

Phenomenology and functional significance of the Vertex Potential

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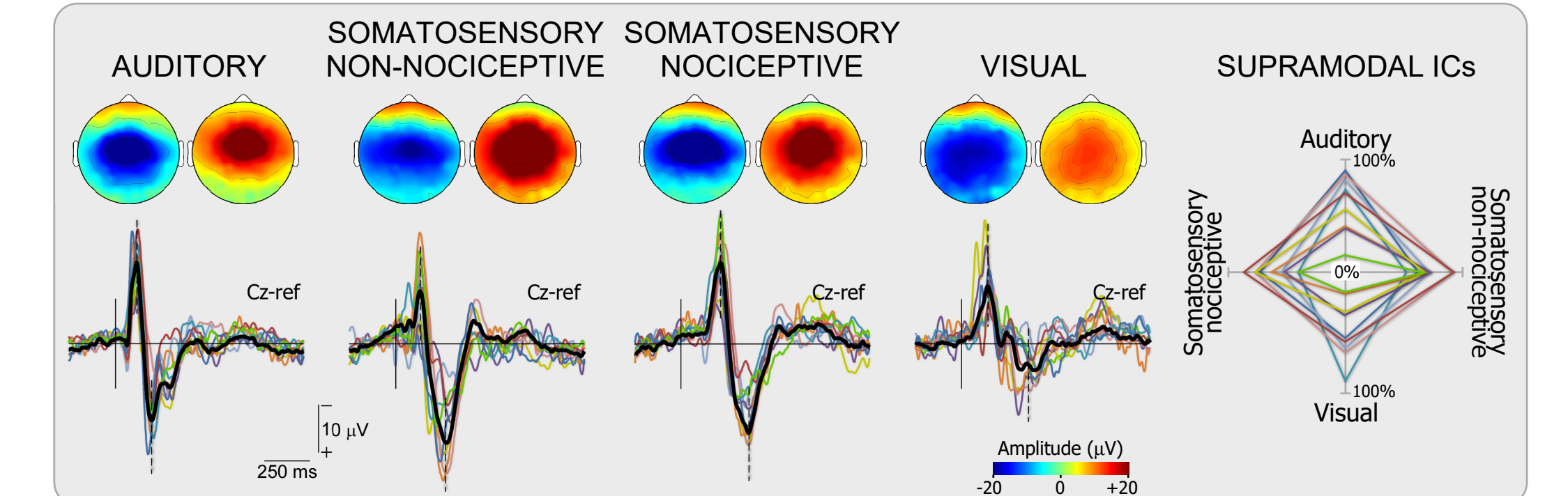
Introduction

Living in rapidly changing environments has shaped animal brains toward high sensitivity to sudden sensory events - often signalling threats or affordances demanding swift motor reactions. Unsurprisingly, such events elicit one of the largest and most widespread electrocortical responses recordable from the scalp: the **Vertex Potential (VP)**.

The VP is often assumed to mostly reflect sensory and unimodal brain processes. However, several studies have convincingly demonstrated that the VP is (1) largely composed of **supramodal neural activity**, and (2) tightly coupled to the preparation of **swift behavioural responses**.

On the basis of this evidence, we hypothesised that the VP reflects a **transient and wide-spread cortical modulation** reflecting the activity of non-specific sensory systems. We are testing this hypothesis in ongoing experiments entailing the simultaneous recording of EEG and intracranial data in rodents and monkeys.

Brain potentials elicited by sudden stimuli of different modalities are all largely contributed by the supramodal Vertex Potential (Mouraux & Iannetti 2009)



EEG response elicited by sudden auditory, tactile, noxious and visual stimuli in humans. Black waveforms show group-level averages, coloured waveforms show single-participant averages. Topographies show the response scalp distribution at the negative and positive peaks. **Note the similarity between the responses across all four modalities.**

These brain responses were then decomposed using probabilistic independent component analysis and the resulting independent components (ICs) were classified according to their contribution to the response in each modality. Radar plots on the right show, for each participant, the proportion of total variance explained in each modality by supramodal ICs (i.e. ICs which contributed similarly to all four modalities).

