



EDITORIAL

Don't turn-off the brain[☆]

No apague el cerebro

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Paradoxically, the analgesics and/or sedatives used to improve the comfort and wellbeing of critical patients can have a negative impact upon their clinical course in the Intensive Care Unit (ICU) or in hospital, with consequences that may even hinder patient return to normal life. Important steps have been taken over the last 20 years to avoid such serious complications. On one hand, the doses and indications of sedative agents have been adjusted. As examples, etomidate is no longer used in continuous infusion; benzodiazepines are increasingly restricted to only concrete indications; and propofol for sedation in critical patients is rarely used at doses above 4.5 mg/kg/h. On the other hand, the complications resulting from a poor sedoanalgesic strategy are known. The non-monitored administration of certain sedatives inevitably results in overdose and drug accumulation, and this in turn prolongs mechanical ventilation (MV) and intubation – with the associated morbidity implied. With the new available drugs, including the incorporation of remifentanyl, dexmedetomidine or new anesthetic gases; the application of sedoanalgesia scales; and the use of cooperative and dynamic sedoanalgesic strategies adapted to the clinical situation of the patient, the prolongation of MV as a consequence of the sedoanalgesic strategy used should be

regarded as a serious adverse event and, indeed, as malpractice on the part of the healthcare professional.¹

However, in recent years a new issue has emerged, with physiopathological implications. The administration of sedating agents for the sedation of critical patients in the ICU, or for carrying out an anesthetic procedure, can cause delirium – with all its associated undesirable consequences – and can give rise to long-term cognitive impairment (LTCl).² Such problems in turn are more common when the drugs used induce deep sedation. The main factor limiting our understanding of this phenomenon is the current lack of knowledge on how the brain works. Achieving such understanding is the aim of the American Brain Research Through Advancing Innovative (BRAIN) project, which includes the participation of hundreds of professionals (physicians, neurobiologists, physicists and engineers), with a budget running into the hundreds of millions of dollars. The director of this project, the Spanish neurobiologist Rafael Yuste, was recently interviewed on television. In reply to the question of how the brain works, the investigator explained that “*We don't know... In fact there is a mystery in neurobiology which we have been unable to explain for over 80 years: the brain is always turned on, always triggering...*”.

Interesting studies have recently appeared – mostly conducted in the experimental setting – that show the importance of having the brain “*always turned on*” as a fundamental factor for neuroregeneration,³ neuroprotection,⁴ and even the control and regulation of phenomena such as inflammation.⁵ We therefore must consider whether the fact of reducing or “*turning off*” patient brain activity for

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sedation or anesthesia – whether for a few minutes, hours or even days – can induce changes in brain function that might have a negative impact upon neurotransmitter balance, neuronal apoptosis and cerebral inflammation, and thus upon the induction of delirium and LTCI. Since 2005 it has been suggested that keeping the bispectral index (BIS®) to under 40/45 during anesthesia may increase the long-term mortality rate.⁶ Later studies in anesthesia and also in critical patients have shown excessive neuronal depression to exert a decisive influence upon the appearance of delirium and LTCI. Deep sedation has its indications and is necessary during general anesthesia or for the sedation of a patient receiving neuromuscular blocker drugs. However, it is essential to distinguish between deep sedation and oversedation, and there monitoring techniques are available for doing so. Sedation scales do not help to discriminate deep sedation levels, and use must be made of electroencephalographic (EEG) processing systems at the patient bedside – BIS® being the most widely used option.⁷ Oversedation is to cause greater sedation than the patient needs. Keeping BIS® to under 40/45 affords no advantages during general anesthesia, and obviously also not for critical patient sedation. Maintaining values of under 40 can trigger the appearance of episodes of brain electrical silence, with suppression rates (SR) on the monitor, and these circumstances in turn are associated to an increased incidence of delirium following either anesthesia⁸ or sedation of the critically ill patient.⁹

The study published in this number of *MEDICINA INTENSIVA* addresses this interesting issue, and the authors conclude that cognitive function over the middle term may be affected in some patients subjected to deep sedation for several days.¹⁰ Unfortunately, with the methodology used, it is not possible to deduce whether the observed LTCI is attributable to the long anesthetic procedure or to the subsequent deep sedation episode during MV in the ICU. Likewise, the authors did not use EEG monitoring in the operating room or ICU, and we therefore cannot know whether the applied deep sedation could be regarded as oversedation. Prolonged deep sedation (for over 24 h), particularly in tracheostomized patients, is not a routine procedure, and its usefulness in preserving graft integrity after microvascular reconstruction is very debatable. For this reason, it would have been a good opportunity for the authors to design a comparative study between groups with BIS® values above or under 40 versus a control group without postoperative deep sedation, in order to either confirm or refute the current evidence. In any case, we congratulate the authors on their article, since it causes us to ponder the importance and impact of deep sedation.

The BRAIN project is an ambitious scientific initiative, and in a period of time which we hope will be as short as possible, it will help us to understand how and why certain neurological disorders develop, and to know why delirium and LTCI occur. Until then, and with the existing knowledge, we can recommend the following in order to reduce the incidence of these two serious complications in the event deep sedation is required: *“Doctor, please don’t turn your patients’ brain off”*.

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