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A SOFTWARE FOR TESTING AND TRAINING VISUO-MOTOR COORDINATION FOR UPPER LIMB CONTROL

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Highlights

- Upper limb rehabilitation can be accelerated through novel computer-based methods
- A specific software has been created to stimulate speed-accuracy tradeoff
- Navigating a cursor through a narrow path required greater attention and reduced speed
- The narrow path induced changes in brain areas related to cognition and motor execution

Abstract

Background: Developing methods to accelerate improvements in motor function are welcomed in clinical practice. Therefore, the aim of this study is to describe changes in brain activity related to the execution of motor tasks implemented on a software – the NeuroMaze – developed specifically to stimulate speed-accuracy tradeoff.

New Method: The NeuroMaze was tested in eleven young and healthy individuals in a single experimental session. The tasks consisted in moving a square appearing on the monitor by holding and dragging it with a mouse across paths of different widths (wide [2 cm] *vs* intermediate [1.5 cm] *vs* narrow [1 cm] widths). The mouse cursor speed and scalp electroencephalography (EEG) from the frontal, somatosensory and motor areas were recorded.

Results: The mouse speed is reduced by 15±6% and 48±7% from the wide to the intermediate and narrow paths respectively ($p<0.005$). Moreover, there was a greater beta EEG relative power in the narrow path in the frontal area of the brain when compared to the wide path ($p<0.05$). Similarly, the narrow path reduced the gamma EEG relative power in motor/sensorimotor areas when compared to the wide path ($p<0.05$).

Comparison with existing methods: The NeuroMaze is introduced as a method to elicit speed-accuracy tradeoff, and the authors are not aware of specific methods to establish fair comparisons.

Conclusion: The NeuroMaze creates conditions to stimulate brain areas related to motor planning, sensory feedback and motor execution using speed-accuracy tradeoff contexts. Therefore, the NeuroMaze may induce adaptations in patients undergoing upper limb rehabilitation.

Keywords: EEG, speed-accuracy tradeoff, motor control, clinical rehabilitation, neuroplasticity.

Introduction

Human motion is based on the refined interplay between the intend of moving and continuous monitoring from sensory information that adjusts such motor action (Bogacz et al. 2010; Heitz 2014; Perri et al. 2014). Single or multi-joint movements may involve high precision, high accuracy or a combination of both. These different movement demands often compete for brain resources, limiting the performance of one or both simultaneously. Therefore, performing highly accurate movements becomes more difficult if faster speed is required. This phenomenon is called Speed Accuracy Tradeoff (SAT), which is an adaptable decision making process highly present in daily life motor gestures (Bogacz et al. 2010; Heitz 2014; Perri et al. 2014). It has been shown that motor tasks involving SAT present with an increased brain activation within the frontal cortex, pre-supplementary motor area (pre-SMA) and dorsolateral pre-frontal cortex area (DLPFC), which are related to motor control/planning and decision making (Alexander and Crutcher 1990; Inase et al. 1999; Shima et al. 2015). Such involvement of various cortical areas in SAT during motor actions (Forstmann et al. 2008; Ivanoff et al. 2008) may provide a rich context for stimulating neuroplasticity in clinical settings. The challenge is to provide an adequate technique for inducing and assessing such neuroplasticity during the performance of SAT.

There is a vast literature describing cortical plasticity following rehabilitation protocols using magnetic resonance imaging (Ivanoff, Branning and Marois, 2008; Belardinelli *et al.*, 2017; Galetto and Sacco, 2017), magnetoencephalography (Jamali et al. 2014; Ang et al. 2015; Mohr et al. 2016; Belardinelli et al. 2017) and non-invasive transcranial magentic stimulation (TMS; Kubis 2016; Stinear 2017). However, the range of movements allowed for scanning is highly restricted, as individuals being scanned must remain stationary and not all patients may tolerate the application of TMS. Movements involving multi-joint control and trunk stability may

provide more ecological validity to rehabilitation settings, as these movements are performed in real life. In such cases, surface electroencephalography (EEG) has been widely used to access electrocortical activity (Gramann et al. 2011; Brauchle et al. 2015; Oliveira et al. 2018; Yoshida et al. 2018). Some advantages of using EEG are its low cost when compared to other brain imaging equipment, high temporal resolution and the possibility of acquiring data in more natural settings (Reis et al. 2014; Hamacher et al. 2015; Oliveira et al. 2016).