This was the first quantitative demonstration that the EEG response elicited by sudden sensory stimuli was largely comprised of supramodal neural activity - which we refer to as the Vertex Potential.

Vertex Potentials are highly sensitive to behavioural-relevance (Iannetti et al, 2008)

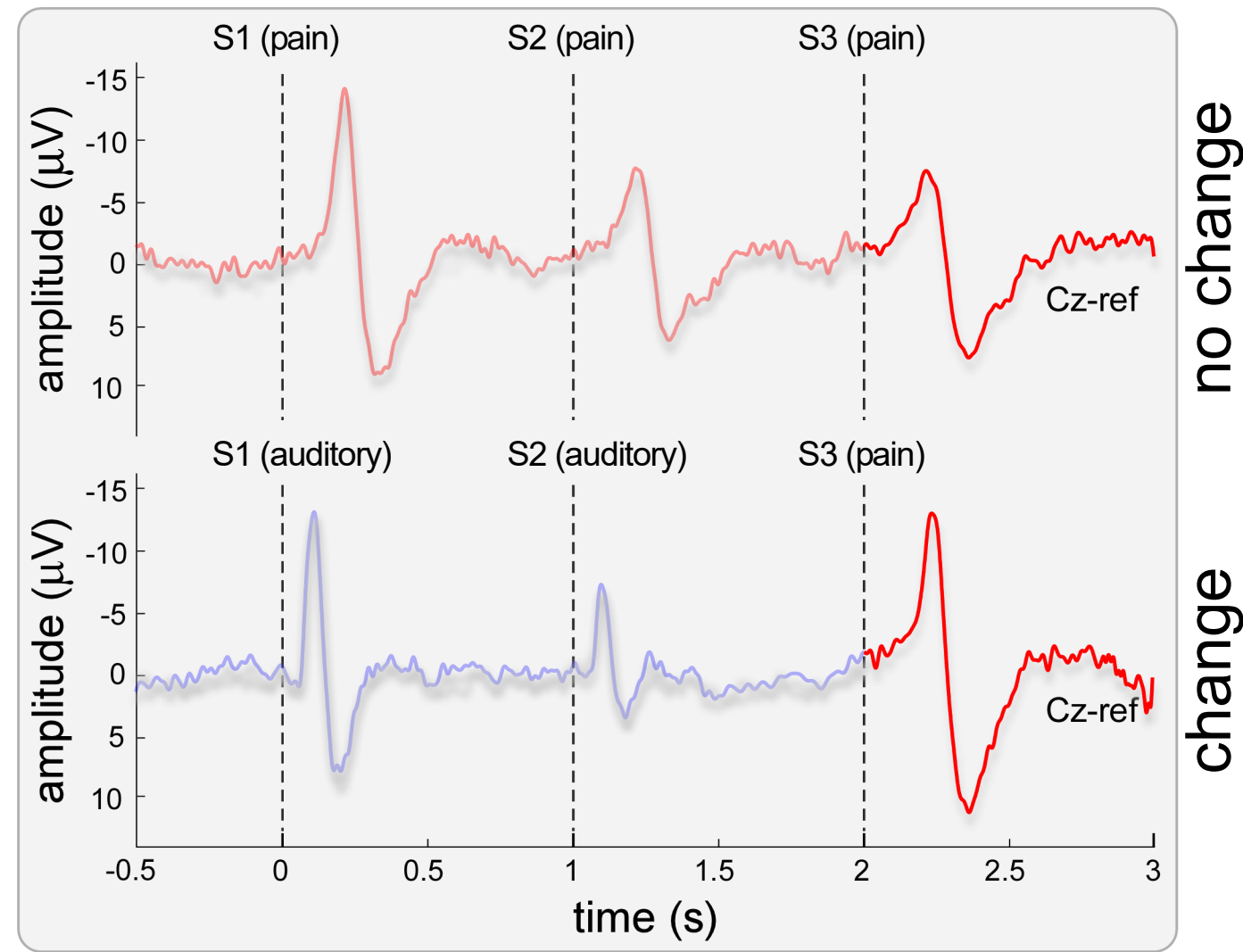
Another important VP feature is its dramatic modulation by **stimulus surprise**.

