unclear. The evidence supporting a defect in vesicle priming in CSPα KO mice is indirect. Direct evidence showing a decrease in the docked vesicle number, the readily releasable vesicle pool size, and/or the rate of vesicle mobilization to the readily releasable pool awaits further study. It also remains untested whether the defects in dynamin 1 polymerization and vesicle recycling cause synapse loss. This possibility has been challenged by a recent study showing that SNAP-25 overexpression is sufficient to rescue synapse loss and degeneration in cultured neurons derived from CSPα KO mice (Sharma et al., 2011a). In addition to SNAP-25 and dynamin 1, there are around 20 other proteins that are reduced in CSPα KO mice (Zhang et al., 2012). Further investigation is needed to understand how these other proteins are regulated by CSPα and whether their decrease contributes to synaptic dysfunction and loss observed in CSPα KO mice. The studies by Rozas et al. (2012) and Zhang et al. (2012) have laid a foundation for future studies that will aim to resolve aforementioned questions.

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Familiarity Breeds Plasticity: Distinct Effects of Experience on Putative Excitatory and Inhibitory Neurons in Inferior Temporal Cortex

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DOI 10.1016/j.neuron.2012.03.020

Primates have a remarkable capacity to recognize a vast array of visual objects, an ability that depends on experience. In this issue of *Neuron*, Woloszyn and Sheinberg (2012) report that putative excitatory and inhibitory neurons in inferior temporal cortex exhibit distinct influences long-term visual experience.

Humans and other primates have an astonishing ability to recognize many thousands of unique visual objects, from faces and food items to natural and man-made objects. We are not born with a large innate library of familiar objects that we are able recognize. Instead, our recognition ability depends on learning and experience. Experience can also produce a significant improvement in visual discrimination. For example, an expert bird watcher might easily distinguish between two individuals from the same species, while a less experienced observer might be unable to distinguish them. In addition to identification and discrimination, humans and other animals are sensitive to whether a stimulus is familiar (Fagot and Cook, 2006), sometimes even for stimuli that had been viewed infrequently in the past and about which no other details can be recalled.

Neurophysiological investigations of object recognition have focused on a hierarchy of cortical areas including area V4 and the posterior and anterior