Surface EEG has recently also been used to describe brain plasticity following motor rehabilitation (Ang et al. 2015; Galetto and Sacco 2017; Iyer 2017). Previous SAT studies have found neural oscillations in the pre-frontal cortex and pre-SMA depending on whether patients should perform movements focusing on speed or accuracy (Forstmann et al. 2008; Wenzlaff et al. 2011; Pastötter et al. 2012; Perri et al. 2014). Specifically, increased activity has been shown in pre-SMA under speed instructions and increased acitivity in DLPFC when patients focused on accuracy (Wenzlaff et al. 2011; Perri et al. 2014). Forstmann et al. (2008) found a focused, highly reliable increase in activity in the right pre-SMA when preparing for fast motor actions (Forstmann et al. 2008). However, to date such measures require a technical expert and are not readily available in the daily clinical setting.

In the current study, we present a novel computer-based software – the NeuroMaze – which aims to assist therapists and patients to conduct training interventions focusing on SAT. The software is editable and can stimulate patients to perform multi-joint upper limb movements in a controlled setting. We tested the NeuroMaze in healthy individuals while surface EEG was acquired from trials where different SAT settings were established. The results showed that the NeuroMaze can elicit specific changes in electrocortical activity depending on the level of

accuracy required to complete the task, being highly suitable for widespread use in clinical settings.

Methods

Participants

Eleven healthy adults (6 males, 5 females, mean±SD age: 23±1.73 yrs, body weight: 78±16.73 kg, height: 177±9.79 cm) with normal or corrected-to-normal vision volunteered for the experiment. Inclusion criteria for the experiment were ageing between 18 and 30 years, and right-hand dominance. Exclusion criteria included left-handed dominance, color blindness or any history of neurological disorders, recent (within 6 months) upper limb injury, or vestibular dysfunction. All participants provided verbal and written consent before participation, and the procedures were in accordance with the ethical committee of Northern Jutland, Denmark.

Experimental Setup

The experiment was conducted in a single session. Initially, participants were familiarized with the testing equipment and the tasks to be performed. Participants were instructed to adjust the height of the chair and of a 22” monitor located in front of them to their comfort. The tasks consisted in moving a square appearing on the monitor by holding and dragging it with a mouse across two distinct paths for three different path widths. As presented in Figure 1, the two paths were a straight line and a multi-directional path, while the three path widths were 2 cm (Wide), 1.5 cm (Medium) and 1 cm (Narrow). Participants were instructed to move this square as fast and as accurate as possible throughout the paths. Therefore, the narrower the path, the more difficult it becomes to move the square quickly through the path. During all tasks, scalp EEG was recorded. Following EEG preparation, participants were allowed to experience the different

paths and widths for approximately 5 minutes. Subsequently, EEG recordings were conducted during the performance of one trial in each path and width for all participants.

INSERT FIGURE 1 HERE

Computer-based interface: NeuroMaze

The NeuroMaze application was implemented on Matlab version R2017a (The Mathworks, Natick, MA). The NeuroMaze tracked the moving square position throughout the duration of the task, and the moving square was immediately frozen in space every time it crossed the path boundaries. The freezing of the square position was relevant because it served as instantaneous punishment related to crossing the path boundary. Moreover, the freezing of the moving square acts to break the ongoing movement planning, forcing the user to re-engage to the task using a fresh movement plan. Moreover, the mouse cursor was not visible when the square was frozen, and the participant should release the square (by unclicking the mouse) whenever the square became frozen. The square was immediately moved towards the center of the path in the exact same travelled distance when the participant released the mouse click, and the participant should hold the square again and keep moving it through the path until reaching its end. An illustrative video of a young healthy individual performing a task on the NeuroMaze has been added as Supplementary video. The NeuroMaze tracked and saved the mouse horizontal and vertical trajectories as output from all trials for all participants (Figure 2A). The mouse data sampling frequency was 1000 Hz.

