

TITLE: BAYESIAN MODELING OF THE PLACEBO RESPONSE IN NEUROPATHIC PAIN

Abstract

In analgesia randomized clinical trials (RCTs), the magnitude and the variability of the placebo response have a negative influence when testing the statistically significant superiority of active compounds compared to placebo. Furthermore, the magnitude of this effect has tended to increase over time, including in peripheral neuropathic pain (PNP) trials. The main objective of this study was to investigate parameters influencing the placebo response as a way to control this major confounding factor.

Eighty-seven PNP patients were enrolled and blindly given a placebo during 4 weeks. The placebo response was estimated as the difference in pain between baseline and end of the treatment. In addition, patients filled a psychological questionnaire at baseline assessing several components of their personality.

We modeled the placebo response from patient's characteristics using a Bayesian machine learning approach: Gaussian processes with a linear kernel. The covariates used in the model were selected using a multivariate recursive feature elimination (RFE). The advantage of this Bayesian modeling is to predict the placebo response and to give confidence intervals on the predictions.

The predictive performances of this model were estimated in a repeated random sub-sampling scheme (or Monte Carlo cross-validation). The model explained almost 30% of the variance in new patients (p-value<0.001).

Using the model predictions as a covariate could thus reduce the placebo variance by 30% in subsequent PNP studies. This reduction of variance could in turns lead to an increased effect size and study power. Such a tool to characterize and predict this important source of variance would thus be of great value in analgesia randomized clinical trials.

Authors

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