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Synaptic Plasticity from Visual Cortex to Hippocampus: Systems Integration in Spatial Information Processing

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The adult cerebral cortex possesses the remarkable ability to change its neuronal connectivity through experience, a phenomenon termed “synaptic plasticity.” Synaptic plasticity constitutes a cellular mechanism that is thought to underlie information storage and memory formation in the brain, and represents a use-dependent long-lasting increase or decrease in synaptic strength. Recent findings, that the adult visual cortex undergoes dynamic synaptic plasticity that is driven by active visual experience, suggest that it may be involved in information processing that could contribute to memory formation. The visual cortex provides a crucial sensory input to the hippocampus, and is a key component for the creation of spatial memories. An understanding of how visual cortical neurons respond with synaptic plasticity to visual experience, and whether these responses influence the induction of hippocampal plasticity, is fundamental to our understanding of the neuronal mechanisms and functional consequences of visuospatial information processing. In this review, we summarize recent findings with regard to the expression of dynamic synaptic plasticity in the visual cortex and how this plasticity may influence information processing in the hippocampus. *NEUROSCIENTIST* 14(6):584-597, 2008. DOI: 10.1177/1073858408315655

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One of the most intriguing of the brain’s complex functions is its ability to store information provided by experience. Memory is not a specialized property of a limited set of cortical areas; rather, all areas of the cortex are capable of experience-dependent change over a wide range of time scales (Gilbert and others 2001). Most experience-dependent learning derives from sensory inputs mediated by visual, auditory, tactile, and olfactory perception. For spatial information processing and the acquisition of declarative memories in general, the visual system dominates in a large number of species, particularly in humans. It had long been assumed that cells in visual areas had fixed properties, passing along the product of a stereotyped operation to the next stage in the visual pathway. But the concept of spatial integration of visual features and the involvement of visual cortex plasticity has been radically modified in the past few years (Gilbert 1998), especially with regard to the role of primary visual cortex. Recent findings suggest that experience-dependent synaptic plasticity occurs in the adult primary visual cortex (Heynen and Bear 2001; Tsanov and Manahan-Vaughan 2007a, 2007b), and that

this phenomenon exerts an influence on subsequent stages of information processing leading to long-term memory. Importantly, synaptic plasticity occurring in the adult primary visual cortex may influence the ability of the hippocampus to integrate spatial episodes in time (Ji and Wilson 2007). This interaction may comprise a key element in neocortico-hippocampal transfer of information and the subsequent formation of spatial memories. In this review, we discuss the evidence for synaptic plasticity in the adult visual system, focusing on synaptic alterations occurring in the primary visual cortex. We relate this plasticity to the mechanisms with which neural circuits have been found to mediate learning along the ventral visual stream. The review summarizes the anatomical and physiological pathway of visual spatial information flow to the hippocampus, and integrates our knowledge of synaptic plasticity and its role in episodic memory formation.

Influence of Sensory Processing on Adult Visual Cortical Plasticity

Although certain functional properties of the visual system, such as ocular dominance, undergo plasticity only during a limited critical period early in postnatal development (Hubel and Wiesel 1977), several other properties can be influenced by visual experience throughout life (Gilbert 1998; Crist and others 2001). Psychophysical evidence shows that the spatial resolution of the adult visual system,

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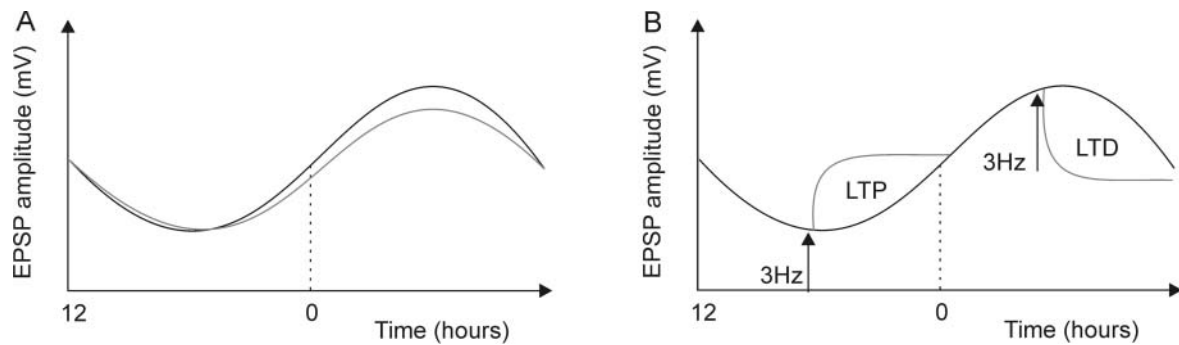


Fig. 1. Modulations of rodent V1 basal synaptic transmission. (A) Diagram of the diurnal oscillation of basal synaptic transmission recorded for 24 hours in freely moving rats. Time 0 on the x axis denotes light on (marked with dotted line), and 12 denotes light off. The relative V1 response to thalamic stimulation is measured as excitatory postsynaptic potential (EPSP) amplitude on the y axis. Prolonged restriction of visual experience causes a smaller response during the augmented part of the cycle, illustrated with the gray line (after Tsanov and Manahan-Vaughan 2007a). (B) Synaptic plasticity induction during different behavioral states results in dissimilar long-term responses. Low-frequency stimulation (3 Hz, 900 pulses) evokes LTP when given during the declining part of diurnal oscillations, and long-term depression (LTD) when given during the augmented part of diurnal oscillations (after Tsanov and Manahan-Vaughan 2007b).

in the form of hyperacuity, can improve with practice (Poggio and others 1992; Fahle and Edelman 1993; Kapadia and others 1994; Beard and others 1995; Saarinen and Levi 1995). Training can also improve discrimination stimulus attributes, including orientation (Vogels and Orban 1985; Shiu and Pashler 1992; Schoups and others 1995), motion (Ball and Sekuler 1982, 1987), texture (Karni and Sagi 1991, 1993), and spatial phase (Fiorentini and Berardi 1980, 1981; Berardi and Fiorentini 1987).

Studies in both humans and animals have shown that training over periods of days to weeks can cause robust and long-lasting improvements in various aspects of visual perception (Fahle and Poggio 2002; Karmarkar and Dan 2006). A growing body of evidence reveals that these long-term effects occur in the early cortical processing of visual information. Application of functional magnetic resonance imaging (fMRI) and transcranial magnetic stimulation have provided more direct evidence that at least some forms of improved visual discrimination involve changes in early circuits such as the primary visual cortex (V1; Furmanski and others 2004; Maertens and Pollmann 2005; Neary and others 2005).

Perceptual learning, or improvement in perceptual abilities with experience or training, involves all areas of the ventral visual pathway from the temporal lobe extending to the primary visual cortex (Gilbert and others 2001). In general, this form of neocortical synaptic plasticity has been best studied at the level of the adult primary visual cortex, because it involves cortical areas at the early stages of visual processing, where most is known about neocortical circuitry, receptive field properties, and functional architecture.

Perhaps the most striking property of the adult cortex is its ability to dynamically modify the processing of visual information according to immediate behavioral requirements (Crist and others 2001). The history of cortical activity is tightly related to changes in the field response evoked either by active visual processing (Tsanov and

Manahan-Vaughan 2007b; Fig. 1A) or by thalamocortical stimulation (Tsanov and Manahan-Vaughan 2007a; Fig. 1B). Basal synaptic transmission in the visual cortex is dynamically regulated by a combination of circadian and light-independent mechanisms, as well as the recent history of visual experience (Tsanov and Manahan-Vaughan 2007b). Visual experience can result in increased neuronal responsiveness and this plastic effect is associated with an increase of gamma oscillations (30–80 Hz) during the preceding visual exploration episode (Tsanov and Manahan-Vaughan 2007b). Gamma oscillations, in cortical structures, are believed to provide temporal windows that bind coherently cooperating neuronal assemblies to enable the representation, processing, storage, and retrieval of information (Singer 1993; Buzsáki and others 1994; Gray 1994; Nase and others 2003; Samonds and Bonds 2005). Gamma oscillations subserve sensory memory and attentional selection (Fries and others 2001). Besides the long-term effects of visual experience, the visual system expresses short-term plastic changes to process information. In the visual cortex, short-term synaptic plasticity, and in particular synaptic depression, is an important component of the nonlinear temporal dynamics that lead to enhancement of responses (Chance and others 1998). Short-term depression on a population level results in enhanced sensitivity of single visual cortex neurons to subtle changes in the firing pattern of their afferents (Abbott and others 1997). This form of plasticity also is correlated to gamma oscillations, indicating that network oscillatory activity and depression of field potentials may act synergistically in the rodent visual cortex (Tsanov and Manahan-Vaughan 2007b).

Plasticity processes in the visual cortex underlie different forms of visual perceptual learning (Hegde 2006; Karmarkar and Dan 2006). Changes in V1 orientation tuning, that accompany improved performance during orientation discrimination in adult monkeys, parallel an increase in the slope of the tuning curve at the trained orientation

(Schoups and others 2001). Following a prolonged learning period, receptive field properties in area V1 vary, depending on task demands. Another form of perceptual learning is associated with changes in the contextual modulation of V1 responses (Li and others 2004). Thus, neuronal activity in V1 can be selectively modulated by behaviorally relevant stimulus elements surrounding the receptive field. This suggests that receptive field properties in V1 are adaptive and can change according to task demands. The relationship between learning and visual cortical changes has been also demonstrated in rodents. Repeated exposure of adult mice to stimuli of a certain orientation induces a specific potentiation of the V1 response to the trained orientation (Frenkel and others 2006). The improvement is specific to the trained eye and develops only across multiple days of training. A common observation from studies in both primates and rodents is that perceptual learning, in the visual system, is mediated primarily by changes in the response strength or tuning of individual neurons (Karmarkar and Dan 2006).

