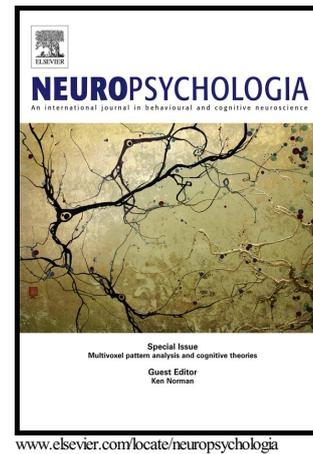


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Enhancing duration processing with parietal brain stimulation

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ABSTRACT

Numerosity and duration are thought to share common magnitude-based mechanisms in brain regions including the right parietal and frontal cortices like the supplementary motor area, SMA. Numerosity and duration are, however, also different in several intrinsic features. For instance, in a quantification context, numerosity is known for being more automatically accessed than temporal events, and durations are by definition sequential whereas numerosity

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can be both sequential and simultaneous. Moreover, numerosity and duration processing diverge in terms of their neuronal correlates. Whether these observed neuronal specificities can be accounted for by differences in automaticity or presentation-mode is however not clear. To address this issue, we used brain stimulation (transcranial random noise stimulation, tRNS) to the right parietal cortex or the SMA combined with experimental stimuli differing in their level of automaticity (numerosity and duration) and presentation mode (sequential or simultaneous). Compared to a non-stimulation group, performance changed in duration but not in numerosity categorisation following right parietal but not SMA stimulation. These results indicate that the right parietal cortex is critical for duration processing, and suggest that tRNS has a stronger effect on less automatic processes such as duration.

Keywords: Duration; Numerosity; transcranial Random Noise Stimulation (tRNS); Parietal cortex; Supplemental Motor Area (SMA); Automaticity; Presentation mode

1. Introduction

Behavioural and neuronal similarities between duration and numerosity processing have been taken to suggest that these dimensions share common mechanisms and neuronal correlates primarily located in the right parietal cortex (e.g. [Walsh, 2003](#)). Duration and numerosity are, however, different in many ways. One is in terms of how automatically these dimensions are accessed, with duration known for being less automatically processed than numerosity in quantification contexts (e.g., [Brown, 1997](#); [Dormal, Seron, & Pesenti, 2006](#); [Roitman, Brannon, Andrews & Platt, 2007](#)). This may explain why task-irrelevant numerosity typically interferes with duration processing, as well as with other magnitude dimensions such as the stimuli physical size (e.g., [Arend, Cappelletti, & Henik, 2014](#); [Dormal & Pesenti, 2013](#); [Henik & Tzelgov, 1982](#); [Javadi & Aichelburg, 2012](#); [Xuan, Zhang, He, & Chen, 2007](#)). Numerosity and duration also differ in terms of how they are typically presented. Temporal stimuli are often sequential in nature, since temporal events are necessarily defined as being before or after other events. In contrast, stimuli to be enumerated can be presented both sequentially (i.e., one element at a time) or simultaneously (i.e., all elements together; [Barth, Kanwisher, & Spelke, 2003](#); [Gallistel & Gelman, 1992](#)).

The extent to which these distinct features of numerosity and duration processes correspond to differences at the neuronal level, especially in the parietal lobes, is not fully understood. Indeed, a right hemispheric dominance has been suggested for duration processing (e.g., [Coull, Davranche, Nazarian, & Vidal, 2013](#); [Dormal, Dormal, Joassin, & Pesenti, 2012](#); [Lewis & Miall, 2003](#)), whilst numerosity processing is reported to recruit the parietal cortices bilaterally (e.g., [Kaufmann et al., 2005](#); [Piazza, Izard, Pinel, Le Bihan, & Dehaene, 2004](#)). Studies using Transcranial Magnetic Stimulation (TMS) have confirmed the crucial role of the right parietal cortex in duration processing ([Alexander, Cowey, & Walsh, 2005](#); [Buetti, Bahrami, & Walsh, 2008](#)), whereas stimulating the left IPS impaired

