

# This Week in The Journal

## ● Cellular/Molecular

### *Handling Synaptic Cargo in C. elegans*

Sandhya P. Koushika, Anneliese M. Schaefer, Rose Vincent, John H. Willis, Bruce Bowerman, and Michael L. Nonet (see pages 3907–3916)

Trafficking of cargo between cell bodies and nerve cell processes involves both anterograde and retrograde transport using distinct molecular motors. Dynein, a microtubule motor protein involved in retrograde transport, performs its function as part of a complex with accessory proteins such as dynactin. Disruption of these complexes can produce features of motor neuron disease or amyotrophic lateral sclerosis (ALS). In this week's *Journal*, Koushika et al. identify *Caenorhabditis elegans* mutants in which retrograde vesicular transport runs afoul. They screened for defects in retrograde transport using GFP-tagged synaptobrevin as a marker. In the identified mutants, including a dynein light intermediate chain (*dli-1*) null mutant, synaptobrevin accumulated in distal neurites. These animals specifically failed to transport synaptobrevin and synaptotagmin but not other synaptic proteins. In addition to the accumulation of synaptic cargo, the worms developed progressive locomotor symptoms and died prematurely. These results illustrate the cargo specificity of retrograde transport and indicate that dynein dysfunction in *C. elegans* can mimic aspects of motor neuron disease.

## ▲ Development/Plasticity/Repair

### *Genes in Contextual Fear Conditioning*

Jonathan M. Levenson, Sangdun Choi, Sun-Young Lee, Yun Anna Cao, Hyung Jin Ahn, Kim C. Worley, Marina Pizzi, Hsiou-Chi Liou, and J. David Sweatt (see pages 3933–3943)

It is now well accepted that consolidation of long-term memory (LTM) requires the synthesis of new mRNAs and proteins. But which genes are transcribed and translated, and when? This week, Levenson et al. screened 12,420 mouse genes for changes in expression in the CA1 and den-

tate region of the hippocampus during contextual fear conditioning, an NMDA receptor-dependent process. Of this total, 4000 genes had detectable hybridization signals in the examined regions. As might be expected, the authors' profiling identified dozens of regulated genes for which expression fluctuated in the hours after conditioning, including transcription factors, signaling molecules, and metabolic enzymes. Notably, the gene expression changes also required NMDA receptor activation. The authors focused in on one gene product, the transcription factor c-Rel, because a number of the memory consolidation-associated genes contained a c-Rel regulatory element. A null mutant c-Rel mouse could not form contextual memories, but associative memory was unaffected, confirming that c-Rel is necessary for hippocampal-dependent LTM.

## ■ Behavioral/Systems/Cognitive

### *Matching the Face with the Place*

Charan Ranganath, Michael X. Cohen, Cathrine Dam, and Mark D'Esposito (see pages 3917–3925)

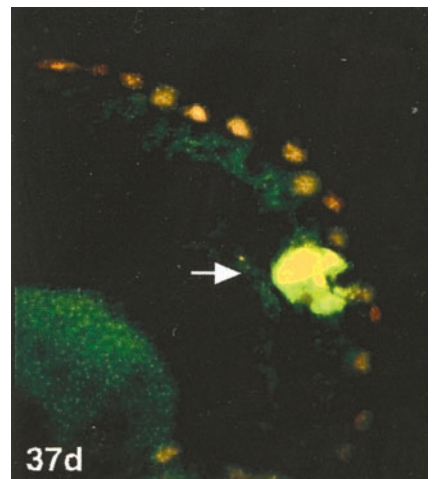
Goal-directed behavior depends on retrieving long-term memories as well as maintaining retrieved information in an active state. In this week's *Journal*, Ranganath et al. use functional magnetic resonance imaging to compare the cortical regions activated by a working memory task with those of an associative memory task. Subjects were trained to associate images of particular faces with particular houses, or were simply shown images of faces or houses alone. In a delayed match-to-sample test, subjects used working memory to hold a previously learned image in mind, while a delayed paired-association task required them to remember and recall a previously formed association. Category-specific areas of inferior temporal cortex lit up selectively; the fusiform face area (FFA) lit up when faces were the stimulus held in active memory, and the parahippocampal place area (PPA) lit up when houses were held in active memory. However, recall from long-term memory activated the anterior prefrontal cortex and hippocampus, providing evidence that these regions supply command signals for linking associative memory to behavioral tasks.

## ◆ Neurobiology of Disease

### *Alzheimer's in the Fly*

Isabell Greeve, Doris Kretzschmar, Jakob-Andreas Tschäpe, Anika Beyn, Claire Brellinger, Michaela Schweizer, Roger M. Nitsch, and Rita Reifegerste (see pages 3899–3906)

We generally think of Alzheimer's disease (AD) as a uniquely human disease marked by  $\beta$ -amyloid ( $A\beta$ ) senile plaques and neurofibrillary tangles. However, as investigators close in on the involvement of key genes in AD, mouse models have played an increasingly vital role. Now Greeve et al. have manipulated these genes in *Drosophila* photoreceptor neurons to create a fly model of Alzheimer's-like amyloidosis. They used the GAL4/UAS system to express the human genes for amyloid precursor protein (APP) and the  $\beta$ -site APP-cleaving enzyme (BACE). The flies also express highly conserved homologs of presenilins 1 and 2 that further process APP. The fly neurons developed "star-like"  $A\beta$  plaques similar to AD and showed photoreceptor degeneration that worsened with age and was reduced by disruption of  $\gamma$ -secretase activity. Ubiquitous expression of APP and BACE in the fly reduced viability. The *Drosophila* model supports a role for  $A\beta$  in AD-induced neuronal death and provides a valuable additional tool for studies of AD pathogenesis and treatment.



Thioflavin S staining revealed amyloid plaques in the degenerated retina of *w; UAS-APP/+; UAS-DPsnL235P/gmr-GAL4* transgenic flies. See the article by Greeve et al. for details.