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| **ISA ISPID  Abstract Submission  Nº: 157**   |  | | --- | | Topics: **SIDS/SUID** | | Type: **Oral** | | **Mechanism of neurodegeneration of Orexin/Dynorphin neurons in Sudden Infant Death Syndrome** | | **Hunt, Nicholas**1; **Waters, Karen**2; **Machaalani, Rita**2 *1 - Department of Medicine, Sydney Medical School; BOSCH Institute of Biomedical Research, University of Sydney, NSW, Australia . 2 - Department of Medicine, Sydney Medical School; BOSCH Institute of Biomedical Research, University of Sydney, NSW, Australia; The Children’s Hospital, Westmead, NSW, Australia.* | | **Introduction** We have previously reported that infants that have died of Sudden Infant Death Syndrome (SIDS) have decreased orexin immunoreactivity in the hypothalamus (Hunt et al., 2015). This study aimed to examine multiple pathways that have previously been shown to promote loss of orexin expression in humans and in animal models of neurodegeneration.  **Material and Methods** Immunofluorescent and immunohistochemical staining for orexin A (OxA), dynorphin (Dyn), cleaved caspase 3 (CC3), terminal-deoxynucleotidyl-transferase-dUTP-nick-end-labelling (TUN), c-fos and the phosphorylated unfolding protein response (UPR) activation markers pancreatic endoplasmic reticular kinase (pPERK) was performed in the tuberal hypothalamus (n=27) of infants (1-10 months) who died from SIDS compared to age matched non-SIDS infants (n=19).  **Results** OxA and Dyn co-localise in orexin neurons with a 20% decrease in expression in SIDS (p=0.001). A 35% increase in co-localised pPERK and OxA was observed in SIDS infants compared to controls (p=0.05). A linear relationship between the decrease in OxA content and the percentage of co-localised pPERK/OxA was seen (p=0.01). No changes in co-localisation of OxA with CC3, TUN or c-fos were observed, nor was there any increase in CC3 or TUN were observed in all hypothalamic neurons in SIDS compared to controls. Furthermore, no correlations were found with risk factors of SIDS that included prone sleeping, cigarette smoke exposure and bed sharing.  **Conclusions** Loss of orexin in SIDS infants appears to be mediated by loss of translation of the orexin peptides following the promotion of the upregulation of pPERK, accumulation of pPERK inhibits the translational of mRNA to protein. This suggests that an ER stress pathway has been promoted in SIDS. These results also suggest that the UPR is occurring in SIDS infants and may be involved in neurodegenerative processes in SIDS. Funding was provided by the SIDS stampede, Australia and the Miranda Belshaw Foundation, Australia. Reference: Hunt, N. J., Waters, K. A., Rodriguez, M. L., & Machaalani, R. (2015). Decreased orexin (hypocretin) immunoreactivity in the hypothalamus and pontine nuclei in sudden infant death syndrome. *Acta neuropathologica*, *130*(2), 185-198. | |  |  |  |  | | --- | --- | | **CONTACT** | | | Name: | **Nicholas** | | Lastname: | **Hunt** | | E-mail: | **nhun3572@uni.sydney.edu.au** | | Country: | **Australia** | | Institution | **Department of Medicine, Sydney Medical School; BOSCH Institute of Biomedical Research, University of Sydney, NSW, Australia** | | Cellphone: | **+61 425 569 108** | | City: | **Sydney** | |