INSERT FIGURE 2 HERE

EEG recordings and processing

EEG data were recorded using a wireless V-Amp 16-channel system (Brain Products Inc., Gilching, Germany), sampled at 500 Hz. The recorded channels were: Fp1, Fp2, F7, F3, Fz, F4, F8, C3, Cz, C4, P3, Pz P4, O1 and O2. Channels F3, C3 and P3 were selected by their location on the contralateral (left) side of the participants, as the task was performed with the right upper limb. The mouse clicks and unclicks were synchronized to the EEG recordings and saved as events into the EEG files. Left mastoid was recorded for re-referencing the EEG channel data. All processing and analysis were performed in Matlab using scripts based on EEGLAB 13.0.1b (//www.sccn.ucsd.edu/eeglab), an open source environment for processing electrophysiological data (Delorme and Makeig 2004). Initially, the EEG files from the straight line path (wide, medium and narrow) as well as the multi-directional path (wide, medium and narrow) were merged into a single dataset. Subsequently this single dataset was band-pass filtered between 1-100 Hz, and also filtered for removing line noise (50 Hz) using the Cleanline technique in EEGLAB (https://www.nitrc.org/projects/cleanline/). The next step was screening the channels for removal using the following methods: 1) channels with magnitude < 30 or > 10000 μV; 2) channels with kurtosis > 5 standard deviations from the mean; 3) channels uncorrelated with the surrounding channels ($r < 0.4$) for more than 1% of the total time; 4) channels with standard deviation substantially higher than the other measured channels. No channel were marked for removal from any subject in this experiment, maintaining all 15 recorded channels for further analysis. Subsequently, independent component analysis was performed on these merged datasets to identify and remove eye blinks (Plöchl et al. 2012; Ries et al. 2014) and artifacts related to muscle activity (Chaumon et al. 2015). On average, 1.3±0.2 eye blink components and 1.8±1.1 artifact components were removed from the EEG datasets. Following the rejection of specific independent components, the remaining independent components were back projected to the EEG channels.

Data analysis – Mouse trajectory

The horizontal and vertical mouse data were extracted in pixels from Matlab and subsequently converted to centimeters based on the screen dimensions provided from Matlab. Both horizontal and vertical mouse position vectors were derived to generate velocity vectors. The resultant instantaneous mouse speed (s, Figure 2B) was computed by using the formula:

$$s[t] = \sqrt{\dot{x}[t]^2 + \dot{y}[t]^2} \qquad (1)$$

where for each time frame t, s was the resultant speed from the mouse velocity vectors in horizontal (x) and vertical directions (y). The resultant mouse speed for a given trial was computed for the periods in which the mouse speed was above 0.1 cm/s, which indicated mouse movements. Likewise, the horizontal and vertical mouse speed were computed using these same events.

Data analysis – EEG spectral power

For each path type and width, the mouse "on" and "off" events were identified in the merged dataset and the power spectrum from each channel and epoch was computed for only these sectors (Hanning windowing,1024 ms FFT, 512 ms point window). The absolute power was subsequently averaged across epochs to obtain the mean EEG absolute power for the theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), gamma 1 (31–50 Hz) and gamma 2 band (51-90 Hz) for all conditions. For each participant, the absolute power extracted from the straight line condition was averaged across all three widths for each frequency band, in order to serve as a normalization parameter for the multi-directional EEG power. Therefore, the EEG power spectrum presented in the results section is relative to the straight line baseline condition. The use of straight paths as normalization parameter provided higher specificity to the baseline

values, with respect to the activation of brain areas related to visuo-motor coordination, motor control and planning and sensorimotor activation. Therefore, the results in this study refer only to the multi-directional path in three different widths, which were described as a percentage of the straight line path. Individual non-normalized power values are available in the Supplementary Table 1.