This sensitivity can be demonstrated by repeating the stimulus eliciting the VP at a constant short latency, a **paradigm that neatly dissociates afferent input and surprise**.

Plots to the right show the VP elicited by a triplet of stimuli delivered at 1Hz (S1-S2-S3).

When the stimulus modality is identical for all three stimuli (top row), the VP magnitude is reduced substantially (i.e. it **habituates**).

Interestingly, if the S3 stimulus changes modality (bottom row), the VP returns to its usual amplitude (i.e. it **dishabituates**; Valentini et al, 2011).

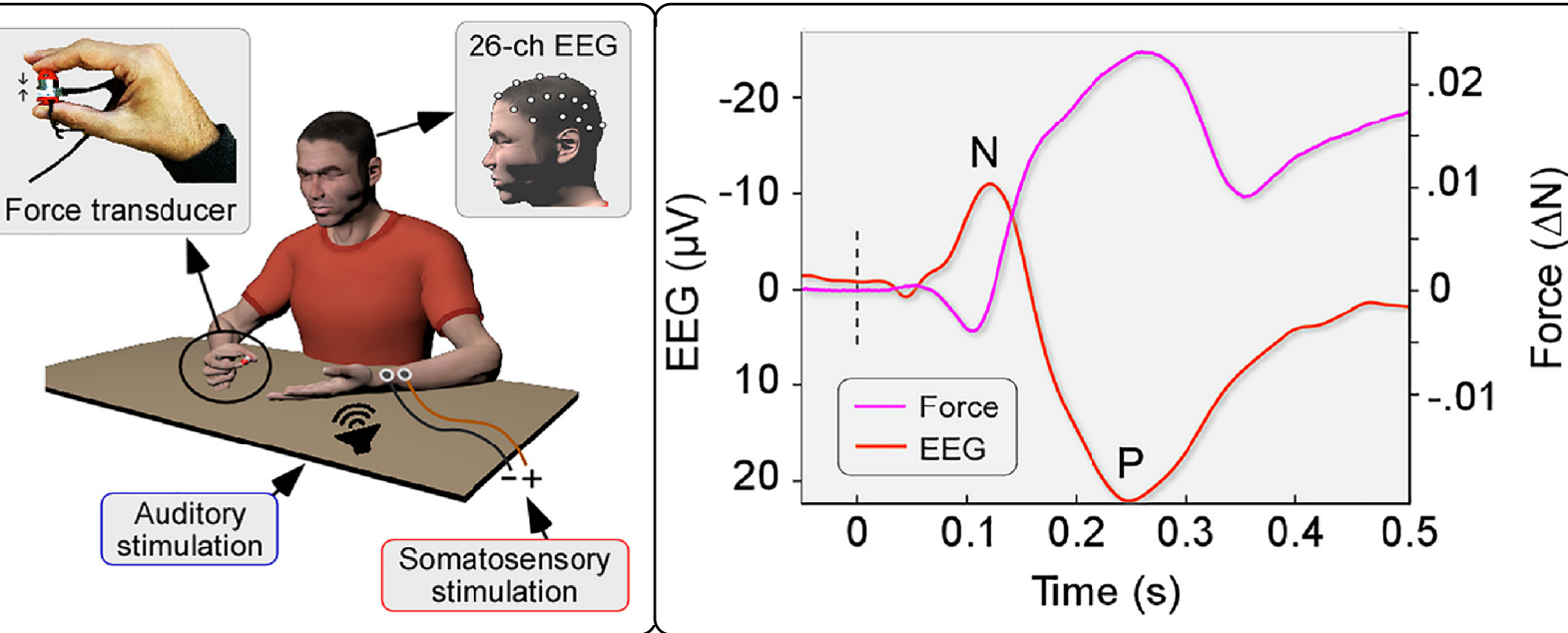


Several other changes of stimulus features result in VP **dishabituation**, including:
 - an increase, but not decrease, of the S3 intensity compared to S1 and S2 (Ronga et al, 2013)
 - a displacement of S3 location towards the core of the body (Moayeddi et al, 2016)
 - randomly varying the inter-stimulus interval such that the stimuli are less predictable (Wang et al, 2010)