A growing amount of data indicates that the adult visual cortex serves as a synaptic network, where the ability to process visual stimuli is dynamically modified by visual experience. Perceptual learning is a process that involves changes in synaptic strength of the neurons comprising the network. This, however, comprises just one component of long-term synaptic modifications of V1 neurons, which influence the functional properties of the visual system. Recently, it has become apparent that the adult visual cortex also participates in dynamic synaptic plasticity that contributes to active visual processing of other forms of sensory information.

Dynamic Synaptic Plasticity in the Adult Visual Cortex

The change of synaptic strength between functionally related neurons is believed to underlie memory processes on a cellular level (Bliss and Collingridge 1993; Bear and Abraham 1996; Braunewell and Manahan-Vaughan 2001; Kemp and Manahan-Vaughan 2007b). Stimulation-induced, bidirectional synaptic plasticity has been observed in the adult visual cortex *in vitro* (Heynen and others 1996; Kirkwood and others 1996), in anesthetized animals (Heynen and Bear 2001), and in freely moving animals (Tsanov and Manahan-Vaughan 2007a). Theta-burst stimulation of the dorsal lateral geniculate nucleus induces reliable and long-lasting potentiation of field potentials evoked in the primary visual cortex of adult anesthetized rats and this potentiation increases the amplitude of visually evoked potentials across a range of spatial frequencies (Heynen and Bear 2001). In humans, a visual tetanus of rapid stimulus presentation enhances a component of visually evoked event-related potentials (Teyler and others 2005), which is reminiscent of synaptic LTP induced *in vitro* by tetanic presynaptic stimulation.

Neuronal responses vary as a function of network activities, which depend, in turn, on behavioral states. A recent study demonstrated that basal synaptic transmission in the visual cortex oscillates between elevated and suppressed levels (Tsanov and Manahan-Vaughan 2007a). The

plasticity properties of both states differ, with low-frequency stimulation (LFS) protocols, in particular, inducing dissimilar synaptic alterations. LFS at 3 Hz leads to long-term depression (LTD) during the nonaroused state and LTP during the aroused state (Fig. 1B). This suggests that in the nonaroused state the modification threshold for induction of LTD is shifted to the left (Bienenstock and others 1982; Bear and others 1987; Kirkwood and others 1995), revealing an occurrence of functionally dependent metaplasticity (Bear and others 1987; Bear and Abraham 1996). These findings indicate that the adult rodent visual cortex is in a perpetually dynamic state, where the direction of change of synaptic strength is driven by the visual experience of the animal during the light-dark cycle.

However, it is still not entirely clear how LTP and LTD relate to naturally occurring long-term plasticity. Frequency-dependent plasticity relies on naturally occurring fast, and very fast, cortical oscillations timed on a slower theta rhythm (Larson and others 1986; Larson and Lynch 1988, 1989; Gray and McCormick 1996; Fig. 2A). In addition to frequency-dependent Hebbian modifications, another mechanism is also known contribute to adult functional V1 plasticity (Yao and Dan 2005). Changes in synaptic efficacy can thus also be based on the precise timing of presynaptic and postsynaptic activity (Levy and Steward 1983; Markram and others 1997; Debanne and others 1998; Fig. 2B). This “spike-timing-dependent plasticity” has several properties that are believed to transform changes in environmental inputs into changes in neural representations (Fu and others 2002; Sur and others 2002). The functional consequence of spike-timing plasticity is that synapses from a presynaptic neuron, which contribute to the firing of the postsynaptic neuron, will be strengthened, whereas synapses which are uncorrelated or antipaired with postsynaptic spike times, will tend to be weakened. Similarly asynchronous visual stimuli flashed at two orientations (Yao and Dan 2001; Yao and others 2004) have been found to induce rapid shifts in orientation tuning, suggesting a functional relevance for the cortical modifications. The dependence on the spiking sequence and interval has been demonstrated in visual cortical slices (Sjostrom and others 2001; Froemke and Dan 2002) and *in vivo* in adult cat V1 (Yao and Dan 2001; Fu and others 2002; Yao and others 2004).

Homosynaptic and heterosynaptic types of plasticity (Fig. 2C, D) occur in primary sensory cortices and at the same time are associated with improvement in perceptual performance, which suggests that the mechanisms of learning may be general to the neocortex as a whole (Crist and others 2001).

Influence of Visual Cortical Plasticity on Synaptic Processing along the Ventral Stream

Given the enormous significance of the visual sensory input to the hippocampus for spatial and declarative memory formation, one possibility is that the visual cortex plays an active role in driving declarative memory formation. But how might synaptic plasticity in the primary visual cortex influence the formation of declarative

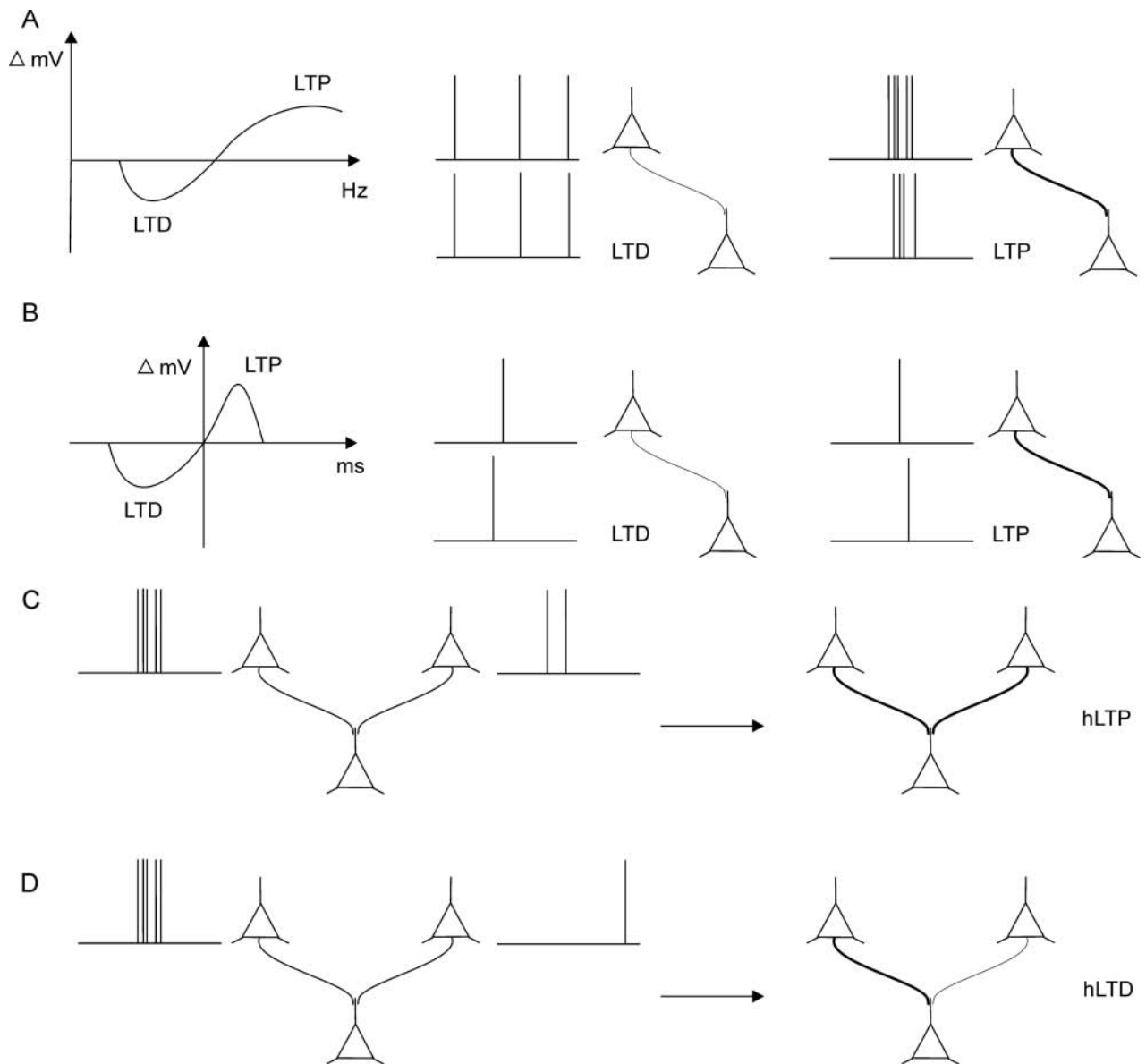


Fig. 2. Models of synaptic plasticity induction. (A) Frequency-dependent synaptic plasticity. *Left:* Diagram showing the dependence of synaptic plasticity, represented on the x axis by the change of the measured neuronal response in mV, on the frequency (Hz) of homosynaptic interaction. A lower frequency, of ~1 Hz, results in LTD, whereas higher frequencies will tend to evoke LTP. Schematic representation of the frequency of the pre- and postsynaptic action potentials (shown with vertical lines) demonstrating the induction of long-term depression (LTD; *middle*) and LTP (*right*). (B) Spike timing-dependent plasticity. (*Left*) Diagram illustrating the importance of the sequence in pre- and postsynaptic activity as well as the importance of a temporal proximity between both events. The timing is expressed in milliseconds on the x axis, with the y axis indicating the moment of coincident activity. (*Middle*) If a presynaptic spike follows the postsynaptic response, LTD is induced. (*Right*) If presynaptic activity precedes the postsynaptic one, LTP is induced. (C) Model for the induction of heterosynaptic plasticity. Temporal pairing of presynaptic high-frequency spiking with another “weak” presynaptic input results in a potentiation (hLTP) of this input. (D) When the second input is silent, the high-frequency activity of the first input induces heterosynaptic depression (hLTD) in the silent one.

memories? To answer this question we need to review it in the context of sensory information processing, which leads to functional integration of physiological processes such as perceptual learning and object recognition, such

that spatial learning and encoding of temporal sequences takes place.