performance in a numerosity comparison task, whilst duration comparison was not affected (Cappelletti, Barth, Fregni, Pascual-Leone, & Spelke, 2007; [Lecce, Didino, Walsh, & Cappelletti, 2015](#); and Dormal, Andres, & Pesenti, 2008 respectively). It is also unclear whether these parietal activations are mode-specific or instead reflect overlapping effects for simultaneous (i.e., through space) or sequential (i.e., through time) presentation of the stimuli (Castelli, Glaser, & Butterworth, 2006; Dormal, Andres, Dormal, & Pesenti, 2010; [Nieder, Diester, & Tudusciuc, 2006](#)). Besides the right parietal cortex, numerosity and duration processing activate other brain regions such as the right frontal cortex (Dormal et al., 2012; [Hayashi et al., 2013](#)), which may support general working memory storage and decision-making (e.g., [Nieder & Miller, 2004](#); Rao, Mayer, & Harrington, 2001). Processing temporal stimuli also activate the supplementary motor area (SMA), which has been taken to suggest a link to the sequential mode of stimuli presentation or to motoric preparation, rather than to magnitude processing *per se* (Dormal et al., 2012; [Macar, Coull, & Vidal, 2006](#)).

Here we aimed to investigate the extent to which differences in automaticity and in the mode of presentation between numerosity and duration may account for the different involvement of the right parietal lobe in these tasks. To this aim, we used right parietal or SMA transcranial random noise stimulation (tRNS) which is known for changing cortical excitability (e.g., [Terney, Chaieb, Moliadze, Antal, & Paulus, 2008](#)). We used a tRNS protocol rather than classical transcranial direct current stimulation (tDCS) for two main reasons: (1) tRNS showed stronger effect than anodal tDCS, at least in a motor task ([Fertonani, Pirulli, & Miniussi, 2011](#)) and (2) tRNS was successfully used in a previous study by our group to enhance nonsymbolic numerical processing (Cappelletti et al., 2013; 2015). We combined tRNS with numerosity and duration tasks that allowed manipulating different levels of automaticity and modes of presentation. We predict that parietal tRNS may result in larger changes in performing the duration task because it relies on a less automatic process,

which in turn is likely to recruit more cognitive resources relative to more automatic processes like numerosity processing ([Andrews, Hoy, Enticott, Daskalakis, & Fitzgerald, 2011](#); [Gill, Shah-Basak, & Hamilton, 2015](#); [Schneider, Dumais, & Shiffrin, 1984](#); [Shiffrin & Schneider, 1977](#)). Indeed, it has previously been shown that noninvasive brain stimulation is likely to impact on a cognitive process when this is sufficiently demanding to recruit more cognitive and neuronal resources ([Gill et al., 2015](#); [Pope & Miall, 2012](#); [Popescu et al., 2016](#)). To assess whether presentation mode may account for some of the differences previously observed between numerosity and duration, we displayed numerosity both simultaneously and sequentially, and we targeted brain areas that are known for being more strongly involved in either magnitude processing (right parietal) or presentation-mode (SMA). Behavioural changes observed after SMA stimulation may suggest that this area is involved in processing both duration and numerosity, while no effect and/or an effect restricted to sequential presentations (sequential numerosity and duration) may indicate that this region is instead implicated in the presentation mode used. Using this comprehensive design with two tasks differing in their level of automaticity (duration and numerosity), two modes of stimuli presentation (sequential and simultaneous), and two target brain regions (right parietal cortex and SMA), in addition to Sham and to a no stimulation group used as control conditions, we aimed to provide a finer characterisation of the cognitive and anatomical features that define duration and numerosity processing.

2. METHOD

2.1 Participants

Thirty-nine right-handed, neurologically healthy volunteers (28 females; mean age: 24 \pm 3.9 years) with normal or corrected-to-normal vision gave written informed consent to take

part in the experiment. They were randomly assigned to one of three groups; thirteen of them received tRNS on the right parietal cortex (Parietal group), thirteen received stimulation on the SMA (SMA group), and thirteen received no stimulation (No Stimulation group). The experimental protocol was approved by the Ethics Committee of University College London, UK.

2.2 Tasks and stimuli

Participants performed three tasks: (1) a duration categorisation of a single dot stimulus (Dur), (2) a numerosity categorisation of sequentially presented dots (SeqN), and (3) a numerosity categorisation of simultaneously presented arrays of dots (SimN). To avoid potential explicit or implicit counting strategies, short durations (i.e., under 1 second) and non-subitizable sets (i.e., above 5 items) were used. Stimuli presentation were controlled by a laptop with a 15.6" screen using E-prime program (Schneider, Eschman, & Zuccolotto, 2002), at the viewing distance from the monitor of approximately 50 cm.