Altogether these results suggest that more surprising and therefore more behaviourally-relevant stimuli elicit VPs of larger magnitude

Vertex Potentials do not reflect a purely sensory brain process (Novembre et al, 2018)

To explore the relationship between VP and motor system, we recorded the EEG response to abrupt sensory stimuli while participants performed a **simple isometric motor task, exerting a constant force** (left panel).

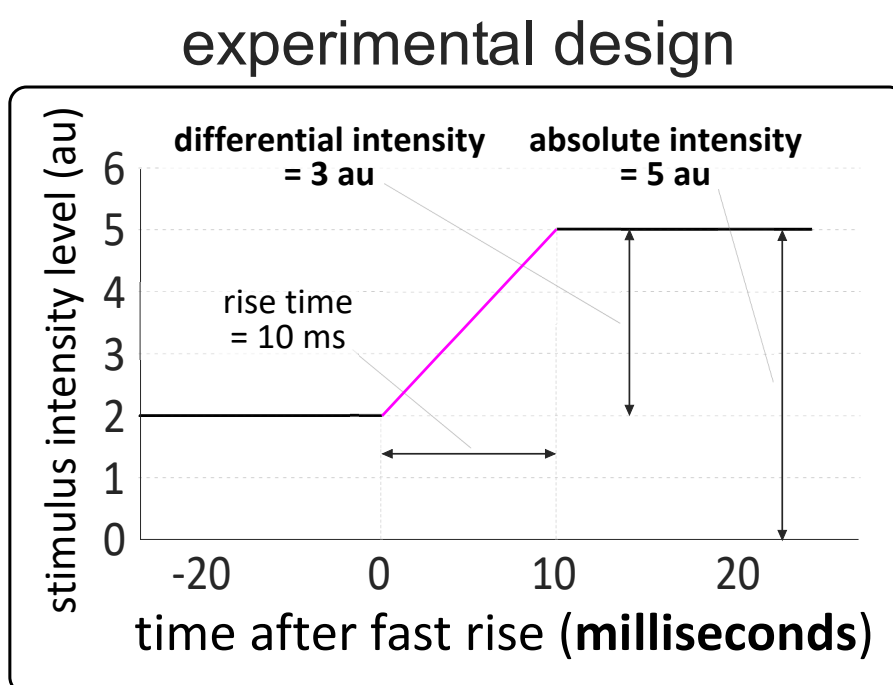


The abrupt stimuli elicited a multipolar pattern of **force modulation highly similar to the VP** in shape and timecourse (right panel). Crucially, trial-by-trial VP amplitude reliably predicted the force modulations (peak R value = ~5), which also habituated with stimulus repetition.

A basic physiological mechanism couples the Vertex Potential with the motor system

