



TAKE CONTROL

MEASURE THE ANS. CONTROL SURGICAL STRESS. IMPROVE OUTCOMES

The Analgesia Nociception Index Technology

"Advances are made by answering questions. Discoveries are made by questioning answers." Bernard Haisch

PAIN is the CONSCIOUS perception of NOCICEPTION

Nociception (from Latin nocere 'to harm or hurt') is the process of the sensory nervous system's response to certain harmful or potentially harmful stimuli. In nociception, intense chemical (chili powder in the eyes), mechanical (cutting, crushing...), or thermal (heat and cold) stimulation of sensory nerve cells called nociceptors produces a signal that travels along a chain of nerve fibers via the spinal cord to the brain.

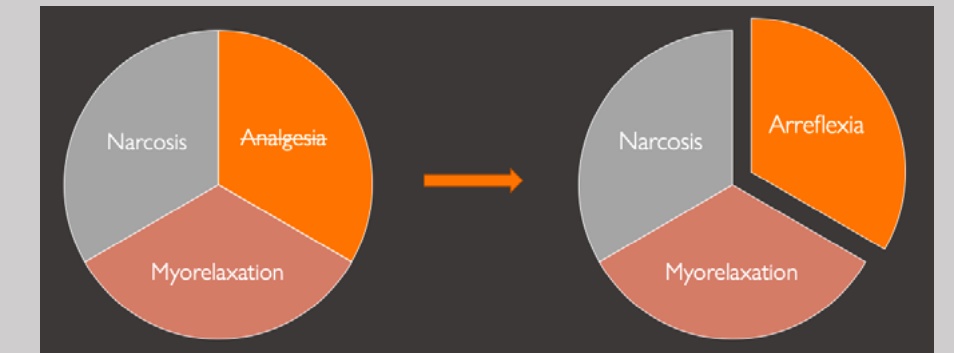
Nociception triggers a variety of physiological changes and usually results in a subjective experience of pain (conscious patient). That is why in unconscious patients, we do not talk about pain but rather nociception.

The physiological changes that occur in the autonomic nervous system, following a nociceptive stimulation, is due to the activation of the sympathetic nervous system. With increased sympathetic activity the production of stress hormones (catecholamines and cytokines) increases which is a major cause of physiological stress.

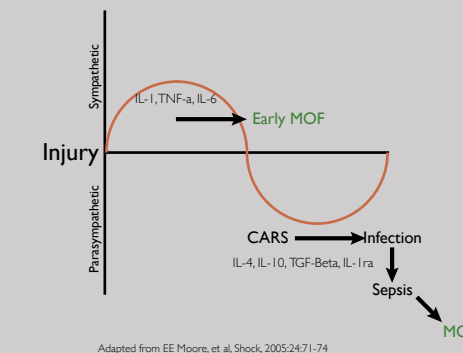


A CHANGE in the anesthesia PARADIGM

In 1960, Dr. Gray changed his previous Pain, Narcosis and Neuromuscular Blockade triad concept substituting pain by areflexia.(1).



Eger defined anesthesia as Amnesia and Areflexia (2) and dr Egan question the use of opioids in general anesthesia (3)



It is the Autonomic Nervous system and its réflex the cause of the activation of the inflammatory response that will affect outcomes (4) morbidity and mortality (5).

(1) Gray C. A reassessment of the signs and levels of anaesthesia. Ir J Med Sci. 1960 Nov;419:499-508. (2) Eger EI 2nd, Koblin DD, Harris RA, Kendig JJ, Pohorille A, Halsey MJ, Trudell JR. Hypothesis: inhaled anesthetics produce immobility and amnesia by different mechanisms at different sites. Anesth Analg. 1997 Apr;84(4):915-8. (3) Egan TD. Are opioids indispensable for general anaesthesia? Br J Anaesth. 2019 Jun;122(6):e127-e135. doi:10.1016/j.bja.2019.02.018. Epub 2019 Mar 28. (4) Moore EE1, Moore FA, Harken AH, Johnson JL, Ciesla D, Banerjee A. The two-event construct of postinjury multiple organ failure. Shock. 2005 Dec;24 Suppl 1:71-4. (5) Tiansheng Sun, Xiaowei Wang, Zhi Liu, Xiaobing Chen, Jianzhong Zhang Plasma concentrations of pro- and anti-inflammatory cytokines and outcome prediction in elderly hip fracture patients. Injury, Int. J. Care Injured 42 (2011) 707-713

