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Title: High-precision voluntary movements are largely independent from preceding vertex potentials elicited by sudden sensory events

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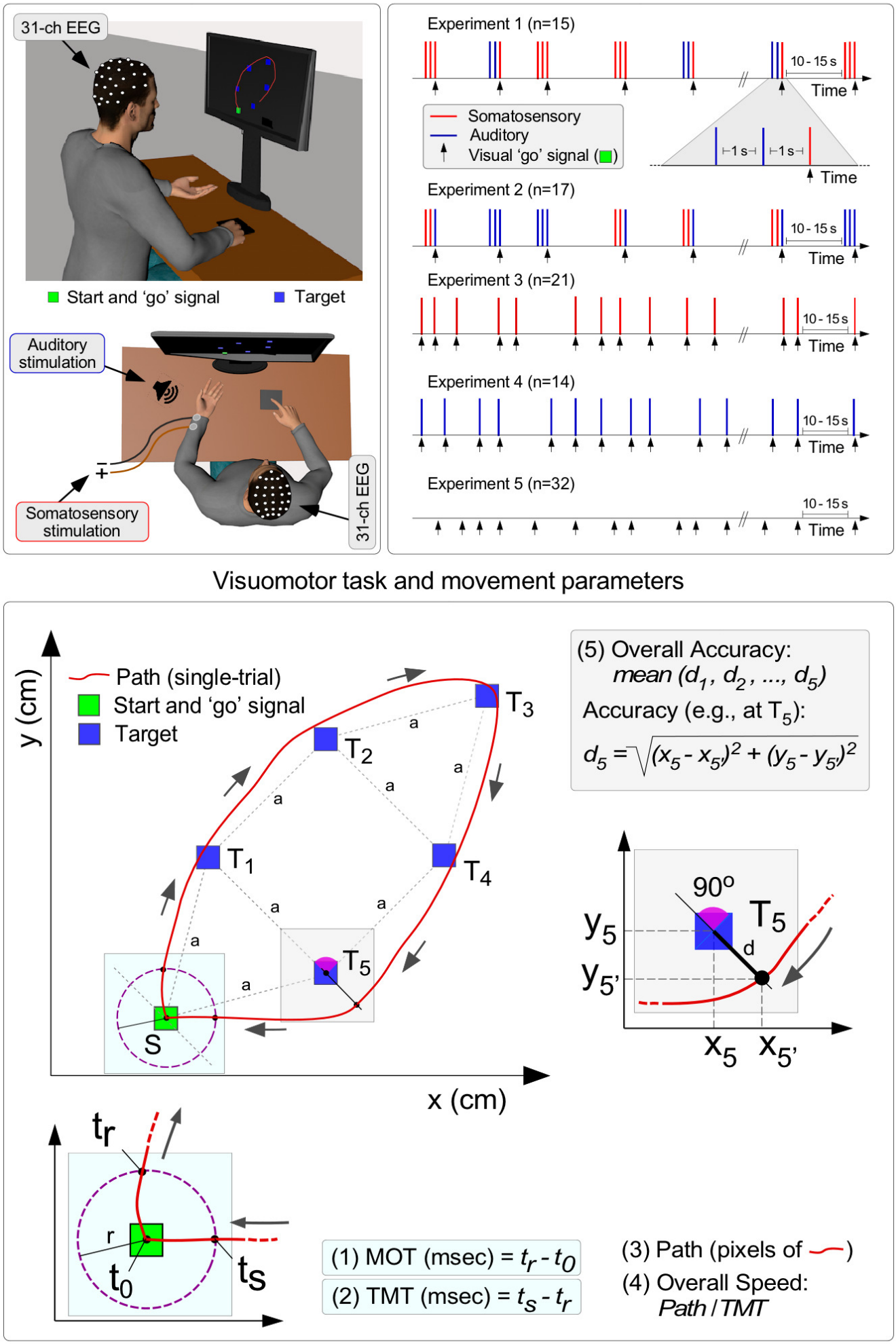
