Effect size and reliability of the Neurological Pain Signature

Xiaochun Han[1], Lauren Y. Atlas[2,3,4], Leonie Koban[5,6], Elizabeth A. Reynolds Losin[7], Mathieu Roy[8], Choong-Wan Woo[9,10], Tor D. Wager[1]

: Xiaochun.han@dartmouth.edu

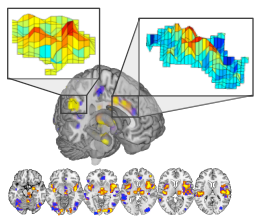
([1]Department of Psychological and Brain Sciences, Dartmouth College, Hanover NH, USA; [2]National Center for Complementary and Integrative Health, National Institutes of Health, Bethesda MD, USA; [3]National Institute of Mental Health, National Institutes of Health, Bethesda MD, USA; [4]National Institute on Drug Abuse, National Institutes of Health, Baltimore MD, USA; [5]INSEAD, Fontainebleau, France; [6]Brain & Spine Institute (ICM), Paris, France; [7]Department of Psychology, University of Miami, Miami FL, USA; [8]Department of Psychology, McGill University, CA; [9]Center for Neuroscience Imaging Research, Institute for Basic Science, Republic of Korea; [10]Department of Biomedical Engineering, Sungkyunkwan University, Republic of Korea.)

Introduction

There is an increasing movement towards establishing neurophysiological markers of mental processes. A priori markers can provide quantitative predictions that can be tested across laboratories, serve as targets for interventions, and increase reproducibility by decreasing analytic flexibility. As markers become more widely shared across labs and translated into practical applications, robust validation of their psychometric properties and performance benchmarks across contexts will become increasingly important.

One such marker is the Neurologic Pain Signature (NPS) [1], a multivariate brain measure trained to track pain induced by nociceptive input. Here, we test the effect size and reliability of the NPS in a large dataset of pain studies.

Neurological Pain Signature (NPS)

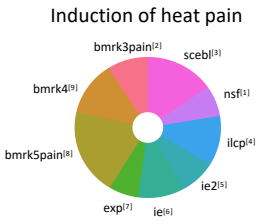


Method

- **Single-trial heat pain database**

The data used for this study are based on a single trial database on healthy subjects during pain tasks, including comprehensive behavioral and fMRI data. Overall, the data set included 16,294 single-trial images of fMRI activity associated with multiple levels of noxious heat and pain ratings across over health 305 participants from 9 studies. In each study, thermal stimulations were delivered to multiple skin sites with temperatures ranging from 41 °C to 50 °C and durations from 1.85 to 16 seconds. On each trial, after the offset of stimulation, participants rated the magnitude of pain they experienced. Quantification of single-trial response magnitudes was done by constructing a GLM design matrix with separate regressors for each trial.

Single-trial database



9 studies
305 subjects
16294 single-trial images

- **Effect size**

We calculated four types of effect size to quantify the performance of NPS in response to heat pain:

- NPS responses in the contrast of [Pain minus Baseline] within each subject
- The correlation of NPS with temperature within each subject
- The correlation of NPS with subjective pain rating within each subject
- The correlation of NPS with subjective pain rating across different subjects

- **Reliability**

We calculate the internal consistency of NPS response and subjective pain ratings of each subject with the split-half correlation and corrected by the Spearman-Brown formula.

- **Three types of pattern similarity representation**

We computed for each trial and each subject a single scalar value representing their expression of the NPS pattern. We also compared with the performance of three commonly used methods used to calculate the expression of the NPS pattern, e.g., dot-product (NPSdot), correlation (NPScorr), and cosine similarity (NPScos).

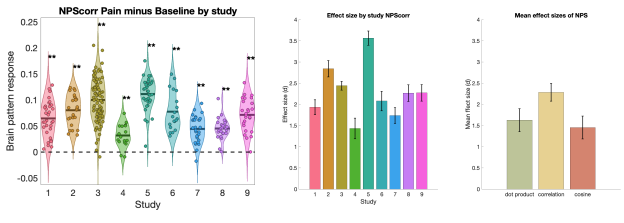
- **NPS vs. Local brain regions**

To test the performance of each brain region within NPS and further test whether the performance of NPS exceeds any individual brain region within NPS, we also computed the pattern expressions for each brain cluster within NPS. We compared the effect size and reliability with the complete NPS pattern representation.

Results

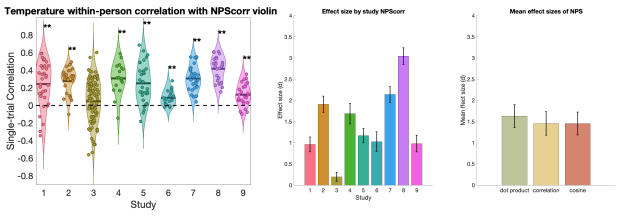
- **NPS responses in the contrast of [Pain minus Baseline]**

The results showed that NPS responses in the contrast of [Pain minus Baseline] are significantly greater than zero in each of 9 studies tested, with effect sizes ranging from Cohen's d = 1.43 to 3.56. Among the three pattern expression indexes, NPScorr has the largest effect size (Cohen's d = 2.29).



