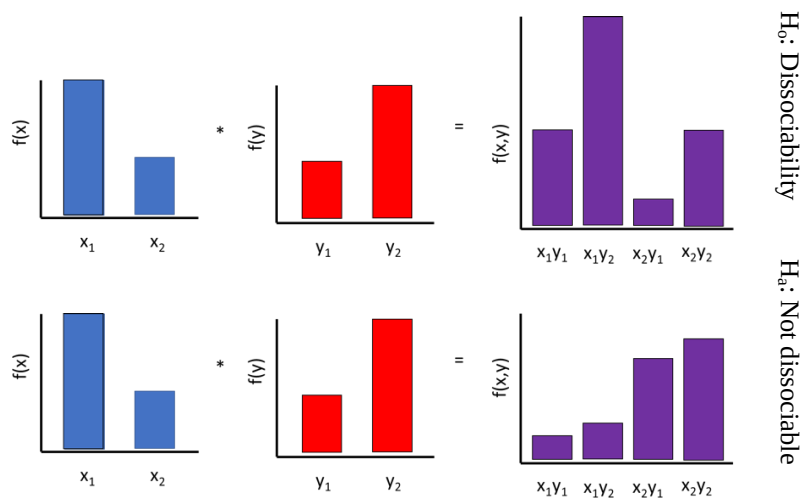


Figure 6: Potential Outcomes. Top figure represents statistical independence and where the effects of variable x and variable y combine such that $f(x, y) = f(x) * f(y)$. Bottom figure represents combinations of effects to which $f(x, y) \neq f(x) * f(y)$ suggesting non-dissociability.

CHAPTER TWO

VALUE AND VALIDITY MODULATIONS TO BEHAVIOR

Introduction

Organisms of all types must be able to make effective decisions under uncertainty to ensure survival. Neural mechanisms have emerged over the course of evolution to facilitate choice among a range of actions – these mechanisms incorporate and prioritize environmental information. Contextualization and balancing information with expected rewards and/or penalties (i.e., negative rewards) is incorporated into decision making. Actions of an agent interact with the environment and produce feedback information encoded by assessing and incorporating prediction errors (Gold and Shadlen, 2007). Cognitive functions such as attention and valuation modulate sensory systems to incorporate meaning and to prioritize processing. In primates, vision dominates subcortical and cortical processing compared to other sensory modalities. Attention, valuation, and prediction systems must interact with the visual system to prioritize, utilize, and perceive salient information related to the given context.

Attention research has exploded since the development of robust psychophysical metrics such as performance and reaction time to characterize attentional facilitation while completing tasks. In these early studies, observers were required to detect targets (visual objects of particularly color and/or shape) presented within a set of distracting stimuli, similar in color and shape. Treisman and Gelade (1980) demonstrated under certain conditions accuracy and speed were correlated with the number of distractors present in the display, suggesting that attention has a narrow spatial focus and was shifted from object to object in the visual scene during search.

(see Carrasco, 2011 for review). About the same time Posner (1980) began long series of studies on attentional orienting, using a partially valid cuing paradigm. In the Posner studies, central fixation is maintained while a transient cue indicates the likely future location of a target stimulus. The target subsequently appears at either the cued (valid) location or an uncued (invalid) location. Posner found that the cue served to orienting attention towards the cued location, leading to improved accuracy and reduced RT on the target detection task (Posner, Snyder, and Davidson, 1980).

The attentional mechanism related to goals (detection of targets) derived from or focused on environmental spaces and features is characterized separately from stimuli that produce attentional capture, seemingly unconsciously. This “bottom-up” attentional capture is distinguished from “top-down” conscious application toward a feature or spatial location in relation to a task known as exogenous and endogenous attention, respectively. Furthermore, endogenous attention can be further subdivided into “overt” attention, where an eye movement physically deploys the foveae to the attended visual field location, and “covert” attention, where attention is directed to a peripheral location in the visual field without moving the eyes (Wolfe, 1994; Marino and Mazer, 2016). Under natural vision conditions, covert attention to a peripheral location is almost always followed by an overt orienting response (i.e., a saccade to the attended location). It is generally well established that saccades, feature, and spatial attention are all interconnected processes, but the extent to which these processes are mediated by the same or overlapping neural circuits remains uncertain (Mazer, 2011).

In addition to “within attention” interactions or confounds, there are also experimental confounds between attention and other important behavioral modulations, for example, reward

processing and the neural representation of expected value. Again, it is becoming increasingly clear that there are interactions between reward signaling and attention in the brain, but the nature of these interactions and the effect on behavior remain unclear (Soltani, Koch, 2010). Selective attention modulates visual processing, which in turn modulates perception (Shore, Spence, and Klein, 2001). Reward valuation is clearly an important part of effective decision making, but it is not entirely clear how reward affects perception. Reward information has been shown to bias perceptual choice toward the more rewarding option (Diederich and Busemeyer, 2006). Reward information has also been proposed to explicitly modulate the sensory processing like selective attention (Liston and Stone, 2008; Voss, et al., 2008) who used behavioral choice and reaction time measures to support their conclusion. At the neurophysiological level, attention and reward can have similar modulatory effects on neural activity. Attention directed in or out of receptive fields can lead to response facilitation and suppression. Similarly, changing the reward associated with a given visual stimulus can either enhance or repress neural firing, depending on the neuron and the task (Desimone and Duncan, 1995; Platt and Glimcher, 1999; Baruni, Lau, and Salzman, 2015; Bisley, et al, 2011).

The confounding elements of reward and attention are unavoidable when using animal models. Almost without exception, animals performing complex cognitive tasks are incentivized during training and testing using either fluid or food rewards. This is also the case in all published animal-model studies of attention. This means that in most studies of attention, attention effects are confounded with the animal's expectation of reward. Similarly, in most studies of reward and valuation, the very real possibility that stimuli associated with higher values might automatically capture attention, possibly in a graded fashion, is not typically

addressed. To understand interactions between attention and reward, we set out to dissociate the effects from value and validity inherent within a task. We developed a novel behavioral task where the amount validity of the spatial cue is independently varied along with reward value. The task is a modified Posner cueing task where observers indicate target detection using a saccadic eye movement. Transient pre-target cues serve to inform the observer about (1) the likely target location, (2) and the validity of the spatial cue and (3) magnitude of the reward that will be delivered following a correct response (See Figure I, Methods). By varying validity and reward magnitude independently in a classic two-by-two experimental design and measuring target detection accuracy and reaction times, we hypothesized that we would be able to determine if attention and reward are behaviorally separable. Our results suggest that at the behavioral level, these systems are coupled and not dissociable, with facilitation correlated with each independent variable and evidence for significant interactions indicative of attention-value coupling.

Methods

Animal Observers

Two adult, male *macaca mulatta* monkeys (Monkey R, 11-15 kg, 16-18 years old; Monkey B, 11-14 kg, 12-14 years old) participated in these experiments. Experimental procedures were approved by the Institutional Animal Care and Use Committee (IACUC) at Montana State University in accordance with the National Institute of Health's Guide for the Care and Use of Laboratory Animals. Both animals had previously participated in neurophysiological studies and been trained to perform basic fixation and saccade to target tasks for other studies. Monkey R had been previously trained to perform a spatial attention task to

investigate the impact of saccades on attentional topography (Marino and Mazer, 2014). Prior to the start of these experiments, both monkeys underwent sterile surgical procedures performed under isoflurane anesthesia to implanted titanium headposts for head stabilization. Posts were attached to the skull using cortical bone screws (see Mazer, et al., 2002 for more details).

Psychophysical Experimental Set-Up

Visual stimuli, behavior, and data collection were controlled by custom software (<https://github.com/mazerj/pype3>). A gamma corrected LCD display (Dell P2210 LCD) presented stimuli with a 75Hz frame rate at a viewing distance of 40 cm. Eye movements were tracked and recorded digitally at 1000 Hz using an infrared eye tracker (EyeLink 1000, SR Research, Mississauga, Canada). Data were imported offline in MATLAB (MathWorks, Natick, Massachusetts) for all statistical analysis and visualization.

Attention-Value Task

Animals were trained for up to 18 months to perform the attention-value task. Animals were initially trained to perform a basic fixation task, signaled by a white fixation target ($0.1-0.3^\circ$ square) appearing on a uniform gray background (26 cd/m^2). Monkeys initiated trials by grasping a capacitive touch bar and required to maintain fixation on the target ($\pm 2^\circ$) for a variable period, after which they received a fluid reward. Fixation times were drawn from a truncated exponential distribution (Min: 500 ms, Max: 2000 ms, Mean: 1500 ms). Fixation breaks were classified as errors and signaled to the monkey by flashing the screen red, followed by a 5s timeout period.

After verification of basic fixation, using the same stochastically determined time allotment, the fixation location was shifted up to 14° left or right (stochastically determined at $p=0.5$). Monkeys had to reacquire the target within 500 ms and maintain fixation for an additional 200 ms to receive a reward. Failure to reacquire the target or subsequent fixation breaks were considered errors. After achieving a stable daily performance level of 70% correct on the basic fixation/saccade task, cues were added to the display during the initial period of fixation. The fixation spot was changed to a yellow to allow the monkey readily to distinguish between the simple fixation/saccade trials and “attention-value” trials. The (now yellow) fixation spot was surrounded with a red ring (color vector: Red:120, Green:1, Blue:1), indicating the target color and the target, now a red square of the same color as the ring appeared 14° left or right of the fixation spot. At the same time, low frequency catch trials (5% of all trials) were introduced stochastically. On catch trials, the target never appeared, and animals were rewarded if they continued to maintain fixation. The introduction of catch trials was intended to discourage animals from guessing or adopting timing strategies. On non-catch trials target onset times were drawn from the same truncated exponential distribution as the original fixation time durations. As monkeys achieved a 70% accuracy on this task, a 100% valid spatial cue was introduced (white bar oriented toward the target location). Spatial cue trials were randomly interleaved with uncued trials with performance and reaction times were tracked and analyzed for statistical differences between uncued and cued condition sets. Once we observed a statistically significant difference between on cued and uncued trials in performance and reaction time, cue validity was reduced to 90%, and the validity level indicated to the monkey as partial filling of cue bar (see Figure 7) such that the fraction of fill was linearly related to the cue’s validity.

This single partial valid cue was instituted until target detection rates for the invalid condition (target appears on uncued side) was over 60%. At this point, a 70% valid cue condition was introduced, appearing randomly interleaved with the 90% valid cue with equal frequency. Once performance stabilized on this task (60% accuracy) a reward cue was introduced. Reward magnitude (number of drops of fluid reward) was signals by white circles surrounding the red ring. A single white circle indicated one drop (small reward), while three circles indicated three drops (large reward). For multi-drop rewards, there was a 200ms gap between each drop delivery. Finally, once animals were reliability performing the full task, task-irrelevant visual probe stimuli (Marino and Mazer...). Probe stimuli were oriented bars of texture noise flashed around the possible target locations (± 10 deg) at a frequency of 10 Hz. Invalid target detection of 60% was again the threshold prior to moving to the behavioral testing phase. Data analyzed in this paper was collected after each animal observer achieved a stable daily performance level of 60% on the full task in the presence of the visual probe stimuli. Behavioral data were collected over a period of 5 months, completing a combined trial count of $n=76,788$ (Monkey B=38,288; Monkey R=38,500). Refer to figure one for final experiment design during testing.