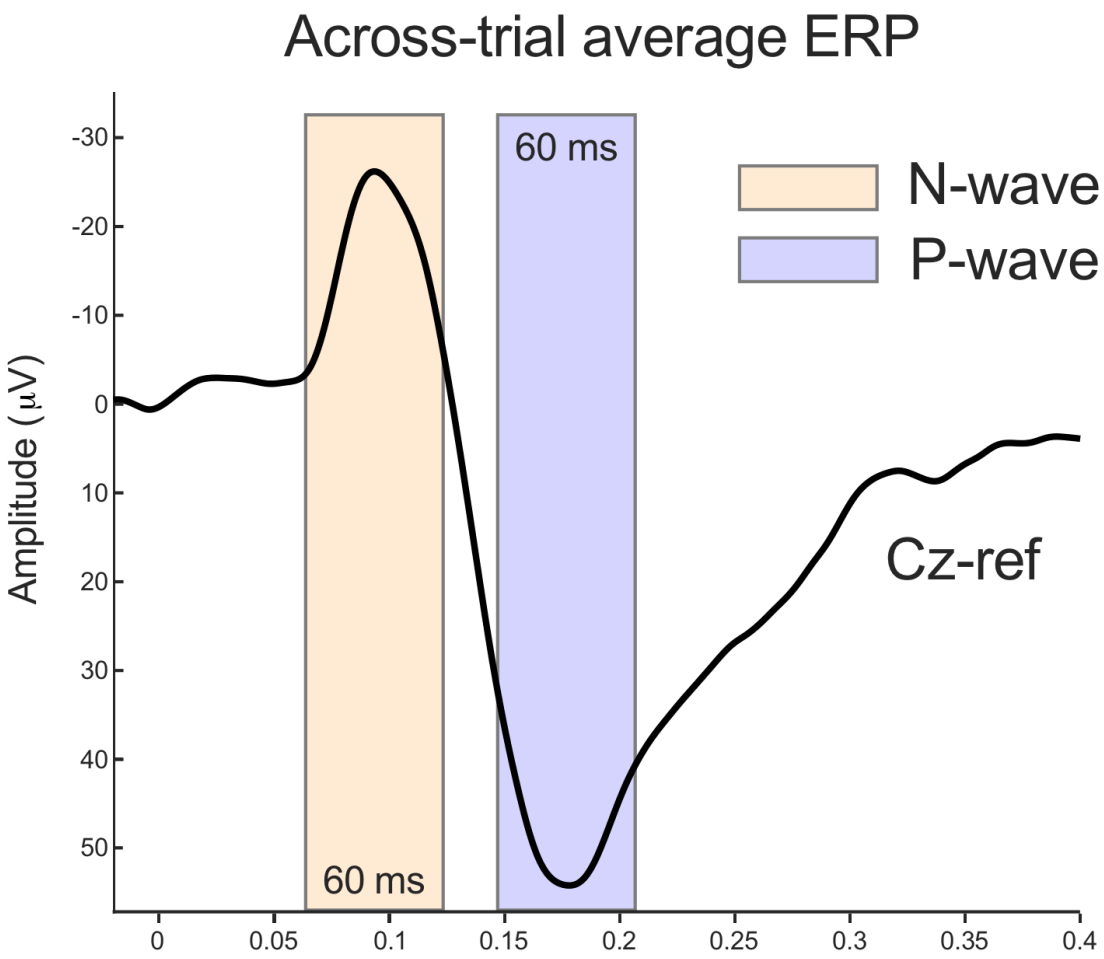
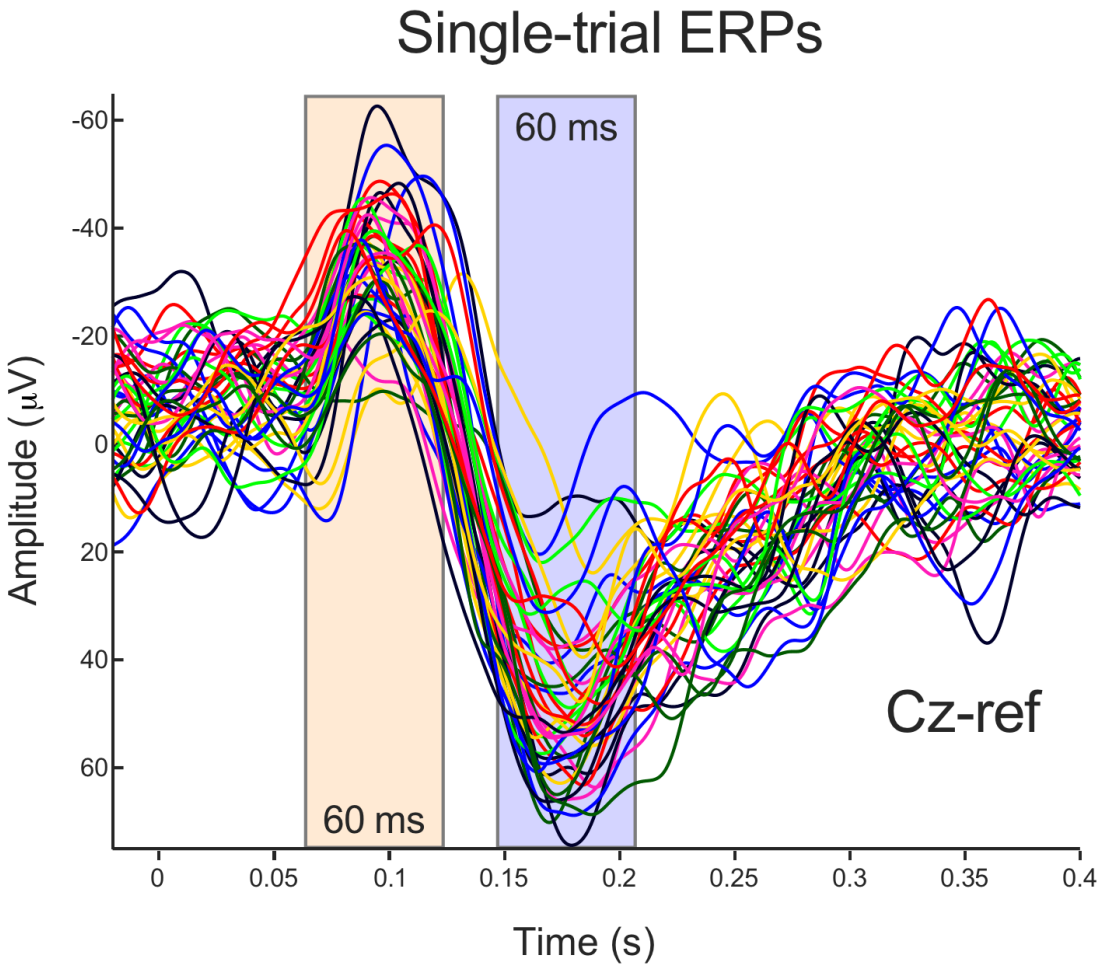
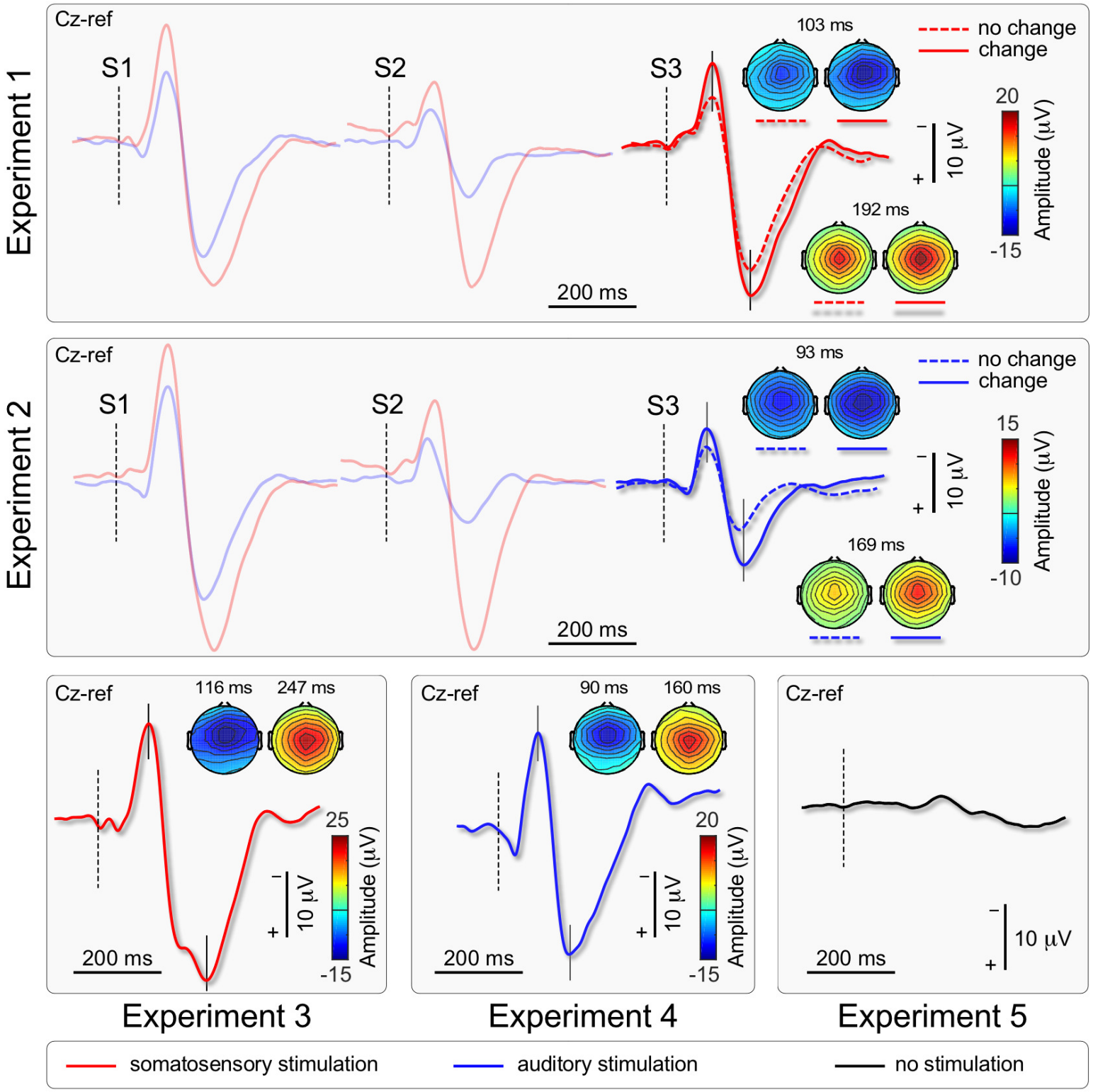