Stimuli in the Dur task were a single black dot (4° diameter) presented at the centre of the screen for short (500 or 600 ms) or long (800 or 900 ms) durations (Figure 1A). The stimuli in the SeqN task were sequences of 5, 6, 7 or 8 black dots (4° diameter) presented one at a time at the centre of the screen (Figure 1A). Sequences with 5 and 6 dots corresponded to the "few" category, those with 7 and 8 dots to the "many" category. The total duration of the sequences was kept constant (1500 ms), whereas the duration of each stimulus and of the inter-stimuli intervals varied randomly between 50 and 270 ms. The stimuli in the SimN task were composed of linear arrays of 5, 6, 7 or 8 black dots displayed in the centre of the screen (Figure 1A) for 150 ms, thus making counting strategies very unlikely to be used. The total length of the arrays was held constant (11.3°), while the diameter of each dot and the inter-

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stimuli spacing varied between 0.4° and 1.7° . The cumulative area covered by the dots in each array was held constant. Non-periodic signals were used such that (i) temporal ratios did not constitute a potential confound as rhythm biases were avoided in the SeqN task; and (ii) spatial ratios and dot size were not confounded with numerosity, such that pattern recognition was avoided in the SimN task (for more methodological details, see Dormal et al., 2006; Dormal & Pesenti, 2007).

