infections, in light of many strains becoming increasingly resistant to antibiotics. However, over time *S. aureus* strains will certainly develop resistance in these nuclease enzymes as well. A more long-lasting therapeutic avenue may be to inhibit NET formation by targeting host enzymes, which will not mutate over time. Since NETs are not only ineffective against these NET-degrading *S. aureus* strains but also enhance microbial virulence, neutrophil elastase inhibitors that block NETosis could be used to treat persistent *S. aureus* infections [20]. This therapeutic strategy may be counter-intuitive but the mechanism uncovered in this recent study suggests that it is worth exploring.

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http://dx.doi.org/10.1016/j.cub.2013.12.027

Neuroscience: Transforming Visual Percepts into Memories

A new study shows that local field potential oscillations in the human entorhinal cortex and hippocampus are correlated with visual awareness.

Ueli Rutishauser

We can reply to the question '*did the image contain an animal?*' with apparent ease, but doing so requires complex visual processing enabled by the cooperation of large numbers of neurons in different areas of the brain. For example, neurons in early sensory cortices respond to local visual features such as oriented edges, whereas neurons in higher visual areas respond to abstract concepts such as faces [1]. Further downstream in the medial temporal lobe (MTL) are areas such as the hippocampus and the amygdala, which receive this highly processed visual information as input. In humans, some neurons in these areas respond only when a specific familiar object or individual is shown [2]. The neural circuits and computations that lead to such abstract visual responses are only beginning to be understood. While early investigations have focused on how single neurons are tuned to visual features or categories, more recent studies have highlighted the importance of synchronized oscillations in coordinating activity among the many neurons involved in object recognition.

A new study [3] reported in this issue of *Current Biology* now shows that awareness of visual objects goes hand-in-hand with certain local field potential (LFP) oscillations within the MTL. The LFP is the low-frequency (<300 Hz) component of the extracellular potential and is measured with a microelectrode. It is predominantly determined by the transmembrane currents caused by synaptic activity around the tip of the electrode [4]. Oscillations in the LFP are thus indicative of oscillations in synaptic activity.

When presenting a sensory stimulus for a short period of time, conscious experience can vary trial-by-trial even for identical inputs. For vision, this phenomenon is readily produced by presenting a picture on a screen for less than 100 ms, followed by a mask (Figure 1A). In this situation, perceptual awareness varies in an abrupt manner, where most stimuli are perceived and subjectively reported as either visible or invisible [5,6]. When a stimulus is invisible and thus failed to reach

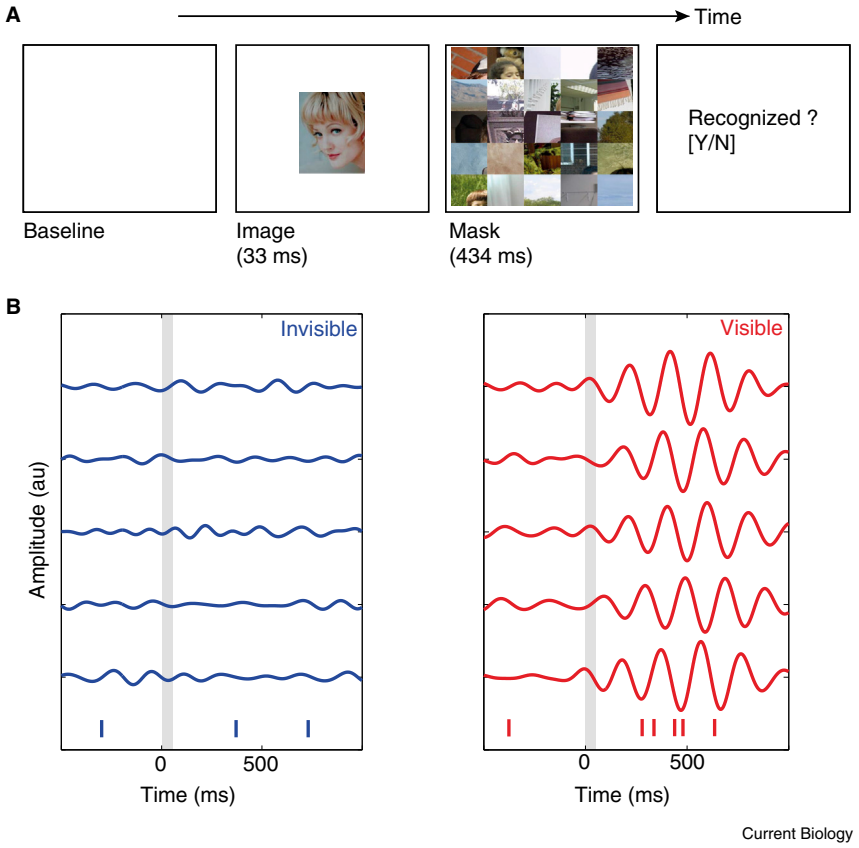

Figure 1. Experimental setup and principal observation of Rey *et al*. [3].

(A) Illustration of the screens the patient saw: a picture was presented for a short period of time (33 ms) and was immediately followed by a mask (434 ms). (B) Illustration of the principal observation: LFP power increased in the theta band for a short period of time (duration about 200–500 ms; see Figure S4 in [3]) after stimulus onset only for visible stimuli (top, frequency 5 Hz). Stimuli were shown on the screen for 33 ms (gray area). Spikes of responsive units (vertical lines at bottom) were present only for stimuli that were recognized by the subject. In this example, spikes that follow visible stimuli occur around the trough of the theta oscillation (bottom right).

awareness, at what point does neuronal processing differ compared with when the same stimulus is perceived? Studies in both humans and non-human primates have used this approach to show that neurons in higher visual areas reflect the subjective percept [6,7]. In contrast, neurons in lower visual areas do not and will respond even if the stimulus has not been perceived [7]. Rey *et al.* [3] exploited a rare opportunity to record the spiking activity of single neurons together with the LFP at the same location in humans: their subjects were patients who had been implanted with depth electrodes with embedded microwires for the purpose of monitoring their seizures [8].

