Correlation between incremental remifentanil doses and the Nociception Level (NoL) index response after intraoperative noxious stimuli

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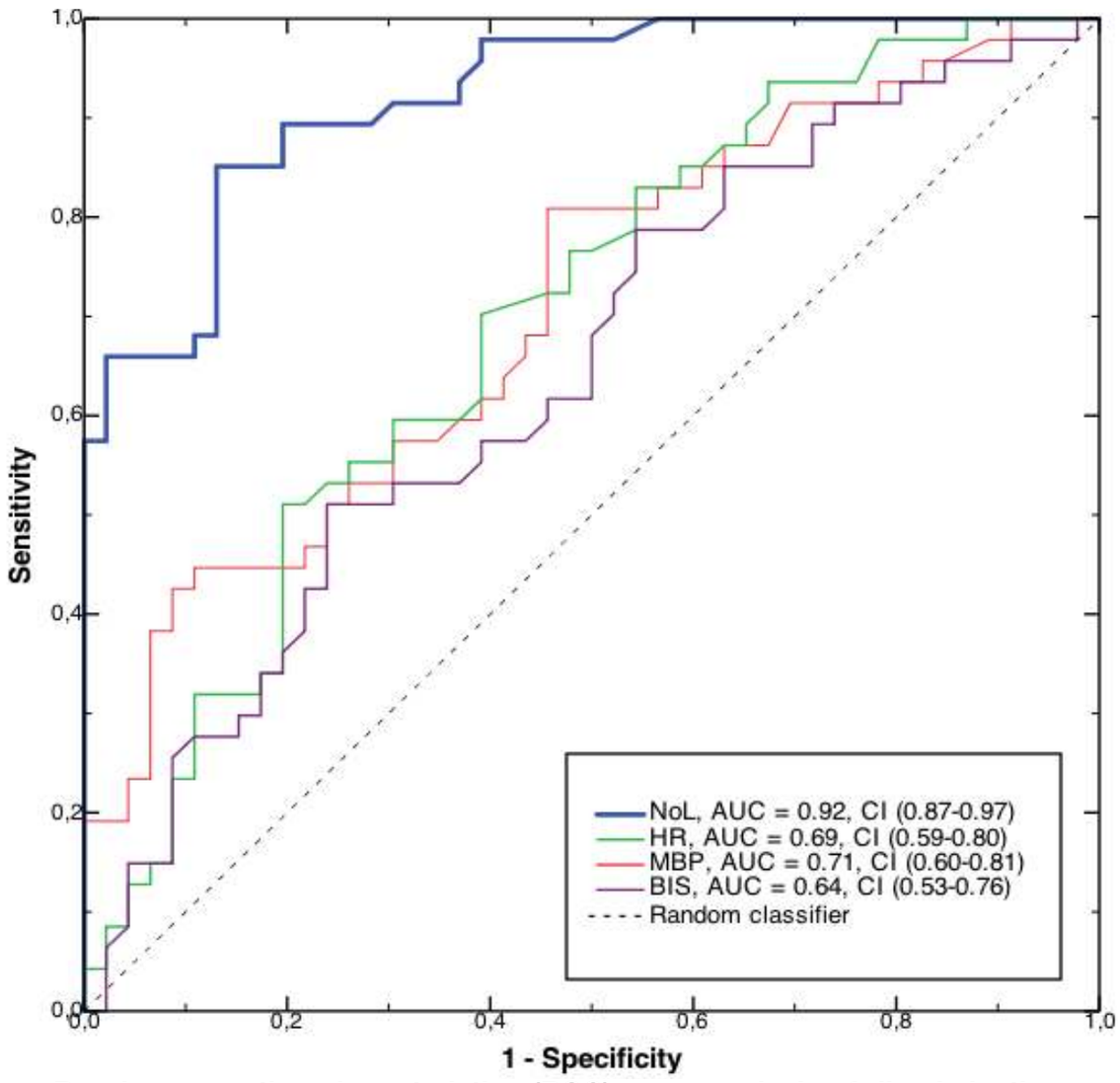
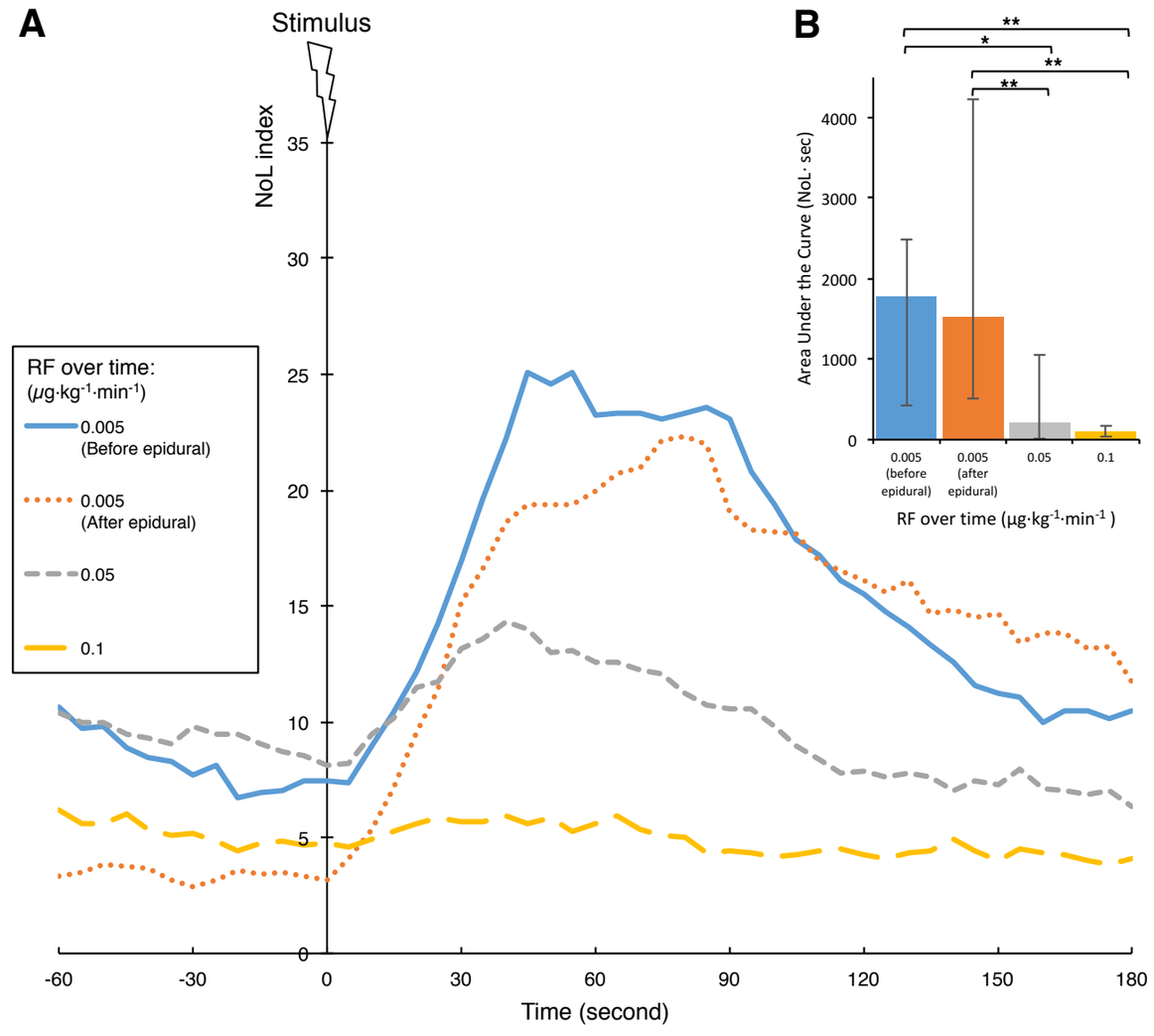


