Separating wrong from right

Neurons that differentiate between correct and incorrect responses on tests of recent verbal memory are functionally and spatially distinct from those that detect errors during identification tasks. This unexpected finding, published recently in *Neuropsychologia*, is based on extracellular recordings from the temporal lobe of epilepsy patients undergoing neurosurgery while awake.

Before surgery, patients were trained on a three-component task that tests the accuracy of both identification and recent memory. Auditory words, text words or object pictures were presented through

a video monitor in three stages. First, the word or object was verbally identified by the patient. This encoding phase was followed by a storage phase, during which the patient identified three additional items of the same modality. Finally, during the retrieval stage, the patient was asked to recall the item that had been presented in the encoding stage.

During surgery, stable recordings of the activity of single neurons at up to four sites were established under local anaesthesia. Patients were then tested as above, and data from trials in which errors occurred were analysed. Significant differences in activity for correct versus incorrect

identification or recall were observed in 22 neurons at 16 sites in 12 patients. Each of these neurons detected errors in identification or memory — never both — and for one modality only.

This clear functional demarcation was reflected in the spatial dimension. Neurons that differentiated correct from incorrect responses on identification tests were preferentially located in medial–basal regions of the temporal lobe, such as the hippocampus and collateral fissure. By contrast, neurons whose activity indicated the accuracy of recent verbal memory were detected only in lateral regions, particularly the superior temporal gyrus.

Anatomical separation also distinguished neurons that detected errors early during test trials from those that indicated accuracy at a later stage. Identification-specific neurons that differentiated accurate from inaccurate responses within

Keeping in synch in the LGN

A study by Hughes *et al.*, published in *Neuron*, provides strong new evidence that activation of a subtype of metabotropic glutamate receptor, mGluR1a, in the thalamus drives the generation of α - and θ -rhythms *in vivo*. These rhythms occur during wakefulness and early sleep, respectively, and the new study highlights the importance of mGluR1a and gap junctions in the thalamus for regulating rhythmic activity.

Electroencephalographic (EEG) recordings in humans show α -rhythms (oscillations in the 8–13 Hz range) during relaxed wakefulness, particularly over the occipital cortex. When subjects become drowsy, the rhythms are replaced by activity in the θ range (2–7 Hz). To investigate previous suggestions that these cortical rhythms are driven by activity in the thalamus, Hughes *et al.* recorded from slices of the lateral geniculate nucleus (LGN) — the part of the thalamus that relays visual information to the cortex.

Rhythmic activity that resembled α - and θ -rhythms was generated in the LGN when the authors applied mGluR1a agonists. Higher concentrations produced α -like oscillations, and lower concentrations gave

rise to θ -rhythms. Single-cell or local field potential recordings of the oscillations showed marked similarities to recordings that were made *in vivo* from the cat LGN during wakefulness or early sleep.

To test whether mGluR1a receptors are important for generating these rhythms *in vivo*, the authors treated cats with the mGluR1a-specific antagonist LY367385. This treatment rapidly suppressed α -rhythm activity in the cat LGN and in EEG recordings over the occipital cortex, and also induced sleepiness in the animals.

What mechanisms are involved in the generation of α - and θ -rhythms in the LGN? Intracellular recordings from thalamocortical neurons in LGN slices showed that treatment with an mGluR1 agonist caused a distinctive form of burst firing, with spontaneous, high-threshold bursts of spikes at 2–13 Hz. The bursts were very similar to those seen in extracellular recordings of α - and θ -activity. They occurred at depolarized membrane potentials and seem to depend on Ni^{2+} -sensitive Ca^{2+} channels.

When investigating how the rhythmic activity is synchronized between cells in the LGN, the authors discovered that blockers of chemical synaptic transmission did not

prevent synchronization. However, blockers of gap junction transmission did, indicating that gap junctions are responsible for synchronized firing in the LGN. In support of this idea, a putative opener of gap junctions, trimethylamine, enhanced α - and θ -oscillations.

When action potentials are transmitted through gap junctions in the thalamus, they give rise to 'spikelets'. The authors recorded bursts of these spikelets, which they term 'burstlets', corresponding to high-threshold bursts transmitted through gap junctions between thalamocortical neurons. These burstlets showed a number of properties that were identical to those of the high-threshold bursts.

Although these results provide compelling evidence that mGluR1 activation in the LGN produces rhythmic activity that is synchronized through gap junctions and that might drive α - and θ -rhythms in the cortex, many questions remain to be investigated. Other areas of the brain are likely to be important for α - and θ -rhythms *in vivo*. It will be essential to investigate how these areas and circuits interact to generate and sustain rhythmic activity under different conditions.

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References and links

ORIGINAL RESEARCH PAPER Hughes, S. W. *et al.* Synchronized oscillations at α and θ frequencies in the lateral geniculate nucleus. *Neuron* **42**, 253–268 (2004)

WEB SITE

Crunelli laboratory: <http://www.thalamus.org.uk/>