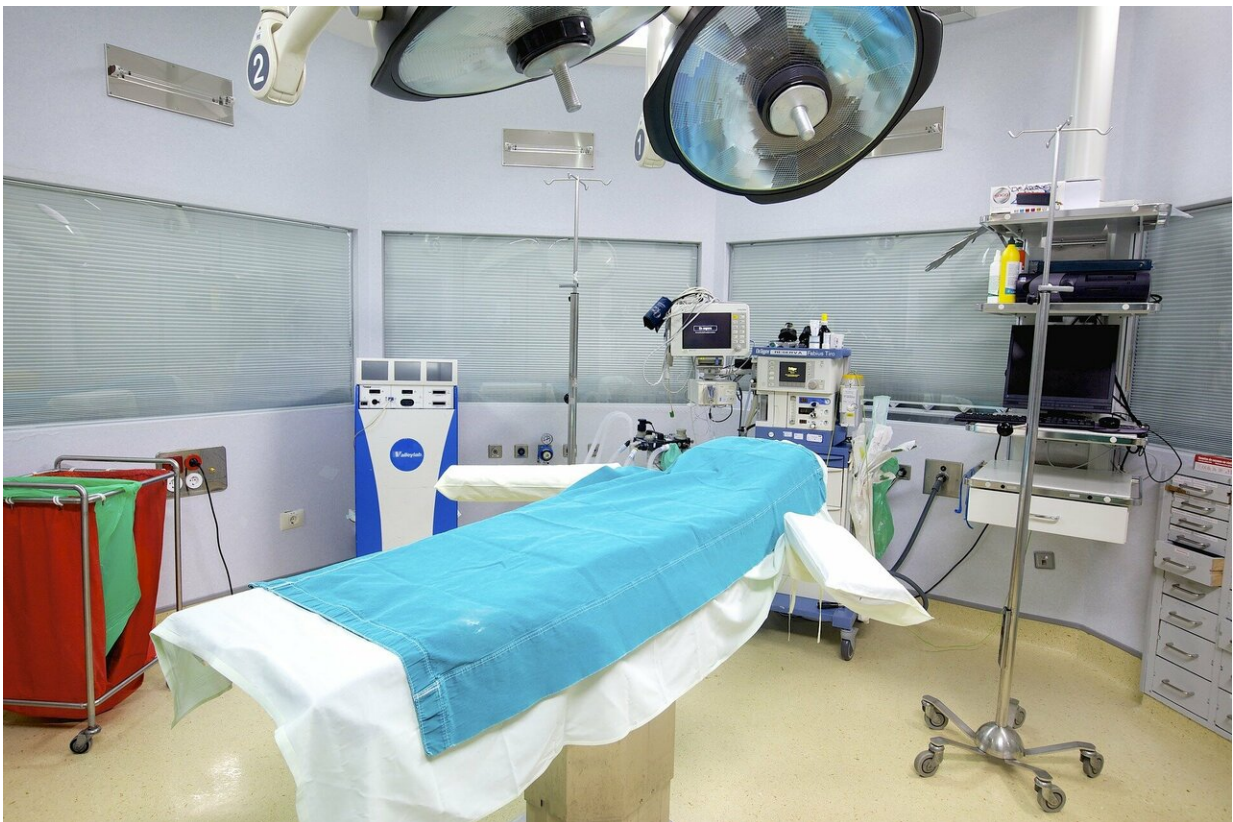


General anesthesia is unlikely to have lasting effects on the developing brains of young children: study

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A single hour of general anaesthesia in early infancy—longer than is necessary to perform the most common types of minor surgeries in

childhood—does not result in measurable neurodevelopmental or behavioural problems up to the age of 5 years, according to the first randomised trial of its kind involving 722 infants in seven countries, published in *The Lancet*.

The trial provides the strongest evidence to date that one brief exposure to [anaesthesia](#) is safe in young children. Nevertheless, the authors caution that most (84%) study participants were male and more research is needed to confirm the findings in girls and children with multiple and prolonged exposure to anaesthesia.

"Nearly half the general anaesthetics given to infants are used for less than one hour, therefore our findings should reassure [health professionals](#) and the millions of parents whose young children undergo surgical or diagnostic procedures with anaesthetic drugs worldwide every year," says Professor Andrew Davidson, Murdoch Children's Research Institute, Australia, who led the study.

