A Systematic Review of Methods Used in Heartbeat Evoked Responses Research

Paul T. Steinfath[1,3*], Maria Azanova[1,2*], Nikolai Kapralov[1,3*], Thomas Loesche[1], Vadim V. Nikulin[1], Arno Villringer[1,4]

[1]Department of Neurology, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany [2]Max Planck School of Cognition, Leipzig, Germany
[3]International Max Planck Research School NeuroCom, Leipzig, Germany [4]LIFE – Leipzig Research Center for Civilization Diseases, University of Leipzig, Germany

*** contributed equally** ✉ *steinfath@cbs.mpg.de*
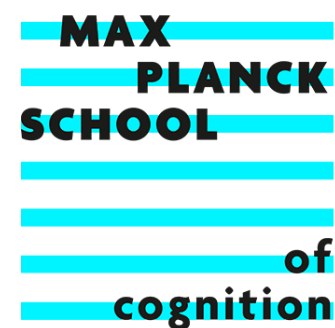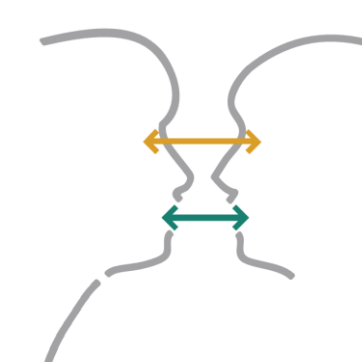
Heartbeat Evoked Responses (HER)

- Neural Responses to Heartbeats
- Involved in a broad range of functions (emotion, perception, various disorders)
- Investigated using brain imaging data time-locked to the heartbeat
- Large variability in HEP amplitude, latency, and waveform (Park & Blanke 2014)
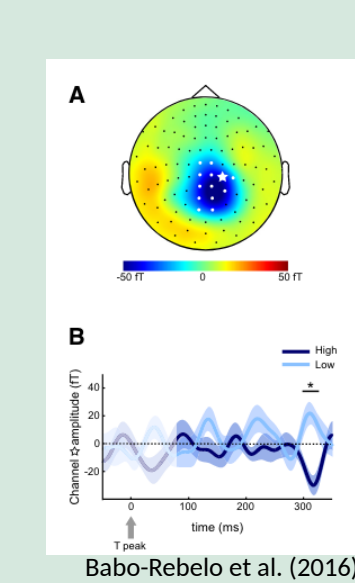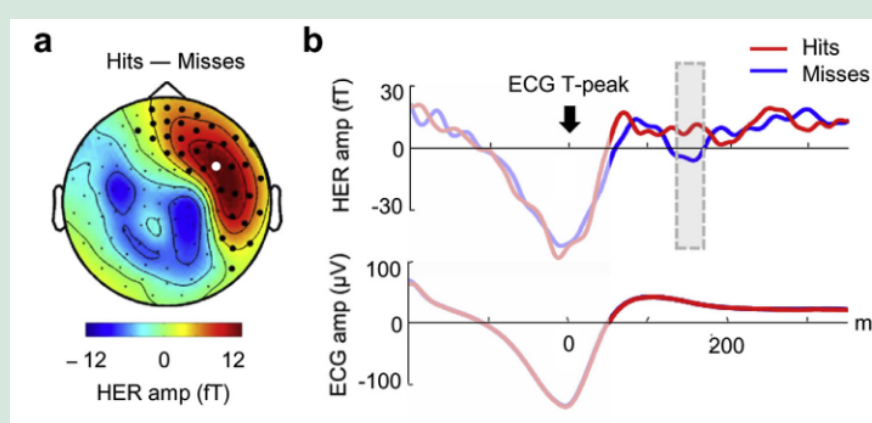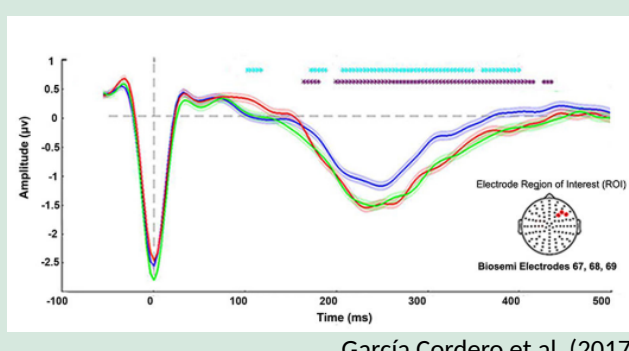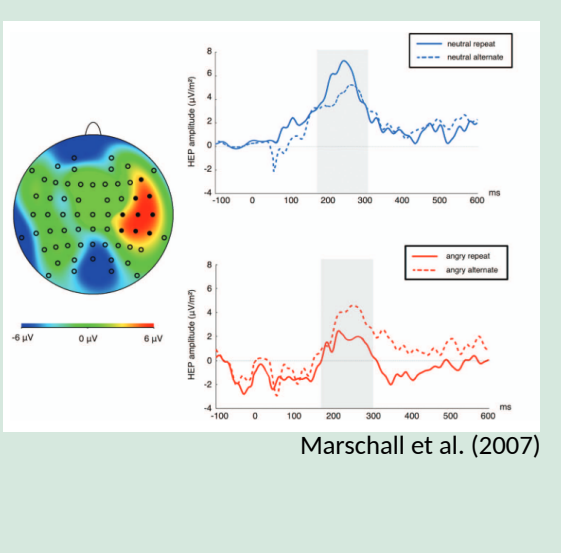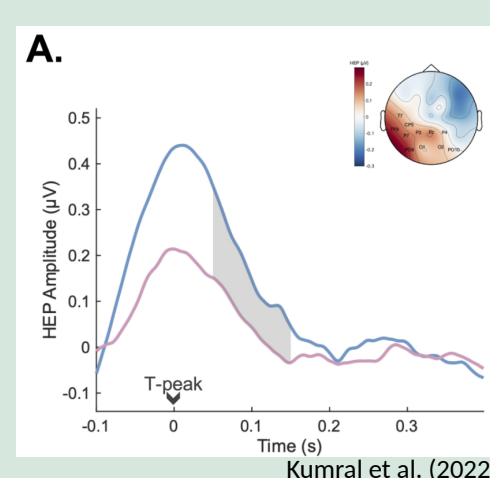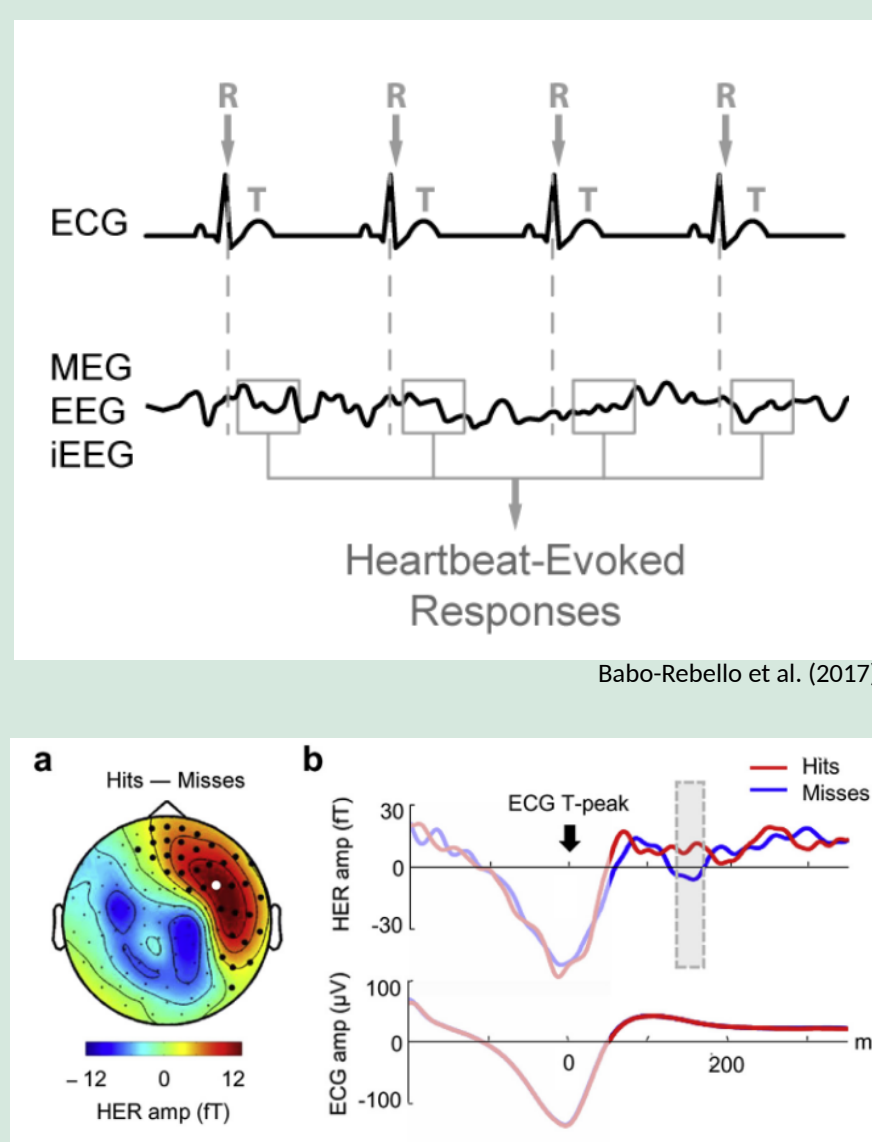
Aim: Elucidate the **methodological variability** in the field of Heartbeat Evoked Responses