Receiver operating characteristics (ROC) curve analysis of discrimination of experimental noxious stimulus
Analysis at minimal remifentanil dosage (0.005 $\mu g.kg^{-1}.min^{-1}$).



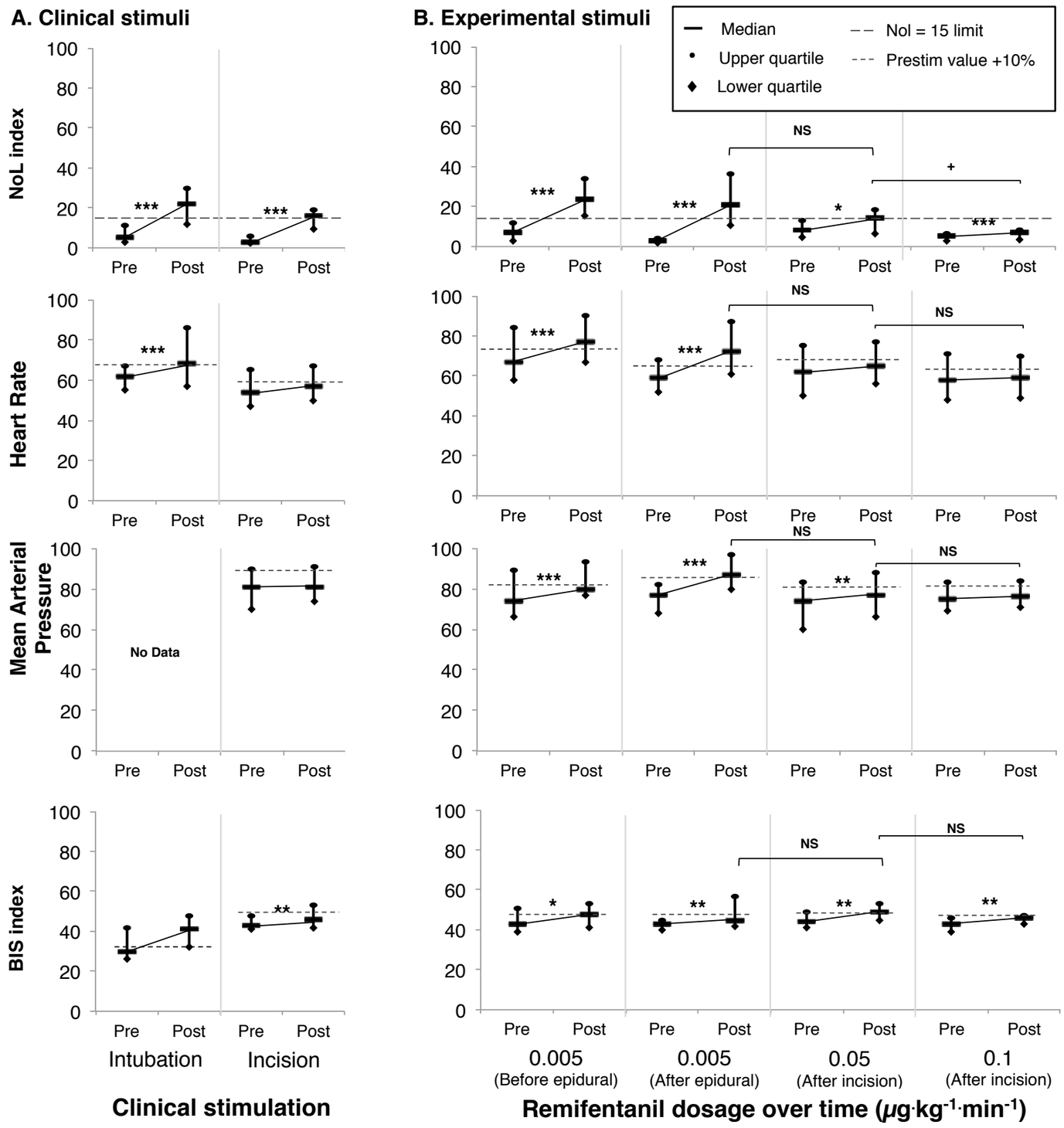
NoL index trend over time during experimental tetanic stimuli.