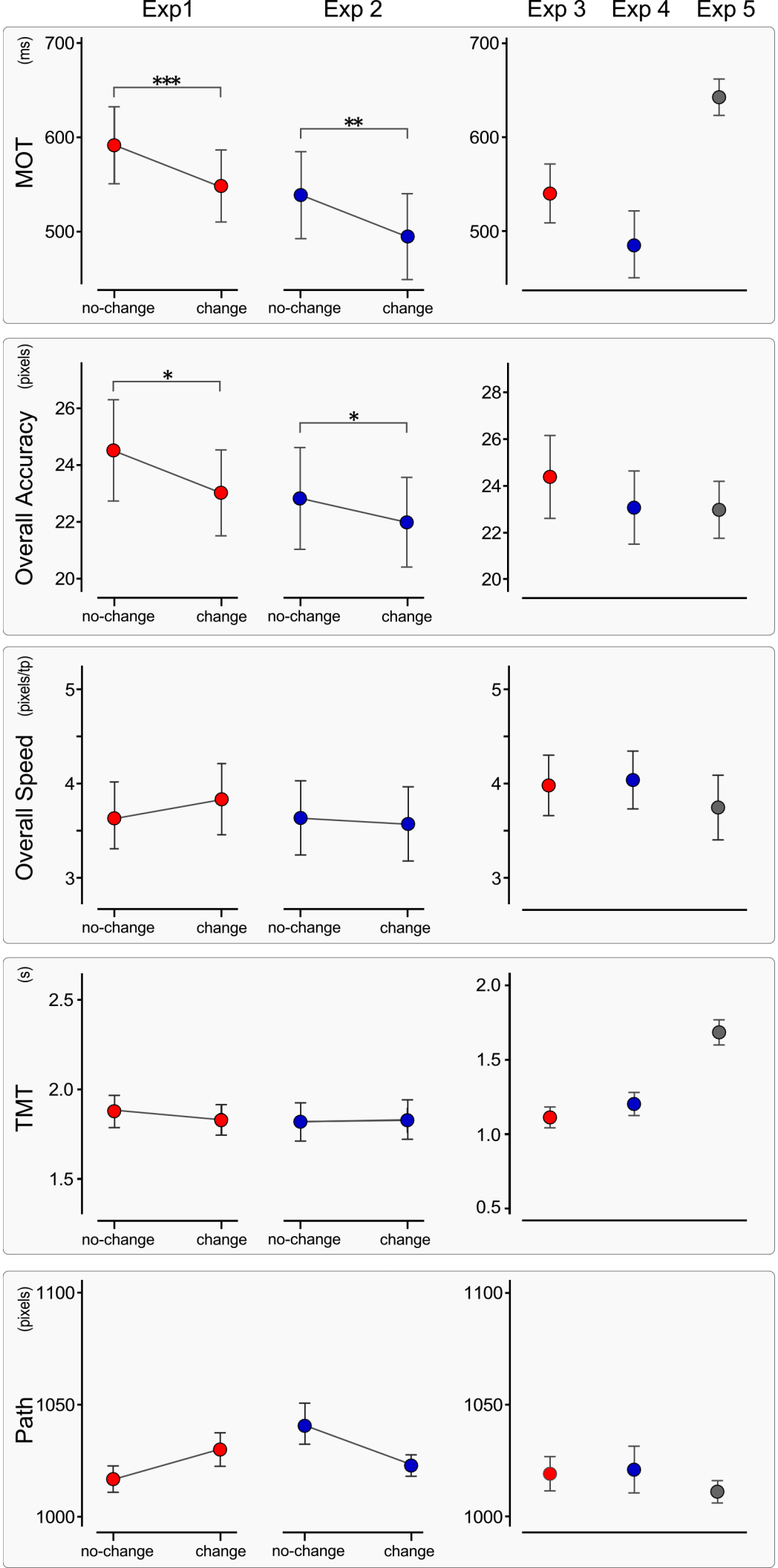
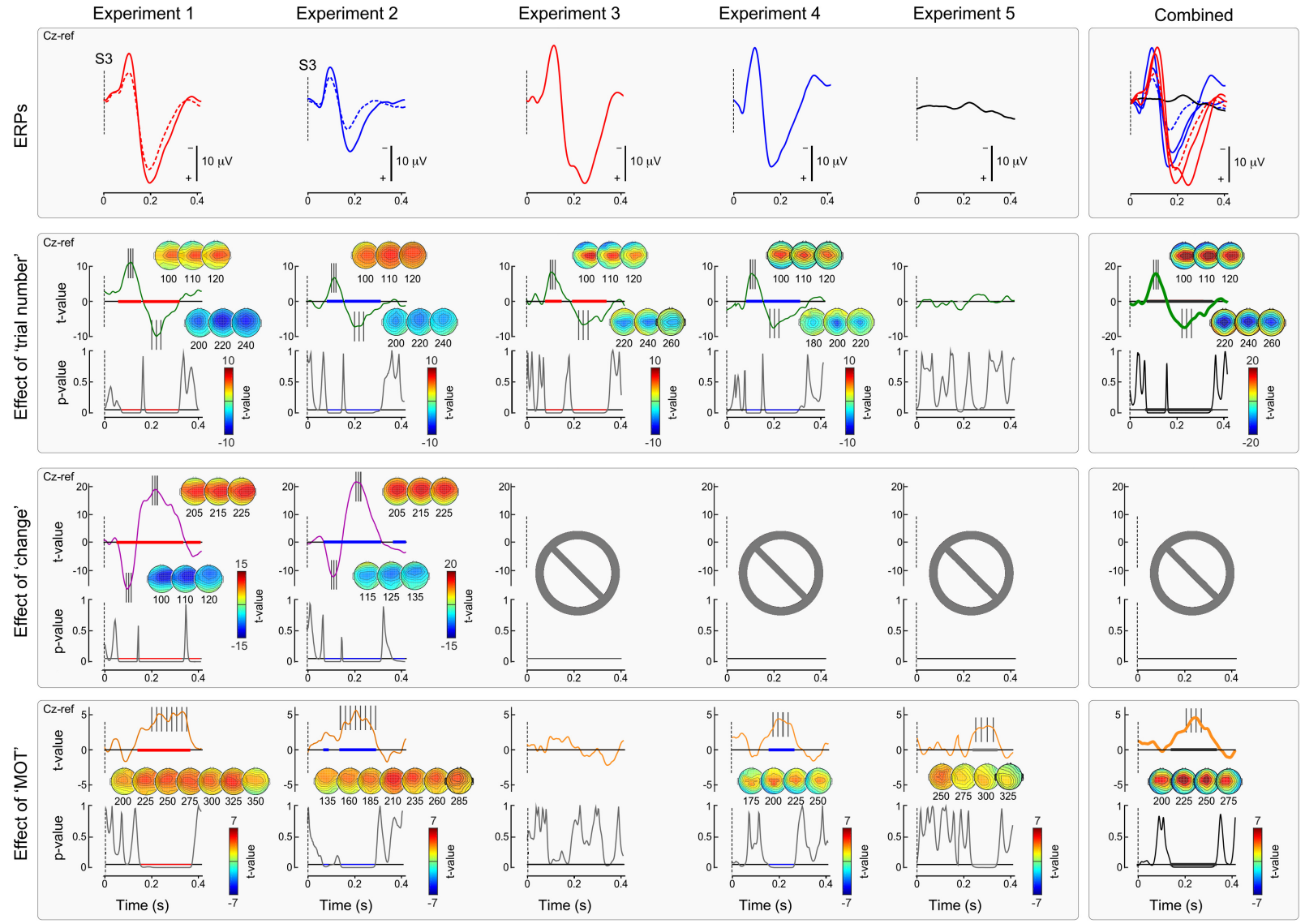