Saccade Detection and Reaction Times

To quantify reaction times saccades were detected offline by determining the first time at which the fixation window was broken for at least 15 ms. Saccades were classified towards the target location or the non-target location if they landed within a 90deg sector centered on the target/non-target locations (0/180deg). Saccades outside these sectors were treated as fixation breaks. Fixation breaks and uninitiated trails were excluded from analysis and when determining

performance thresholds during training. Saccade reaction times (sRTs) for correct trials were calculated for different target onset times and saccade direction.

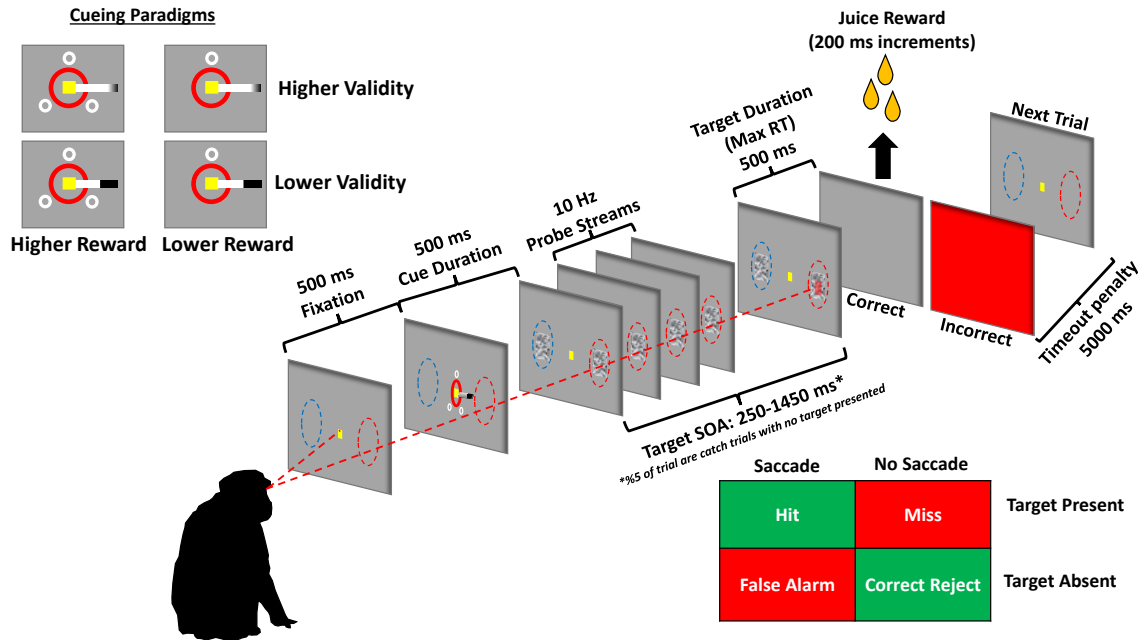


Figure 7. Attention-Value Behavioral Task. Animal observers initially fixate on a central square and are presented with a set of cues indicating target color, a spatial cue indicating both the likely location of the target and the validity of the spatial cue. Reward size for correct trial outcome is indicated simultaneously. After the cues are extinguished, two streams of dynamic visual probe stimuli (textured noise patterns flickering at 10 Hz) appear and remain visible for the remainder of the trial. At a randomly selected time (250-1450 ms), a target appears at the center of one of the probe streams and observers must make a single accurate saccade to the target within 500 ms. Following an accurate saccade to the target, animals receive the reward. Errors (saccades to the wrong location or missed targets) are signaled by briefly flashing the screen red and a short timeout period. On 5% of trials no target appears (catch trial) and observers must maintain fixation until the end of the trial to obtain the reward. Cue configurations: The ring surrounding the fixation square indicates the color of the target, which remains constant (red). The horizontal black and white bar serves two functions: the direction of the bar indicates the likely location of the target and white/black ratio indicates the spatial cue's validity (90% white = 90% valid, 70% white = 70% valid, etc). The small circles indicate the number of drops of juice the observers will receive on a correct trial.

Dissociability

Metrics. Three metrics will be used to assess dissociability and characterize performance; false alarm rate, hit rate, and saccade reaction time. False alarm rates are calculated by the following equation: $False\ Alarm\ Rate = \frac{\#False\ alarms_{Condition}}{\#Trials_{Condition}}$. Hit rates are calculated as follows: $Hit\ Rate = \frac{Saccade\ to\ Target_{Condition}}{\#Targets\ Presented_{Condition}}$. Saccade reaction time (sRTs) is determined by the difference between saccade detection and target onset time for a particular trial. In both hit rate and sRTs, references to “Cued” represent “Valid” and “Uncued” represent “Invalid” cues as per convention in attention literature.

Step-Change Analysis. Value and validity variables were presented in one of two conditions, categorically separated as “high” and “low.” Spatial location was categorized as “Cued” and “Uncued” to delineate between visual hemifields. Each step change (the difference in metric from high to low) was assessed for each second variable condition as well as the average. Function outputs and difference metrics will be bootstrapped (n=1000) with and a t-test between step changes to detect statistically significant difference.

An example is as follows:

For each spatial location (cued or uncued):

Let $X = \{High\ Value, Low\ Value\}$

Let $Y = \{High\ Validity, Low\ Validty\}$

Let $f(\cdot) = Observed\ metric\ (false\ alarm\ rates, hit\ rates, saccade\ reaction\ times)$

Let $\Delta x := E[f(x_2)] - E[f(x_1)]$

Let $\Delta x_{y_1} := E[f(x_2, y_1)] - E[f(x_1, y_1)]$

Let $\Delta x_{y_2} := E[f(x_2, y_2)] - E[f(x_1, y_2)]$

If $\Delta x_{y_1} \neq \Delta x_{y_2} \neq \Delta x$ demonstrates y changes $f(x)$ suggesting no statistical independence

$$\text{Let } \Delta y := E[f(y_2)] - E[f(y_1)]$$

$$\text{Let } \Delta y_{x_1} := E[f(x_1, y_2)] - E[f(x_1, y_1)]$$

$$\text{Let } \Delta y_{x_2} := E[f(x_2, y_2)] - E[f(x_2, y_1)]$$

If $\Delta y_{x_1} \neq \Delta y_{x_2} \neq \Delta y$ demonstrates x changes $f(y)$ suggesting no statistical independence

Difference Metrics. Permutated t-tests will be used to test significance of difference metrics for each condition and between conditions. Difference metrics were calculated via bootstrap (n=1000) looking at differences in effect between spatial location, validity, and value with permutated t-tests detecting significant differences. The following cartesian products are used for this analysis:

Cued (Valid)-Uncued (Invalid) Conditions		
Value/Validity	V (High Validity)	v (Low Validity)
R (High value)	RV	Rv
r (Low Value)	rV	rV

High-Low Value Conditions		
Validity/Hemifield	C (Cued)	U (Uncued)
V (High Validity)	VC	VU
v (Low Validity)	vC	vU

High-Low Validity Conditions		
Validity/Hemifield	C (Cued)	U (Uncued)
R (High Value)	RC	RU
r (Low Value)	rC	rU

N-Way ANOVAs. N-way ANOVAs were conducted for false alarms rates, hit rates, and saccade reaction times. For false alarm ANOVAs the response variable was coded with binary digits with “1” representing a false alarm trial, and zero a non-false alarm trial. Reward and Validity vectors were designated as predictor variables. Alpha was set at 0.05 and interactions between terms were included. Hit rates and sRTs ANOVAs included another predictor term, ‘Hemifield,’ to designate whether the target appeared in the cued hemifield or not. Interactions between all these terms were included in ANOVAs.

Results

False Alarm Rates

Each trial of attention-value tasks presents an opportunity for the animal to commit a “False Alarm,” making a saccade to one of the two target locations prior to the target stimulus appearance. Potential target locations were categorized as either “cued” or “uncued.” Step change analysis was conducted for both validity and value variables. (See methods). In cued conditions, each variable affected the step-change of the other, yielding significantly different averages (See Table 1).

False alarm rates and differences between condition sets were computed by bootstrapping 75% of trials (n=1000) and calculating false alarms rates. In each instance of the individual variable conditions, the difference cued and uncued conditions was significantly above zero in pooled and individual animal observers ($p < 0.001$ in all cases). Data was then pooled for additional condition comparing (See Figure 8). High Reward conditions were significantly lower than low rewarded condition sets. In the validity condition sets, this effect was reversed with higher validity significantly higher than lower validity. Conditions between high/low reward, high/low validity, and cued/conditions sets computed and differences compared. Cue/Uncued differences between conditions sets were all significantly above zero.

Table 1. False Alarm Rate Step Change Analysis				
	$\Delta \text{Validity} \text{Value}_{\text{Low}}$	$\Delta \text{Validity} \text{Value}_{\text{High}}$	$\Delta \text{Validity (All)}$	$\neq$
C	$\bar{x} = 3.70e^{-3}, \sigma_x = 8.01e^{-4}$	$\bar{x} = 2.90e^{-3}, \sigma_x = 6.47e^{-4}$	$\bar{x} = 3.30e^{-3}, \sigma_x = 5.14e^{-4}$	1
U	$\bar{x} = -1.30e^{-3}, \sigma_x = 4.29e^{-4}$	$\bar{x} = -1.20e^{-3}, \sigma_x = 4.21e^{-4}$	$\bar{x} = -1.30e^{-3}, \sigma_x = 2.98e^{-4}$	0
	$\Delta \text{Value} \text{Validity}_{\text{Low}}$	$\Delta \text{Value} \text{Validity}_{\text{High}}$	$\Delta \text{Value (All)}$	
C	$\bar{x} = -6.30e^{-3}, \sigma_x = 6.87e^{-4}$	$\bar{x} = -7.00e^{-3}, \sigma_x = 7.74e^{-4}$	$\bar{x} = -6.70e^{-3}, \sigma_x = 5.19e^{-4}$	1
U	$\bar{x} = 4.66e^{-5}, \sigma_x = 4.50e^{-4}$	$\bar{x} = 2.02e^{-4}, \sigma_x = 3.98e^{-4}$	$\bar{x} = 1.25e^{-4}, \sigma_x = 2.97e^{-4}$	0
C= Cued U= Uncued $\neq$ = significantly different Δ 's				

Conditions sets were examined between high/low value between condition sets (Figure 3, Upper Right). The differences in this effect between cued and uncued conditions were significant in the low validity and high validity cued conditions. The differences in this effect between high validity and low validity were also significant in the cued but not uncued. High/Low validity differences were also quantified across condition sets (Figure 3, lower right). Cued and uncued differences in this effect were significant in high reward and low reward cue conditions.

Differences in high/low reward in this effect in cued conditions proved significant but not in the uncued condition.