Statistical analysis

A one-way, repeated measures analyses of variance (RM ANOVA) was used to assess the effect of different path width (Wide *vs.* Medium *vs.* Narrow) on the time to complete the path, resultant mouse speed, horizontal and vertical mouse speed, as well as the EEG relative power in different frequency bands. Post-hoc tests were conducted using Bonferroni pairwise comparison. To account for multiple comparison, the p-value was reduced to $p<0.007$ and $p<0.004$ for the mouse speed and EEG absolute relative statistical analysis, respectively. Bonferroni tests were used as pairwise post-hoc analysis. Moreover, partial eta-squared effect size (ηp^2, defined as the ratio between the sum of squares from a given effect by the total sum of squared from all effects and interactions) were computed for each RM ANOVA test. All values expressed in the text and supplementary tables are mean ± SD. The statistical p-values from the EEG relative power were reported in scalp maps, in which the values below the significance level were color coded, whereas the values above significance level were masked in green.

RESULTS

There was a significant effect of the path width on the task duration ($F(2,20) = 107.36$, $\eta p^2 = 0.915$, $p<0.0001$). Participants moved the square through the widest path in 3.54±1.40 s, and this task duration increased for the Medium path (8.49±2.35 s) and especially for the Narrow

path (17.40±4.44). Post-hot tests revealed significant difference between all pairwise comparisons ($p < 0.005$).

Mouse speed

There was a significant effect of the path width on the resultant mouse speed ($F(2,20) = 127.78$, $\eta p^2 = 0.927$, $p<0.00001$, Figure 3), as well as the horizontal ($F(2,20) = 27.38$, $\eta p^2 = 0.859$, $p<0.005$) and vertical ($F(2,20) = 86.90$, $\eta p^2 = 0.915$, $p<0.001$) mouse speed separately. It was found that navigating the path with Medium and Narrow widths reduced the mouse speed by 15±6% and 48±7%, respectively, when compared to the Wide width. Post-hot tests revealed significant difference between all pairwise comparison in all three variables ($p < 0.001$).

INSERT FIGURE 3 HERE

EEG relative Power

There was a significant effect of the path on the EEG relative power for the channel Fz at the beta band ($F(2,20) = 6.40$, $\eta p^2 = 0.387$, $p<0.01$, Figure 4), as well as for the channels F3 and C3 at both Gamma 1 and Gamma 2 bands ($F(2,20) = 9.76$, $\eta p^2 = 0.494$, $p<0.001$). It was found that navigating the path with Narrow width reduced the Fz beta power when compared to the Wide width. In addition, navigating the Narrow path width reduced the F3 and C3 gamma 1 and 2 power when compared to the Wide width. Channels C3 and Pz presented trends ($p<0.05$) of significant changes related to the path width at the beta band. It was found that navigating the path with Narrow width increased the Pz beta power when compared to the Wide width. The mean and standard deviation for all data presented in Figure 4 are available in the Supplementary Table 2. An additional analysis was conducted using the EEG absolute power from the straight line path (Supplementary results), which was used as a normalization index for the more complex path. A similar RM ANOVA on the data from channel C3 revealed no

significant effects of the path width for the theta, alpha and beta bands, but there was a trend for significant reductions in the absolute power for both gamma 1 and gamma 2 bands ($F(2,20) = 3.45$, $\eta p^2 = 0.134$, $p = 0.055$).

INSERT FIGURE 4 HERE

DISCUSSION

This study aimed to design and test a novel computer-based tool to stimulate speed-accuracy tradeoff, which may be useful in rehabilitation programs. The developed computer software offered two types of paths and three different widths, diversifying the difficulty level for moving the mouse cursor across the paths. The results demonstrated that healthy individuals significantly reduce the mouse speed when navigating through narrower paths. Moreover, narrower paths induced greater beta EEG power in the frontal area of the brain, and reduced gamma power in areas related to sensorimotor control. These results suggest that this novel tool creates ideal conditions to stimulate brain areas related to motor planning, sensory feedback and motor execution using speed-accuracy tradeoff contexts. Therefore, it may contribute to induce positive adaptations in patients undergoing upper limb rehabilitation programs.