Our capacity to identify visual objects in space relies on a large neural network, extending from the retina to

the hippocampal region, and which includes the so-called ventral pathway, a set of cortical areas spanning from the primary visual cortex to the inferior temporal cortex (Fig. 3). The ventral pathway can be characterized by a hierarchical architecture in which neurons in higher areas code for progressively more complex representations by pooling information from lower areas (Logothetis and Sheinberg 1996; Rolls 2000a). Thus, neurons in V1 code for relatively simple features such as local contours and colors, whereas neurons in higher cortical areas represent increasingly complex characteristics of images, objects, and categories (Maunsell and Newsome 1987; Vogels and Orban 1996). Higher neurons are also less dependent on coincidental spatial features, such as precise location, retinal size, viewpoint, lighting, and color (Hochstein and Ahissar 2002). Structurally this hierarchical organization of the visual system is linked to the size of the receptive fields (RFs). V1 neurons have small RFs, hence providing precise information about the position of the stimulus in the visual field. As each higher level of the visual system receives convergent inputs from lower areas, integrating information from broad areas of the visual field, the RFs consequently become larger (Boussaoud and others 1991; Kobatake and Tanaka 1994; Op De Beeck and Vogels 2000). Therefore, the ventral pathway possesses the capacity to very rapidly build the representation of an isolated object that is finally encoded in inferior temporal areas (TEO and TE).

Large RFs imply that TE neurons are able to encode several coarse object representations simultaneously during a short time after stimulus onset. This property enables the ventral pathway, via V4, TEO, and the TE neurons, to build up the spatial configuration of visual features that are processed in a receptive field. Such an ability underlies our capacity for parallel processing of different visual features, enabling recognition of a complex object independently of its size and position (Hasselmo and others 1989; Gross 1992; Rolls 1992; Logothetis and others 1995; Wallis and Rolls 1997; Booth and Rolls 1998; Rolls and Treves 1998). With experience, the temporal pathway can encode several objects and their relationships at once. This may occur by means of neuronal encoding of full objects, as well as object parts (Rousselet and others 2004). In keeping with this idea, the response of many TE neurons appears to be tuned to diagnostic elements of stimuli (Sigala and Logothetis 2002) and some neurons can be highly selective to one or very few objects among a large set (Tamura and Tanaka 2001). Thus, perceptual learning of visual stimuli and their spatial relation may improve the velocity of object recognition, without relying on highly detailed representations that require additional processing time (Wallis and Rolls 1997; Riesenhuber and Poggio 2002; Wersing and Korner 2003).

Rapid processing presumably depends on the ability of the visual system to learn to recognize familiar visual forms in an unsupervised manner (Masquelier and Thorpe 2007). The ventral pathway can deal with two or more objects simultaneously, overcoming the so-called binding

problem (Rousselet and others, 2004). This important characteristic is possibly due to the combination of intraregional and interregional learning processes. They start with neurons in V1, which encode simultaneously low-level properties such as orientation, color, and spatial frequency (Bullier and Nowak 1995; Leventhal and others 1995) and also integrate information from outside their classical RF (Lee 2003; Fig. 4). Furthermore, V2 integrates converging information from different orientations to build complex orientations. Hence, the process of binding the different elements that compose an object begins already in V1 and continues in V2, V4, and temporal lobe areas TEO and TE, as neurons code for more and more complex conjunctions of elements processed in the previous stages. These visual invariances are learned first over small regions of space, and for quite simple feature combinations, and then over successively larger and more complex regions (Rolls 2000a). It is assumed that this process, which takes place gradually from V1 to TE, obeys the Hebbian learning rule, and includes a short memory trace of preceding neuronal activity (Foldiak 1991; Rolls 1992; Wallis and Rolls 1997). Experimental evidence confirms that the selectivity to the "relevant" features for a given recognition task can be enhanced in V4 (Bichot and others 2005; Raiguel and others 2006) and TE (Rolls and others 1989; Higuchi and Miyashita 1996; Tovee and others 1996; Sigala and Logothetis 2002).

Experience-dependent synaptic plasticity modifies the neurons throughout the ventral stream so that they become selective to patterns that are reliably present in the input, whereas their latencies decrease, leading to both fast and informative responses (Masquelier and Thorpe 2007). The final outcome of this functional syncytium is the error-free learning of spatial combinations of elements from different objects. However, the structural and functional plasticity properties of the primary visual cortex should not be considered as an isolated phenomenon, but should be regarded in the context of visual information processing along the ventral (as well as dorsal) pathway. Each stage of ventral pathway processing integrates experience-dependent plasticity changes of the preceding stage, thus forming a hierarchical mechanism that can learn complex images. The integration of sensory stimuli does not finish in the ventral pathway, however, but continues in the adjacent medial temporal cortex with the subsequent stages of declarative memory formation.

Visual Cortical-Hippocampal Information Transfer

From the inferior temporal cortex, visual information reaches the primate hippocampus via the perirhinal cortex and the entorhinal cortex, which then projects to the hippocampus (Suzuki and Amaral 1994b). The structural integrity between the TE neurons and the adjacent perirhinal cortex is enabled by the massive backprojections between these regions (Suzuki and Amaral 1994a, 1994b). The identity of a complex object is represented by area TE, and the ability to associate this object with its name, for example (so that this identity can be recollected

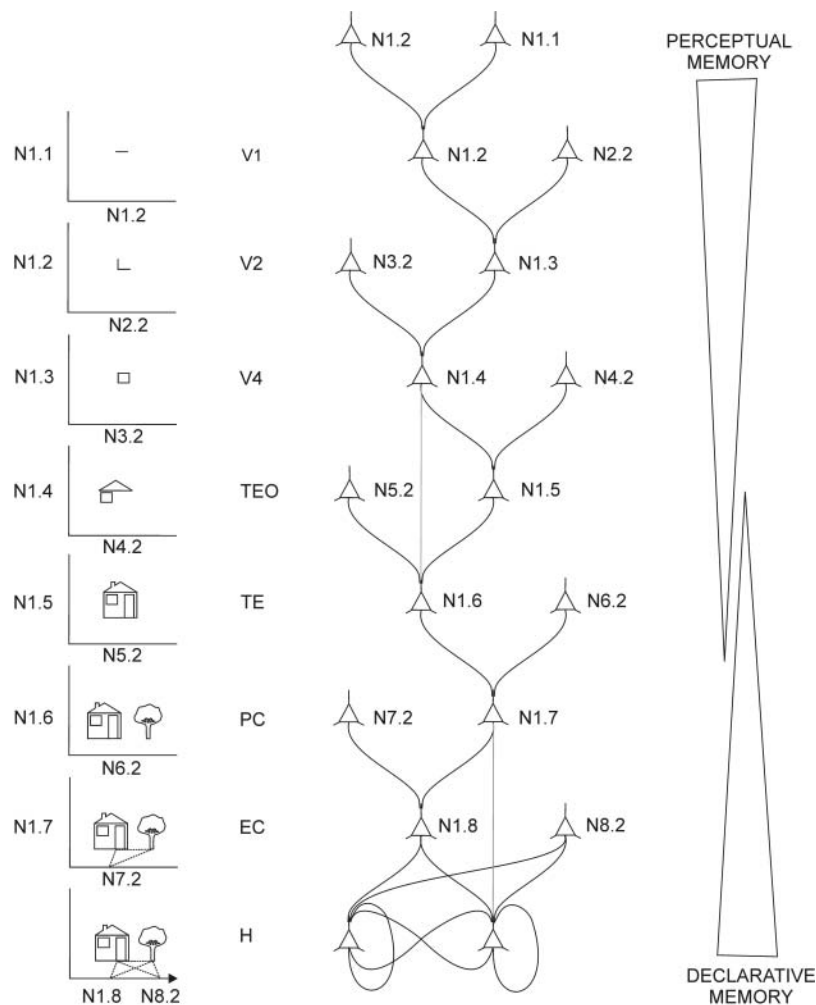


Fig. 4. Schematic representation of the functional convergence along the ventral visual pathway. Complex selectivities are built, step by step, from simpler ones. (*Left*) Examples of elements that are selectively encoded by neurons from the lower order hierarchical level are represented in a coordinate system per each level. The first visual feature presented (*top left*) is orientation selectivity in V1. The simple cells N1.1 and N1.2 encode the response of a complex cell for a horizontal orientation. The same complex cell (N1.2) together with a complex cell that encodes vertical orientation (N2.2) determines a particular responsiveness in V2. The resulting representation, N1.3, in combination with another cell in V2 forms a response in V4 to a particular shape: a square. Thus from orientation selectivity in V1, neurons can build receptive fields selective to complex shapes through objects and categories in inferior temporal cortex. Neurons at higher levels typically receive inputs from more than one object at a time during natural scene perception, encoding spatial conjunctions of elements. Area TE encodes complex invariant visual features, and as an example, it is shown here that the converging inputs from the preceding level (N1.5 and N5.2) form the representation of a “house.” Further on, in the perirhinal cortex (PC) the complex shapes are associated with other complex shapes, other sensory inputs, or abstractions. In this case, the “house” is associated with a “tree.” The next level, the entorhinal cortex (EC), integrates different perirhinal inputs and also adds idiothetic information. Finally, the visual information converges in the hippocampus (H) as a sequence of allocentric visual episodes (N1.8 and N8.2) encoded in time (indicated by the arrow of the *x* axis). (*Middle*) In the second column, schematic representation of the neuronal connectivity shows the hierarchical plasticity of the ventral visual stream. It is suggested that this process takes place gradually over most stages of the ventral pathway, with each stage converging inputs from a small part of the preceding stage, so that invariances are learned first over small regions of space, about quite simple feature combinations, and then over successively larger regions (Rolls 2000b). Each stage is assumed to operate essentially as a competitive network (Rolls and Treves 1998) that can learn such feature combinations. The trace rule can then learn invariant representations of such spatially bound feature combinations (Rolls 1992). Feedback and horizontal connections are not shown but are often essential to build up object representations. Gray lines indicate the direct connections between V4 and TE, and PC and hippocampus, respectively (Zola-Morgan and others 1989; Suzuki and Amaral 1994b; Zola-Morgan and others 1994; Suzuki and others 1997). (*Right*) Schematic illustration of the memory types that summarize the learning processes at each stage. The early visual system represents only the consequences of perceptual learning, whereas the inferior temporal cortex already takes part in semantic associations (Nakamura and others 2000). The continuous association of different visual episodes represents the formation of episodic memory and this unique sequence is mediated by the hippocampal “view” or “place” cells. Therefore, the quantum of information carried by each cell represents the convergence of visual features throughout the ventral (as well as dorsal) pathway and emphasizes the formation of episodic declarative memory.