PRISMA-Flowchart

We retrieved publications from Pubmed that included measurement of Heartbeat Evoked activity in EEG or MRI in Humans until 05.08.2024.
In total we screened 749 publications, from which we included 132 studies in our systematic review.

Data Aquisition & Preprocessing Methods used

Across data aquisition and preprocessing steps we can observe some popular choices, like a sample size between 10-100 subjects, EEG as recording modality, and Common Average as a reference.

LM: Linked Mastoids, N/M: not mentioned, CMS: Common Mode Sense, CAR: Common Average Reference, LE: Linked Ears, LAP: Laplacian

ECG Derivations Matter!

N/M: not mentioned

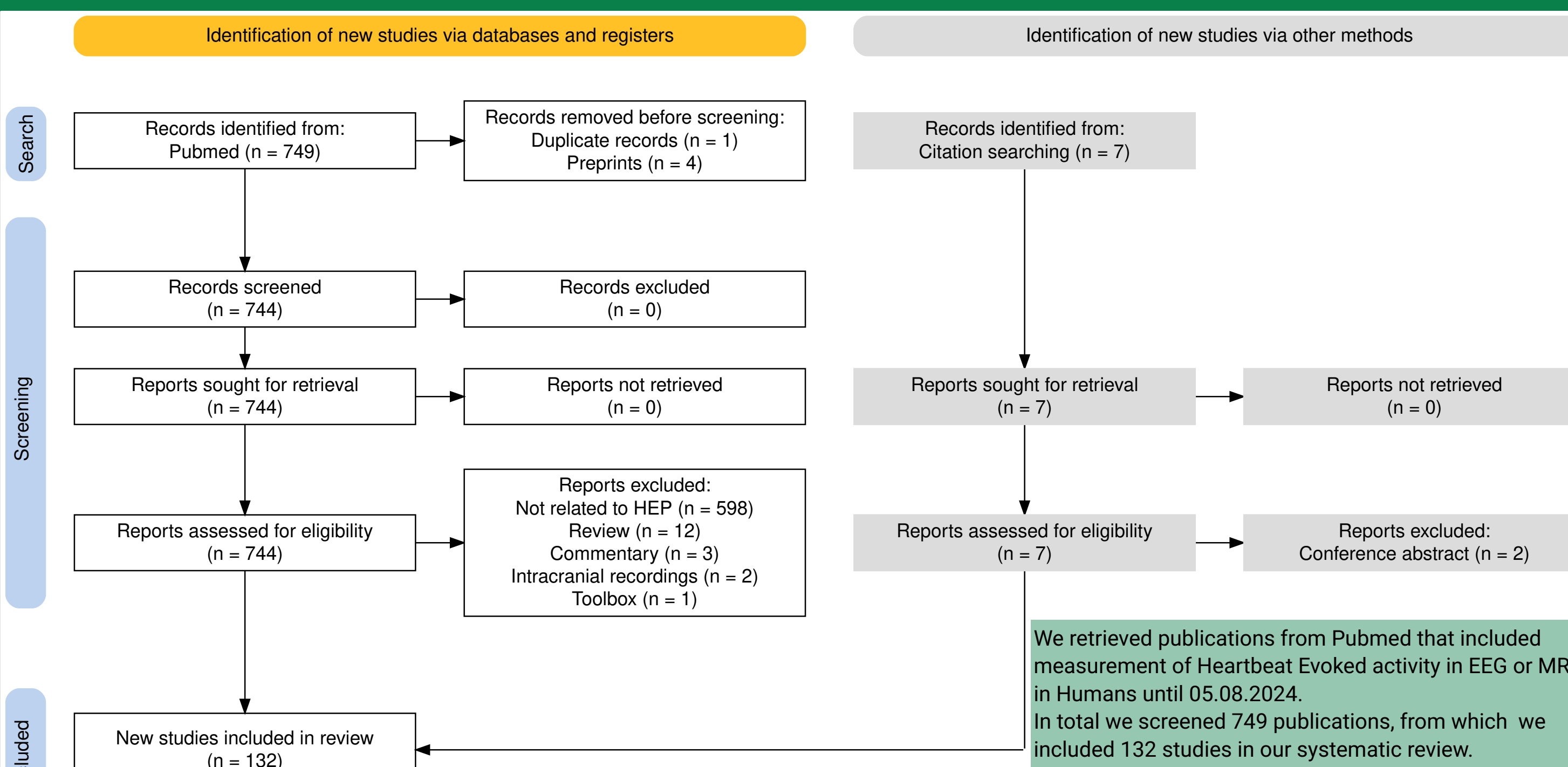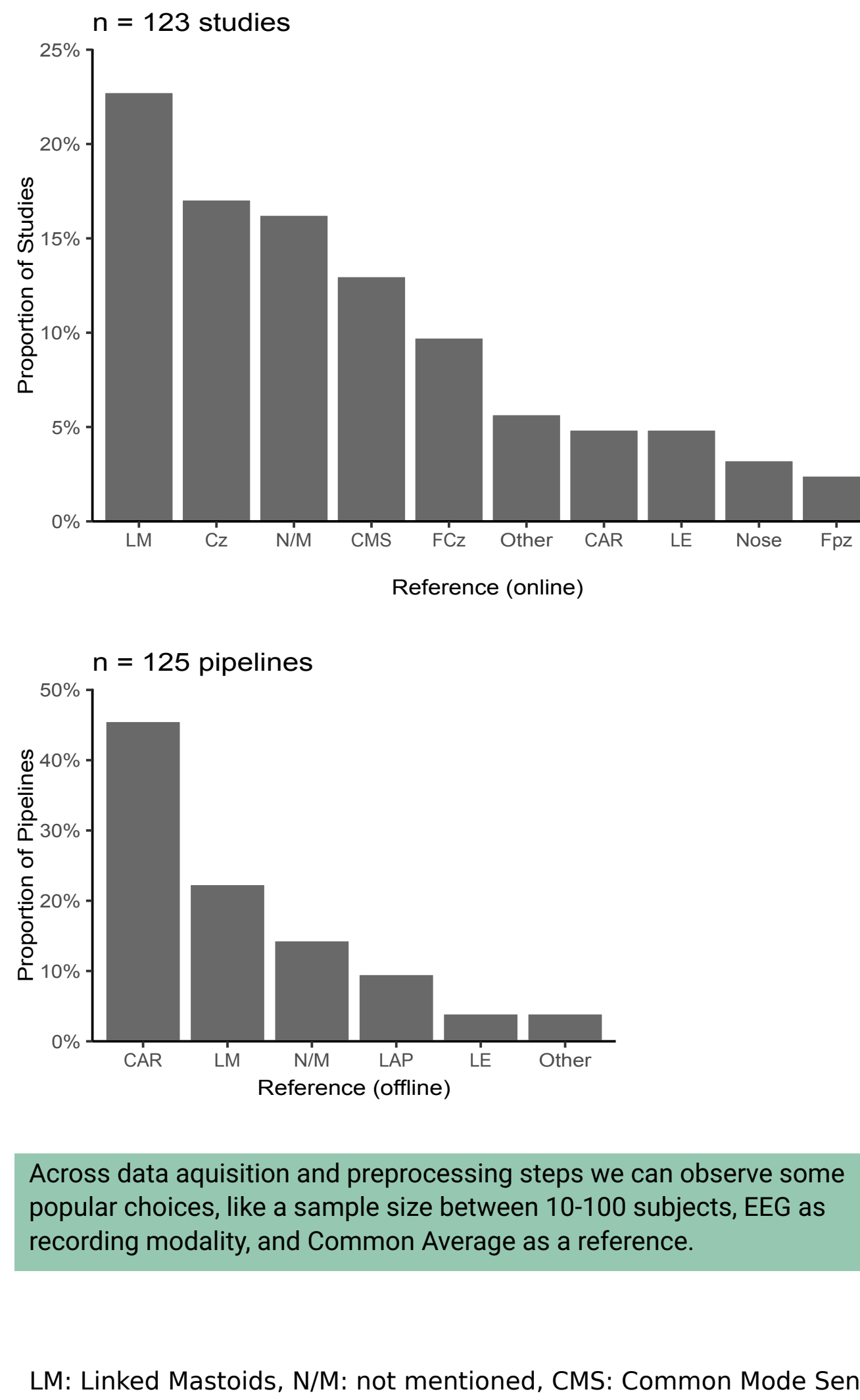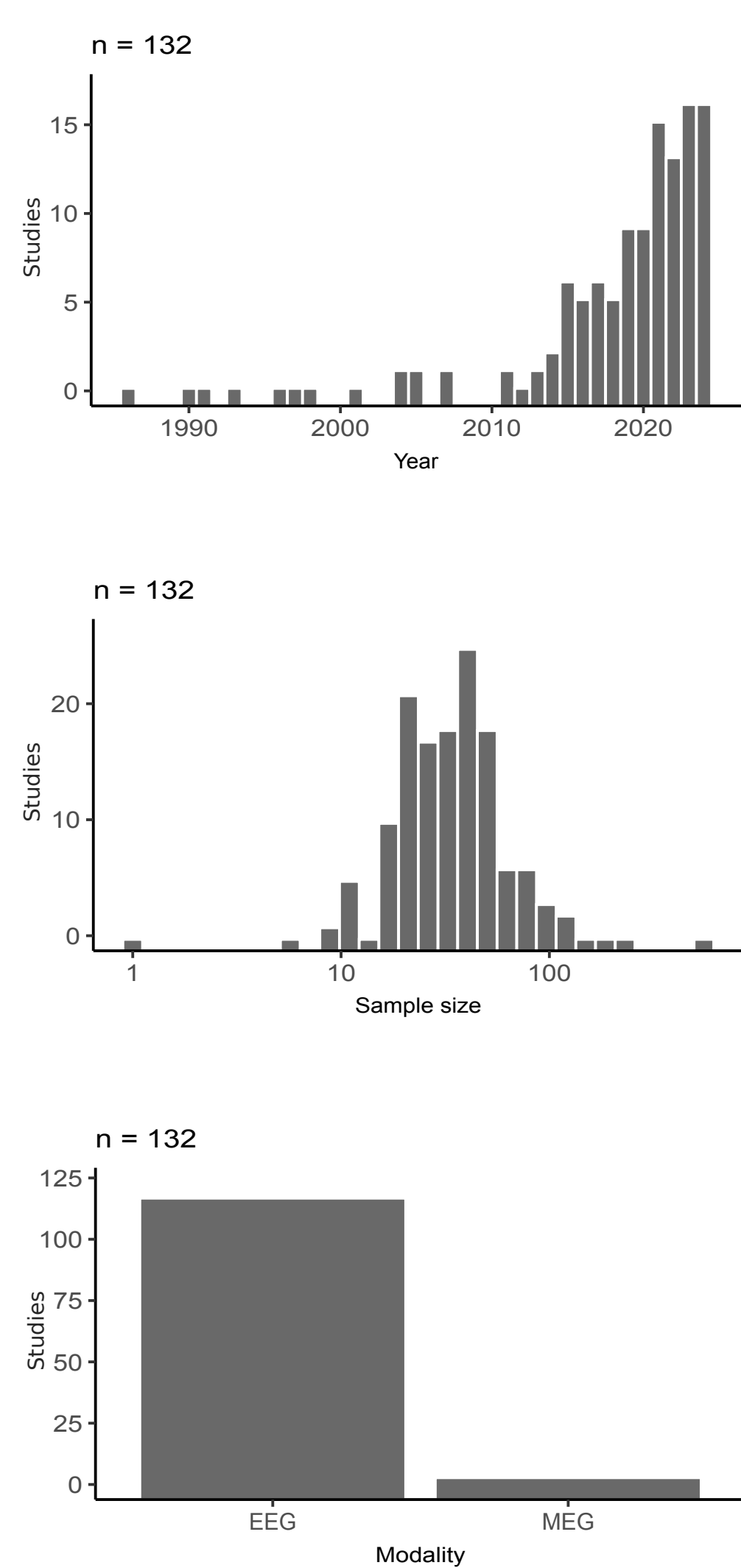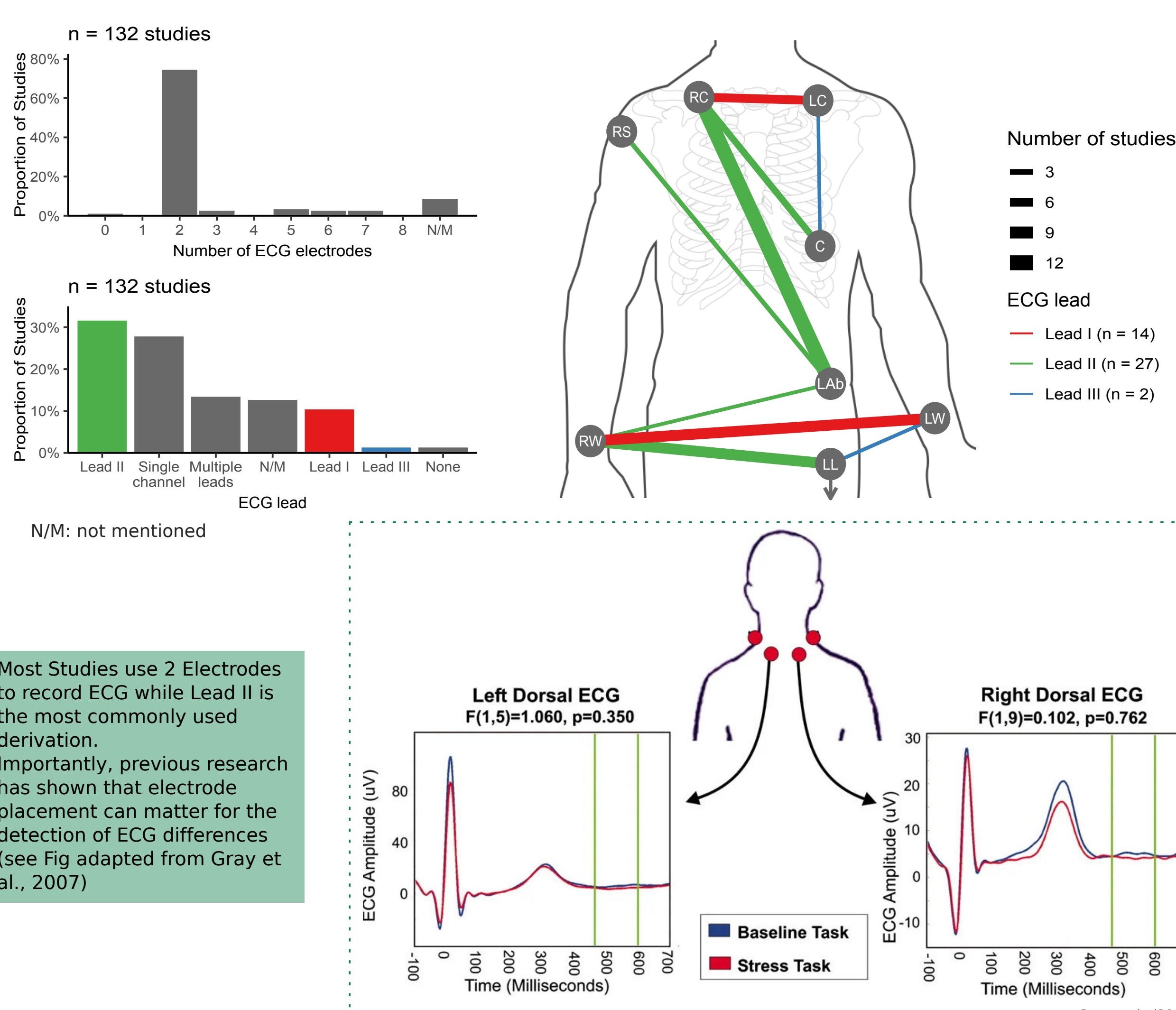Most Studies use 2 Electrodes to record ECG while Lead II is the most commonly used derivation.
Importantly, previous research has shown that electrode placement can matter for the detection of ECG differences (see Fig adapted from Gray et al., 2007)