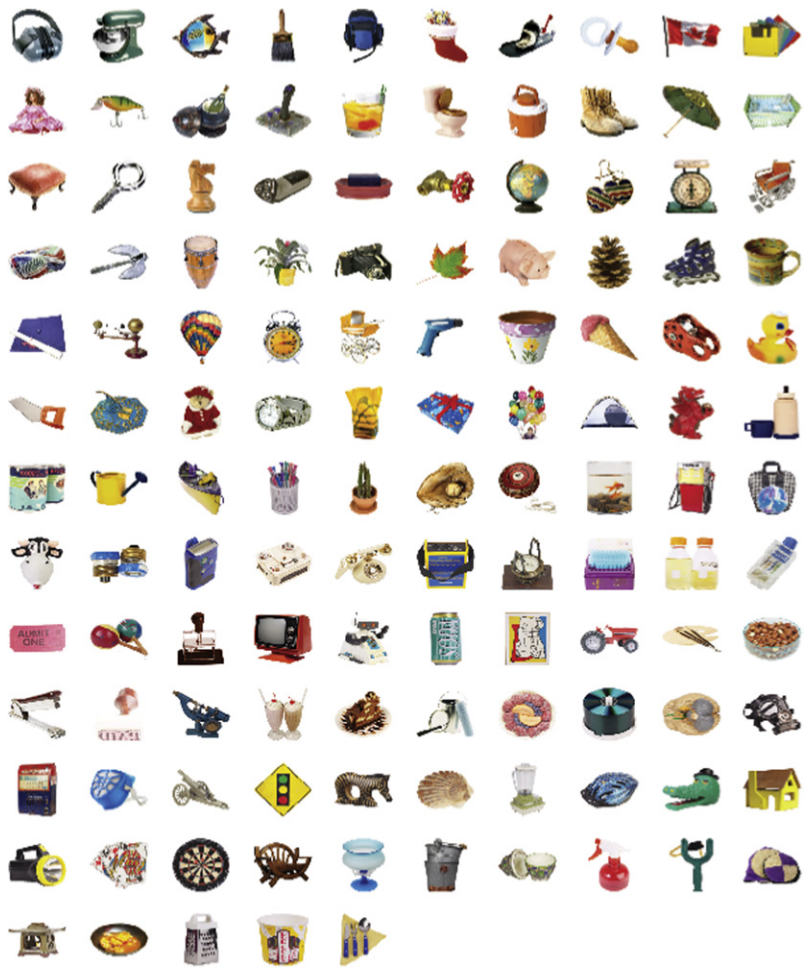

Figure 1. Examples of Familiar Stimuli used in the Woloszyn and Sheinberg Study

inferior temporal cortex (ITC). Studies of the visual selectivity of neurons in these areas have revealed tuning to combinations of visual features and increasing complexity of preferred stimuli from more posterior areas to anterior ITC (for a recent review, see Connor et al., 2009). Well-known examples of neuronal object selectivity are "face cells" in ITC which respond preferentially to images containing faces. While recent work suggests that face processing may depend on a specialized network of areas within ITC (Moeller et al., 2008), strong neuronal responses and selectivity are observed throughout ITC for a wide range of stimuli including abstract geometric patterns, natural and man-made objects, and natural scenes.

A number of studies, including that by Woloszyn and Sheinberg (2012) in the current issue of *Neuron*, have demonstrated that both passive exposure and explicit training can impact neuronal activity in ITC, often in ways that enhance or sharpen object representations. However, the patterns of experience-dependent changes in ITC have varied across studies for reasons that are not fully understood. For example, several studies in ITC suggest that passive experience or explicit training results in sharper tuning for trained stimuli, as well as increased response strength for neurons' preferred stimuli (Kobatake et al., 1998; Logothetis et al., 1995). However, other groups reported that, while ITC selectivity was enhanced for familiar or trained stimuli, experience led to *weaker* average responses to familiar compared to novel stimuli (Li et al., 1993; Fahy et al., 1993) and that enhanced selectivity may result from decreased responses to nonpreferred stimuli rather than increases to preferred stimuli (Freedman et al., 2006).

In the current issue of *Neuron*, Woloszyn and Sheinberg (2012) shed new light on the plasticity of ITC shape representations and help reconcile the disparate results of the prior studies mentioned above. They examined ITC activity while monkeys viewed visual stimuli that were either novel or highly familiar (Figure 1). They classified their ITC population into putative excitatory and inhibitory cells by virtue of the width of neurons' spike waveforms and examined whether these distinct neuronal populations exhibited different patterns of selectivity and learning effects. Narrow spiking neurons usually correspond to inhibitory interneurons while broad spikes are typically generated by excitatory pyramidal neurons (McCormick et al., 1985). Recent studies in V4, posterior parietal cortex, and prefrontal cortex found that these two neuron classes showed distinct patterns of effects during attention (Mitchell et al., 2007), discrimination (Hussar and Pasternak, 2009), and numerical categorization (Diester and Nieder, 2008).

Woloszyn and Sheinberg (2012) show that in ITC, putative excitatory and inhibitory neurons exhibit very different effects of experience—excitatory neurons typically showed experience-dependent *increases* in activity that were specific to their preferred stimuli (i.e., the images in the stimulus set that elicited the strongest responses). In contrast, inhibitory neurons showed global *decreases* to familiar compared to novel stimuli (including the most preferred stimuli in the tested sets). Notably, putative excitatory neurons also showed widespread decreases in firing rate to nonpreferred familiar stimuli. These results suggest that the net effect of experience on putative excitatory neurons is to boost responses to neurons' preferred stimuli, potentially leading to sparser representations with a higher signal-to-noise ratio. These stronger and sharper representations of familiar stimuli could have a greater impact on downstream neurons, potentially enhancing the read out information from ITC. Long-range

connections between cortical areas originate predominantly from excitatory pyramidal neurons; thus, the stronger and sharper representations of familiar stimuli would support more efficient read-out of object identity from excitatory ITC neurons.