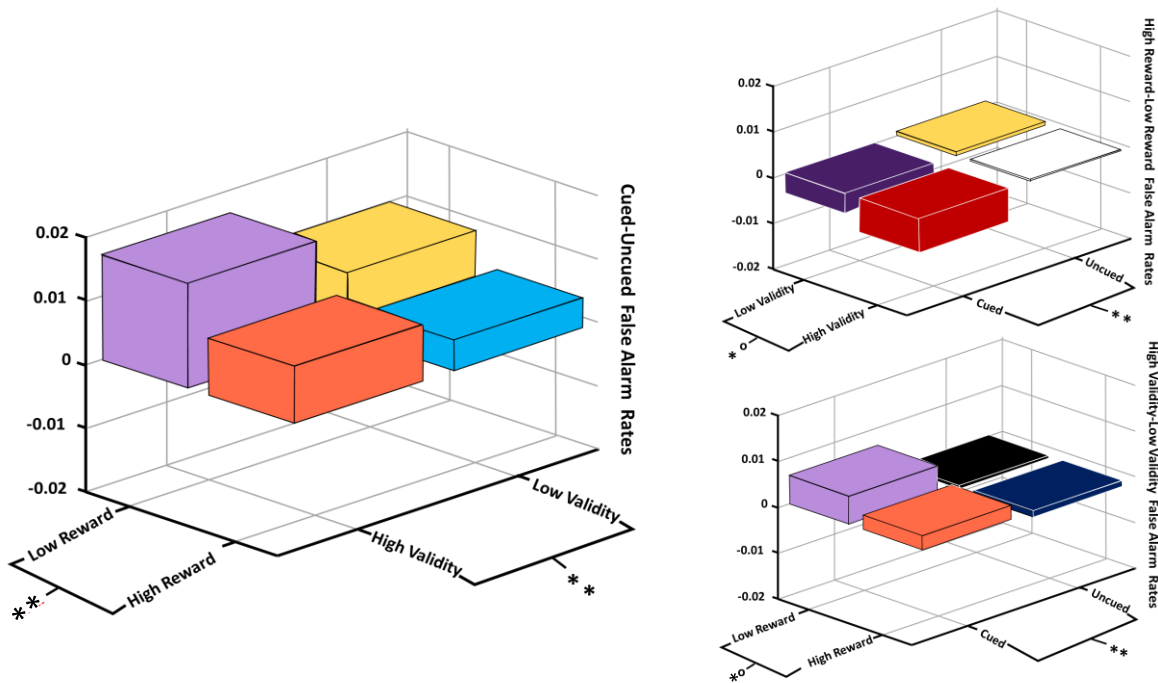


Figure 8: False Alarm Analysis. Data from the two animals were pooled and 75% bootstrapped ($n=1000$). Significant effects are represented by colored squares with hue differences (dark=negative, light=positive) delineating effect size. No significance is represented by a white (positive, $p>0.05$) and black (negative, $p>0.05$). Significant difference in this effect size between axis conditions is represented by an asterisk and non-significance by a black circle arranged by axis depth (i.e. In the Lower right, Validity differences between cued and uncued conditions in the High reward and low reward conditions were significant. Whereas validity differences between high and low reward conditions were not significant in the uncued condition but significant in the cued condition).

Independent variable conditions of high/low value and high/low validity demonstrated opposing effects on false alarm rates. Higher reward conditions had less differences between the cued/uncued compared with low reward with a sign difference in higher validity contrasted with lower. The lowest difference in these values occurred in the most uncertainty and highest reward

condition set. When the other dimension differences were analyzed, cued and uncued conditions had opposing sign differences in both high and low validity, with the cued condition enhancing the effect, with lower false alarm rates in high reward conditions than that of low reward conditions.

While high reward reduced the effect in validity differences in the cued condition (no significant difference detected in the uncued condition.) In both high/low reward conditions the cued condition enhanced the effect of the differences in validity, with cued conditions invoking larger false alarm rates than uncued ones. An Analysis of variance ($\alpha=.05$) was conducted with reward and validity as predictors of a false alarm trial. Both value and validity were significant, while their interaction was not (See Table 2).

Table 2. False Alarm Rate N-Way ANOVA					
Source	Sum Sq.	Deg f.	Mean Sq.	F	Prob>F
Value	0.82	1	0.8193	40.43	4.21E-04
Validity	0.08	1	0.0821	4.05	0.0441
Value * Validity	0	1	0.00212	0.1	0.074
Error	1556.17	76784	0.02027		
Total	1557.08	76787			

Hit Rates

Trials where a target appeared were categorized by cue conditions. Targets that appeared in the uncued hemifield in literature are labeled “Invalid” in contrast with “Valid” when appearing in the cued hemifield. Step change analysis was conducted (See Methods). For both valid and invalid targets, hit rate differences between value or validity were affected by the value of the other variable (See Table 3).

Data was then bootstrapped (n=1000) by taken 75% of data and computing raw and difference metrics between condition sets. High/low value and high/low validity conditions were pooled and the differences between cued and uncued conditions computed (See Figure 9). The differences in high value and low value in cued – uncued conditions were significant. High validity and low validity were also significant.

Table 3. Hit Rate Step Change Analysis				
	$\Delta\text{Validity} \text{Value}_{\text{Low}}$	$\Delta\text{Validity} \text{Value}_{\text{High}}$	$\Delta\text{Validity (All)}$	$\neq$
C	$\bar{x} = 2.85e^{-4}, \sigma_x = 2.70e^{-3}$	$\bar{x} = -3.10e^{-3}, \sigma_x = 2.80e^{-3}$	$\bar{x} = -1.50e^{-3}, \sigma_x = 1.90e^{-3}$	1
U	$\bar{x} = -6.30e^{-3}, \sigma_x = 7.30e^{-3}$	$\bar{x} = -1.89e^{-2}, \sigma_x = 7.80e^{-3}$	$\bar{x} = -1.23e^{-2}, \sigma_x = 5.40e^{-3}$	1
	$\Delta\text{Value} \text{Validity}_{\text{Low}}$	$\Delta\text{Value} \text{Validity}_{\text{High}}$	$\Delta\text{Value (All)}$	
C	$\bar{x} = -4.30e^{-3}, \sigma_x = 2.90e^{-3}$	$\bar{x} = -7.70e^{-3}, \sigma_x = 2.60e^{-3}$	$\bar{x} = -6.20e^{-3}, \sigma_x = 1.90e^{-3}$	1
U	$\bar{x} = -1.68e^{-2}, \sigma_x = 5.20e^{-3}$	$\bar{x} = -2.94e^{-2}, \sigma_x = 8.90e^{-3}$	$\bar{x} = -1.99e^{-2}, \sigma_x = 4.50e^{-3}$	1
C= Cued U= Uncued $\neq$ = significantly different Δ 's				

Differences between high/low value, high/low validity, and cued/uncued were computed for each single condition set. Cued – Uncued hit rates were calculated and all showed significant effects, with a negative effect in the low value/low validity condition. Differences were also computed between high/low value and validity conditions. The differences in value for high validity and low validity both were significant with an increased effect from a higher value. The differences in validity for high value and low value were both significant with a reduced effect in the high value condition.

High/low value hit rate comparisons were computed for each conditions set. Negative effects from a higher value condition were present in all except the low validity condition, where the highest effect was detected. Differences between high/low validity in cued was significant

but not in uncued conditions. Cued/Uncued difference in value were significant in the high validity and low validity conditions. Higher validity and lower validity had difference

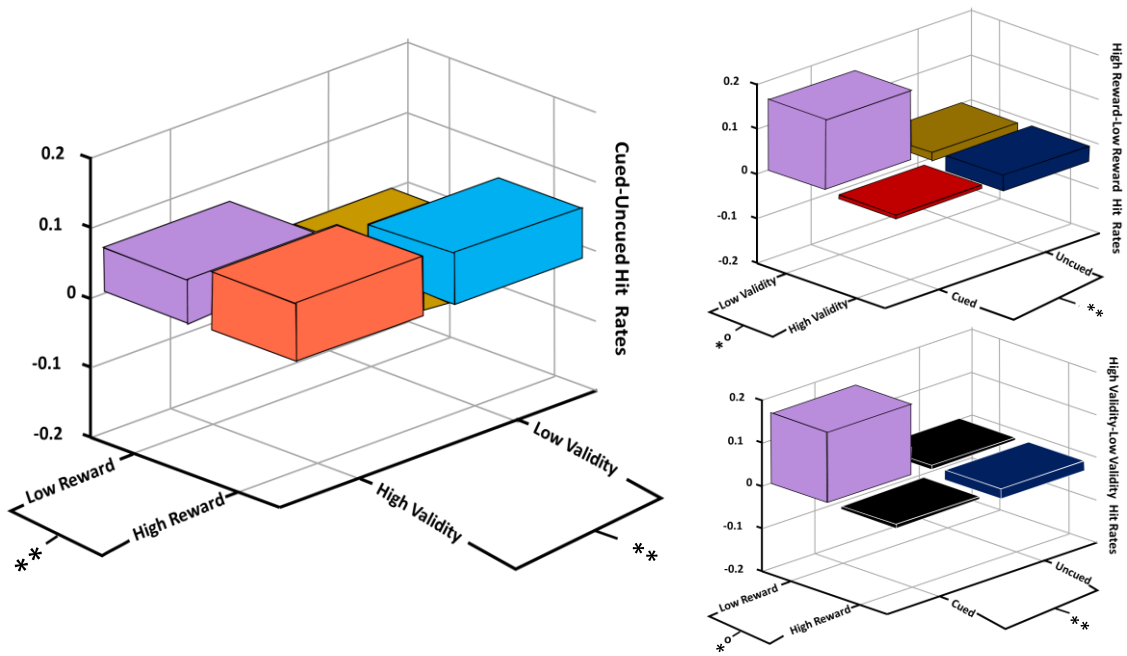


Figure 9: Hit Rate Analysis. Data from the two animals were pooled and 75% bootstrapped ($n=1000$). Significant effects are represented by colored squares with hue differences (dark=negative, light=positive) delineating effect size. No significance is represented by a white (positive, $p>0.05$) and black (negative, $p>0.05$) Significant difference in this effect size between axis conditions is represented by an asterisk and non-significance by a black circle arrange by axis depth (i.e. In the Lower right, Validity differences in low reward, cued conditions were positive and significant, whereas in the high reward, uncued condition they were negative and significant.)

enhancement between cued and uncued conditions, with lower validity increasing in effect while higher validity reduced it.

High/low validity hit rate comparisons were computed for each condition set. The differences between high and low value conditions in cued was significant while uncued was not. In cued/uncued difference were significant in both high value and low value conditions. ANOVA

analysis detected significant effect from value and which hemifield the target, indicating whether the target was valid or not but not validity (See Table 4).

Table 4. Hit Rate N-Way ANOVA					
Source	Sum Sq.	Deg f.	Mean Sq.	F	Prob>F
Value	1.64	1	1.6419	11.86	0.0006
Hemifield	34.43	1	34.4329	248.79	7.55e-5
Validity	0.35	1	0.355	2.56	0.1093
Value*Hemifield	0.51	1	0.5115	3.7	0.0546
Value*Validity	0.08	1	0.0795	0.57	0.4484
Hemifield*Validity	0.23	1	0.2308	1.67	0.1966
Error	7955.16	57478	0.1384		
Total	7996.80	57484			

Saccade Reaction Times

Saccade reaction times were gathered from correct trials only. Step change analysis was conducted (See Methods). For both valid and invalid sRTs, differences between value or validity were affected by the value of the other variable. (See Table 5).

