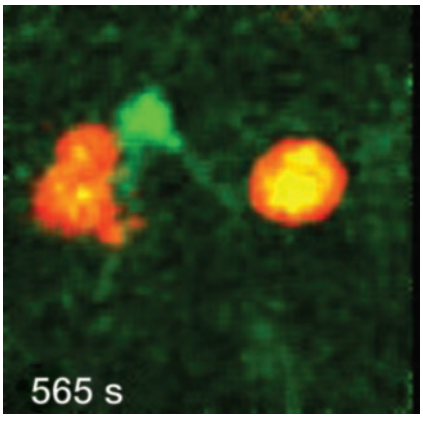
This Week in The Journal

● Cellular/Molecular

Close Encounters between T Cells and Neurons

Robert Nitsch, Elena E. Pohl, Alina Smorodchenko, Carmen Infante-Duarte, Orhan Aktas, and Frauke Zipp
(see pages 2458–2464)

Autoimmune disease is accompanied by T-cell invasion of the CNS, a realm from which they are normally banned. But while we generally think of oligodendrocytes as the primary victims in demyelinating autoimmune disorders such as multiple sclerosis (MS), Nitsch et al. show this week that neurons themselves are under attack from T cells as well. The authors exposed mouse brain slices with intact cellular architecture to activated T cells. T cells were stimulated with oligodendrocyte-derived proteolipid protein (PLP) or ovalbumin (not expressed in mice). The T cells encountered, bound, and killed neurons, whereas unstimulated T cells did not invade the slice. Using two-photon microscopy and ion-sensitive dyes, the authors tracked the real-time movements of the stimulated T cells. T cells, traveling quickly (2.5 μm/sec at 34°C), assailed neurons with a veritable neuronal kryptonite: calcium oscillations. They identified two seemingly cooperative pathways for the excitotoxic calcium: perforin release from T cells and neuronal glutamate receptor activation. Click the movie and watch them go!



Interaction of PLP-specific T cells (red) obtained from SJL/J (H-2^s) mice with hippocampal neurons (green) in living brain tissue from B10.PL (H-2^u) mice. Note the oscillations in neuronal calcium on contact with the T cell. The video shows a 10 sec sequence. See the article by Nitsch et al. for details.

▲ Development/Plasticity/Repair

Retinotectal Mapping without EphA Receptors

David A. Feldheim, Masaru Nakamoto, Miriam Osterfield, Nicholas W. Gale, Thomas M. DeChiara, Rajat Rohatgi, George D. Yancopoulos, and John G. Flanagan
(see pages 2542–2550)

Visual information reaches the retina as a spatially ordered image that must reach higher centers intact for it to be useful to the organism. This task requires topographical mapping between the retina and the tectum (in the chick) or superior colliculus (in mammals). Multiple EphA receptors and their ephrin ligands are expressed in gradients across the projection and target areas, forming a crisscrossed web of repellant molecules that guides retinal axons to their destinations. Now Feldheim et al. have created loss-of-function mutants of the EphA5 receptor in mice and the EphA3 receptor in the chick to ascertain their role in retinotectal mapping. Deletion of the cytoplasmic domain of the receptors disrupted the map but still allowed complete innervation. Their work confirms a functional role for the intracellular domain of the receptor and supports a "competition" model of mapping, in which retinal axons compete to fill the target area and create a map even without a key guidance molecule.

■ Behavioral/Systems/Cognitive

Discriminating Time

Maria A. Pastor, Brian L. Day, Emiliano Macaluso, Karl J. Friston, and Richard S. J. Frackowiak
(see pages 2585–2591)

The somatosensory system can identify independent stimuli that occur within milliseconds, or millimeters, of one another, but only within limits. The threshold for discrimination of separate events is determined by the biophysical properties of neurons and by their circuitry. Do specific brain areas oversee this discrimination? Certain lesions and diseases of the basal ganglia raise the threshold for discrimination, but little more is known about specific circuits mediating temporal and spatial discrimination. In this week's *Journal*, Pastor et al. take a closer look with functional magnetic resonance imaging. Healthy subjects performed the tasks of detecting electrical stimuli to the arm or discriminating between closely spaced or timed events. Not surprisingly, discrimination activated more brain areas than did detection, but temporal discrimination utilized regions even beyond those used for spatial discrimination. The report reveals a cortical "timing circuit" in the pre-supplementary motor area (pre-SMA) and the anterior cingulate.

♦ Neurobiology of Disease

Amyloid Imaging

Nobuyuki Okamura, Takahiro Suemoto, Hiroshi Shimadzu, Masako Suzuki, Tsuyoshi Shiomitsu, Hiroyasu Akatsu, Takayuki Yamamoto, Matthias Staufenbiel, Kazuhiko Yanai, Hiroyuki Arai, Hidetada Sasaki, Yukitsuka Kudo, and Tohru Sawada
(see pages 2535–2541)

Alzheimer's disease (AD) causes dementia and memory loss accompanied by neuronal death. AD pathology has been linked to accumulation of senile plaques (SP) containing amyloid-β (Aβ) peptides, but the diagnosis is still a clinical one, because there is no reliable presymptomatic test. This week, Okamura et al. report on a series of styrylbenzoxazole derivatives for use as potential diagnostic tools with positron emission tomography (PET) or single-photon emission computed tomography (SPECT) imaging. Their quest presented multiple challenges. They needed a compound that binds specifically to Aβ, can be tagged with a radioactive isotope, readily crosses the blood–brain barrier, and is quickly cleared from the brain. They report that 6-(2-fluoroethoxy)-2-[2-(4-methylaminophenil) ethenyl]benzoxazole (BF-168) fulfills these criteria and labels both neuritic and diffuse Aβ plaques in transgenic mice. This synthetic compound may hold future promise for earlier AD detection in humans.