

CoA-dependent activation of mitochondrial acyl carrier protein links four neurodegenerative diseases

What does the paper say?

In order to develop a treatment for a disease, it is important to understand the symptoms of a disease. The manuscript by Lambrechts et al explains some of the characteristics of PKAN and explains why some symptoms of PKAN are comparable to symptoms of 3 other diseases. These other diseases are CoPAN, MePAN and PDH-E2 deficiency. The presence of similar symptoms suggests that the 4 diseases share comparable metabolic defects. The manuscript describes and explains these shared metabolic defects in a fruitfly model and in human cells. One of the key findings of the manuscript is that the protein mtACP is less active in PKAN. A defect in mtACP has never been considered nor investigated in relation to PKAN and this provides important insights why mutations in PANK2 gene cause the disease PKAN. A less active mtACP explains also the metabolic defects observed in cells of PKAN patients and the iron accumulation reported in the manuscript of the OHSU group in the PKAN mouse model. The results presented in the Lambrechts et al manuscript also explain why 4-phosphopantetheine corrects the metabolic defects in PKAN as elegantly demonstrated in the Jeong et al manuscript.

What does it mean for people with PKAN?

The manuscript further supports the findings of the OHSU group that the mouse model is a valuable model to understand PKAN and is in agreement with the findings of the OHSU group that 4-phosphopantetheine might help people with PKAN.

What does it mean for people with CoPAN, MePAN and PDH-deficiencies?

Based on the results of the fly model, the results suggest that 4-phosphopantetheine most likely is not promising for CoPAN, MePAN and PDH-E2 deficiency patients. For these diseases the manuscript suggests other treatment strategies. These strategies need to be further explored before they can be implemented in the clinic.