Table 5. Saccade Reaction Time Step Change Analysis				
	Δ Validity Value _{Low}	Δ Validity Value _{High}	Δ Validity (All)	$\neq$
C	$\bar{x} = 0.39, \sigma_x = 0.69$	$\bar{x} = -0.85, \sigma_x = 0.60$	$\bar{x} = -0.24, \sigma_x = 0.44$	1
U	$\bar{x} = -0.62, \sigma_x = 1.59$	$\bar{x} = 2.63, \sigma_x = 1.63$	$\bar{x} = 0.94, \sigma_x = 1.10$	1
	Δ Value Validity _{Low}	Δ Value Validity _{High}	Δ Value (All)	
C	$\bar{x} = -1.17, \sigma_x = 0.66$	$\bar{x} = -2.41, \sigma_x = 0.58$	$\bar{x} = -1.86, \sigma_x = 0.44$	1
U	$\bar{x} = 0.31, \sigma_x = 1.10$	$\bar{x} = 3.56, \sigma_x = 2.02$	$\bar{x} = 1.10, \sigma_x = 0.94$	1
C= Cued U= Uncued $\neq$ = significantly different Δ 's				

Saccade reaction times (sRTs) were pooled from animal observers, categorized, and separated by condition type and bootstrapped ($n=1000$) for means and differences in means (see methods). High value, low value, high validity, and low validity conditions were pooled and the difference in cued-uncued conditions examined for differences. Significant value differences were detected with higher value enhancing the difference between cued and uncued condition sets. Validity differences were not detected above significance.

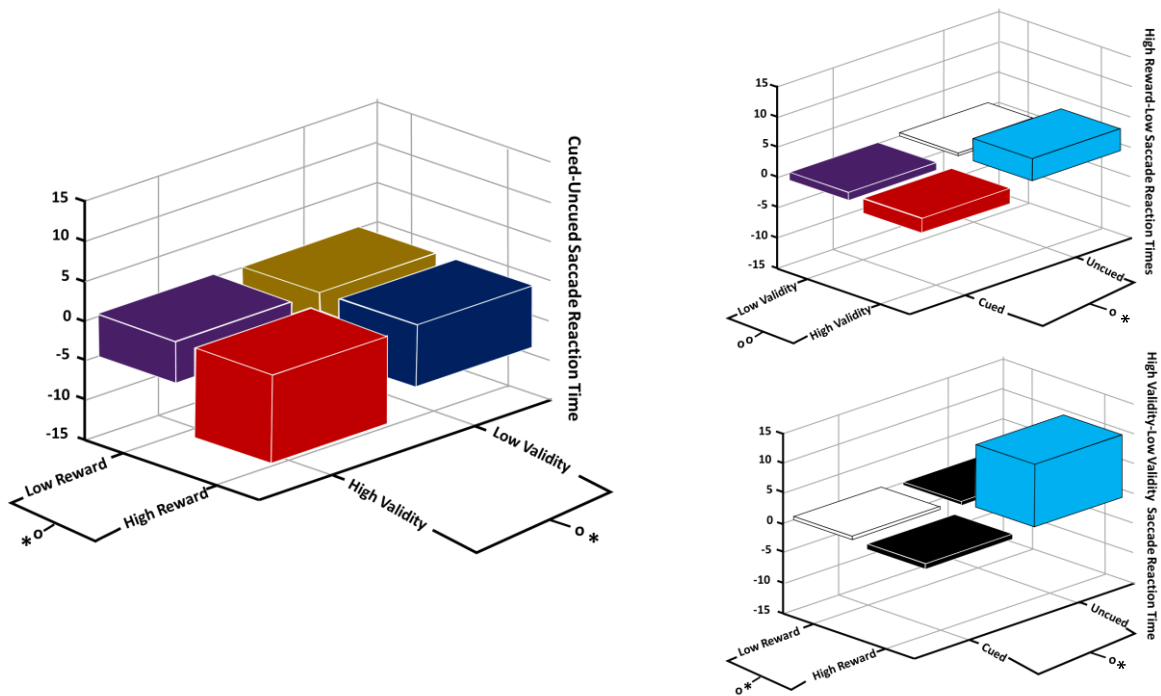


Figure 10: Saccade Reaction Time Analysis. Data from the two animals were pooled and 75% bootstrapped ($n=1000$). Significant effects are represented by colored squares with hue differences (dark=negative, light=positive) delineating effect size. No significance is represented by a white (positive, $p>0.05$) and black (negative, $p>0.05$) Significant difference in this effect size between axis conditions is represented by an asterisk and non-significance by a black circle arrange by axis depth (i.e. In the Lower right, Validity differences in low reward, cued conditions were positive and significant, whereas in the high reward, uncued condition they were negative and significant.)

Differences in cued and uncued were significant across all conditions. Differences in the value cue difference were significant for high validity but not in low validity conditions. In high

value conditional differences in validity cue-uncued were significant but not in lower value conditions. High value and high validity conditions enhanced the effect of the reduction in reaction time between cued and uncued conditions.

Differences in value was computed across condition sets. The only significant differences detected were between cued and uncued high validity conditions with cueing reducing the effect of value differences. Validity differences were also computed across conditions. Significant differences between cued and uncued validity differences were detected in high value and between high and low value in uncued conditions.

An ANOVA was conducted and detected significant effect from only whether a target was valid or not (categorized as “hemifield”). value and which hemifield the target, indicating whether the target was valid or not but not validity (See Table 6).

Table 6. Saccade Reaction Time N-Way ANOVA					
Source	Sum Sq.	Deg f.	Mean Sq.	F	Prob>F
Value	972.3	1	0.8953	6.14	0.6794
Hemifield	325072.2	1	25.1245	57.09	1.72e-5
Validity	850.2	1	0.5473	0.15	0.6992
Value*Hemifield	14488.2	1	1.1334	2.54	0.1107
Value*Validity	830	1	0.0038	0.15	0.7026
Hemifield*Validity	2035.5	1	2035.5	0.36	0.5499
Error	2713635878	47659	5693.9		
Total	271794304	47665			

Discussion

Reward magnitude, target spatial location, and spatial location cue validity were endogenously cued to dissociate the effects of value and validity on behavior. The standard approach in visual attention research is to quantify the differences in performance, e.g., sensitivity, accuracy, reaction time, etc., for target appearing at the cued and uncued locations. In this study, we have added additional experimental manipulations that can affect performance, namely, reward magnitude and information about the validity of the spatial cue. This means there are four critical experimental conditions: high value/high validity, high value/low validity, low value/high validity, and low value/low validity. When we pooled data across value and validity conditions, we detected significant effects in false alarm rates, hit rates, and saccade reaction times comparing cued and uncued performance metrics.

Statistical independence between variables x and y are defined as $\frac{f(x,y)}{f(x)*f(y)} = 1$ with $f(x)$ being the probability density function (pdf) of x , $f(y)$ the pdf of y , and $f(x, y)$ as the joint pdf. With only two elements in each set, a sufficient test for statistical independence is difficult. However, in the step change analysis, the difference between value depended on which validity element was presented (and vice versa) suggesting interdependence, thus non-dissociability. This was observed in false alarm rates, hit rates, and reaction times.

The signal detection theory can be used to estimate for sensitivity of a detector (d') as $Z(\text{Hit Rate}) - Z(\text{FA Rate})$. Several studies have suggested that attention increases sensitivity within the attentional locus by suppressing the responses outside the locus (Cameron, et al., 2004; Eckstein, Palmer, and Shimozaki, 2000). This “filtering” model is consistent with physiological evidence from area V4 (Reynolds and Pasternak, 2000). In the attention-value task, while animal

observers showed higher false alarm rates in cued conditions, but this was smaller than the effect on hit rates, leading to a net change in increased sensitivity for the cued side which is consistent with literature. The increased propensity for false alarms to the cued side would be consistent with a gain model, as noise is amplified along with signal, thus producing more false alarms. High reward, low validity interactions are of particular interest as their interaction reduced false alarm rate differences between hemifields (figure 8). In cued conditions low validity increased the differences in value hit rates, while high value decreased validity differences. Saccade reaction times difference in validity were increased in high value conditions, with low validity having faster reaction times to the uncued side.

Saccade reaction times showed a significant reduction in all cued-uncued comparison across conditions sets consistent with literature using the Posner cueing paradigm (Posner, 1980; Carrasco, 2011). Animal observers had opposing effects with respect to high value-low value differences with Monkey B showing a longer response time in high value conditions while Monkey R showed a reduction in reaction times. Lower validity, high value conditions in uncued locations had much faster reaction times than higher validity, high value, cued locations. Animal observer differences in weighting probability and magnitude information are consistent with human behavior of subjective utility studies on choice behavior (Kahneman, D., and Tversky, A, 1979; Spitmaan, Chu, and Soltani, 2019). These studies along with our results suggest that information about value magnitude and probability is encoded and categorized, but there are significant individual differences between observers.

Saccade reaction time reduction in cued conditions is consistent with spatial attention literature in human and primate observers (Gilbert and Lee, 2013; Carrasco, 2011). In both

animal observers, the added uncertainty of cue validity decreased reaction times in high rewarded uncued conditions compared the high validity condition. Saccade reaction time reduction via higher expected value induced by reward and probability is consistent with previous research (Gold, & Shadlen, 2007; Anderson, B., 2016). The reduction of reaction time with increased uncertainty of cue validity in higher payoff trials may induce a spread of the attention resources to multiple locations as suggested by Cavanaugh and Intriligator (Intriligator, J., and Cavanagh, P. 2001). Their study showed that selective attention has a reduced resolution compared to the resolution of vision and theorized the parietal area as the most likely locus of this selection mechanism, acting as a pointer to spatial coordinates of items of interest, not their visual representations. However, in their study there was no modification of the payoff from these items, which are associated with action value.

These results demonstrate that while there is some degree of dissociation between the behavioral effects from reward magnitude and spatial validity, there are interactions between these signals, which may indicate coupling or even shared circuitry at the neural level. Recordings in area V4 have consistently shown modulatory effects in spatial attention experiments across a wide range of behavioral tasks and neurophysiological recording methods (Roe, et al., 2012). Baruni et al (2105) also demonstrated that V4 neurons encode information about absolute reward magnitude. Baruni et al suggested that downstream selection areas known to be involved in valuation, namely the LIP (Platt and Glimcher, 1999), might be the source of the modulation they observed in V4. In V4 spatial attention targeted in retinotopic coordinates (Golomb, Chun, and Mazer, 2008; Marino and Mazer, 2018). The observation that reward modulation can be observed in a nominal “attention area” (i.e., V4) is somewhat problematic

given the lack of experimental dissociation between attention and reward in virtually all published attention studies and was, in part, the motivation for the studies described in this and the following chapter.

The results of this study unambiguously indicate that both attention and reward contingencies can influence visually guided behavior. However, these influences are not readily separable – that is, they are not fully independent processes. More specifically, our results suggest the systems representing reward magnitude and spatial validity information are only dissociable in their effect in a specific environment but remained coupled in how they interact with each other, such that at times they appear to exhibit opposing influences. Further behavioral and research, as well as neurophysiological studies, will be required to fully tease these two effects apart (see Chapter 3).