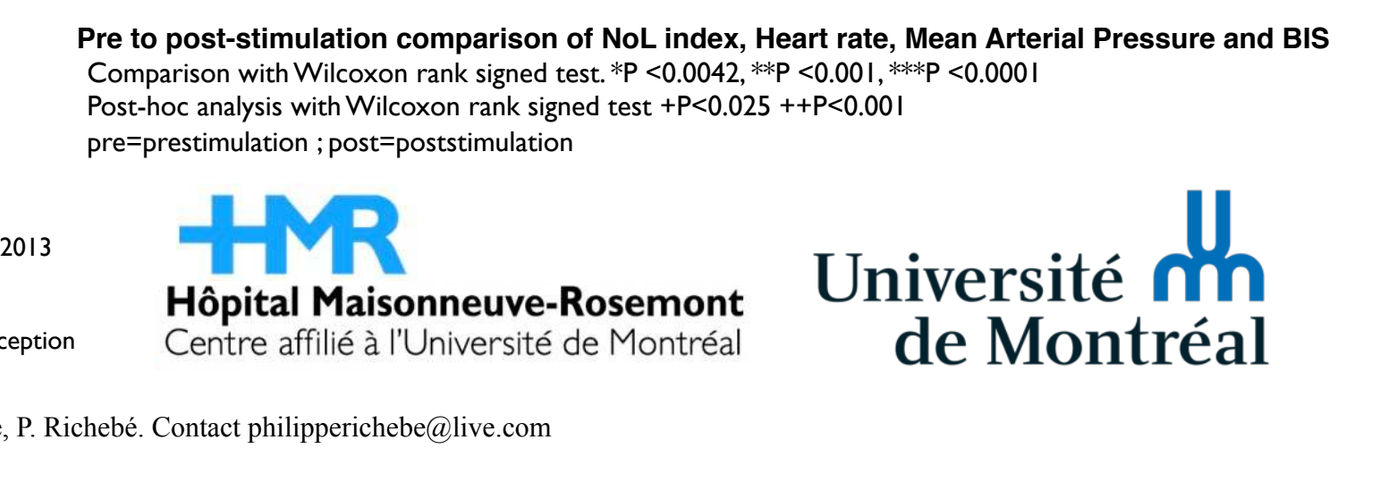
Background: Several single-parameter based indices have been used to monitor nociception intensity under general anesthesia. The Pain Monitoring Device (PMD) monitor (Medasense Biometrics, Israel) uses the Nociception Level (NoL) index, a multiparametric approach, and has recently shown a good sensitivity and specificity to detect noxious stimuli. With the latest version PMD200, we assessed the NoL response during noxious stimuli at various doses of remifentanil to study the association between remifentanil dose and NoL.

Methods: Twenty-six patients undergoing midline laparotomy received desflurane-remifentanil based anesthesia with an epidural analgesia. A tetanic stimulation was applied to the forearm of the patients at different remifentanil doses. NoL variations after experimental and clinical stimuli were compared to heart rate (HR), mean arterial pressure (MAP) and Bispectral Index™ (BIS). NCT#02884778.

Results: The correlation between post tetanic stimulation NoL values and remifentanil doses was moderate with r = -0.584 ($P<$ 0.0001). Only the NoL index respond significantly to all noxious stimuli, regardless of the remifentanil dose. NoL outperformed all other single parameters in discriminating noxious from non-noxious state, with a sensitivity of 85% and a specificity of 87%. The area under the curve to discriminate noxious from non-noxious states was 0.92 for NoL vs 0.69, 0.71, 0.64 for HR, MAP and BIS, respectively.

Conclusions: NoL value after noxious stimulus decreased with incremental remifentanil doses, showing an inverse correlation between the NoL index and opioid doses. The high sensitivity and specificity of the NoL index suggests a great potential as a monitor of nociception intensity during anesthesia.





Pre to post-stimulation comparison of NoL index, Heart rate, Mean Arterial Pressure and BIS
Comparison with Wilcoxon rank signed test. *P <0.0042, **P <0.001, ***P <0.0001
Post-hoc analysis with Wilcoxon rank signed test +P<0.025 ++P<0.001
pre=prestimulation ; post=poststimulation

1. Ben-Israel et al, Monitoring the nociception level: a multi-parameter approach. J Clin Monit Comput 2013
2. Martini et al. Ability of the Nociception Level, a Multiparameter Composite of Autonomic Signals, to Detect Noxious Stimuli during Propofol–Remifentanil Anesthesia. Anesthesiology 2015
3. Edry et al. Preliminary Intraoperative Validation of the Nociception Level Index: A Noninvasive Nociception Monitor. Anesthesiology 2016

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