Left Dorsal ECG $F(1,5)=1.060, p=0.350$
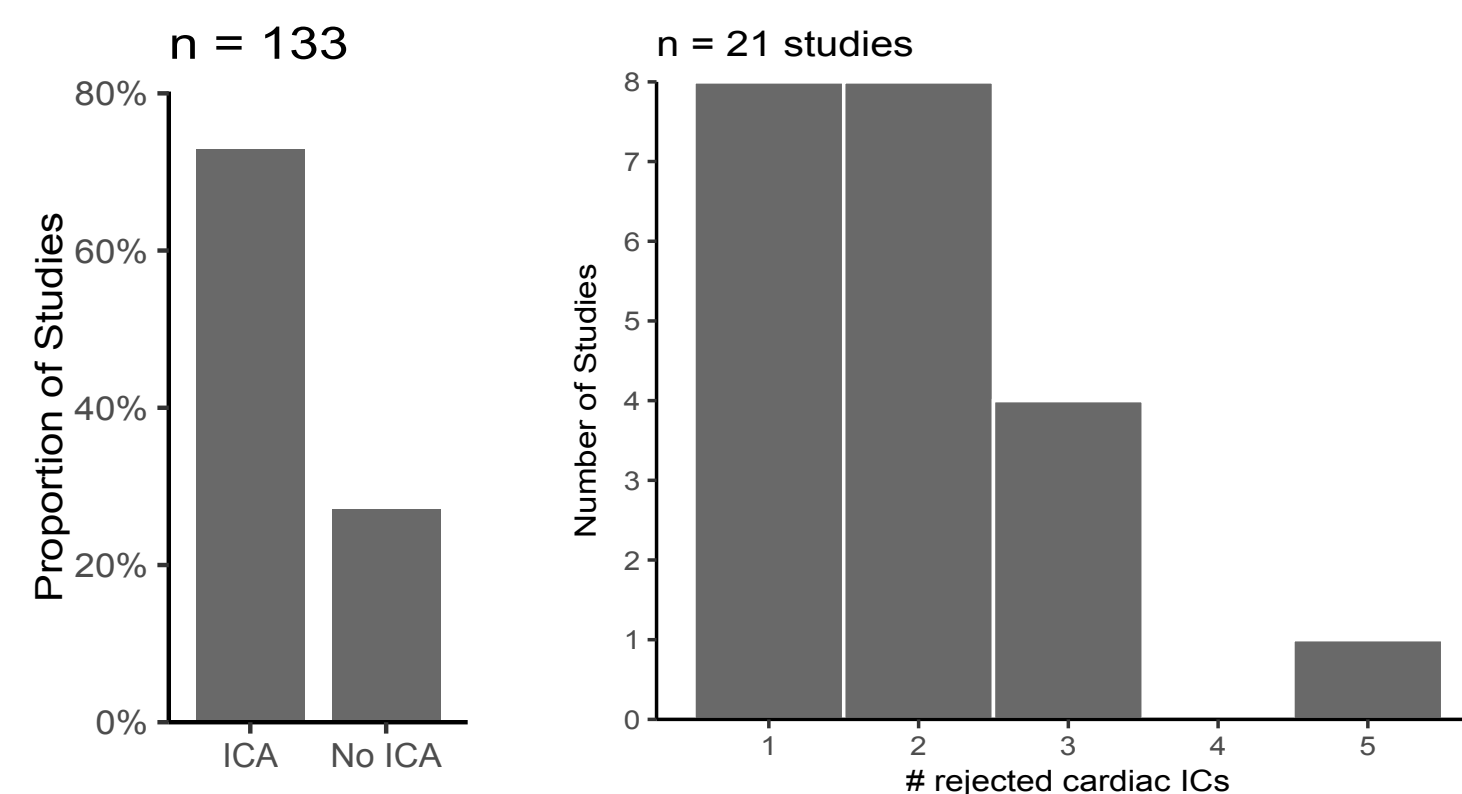**Right Dorsal ECG** $F(1,9)=0.102, p=0.762$
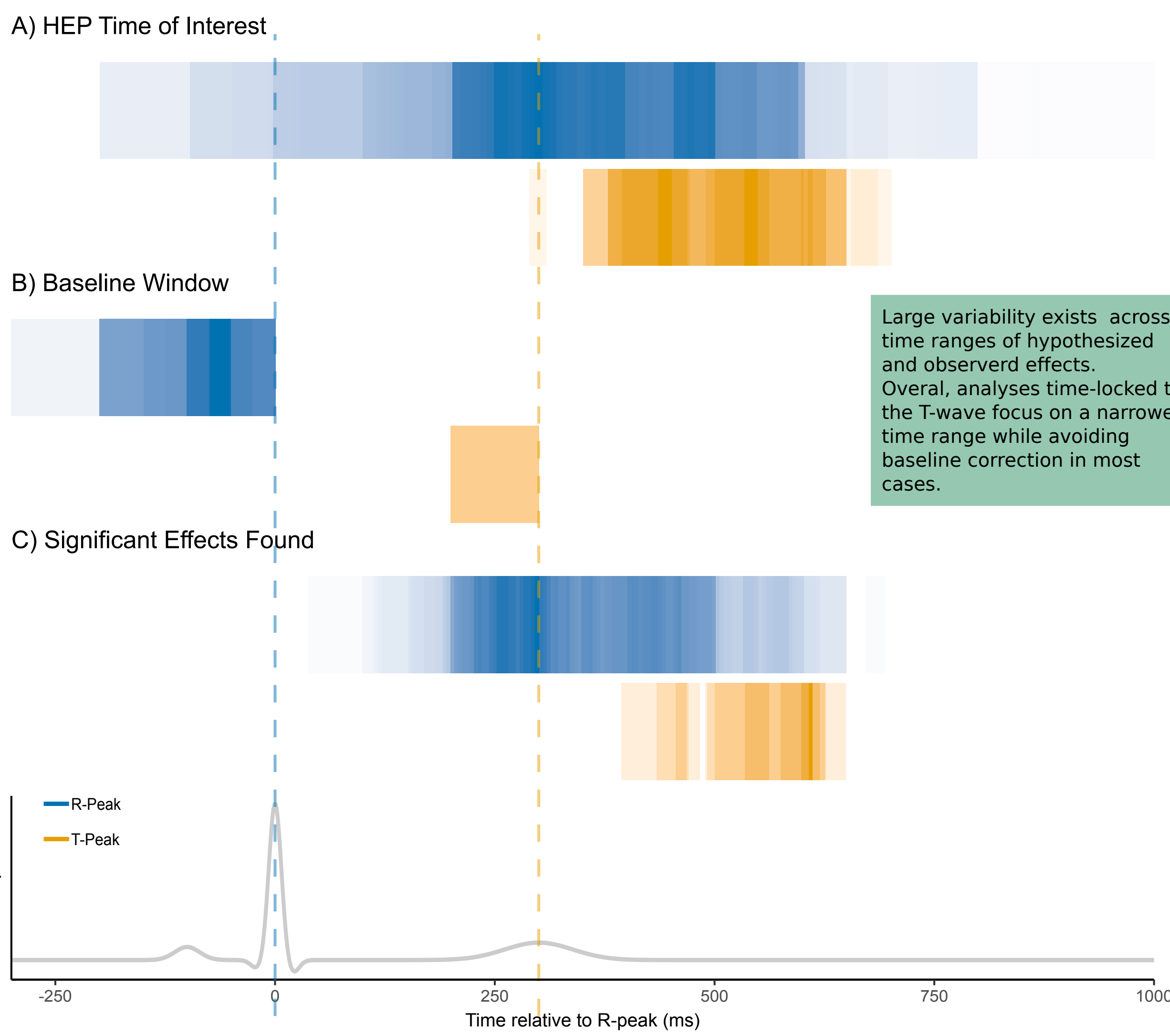
Baseline Task / Stress Task