Buckley and Gaffan 1998) or with abstractions (Liu and others 2000; Murray and Richmond 2001). It also plays a role in associating objects with other sensory representations as tactile (Goulet and Murray 2001) and gustatory information with objects (Parker and Gaffan 1998). Thus, this step of visual information processing associates different views of objects and their various nonvisual attributes, thereby binding the various attributes of an object into a completed representation. A neural network model of how the perirhinal cortex could implement such memory has been proposed to use Hebbian associative learning (Ziakopoulos and others 1999; Winters and Bussey 2005).

The next stage of visual information processing comprises the entorhinal cortex. Consistent with its anatomical relations this region operates as a junctional region between the perirhinal cortex and the hippocampus, assimilating information about both complex visual cues and idiothetic (body motion or head motion) stimuli (Quirk and others 1992; Suzuki and others 1997; Young and others 1997; Xiang and Brown 1998). Neurons in the entorhinal cortex fire in relation to the animal's spatial orientation, suggesting that the representation of position, distance, and direction may come together in this region (Hafting and others 2005). The temporal encoding of allocentric spatial information into sequences enables us the merging of environmental information. A good example of this is the estimation of our location in the surrounding space. Remembering the order of spatial cues allows us to predict their location or to create a virtual spatial map of the environment. This sequence encoding is thought to occur in the hippocampus (Eichenbaum and others 1999; Lisman 1999) and is mediated by the firing frequency of the hippocampal neurons. The primate hippocampus contains spatial cells that respond when the monkey looks at a certain part of space, "view" neurons (Rolls and O'Mara 1995), whereas the rodent hippocampus is characterized by "place cell" neurons that encode the rat's location (O'Keefe 1976). Sensory and idiothetic representations in the hippocampus are translated into neural firing patterns, which encode the sequence of events that compose a unique, personal experience known as episodic memory. Human memory is generally distinguished into declarative and a nondeclarative forms. Declarative memory can be semantic, for example, memory for facts, or episodic, for example, memory for events (Eichenbaum 2000). Perceptual learning in the visual system gives rise to nondeclarative perceptual memory. Along the ventral pathway, memory traces can be defined as nondeclarative (unconscious) or perceptual in the early stages (V1) and as declarative in perirhinal cortex. As the transition happens in the temporal region, with the formation of semantic associations, we hypothesize that episodic memory represents a quantum of information that converges on a single hippocampal "view" or "place" cell, respectively (Fig. 4). This quantum can be stored, and declaratively recollected, on a long time scale in the hippocampus, and on a very long time scale in the prefrontal cortex. It is therefore not possible to recollect a pure perceptual memory

separately and without a hierarchically enriched context. In this manner, perceptual memory resembles procedural memory, which describes the ability to learn skills. Accordingly, we can recollect the process of cycling a bike, but we cannot recollect the exact timing and firing order of each muscle fiber that participates in this process.

Other insights as to the interregional component of memory formation comes from fMRI studies. The ability to imagine an object is a form of memory recollection (Schacter and others 2007). It has been shown that ventral stream is also activated during mental imagery of visual objects in the absence of visual input (Kosslyn and others 1995, 1997; Ganis and others 2004; Amedi and others 2005; Newman and others 2005). Importantly, when precise visual discriminations are used, earlier stages, and particularly V1, are predominantly involved in this process (Kosslyn and others 1999; Kosslyn and Thompson 2003). If the recollection of visual items is related to the perceptual learning of the ventral stream, the same process should also involve a response from the declarative system. In agreement with this idea, single neurons in the human hippocampus and entorhinal cortex have been shown to alter their firing rates while the subjects were asked to imagine previously viewed images (Kreiman and others 2000). Similarly, rapid eye movement (REM) dreaming, a process that is based on internal sources of visual information, reveals an involvement of the ventral visual system (Maquet and others 1996; Braun and others 1998; Hobson and others 1998; Maquet 2000; Schwartz and Maquet 2002) in parallel with hippocampal activity (Maquet and others 1996; Braun and others 1997; Hobson and others 1998; Maquet 2000; Schwartz and Maquet 2002).

Memory formation is not a process encapsulated in particular structures, but represents the synchronized activity of hierarchically interrelated regions. The ventral visual pathway is one of the major informational sources for the formation of declarative memory. The learning processes involved in the early stages of the ventral pathway lead only to perceptual memory traces, but with the increasing informational convergence along the inferior temporal structures, a formation of complex associations occurs. The hippocampus then integrates different sensory sources into a temporal sequence, the unique combination of which forms subjective episodic memories.

Visual Processing Influence on Hippocampal Plasticity

To confirm the hypothesis that the hippocampal formation uses visual information, which has already undergone plasticity modulation along the ventral stream, we need proof that synaptic alterations at early visual system stages can evoke plastic responses in the hippocampus. Recent findings indeed demonstrate this phenomenon. Parallel field recordings from the visual cortex and dentate region in hippocampus of freely behaving adult rats revealed an interaction between synaptic alterations in both structures

(Tsanov and Manahan-Vaughan 2006a). Theta-burst stimulation of the thalamocortical pathway drives a long-term enhancement of granule cell excitability in the hippocampus that is preceded by a concurrent potentiation of the V1 response (Fig. 5A, B). The evoked potentiation in V1 correlates with the enhancement of intrinsic dentate gyrus excitability that may facilitate the induction of synaptic plasticity in the hippocampus (Fig. 5E). Furthermore, the spectral power of theta oscillations in the dentate gyrus increases soon after tetanization-driven high-frequency rhythms in V1 (Tsanov and Manahan-Vaughan 2006b; Fig. 5C). Field potential oscillations at theta frequency (5–12 Hz) are believed critical for the acquisition of new information by active hippocampal ensembles (Buzsáki and others 2002) and are, in fact, a typical feature of network activity during novel spatial exploration. These data suggest that synaptic plasticity and network activity in the primary visual cortex that occurs as a consequence of active sensory processing strongly influences dentate gyrus excitability and may comprise one of the endogenous triggers for synaptic plasticity in the hippocampal region.

For memory traces to persist in time they need to be reactivated occasionally—a process known as memory consolidation (McGaugh 2000). Off-line memory reprocessing is believed to occur during sleep periods (Alvarez and Squire 1994; Stickgold and others 2001; Kali and Dayan 2004). A recent study demonstrates the simultaneous reactivation of coherent memory traces in the cortex and hippocampus during sleep (Ji and Wilson 2007). Multicell spiking patterns in both the visual cortex and the hippocampus in rats shared sequences evoked by awake experience, which were replayed during slow-wave sleep in both regions (Fig. 6). Furthermore, replay events in the sensory cortex and hippocampus were coordinated to reflect the same experience. The fact that cortical frames led hippocampal frames by about 50 milliseconds indicates that hippocampal frames may be the result of cortical drive rather than intrinsic state change. Recently, hippocampal interneurons have been found to be phase-locked to cortical up- and down-state transitions (Hahn and Mehta 2006), indicating that the frame structure in the hippocampus may be primarily driven or shaped by the interneuron activity. Therefore, during slow oscillatory periods an interregional communication between visual cortices and the hippocampal region continues, suggesting processes of memory consolidation.

Encoding by Hippocampal Synaptic Plasticity of Visual Spatial Information

The hippocampus has long been implicated in learning and memory in both humans and animals. Extensive evidence implicates the hippocampus and related structures in the formation of episodic memories in humans (Aggleton and Brown 1999; Reilly 2001) and in consolidating information into long-term declarative memory (Mumby and others 1999). It has also been recognized that memory traces of past events are eventually transferred or rerepresented in

the neocortex (Otto and Eichenbaum 1992; Squire 1992). A careful analysis of performance in different spatial learning tasks has led to the suggestion that the integrity of connections between the hippocampus, subiculum, and cortical areas is necessary for synthesis of all components of spatial learning (Squire 1992). A major task, therefore, is to reveal the neuronal mechanisms responsible for the modification of the neuronal connectivity within the hippocampus and between the neocortex and the hippocampal formation.

Neocortico-hippocampal transfer of new spatial information occurs during exploratory behavior. Modification of synaptic weights is likely to happen very fast during the activated state of the hippocampus (Buzsáki 1996), and entorhinal-hippocampal network oscillations at theta frequency play a crucial role in this process (Kamondi and others 1998). The neuronal burst probability is highest for hippocampal neurons that discharge at theta frequencies of 6 to 8 Hz, where an optimal balance between excitation and suppression is formed (Harris and others 2001), and the bursting mode of neuronal activity is known to change the intracellular calcium dynamics (Wong and Prince 1978; Regehr and others 1989; Jaffe and others 1992). Calcium entry into cells, a prerequisite for the induction of plasticity and gene expression in neurons (Bading and others 1993; Bliss and Collingridge 1993), may exert a long-term change on synaptic connectivity.