Previous literature has shown that performing highly accurate movements requires greater focus on movement control. Imposing the increase on movement speed in such conditions increased the likelihood of reducing precision (Bogacz et al. 2010; Heitz 2014; Perri et al. 2014). The results from the presented study corroborate such findings, as task duration increased as a function of the reduced path width, in which a higher emphasis on accuracy was required. Therefore, changes in path width can be a simple yet effective way to induce substantial changes in motor performance. It is expected that patients with brain disorders may have direction-

dependent changes in movement speed. Previous studies (Winstein and Pohl 1995; Rodrigues et al. 2017) have found changes in movement speed and accuracy of exercises among stroke patients compared to healthy participants during different directional motor tasks. Our population consisted of healthy participants doing movements in vertical and horizontal directions. They had no direction-dependent problems during the task contrary to the stroke patients from previous mentioned studies with comparable experiments. Therefore, the Neuro-Maze may contribute to rehabilitation training of patients with brain disorders such as Parkinson's disease, stroke, paralysis etc. who suffer from direction-dependent changes in movement speed. There have been studies implementing upper limb tasks for rehabilitation, which may be effective in improving motor function. Some tasks are robot-assisted to allow severely inflicted patients to perform movements, which are mostly available only for research-based clinical experiments (Krebs et al. 2004; Babaiasl et al. 2015; Hsieh et al. 2018). Exercises not involving movement-assisted control can also help patients to improve reaching skills through varying movement speed from between slow and fast (Hammerbeck et al. 2017). Therefore, the proposed NeuroMaze task may provide relevant stimulus to implement changes in movement speed combined with accuracy constraints.

Studies have shown an event-related desynchronization in the beta band approximately two seconds prior to a movement onset, while an event-related synchronization in the beta band occurs throughout the movement monitoring phase (Pfurtscheller et al. 2003; Wenzlaff et al. 2011). The intensity of the desynchronization and synchronization in the beta power increases proportionally to the accuracy demands and the number of repetitions (Houweling et al. 2008). Thus, beta rhythms are likely important for movement planning and this is enhanced according to the accuracy of the movement, especially in the contralateral hemisphere (Pfurtscheller et al. 2003; Houweling et al. 2008; Wenzlaff et al. 2011). The presented results showed intensified

beta synchronization as a function of reduced path width in Fz, equivalent to the pre-frontal cortex. Beta oscillations also appear relevant for muscle tonus prior to movements, since they increase as the steadiness of the movement increases according to the accuracy (Pogosyan et al. 2009). Therefore, the proposed application is highly promising to conduct training and testing protocols that will stimulate relevant brain areas involved in motor planning and control.

Gamma band oscillations, especially at higher frequencies (above 70 Hz) have been associated with movement control and are currently widely used in brain-computer interfaces (Darvas et al. 2013). Gamma band desynchronization occurs in the contralateral motor cortex during abduction of the index fingers, flexion and extension of the elbow and dorsiflexion of the feet, suggesting that gamma bands are relevant for controlling precision (Cheyne et al. 2008). Darvas et al. (2013) found significant changes in high gamma in the left motor area for right-handed individuals while watching hand movements. The study also found a significant difference in high gamma between contralateral and ipsilateral motor areas for individuals watching hand movements (Darvas et al. 2013) Another study by Darvas et al. (2010) found that a rise of high gamma activity begins in the contralateral pre-frontal cortex, moving to the motor cortex, and to the ipsilateral side as the movement is executed (Darvas et al. 2010). The fact that changes in power found in our results were focused on somatotopic brain areas, measured by C3 and F3, confirms the relevance of gamma bands to movement control. Moreover, the trend for reductions in gamma power for channel C3 in the simplest narrow straight line (Supplementary Results) indicates that the path width can influence the control of simple upper limb trajectories.

