



# Intense Noxious Stimulus during an Adequate Depth of General Anesthesia Produces a Transient Burst Suppression Pattern in a Density Spectral Array

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## Abstract

There has been renewed interest in utilizing electroencephalogram (EEG)/processed EEG to assess the response to noxious stimuli under general anesthesia (GA). We are submitting multiple observations that explore the intriguing phenomenon of the transient burst suppression pattern (BSP) in the density spectral array (DSA) of the SedLine Masimo during intense noxious stimulation under GA. Three patients underwent spine surgery under sevoflurane/total intravenous anesthesia with adequate depth. Sudden transient BSP was noted on the DSA during an intense noxious stimulus. Traditionally, BSP on the processed EEG/DSA under GA in a hemodynamically stable patient indicates excessive hypnosis. It is usually treated by reducing the dose of a hypnotic agent. Decreasing the depth of anesthesia (DOA) in the presence of intense pain can have adverse consequences, especially in high-risk patients. Awareness of processed EEG/DSA changes associated with intense noxious stimuli, helps the anesthesiologist to titrate analgesia without altering DOA.

## Keywords

- ▶ electroencephalography
- ▶ general anesthesia
- ▶ neurophysiological monitoring
- ▶ pain

## Introduction

Processed electroencephalography (EEG)-based monitors such as Bispectral Index (BIS Medtronic, Dublin, Ireland), State Response Entropy (SE/RE; GE Health Care, Helsinki, Finland), and Patient State Index (PSI; SedLine, Masimo, Irvine, California, United States) are commonly utilized depth of anesthesia (DOA) monitors for titrating hypnosis.<sup>1,2</sup> These DOA monitors measure relatively high-frequency EEG power rather than low-frequency activity. Hence, they mainly focus on the EEG changes associated with various depths of hypnosis and not the EEG changes associated with noxious stimuli.

Recently, there has been a renewed interest in utilizing the EEG/processed EEG to assess pain response to noxious stimuli.<sup>3-5</sup> Although the EEG response to noxious stimuli was first reported in the early 90s, it has seldom received attention for pain assessment.<sup>6-8</sup> Beta arousal (increase in  $\beta$  power in 12–25 Hz band), alpha dropout (decreased  $\alpha$  power in

8–12 Hz), and delta arousal (increased delta power in 0.5–4 Hz) are the three EEG patterns reported in the literature in response to noxious stimuli.<sup>2,3</sup>

Increased cortical depolarization to noxious stimuli during the light plane of anesthesia produces a beta arousal pattern. The alpha dropout and delta arousal patterns are observed during adequate DOA with inadequate analgesia. Exaggerated GABAergic negative feedback loops in the brainstem and thalamic regions convert intense noxious stimulation to slow-wave activity, producing delta arousal. Cortical hyperpolarization due to sufficient intrinsic inhibitory GABAergic drug effects is responsible for alpha dropout. Both delta arousal and alpha dropout need to be treated with analgesics without altering the DOA, while beta arousal should be treated with increasing the DOA along with analgesics.<sup>3</sup>

We are submitting multiple observations that explore the intriguing phenomenon of the transient burst suppression pattern (BSP) in density spectral array (DSA) display of SedLine

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Masimo, which is associated with intense noxious stimulation at various stages of spine surgery under an adequate depth of general anesthesia (GA) using sevoflurane/total intravenous anesthesia (propofol and fentanyl). This observation has not been reported in the literature.

## Case Series

### Case 1

A 61-year-old male with diabetes, hypertension, and a history of coronary artery bypass grafting for triple-vessel disease was diagnosed with L2–3 central disc prolapse. He underwent L2 laminectomy, and L2–3 discectomy under sevoflurane anesthesia (PSI ranged 25–35) with bilateral erector spinae block at the L2-L3 level. As the block worked well, the patient’s hemodynamics remained stable throughout the surgery. During discectomy, the surgeon retracted the nerve root (intense noxious stimuli), which resulted in a sudden transient drop in PSI along with BSP in DSA (►Fig. 1A) of SedLine Masimo along with a transient increase in blood pressure and heart rate (►Fig. 1B). The response was treated with fentanyl (30 µg) and propofol (30 mg), which resulted in the disappearance of BSP with normalization of vital signs.