CHAPTER THREE

ENCODING OF VALUE AND VALIDITY IN THE EXTRASTRIATE AND THE
POSTERIOR PARIETAL CORTEXIntroduction

Natural scenes are complex and cluttered with objects, features, and locations in competition for scarce cognitive resources. Allocation of limited neural resources for sensory processing and decision making is essential. The human brain (or any brain) is not capable of processing all aspects of all stimuli in the visual field. It has been established that attention can be focused on, or attracted to, specific objects, isolated features, and locations in the visual system (Carrasco, 2011). Visual search models are based on a *saliency map* (Itti and Koch, 1999), an explicit two-dimensional map that encodes spatial task-relevance or “illumination” of a location. (i.e., an unexpected bright or moving object). Orienting responses (motor actions that direct gaze towards salient scene features) and specialized neural machinery to support fast, accurate orienting, is ubiquitous in vertebrate species and widely regarded as an essential survival mechanism.

Environmental cues provide information used by organisms to determine appropriate action patterns to support essential activities such as foraging for food or seeking shelter. Visual information associated with cues aids in decision making and through iterative feedback. Salient spatial and feature cues inform agents of context and of targets for prioritized processing, meaning stimuli can both direct attention and as well as become a target of it (Posner, 1980,

Moran and Desimone, 1985). Simultaneously, visual stimuli can provide information to support decision making (Gold and Shadlen, 2007).

Economic theories of optimal decision making have developed emphasizing the expected value, or reward, associated with a decision option. While the mechanisms of spatial saliency and encoding of expected values may seem independent, what happens when orienting towards a stimulus is a high expected value action? Does the high value draw attention to that stimulus regardless of voluntary control? It is not clear that value encoding, and spatial attention differences driven by partially valid cues are independent of one another. Moreover, the variety of differential weighting, or emphasis on a piece of information between reward and probability has been observed in humans (Spitmaan, Chu, Soltani, 2019), and is consistent with the subjective valuation conveyed in prospect theory (Kahneman and Tversky, 1979) further complicating matters with probabilistic outcomes. Probability is a component of partial valid potential target locations. How environmental cues which simultaneously provide information about both spatial salience and expected action value modulate visual behavior and neural circuitry is not well understood.

In non-human primate animal models, neurophysiology has mostly conducted on the cortical surface for a variety of reasons (general welfare, risks, accessibility, etc.) Investigations in this field of research into valuation, decision-making, and attention utilize the visual modality to test hypothesis. In valuation experiments along these lines of investigation, the parietal cortex is a common target for measuring and analyzing neural activity. Platt and Glimcher's (1999) study of the lateral intraparietal cortex (LIP) was the first to show neural correlates of decision variables in the primate brain and revealed that the activity of many LIP neurons encodes the

expected value of stimuli in their receptive fields. Parietal cortex has been the location of decision variable studies (Gold and Shadlen, 2007), however, it is not the only cortical area associated with the visual modality with evidence of encoding value. Encoding of reward magnitudes associated with visual stimuli has also been demonstrated in area V4 neurons (Baruni, Lau, and Salzman, 2015).

The tendency for utilizing the visual system is true for characterizing spatial, feature, and object modulatory profiles in experiments for similar reasons as stated above. The similarities in lines of investigation are not constrained to anatomy. At the scale of behavior, performance improves, and reaction times are reduced in for higher rewarded choices and for spatially cued task-relevant stimuli (Bisley, et al, 2011; Gilbert and Li, 2013; Pessoa, 2015). Because of its invasive nature, animal models are the mainstay of neurophysiology. Training animals to perform the tasks required to investigate attention and decision making requires incentivization, typically in the form liquid or food rewards. This presents a potential confound of reward magnitude and spatial probability information modulations to visual processing and between profiles of reward processing and attention cognitive function. A confounding of neural activity attributed to spatial attention may be that of associated payoff and vice versa.

To examine interactions between value-coding and attentional modulation at the neural level we defined a novel “attention-valuation” task where the validity of a spatial cue can be varied independently of reward magnitude. We then targeted recordings to extrastriate and posterior parietal cortex, specifically targeting visual areas V4 and LIP, where there is arguably the best experimental evidence of activity modulations related to both attention and reward (see Carrasco, 2011; Glimcher and Fehr, 2013 for review). V4 and LIP are also both critical hubs of

neural connectivity required for intermediate visual processing (Sporns, 2003). Chronically implanted movable electrodes were used to record neural activity from these target areas to examine the degree of separability between attentional modulation and reward magnitude coding in intermediate visual cortex. The results reveal a complex pattern of heterogeneous modulation profiles. Results show an increase to the number of individually modulated neurons but a decrease in the modulation sizes with increased uncertainty due to a lower validity cue when coupled with a higher rewarded trial. Results also suggest an anticipatory reward feedback network that is modulated based on pre-task environmental cueing of reward magnitude. The concerns of confounding the attribution of neural activity modulation to attention or valuation were affirmed, making assumptions into the dissociability of validity and value information not a safe one to make.

Methods

Data Acquisition

Animal Observers. A male *macaca mulatta* monkey (Monkey B, 11-14 kg, 12-14 years old) participated in these experiments. Experimental procedures were approved by the Institutional Animal Care and Use Committee (IACUC) at Montana State University in accordance with the National Institute of Health's Guide for the Care and Use of Laboratory Animals. Monkey B had been previously trained to perform a saccade to target task. Prior to training, Monkey B underwent sterile surgical procedures performed under isoflurane anesthesia

and implanted with titanium headposts for head stabilization, anchored to the bone with cortical bone screws. One the animal was fully trained to perform the behavioral task described in Chapter 2, two 32-Channel recording chambers (Gray Matter Research, LLC; Dotson, Hoffman, Goodell, and Gray, 2017). were implanted in a sterile surgical procedure under isoflurane anesthesia. MRI scans were used to target lunate and interparietal sulci stereotaxically used to center each chamber (3D Slicer, slicer.org, Fedorov, et al.,2012). During the surgery A craniotomy and durotomy were performed to allow electrode access and chambers were anchored to the bone with cortical bone screws and sealed with acrylic cement.

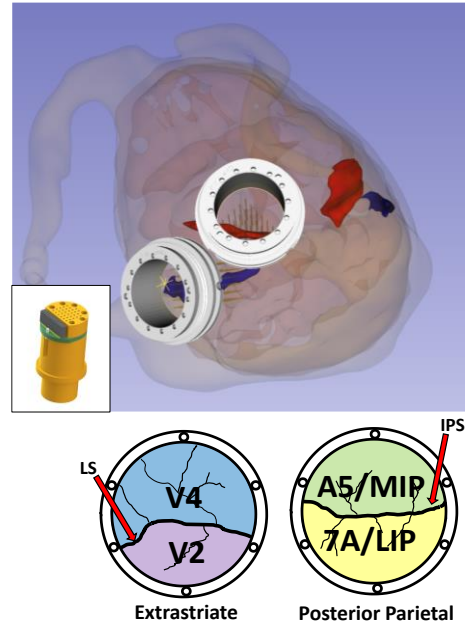


Figure 11: Chamber and Placement. Lunate Sulcus (Blue) and the Interparietal Sulcus (Red) were identified and used to identify stereotaxic coordinates. 32-channel microdrives were placed on each chamber.

Electrophysiological Recordings. Three metrics Broadband signals (0.1 Hz - 9 kHz, sampled at 32 kHz) were recorded using a 256-channel Digital Lynx system (Neuralynx) and with high impedance (nominally 1 MU at 1 kHz) glass coated tungsten microelectrodes (250-350 mm diameter, Alpha Omega Engineering, Alpharetta, GA). A threshold of three standard deviations of background signal was used to identify spike events. Thirty-two data points were saved for each spike. Waveforms were analyzed with custom algorithms in MATLAB software using a combination of principal component analysis and k-means clustering to isolate single neurons. Recordings were classified as “single unit” if they exhibited clear clustering in the PCA

space and low waveform standard deviation, recordings without clear clustering or overlapping waveforms between clusters were labeled as “multiunit” and initially analyzed separately from the single neuron data. Single-unit and multi-unit spike event times were collected in MATLAB for statistical analysis and visualization. During analysis, we observed no significant differences between single- and multiunit data (data not shown); results below are based on analysis of the pooled data.

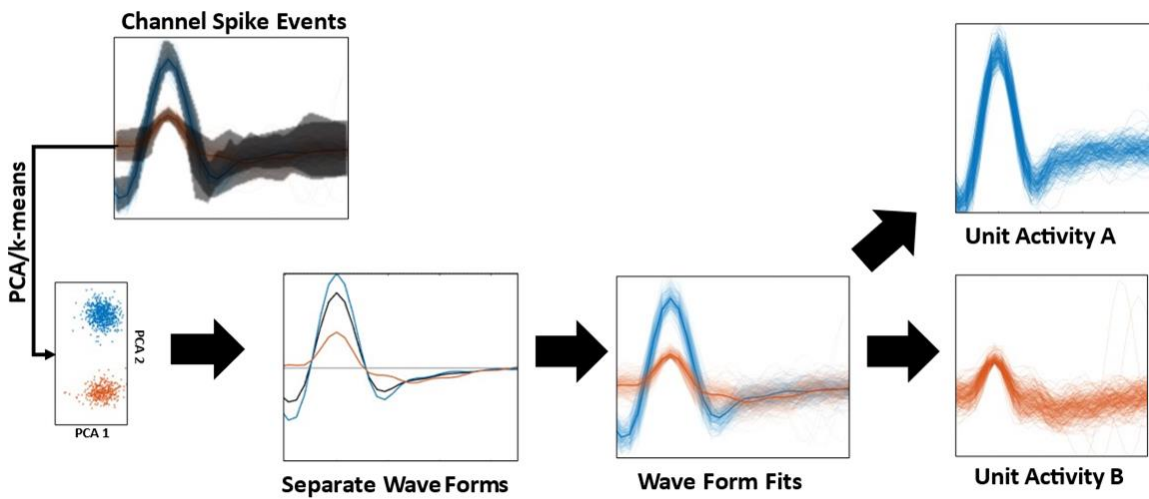


Figure 12. Spike Sorting Pipeline. High-pass broadband signals 3σ above background were logged as spike events. Principle component analysis and k-means clustering algorithms were used to determine separability between waveform features. Separate wave form averages were used to fit spike events and designated into separate unit activity sites. Units were designated as “single” with low variance waveform features consistent across spike event window. Above is an example from experiment 1450, Channel 43 (A5/MIP), A was designated as a single unit, b as multi-unit activity.