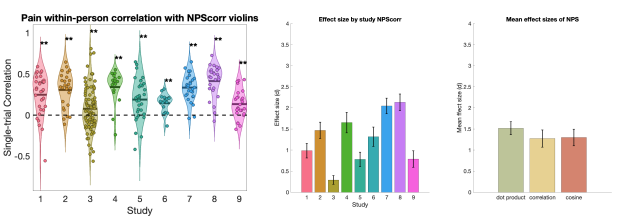
- **Correlation of NPS with temperature**

The results showed that the correlations of NPS responses with temperature are significantly greater than zero in 8 out of 9 studies tested, with effect sizes ranging from Cohen's d = 0.19 to 3.04. Among the three pattern expression indexes, NPSdot has the largest effect size (Cohen's d = 1.63).



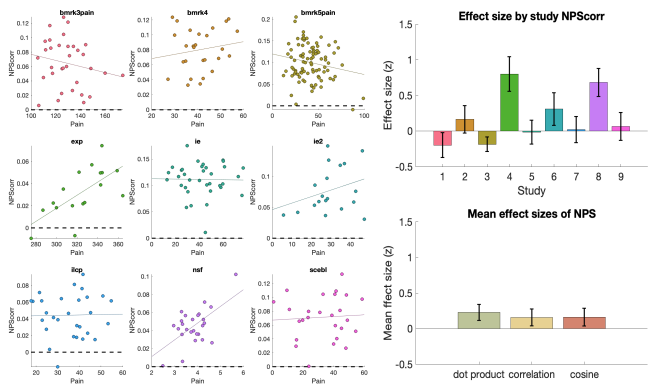
- **Correlation of NPS with subjective pain ratings**

The results showed that the within-subject correlations of NPS responses with the subjective pain ratings are significantly greater than zero in each of 9 studies tested, with effect sizes ranging from Cohen's d = 0.29 to 2.13. Among the three pattern expression indexes, NPSdot has the largest effect size (Cohen's d = 1.52).



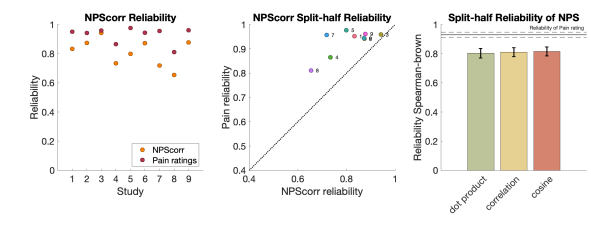
- **Correlation of NPS with subjective pain rating between subjects**

The results showed that the between-subject correlations of NPS responses with the subjective pain ratings are significantly greater than zero in 3 out of 9 studies tested, with effect sizes ranging from Fisher's z = -0.2 to 0.8. Among the three pattern expression indexes, NPSdot has the largest effect size (Fisher's z = 0.23).



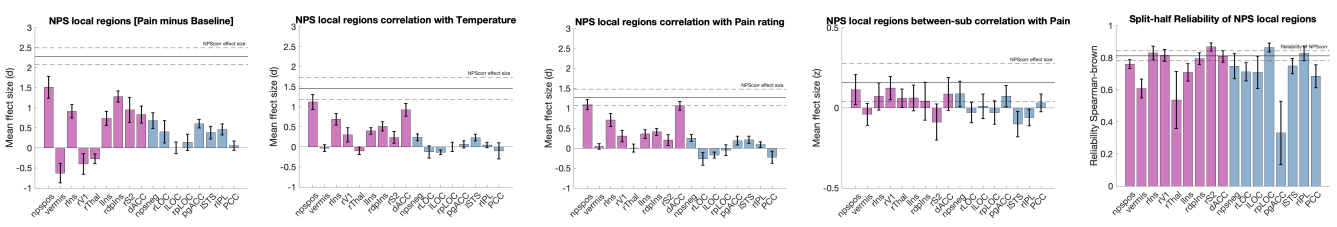
- **Reliability of NPS response and subjective pain ratings**

Reliability tests of NPS show that the average Spearman-Brown first-second half reliability is 0.81, ranging from 0.65 to 0.94. Three pattern expression indexes showed similar reliabilities, and NPScos has the relatively largest reliability (0.82). Reliability tests of pain ratings show that the average Spearman-Brown first-second half reliability is 0.93, ranging from 0.81 to 0.98.



- **Performance of NPS local brain regions**

The effect sizes of NPS local brain regions' responses in the contrast of [Pain minus Baseline] range from Cohen's d = -0.63 to 1.51. The effect sizes of the correlations between NPS local brain regions and temperature range from Cohen's d = -0.14 to 1.12. The effect sizes of the correlations between NPS local brain regions and subjective pain ratings range from Cohen's d = -0.27 to 1.09. The effect sizes of the between-subject correlations between NPS local brain regions and subjective pain ratings range from Fisher's z = -0.10 to 0.12. Reliability tests of NPS local brain regions show that the average Spearman-Brown first-second half reliability range from 0.33 to 0.87.



Conclusion

- NPS showed a decent performance in effect size and reliability across different studies, superior to the performance of local brain regions.
- The performances of three types of pattern similarity representations of NPS are similar, with some minor differences in different statistics.
- The reliabilities for NPS and pain ratings are much higher than their correlations, suggesting that two measurements may be suspected to different sources of inter-individual variability and are not redundant.
- These studies were heterogeneous in preprocessing methods, pain duration, scanner, population, body site, and concurrent contexts/cognitive tasks. While this is a strength in demonstrating generalizability, it also limits effect sizes and reliability. Advances could be made by customizing models for particular types of populations/body sites/stimulus durations/contexts.

References

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