MEASURE THE AUTONOMIC NERVOUS SYSTEMS

Heart rate variability is a well-known phenomenon that controls the regulation of the cardiovascular system via the autonomic nervous system. By analysing the heart rate variability oscillations it reflects the activity of the sympathetic and parasympathetic nervous systems.(6)

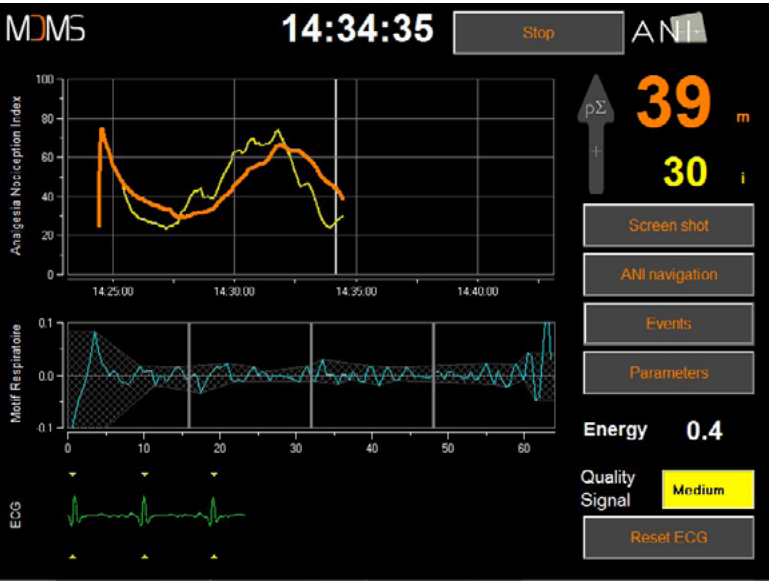
All mammals exhibit what is known as respiratory sinus arrhythmia. The latter process is controlled by the sympathetic and the parasympathetic branch of the n.accumbens and ambiguus, causing the heart to beat slower during expiration due to vagal activation and faster in inspiration as a result of sympathetic innervation.(7)

The ANI express in percentage the parasympathetic activity of the patient. Thus, an ANI of 50 means that 50% of the total energy of the ANS is related to parasympathetic.

The total energy of the ANS is shown in the screen of the monitor.

During general anaesthesia the ANI range [50-70] relates to adequate analgesia, which means that antinociception is adequate and that the parasympathetic activity is mildly predominant over sympathetic activity.

When the ANI value falls below 50, the occurrence of a hemodynamic response within the following 10 minutes is very likely.(8) Anesthetists can use this information in order to predict and avoid a hemodynamic response by increasing analgesia.

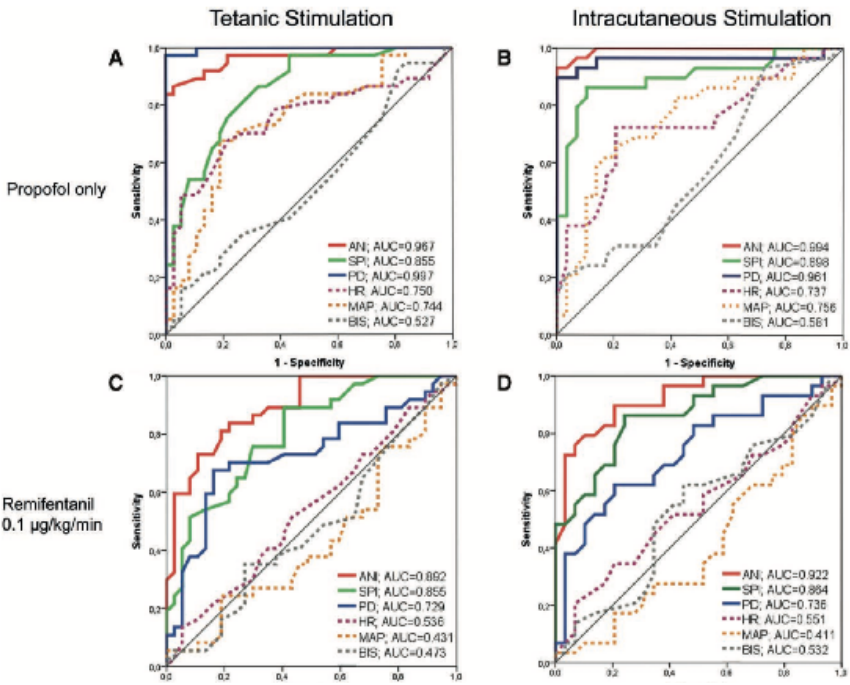


Screenshot ANI technology



In Anesthesiology 2017, Funcke et al showed that the ANI was the best in class detecting nociception versus other parameters.(9).