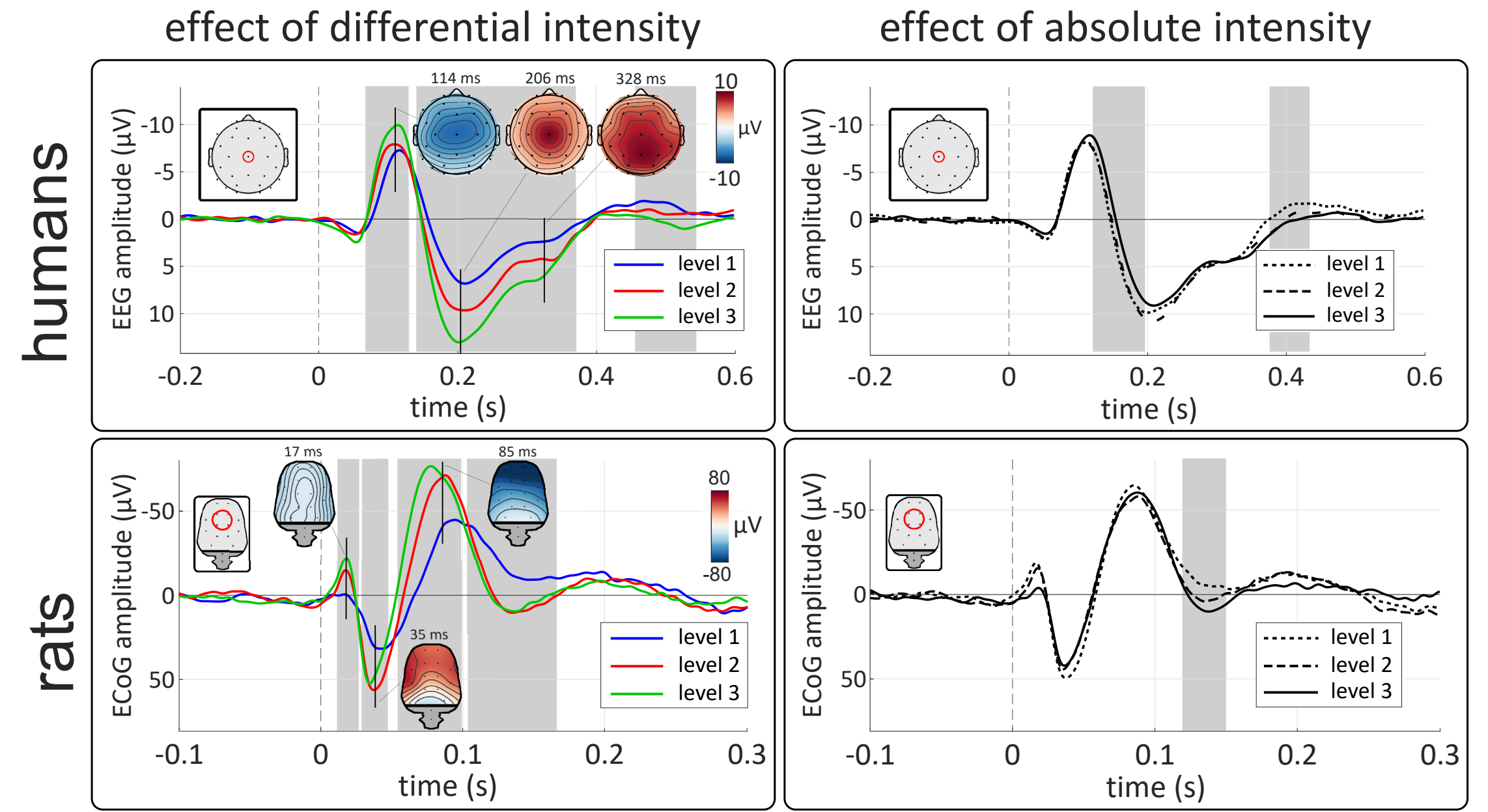
Vertex Potentials are sensitive to abrupt changes of stimulus intensity in humans and rodents (Somervail et al, 2021, 2022)

VP magnitude is known to be largely determined by stimulus intensity. We dissociated two aspects: the degree of intensity change (**differential intensity**) and the **absolute intensity** at which the change took place (*experimental design*, right).

