

The Lullaby Trust: Overview of potential mechanisms underlying SIDS

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The following information is based primarily on a review paper about sudden infant death syndrome (SIDS)¹. The information aims to outline the key mechanisms suggested to be involved in SIDS. It should be emphasised that despite lots of theories being explored, it's not yet known exactly what causes SIDS and there are likely to be several factors involved. Research is ongoing into trying to understand the mechanism(s) underlying SIDS.

The triple risk hypothesis

Data from population (epidemiological) studies indicate that there are numerous risk factors for SIDS that act together to increase or decrease the chance of death. SIDS is therefore thought to be due to multiple factors acting in a given situation. The 'triple risk hypothesis' has been suggested as a model of how risk factors might act to cause SIDS. This model suggests that SIDS occurs due to a combination of factors including:

1. The infant is vulnerable (e.g. they may have a physiological impairment of some kind)
2. The infant is at a critical period of development
3. There is an external factor in action (e.g. the infant is placed prone to sleep)

While this model may help to explain how risk factors might act together when SIDS occurs, we still need to know exactly what is happening in the body to cause SIDS even if these factors are present – i.e. the potential 'mechanisms' underlying the syndrome.

Potential mechanisms

Over the years a huge number of possible mechanisms of SIDS have been suggested, most of which have not been substantiated by published evidence and even fewer of which have stood the test of time. The following are the most generally accepted possible mechanisms by which death may occur in SIDS.

1. Autonomic control and arousal

Although the specific cause of SIDS is unknown, abnormalities or immaturity of autonomic control and failure of arousal responsiveness from sleep may be important factors.

What does 'autonomic control' mean?

Autonomic is a term usually referring to the nervous system that controls involuntary or unconscious actions, such as control of heart rate, respiratory rate, salivation, digestion and perspiration. If the autonomic control system is impaired in some way it could affect essential bodily functions, potentially leading to serious complications such as heart problems, blood pressure problems and trouble with breathing or swallowing.

¹ Moon RY, Horne RSC, Hauck FR. Sudden infant death syndrome. *Lancet*. 2007; 370:1578-87

What does 'arousal' mean?

Arousal refers to waking from sleep. Arousal from sleep is an important survival response to a life-threatening event, such as low blood pressure or sleep apnoea (when breathing temporarily stops during sleep). Arousal from sleep can occur spontaneously in response to internal physiological changes, and can also be brought about by external environmental factors.

What happens during arousal from sleep?

Arousal involves both autonomic and behavioural components. Heart rate, blood pressure and breathing are increased (autonomic components) and a behavioural response is prompted, allowing body movements aimed at avoiding a life-threatening situation (e.g. moving the head to avoid suffocation if the mouth is accidentally covered by a blanket during sleep). Cardiorespiratory responses at arousal are similar to fight-or-flight reactions, which also increase heart rate, blood pressure and breathing. The defence-alerting responses range from mild cardiorespiratory activation (e.g. a sigh), through awakening, and finally to redistribution of blood flow and gasping during oxygen deprivation.

What is the link between arousal and SIDS?

Abnormalities of arousal have been associated with cases of SIDS. Studies of infants who subsequently died from SIDS found fewer spontaneous arousals from sleep and immature sleep patterns in some of these infants, compared with infants who survived, suggesting the arousal mechanism was impaired in those infants who died. Many studies of sleep and arousal responses in healthy infants exposed to major SIDS risk factors have shown that these risk factors can alter the sleep patterns and physiology of infants, and may impair infant arousal responses to both internal and external stimuli.

Infants who died of SIDS are sometimes found to have alterations in the brain in areas associated with autonomic control, control of respiration, sleep and arousal.

While it seems that problems with the autonomic nervous system or failure of arousal from sleep might be significantly involved in SIDS, the causes of why such problems occur haven't yet been determined.

2. Genetic factors***What are genes?***

Genes are small portions of DNA. Genes provide sets of instructions for different parts and functions of the body.

What is the link between genetics and SIDS?

Genetic variations may lead to alterations of autonomic control and failure of arousal. Studies have found differences in the genetics of some infants who died from SIDS which might be linked to physiological impairments resulting in SIDS. However, these findings are mainly observations of particular genetic differences between some infants who died of SIDS and healthy infants, but are not studies proving a causal link between the genetic variations and SIDS. As such, a specific genetic variation proven to cause SIDS has not yet been identified. Researchers are investigating new genetic variations frequently in the search for a proven link.

3. Infection

There is some evidence to suggest that infection might have a role in some cases of SIDS. Bacteria that can cause serious illness in infants are found more frequently in SIDS cases than non-SIDS cases and it has been suggested that either a response to these bacteria, or possibly substances that the bacteria produce (toxins), might be important in some SIDS cases. It has also been suggested that an inherited (genetic) alteration in how some infants' bodies respond to bacteria might be important. However, at present it is very difficult to know whether infection caused a death in an individual case and research is ongoing to try to develop better tests for use at autopsy.

Potential mechanisms linked to some known SIDS risk factors

A. Factors associated with a increased risk of SIDS

Prone sleeping

Prone sleeping has been shown to increase the amount of time that infants spend asleep and the time spent in quiet sleep, a state of reduced arousability. In addition, it has been found that infants sleeping on their fronts have significantly decreased arousability compared with those sleeping on their backs. Prone sleeping has also been associated with altered autonomic control, seen as raised heart rates and decreased heart rate variability, amongst other responses.

Smoking

Infants exposed to smoke in the womb have been found to have decreased arousability and altered autonomic control. Prenatal smoke exposure can result in decreased lung volume and ease of expansion, and decreased heart rate variability to stress. In addition, nicotine interferes with normal development of the embryo resulting in changes in autonomic pathways, including decreased arousal to low oxygen in the body and other stimuli. Smoking might also affect the way the lung develops and how surfactant, an important substance which keeps the lungs inflated, might function.

Premature infants

Research has shown that before neonatal unit discharge, infants born prematurely slept longer, had fewer arousals from sleep and more sleep apnoeas when sleeping prone. Premature infants are often placed prone in intensive care settings to enhance respiration. The lungs of premature infants may also show abnormal development.

B. Factors associated with a decreased risk of SIDS

Breastfeeding

Studies have shown that breastfed infants arouse from sleep more readily at age 2-3 months (a time of particularly increased SIDS risk) than formula-fed infants do. In addition, research has found that formula-fed infants who died of SIDS have much lower concentrations of a fatty acid (docosahexaenoic acid) in their brains than breastfed infants. This fatty acid is essential for the normal development of the brain in infants and has also been associated with more mature infant sleep patterns.

Dummy use

Several mechanisms have been suggested for why dummy use may reduce the risk of SIDS. One study found a lower arousal threshold in infants who frequently used a dummy during sleep than those who did not, which might lead to a heightened response to a life-threatening situation (e.g. apnoea caused by obstruction in the airway, irregular heartbeat or external conditions leading the body to be deprived of oxygen). Other theories include an improved ability to breathe through the mouth if the nasal airway becomes blocked, and decreased likelihood of obstruction in the back of mouth / top of the throat by bringing the tongue forward. Displacement of the dummy during sleep might also contribute to increased sleep disruption and greater arousability of the infant.

While a large amount of research has been carried out and numerous risk factors for SIDS identified, the exact reasons why a particular infant died, with or without those risk factors present, remains uncertain. Ongoing research is required to find out exactly what the process is that leads to death in SIDS cases to improve our understanding of how to lessen the chance of this happening.

Additional references:

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