Anesthesiologists titrate analgesics based on heart rate and blood pressure. Funcke et al., demonstrated that the Analgesia Nociception Index has a higher sensitivity and specificity detecting noxious stimulations compared to standard hemodynamic parameters and other technology available in adults (9) and children (9').

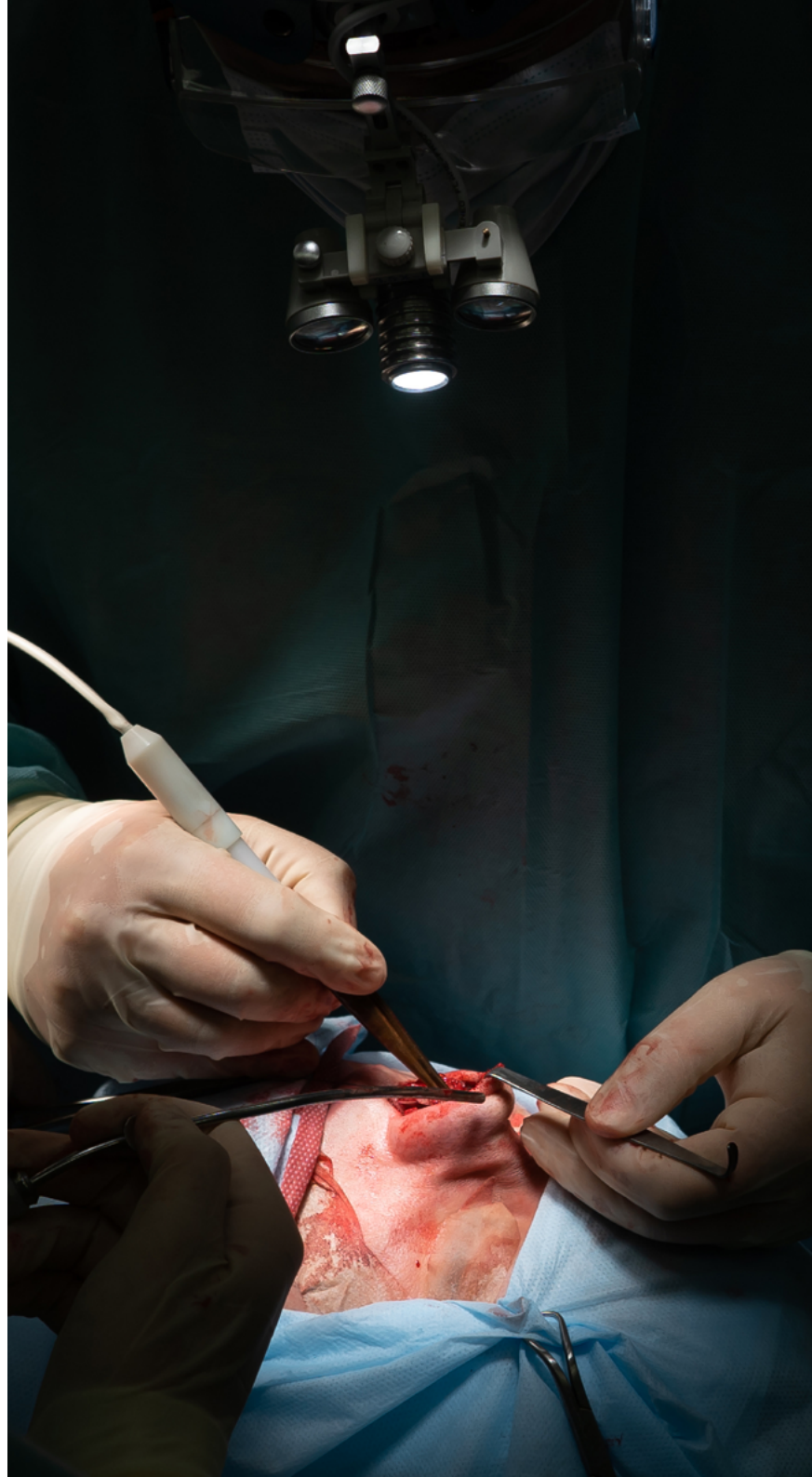


Source: Funcke et al.

