What does it take to make a memory? Study says new proteins

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Credit: Rice University

While the romantic poets' idea of memories being akin to spirits may have poetic merit, the scientists' perspective is that memories are concrete, physical entities that can be visualized within various regions of the brain.

Scientists from the Florida campus of The Scripps Research Institute (TSRI) have now for the first time identified a sub-region in the brain that works to form a particular kind of memory: fear-associated with a specific environmental cue or "contextual fear memory."

The study, recently published in the journal *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, was led by TSRI Associate Professor Sathyanarayanan V. Puthanveettil.

"Much is still unknown about the identities of proteins synthesized to produce long-term memory," Puthanveettil said. "The most striking observation from the new study is that the medial prefrontal cortex is the site of this early protein synthesis. We have also identified what proteins are newly synthesized in the medial prefrontal cortex."

In particular, the study showed new protein synthesis in a specific sub-region of the prefrontal cortex known in rodents as the prelimbic. In humans, this area corresponds to the anterior cortex, which has been linked to processing emotional responses.

Initially, Puthanveettil and his colleagues ignored the medial prefrontal cortex because no one believed that it had anything to do with early encoding of long term memories.

However, when they closely examined the effects on the brain of conditioning rodents with a mild foot shock, the scientists found several messenger RNAs recruited to polyribosomes in the medial prefrontal cortex—a clear indication of new protein synthesis there.

Puthanveettil and his colleagues also discovered that if they inhibited new protein synthesis in the prelimbic region right after fear conditioning took place, those memories did not form. But if the researchers waited just a few hours, inhibiting protein synthesis in prelimbic cortex had no impact and the memories took hold. There is temporal and spatial regulation of new protein synthesis in the medial prefrontal cortex.

"It may be that the first wave of protein synthesis is critical for encoding contextual fear memory, while second wave in other sub-regions is important for memory storage," he said.

It remains to be determined if other sub-regions of the cortex are also be involved in the synthesis of memory proteins.

"The medial prefrontal cortex has many sub-regions," said TSRI Senior Research Associate Bindu L. Raveendra, co-first author of the study with Valerio Rizzo, Khalid Touzani and Supriya Swarnkar, all of TSRI at the time of the study. "But the specific roles of these sub-regions in encoding, expression and retrieval, as well as their underlying molecular mechanisms, remain to be unraveled."

Other authors of the study, "Encoding of Contextual Fear Memory Requires De Novo Proteins in The Prelimbic Cortex," include Beena M. Kadakkuzha and Xin-An Liu of TSRI; Joan Lora and Robert W. Stackman of Florida Atlantic University; and Chao Zhang and Doron Betel of Weill Cornell Medical College.

More information: Valerio Rizzo et al. Encoding of Contextual fear Memory Requires de novo Proteins in the Prelimbic Cortex, *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* (2016). DOI: 10.1016/j.bpsc.2016.10.002

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