**ISA ISPID  
  
Abstract Submission  
  
Nº: 183**

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| Topics: **SIDS/SUID** |
| Type: **Oral** |
| **Apoptotic pathways in the Sudden Infant Death Syndrome (SIDS) medulla.** |
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| **Introduction** Sudden infant death syndrome (SIDS) is the leading cause of post-neonatal death in Australia and the developed world. Previous studies within our laboratory have identified that apoptotic markers are upregulated in two cohorts of SIDS infants; a Canadian population from the mid 1990’s1 and an Australian cohort spanning 1997-20022. The involvement of the intrinsic, extrinsic, and alternative apoptotic pathways are currently unknown.  **Material and Methods** This study aimed to (i) characterise a new infant dataset spanning 2008-2012; (ii) investigate the expression of three apoptotic markers; active caspase-3, active caspase-9 (intrinsic pathway marker), and TUNEL in the rostral medulla of SIDS (n=20) and non-SIDS (n=10) using immunohistochemistry; (iii) to determine any correlation with infant characteristics and/or SIDS risk factors.  **Results** *Characteristics:* The two groups were well matched for age, gender, and anthropometric data. At death nearly half (48%) of SIDS infants were reported as being found in the prone sleeping position despite no cases reported as being placed in this position (p=0.001). The incidence of cigarette smoke exposure was 48% in SIDS infants. *Apoptotic expression between SIDS and non-SIDS:* An increase in caspase-9 was observed in three nuclei; the hypoglossal nucleus (XII), the cuneate nucleus (Cun), and the inferior olivary nucleus (ION), in SIDS compared to non-SIDS (p<0.05). Only the XII demonstrated a significant increase in caspase-3 (p<0.05). TUNEL was increased only in the Cun of SIDS compared to non-SIDS (p<0.05). Co-localised expression of caspase-3 and caspase-9 with TUNEL were not significantly different between the two diagnostic groups in any of the nuclei. Despite this positive correlations were observed in the SIDS cohort between caspase-3 and TUNEL in the ION and between caspase-3 and caspase-9 in the XII. *Correlation with infant characteristics and/or SIDS risk factors:* Regardless of diagnosis, the increased expressions of the three markers correlated with gliosis, the presence of *Staphylococcus aureus,* and an upper respiratory tract infection predominantly for the Cun, ION, vestibular nucleus, and nucleus of the spinal trigeminal tract. The only association with the two major SIDS risk factors: prone sleeping and cigarette smoke exposure, was observed in the dorsal motor nucleus of the vagus in SIDS infants with a history of exposure having a decrease in caspase-3 expression (p=0.004).  **Conclusions** Findings from this study add to the amassing evidence of increased apoptotic pathways in the brainstem of SIDS infants, still present three decades from its first report1. Although the Cun neurons were found to be at the final stage of cell death (TUNEL) within SIDS, the XII and ION are also implicated but at the earlier stages of cell death. This may suggest impairment of these neurons in the lead up to a SIDS death with possible consequential functional loss including fine touch and proprioception of the upper body (Cun), control of the tongue (XII), and control and execution of movement (ION). **Funding Source:**SIDS Stampede and Miranda Belshaw Foundation. **References:**1- Waters, KA et al.,1999, *Pediatric Research*, *45*(2), 166-172. 2- Machaalani, R & Waters, KA, 2008, *Brain*,*131*(1), 218-228. |
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