Sudden Infant Death Syndrome: a potential breakthrough?

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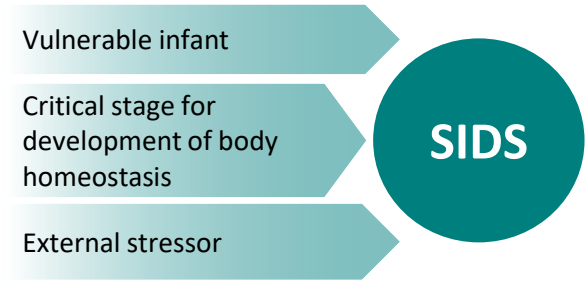
The term **Sudden Infant Death Syndrome** (SIDS) describe the unexplained death during sleep of an otherwise apparently healthy infant under one year of age. **Major risk factors** have been identified in **prematurity, prone sleeping, maternal smoking and overheating**[1], yet SIDS remains a poorly understood phenomenon, in which multiple factors are likely to play a role.

Public health initiatives targeting the known risk factors have been largely successful in reducing the incidence of SIDS.[3]
However,...

The "Triple risk model" of SIDS[2]



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"Usually, if a baby is confronted with a life-threatening situation [...] they will arouse and cry out. What this research shows is that some babies don't have this same robust arousal response."[1]

SIDS still accounts for nearly half of post-neonatal deaths in Western countries, therefore any insight into its pathophysiology would be highly valuable. The proposed association between SIDS and autonomic dysfunction has led researchers to investigate the role of cholinergic enzyme butyrylcholinesterase (BChE), which is thought to modulate CNS arousal responses, among other autonomic functions.[3]

Butyrylcholinesterase is a potential biomarker for Sudden Infant Death Syndrome[3]

Objective

- To evaluate BChE levels and activity in **infants who had died from SIDS** and infants who had **died from other causes** vs **healthy controls**.

Methods

- The study compared 26 SIDS and 30 non-SIDS deaths to 254 and 291 matched surviving controls, respectively.
- **BChE specific activity (BChEsa)** and total BChE were assayed from the eluate of 5µL samples from **dried blood spots (DSB) taken at birth.**
- BChEsa was calculated by dividing BChE activity (mU/ml) by total protein content (µg/ml).

Results

- BChE activity was retained after elution, with good correspondence between plasma and DBS QCs.
- **Mean BChEsa was significantly lower in SIDS cases**, but not in non-SIDS cases, compared to respective controls.
- There was a **strong linear association between lower BChEsa and death in SIDS cases**, which was not observed in non-SIDS deaths.

Butyrylcholinesterase specific activity and correspondent risk of death in SIDS and non-SIDS deaths vs healthy controls[3]

Cause of death	SIDS		Non-SIDS	
	Cases (n = 26)	Controls (n = 254)	Cases (n = 30)	Controls (n = 291)
BChEsa, U/mg, mean (SD)	5.6 (2.1)	7.7 (3.6)	8.5 (4.2)	8.5 (3.4)
OR per BChEsa unit (95% CI)	0.73 (0.60—0.89)		1.001 (0.89—1.13)	
P value	0.0014		0.99	

Our thoughts:

- The study presents a few limitations, mainly that it is difficult to compare DSB BChE levels with known post-natal BChE reference points; also, no information was available on BChE levels at the time of death.
- Further research is necessary to address the above limitations and to gather data on the distribution of BChE activity in the general population.
- If confirmed, however, this finding would be a breakthrough in SIDS prevention. With a **biomarker** that could be reliably assayed as part of **routine neonatal screening**, vulnerable babies could be identified early on, **improving the efficacy of postnatal monitoring and targeted interventions**.

References

1. World first breakthrough could prevent SIDS | Sydney Children's Hospitals Network (nsw.gov.au)
2. Filiano J, J, Kinney H, C: A Perspective on Neuropathologic Findings in Victims of the Sudden Infant Death Syndrome: The Triple-Risk Model. Neonatology 1994;65:194-197. doi: 10.1159/000244052
3. Harrington CT, Hafid NA, Waters KA. Butyrylcholinesterase is a potential biomarker for Sudden Infant Death Syndrome. EBioMedicine. 2022 May 6;80:104041. doi: 10.1016/j.ebiom.2022.104041