The context of reaching a target by moving a cursor from one point to another is present in previous research using such assistive devices (Krebs et al. 2007; Babaiasl et al. 2015; Hsieh et al. 2018). Despite the unquestionable relevance of these rehabilitation devices and software, the

restriction imposed for the cursor movement is only marked as a boundary on the task background. Therefore, the user/patient may extrapolate the boundary limits with no penalties to the task accomplishment. The NeuroMaze has been designed to impose a direct constrain to the path limit, which may increase the attentional aspect of the task. Moreover, combining the constraint to the varying path width increased the complexity of the sensorimotor integration towards maximizing movement precision. These aspects have not been explored in previous studies and may be relevant to improve visuo-motor coordination and movement planning/execution in patients undergoing upper limb rehabilitation. The practical benefits of such constraint to movement planning and performance in patients is yet to be proven, but results acquired from healthy young adults were encouraging.

This study successfully demonstrated that the use of speed-accuracy tradeoff contexts can elicit relevant changes in brain activation. However, only one path has been used for this demonstration. For future studies, the description of results from different paths and/or movement directions could provide additional insights into the use of computer-based software such as the NeuroMaze to stimulate brain plasticity. It is noteworthy that the current version of this software runs only on a specific programming language for research purposes. However, a stand alone version of the NeuroMaze as an executable software is being generated to eliminate the need for Matlab installation. This version is intended for clinical usage, where clinician will be able to generate reports and save the results from specific patients and sessions for long-term tracking of simple variables, such as number of errors and movement speed. Finally, there is a large inter-subject variability in the effect of path width on EEG spectral power. This result is somewhat expected, as a recent study showed that different subjects/participants are the largest source of variance on an EEG experiment, being larger than different types of EEG systems or different recording sessions (Melnik et al. 2017).

In summary, our results showed that the restrictions in path width and increased path complexity using the NeuroMaze can evoke changes in electrocortical activity in brain areas related to both motor control and motor planning in healthy individuals. These results indicate the potential of the NeuroMaze to stimulate brain areas affected by brain disorders in rehabilitation settings, potentially inducing the neuroplastic stimuli to improve motor function.

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Figure captions

Figure 1. Illustrative images of the different paths and width created using the NeuroMaze interface.