Synaptic plasticity implies either an increase of transmission between the neurons in a given network, termed LTP (Castro and others 1989), or a decrease of transmission, known as LTD (Manahan-Vaughan and Braunewell 1999; Kemp and Manahan-Vaughan 2004). It has become increasingly apparent that hippocampal LTP and LTD may engage in the encoding of different aspects of visual spatial information (Kemp and Manahan-Vaughan 2007b). There are a substantial number of reports that LTP is consistently facilitated when a stimulation protocol that normally elicits short-term potentiation is coupled with novel exploration of an empty environment (Manahan-Vaughan and Braunewell 1999; Straube and others 2003a, 2003b; Kemp and Manahan-Vaughan 2004; Uzakov and others 2005). What is striking is that these effects have been reported for all three major synapses of the trisynaptic circuit, namely, the perforant path-dentate gyrus synapse, the mossy fiber-CA3 synapse, and the Schaffer collateral-CA1 synapse (Manahan-Vaughan and Braunewell 1999; Straube and others 2003a, 2003b; Kemp and Manahan-Vaughan 2004, 2007a; Hagena and Manahan-Vaughan 2007). Thus, exposure to a new environment appears to trigger LTP as a kind of global response across the hippocampus. This is quite distinct from the involvement of LTD in information encoding (Kemp and Manahan-Vaughan 2007b). Although LTD appears to occur intrinsically as a response to changes in environmental detail (Manahan-Vaughan and Braunewell 1999; Lemon and Manahan-Vaughan 2006), the hippocampal subregions appear to process different aspects of this: LTD in the CA1 region is facilitated by exposure to contextual

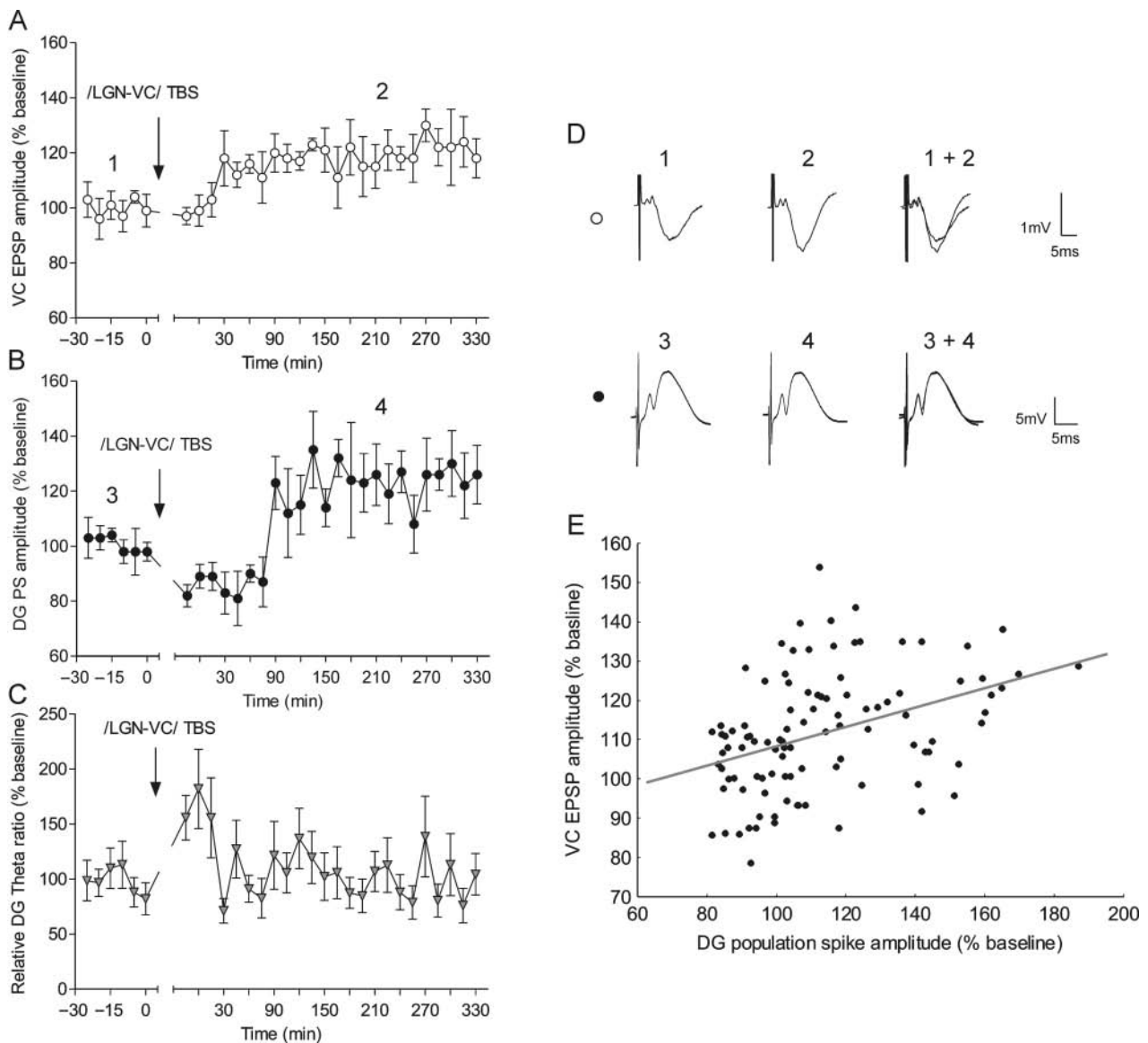


Fig. 5. Synaptic plasticity in the visual cortex parallels hippocampal excitability potentiation. (A) Theta-burst stimulation (TBS) of lateral geniculate nucleus (LGN) in the primary visual cortex (VC) of adult freely moving rats. The stimulation protocol induces potentiation of the VC field response, measured by field excitatory postsynaptic potential (EPSP) amplitude (analysis of variance [ANOVA], $n = 6$, $P < .05$). (B) Parallel recorded field potentials in dentate gyrus (DG), evoked by medial perforant path stimulation, show that TBS of LGN is able to drive a late-onset enhancement of the population spike response (ANOVA, $n = 6$, $P < .05$). Population spike (PS) amplitude potentiation developed 90 minutes after the high-frequency protocol and continued till the end of the 4-hour recording period. (C) Immediately after LGN stimulation a significant increase in the theta ratio (ratio between theta and delta spectral powers) was observed in the dentate gyrus granule cell layer (t -test, $n = 6$, $P < .01$). (D) Analog traces represent an average of five field potentials evoked at the points marked in A and B. Horizontal bar: 5 msec, vertical bar: 5 mV (DG) and 1 mV (VC). (E) A significant correlation (Pearson, $n = 5$, $P < .0001$, $r = 0.3880$) between TBS-induced cortical EPSP amplitude enhancement and dentate PS amplitude potentiation was demonstrated by the comparison of the individual values from all subsequent recordings (Tsanov and Manahan-Vaughan 2006 a, b).

changes in small features of an environment (Kemp and Manahan-Vaughan 2004), whereas LTD in the dentate gyrus is facilitated by contextual changes in landmark or orientational features of an environment (Kemp and

Manahan-Vaughan 2007a). This suggests LTP and LTD encode different aspects of spatial memory and that the hippocampal subregions may engage in a hierarchical encoding of certain types of spatial memory.

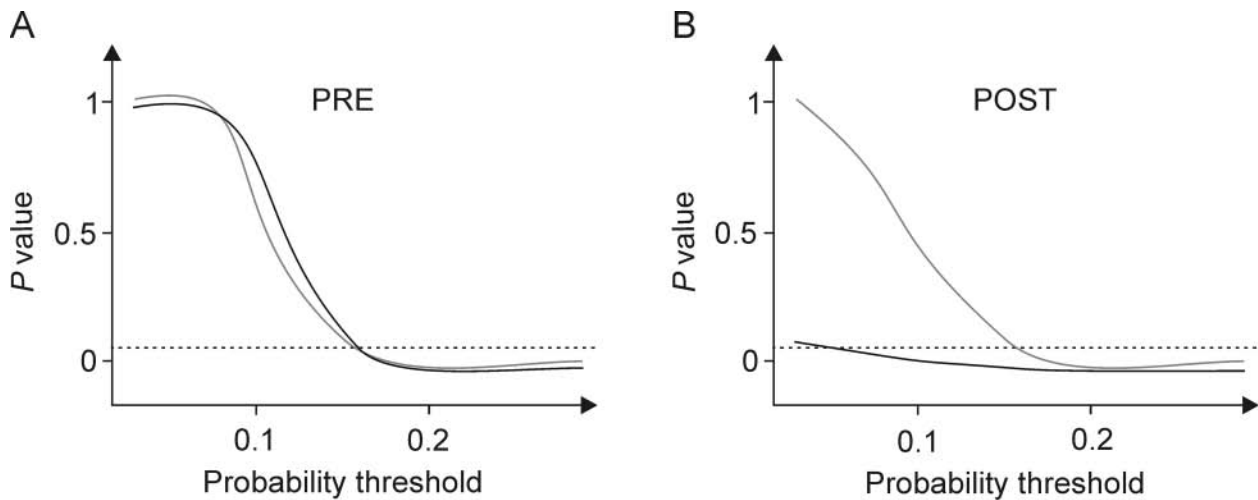


Fig. 6. Coordinated spiking activity replay in the visual cortex and hippocampus during sleep. Schematic diagrams illustrating the modification of cortico-hippocampal firing patterns after spatial learning experience. Visual cortical and hippocampal spiking activities were organized as frames during slow-wave sleep. A 1- to 2-hour sleep session before a 20- to 40-minute maze running session was indicated as PRE, and a 1- to 2-hour sleep session after the run as POST. The x axis represents the matching probability that defines how robust is the overlapping effect of the replaying frames. Dependence of the significance P values of the observed numbers (y axis) on the matching probability threshold in PRE (A) and POST (B). Black lines indicate the same trajectory; gray lines, different trajectory; dotted horizontal lines, significance level $P = .05$ (after Ji and Wilson 2007).