### Case 2

A 64-year-old hypertensive male presented with clinical features of compressive myelopathy at C5–6 and C6-C7 levels due to central disc prolapse and ligamentum flavum hypertrophy

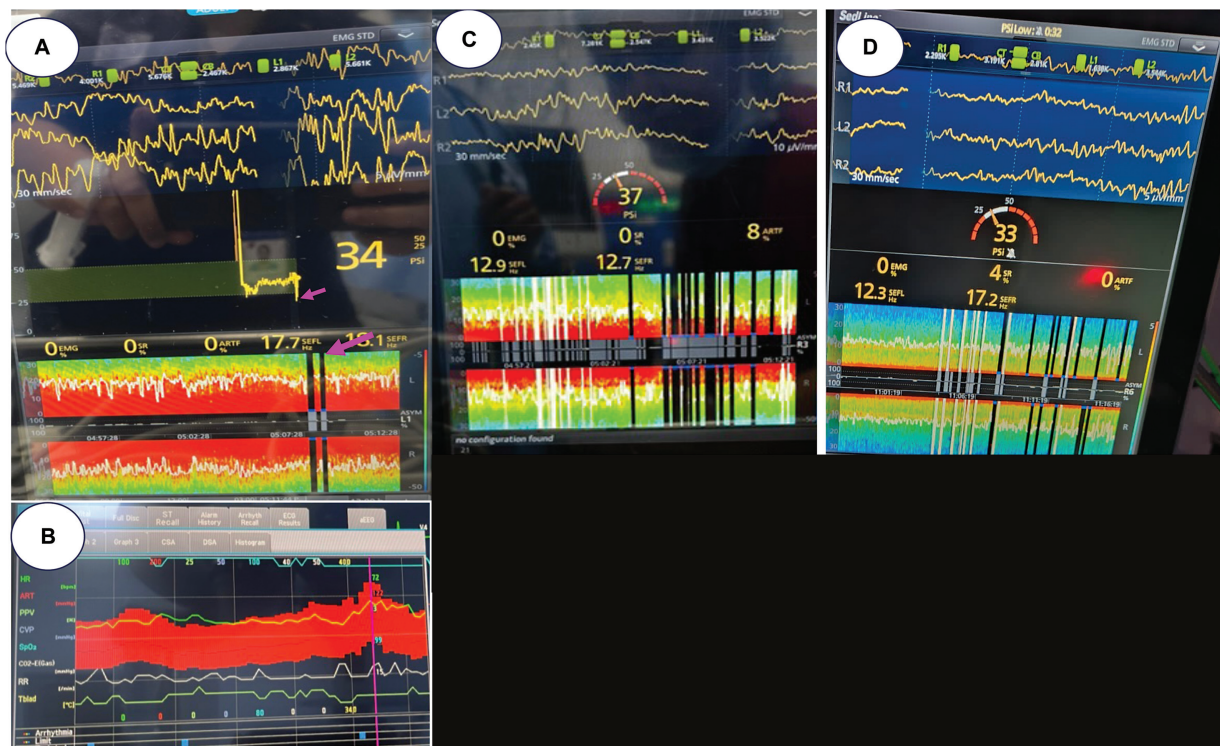
with spinal cord signal changes at the C6–7 level. He underwent a C6 corpectomy with instrumented fusion under sevoflurane anesthesia. The patient’s DOA was stable during surgery (PSI ranged between 28 and 40). At the time of cage placement, multiple BSPs were noted on the DSA that lasted for 8 to 10 minutes and were treated with a fentanyl bolus without altering the DOA. Subsequently, the BSP disappeared (►Fig. 1C).