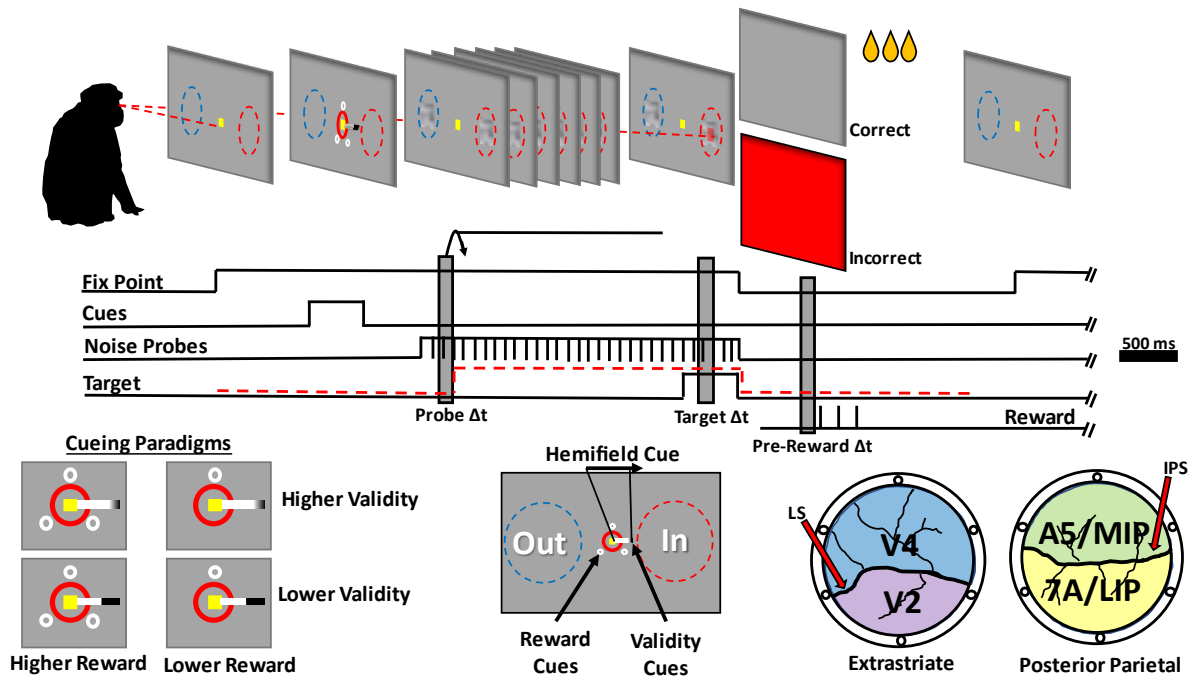


Figure 13. Attention-Value Experimental Design. Animal observers initially fixate on a central square and are presented with a set of cues indicating target color, a spatial cue indicating both the likely location of the target (left or right) and the validity of the spatial cue, and reward size for correct trial outcome. After the cues are extinguished, two streams of dynamic visual probe stimuli (textured noise patterns flickering at 10 Hz) appear and remain visible for the remainder of the trial. At a randomly selected time, a target appears at the center of one of the probe streams and observers must make a single accurate saccade to the target within 500 ms. Following an accurate saccade to the target, animals receive the reward. Errors (saccades to the wrong location or missed targets) are signaled by briefly flashing the screen red and a short timeout period. On 5% of trials no target appears (catch trial) and observers must maintain fixation until the end of the trial to obtain the reward. Neural activity was recorded and analyzed in three different temporal windows (gray shading), probe onset, target onset, and prior to reward delivery. Activity was recorded from four separate cortical surface areas delineated by sulci (lunate sulcus, LS, interparietal sulci, IPS) bifurcating the chamber area. V4 (blue), V2 (purple), A5/MIP (green), 7A/LIP (yellow).

Data Analysis

Initial Screening. An N-way ANOVA with categorical factors (reward magnitude, cue validity, cue location) was applied to the spike count data collected from each neuron ($\alpha=0.05$, see Figure 1) to determine which aspects of the behavioral task modulated neural activity. We computed the fraction of neurons significantly modulated by each factor in each brain region we recorded from. Significant percentages were bootstrapped ($n=1000$) by taking 75% of the cells in each area. Only correct trials were used.

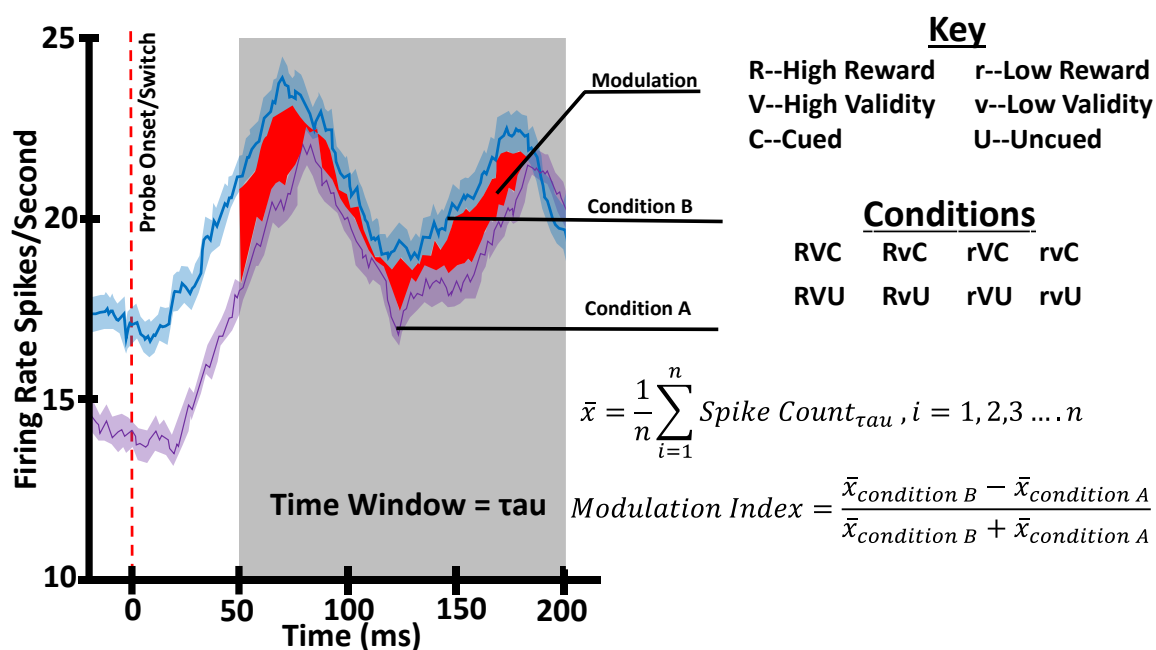
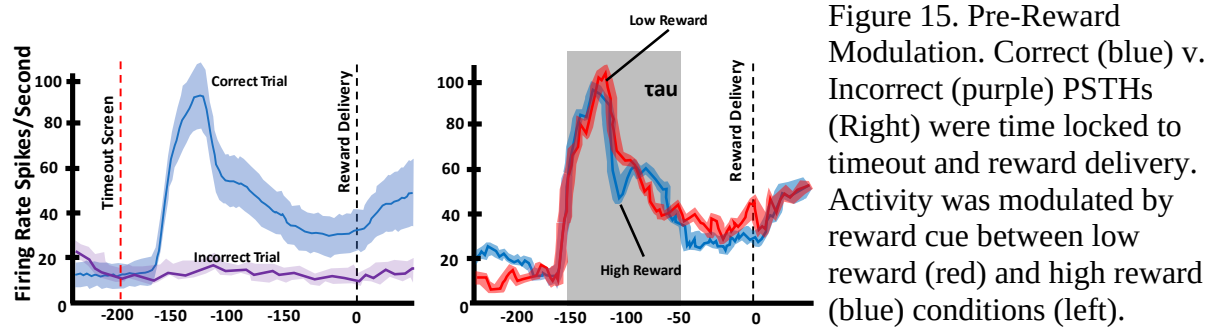


Figure 14: Neural Activity Analysis. Responses were time-locked to stimuli onset and spike counts were recorded during time period τ (gray box). Spike count averages were used to quantify modulation (red Area) between condition A (purple) and condition B (blue). Modulation indexes were recorded and screened for significance (permuted t-test, $\alpha=0.05$) between each condition type for reward, validity, and hemifield and used for further analysis.

Pre-Reward Activity. An increase of neural activity was observed prior to reward delivery in the attention-value task. This activity does not occur in incorrect trials. Modulations to this signal was observed in neurons with significant activity (see Figure 15).



Modulation Indexes. Spike count averages were used to quantify and characterize modulation profiles of each neuron. Modulations were transformed into a non-linear space (Michelson, 1927) to compare across a range of baseline firing rates (See figure 13; Marino and Mazer, 2018). A permuted t-test ($\alpha=0.05$) was used to determine modulation significance. After significance was determined, modulation sizes were bootstrapped ($n=1000$, 75% sampled with replacement). Positive and negative modulations were categorized between the twelve modulation categories. Neurons with detected modulations in a particular epoch were screened for modulations in other two epochs (See figure 14).

Results

Thirty recording sessions yielded activity from 622 units across both chambers (V4: 94, V2: 15, 7A/LIP: 232, A5/MIP: 281; recording sites identified based on combination stereotaxic

coordinates, sulcal landmarks recorded intraoperatively and reference to pre-operative MRI scans). Spike counts in probe, target, and pre-reward analysis windows underwent an ANOVA-N ($\alpha=0.05$) with reward, validity, and hemifield variables. Main and interaction effects were quantified by the amount of ANOVA-N significant cells as a ratio to cell totals (See Figure 16).

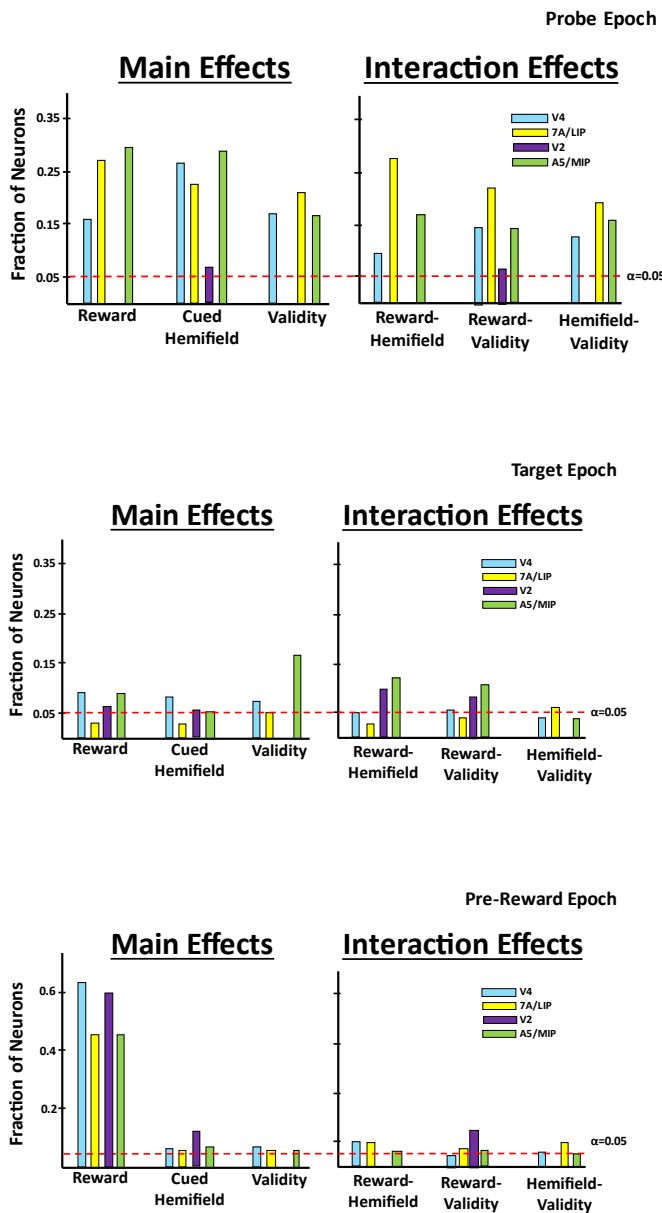


Figure 16: N-way ANOVA. Spike counts during probe epoch (top), target epoch (middle), and pre-reward epoch (bottom) were analyzed with N-way ANOVA with spike counts as response variables and categorical factors as predictors (see methods).