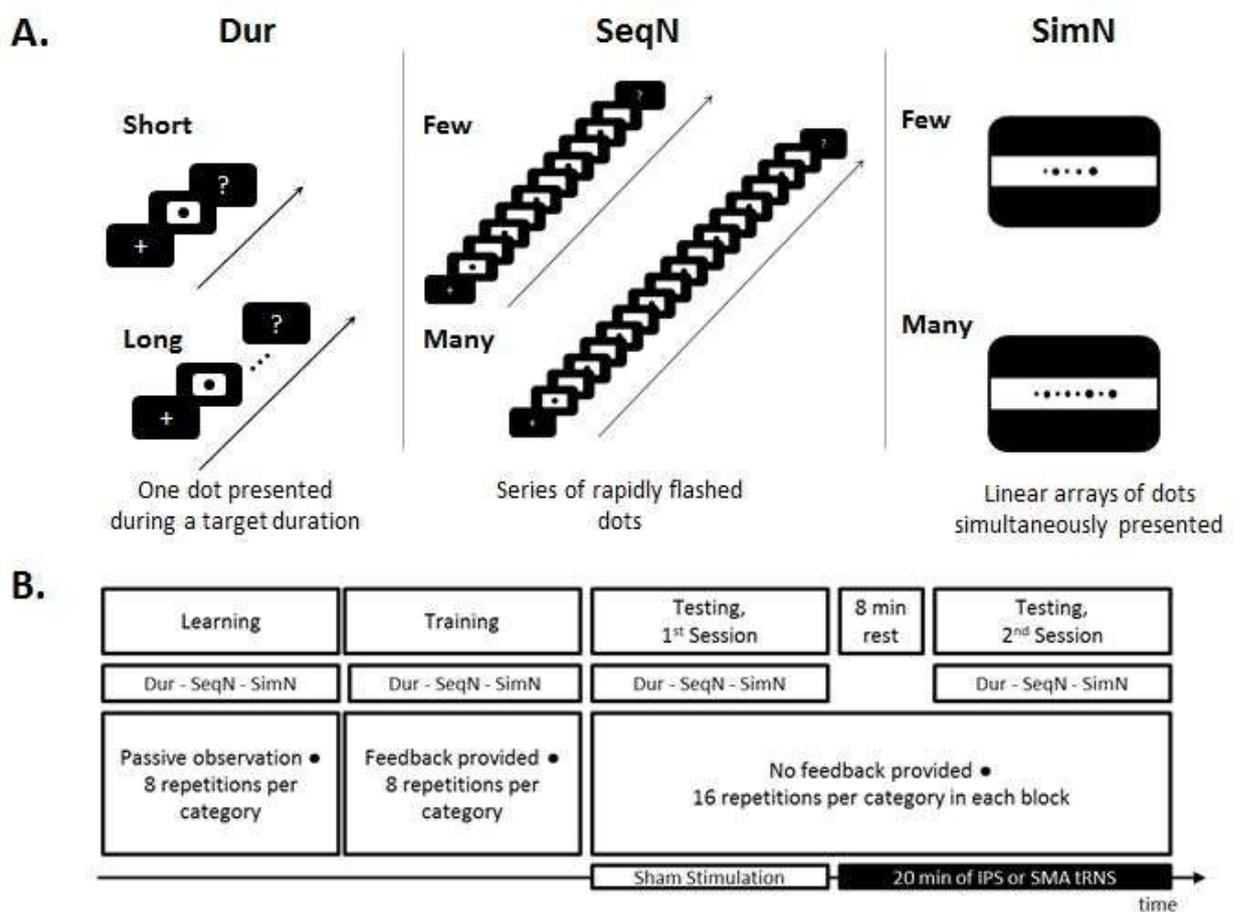


Figure 1. Experimental stimuli and design. (A) Example of stimuli for each category of the three categorisation tasks (Dur: Duration; SeqN: Sequential numerosity; SimN: Simultaneous numerosity). In each categorisation task, participants decided with a button-press whether a dot was presented for a “short” or a “long” period (Dur task), and whether each array contained “few” or “many” dots (SeqN and SimN tasks). (B) Each participant was informed of the three stages of the experiment, namely

learning, training and testing, and randomly assigned to one condition group (i.e., IPS, SMA or No Stimulation). The numerosity and duration tasks were presented in one of three pseudo-randomised orders.

2.3. Experimental procedure and tRNS protocol

In each group, participants performed two testing sessions in the same day; each testing session consisted of one block of each task (Dur, SeqN and SimN), with each block containing 64 trials corresponding to 16 presentations of each magnitude. In the Dur task, participants categorised each dot as being presented for a “short” (i.e., 500 or 600 ms) or a “long” (i.e., 800 or 900 ms) duration by pressing a left- or right-hand response button (letters “S” and “L” on the computer keyboard). In the SeqN and SimN tasks, participants decided whether each sequence/array of dots contained “few” (i.e., 5 or 6) or “many” (i.e., 7 or 8) dots by using the same two-choice button-presses. Participants were instructed to answer as accurately as possible; in each task, response latencies (RLs) corresponded to the time elapsed between the disappearance (i.e., offset) of the stimulus and the response key press.

Before the testing phase and for each categorisation task, participants learned the different experimental categories. The preliminary phase consisted of a learning block and a training block with feedback (Figure 1B). In the learning block, 8 trials of “short” and 8 trials of “long” duration were presented for the Dur task, and 8 trials of “few” and 8 trials of “many” stimuli for the SeqN and SimN tasks. Participants were instructed to observe each trial passively, with no mention of the duration of the presentation of a single dot or the numerosity of the sequences/arrays. The training block was identical to the testing block except that, after each trial, a visual feedback informed participants whether or not their answer was correct. Eight stimuli from each category (short/long or few/many) were

presented in a randomised order within each block and participants had to categorise each of them.

After the preliminary phase, each participant was randomly assigned to one group (Parietal, SMA or No Stimulation) and carried out two testing sessions consecutively, each session composed of one block of each categorisation task (Figure 1B). Participants in the Parietal or SMA groups performed the first session while they received sham stimulation. Immediately after, they performed the task again while receiving tRNS via a 5 x 7cm electrode positioned over the right parietal cortex (P4) or the SMA (FCz)¹ based on the international 10-20 EEG electrode placement (Figure 2A). A reference electrode (5 x 7cm) was fixed extra-cephalically on participants' left wrist, in order to avoid any confounding effect that could derive from positioning the reference electrode on the brain (Nitsche et al., 2008). Electrodes were encased in saline-soaked synthetic sponges and stimulation was delivered by a NeuroConn DC Brain Stimulator Plus unit (Rogue Resolutions, Wales, UK). Random noise stimulation (0.1 – 640 Hz) varying between ± 1.5 mA with fade-in and fade-out phase lasting 15 seconds was administered for 20 minutes. After 8 minutes of stimulation during which participants sat at rest, they performed the second testing session composed of the same three categorisation tasks. The initial sham condition was identical to the real stimulation (i.e., the electrodes were positioning on the same sites), except that the stimulation stopped after 30 seconds. The direct comparison between the sham and the active conditions allowed us to exclude unspecific effects of tRNS. The first session always corresponded to the sham stimulation in order to avoid any possible undesired residual effect of stimulation on the second session. To assess order or learning effects, a third group of new participants who received no stimulation was also tested. Participants of this third group performed the two

¹ Note that due to the size of the electrode (5x7cm) and the position of the SMA, the electrical stimulation necessarily targets the SMA in both hemispheres.

testing sessions without any stimulation. The order of the tasks was counterbalanced across participants.

