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Invited reply

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Reply to Coll *et al.* 'Important methodological issues regarding the use of transcranial magnetic stimulation to investigate interoceptive processing' (2017)

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We want to respond to the two main points raised by Coll, Penton and Hobson as comment on our article 'Changes in interoceptive processes following brain stimulation' [1,2]. First, we want to discuss in more detail the question raised by Coll and co-workers in their comment, namely which regions were stimulated by our set-up. We are grateful to the authors providing results of a simulation of field distribution using SimNIBS. Indeed, as we already addressed in the discussion of our article, we cannot be sure that transcranial magnetic stimulation (TMS) directly reaches the anterior insula (AI). We also refer to the arguments already discussed in our article, but especially important for this issue: The topographic situation when stimulating the AI is directly comparable with the attempts to stimulate primary auditory cortex in the case of tinnitus referring to the auditory cortex. And is has been shown that chronic tinnitus can be modulated by rTMS [3,4], despite the larger distance of the coil to the primary auditory cortex (planum temporale, e.g. [5]). However, field simulation only demonstrates field distribution relative to a given range. As it is not yet possible to determine a threshold for a cortical stimulation site (with the exception of primary motor cortex and visual cortex) we do not know down to which relative field strength neurons respond to the TMS pulses. Using the field model provided by Coll, Penton and Hobson in their comment, we compared the field distribution windowed from 0 to 2.2 (maximum of norm E-field) with a window from 0 to 1 norm E-field (figure 1). Here, at least the upper part of the AI is directly reached by a field strength of about 0.5, about a quarter of the maximum norm E-field. Of course, large parts of prefrontal and temporal cortex covering the insula are exposed to a higher field strength. We can neither exclude a trans-synaptic activation of the AI from prefrontal cortex closer to the skull, nor a direct contribution of areas exposed under the coil to the observed effects.

The second main point refers to the question whether these effects are specific to interoceptive processes. The authors argue that the study lacks a control condition not related to interoceptive processes targeting attention processes or working memory performance in general that might be affected by frontal stimulation. We want to argue against the claim that attention processes or working memory performance in general might underlie the observed results after frontal stimulation. Effects of inhibiting somatosensory cortices were comparable in many aspects to effects of inhibiting AI, both on performance level as well as on EEG level as assessed by the HEP. These results contradict the idea that a change in interoceptive processes might be due to side effects of the TMS frontal stimulation site and therefore a general effect of affecting attention or working memory circuits. We in contrast argue that the fact that major results were comparable between stimulation sites aiming to inhibit AI and somatosensory cortices is a strong empirical evidence that indeed nodes of the interoceptive network were affected by TMS and that these effects were specific for interoceptive processes and are not related to other main functions

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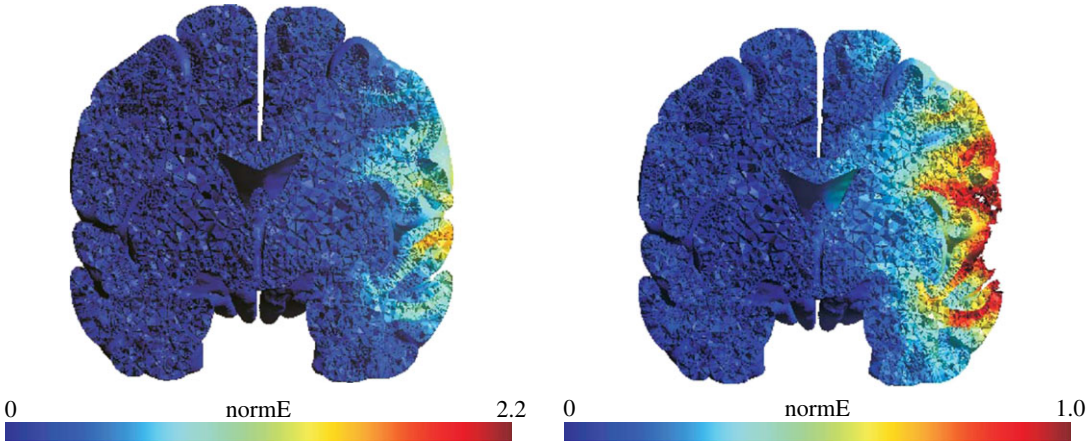

Figure 1. Simulation of normalized E-field distribution on a coronar section using SimNIBS, using different colour code windows. Top: colour code from 0 to 2.2 (maximum of E-field), bottom: colour code from 0 to 1.0.

in attention or working memory. We agree with the authors that a control task e.g. assessing performance and acoustic evoked potentials measured by EEG might have been a useful condition to prove whether TMS stimulation sites have an impact on other functions not related to interoceptive processes, but as TMS effects are time critical we decided to use a control site instead of a control condition as suggested by the authors.

We conclude that further empirical evidence is needed to further elucidate whether observed results can be replicated and are specific for interoceptive target areas, e.g. using new methodological approaches such as protocols with combined TMS stimulation and neuroimaging.

Competing interests. We declare we have no competing interests.
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References

1. Pollatos O, Herbert BM, Mai S, Kammer T. 2016 Changes in interoceptive processes following brain stimulation. *Phil. Trans. R. Soc. B* **371**, 20160016. (doi:10.1098/rstb.2016.0016)
2. Coll M-P, Penton T, Hobson H. 2017 Important methodological issues regarding the use of transcranial magnetic stimulation to investigate interoceptive processing: a Comment on Pollatos *et al.* (2016). *Phil. Trans. R. Soc. B* **372**, 20160506. (doi:10.1098/rstb.2016.0506)
3. Plewnia C. 2011 Brain stimulation: new vistas for the exploration and treatment of tinnitus. *CNS Neurosci. Therapeutics* **17**, 449–461. (doi:10.1111/j.1755-5949.2010.00169.x)
4. Plewnia C, Reimold M, Najib A, Brehm B, Reischl G, Plontke SK, Gerloff C. 2007 Dose-dependent attenuation of auditory phantom perception (tinnitus) by PET-guided repetitive transcranial magnetic stimulation. *Hum. Brain Mapp.* **28**, 238–246. (doi:10.1002/hbm.20270)
5. Langguth B, Zowe M, Landgrebe M, Sand P, Kleinjung T, Binder H, Hajak G, Eichhammer P. 2006 Transcranial magnetic stimulation for the treatment of tinnitus: a new coil positioning method and first results. *Brain Topogr.* **18**, 241–247. (doi:10.1007/s10548-006-0002-1)