The fraction of neurons for each area (V4: light blue, V2: purple, 7A/LIP: yellow, A5/MIP: Green) is represented on the y-axis. Red dashed line is chance level detection at $\alpha = 0.05$. Main effects from value (reward), spatial location (cued hemifield), and validity along with interaction effects. Pre-reward epoch yielded higher fraction of neurons as indicated by the y-axis (fraction of neurons).

In 51/622 cells we observed a large increase in firing rate after the animal responded, but before the reward was delivered (started 150-200 ms before reward delivery; V4: 35/94, V2: 7/15, 7A/LIP: 1/225 A5/MIP: 8/255). Incorrect trials were compared with timeout screen onset with a latency of 50ms to 200 ms (See methods). Firing rates during this pre-reward delivery period were modulated in cells with a high rise in firing rate, but also in cells with a more attenuated signal. Spike count ANOVA-N detected large fractions of reward effects across all neurons.

Initial screening during ANOVA showed effects from value, validity, and location in fractions of neurons above what is expected by chance in all areas except V2 during the probe epoch, with little effects detected in all areas during the target epoch. Modulations from value, validity, and location were seemingly dependent on other categorical factors (see Chapter 2), a justification for use of more detailed modulation index analysis to address our hypothesis of non-dissociability between value and validity encoding.

Two variables were held constant while the modulation index (see methods) was calculated via bootstrapped with replacement ($n=1000$, 75%) and averages recorded. Bootstrapped mean modulation indexes for both negative and positive modulations for each condition were compared across conditions. Modulation absolute values were used to determine fraction of neurons with modulation. Modulation Indexes were calculated as in probe, target, and pre-reward time periods (See Figures 17, 18, 19).

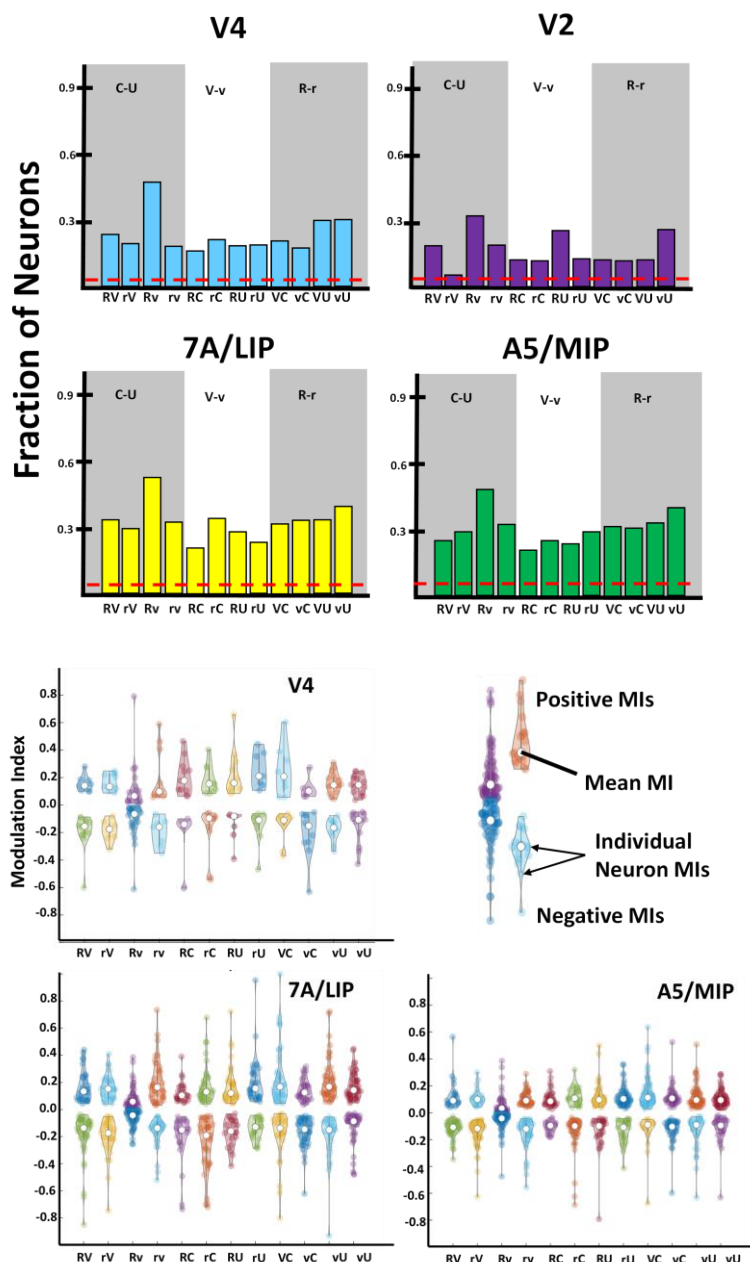


Figure 17: Probe Epoch Modulation Index Analysis. (Top) Spike counts averages per condition were tested for significance (see methods). Fraction of neurons for each of the twelve possible modulatory conditions were broken down by area. C-U represents MIs associated with hemifield, R-r reward, and V-v validity.

(Bottom) If significant, modulation index size was bootstrapped ($n=1000$, 75% with replacement). Positive and negative modulations were plotted separately. The different colors of violin plots were used to distinguish between individual plots. White circles indicate mean modulation index for a given condition (positive and negative). Variance is indicated by boundary of each plot, with individual measurements indicated by a small dense circle of the same plot color.

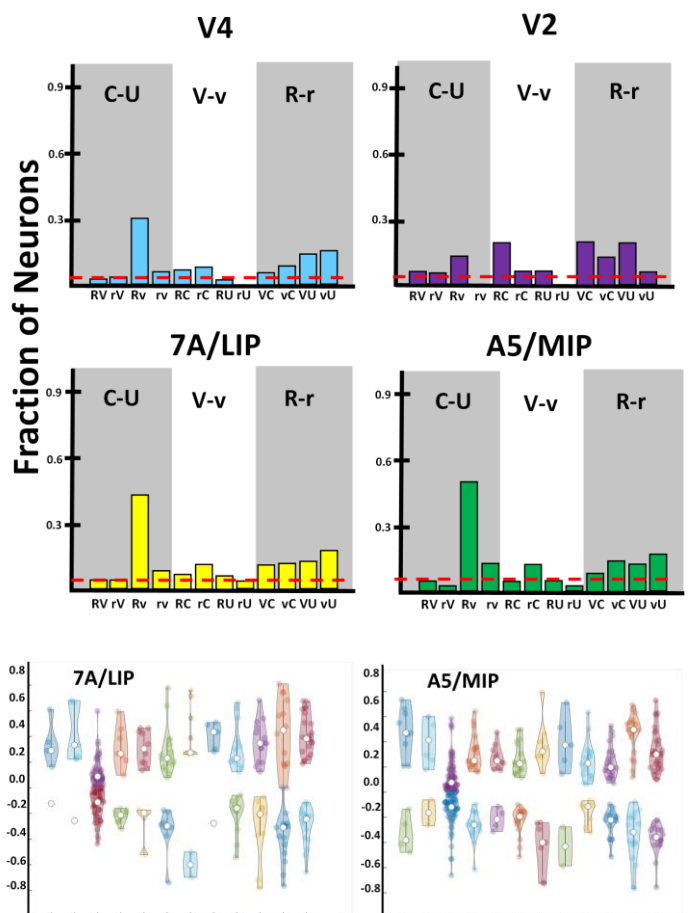


Figure 18: Target Epoch Modulation Index Analysis. (Top) Spike counts averages per condition were tested for significance (see methods). Fraction of neurons for each of the twelve possible modulatory conditions were broken down by area.

(Bottom) If significant, modulation index size was bootstrapped ($n=1000$, 75% with replacement). Positive and negative modulations were plotted separately. The different colors of violin plots were used to distinguish between individual plots. White circles indicate mean modulation index for a given condition (positive and negative). Areas V2 and V4 did not have enough modulations to warrant a violin plot.

In all probe epochs and areas, modulations between hemifields in the high value/low validity conditions were most prevalent. Modulation index values in this condition were also closest to zero, with absolute values statistical significantly different than other conditions, permitted enough modulation indexes were detected (permutated t-tests, $n=1000$, $p<0.001$), no permutated t-test was conducted if total MIs detected were less than ten observations. Modulations induced by value and validity differences were most prevalent during the probe

epoch. Reward modulations in target and pre-reward epochs were higher than the probe epoch.

Validity modulation was not prevalent outside the probe epoch.

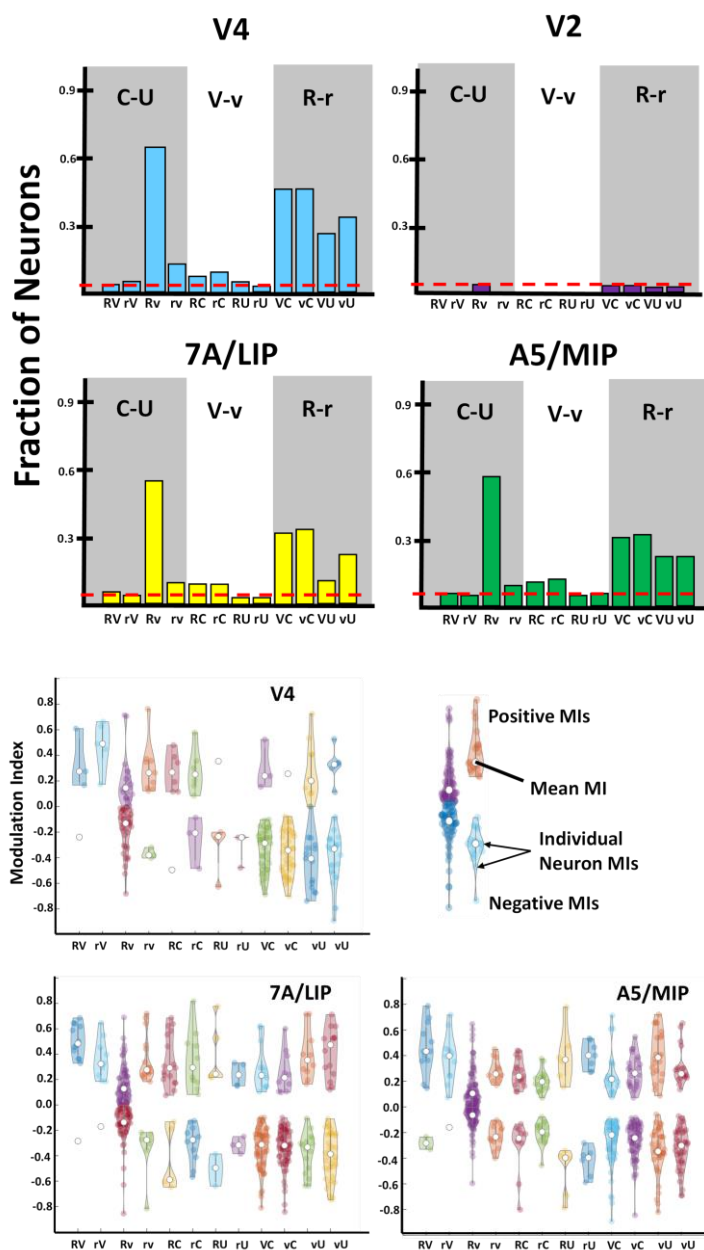


Figure 19: Pre-Reward Epoch Modulation Index Analysis. (Top) Spike counts averages per condition were tested for significance (see methods). Fraction of neurons for each of the twelve possible modulatory conditions were broken down by area. C-U represents MIs associated with hemifield, R-r reward, and V-v validity.