3. Results

3.1 Task differences and difficulty effect without stimulation

Possible differences in the level of difficulty across the tasks were measured in terms of the classical distance effect ([Moyer & Landauer, 1967](#)). Durations were classified as ‘easy’ or ‘difficult’: easy durations corresponded to sequences lasting 500 and 900 ms, which are respectively at the lower or upper extreme of the range and are thus easier to discriminate; difficult durations corresponded to sequences of 600 and 800 ms. Following the same logic, sequences of 5 and 9 dots constituted the ‘easy’ numerosity, while sequences with 6 and 8 dots the ‘difficult’ numerosity.

To test whether the three tasks were equivalent in difficulty level, two initial analyses of variance (ANOVAs) were independently performed on the mean RLs of correct trials and error rate (ER) of the first session only, with GROUP (Parietal, SMA, No Stimulation) as a between-subject variable, TASK (Dur, SeqN vs. SimN) and DIFFICULTY (Easy vs Difficult) as within-subject variables. A main effect of DIFFICULTY was observed for both RLs ($F_{(1,36)} = 102.239, p < 0.001, \eta^2 = .740$) and ER ($F_{(1,36)} = 363.09, p < 0.001, \eta^2 = .910$): participants were slower and made more errors in more difficult items (RLs: 454 ± 80.8 ms; ER: $21.1 \pm 6.1\%$) relative to easier ones (RLs: 414 ± 68.9 ms; ER: $4.7 \pm 2.9\%$). No main effect of TASK (RLs: $F_{(2,72)} = 1.695, p = 0.191$; ER: $F_{(2,72)} = 1.132, p = 0.328$) and no interaction with GROUP (RLs: $F_{(4,72)} = 1.382, p = 0.249$; ER: $F_{(2,72)} = 0.723, p = 0.579$) were observed, suggesting that the three categorisation tasks were equivalent in terms of processing speed (Dur: 423 ± 82.1

ms; SeqN: 427 ± 87.7 ms; SimN: 452 ± 115.9 ms)² and difficulty (Dur: $13.1 \pm 6.1\%$; SeqN: $13.6 \pm 6.3\%$; SimN: $11.9 \pm 4.9\%$).

3.2 Test-retest and tRNS effects

To test for any tRNS effects, two ANOVAs were performed on the mean RLs of correct trials and the ER with GROUP (Parietal, SMA and No Stimulation) as a between-subject variable, SESSION (Session1³ and Session2), TASK (Dur, SeqN and SimN) and DIFFICULTY (Easy and Difficult) as within-subject variables.

The RLs analysis showed a main effect of SESSION ($F_{(1,36)} = 21.778$, $p < 0.001$, $\eta^2 = .377$) and of DIFFICULTY ($F_{(1,36)} = 79.427$, $p < 0.001$, $\eta^2 = .688$): irrespective of the group, participants were faster in the second session (406 ± 82.4 ms) compared to the first one (434 ± 74.1 ms), and they were also faster in the easier items (402 ± 68.8 ms) compared to the difficult ones (437 ± 84.1 ms). A main effect of TASK was also found ($F_{(2,72)} = 3.791$, $p = 0.027$, $\eta^2 = .095$) because the SimN task (444 ± 115.6 ms) was performed slower than the Dur task (404 ± 83.7 ms; $t_{(38)} = 2.600$, $p = 0.039$), while no difference was observed between the other tasks (SeqN: 411 ± 82.1 ms; SeqN vs. SimN: $t_{(38)} = 1.972$, *ns*; SeqN vs. Dur: $t_{(38)} = 0.404$, *ns*).

Importantly, a significant interaction between SESSION, TASK and GROUP was observed ($F_{(4,72)} = 3.105$, $p = 0.020$, $\eta^2 = .147$). In order to decompose this triple interaction, separate ANOVAs for each task were performed with GROUP (Parietal, SMA and No Stimulation) as a between-subject variable and SESSION (Session1 and Session2) as within-subject variable. While this analysis on SimN task revealed no main effects or interactions (all p -values > 0.1), the SeqN task showed a main effect of SESSION only ($F_{(1,36)} = 24.045$, $p < .001$, $\eta^2 = .400$):

² Despite no significant difference, a tendency to process the SimN task more slowly was observed. This difference might appear because participants could anticipate their answer in the sequential tasks (i.e., Dur and SeqN), but not in the SimN task. This therefore suggests that the error rate is a more valid measure to assess the equivalence of the three tasks.