Stimulation and Recording
31-ch EEG
Start and 'go' signal
Target
Auditory stimulation
Somatosensory stimulation
31-ch EEG
Experimental paradigms
Experiment 1 (n=15)
10 - 15 s
Time
Somatosensory
Auditory
Visual 'go' signal
1 s
1 s
Time
Experiment 2 (n=17)
10 - 15 s
Time
Experiment 3 (n=21)
10 - 15 s
Time
Experiment 4 (n=14)
10 - 15 s
Time
Experiment 5 (n=32)
10 - 15 s
Time
Visuomotor task and movement parameters
y (cm)
Path (single-trial)
Start and 'go' signal
Target
T1
T2
T3
T4
T5
S
a
x (cm)
(5) Overall Accuracy:
mean (d1, d2, ..., d5)
Accuracy (e.g., at T5):
d5 = √((x5 - x5')2 + (y5 - y5')2)
90°
T5
d
y5
y5'
x5
x5'
tr
ts
t0
r
(1) MOT (msec) = tr - t0
(2) TMT (msec) = ts - tr
(3) Path (pixels of)
(4) Overall Speed:
Path / TMT

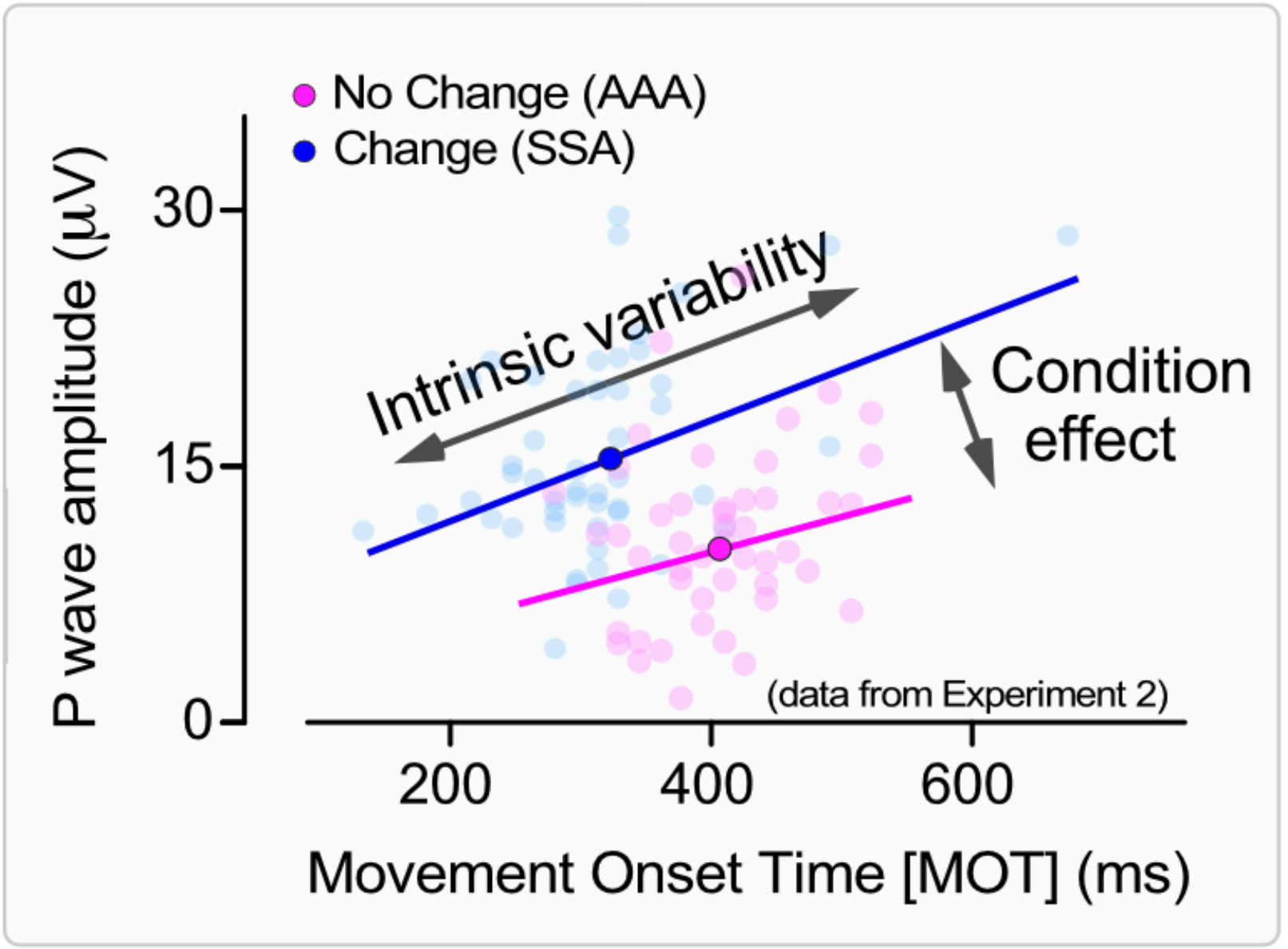

Across-trial average ERP
