High fat diets (HFD) rich in saturated fatty acids such as palmitic acid (PA) increase oxidative stress, apoptosis, and pro-inflammatory cytokines in both peripheral tissue and brain (1-4). In in vitro models, PA increases lipid peroxidation and cell death. High fat diets have been linked to neuronal degeneration of hypothalamic sites important in regulating energy balance in vivo, but the underlying cause of this dysregulation remains unclear.

Recent evidence suggests that orexin A (OXA), hypoxia 1 (HIF1a), a hypoxia-protective peptide, protects against oxidative stress and neuroinflammation (5-6). In an in vitro hypothalamic cell culture model, we showed that OXA reduces lipid peroxidation, decreases PA-induced apoptosis, and stabilizes the pro-apoptotic protein B-cell lymphoma 2 (Bcl-2). Does PA decrease pro-survival gene expression and in part OXA against pro-inflammatory cytokines in arcuate hypothalamic microglial cells? We hypothesize that PA-induced microglial activation affects neuronal response to PA-induced toxicity. Together, these studies were designed to answer three main questions:

1) Does OXA increase HIF1-a in arcuate nucleus and caudal lateral hypothalamic explants?
2) Does PA decrease pro-survival gene expression and increase cytoktocity in Arc and CAH explants?
3) Does PA increase mitochondrial activity and microglial activation in immortalized microglial cells?

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Acknowledgements

References

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