Integral Relationship Between Vitamin B1 and Hypoxia Inducible Factor-1alpha

Abstract

My primary research interests surround the pathophysiological implications of Vitamin B1 (thiamine) deficiency and supplementation. These research efforts have centered on how HIF1α impacts thiamine homeostasis and how changes in thiamine status can in turn regulate HIF1α. HIF1α is an essential adaptive stress response transcriptional factor that can contextually mediate either pro-survival or pro-death cellular responses. In hypoxic tumor microenvironments, HIF1α was found to be a direct transcriptional activator for the thiamine transporter SLC19A3. Furthermore, HIF1α upregulates thiamine pyrophosphokinase-1 (TPK1). Thus, HIF1α activation during hypoxic conditions attempts to upregulate thiamine homeostasis in a pro-survival capacity. In contrast, thiamine deficiency (TD) can activate HIF1α independent of low oxygen conditions. Reduced activity of thiamine dependent enzyme PDH during TD resulted in a buildup of pyruvate capable of activating HIF1α. Activation of HIF1α during TD mediated pro-apoptotic and amyloidogenic processes. Therefore, HIF1α may be a possible transcriptional mediator promoting neurological injury in TD associated neuropathologies.