(Bottom) If significant, modulation index size was bootstrapped ($n=1000$, 75% with replacement). Positive and negative modulations were plotted separately. The different colors of violin plots were used to distinguish between individual plots. White circles indicate mean modulation index for a given condition (positive and negative). Area V2 did not have enough modulations to warrant a violin plot.

To further assess the dissociability of value and validity, modulation categories were checked for isolation with respect to modulation (i.e., neuron X is modulated by location but not

Discussion

The effects of cues on spike counts during the probe response period were heterogeneous in all brain regions recorded from. The cues that provide expected value maps with only low-resolution encoding detectable, precise probability is not as likely as one of qualitative probability as studies have suggested in primate and humans (Kable and Glimcher, 2007; Liston and Stone, 2008; Krajbich, and Rangel, 2011; Rushworth and Behrens, 2008; Gold and Shadlen, 2007) encoded as a range of probabilities with observable categorical effects between contrasting magnitudes.

The experimental design of the attention-value task is meant to test the differences between attentional facilitation between conditions. Early investigations into feature attention suggested a parallel processing network to accommodate simple forms of visual search (e.g., “singleton” search, where targets are uniquely defined by a single perceptual dimension, like color), discarding irrelevant features, enabling the “pop-out” (Treisman and Gelade, 1980). When search is more complex (e.g., “conjunction” search, where two or more perceptual dimensions must be checked to identify a stimulus as the target), search becomes serial and requires some sort of focal attention which is thought to scan the visual field in a serial manner (Wolfe, 1994).

Spatial attention resolution of the attentional locus is theorized to change size or spread between multiple locations (Intriligator, J., and Cavanagh, P. 2001). The higher number of modulations but of smaller effect size between locations in high-value/low-validity may be evidence in support of attentional locus spread during these conditions, though not definitive. A higher number of modulatory neural activity sites suggest an increase of attention facilitation,

consistent with theories on reward predictions in eliciting attention (Sali, Anderson, and Yantis, 2014; Rombouts, et al., 2015; Anderson, 2016). These suggest a variability to the either radius or resolution of the attentional locus based on environmental information while conducting repetitive tasks.

We rarely observed cells that were modulated by a single experimentally controlled independent variable. Spike count ANOVAs are not sensitive enough to detect the variable of modulation different condition sets. The sign of reward modulation can change depending on the location of the attentional focus, (i.e., ipsilateral, or contralateral to the neuron's receptive field). The coupling of reward magnitude and probability information allocates the attentional locus in ways that perceptual studies suggest information has subjective weight differences (Spittman, Chun, and Soltani, 2019) between observers, and based on the results of this study, is contingent on condition parameters, suggesting non-dissociability of value and validity.

Gain and suppression modulations detection often occurred in the same neuron on a given factor (location, value, or validity), contingent upon specific conditions of dependent on the other categorical factors. However, at the population level, similar characteristics emerged across all areas, most notably the modulation abundance between cued and uncued conditions with high reward and low validity and a reduction in modulation magnitudes.

Evidence has suggested attention reduces noise correlations in firing rates of the attended hemifield (Cohen and Maunsell, 2009). However, there is little evidence prior to this study of interareal signatures as observed in modulation index analysis, consistent across areas in specific condition sets. Until recently, technological limitations limited recording to single neurons in succession or multiple neurons of a single area. The heterogenous profiles of individual neurons

contrasted with more structure population characteristics implies systemic modulation that modulates individual neurons differently depending on cue conditions and temporal measurements but with structured population effects. There are several explanations as to the source of system wide modulations. FEF has is hypothesized to directly modulate extrastriate and parietal areas via cortical feedback circuits, or indirectly through subcortical structures like SC and the striatum (Noudoost and Moore, 2011). Neuromodulator's dopamine, acetylcholine, and epinephrine have been correlated with attention, posing questions as too their concentration levels with respect to each other, potentially different depending on environmental context. Extrastriate and post-parietal connectivity profiles invite numerous avenues for correlated interareal excitation, inhibition, and modulation and more resolution at all scales is needed to continue to develop and test hypothesis at neuron population levels.

The strongest signal detected during this study was the observed change in activity during the pre-reward period contingent on whether the trial was correct or incorrect. On correct trials we observed a significant increase in firing rate compared to incorrect trials (which generally showed no change in firing rate during the pre-reward interval). Because animals received visual feedback indicating whether the trial was correct (light gray screen) or incorrect (red screen), it is difficult to know whether this modulation is linked to the feedback or the animals' internal state. However, the observed modulation resembles previous reports (see Schultz, 1998 for review) recorded in dopaminergic neurons of the dorsal and ventral striatum, caudate and putamen areas of the thalamus, the substantia nigra. A substantial number of unit activity sites had detected modulations in reward in all conditions and a high number of cue modulations in high reward and low validity conditions in sensory neurons not reported previously.

At the scale of neuromodulators, studies into dopamine (DA) suggest that DA can modulate the efficacy of excitatory responses in way that is optimized for DA level whereas the synaptic efficacy declines outside of this amount (Noudoost & Moore, 2011). In a simultaneous recording of V4 and FEF neurons, D1R-mediated FEF activity was manipulated by injecting a D1 antagonist into sites within FEF. V4 neurons with similar spatial receptive fields as corresponding FEF manipulated neurons, the visual stimulus inside the RF was chosen more often as a saccade target. It was also observed that during passive fixation, the gain of visual signals showed an enhanced magnitude of response, a more selective stimulus orientation tuning and a more coherent response profile, all similar effects of covert attention in the extrastriate cortex. Manipulation of D2R yielded no enhancement of response yet did show preference to target selection (Noudoost & Moore, 2011). Their study did not address the time epoch prior to reward delivery, but the overlapping mechanisms suggested by literature and observations of this study point to potential lines of investigation to better understand this “anticipatory” response.

During probe periods, reward information interacted with spatial location and validity cues. The heterogeneity observed in modulation profiles of unit activity sites is reduced in target periods and reduced even further in pre-reward epochs with only reward modulations detectable above population chance levels. Probe epochs had substantially more sample sizes (~5 to 1) compared to targets, which can explain the reduction in detectability of other modulation types, but in the pre-reward epoch the same ratio exists with a significant signal present.

Correlations between significantly modulated neurons in between epochs yielded interesting results, with probe/target and probe/pre-reward modulations of the same neurons, whereas none existed between target/pre-reward epochs despite similar modulation index

profiles. This may provide evidence of dissociability of attention and reward neural activity in sensory areas and warrants more investigation into the differences between continuity of modulation during different task epochs.

In total, the data suggests separate systems with overlapping activity during the probe epoch. Analysis conducted during this study could not dissociate between value and validity effects on neural activity, regardless of area. Validity effects were less prevalent and nearly non-existent in anticipatory reward and target epochs, suggesting a potential avenue for dissociability between circuitry responsible for value and validity modulation. Reward information implicit in the endogenous cues may be a separate system interacting with probability information to detect a target from that of anticipatory or feedback modulations concentrated sensitive to value cues.

Using a stochastic reward schedule and/or varying reward validity in future work would help clarify the nature and possible sources of the pre-reward modulation observed here. Stochastic reward has shown to modulate decision making and neural activity in humans and primates (Rakhshan, et al., 2018; Baruni, Lau, Saltzman, 2015; Henschke, et al., 2020; Liston, 2008, Louie, et al., 2011; Murty, et al., 2017). The interaction with spatial validity is not present once the target has appeared (the probability of a target at a location is now effectively 1 or 0) and after months of training, reward delivery 100% consistent with reward cueing, with temporal precision (<5 ms). An introduction of reward cue validity may disrupt the certainty of reward, sending modulatory profiles into more heterogeneous make up such as those observed during probe epochs, possibly linking observations of a single systems under diverse conditions instead of two separate systems. Further investigation is required to substantiate the separability of reward information processing in sensory neurons and categorize differences in observers.

CONCLUSIONS

“We assumed that visual attention can be treated as conceptually separable from other elements of the decision-making process” –Platt and Glimcher, Nature, 1999

Three performance metrics were used to characterize modulations between endogenous cue conditions in the attention-valuation task. High reward and low validity cue false alarm rates were significantly detectable but the closest to net zero compared with other conditions. Reward modulations were closer to zero in uncued conditions but increased false alarm rates at cued locations suggesting an increased level of alertness during higher rewarded trials. Hit rates differences of over 10 percent for higher reward in cued low validity conditions and likewise for higher validity low reward cued conditions, similar across both animal observer. Saccade reaction times to the uncued side were ten milliseconds faster between higher validity and lower validity in high reward uncued conditions.

In total, the confidence in information in higher validity led to increased false alarms, hit times, and a reduction in reaction times. These effects were eliminated in lower validity trials, especially when combined with higher reward cues. These observations suggest that high reward and low validity cue interactions induce a different state of the system, at least compared to other variable combinations. The significant differences in effects of validity, spatial cue, and reward information and diversity of modulation profiles suggests a coupling of systems that interact in ways that are detectable but not orthogonal.

622 neurons from different areas produced diverse individual modulatory profiles, but similar population profiles most notably when metrics were transformed into modulation indexes and characterized, were observed in all areas. A pre-reward signal was strongly present in

Individual neurons encode reward, validity, and hemifield modulations differently, but produce similar distributions of modulation indexes at population level.

A pre-reward anticipatory signal modulation by reward was observed in the period prior to reward delivery in correct trials. Modulations of this signal were detected in all areas in much higher percentages than during probe periods, with the most activity occurring between cue modulations in high reward, low validity conditions.

The hypothesis inspiring this body of work is that modulations due to reward and spatial attention are not dissociable. The best evidence for dissociability is in increased reward modulated anticipatory signals with elevated structure in high reward and low validity conditions. Firing rates in anticipation of reward, modulate their firing rates based on the expectation. Reward magnitude cue were 100% valid and elicited individual neurons levels above chance in 3/4 recorded areas during all time epochs of the task.

However, the original hypothesis was developed specifically for the probe epoch in assessing attention and reward modulation. Given the heterogeneity of modulation indexes of any given cell but structure in aggregate, presents a picture of systemic modulations which could be an emergent phenomenon based on network arrangement of relationships than individual node computation. At the individual neuron level, the null hypothesis can be rejected, however at population and behavioral scales it cannot be dissociated.

Without a second animal observer it is difficult to assess individual variability contributions to the results. This leaves uncertainty of the impact of the results of this study. Discontinuity between animal observers at the level of behavior without neural data to test whether behavior and neural activity emphasis on probability or reward cues for any given time

epoch is consistent with behavioral modulation profiles or the same as the other observer at individual and population of neurons.

A second avenue of critique can be levied by the position of what is classified as attention vs reward modulations in the past. Perceptual learning via plasticity may render the use of attentional deployment a waste of resources to be reserved when the reliability of perceptual cue associations is degraded such as in lower validity conditions. The brain's properties of plasticity are not fully understood and creates multiple solution pathways to an optimization problem, the hallmark of an evolutionary process in response to diverse environmental conditions.

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