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#### CONTINUING EDUCATION

#### Monitoring of nociception, reality or fiction?<sup>☆</sup>

A. Abad-Gurumeta<sup>a,\*</sup>, J. Ripollés-Melchor<sup>a</sup>, R. Casans-Francés<sup>b</sup>, J.M. Calvo-Vecino<sup>c</sup>

- <sup>a</sup> Servicio de Anestesiología y Reanimación, Hospital Universitario Infanta Leonor, Madrid, Spain
- <sup>b</sup> Servicio de Anestesiología y Reanimación, Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain
- <sup>c</sup> Servicio de Anestesiología y Reanimación, Hospital Universitario de Salamanca, Salamanca, Spain

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#### **KEYWORDS**

Nociception monitoring; Surgical pleth index; Analgesia nociception index; Pupillometry; Spectral entropy; Composite variability index; qNOX **Abstract** There are currently various projects underway that attempt to monitor the nociceptive responses caused by surgical stress and ensure patients the best analgesic conditions.

The systemic response to surgical stress has repercussions in the postoperative period, such as worse pain control, delayed recovery, greater complications, longer stay in resuscitation and hospital units, and increased healthcare costs. However, treatment with higher doses of opioids than necessary may lead to slower awakening, increased drowsiness and adverse effects, as well as situations of postoperative opioid-induced hyperalgesia.

There are 2 large groups of nociceptive monitoring according to the origin of the theoretical objective of monitoring response to the stimulus, that may derive from changes in the electroencephalogram or the response of the autonomic nervous system.

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#### PALABRAS CLAVE

Monitorización de la nocicepción; Índice de pletismografía quirúrgico;

#### Monitorización de la nocicepción, ¿realidad o ficción?

**Resumen** En la actualidad han aparecido diferentes proyectos para intentar monitorizar las respuestas nociceptivas provocadas por el estrés quirúrgico y para mantener a los pacientes en las mejores condiciones analgésicas.

La respuesta sistémica al estrés quirúrgico tiene repercusiones en el postoperatorio, como son el peor control del dolor, una recuperación más tardía, mayores complicaciones, mayor tiempo de estancia en unidades de reanimación y hospitalaria, e incremento del coste de los

E-mail address: alfredoabadgurumeta@gmail.com (A. Abad-Gurumeta).

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<sup>\*</sup> Corresponding author.

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Analgesia nociception index; Pupilometría; Entropía espectral; Índice de variabilidad compuesto; qNOX servicios sanitarios. Sin embargo, el tratamiento con mayores dosis de opiáceos de las necesarias puede suponer situaciones de despertar más lento, mayor somnolencia y efectos adversos, pero también situaciones de hiperalgesia postoperatoria por opiáceos.

Existen 2 grandes grupos de monitorización nociceptiva según el origen del objetivo teórico de vigilancia de la respuesta al estímulo, pudiendo ser derivados de cambios en el electroence-falograma o de la respuesta del sistema nervioso autónomo.

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#### Introduction

Various systems for monitoring nociceptive responses caused by surgical stress and for maintaining an optimal nociceptive/antinociceptive balance have been put forward in recent years.<sup>1</sup>

The systemic response to surgical stress has repercussions in the postoperative period, such as poor pain control, delayed recovery with worse outcomes, greater number of complications, longer stay in recovery rooms and hospital wards, and higher healthcare costs. However, administering higher doses of opioids than necessary may delay awakening, increase somnolence and the risk adverse effects, <sup>2,3</sup> and can also lead to postoperative hyperalgesia, particularly with remifentanil. <sup>4</sup>

There are 2 major approaches to nociceptive monitoring, based on the theoretical objective of detecting response to stimuli (through electroencephalogram (EEG) readings or autonomic nervous system responses), although alternative systems, such as nociceptive flexion reflex, which measures muscle withdrawal in response to nociceptive stimuli, have also been developed (Table 1; Fig. 1).

#### Electroencephalogram monitoring

#### Composite variability index

The bispectral index, or BIS® (Covidien, Boulder, CO, USA) was the first system for measuring depth of hypnosis to be approved by the American Food and Drug Administration. It is based on the observation that frontal electromyography (FEMG) increases during painful stimulation,<sup>5</sup> and that this, in addition to opioid-related changes, 6 may be used to detect inadequate analgesia. This led to the development of the composite variability index, based on the analysis of changes in BIS® values and EMG readings over a period of 3 min to show the nociception/antinociception balance on a scale of 0 (low nociceptive level) to 10 (high nociceptive level). Preliminary tests showed that the composite variability index was more likely to provide early detection of somatic events (standardised by electrical and tetanic stimulation) than heart rate or blood pressure<sup>7,8</sup> monitoring. However, it was noted that the index could not predict movement prior to stimulus, or to predict an inadequate level of analgesia.<sup>7,9</sup> Studies have shown that some factors that could influence  ${\sf BIS}^{\circ}$  and EMG variability include the use of electric scalpels, intense or deep neuromuscular blockade or complete absence of blockade, and the type of hypnotic agent used.  $^{8}$ 

#### Spectral entropy

Spectral entropy® (GE Healthcare, Helsinki, Finland) is another EEG and FEMG-derived variable used to measure hypnosis. The algorithm calculates 2 values that indicate the depth of anaesthesia: state entropy (SE) and response entropy (RE). The full description of the algorithm has been published. 10 SE shows EEG activity in the spectral domain on a scale of 0 (deep hypnosis) to 91 (fully awake), while RE shows most of the spectrum and also includes the higher FEMG frequencies (gamma waves, from 0 to 50 Hz and from 50 to 150 Hz), shown on a scale of 0-100. SE, therefore, is used to measure cortical changes and the hypnotic component of anaesthesia. 10 RE, and the RE – SE difference, meanwhile, reflect FEMG activity, and were proposed as indirect measurements of depth of analgesia. In a comparative study in sevoflurane-induced anaesthesia, SE values were significantly altered in patients who moved in response to stimulation compared to those that did not. 11 In addition to potentially detecting pain, the system was also shown to moderately predict motor, though not haemodynamic, response. 12 Incorporating EMG signal in EEG analysis could provide important additional information. Therefore, the RE – SE difference would reflect EMG activity, and could be successfully integrated into an automated opioid administration algorithm. 13 Entropy-guided anaesthesia based on a target SE of 40-60 for adequate hypnosis and an RE – SE difference of <10 for analgesia was associated with a significant reduction in remifentanil use and adverse events. 14 Measurement limitations were the same as those encountered with the BIS<sup>®</sup>.

#### The qNOX index

The qNOX index (Quantium Medical, Mataro, Barcelona, Spain) in an optional index for qCON depth of anaesthesia monitors. The qNOX index is obtained from frontal EEG signals recorded through a single channel, and is based on 4 frequency bands analysed using an advanced digital processing algorithm, the Adaptive Neuro-Fuzzy

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