Synthesis and Conclusions

Processing of visual information is not a static process, but a dynamic mechanism underlying the formation of visually driven memories. All levels of cortical processing are hierarchically interconnected and converge frames of learned features into complex configurations. Substantial progress has been made in understanding how experience modifies synaptic strength among the neurons in the visual cortex and how this process influences the functional properties of the visual and the hippocampal systems. Recent findings suggest not only that the adult visual cortex undergoes dynamic synaptic plasticity that is driven by behavioral state and active visual experience, but that this process may influence subsequent visuospatial memory formation encoded through synaptic plasticity in the hippocampus.

References

Abbott LF, Varela JA, Sen K, Nelson SB. 1997. Synaptic depression and cortical gain control. *Science* 275:220–4.

Aggleton JP, Brown MW. 1999. Episodic memory, amnesia, and the hippocampal-anterior thalamic axis. *Behav Brain Sci* 22:425–44.

Alvarez P, Squire LR. 1994. Memory consolidation and the medial temporal lobe: a simple network model. *Proc Natl Acad Sci U S A* 91:7041–5.

Amedi A, Malach R, Pascual-Leone A. 2005. Negative BOLD differentiates visual imagery and perception. *Neuron* 48:859–72.

Bading H, Ginty DD, Greengard ME. 1993. Regulation of gene expression in hippocampal neurons by distinct calcium signaling pathways. *Science* 260:181–6.

Ball K, Sekuler R. 1982. A specific and enduring improvement in visual motion discrimination. *Science* 218:697–8.

Ball K, Sekuler R. 1987. Direction-specific improvement in motion discrimination. *Vision Res* 27:953–65.

Bear MF, Abraham WC. 1996. Long-term depression in hippocampus. *Annu Rev Neurosci* 19:437–62.

Bear MF, Cooper LN, Ebner FF. 1987. A physiological basis for a theory of synaptic modification. *Science* 237:42–48.

Beard BL, Levi DM, Reich LN. 1995. Perceptual learning in parafoveal vision. *Vision Res* 35:1679–90.

Berardi N, Fiorentini A. 1987. Interhemispheric transfer of visual information in humans: spatial characteristics. *J Physiol* 384:633–47.

Bichot NP, Rossi AF, Desimone R. 2005. Parallel and serial neural mechanisms for visual search in macaque area v4. *Science* 308:529–34.

Bienenstock EL, Cooper LN, Munro PW. 1982. Theory for the development of neuron selectivity: orientation specificity and binocular interaction in visual cortex. *J Neurosci* 2:32–48.

Bliss TVP, Collingridge GL. 1993. A synaptic model of memory: long-term potentiation in the hippocampus. *Nature* 361:31–9.

Booth MCA, Rolls ET. 1998. View-invariant representations of familiar objects by neurons in the inferior temporal visual cortex. *Cereb Cortex* 8:510–23.

Boussaoud D, Desimone R, Ungerleider LG. 1991. Visual topography of area TEO in the macaque. *J Comp Neurol* 306:554–75.

Braun AR, Balkin TJ, Wesensten NJ, Carson RE, Varga M, Baldwin P, and others. 1997. Regional cerebral blood flow throughout the sleep-wake cycle. An H2(15)O PET study. *Brain* 120:1173–97.

Braun AR, Balkin TJ, Wesensten NJ, Gwadrly F, Carson RE, Varga M, and others. 1998. Dissociated pattern of activity in visual cortices and their projections during human rapid eye movement sleep. *Science* 279:91–5.

Braunewell K-H, Manahan-Vaughan D. 2001. Long-term depression: a cellular basis for learning? *Rev Neurosci* 12:121–40.

Brown MW, Aggleton JP. 2001. Recognition memory: what are the roles of the perirhinal cortex and hippocampus? *Nat Rev Neurosci* 2:51–61.

Buckley MJ, Gaffan D. 1998. Perirhinal cortex ablation impairs configural learning and paired-associate learning equally. *Neuropsychologia* 36:535–46.

Bullier J, Nowak LG. 1995. Parallel versus serial processing: new vistas on the distributed organization of the visual system. *Curr Opin Neurobiol* 5:497–503.

- Buzsáki G. 1996. The hippocampo-neocortical dialogue. *Cereb Cortex* 6:81–92.
- Buzsáki G, Csicsvari J, Dragoi G, Harris K, Henze D, Hirase H. 2002. Homeostatic maintenance of neuronal excitability by burst discharges in vivo. *Cereb Cortex* 12:893–9.
- Buzsáki G, Llinás R, Berthoz A, Christen Y. 1994. Temporal coding in the brain. Berlin: Springer-Verlag.
- Castro CA, Silbert LH, McNaughton BL, Barnes CA. 1989. Recovery of spatial learning deficits after decay of electrically induced synaptic enhancement in the hippocampus. *Nature* 342:545–8.
- Chance FS, Nelson SB, Abbott LF. 1998. Synaptic depression and the temporal response characteristics of V1 cells. *J Neurosci* 18:4785–99.
- Crist RE, Li W, Gilbert CS. 2001. Learning to see: experience and attention in primary visual cortex. *Nat Neurosci* 4:519–25.
- Debanne D, Gahwiler BH, Thompson SM. 1998. Long-term synaptic plasticity between pairs of individual CA3 pyramidal cells in rat hippocampal slice cultures. *J Physiol* 507:237–47.
- Eichenbaum H. 2000. A cortical-hippocampal system for declarative memory. *Nat Rev Neurosci* 1:41–50.
- Eichenbaum H, Dudchenko P, Wood E, Shapiro M, Tanila H. 1999. The hippocampus, memory, and place cells: is it spatial memory or a memory space? *Neuron* 23:209–26.
- Fahle M, Edelman S. 1993. Long-term learning in vernier acuity: effects of stimulus orientation, range and of feedback. *Vision Res* 33:397–412.
- Fahle M, Poggio T. 2002. *Perceptual learning*. Cambridge (MA): MIT Press.
- Fiorentini A, Berardi N. 1980. Perceptual learning specific for orientation and spatial frequency. *Nature* 287:43–4.
- Fiorentini A, Berardi N. 1981. Learning in grating waveform discrimination: specificity for orientation and spatial frequency. *Vision Res* 21:1149–58.
- Foldiak P. 1991. Learning invariance from transformation sequences. *Neural Comput* 3:193–9.
- Frenkel MY, Sawtell NB, Diogo AC, Yoon B, Neve RL, Bear MF. 2006. Instructive effect of visual experience in mouse visual cortex. *Neuron* 51:339–49.
- Fries P, Neuenschwander S, Engel AK, Goebel R, Singer W. 2001. Rapid feature selective neuronal synchronization through correlated latency shifting. *Nat Neurosci* 4:194–200.
- Froemke RC, Dan Y. 2002. Spike-timing-dependent synaptic modification induced by natural spike trains. *Nature* 416:433–8.
- Fu YX, Djupsund K, Gao H, Hayden B, Shen K, Dan Y. 2002. Temporal specificity in the cortical plasticity of visual space representation. *Science* 296:1999–2003.
- Furmanski C, Schluppeck D, Engel SA. 2004. Learning strengthens the response of primary visual cortex to simple patterns. *Curr Biol* 14:573–8.
- Ganis G, Thompson WL, Kosslyn SM. 2004. Brain areas underlying visual mental imagery and visual perception: an fMRI study. *Brain Res Cogn Brain Res* 20:226–41.
- Gilbert CD. 1998. Adult cortical dynamics. *Physiol Rev* 78:467–85.
- Gilbert CD, Sigman M, Crist RE. 2001. The neural basis of perceptual learning. *Neuron* 31:681–97.
- Goulet S, Murray EA. 2001. Neural substrates of crossmodal association memory in monkeys: the amygdala versus the anterior rhinal cortex. *Behav Neurosci* 115:271–84.
- Gray CM. 1994. Synchronous oscillations in neuronal systems: mechanisms and functions. *J Comput Neurosci* 1:11–38.
- Gray CM, McCormick DA. 1996. Chattering cells: superficial pyramidal neurons contributing to the generation of synchronous oscillations in the visual cortex. *Science* 274:109–13.
- Gross CG. 1992. Representation of visual stimuli in inferior temporal cortex. *Philos Trans R Soc London Ser* 335:3–10.
- Hafting T, Fyhn M, Molden S, Moser MB, Moser EI. 2005. Microstructure of a spatial map in the entorhinal cortex. *Nature* 436:801–6.
- Hagena H, Manahan-Vaughan D. 2007. Frequency-facilitation at mossy fiber-CA3 pyramidal synapses *in vivo* precedes short-term synaptic depression. *Soc Neurosci Abstr* 361.7.
- Hahn TT, Sakmann B, Mehta MR. 2006. Phase-locking of hippocampal interneurons' membrane potential to neocortical up-down states. *Nat Neurosci* 9:1359–61.
- Harris KD, Hirase H, Leinekugel X, Henze DA, Buzsáki G. 2001. Temporal interaction between single spikes and complex spike bursts in hippocampal pyramidal cells. *Neuron* 32:141–9.
- Hasselmo ME, Rolls ET, Baylis GC, Nalwa V. 1989. Object-centered encoding by face-selective neurons in the cortex in the superior temporal sulcus of the monkey. *Exp Brain Res* 75:417–29.
- Hegde J. 2006. Search for the neural correlates of learning to discriminate orientations. *J Neurosci* 26:8877–8.
- Heynen AJ, Abraham WC, Bear MF. 1996. Bidirectional modification of CA1 synapses in the adult hippocampus *in vivo*. *Nature* 381:163–6.
- Heynen AJ, Bear MF. 2001. Long-term potentiation of thalamocortical transmission in the adult visual cortex *In vivo*. *J Neurosci* 21:9801–13.
- Higuchi S, Miyashita Y. 1996. Formation of mnemonic neuronal responses to visual paired associates in inferotemporal cortex is impaired by perirhinal and entorhinal lesions. *Proc Natl Acad Sci U S A* 95:739–43.
- Hobson JA, Stickgold R, Pace-Schott EF. 1998. The neuropsychology of REM sleep dreaming. *Neuroreport* 9:R1–14.
- Hochstein S, Ahissar M. 2002. View from the top: hierarchies and reverse hierarchies in the visual system. *Neuron* 36:791–804.
- Hölscher C, Rolls ET, Xiang J-Z. 2003. Perirhinal cortex neuronal activity related to long-term familiarity memory in the macaque. *Eur J Neurosci* 18:2037–46.
- Hubel DH, Wiesel TN. 1977. Functional architecture of macaque monkey visual cortex. *Proc R Soc Lond B Biol Sci* 198:1–59.
- Jaffe DB, Johnston D, Lasser-Ross N, Lisman JE, Miyakawa H, Ross WN. 1992. The spread of Na⁺ spikes determines the pattern of dendritic Ca²⁺ entry into hippocampal neurons. *Nature* 357:244–6.
- Ji D, Wilson MA. 2007. Coordinated memory replay in the visual cortex and hippocampus during sleep. *Nat Neurosci* 10:100–7.
- Kali S, Dayan P. 2004. Off-line replay maintains declarative memories in a model of hippocampal-neocortical interactions. *Nat Neurosci* 7:286–94.
- Kamondi A, Acsady L, Wang XJ, Buzsáki G. 1998. Theta oscillations in somata and dendrites of hippocampal pyramidal cells *in vivo*: activity-dependent phase-precession of action potentials. *Hippocampus* 8:244–61.
- Kapadia MK, Gilbert CD, Westheimer G. 1994. A quantitative measure for short-term cortical plasticity in human vision. *J Neurosci* 14:451–7.
- Karmarkar UR, Dan Y. 2006. Experience-dependent plasticity in adult visual cortex. *Neuron* 52:577–85.
- Karni A, Sagi D. 1991. Where practice makes perfect in texture discrimination: evidence for primary visual cortex plasticity. *Proc Natl Acad Sci U S A* 88:4966–70.
- Karni A, Sagi D. 1993. The time course of learning a visual skill. *Nature* 365:250–2.
- Kemp A, Manahan-Vaughan D. 2004. Hippocampal long-term depression and long-term potentiation encode different aspects of novelty acquisition. *Proc Natl Acad Sci U S A* 101:8192–7.
- Kemp A, Manahan-Vaughan D. 2007a. The hippocampal CA1 region and dentate gyrus differentiate between environmental and spatial feature encoding through long-term depression. *Cereb Cortex*. E-pub ahead of print.
- Kemp A, Manahan-Vaughan D. 2007b. Hippocampal LTD: master or minion in declarative memory processes? *Trends Neurosci* 30:111–8.
- Kirkwood A, Lee H-K, Bear MF. 1995. Co-regulation of long-term potentiation and experience-dependent plasticity in visual cortex by age and experience. *Nature* 375:328–31.
- Kirkwood A, Rioult MG, Bear MF. 1996. Experience-dependent modification of synaptic plasticity in visual cortex. *Nature* 381:526–8.
- Kobatake E, Tanaka K. 1994. Neuronal selectivities to complex object features in the ventral visual pathway of the macaque cerebral cortex. *J Neurophysiol* 71:856–67.
- Kosslyn SM, Pascual-Leone A, Feliciano O, Camposano S, Keenan JP, Thompson WL, and others. 1999. The role of area 17 in visual imagery: convergent evidence from PET and rTMS. *Science* 284:167–70.