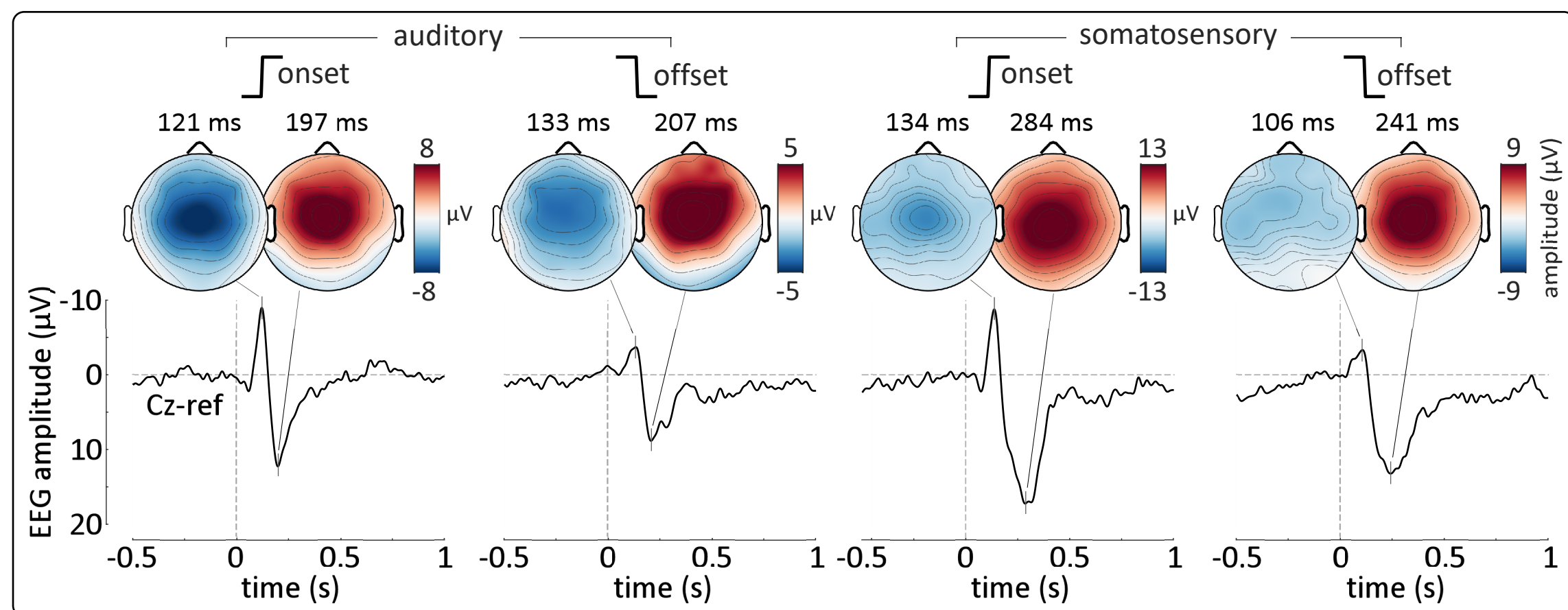


VP magnitude was highly sensitive to differential intensity, and insensitive to the absolute intensity (although a small effect on latency was present). This observation was **invariant to the stimulus modality**, showing that the sensitivity to differential intensity was **supramodal**.

We also replicated this result in rats, suggesting that **this sensitivity to environmental changes is highly conserved across mammals**.



Highly similar VPs can be elicited by both increases (onsets) and decreases (offsets) of sensory intensity. These onset- and offset-evoked VPs (1) have highly similar scalp topography, (2) are similarly supramodal, (3) habituate when the stimulus is repeated at a short and predictable inter-stimulus interval and (4) are both tightly coupled to the motor system.



Together with previous experiments, these results demonstrate that the VP is primarily sensitive to abrupt, surprising and therefore behaviourally-relevant, changes in the sensory environment.

Do Vertex Potentials reflect the cortical consequence of the activation of the extralemnisal system?

There is strong empirical evidence that the **VP does not primarily reflect the canonical "lemniscal" pathways** - which transmit high-fidelity sensory information from one modality to its corresponding primary sensory cortex, via 'core' cells in specific thalamic "relay" nuclei.