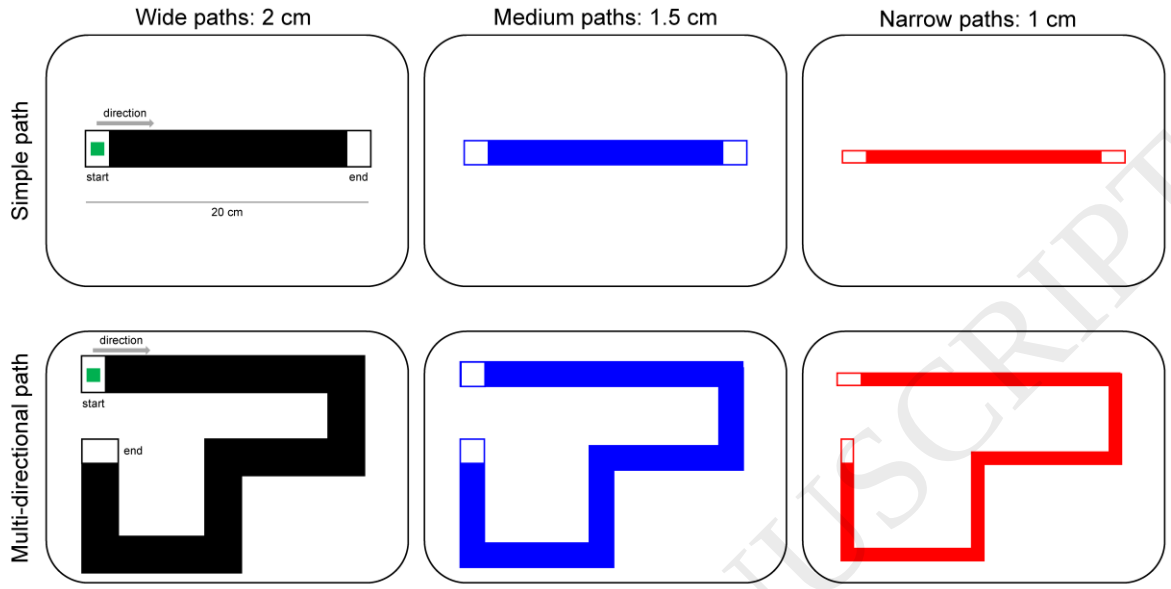

Figure 2. Mouse trajectory (A) across the multi-directional path for the Wide (black trace), Medium (blue trace) and Narrow (red trace) from a representative participant. In B, the respective mouse speed across the path for the three proposed path width conditions.