Gray et al., (2007)

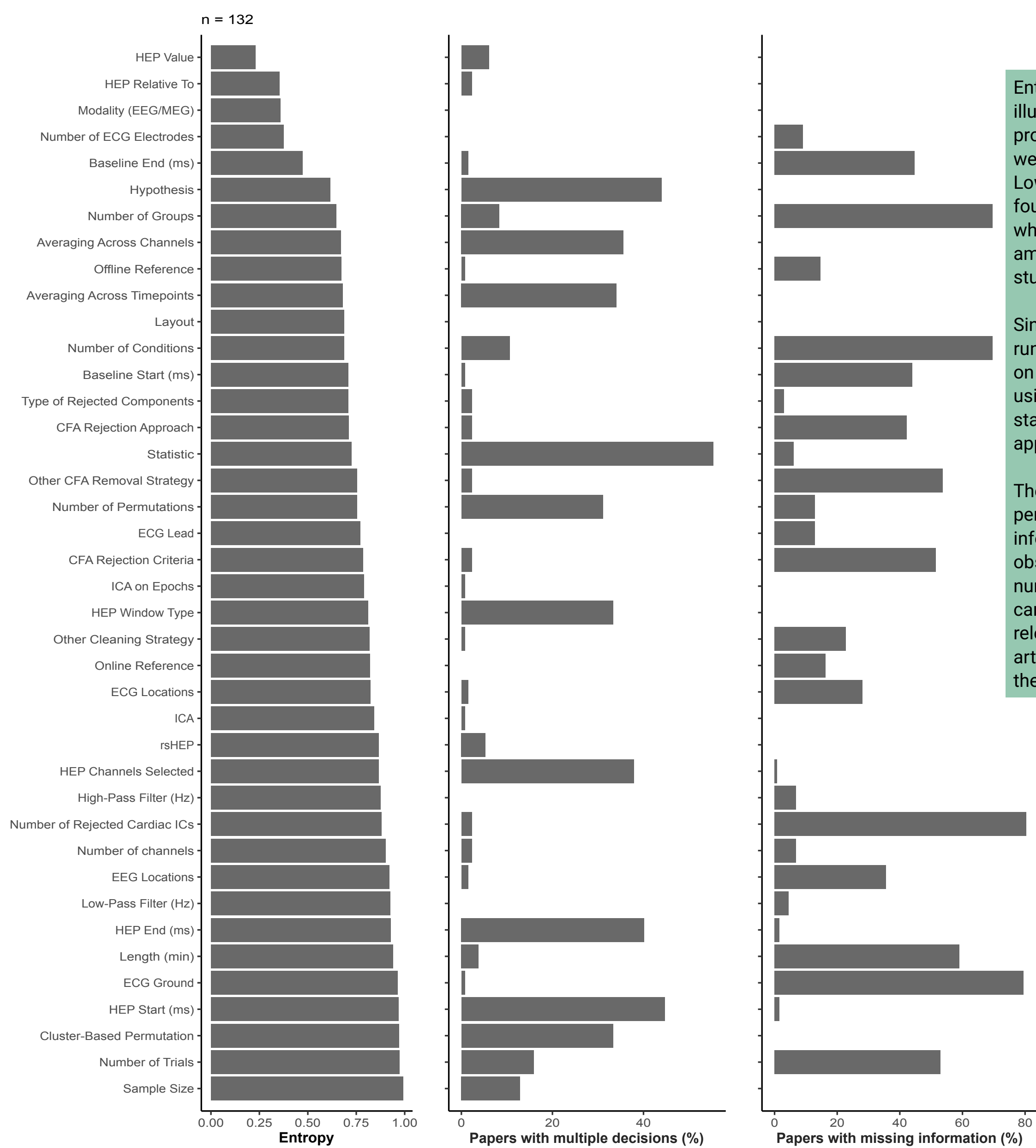## Diverse Approaches to address Cardiac Artifacts

Cardiac Artefacts are frequently addressed by Independent Component Analysis (ICA) based correction. However, no consensus exists on the right amount of removed components.

Furthermore, overlap with artefacts is prevented by excluding trials with short R-R interval or setting of the time range of interest for anlysis.

Buot et al., (2021)

