Examining the Therapeutical Effects of Lanthionine Ketimine (LK) in Neuronal Connectivity

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Abstract
Collapsin response mediator proteins (CRMPs), are cytoskeletal adapter molecules involved in a variety of normal cellular functions including alteration of cell shape and cell communication. CRMP2s have also been associated with pathological disorders and neurological diseases. For instance, CRMP2 protein collects in cytoskeletal tangles in Alzheimer’s disease, which may contribute to neural degeneration in this disorder. In other examples, differences in CRMP2 expression have been documented in some subsets of patients suffering paranoid schizophrenia. Lastly, the anticonvulsant drug lamotrigine (VimPat) was found to act by binding to CRMP2, which unmasked the pharmacological importance of CRMP2-binding in epilepsy. Thus, based on these observations, we hypothesize that CRMP2 plays a central role in neuronal connectivity and may represent a critical junction linking neural brain function and potential for therapeutic manipulation using the nematode C. elegans.

Results
5. LKE has a positive affect on ventral nerve cord development of unc-33 (e204) nematodes over-expressing GFP

Figure 5. unc-33 (e204) nematodes over-expressing GFP in neurons and grown in 0.5 mM LKE exhibited a lower frequency of premature terminating commissures. A: unc-33 (e204) nematodes over-expressing GFP in GABAergic neurons grown in 0.5mM LKE. B: unc-33 (e204) nematodes over-expressing GFP in GABAergic neurons grown in 0.5mM LKE. C: Quantification of the frequency of early terminating commissures in 20 individuals per treatment showed that LKE results in a significant decrease in premature termination. * p<0.001

Conclusions
• This research corroborates previous findings using a cholinergic fluorescent marker.
  • In brief, we demonstrated that LKE partially rescued unc-33 (e204) mutant synaptic phenotype.
  • More specifically, LKE treatment significantly decreased the number of gaps observed at the ventral nerve cord. The size of the gaps, as well as the proportion of early terminated commissures.

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