³ For the Parietal and SMA groups, Session 1 always corresponded to sham stimulation.

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irrespective of the group, participants were faster in Session2 (394 ± 81.2 ms) compared to Session1 (427 ± 87.7 ms; Figure 2B). A main effect of SESSION was also present in the Dur task, ($F_{(1,36)} = 13.380$, $p = 0.001$, $\eta^2 = .271$), this time interacting significantly with GROUP ($F_{(2,36)} = 6.620$, $p = 0.004$, $\eta^2 = .269$). Therefore, participants of the Parietal group were faster in Session2 (344 ± 58.84 ms) compared to Session1 (432 ± 105.9 ms; $t_{(12)} = 4.992$, $p < 0.001$), while no difference between the two sessions was observed in the SMA and the No Stimulation groups (all p -values > 0.4 ; Figure 2B).

An equivalent analysis of ER revealed only significant main effects of TASK ($F_{(2,72)} = 3.964$, $p = 0.023$, $\eta^2 = .099$) and DIFFICULTY ($F_{(1,36)} = 476.905$, $p < 0.001$, $\eta^2 = .930$). Irrespective of the group, participants made more errors in performing difficult items (20.3 ± 5.6 %) compared to the easy ones (4.5 ± 2.5 %); and they made fewer errors in the SimN task (10.8 ± 3.7 %) compared to the Dur (13.3 ± 6.3 %; $t_{(38)} = 2.481$, $p = 0.054$) and SeqN (13.2 ± 5.4 %; $t_{(38)} = 2.589$, $p = 0.042$) tasks, the latter tasks not differing ($t_{(38)} = 0.122$, ns). No significant main effect of GROUP and no interaction including this variable were observed (all p -values > 0.1).

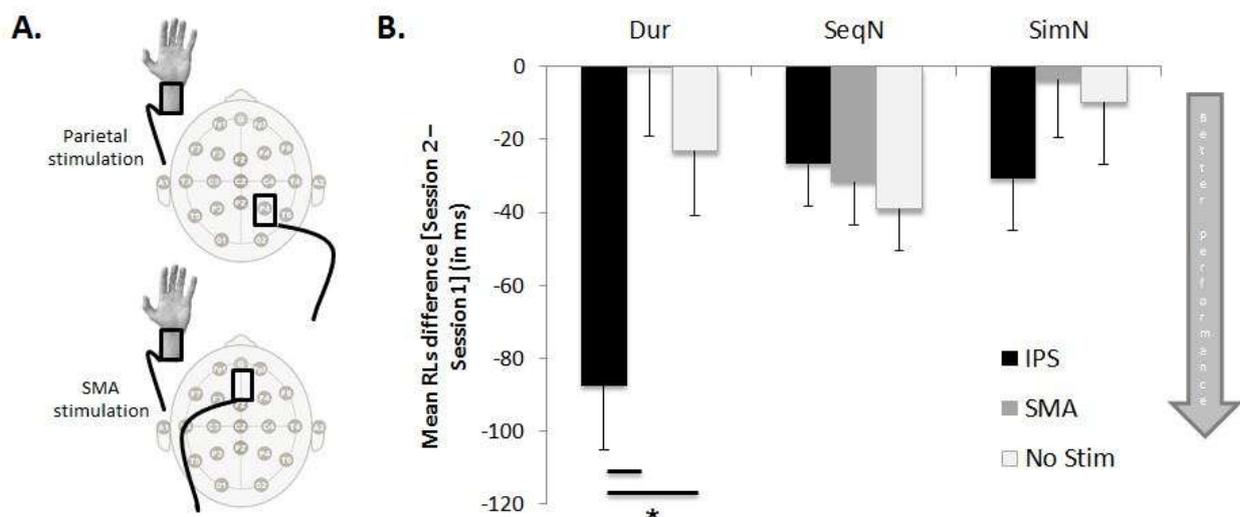


Figure 2. Stimulation design. (A) Stimulation sites: the right IPS and SMA areas were stimulated, corresponding to P4 and FCz according to the international 10-20 EEG system. An extra-cephalic reference electrode was used. (B) Difference in mean response latencies (RLs) between testing Session 2 and Session 1 (\pm SE) in the three tasks (Dur, SeqN and SimN) and stimulation groups (IPS, SMA and No Stimulation). Shorter RLs, namely an improvement, in the second session relative to the first correspond to a negative value, whereas longer RLs, namely a decline, correspond to a positive value. The asterisk indicates significant difference between groups ($p < 0.05$).