Minimum RR Intervals

Reference — T-peak — R-peak

HEP windows for minimal artifact
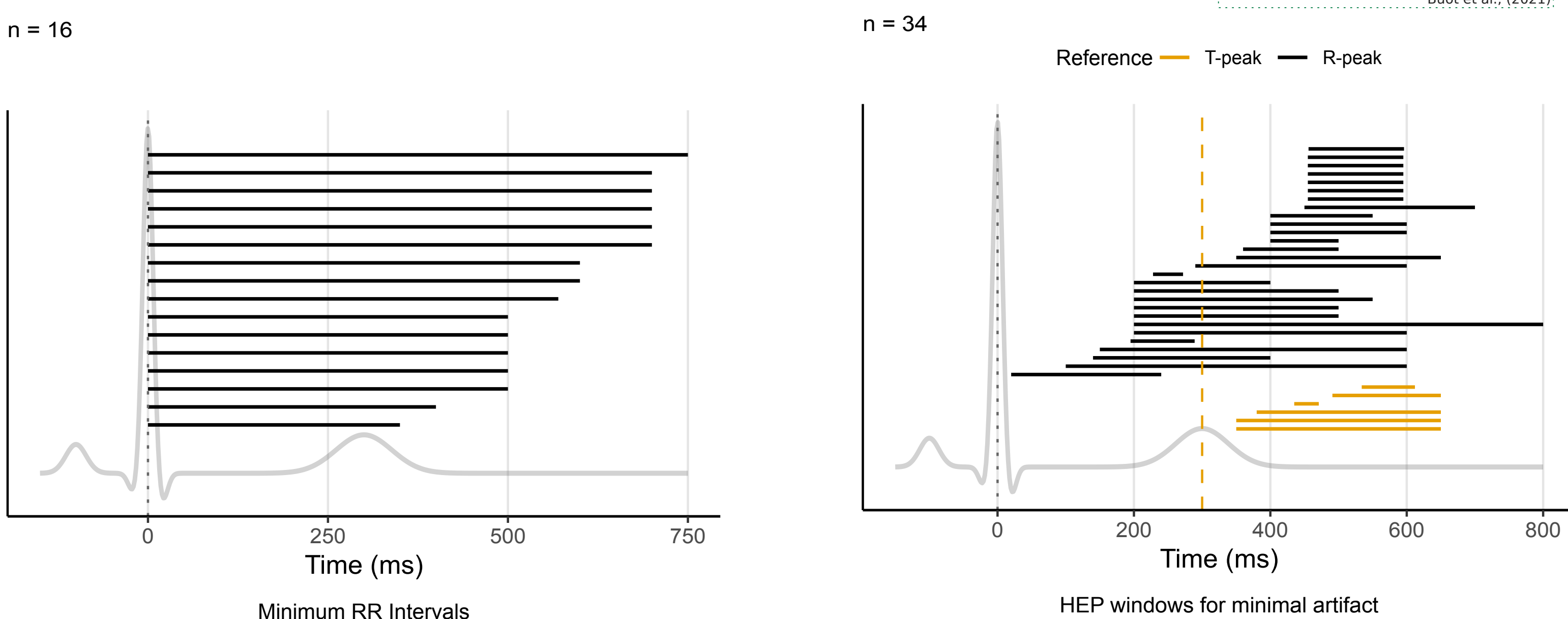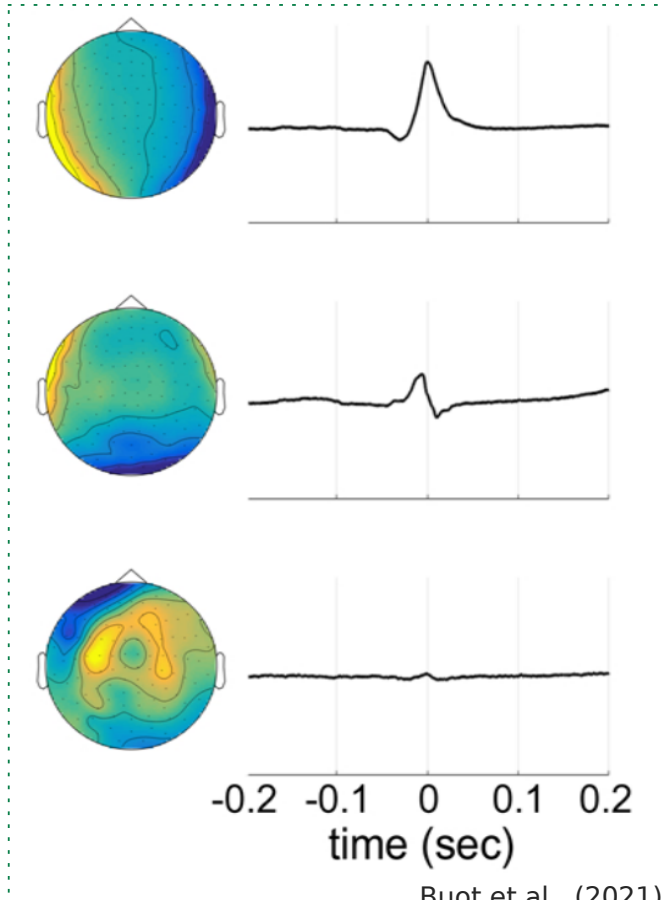
Hypothesized and Detected HER Effects