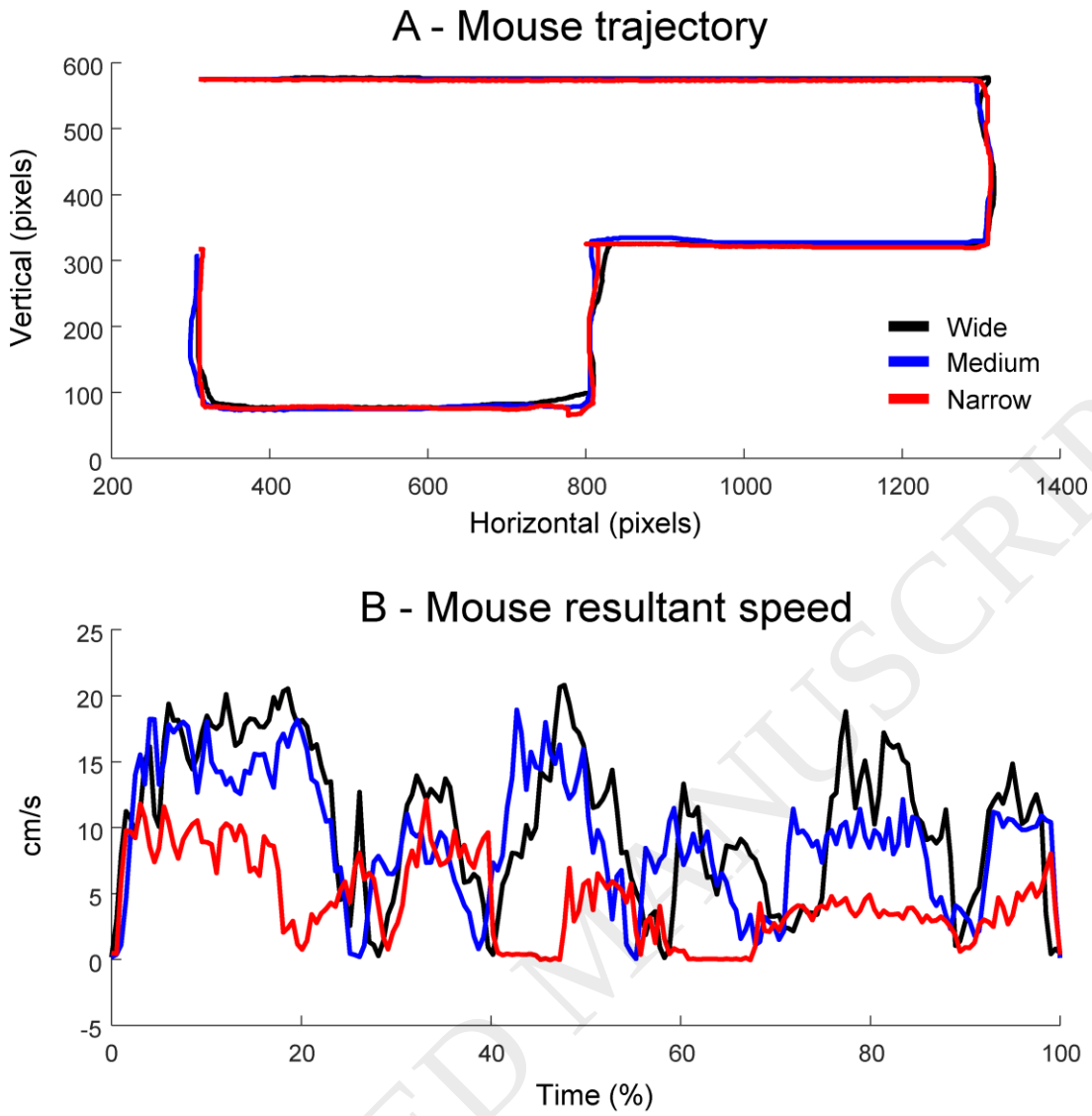

Figure 3. Mean ±SD resultant mouse speed (*left*), horizontal mouse speed (*center*) and vertical mouse speed (*right*) across the multi-directional path for the Wide, Medium (Med) and Narrow (Narr) conditions. * denotes significant difference in relation to Wide ($p<0.01$); † denotes significant difference in relation to Medium ($p<0.01$).

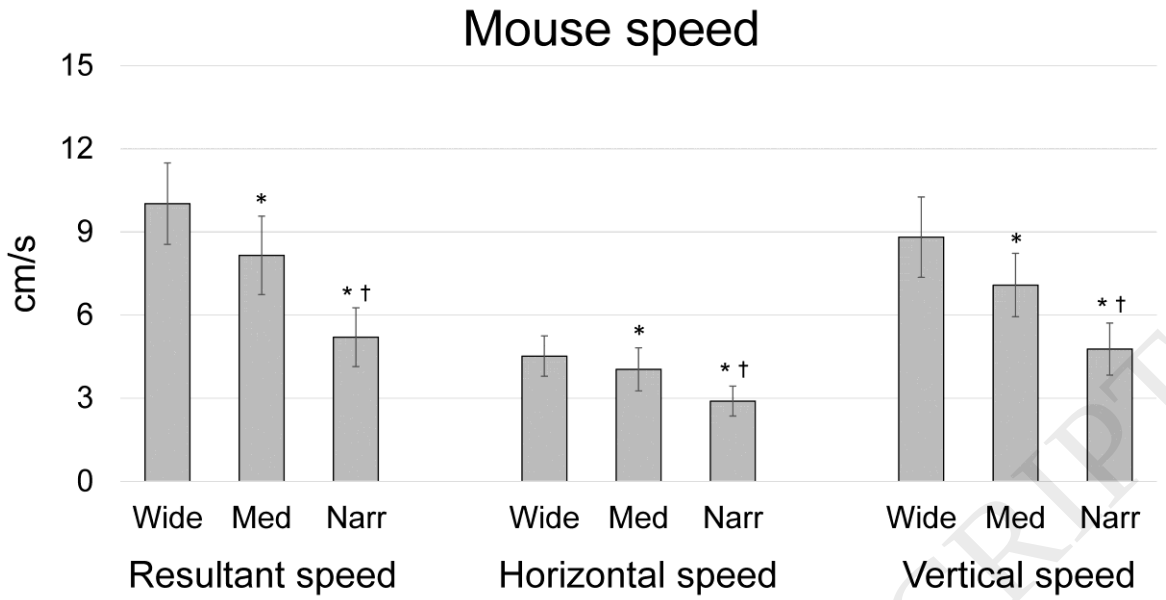

Figure 4. Grand average scalp maps illustrating the EEG relative power across all 15 channels recorded while participants moved the target square across the multi-directional path for the Wide, Medium and Narrow conditions. The columns represent the EEG frequency bands, while the rows represent the different width levels. Significant differences across conditions were marked in dark blue ($p<0.01$), while trends to significance ($p<0.05$) were marked in green/yellow. The remaining irrelevant/non-significant results were masked in dark red.