

## Long Term Neurocognitive Outcome after Anaesthesia and Surgery in Children; Is There a Problem?

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There is increasing evidence that general anaesthetic exposure to the developing brain of rodents results in neuronal apoptosis and abnormal neuronal development. There is also some evidence for this in the developing primate brain. It appears to be a dose effect and there are also periods of development when the neuron is most susceptible. The mechanism may be due to relative reduction in neuronal activity but there are still inconsistencies and questions surrounding exact mechanism. Some animal studies demonstrate long term cognitive or behavioural affects while others do not.

It is very difficult to know how these animal studies relate to humans. While they are cause for concern, it is not certain they translate to clinically significant human outcomes. The period of vulnerability in the human, the dose and the recovery capacity in humans are all unknown. It is also unknown what effect the surgery itself has on the injury. The inflammatory and humoral response of surgery may itself harm the developing neuron and, given the neuroprotective qualities of anaesthesia and analgesia, it is plausible that in the clinical setting anaesthesia is relatively protective.

Human clinical studies repeatedly demonstrate a weak association between surgery in infancy and delay in neurodevelopmental milestones. In spite of efforts to control for confounding influences, it is unknown if this association is due to coexisting morbidities such as prematurity or general illness. It is also not possible to determine if the association is due to the surgery *per se* rather than the anaesthesia. Interestingly there is some evidence that children requiring one operation have no injury but those needing repeated operations do worse. This may be the confounding influence of having a condition that requires multiple surgeries. Such cohort studies are also difficult to interpret as it is unclear if the populations studied are those at greatest risk and the appropriate outcome measure to use is not clear.

The issue of potential anaesthetic neurotoxicity to the developing brain has generated considerable interest but there are as yet no firm clinical guidelines apart from a general and vague recommendation to avoid unnecessary elective surgery in children less than 6 months. Many studies are underway to address the issue, but it may be some time before all the questions are answered. In the meantime a general consensus is that anaesthesia should not be withheld when it is needed, and the mode of anaesthesia should be that which the practitioner is most familiar with.