"Parents and clinicians may want to delay necessary procedures—particularly in very [young children](#). These findings mean children no longer need to be subjected to the potential medical and developmental risks of delaying surgery, and anaesthetists do not have to avoid general anaesthetics in favour of less well established anaesthetic techniques."

The study is the first randomised trial to investigate whether exposure to general anaesthesia in infancy (aged 60 weeks of postmenstrual age or younger), a time of high brain vulnerability, negatively impacts the growing brain at age 5.

During the first 3 years of life, around 1 in 10 children in developed countries—equating to millions of children every year—undergo surgical, medical, and diagnostic procedures under general anaesthesia

including hernia repair, tonsillectomy, imaging, and endoscopies.

For over a decade, the potential neurotoxicity of commonly used anaesthetic drugs in children has been debated. In 2017, the US Food and Drug Administration warned that prolonged or repeated anaesthesia in children younger than 3 years of age might affect brain development. However, this warning was based largely on animal studies which showed increased cell death in developing animals.

So far, research in humans has been limited to observational studies that have reported conflicting findings, and are unable to conclude whether anaesthesia itself is causing problems, or if other factors such as the underlying medical conditions that make surgery necessary, or the surgical procedure itself, might be to blame.

To provide more evidence, the General Anaesthesia compared to Spinal anaesthesia (GAS) study recruited 722 children undergoing surgical repair of inguinal hernia (one of the most common operations of early childhood) at 28 hospitals in Australia, Italy, the USA, the UK, Canada, the Netherlands, and New Zealand between February 2007 and January 2013. Participants were randomly assigned to general anaesthesia (363 children) or awake-regional (local) anaesthesia (which does not cause brain injury in animal models; 359 children).

In 2016, interim results found that neurodevelopmental outcomes at age 2 years did not significantly differ between the general anaesthesia and awake-regional groups.

Here, the researchers report the final results of the GAS trial at 5 years of age—a time when intelligence testing is strongly predictive of future achievement. Child psychologists used standard measures to assess the children's IQ score, memory, attention, executive function (skills that help with memory, impulse control, and planning), and behaviour.

Due to deviations from the treatment protocol (some children in the awake-regional group also had to be given a general anaesthetic) and loss to follow up, only 205 of 363 children in the awake-regional group and 242 of 359 children in the general anaesthesia group were included in the final analysis. The average duration of general anaesthesia was 54 minutes.

Results showed no significant difference in IQ scores between the children exposed to general anaesthesia (average IQ score 98.87) and awake-regional anaesthesia (99.08), after adjusting for age at birth and country, and accounting missing data. There were no significant differences in a range of other tests of neurocognitive function.

The authors note several limitations, including that there were a substantial number of deviations from the treatment protocol in the awake-regional group because children had to be given general anaesthesia, and a number of children were lost to follow up over the 5 years. They also point out that although several [general anaesthetics](#) are commonly used in children, participants in the trial only received sevoflurane, which could limit the generalisability of the findings. Additionally, 5 years of age may be too young to detect some executive functions and social-emotional skills which do not develop until later in life.

Commenting on the implications of the findings, Dr. James O'Leary from the University of Toronto in Canada says that the study provides the "strongest evidence to date" that a single, brief exposure to general anaesthesia during infancy is not harmful to neurodevelopment. However, he cautions: "Adverse neurodevelopment in childhood results from interactions among multiple risk and protective factors, including health-care-related, genetic, familial, and environmental factors. Consequently, potential contributing factors other than general anaesthesia (eg, type of surgery, sex [84% of [study participants](#) were

male]) should be considered when interpreting and generalising these findings. Perhaps most importantly, the study results cannot be extrapolated to [children](#) who undergo prolonged or repeated exposures to [general anaesthesia](#) or receive multiple anaesthetic drugs for the same [surgical procedure](#)...Whether anaesthesia causes neurological injury in patients under these conditions remains to be established."

More information: *The Lancet* (2019).
[www.thelancet.com/journals/lan ... \(18\)32485-1/fulltext](http://www.thelancet.com/journals/lan ... (18)32485-1/fulltext)

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