4. Discussion

Duration and numerosity processing are thought to rely on a common magnitude-based mechanism relying on brain areas around the right intraparietal sulcus, among other brain regions. However, duration and numerosity differ in terms of how automatically they are processed, with duration being processed less automatically than numerosity. These dimensions also differ with regard to how they are usually presented: temporal stimuli are by default sequential, whereas numerosity can also (and often) be simultaneous. Here, we tested whether differences in the gradient of automaticity and in the presentation mode between numerosity and duration may be reflected in two distinct brain areas being differently critical for numerosity and duration processing. Using parietal or SMA brain stimulation in combination with duration, sequential or simultaneous numerosity categorisation tasks, we showed that, relative to sham, right parietal-tRNS but not SMA-tRNS enhanced performance in the duration task only. This result supports the idea that the right parietal cortex plays a critical role in duration processing.

In contrast, we found no effect of right parietal stimulation on small numerosity processing irrespective of whether the stimuli were presented sequentially or simultaneously. This is in line with a previous TMS study showing no effect of right parietal stimulation on

small numerosity processing (Dormal et al., 2008), and suggests that the modulation of performance by tRNS in the DUR task does not merely come from the sequential mode of presentation of the stimuli in this task. Since before stimulation the three tasks did not differ in terms of difficulty, the effect of right parietal stimulation on duration processing is unlikely to be related to differences in attentional or difficulty demands between the tasks. The specific effect of parietal stimulation on duration processing thus suggests that processes sustained by similar brain areas but differing in terms of their automaticity could be differentially modulated by tRNS: a less automatically processed dimension (duration) may be more strongly modulated by stimulation whereas a more automatically processed dimension (numerosity), possibly recruiting less cognitive resources, is not. This result is in line with evidence showing that the behavioural effect of stimulation can be influenced by the cognitive demand of the task ([Andrews et al., 2011](#); [Gill et al., 2014](#); [Pope & Miall, 2012](#); [Popescu et al., 2016](#)). For tRNS to influence more automatic processes like numerosity manipulation, modification of the tasks or the stimulation design may be needed. Indeed, previous studies showing significant enhancement of numerical estimation abilities used a comparison task with a larger range of numerosities (i.e., between 5 and 16 dots) and with different ratios ([Cappelletti et al., 2013, 2015](#)). Moreover, as some neuroimaging studies revealed a bilateral activation of the parietal cortex during numerosity processing (e.g., [Kaufmann et al., 2005](#); [Piazza et al., 2004](#)), these two parietal regions could potentially play a crucial role and the stimulation of the left and the right parietal region with a dual-tRNS setting (i.e., two electrodes, one on the left and one on right parietal lobe) may be needed to observe significant changes of performance.

Neuroimaging studies have frequently showed that SMA is activated in duration processing (e.g., [Macar et al., 2006](#); [Wiener et al., 2010](#)). Similar effects have been found regardless of the task used (motor or perceptual timing), the range of durations considered

(sub- or supra-second intervals), as well as in sequential numerosity processing (e.g., Dormal et al., 2012). In our study, however, SMA tRNS did not impact on duration and numerosity categorisation performance, suggesting that despite being involved in these processes, the SMA may not be critical for them.

In conclusion, our findings indicate that differences in the level of automaticity between numerosity and duration are reflected in neuronal differences between these magnitude dimensions. Specifically, the right parietal lobe appears critical for sub-second time processing but not for the manipulation of small numerosity sets.

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Enhancing duration processing with parietal brain stimulation

Highlights (3-5 bullet points, max 85 characters including spaces)

- Numerosity and duration share common mechanisms and neuronal correlates
- They differ in terms of automaticity and presentation mode
- Whether these differences modulate performance and neuronal correlates is unknown

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- Right parietal and SMA tRNS was used during numerosity and duration processing
- Increase in duration discrimination only was observed after right parietal tRNS

Accepted manuscript