60 ms
N-wave
P-wave
Amplitude (μV)
-30
-20
-10
0
10
20
30
40
50
60 ms
Cz-ref
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4

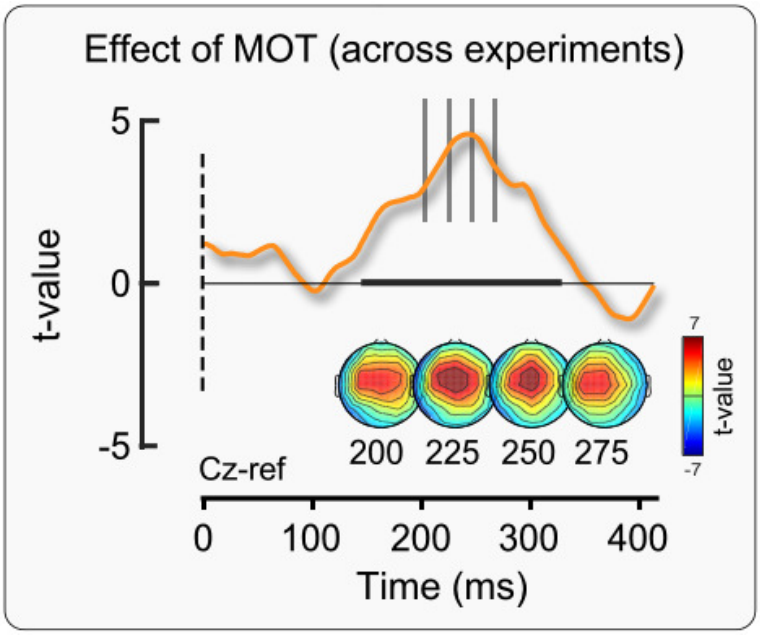

Single-trial ERPs
60 ms
Amplitude (μV)
-60
-40
-20
0
20
40
60
60 ms
Cz-ref
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
Time (s)

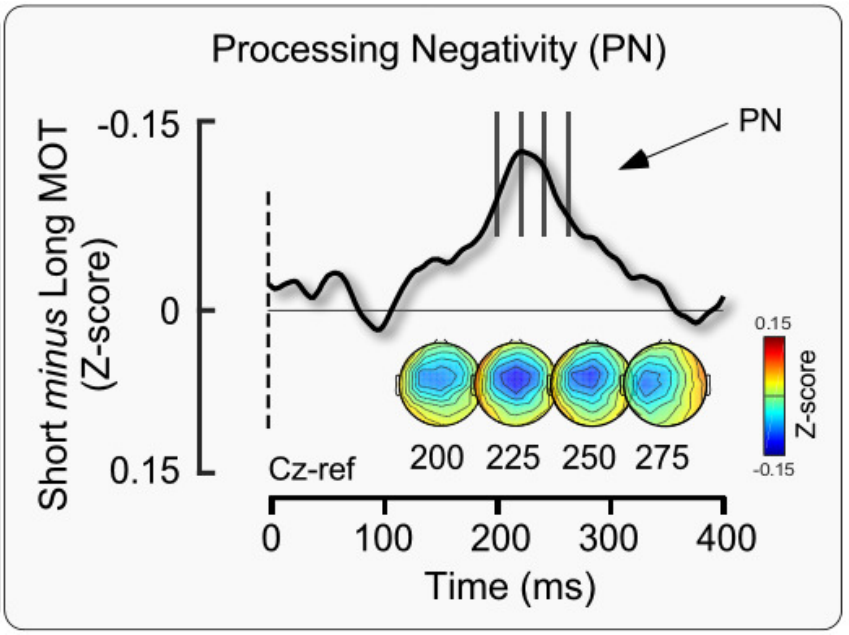

Experiment 1
Cz-ref
S1
S2
S3
103 ms
192 ms
no change
change
20
-15
Amplitude (μV)
10 μV
200 ms
Experiment 2
Cz-ref
S1
S2
S3
93 ms
169 ms
no change
change
15
-10
Amplitude (μV)
10 μV
200 ms
Cz-ref
116 ms
247 ms
25
-15
Amplitude (μV)
10 μV
200 ms
Experiment 3
Cz-ref
90 ms
160 ms
20
-15
Amplitude (μV)
10 μV
200 ms
Experiment 4
Cz-ref
10 μV
200 ms
Experiment 5
somatosensory stimulation
auditory stimulation
no stimulation


