We welcome the comprehensive summary and insightful comments made in the Journal Club by Rahnev (Rahnev, 2013) on our publication “Causal frequency-specific contributions of frontal spatiotemporal patterns induced by non-invasive neurostimulation to human visual performance” published in March in this same journal (Chanes et al., 2013). The author does an outstanding job of presenting the framework and contributions of our manuscript. There are, however, some issues we would like to comment on further, as due to space limitations we fear they might have remained unclear.

Methodologically, our study is indebted to the pioneering ideas of Thut and Miniussi who put forward the notion of using Transcranial Magnetic Stimulation (TMS) patterns to artificially induce, emulate and manipulate oscillatory activity (Thut and Miniussi, 2009). The interest of this method is that it could help establish causation between spatiotemporal brain activity patterns and cognitive processes and relate them non-invasively, to specific cortical locations and their associated networks. In our study, we originally contributed to improve prior rhythmic TMS approaches by comparing the impact on specific visual behaviors of frequency-specific and non-frequency-specific patterns. This simple procedure, allowed us to isolate the causal effect of pattern frequency on performance and avoid the biases one incurs when comparing burst of different frequencies equated either in number of pulses or pattern duration.

Two frequency patterns, either 30 or 50 Hz and their associated non-frequency specific
patterns, two embedded TMS modalities for each, active or sham, and the dissociations found for the modulation of either visual sensitivity (d’) with high-beta or response criterion (beta) for gamma right FEF patterns come in support of the magnetic nature, pattern frequency and behavioral specificity of our findings. The visual paradigm we used evaluates two serially presented visual tasks performed on the same near-threshold target: a visual discrimination (evaluated through performance) and a conscious visual detection task (assessed by the SDT measures indicated above). We used lateralized target presentation as we aimed to manipulate the FEF’s role in visuo-spatial allocation signaled by specific oscillations to drive visual improvements, emulating to a certain extent the details of a non human primate study that inspired the use of beta and high gamma frequencies as related to attentional orienting (Buschman and Miller, 2007). Signal detection Theory (SDT) outcome measures for the detection of lateralized stimuli have been widely used without raising major criticisms (Grosbras and Paus, 2003; Chica et al., 2011; Leo et al., 2011; Chanes et al., 2012; Chica et al., 2012). Particularly in our paper, the attribution (left or right) errors Rahnev makes reference to, were equally distributed across conditions, accounted for a small proportion (3-7%) of the trials in which participants reported to have seen the target (Chanes et al., 2013), and as we tested, did not modify the results when fully integrated in our analyses as responses.

Suggestions for separating detection and discrimination blocks, the use of centrally presented targets, or their combination with peripheral cues suggested by Rahnev in his Journal Club are all very interesting options, but they would change the nature of the task and their underlying processes. One could easily hypothesize different signaling mechanisms and reduced leverage for oscillation-based modulations of eccentric, as compared to foveal target detections in absence of spatial uncertainty. Recent research has also shown the ability of visual cues to sculpt according to their spatial validity the effects of TMS pulses by manipulating the state of the FEF and its associated network (Chanes et al., 2012; Quentin et al., 2013), a process that could modify per se the nature of the interregional interactions underlying behavioral modulations by rhythmic
Supplementing the arguments by Rahnev, the lack of a grating discrimination effect (a proven sensitive marker of attentional orienting in lateralized cuing tasks, particularly when assessed through response reaction times) could be an additional proof suggesting a non attentionally-mediated effect for visual sensitivity improvements (Chica et al., 2011). One must remain cautious, since participants were requested to respond to this task as accurately as possible. Accordingly, discrimination was assessed in terms of performance instead of reaction times, which could have been a more sensitive marker of attentional orienting. Moreover, additional differences in the perceptual nature, precise behavioral demands and response conditions makes the interpretation of the dissociation between discrimination and attention challenging (see discussion in Chanes et al., 2012). A likely direct connectivity-mediated impact of frontal oscillatory patterns on cortical or subcortical (Quentin et al., 2013) visual nodes as also suggested by Rahnev, or an effect on neural substrates modulating access to visual consciousness, or decision making processes independently of attentional orienting need to be ruled out in further ad hoc studies.

Rhythmic TMS approaches are based on assuming an association between the input frequency and the rhythm of the oscillations entrained in neural assemblies within the targeted area. Coupled TMS-EEG recordings have shown that brief bursts of focal non-invasive neurostimulation have the ability to either induce phase setting effects, entrain oscillatory activity and/or boost the underlying natural oscillation frequency of the stimulated region. On the basis of evidence provided for TMS entrained alpha occipito-parietal oscillations related to attentional orienting in absence of task performance (Thut et al., 2011), it is reasonable to think that similar effects could be extrapolated to other input frequencies. Unfortunately, the evidence for entrainment at higher frequencies (such as high-beta or gamma) requested by Rahnev might remain for some time elusive given the short interpulse time lag left to record artifact-free data for reliable time frequency analyses, among other technical hurdles that need to be overcome. Significant effort through the use of more sophisticated TMS-EEG recording technologies in humans, but particularly intracortical
stimulation and recording approaches in animals by means of multi-electrodes (which might prove less sensitive to stimulation artifacts) will have to be invested to provide entraining research with further support in the decades to come. This should not stop the field from progressing and using in humans safe patterns of invasive and non-invasive rhythmic neurostimulation to keep providing relevant causal insights on the oscillatory basis of cognition, whose underlying mechanisms could be then explored further in invasive non-human primate experiments.

Indeed, the interest in rhythmic neurostimulation remains very high as brain networks could be characterized with regards to their nodes, connections and temporal dynamics but also according to their malleability to external perturbations and entrainment properties induced by magnetic fields or electrical currents. From a therapeutic point of view, rhythmic or arrhythmic random patterns of stimulation could be of particular interest not only to restore normal oscillatory rhythms tied to specific cognitive processes but also to prevent a build up of abnormal frequency-specific local or interregional synchrony. As an example, a recent MEG study (Rastelli et al., 2013) in right hemisphere stroke patients identified a brief build up of low beta activity in left prefrontal locations prior to target onset with visual omissions, and thus one could easily envision the use of episodic random arrhythmic patterns to provide such correlations with a causal basis and eventually reduce performance impairments.

All in all, in spite of the insightful caveats raised by Rahnev on future uses of rhythmic TMS, the neuroscience community must remain optimistic and excited about such new avenues. The developing field of oscillation-tailored neurostimulation for the causal exploration of cognition and its associated therapeutic applications have the potential to provide focal stimulation techniques such as TMS with a new life and novel uses in the cognitive neurosciences, and contribute to the advancement of brain science. Let’s allow such to sprout, grow and develop in the years to come.

References