- Kosslyn SM, Thompson WL. 2003. When is early visual cortex activated during visual mental imagery? *Psychol Bull* 129:723–46.
- Kosslyn SM, Thompson WL, Alpert NM. 1997. Neural systems shared by visual imagery and visual perception: a positron emission tomography study. *Neuroimage* 6:320–34.
- Kosslyn SM, Thompson WL, Kim IJ, Alpert NM. 1995. Topographical representations of mental images in primary visual cortex. *Nature* 1995:496–8.
- Kreiman G, Koch C, Fried I. 2000. Imagery neurons in the human brain. *Nature* 408:357–61.
- Larson J, Lynch G. 1988. Role of N-methyl-D-aspartate receptors in the induction of synaptic potentiation by burst stimulation patterned after the hippocampal theta-rhythm. *Brain Res* 441:111–8.
- Larson J, Lynch G. 1989. Theta pattern stimulation and the induction of LTP: the sequence in which synapses are stimulated determines the degree to which they potentiate. *Brain Res* 489:49–58.
- Larson J, Wong D, Lynch G. 1986. Patterned stimulation at the theta frequency is optimal for the induction of hippocampal long-term potentiation. *Brain Res* 368:347–50.
- Lee TS. 2003. Computations in the early visual cortex. *J Physiol Paris* 97:121–39.
- Lemon N, Manahan-Vaughan D. 2006. Dopamine D1/D5 receptors gate the acquisition of novel information through hippocampal long-term potentiation and long-term depression. *J Neurosci* 26:7723–9.
- Leventhal AG, Thompson KG, Liu D, Zhou Y, Ault SJ. 1995. Concomitant sensitivity to orientation, direction, and color of cells in layers 2, 3, and 4 of monkey striate cortex. *J Neurosci* 15:1808–18.
- Levy WB, Steward D. 1983. Temporal contiguity requirements for long-term associative potentiation/depression in the hippocampus. *Neuroscience* 8:791–7.
- Li W, Piech V, Gilbert CD. 2004. Perceptual learning and top-down influences in primary visual cortex. *Nat Neurosci* 7:651–7.
- Lisman JE. 1999. Relating hippocampal circuitry to function: recall of memory sequences by reciprocal dentate/CA3 interactions. *Neuron* 22:233–42.
- Liu Z, Murray EA, Richmond BJ. 2000. Learning motivational significance of visual cues for reward schedules requires rhinal cortex. *Nat Neurosci* 3:1307–15.
- Logothetis NK, Pauls J, Poggio T. 1995. Shape representation in the inferior temporal cortex of monkeys. *Curr Biol* 5:552–63.
- Logothetis NK, Sheinberg DL. 1996. Visual object recognition. *Annu Rev Neurosci* 19:577–621.
- Maertens M, Pollmann S. 2005. fMRI reveals a common neural substrate of illusory and real contours in V1 after perceptual learning. *J Cogn Neurosci* 17:1553–64.
- Manahan-Vaughan D, Braunwell K-H. 1999. Novelty acquisition is associated with induction of hippocampal long-term depression. *Proc Natl Acad Sci U S A* 96:8739–44.
- Maquet P. 2000. Functional neuroimaging of normal human sleep by positron emission tomography. *J Sleep Res* 9:207–31.
- Maquet P, Pétters J, Aerts J, Delfiore G, Degueldre C, Luxen A, and others. 1996. Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. *Nature* 383:163–6.
- Markram H, Lubke J, Frotscher M, Sakmann B. 1997. Regulation of synaptic efficacy by coincidence of postsynaptic APs and EPSPs. *Science* 275:213–5.
- Masquelier T, Thorpe SJ. 2007. Unsupervised learning of visual features through spike timing dependent plasticity. *PLoS Comput Biol* 3:e31.
- Maunsell JH, Newsome WT. 1987. Visual processing in monkey extrastriate cortex. *Annu Rev Neurosci* 10:363–401.
- McGaugh JL. 2000. Memory—a century of consolidation. *Science* 287:248–51.
- Mumby DG, Astur RS, Weisend MP, Sutherland RJ. 1999. Retrograde amnesia and selective damage to the hippocampal formation: memory for places and object discriminations. *Behav Brain Res* 106:97–107.
- Murray EA, Gaffan D, Mishkin M. 1993. Neural substrates of visual stimulus–stimulus association in rhesus monkeys. *J Neurosci* 13:4549–61.
- Murray EA, Richmond BJ. 2001. Role of perirhinal cortex in object perception, memory, and associations. *Curr Opin Neurobiol* 11:188–93.
- Nakamura K, Kawashima R, Sato N, Nakamura A, Sugiura M, Kato T, and others. 2000. Functional delineation of the human occipito-temporal areas related to face and scene processing. A PET study. *Brain* 123:1903–12.
- Nase G, Singer W, Monyer H, Engel AK. 2003. Features of neuronal synchrony in mouse visual cortex. *J Neurophysiol* 90:1115–23.
- Neary K, Anand S, Hotson JR. 2005. Perceptual learning of line orientation modifies the effects of transcranial magnetic stimulation of visual cortex. *Exp Brain Res* 162:23–34.
- Newman SD, Klatzky RL, Lederman SJ, Just MA. 2005. Imagining material versus geometric properties of objects: an fMRI study. *Brain Res Cogn Brain Res* 23:235–46.
- O’Keefe J. 1976. Place units in the hippocampus of the freely moving rat. *Exp Neurol* 51:78–109.
- Op De Beeck H, Vogels R. 2000. Spatial sensitivity of macaque inferior temporal neurons. *J Comp Neurol* 426:505–18.
- Otto T, Eichenbaum H. 1992. Neuronal activity in the hippocampus during delayed non-match to sample performance in rats: evidence for hippocampal processing in recognition memory. *Hippocampus* 2:323–34.
- Parker A, Gaffan D. 1998. Lesions of the primate rhinal cortex cause deficits in flavour–visual associative memory. *Behav Brain Res* 93:99–105.
- Poggio T, Fahle M, Edelman S. 1992. Fast perceptual learning in visual hyperacuity. *Science* 256:1018–21.
- Quirk GJ, Muller RU, Kubie JL, Ranck JBJ. 1992. The positional firing properties of medial entorhinal neurons: description and comparison with hippocampal place cells. *J Neurosci* 12:1945–63.
- Raiguel S, Vogels R, Mysore SG, Orban GA. 2006. Learning to see the difference specifically alters the most informative V4 neurons. *J Neurosci* 26:6589–602.
- Regehr W, Connor J, Tank D. 1989. Optical imaging of calcium accumulation in hippocampal pyramidal cells during synaptic activation. *Nature* 341:533–6.
- Reilly CE. 2001. Hippocampus selectively supports episodic memory retrieval. *J Neurol* 248:1014–5.
- Riesenhuber M, Poggio T. 2002. Neural mechanisms of object recognition. *Curr Opin Neurobiol* 12:162–8.
- Rolls ET. 1992. Neurophysiological mechanisms underlying face processing within and beyond the temporal cortical visual areas. *Philos Trans R Soc London Ser* 335:11–21.
- Rolls ET. 2000a. Functions of the primate temporal lobe cortical visual areas in invariant visual object and face recognition. *Neuron* 27:205–18.
- Rolls ET. 2000b. Memory systems in the brain. *Annu Rev Psychol* 51:599–630.
- Rolls ET, Baylis GC, Hasselmo ME, Nalwa V. 1989. The effect of learning on the face selective responses of neurons in the cortex in the superior temporal sulcus of the monkey. *Exp Brain Res* 76:153–64.
- Rolls ET, Franco L, Stringer SM. 2005. The perirhinal cortex and long-term familiarity memory. *Q J Exp Psychol B* 58:234–45.
- Rolls ET, O’Mara SM. 1995. View-responsive neurons in the primate hippocampal complex. *Hippocampus* 5:409–24.
- Rolls ET, Treves A. 1998. Neural networks and brain function. Oxford (UK): Oxford University Press.
- Rousselet GA, Thorpe SJ, Fabre-Thorpe M. 2004. How parallel is visual processing in the ventral pathway? *Trends Cogn Sci* 8:363–70.
- Saarinen J, Levi DM. 1995. Perceptual learning in vernier acuity: what is learned? *Vision Res* 35:519–27.
- Samonds JM, Bonds AB. 2005. Gamma oscillation maintains stimulus structure-dependent synchronization in cat visual cortex. *J Neurophysiol* 93:223–36.
- Schacter DL, Addis DR, Buckner RL. 2007. Remembering the past to imagine the future: the prospective brain. *Nat Rev Neurosci* 8:657–61.
- Schoups A, Vogels R, Quian N, Orban G. 2001. Practising orientation identification improves orientation coding in V1 neurons. *Nature* 412:549–53.

