## Breathe in, breathe out: how respiratory phases modulate brain-heart interactions

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## Abstract

The functions of respiration go far beyond that of supplying the organism with oxygen. In recent years, several studies both in animals and in humans have revealed the fundamental role of respiratory activity in modulating sensorimotor, cognitive, and emotional functions by shaping brain activity and connectivity. However, the psychophysiological basis of respiratory-related brain changes is not yet clarified. We recently hypothesised that a crucial mechanism can be related to changes of interoception across the respiratory cycle, that is how the brain receives, elaborates and interprets bottom-up signals that represent the physiological condition of the body.

We recently found higher Heartbeat Evoked Potential (HEP) during exhalation compared to inhalation ( $\Delta$ HEP) in healthy humans during a resting-state, mind-wandering condition, showing increased cortical processing of heartbeats. Additionally,  $\Delta$ HEP was higher while performing the Interoceptive Condition of the Heartbeat Detection task, compared to the Exteroceptive Condition. Finally,  $\Delta$ HEP was linked to interoceptive accuracy, suggesting interoceptive optimization across the respiratory cycle. However, these findings raised the question as to whether the observed effects were specific for cardiac interoception.

In a second study, we assessed whether respiratory phase-related HEP modulations were specific for cardiac interoception, or they were also present in other domains of interoception, by directly comparing a cardiac interoceptive task (Heartbeat Counting Task - HCT) with a respiratory interoceptive task (Breath Counting Task - BCT) in 28 healthy volunteers. We used a cardiac and a respiratory Tone Counting Task as Exteroceptive control conditions. We found non-specific HEP activity increases while performing the Interoceptive conditions of the HCT and the BCT, compared to their respective Exteroceptive conditions. Notably, we found increased  $\Delta$ HEP specifically during the Interoceptive condition of the HCT, compared to the Interoceptive condition of the BCT.

Overall, present data showed that respiratory activity shape brain-heart interactions, modulating cardiac interoception at the behavioural and neurophysiological levels. In addition, HEP changes

across the respiratory cycle could represent a physiological signature of heartbeats' cortical processing optimization, which is mediated by cardiac interoceptive attention.