(6) European Heart Journal (1996) 17, 354–381. Guidelines Heart rate variability Standards of measurement, physiological interpretation, and clinical use Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology (Membership of the Task Force listed in the Appendix) (7) Jeanne M, Logier R, De Jonckheere J, Tavernier B. Validation of a graphic measurement of heart rate variability to assess analgesia/nociception balance during general anesthesia, IEEE Proceedings 2009. doi: 10.1109/IEMBS.2009.5332598. (8) Jeanne M, Delecroix M, De Jonckheere J, Kerbedj A, Logier R, Tavernier B. Variations of the Analgesia Nociception Index during propofol anesthesia for total knee Replacement. Clin J Pain 2014 Dec; 30(12):1084-8. doi: 10.1097/AJP.0000000000000083.

(9') Sabourdin N, Arnaout M, Louvet N, Guye M-L, Piana F & Constant I. Pain monitoring in anesthetized children: first assessment of skin conductance and Analgesia Nociception Index at different infusion rates of remifentanyl. Pediatric Anesthesia 2013 Feb; 23(2):149-55. doi: 10.1111/pan.12071

CONTROL SURGICAL STRESS



Using ANI, doctors will always know the sympathetic/parasympathetic balance allowing them to TAKE CONTROL OF THE SURGICAL STRESS.

Measuring the ANS will help doctors to provide optimal analgesic levels to avoid:

- Longer time recovery (10)
- PONV (10)
- Urine retention (10)
- Shivering (10)
- Thromboembolism (11)
- Pulmonary complications (11)
- Bradycardia (12)
- Hypotension (12)
- Ileum (13)
- Respiratory failures (13)
- Post-op hyperalgesia (14)
- Delirium (15)(16)
- POCD (17)
- Stimulates cancer progression (17)
- Chronic Pain (18)

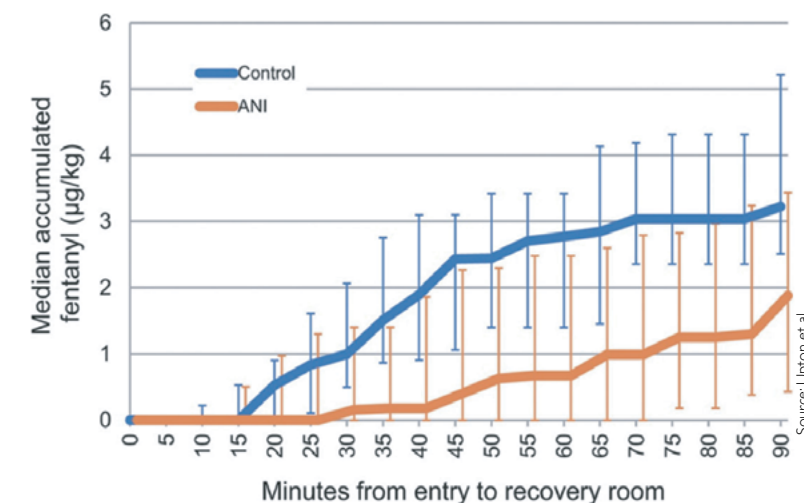
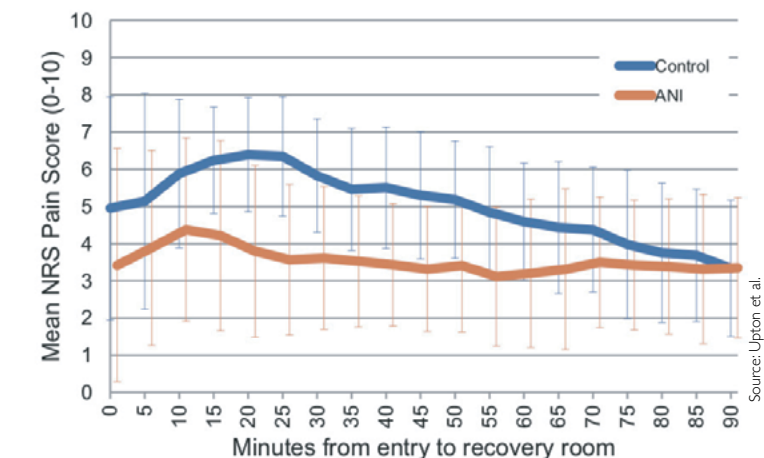
(10) de Boer HD, Detrich O, Forget P. Opioid-related side effects: Postoperative ileus, urinary retention, nausea and vomiting, and shivering. A review of the literature. *Best Pract Res Clin Anaesthesiol.* 2017 Dec;31(4):499-504. doi: 10.1016/j.bpa.2017.07.002. Epub 2017 Jul 8. (11) Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. *Br J Anaesth.* 1997 May;78(5):606-17. (12) Joshi GP, Warner DS, Twersky RS, Fleisher LA. A comparison of the remifentanyl and fentanyl adverse effect profile in a multicenter phase IV study. *J Clin Anesth.* 2002 Nov;14(7):494-9. (13) Imam MZ, KA, Ghassabian S, Smith MT. Progress in understanding mechanisms of opioid-induced gastrointestinal adverse effects and respiratory depression. *Neuropharmacology* 2018; 131: 238–55. (14) Colvin LA, Bull F, Hales TG. Perioperative opioid analgesia-when is enough too much? A review of opioid-induced tolerance and hyperalgesia. *Lancet.* 2019 Apr 13;393(10180):1558-1568. doi: 10.1016/S0140-6736(19)30430-1. (15) Relationship Between Pain and Opioid Analgesics on the Development of Delirium Following Hip Fracture. *Journal of Gerontology: MEDICAL SCIENCES*. The Gerontological Society of America 2003, Vol. 58A, No. 1, 76–81 (16) The Comparative Risk of Delirium with Different Opioids: A Systematic Review. *Drugs Aging.* 2017; 34(6): 437–443. Published online 2017 Apr 12. (17) Iwasaki M, Edmondson M, Sakamoto A, Ma D. Anesthesia, surgical stress, and «long-term» outcomes. *Acta Anaesthesiol Taiwan.* 2015 Sep;53(3):99-104. doi: 10.1016/j.aat.2015.07.002. Epub 2015 Jul 30. (18) Glare P, Aubrey KR, Myles PS. Transition from acute to chronic pain after surgery. *Lancet* 2019; 393: 1537–46.