- Schoups AA, Vogels R, Orban GA. 1995. Human perceptual learning in identifying the oblique orientation: retinotopy, orientation specificity, and monocularly. *J Physiol* 483:797–810.
- Schwartz S, Maquet P. 2002. Sleep imaging and the neuro-psychological assessment of dreams. *Trends Cogn Sci* 6:23–30.
- Shiu LP, Pashler H. 1992. Improvement in line orientation discrimination is retinally local but dependent on cognitive set. *Percept Psychophys* 52:582–8.
- Sigala N, Logothetis NK. 2002. Visual categorization shapes feature selectivity in the primate temporal cortex. *Nature* 415:318–20.
- Singer W. 1993. Synchronization of cortical activity and its putative role in information processing and learning. *Annu Rev Physiol* 55:349–74.
- Sjostrom PJ, Turrigiano GG, Nelson SB. 2001. Rate, timing, and cooperativity jointly determine cortical synaptic plasticity. *Neuron* 32:1149–64.
- Squire LR. 1992. Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. *Psychol Rev* 99:195–231.
- Stickgold R, Hobson JA, Fosse R, Fosse M. 2001. Sleep, learning, and dreams: off-line memory reprocessing. *Science* 294:1052–7.
- Straube T, Korz V, Balschun D, Frey JU. 2003a. Requirement of beta-adrenergic receptor activation and protein synthesis for LTP-reinforcement by novelty in rat dentate gyrus. *J Physiol* 552:953–60.
- Straube T, Korz V, Frey JU. 2003b. Bidirectional modulation of long-term potentiation by novelty-exploration in rat dentate gyrus. *Neurosci Lett* 344:5–8.
- Sur M, Schummers J, Dragoi V. 2002. Cortical plasticity: time for a change. *Curr Biol* 12:R168–70.
- Suzuki WA, Amaral DG. 1994a. Perirhinal and parahippocampal cortices of the macaque monkey—cortical afferents. *J Comp Neurol* 350:497–533.
- Suzuki WA, Amaral DG. 1994b. Topographic organization of the reciprocal connections between the monkey entorhinal cortex and the perirhinal and parahippocampal cortices. *J Neurosci* 14:1856–77.
- Suzuki WA, Miller EK, Desimone R. 1997. Object and place memory in the macaque entorhinal cortex. *J Neurophysiol* 78:1062–81.
- Tamura H, Tanaka K. 2001. Visual response properties of cells in the ventral and dorsal parts of the macaque inferotemporal cortex. *Cereb Cortex* 11:384–99.
- Taylor TJ, Hamm JP, Clapp WC, Johnson BW, Corballis MC, Kirk IJ. 2005. Long-term potentiation of human visual evoked responses. *Eur J Neurosci* 21:2045–50.
- Tovee MJ, Rolls ET, Ramachandran VS. 1996. Rapid visual learning in neurones of the primate temporal visual cortex. *Neuroreport* 7:2757–60.
- Tsanov M, Manahan-Vaughan D. 2006a. Synaptic plasticity in the visual cortex influences excitability and plasticity of dentate gyrus granule cells in freely moving rats. *Fed Eur Neurosci Soc Abstr* A049.21.
- Tsanov M, Manahan-Vaughan D. 2006b. Visual cortex plasticity parallels theta-frequency stimulation-induced synaptic alterations in dentate gyrus. *Soc Neurosci Abstr* 31.4.
- Tsanov M, Manahan-Vaughan D. 2007a. The adult visual cortex expresses dynamic synaptic plasticity that is driven by the light-dark cycle. *J Neurosci* 27:8414–21.
- Tsanov M, Manahan-Vaughan D. 2007b. Intrinsic, light-independent and visual-activity dependent mechanisms cooperate in the shaping of the field response in rat visual cortex. *J Neurosci* 27:8422–9.
- Uzakov S, Frey JU, Korz V. 2005. Reinforcement of rat hippocampal LTP by holeboard training. *Learn Mem* 12:165–71.
- Vogels R, Orban GA. 1985. The effect of practice on the oblique effect in line orientation judgments. *Vision Res* 25:1679–87.
- Vogels R, Orban GA. 1996. Coding of stimulus invariances by inferior temporal neurons. *Prog Brain Res* 112:195–211.
- Wallis G, Rolls ET. 1997. Invariant face and object recognition in the visual system. *Prog Neurobiol* 51:167–94.
- Wersing H, Korner E. 2003. Learning optimized features for hierarchical models of invariant object recognition. *Neural Comput* 15:1559–88.
- Winters BD, Bussey TJ. 2005. Glutamate receptors in perirhinal cortex mediate encoding, retrieval, and consolidation of object recognition memory. *J Neurosci* 25:4243–51.
- Wong RKS, Prince DA. 1978. Participation of calcium spikes during intrinsic burst firing in hippocampal neurons. *Brain Res* 159:385–90.
- Xiang JZ, Brown MW. 1998. Differential neuronal encoding of novelty, familiarity and recency in regions of the anterior temporal lobe. *Neuropharmacology* 37:657–76.
- Yao H, Dan Y. 2001. Stimulus timing-dependent plasticity in cortical processing of orientation. *Neuron* 32:315–23.
- Yao H, Dan Y. 2005. Synaptic learning rules, cortical circuits, and visual function. *Neuroscientist* 11:206–16.
- Yao H, Shen Y, Dan Y. 2004. Intracortical mechanism of stimulus timing-dependent plasticity in visual cortical orientation tuning. *Proc Natl Acad Sci U S A* 101:5081–6.
- Young BJ, Otto T, Fox GD, Eichenbaum H. 1997. Memory representation within the parahippocampal region. *J Neurosci* 17:5183–95.
- Ziakopoulos Z, Tillett CW, Brown MW, Bashir ZI. 1999. Input-and layer-dependent synaptic plasticity in the rat perirhinal cortex in vitro. *Neuroscience* 92:459–72.
- Zola-Morgan S, Squire LR, Amaral DG, Suzuki WA. 1989. Lesions of perirhinal and parahippocampal cortex that spare the amygdala and hippocampal formation produce severe memory impairment. *J Neurosci* 9:4355–70.
- Zola-Morgan S, Squire LR, Ramus SJ. 1994. Severity of memory impairment in monkeys as a function of locus and extent of damage within the medial temporal lobe memory system. *Hippocampus* 4:483–94.