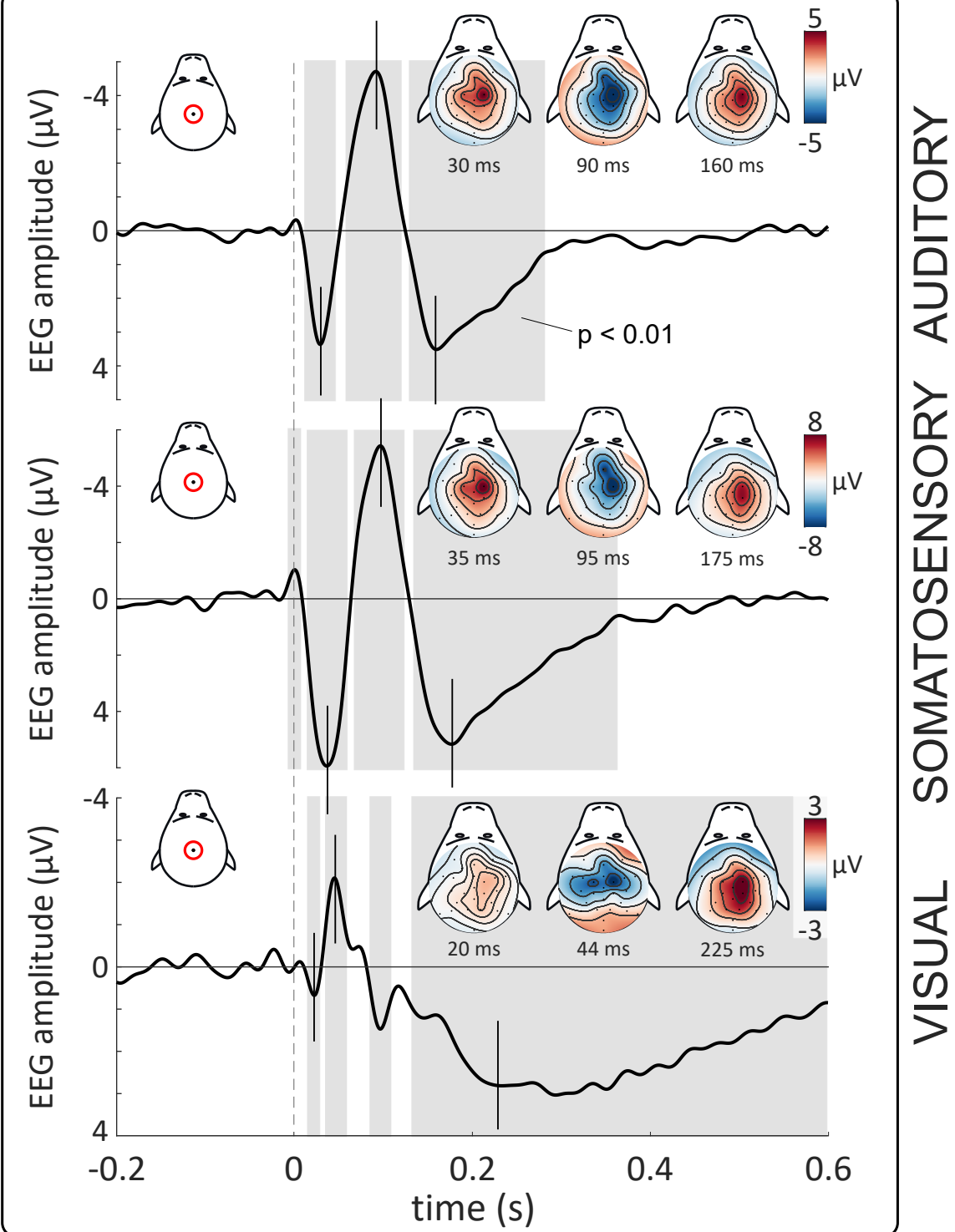
Instead, there is accumulating evidence that the **VP reflects the cortical consequence of the activation of the extralemnisal system** - which carries supramodal sensory information from 'matrix' cells in non-specific thalamic nuclei across the brain.