These results help to reconcile the conflicting findings from earlier studies. As the authors point out, previous studies which reported stronger responses to familiar stimuli tended to use large and diverse stimulus sets and/or screened neurons to identify their preferred stimuli. Thus, these studies were more likely to test neurons with preferred stimuli that would drive strong responses. Studies which found either weaker or equivalent firing rates for familiar compared to novel stimuli often used smaller stimulus sets, chose stimuli from a relatively restricted region of object space, or made no efforts to identify neurons' preferred stimuli. Furthermore, all prior studies almost certainly sampled both excitatory and inhibitory neurons, but did not analyze those populations separately. The authors point out that when both classes of neurons are combined in population analyses, the increased response of the excitatory population to preferred familiar stimuli would be at least partially counterbalanced by the opposite effect in the inhibitory population. Along with the differences in the stimuli and experimental procedures, this may account much of the variability across previous studies.

This study lends support to the idea that object recognition is mediated by a sparse code in ITC, in which objects are each represented by small populations of exquisitely tuned neurons. The current study suggests that learning would facilitate this coding scheme by increasing the response rate and sharpness of selectivity for neurons' preferred familiar stimuli. As described above, this could lead to improvements in the ability of downstream areas to read out object information from excitatory projection neurons in ITC. Important questions remain regarding the encoding of object representations in ITC. For example, studies which did not optimize stimuli or used small or homogeneous stimulus sets typically find highly significant stimulus selectivity for the tested stimuli despite weaker firing rates (Baker et al., 2002; Sigala and Logothetis, 2002; Freedman et al., 2006). Thus, in addition to responding very strongly to an optimal stimulus, ITC neurons also have the ability to discriminate between their nonpreferred stimuli. However, the degree to which object recognition is mediated by the few neurons that are optimally tuned for a stimulus or, instead, by the larger and more distributed population that is responding selectively (but at nonoptimal rates) remains to be determined.

A number of related questions remain to be examined in future work. For example, the current study examined ITC activity during a passive viewing task with limited behavioral demands. Thus, it will be interesting to compare the patterns of selectivity in putative excitatory and inhibitory neurons during more active and demanding tasks such as discrimination or memory-based matching. One way to assess whether recognition relies predominantly on the subset of strongly responsive excitatory neurons is to ask whether the activity of those neurons is better correlated with animals' trial-by-trial perceptual judgments than other neuronal populations. A second question to explore is how ITC object representations change during the learning process itself. In the current study, monkeys were familiarized with a set of stimuli for several months prior to ITC recordings. Additional work is needed to characterize the time course of experience-dependent changes in ITC, and to explore whether putative excitatory and inhibitory neurons play distinct roles during the learning process as they appear to do once learning is complete.

An intriguing effect observed in both this study and previous work is that experience results in a marked decrease in average activity across the ITC population (Li et al., 1993; Fahy et al., 1993; Freedman et al., 2006)—except for the (presumably few) excitatory neurons that happen to be well tuned to the currently-viewed stimulus. As noted above, humans and other animals are highly sensitive to whether a stimulus is familiar or novel. An interesting issue for future work will be to examine the relationship between neuronal familiarity effects in ITC and behavioral effects of novelty and familiarity. One hypothesis is that the widespread experience-dependent suppression of activity in ITC underlies our ability to detect novelty and familiarity. Further, it will be interesting to examine how novelty and familiarity signals in ITC relate to attention, as novel or unexpected stimuli are often highly effective for capturing attention.

In summary, the results of this study are an important contribution to our understanding of the neural circuitry underlying visual object recognition and, in particular, how experience influences shape selectivity in ITC. More broadly, the observation that different cell classes show distinct effects of learning points out the need for new tools, analytical approaches, and in vivo data acquisition techniques for recording neuronal activity along with anatomical and morphological information about the recorded neurons (e.g., neuron type, cortical layer, and pattern of connections). This will ultimately be essential for developing a detailed circuit-level understanding of the neural basis of visual recognition.

ACKNOWLEDGMENTS

The author thanks Jillian McKee and Sruthi Swaminathan for comments and helpful discussions regarding this manuscript.

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