Research shows spaced training improves long term memory in mice with fragile X syndrome

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Prominent characteristics of the syndrome include an elongated face, large or protruding ears, and low muscle tone. Credit: Wikipedia

(Medical Xpress)—Research on mice with fragile X syndrome (FXS) suggests that multiple, spaced training sessions can enhance learning and long term memory when longer, continuous sessions do not. Christine

Gall and colleagues at the University of California Irvine tested mice with FXS on their ability to remember objects and locations and found that multiple training sessions, with 60-minutes breaks, allowed them to perform as well as healthy mice. The research appears in the *Proceedings of the National Academy of Sciences*.

FXS is the most common cause of inherited intellectual disability. Previous studies have shown that mice with this condition have a problem with synaptic signaling in the hippocampus, which affects their ability to create long term memories.

Gall's team wanted to see if they could create a training regime that would help overcome synaptic signaling problems and enable mice with FXS to learn normally. They knew that individuals tend to learn better when trained in short, spaced trials rather than a single, long training episode, so they tested whether spaced training would help FXS mice.

The researchers tested the mice on object location memory (OLM) and novel object recognition (NOR). To test OLM, they placed a mouse in a chamber that also contained two identical objects. They gave the mouse time to examine the objects and remember their locations, and then removed the mouse. When the mouse was gone, the researchers moved one of the objects. They then returned the mouse to the chamber. If the mouse spent more time exploring the new location than the old location, it was a sign that it had remembered the original location.

NOM testing involved replacing one of the identical objects with a different object, without changing its location. Mice that spent more time examining the new object showed that they had remembered the original object.

After undergoing five minutes of continuous training and being removed from the chamber for 24 hours, wild mice recognized that one of the

objects had moved or been replaced, but FXS mice did not. However, when the researchers divided the training into three 100-second trials, with 60-minute intervals between them, the FXS mice performed about as well as the wild mice.

Gall's team examined hippocampal tissue from the mice and found that control FXS mice had problems with the activation of ERK1/2, a kinase needed for memory encoding. Spaced training corrected this problem and restored proper signaling between synapses.

More information: Spaced training rescues memory and ERK1/2 signaling in fragile X syndrome model mice, *PNAS*, Ronald R. Seese, DOI: 10.1073/pnas.1413335111

Abstract

Recent studies have shown that short, spaced trains of afferent stimulation produce much greater long-term potentiation (LTP) than that obtained with a single, prolonged stimulation episode. The present studies demonstrate that spaced training regimens, based on these LTP timing rules, facilitate learning in wild-type (WT) mice and can offset learning and synaptic signaling impairments in the fragile X mental retardation 1 (Fmr1) knockout (KO) model of fragile X syndrome. We determined that 5 min of continuous training supports object location memory (OLM) in WT but not Fmr1 KO mice. However, the same amount of training distributed across three short trials, spaced by one hour, produced robust long-term memory in the KOs. At least three training trials were needed to realize the benefit of spacing, and intertrial intervals shorter or longer than 60 min were ineffective. Multiple short training trials also rescued novel object recognition in Fmr1 KOs. The spacing effect was surprisingly potent: just 1 min of OLM training, distributed across three trials, supported robust memory in both genotypes. Spacing also rescued training-induced activation of synaptic ERK1/2 in dorsal hippocampus of Fmr1 KO mice. These results show

that a spaced training regimen designed to maximize synaptic potentiation facilitates recognition memory in WT mice and can offset synaptic signaling and memory impairments in a model of congenital intellectual disability.