

November 1, 2017

In response to the recent abstract “Cognitive deficits and increases in creatine precursors in a brain-specific knockout of the creatine transporter gene *Slc6a8*” <https://www.biorxiv.org/content/early/2017/09/29/196063>, ACD Scientific Advisory Board Member, Dr. Matthew Skelton issued the following comments:

This paper represents an important control study for our lab. To test a mouse’s learning ability, we put them through a swimming task where they find an invisible platform in a pool of water. Our mice that lack the creatine transporter (known as knockouts) throughout their whole bodies are much smaller than mice that have the gene (known as wild-type). The knockout mice also swam slower than their wild-type counterparts. Based on a 2016 paper published by our lab, it appears that the weight difference is due to a loss of muscle, as fat levels are similar between knockout and wild-type mice. Taken together, we were concerned that the poor performance in the swimming task could be due to motor problems instead of changes in the brain. This could make interpreting results from treatment studies difficult. To eliminate this concern, we removed the creatine transporter from the brain while leaving creatine levels in other tissues at normal levels. This “brain specific” knockout showed deficits in the swimming task comparable to mice that lacked creatine throughout the body. In addition, they showed deficits in two other learning tasks that do not require swimming. The results of this study allow us to use the mice that lack creatine throughout the body to test treatments and better understand CTD. This is important because mice the brain-specific knockout mice do not represent the normal physiology of human CTD patients. They have a working creatine transporter in the intestine, muscle, and at the blood-brain barrier which could lead to incorrect results if the brain-specific mice are used to test treatments. Clearing the way for the use of whole-body knockout could lead to the development of better therapeutics for CTD.