IMPROVE OUTCOMES

Upton et al., showed that ANI guided analgesia was able to reduce postoperative pain scores in the PACU and subsequently, less postoperative use of fentanyl versus standard practice.

Compared to the control group, patients in the ANI group had :
- 64% lower recovery room total fentanyl administration.
- 82% lower nausea scores.
- 23% less shivering.

The total intraoperative amount of fentanyl was the same in the two groups, but not the way and when it was administered. The authors concluded that ANI helped them to detect the noxious stimuli, avoiding neuromodulation. (19)



THE MAIN BENEFITS OF USING THE ANI TECHNOLOGY

- ✓ Anticipate hemodynamic reactivity (22)
- ✓ Diagnose the etiology of a hemodynamic event (23)
- ✓ Titrate opioids (20)
- ✓ Anticipate post-operative pain (22)

(19) Henry D, Upton, MBBS, BMedSc (Hons), Guy L, Ludbrook, MBBS, FANZCA, PhD, Andrew Wing, BMBS (Hons), BSc (Hons), FANZCA, and Jamie W, Sleight, MD Intraoperative "Analgesia Nociception Index"-Guided Fentanyl Administration During Sevoflurane Anesthesia in Lumbar Discectomy and Laminectomy: A Randomized Clinical Trial. *Anesthesia & Analgesia* July 2017. doi: 10.1213/ANE.0000000000001984.
(20) Daccache G, Caspersen E, Pegoix M, Monthé-Sagan K, Berger L, Fletcher D, Hanouz JL. A targeted remifentanyl administration protocol based on the analgesia nociception index during vascular surgery. *Anaesth Crit Care Pain Med.* 2017 Aug;36(4):229-232. doi:10.1016/j.jaccpm.2016.08.006. (21) Logier R, De Jonckheere J, Kerbedj A, Jeanne M, Journez R, Tavernier B. Heart Rate Variability analysis for arterial hypertension etiological diagnosis during surgical procedures under tourniquet. *IEEE Proceedings* 2011. doi:10.1109/EMBS.2011. (22) Boselli E, Bouvet L, Bégou G, Dabouz R, Davidson J, Deloste J-Y, Rahali N, Zadani A, Allaouchiche B. Prediction of immediate postoperative pain using the Analgesia Nociception Index: a prospective observational study. *Br J Anaesth.* 2014 Apr;112(4):715-21. doi:10.1093/bja/aet407



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