Subjects were asked by Rey *et al.* [3] to indicate whether they were able to recognize pictures presented on a screen for a short period of time (Figure 1A). Subjects reported verbally what they saw. While subjective and difficult to control, this avoids challenging potential confounds that similar primate-based studies face. It has previously been reported that the responses of individual neurons in the human MTL mirror visual awareness — there was no response for invisible stimuli [9,10]. Now, Rey *et al.* [3] report that the power of theta (4–8 Hz) and high gamma-band (70–200 Hz) oscillations increased at about 200–250 ms after stimulus onset if and only if subjects recognized the stimulus. The gamma-band increase was local and most prominent only on the same microwire where a selective neuron had been observed [6]. In contrast, the theta-band response was global and could be observed on all wires regardless of whether a selective unit for that stimulus was identified. This result is the most interesting aspect of this new study and raises a multitude of new questions on the role of theta-oscillations in primates. While intensively studied in rodents, the role of theta-oscillations in primates has remained little studied until recently [11–13].

The network-scale coordination of activity between populations of neurons is thought to enable efficient communication between different brain areas [14]. One way to achieve such coordination is to provide common oscillatory synaptic input, which leads to synchronization. Theta-frequency oscillations are a prominent type of oscillation found in the LFP. They coordinate the activity in and between a number of cortical and subcortical areas, as demonstrated, for example, by the phase-locking of single neuron activity in one area to oscillatory activity in another area [15]. Theta oscillations also modulate plasticity: spikes that arrive at a particular phase of the theta oscillation are more likely to result in synaptic plasticity [16] compared to other phases. The novel finding that successful recognition of an object goes along with area-wide increases of theta-band power (as well as a phase reset) thus means that, whenever a stimulus is recognized, activity of many neurons within the MTL becomes coordinated by selectively enforcing phase-locking (Figure 1B).

Rey *et al.* [3] further highlight the selectivity of phase locking: responsive neurons phase-lock to theta only after stimulus onset. In contrast, non-responsive units do not phase lock even after stimulus onset and units that phase lock to gamma oscillations do so both before and after stimulus onset. This suggests that theta oscillations coordinate network-wide activity only if stimuli are consciously perceived. Thus, theta-sensitive mechanisms such as plasticity [16] would only be engaged for perceived stimuli. Further, using the same mechanism a hypothetical downstream readout neuron could efficiently determine whether a stimulus was recognized and which neurons responded to the stimulus (without knowing their tuning).

Where does the theta rhythm in the human MTL originate? Is it different from theta rhythms observed in cortex, such as visual area V4 [13], prefrontal cortex or the cingulate [17]? While

intensively studied in the case of the hippocampus in rodents during spatial navigation, the origins and function of theta-rhythms in primates are comparatively poorly understood. Evidence is accumulating, however, that theta-frequency synchronization between areas has a general role in coordinating dynamic cell assemblies between different brain areas. Apart from the hippocampus itself, theta rhythms have been observed in other limbic structures such as the amygdala or cingulate but also in many other neocortical areas. Such theta rhythms can, for example, be observed during the maintenance period of working memory tasks [13,14].

The analysis reported by Rey *et al.* [3] adds visual awareness to this list, but at the same time raises new wide-ranging questions. Does successful visual recognition require theta oscillations and if so can signatures of the same process be found in visual cortex? Are visual recognition processes interacting directly with the principle generator of theta activity in the brain, the cholinergic septum [16,18]? Clearly, subjects without a functioning hippocampus and surrounding areas (where the neurons reported here were recorded) are capable of performing object recognition tasks and have visual awareness [19], but they are unable to form new declarative memories. The long response latency of human MTL neurons further questions their direct involvement in recognition processes [20]. An alternative hypothesis is thus that, as a consequence of visual recognition, theta-oscillations are modulated to facilitate plasticity in the MTL. This is compatible with the crucial role theta oscillations have in regulating and coordinating synaptic plasticity [12,16]. New experimental designs are needed to disambiguate these processes — for example, can situations be created in which subjects recognize but not learn or learn but not recognize? If so, these would be powerful candidates to further deepen our understanding of how recognition and learning interact and what the role of theta oscillations is in this interaction.

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http://dx.doi.org/10.1016/j.cub.2013.12.021

Ribosomes: Lifting the Nuclear Export Ban

A recent study shows that nuclear export of the large ribosomal subunit is regulated by a GTPase that blocks recruitment of the nuclear export factor Nmd3 until remodeling of the pre-ribosome by the AAA-ATPase Rea1 (Midasin).

Arlen W. Johnson

The ribosome is tasked with decoding our genetic information, converting nucleotide sequence into protein sequence. It must do this with sufficient speed to support cell growth and with sufficient fidelity to avoid triggering disease states. The ribosome is a highly complex nanomachine composed of ~80 proteins and more than 4,000 nucleotides of RNA that must fold into a stable but dynamic three-dimensional structure. The ribosome must sequentially bind and release multiple ligands, including tRNAs, mRNA, translation initiation and elongation factors, and chaperones. How does a cell accomplish the daunting task of assembling such complex but flexible machines? Matsuo *et al.* [1] now show that during nuclear export of the large (60S) subunit, the acquisition of a critical