

## **Does calcium leak in the brain cause mental retardation?**

### **Results:**

Some patients with inherited mutations in the ryanodine receptor (RyR2) only develop cardiac arrhythmias, whereas others also develop mental retardation. We tested the hypothesis that mutation R176Q in RyR2 – identified in patients with arrhythmias – also exhibit defects in learning and memory.

First, the passive avoidance test was performed for contextual and emotional memory. The R176Q/+ mutant mice did not show decreased latencies to enter the dark side in the passive avoidance test.

Second, general anxiety evaluated with the passive avoidance task was normal. We conducted an open field test as a control experiment, to measure anxiety and locomotor activity. Wildtype and R176Q/+ mice behaved similarly in the open field test. The light-dark test revealed that R176Q/+ mice did not demonstrate altered exploratory behavior. Moreover, the R176Q/+ mice did not show altered exploratory behavior.

Third, the Morris Water Maze was performed to test for learning and memory. There were no significant differences between WT and R176Q/+ mice. Moreover, there were no significant differences in the time to reaching the visible platform comparing both groups. The Rotarod test was performed a control for the Morris water maze test. Our results show that R176Q/+ mice have similar learning performance to WT mice on the rotarod.

In conclusion, our results show that knockin mice with the R176Q/+ mutation, found in patients with cardiac arrhythmias, exhibit normal learning and memory abilities. These findings suggest that mutations of different residues within RyR2 may either cause cardiac or neuronal defects.

### **Areas of interest:**

Calcium channels, electrophysiology, brain/heart interactions

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**Researchers contact:**

Xander H.T. Wehrens, MD, PhD  
Director, Cardiovascular Research Institute  
Juanita P. Quigley Endowed Chair in Cardiology  
Professor, Dept. of Molecular Physiology and Biophysics  
Professor, Dept. of Medicine (in Cardiology)  
Co-Director, Medical Scientist Training Program (MSTP)

Baylor College of Medicine  
One Baylor Plaza, BCM335  
Houston, TX 77030  
T. 713-798-4261 (direct)  
F. 713-798-3475  
E. wehrens@bcm.edu