A) HEP Time of Interest
B) Baseline Window
C) Significant Effects Found

R-Peak / T-Peak

Large variability exists across time ranges of hypothesized and observerd effects. Overal, analyses time-locked to the T-wave focus on a narrower time range while avoiding baseline correction in most cases.
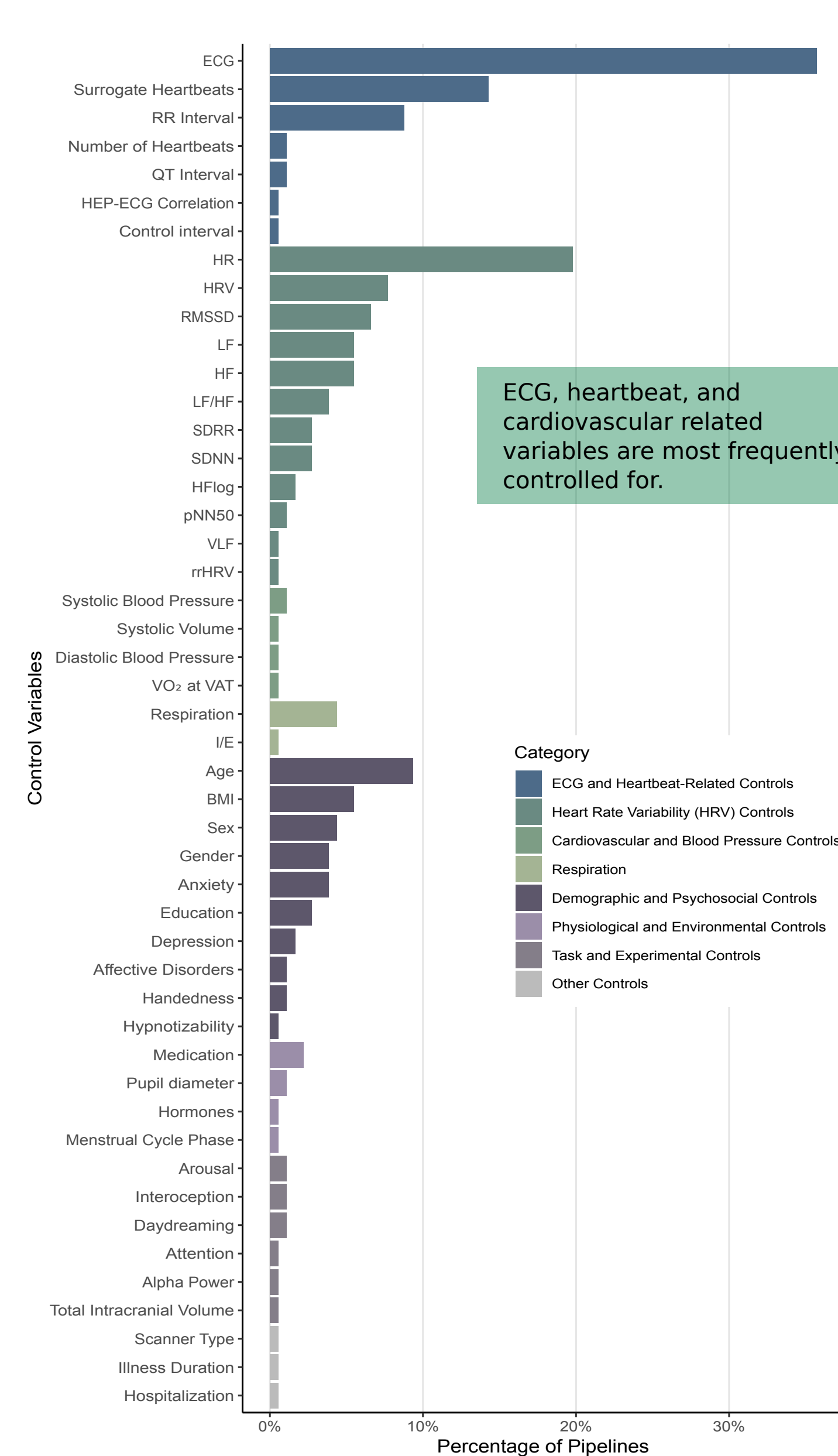
Methodological Variability and Reporting Inconsistencies

Entropy was used to illustrate how diverse processing choices were across studies. Lowest entropy was found for HER value which is defined as amplitude in most studies.

Single studies often run several analysis on HERs, specifically using several statistical approaches.

The highest percentage of missing information could be observed for the number of rejected cardiac ICs, which is a relevant parameter for artefact correction int the HER field.

Control Variables

ECG, heartbeat, and cardiovascular related variables are most frequently controlled for.

Reporting Check-List

- Surrogate heartbeat analysis
- ECG control analyses
- EEG
  - Reference online/offline
  - High- and low-pass
  - Number of channels and layout
- ICA
  - Algorithm
  - Epochs or continuous data
  - Type of rejected components
  - Number of rejected components (overall and cardiac)
  - Explained variance
  - Rejection approach (manual, automatic) and criteria (topography, time course...)

- ECG:
  - Locations, ground, lead(s)
- Analysis (for each test):
  - Number of groups
  - Subjects in groups
  - Conditions, trials
  - Number of epochs averaged to obtain HEP
  - Start and end of analysis window and of baseline
- For permutation clustering:
  - Which statistic was used
  - How many permutations
- For significant results:
  - exact location and relevant
  - significance values
  - average statistic in a cluster

Discussion & Open Questions

- Large variability across many processing choices & Results
- Effects of different settings largely unknown
- field agrees on: R-peaks as HER marker, EEG as recording method, and Amplitude as outcome measure

- To check systematically:
  - CFA (and ocular/muscle) removal effects
  - ICA on epochs vs continuous data
  - ECG electrode placement
  - Role of baseline-correction
  - Effects of different filter cutoffs
  - How combinations of steps affect results (Multiverse)

Babo-Rebelo,M., Buot, A., & Tallon-Baudry, C. (2019). Neural responses to heartbeats distinguish self from other during imagination. Neuroimage, 191, 10-20. https://doi.org/10.1016/j.neuroimage. 2019.02.012
Babo-Rebelo, M., Richter, C. G., & Tallon-Baudry, C. (2016). Neural responses to heartbeats in the default network encode the self in spontaneous thoughts. Journal of Neuroscience, 36(30), 7829-7840. https://doi.org/10.1523/JNEUROSCI.0262-16.2016
Buot, A., Azzalini, D., Chaumon, M., & Tallon-Baudry, C. (2021). Does striato-limbic volume heartbeat evoked potential. Biological Psychology, 1 (58)(0). https://doi.org/10.1016/j.biopsycho.2021.108103
Garcia-Cordero, I., Esteves, S., Mikulan, E. P., Hesse, E., Baglivo, F. H., Silva, W., Garcia, M. del C., Vaucheret, E., Ciraolo, C., Garcia, H. S., Adolfi, F., Pietto, M., Herrera, E., Legaz, A., Manes, F., Garcia, A. M., Sigman, M., Bekinschtein, T. A., Ibáñez, A., & Sedeño, L. (2017). Attention, in and out: Scalp-level and intracranial EEG correlates of interoception and exteroception. Frontiers in Neuroscience, 11(JUL). https://doi.org/10.3389/fnins.2017.00411
Gray, M. A., Taggart, P., Sutton, P. M., Groves, D., Holdright, D. R., Bradbury, D., Brull, D., & Critchley, H. D. (2007). A cortical potential reflecting cardiac function. Proceedings of the National Academy of Sciences, 104(16), 6818-6823. https://doi.org/10.1073/pnas.
Kumral, D., A. C., Cesnaite, E., Kornej, J., Sander, C., Hensch, T., Divarkova, S., Stadvhalk, S., Hagendorf, A., Laufs, U., Wachter, R., Nikulin, V., & Villringer, A. (2022). The Neural Representation of the Heart is Strongly Attenuated in Patients with Atrial Fibrillation. SSRN Electronic Journal. https://doi.org/10.2139/ssrn.4079330
Marshall, A. C., Gentsch, A., Jelinčić, V., & Schütz-Bosbach, S. (2017). Exteroceptive expectations modulate interoceptive processing: Repetition-suppression effects for visual and heartbeat evoked potentials. Scientific Reports, 7(1), 1-11. https://doi.org/10.1038/s41598-017-16595-9
Park, H. D., & Blanke, O. (2019). Heartbeat-evoked cortical responses: Underlying mechanisms, functional roles, and methodological considerations. NeuroImage, 197(April), 502-511. https://doi.org/10.1016/j.neuroimage.2019.04.081