Indeed, the VP and the electrophysiological responses of non-specific thalamic nuclei share several properties:
 - both consist of longer latency responses elicited by several sensory modalities (Jones, 2001)
 - both are effectively activated by abrupt changes of sensory input and relatively insensitive to absolute stimulus features (e.g. Albe-Fessard & Kruger, 1962, Peschanski et al, 1981)
 - both habituate when stimuli are repeated at short inter-stimulus interval (e.g. Peschanski et al, 1981)
 - auditory-evoked VP in rats is unaffected by lesioning the primary auditory cortex, while general anaesthetic abolishes both the VP and responses in non-specific thalamus (Simpson & Knight, 1993)

We therefore hypothesise that the VP reflects a phenomenon similar to the cortical down-up states typically observed in sleep (Massimini et al, 2003) and mediated by the extralemnisal pathways and related arousal systems. The consequent reset of the ongoing brain state might facilitate rapid behavioural reactions to potentially threatening stimuli.

Simultaneous EEG and intracranial recordings in monkeys (preliminary results)

To test this hypothesis more thoroughly, we recorded **simultaneous EEG and intracranial signals in two monkeys** while delivering abrupt auditory, somatosensory and visual stimuli.



On the right we show the averaged waveforms from a single monkey for the three sensory modalities. **Note the similarity of the waveforms and scalp topographies across all modalities.**

We will perform a regression to predict the magnitude of the supramodal VP component using LFPs recorded in a pre-motor area at different electrode depths.

If the VP is the cortical output of the extralemnisal system, it should be strongly predicted by LFPs at more superficial cortical layers, even in this non-sensory area.

Additionally, we can explore the **single-unit activity** for evidence of **cortical down-up states**, similar to those found in slow-wave sleep (Massimini et al, 2003).

This result would demonstrate that the VP reflects a widespread "brain reset".

Conclusion & Future Directions

We have shown that, despite its common interpretation as a purely-sensory unimodal response, the **Vertex Potential** elicited by sudden sensory stimuli is largely comprised of **supramodal neural activity**, likely related to the preparation for **urgent behaviours**.

We are now testing the hypothesis that this **supramodal neural activity** is the cortical consequence of the activation of the widely-projecting **extralemnisal pathways from non-specific thalamus**.

We also plan to explore this hypothesis with **high-resolution fMRI of the thalamus & cortex**.

References

Albe-Fessard D, Kruger L. 1962. *J Neurophysiol*. 25:3-20.
 Iannetti GD, Hughes NP, Lee MC, Mouraux A. 2008. *J Neurophysiol*. 100:815-828.
 Jones EG. 2001. *Trends Neurosci*. 24:595-601.
 Massimini M, Rosanova M, & Mariotti M. 2003. *J Neurophysiol*. 89:1205-1213.
 Moayeddi M, Di Stefano G, Stubbs MT, Djougum B, Liang M, Iannetti GD. 2016. *eNeuro*. 3:399-418.
 Mouraux A, Iannetti GD. 2009. *J Neurophysiol*. 101:3258-3269.
 Novembre G, Pawar VM, Bufacchi RJ, Kilintari M, Srinivasan M, Rothwell JC, Haggard P, Iannetti GD. 2018. *J Neurosci*. 38:2385-2397.
 Peschanski M, Guilbaud G, Gautron M. 1981. *Exp Neurol*. 72:226-238.
 Ronga I, Valentini E, Mouraux A, Iannetti GD. 2013. *J Neurophysiol*. 109:692-701.
 Simpson G V, Knight RT. 1993. *Brain Res*. 602:251-263.
 Somervail R, Bufacchi RJ, Salvatori C, Neary-Zajicek L, Guo Y, Novembre G, Iannetti GD. 2022. *Cereb Cortex*. 1-14.
 Somervail R, Zhang F, Novembre G, Bufacchi RJ, Guo Y, Crepaldi M, Hu L, Iannetti GD. 2021. *Cereb Cortex*. 31:949-960.
 Valentini E, Torta DME, Mouraux A, Iannetti GD. 2011. *J Cogn Neurosci*. 23:2822-2837.
 Wang AL, Mouraux A, Liang M, Iannetti GD. 2010. *J Neurophysiol*. 104:2116-2124.