### Case 3

A 65-year-old male, a diabetic, hypertensive, and heavy smoker with severe chronic obstructive lung disease, presented with clinical features of T6 compressive myelopathy. Magnetic resonance imaging spine revealed severe cord compression at the T6 level with ventral tethering. The patient underwent T5–T8 posterior fusion, followed by T5–7 laminectomy and ventral untethering under total intravenous anesthesia using propofol (150–200 µg/kg/min) and fentanyl (1–2 µg/kg/hr) with motor-evoked potential monitoring. His hemodynamics and DOA were stable throughout the surgery. At the time of ventral untethering (cord retraction and root stretch), we observed BSP on the DSA of SedLine Masimo, which was treated with fentanyl bolus, followed by increasing the fentanyl infusion rate. Subsequently, the BSP did not reappear (►Fig. 1D).

## Discussion

From our case series, we observed transient BSP pattern during intense noxious stimulation in hemodynamically



**Fig. 1** (A) Case no 1: SedLine Masimo, showing the transient drop in patient state index (PSI) along with burst suppression pattern (pink arrows) in the density spectral array (DSA) at the time of root handling (noxious stimuli) during L2-L3 discectomy. (B) Shows the vital trends; at the time of root stimulation, there is a transient elevation in blood pressure (BP) and heart rate (pink line). (C) Case no 2: SedLine Masimo – DSA display showing transient burst suppression pattern (vertical black lines) in a patient undergoing C6 corpectomy at the time of cage placement (noxious stimuli). (D) Case no 3: SedLine Masimo – DSA display showing multiple transient burst suppression patterns (vertical black lines) for a few minutes at the time of ventral untethering at T6 (cord retraction with root stretching lead to noxious stimuli).

stable patients at various stages of spine surgeries with adequate DOA. This pattern was observed without the delta arousal or alpha dropout pattern on DSA. Traditionally, in a hemodynamically stable patient, during the maintenance phase of GA, the appearance of BSP on EEG/processed EEG generally indicates excessive hypnosis. It is usually treated with decreasing the DOA by reducing the dose of hypnotic agents (inhalational agents/propofol). Decreasing the DOA in the presence of noxious stimuli can lead to adverse consequences, especially in high-risk patients.

There are various physiological and pathological causes for intraoperative BSP on EEG, such as hypoxia, severe hypotension, intraoperative stroke, severe hypothermia, refractory status epilepticus, and raised intracranial pressure with low cerebral perfusion pressure.<sup>9</sup> All these factors will cause persistent BSP pattern on EEG/processed EEG. In our case series, all patients had sudden, transient BSP associated with noxious stimuli. All of them underwent spine surgeries with stable hemodynamics, and none of them had intraoperative hypotension or hypoxic events. None of them had any intracranial pathology or woke up with neurological deficits indicative of stroke.

Animal studies have shown that the administration of N-methyl-D-aspartate receptor antagonists in patients receiving GABAergic agonists also causes transient BSP by increasing the DOA and accelerating the recovery through the cholinergic mechanism.<sup>10</sup> However, in our case series, none of them received ketamine for intraoperative analgesia. Studies have shown that the duration of BSP has a positive correlation with postoperative cognitive dysfunction and delirium.<sup>9</sup> In our case series, since the BSP was transient, none of the patients had postoperative delirium or cognitive dysfunction.

There is no standard monitoring method for assessing pain under GA. Traditionally, cardiovascular parameters, autonomic signs, and somatic responses have been used to assess pain responses under GA. However, all these parameters have low sensitivity and specificity, especially with adequate DOA. Recently, various monitors have been used to monitor nociception based on autonomic nervous system indices, EEG-based monitoring, and spinal reflex-based monitoring.<sup>2,3</sup> Nociception monitor with high sensitivity and specificity is yet to be elucidated.

Awareness regarding these processed EEG/DSA changes associated with intense noxious stimuli helps the anesthe-

siologist titrate analgesia without altering the DOA. The long-term clinical consequences of BSP with noxious stimulation remain unknown. Future studies are needed to determine whether processed EEG/DSA can be utilized as a potential biomarker of pain perception and to elucidate the long-term effects of noxious stimuli-induced BSP and its clinical outcome.

#### Conflict of Interest

None declared.

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