Exp1
Exp 2
Exp 3
Exp 4
Exp 5
MOT
(ms)
700
600
500
***
**
no-change
change
Overall Accuracy
(pixels)
26
24
22
20
28
*
Overall Speed
(pixels/tp)
5
4
3
TMT
(s)
2.5
2.0
1.5
1.0
0.5
Path
(pixels)
1100
1050
1000


Experiment 1
Experiment 2
Experiment 3
Experiment 4
Experiment 5
Combined
ERPs
Effect of 'trial number'
Effect of 'change'
Effect of 'MOT'
Cz-ref
S3
10 µV
t-value
p-value
Time (s)


No Change (AAA)
Change (SSA)
P wave amplitude (μV)
30
15
0
Intrinsic variability
Condition effect
(data from Experiment 2)
200
400
600
Movement Onset Time [MOT] (ms)


Effect of MOT (across experiments)
t-value
5
0
-5
Cz-ref
200 225 250 275
7
-7
t-value
0
100
200
300
400
Time (ms)


Processing Negativity (PN)
Short minus Long MOT (Z-score)
-0.15
0
0.15
PN
Cz-ref
200 225 250 275
0.15
-0.15
Z-score
0
100
200
300
400
Time (ms)

High-precision voluntary movements are largely independent from preceding vertex potentials elicited by sudden sensory events

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Number of figures: 7

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Table of contents category: Research Paper

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Key Points Summary

- Salient and sudden sensory events generate a remarkably large response in the human brain, the vertex wave (VW)

- The VW is coupled with a modulation of a voluntarily-applied isometric force

- Here, we tested whether the VW is also related to executing high-precision movements

- The execution of a voluntary high-precision movement remains relatively independent of the brain activity reflected by the preceding VW

- The apparent relationship between the positive VW and the movement onset time is explained by goal-related but stimulus-independent neural activities

- These results highlight the need of considering such goal-related but stimulus-independent neural activities when attempting to relate ERP amplitude with perceptual and behavioural performance

Abstract

Salient and fast-rising sensory events generate a large biphasic vertex wave (VW) in the human electroencephalogram (EEG). We recently reported that the VW is coupled with a modulation of concomitantly-applied isometric force. Here, in five experiments we tested whether the VW is also related to high-precision visuomotor control. We obtained three results. First, the saliency-induced increase in VW amplitude was paralleled by a modulation in two of the five extracted movement parameters: a reduction in the onset time of the voluntary movement ($p<0.005$) and an increase in movement accuracy ($p<0.05$). Second, spontaneous trial-by-trial variability in vertex wave amplitude, for a given level of stimulus saliency, was positively correlated with movement onset time ($p<0.001$ in four out of five experiments). Third, this latter trial-by-trial correlation was explained by a widespread EEG negativity independent from the occurrence of the positive VW, although overlapping in time with it. These results indicate that (1) the execution of a voluntary high-precision movement remains relatively independent of the neural processing reflected by the preceding VW, with (2) the exception of the movement onset time, for which saliency-based contextual effects are dissociated from trial-by-trial effects. These results also indicate that (3) attentional effects can produce spurious correlations between ERPs and behavioural measures. Whereas sudden salient stimuli trigger characteristic EEG responses coupled with distinct *reactive* components within an ongoing isometric task, the present results indicate that the execution of a subsequent *voluntary* movement appears largely protected from such saliency-based modulation, with the exception of the movement onset time.

Key words: saliency, vertex potential, event-related potentials, voluntary movement, motor control.

1. Introduction

Nervous systems have evolved to sense the external world, and make decisions resulting in actions that are appropriate to cope effectively with environmental changes. The detection of sudden and unexpected events is of paramount importance, as they often signal environmental threats or affordances that need to be reacted to swiftly.

Salient and fast-rising sensory events delivered to awake humans generate a remarkably large synchronization in the electroencephalogram (EEG), which takes the form of a biphasic potential, widespread and maximum over the scalp vertex ('Vertex Wave', VW; Bancaud et al., 1953). This biphasic vertex wave is evoked by stimuli of any modality, provided that they are salient enough (Bancaud et al., 1953; Walter, 1964; Mouraux and Iannetti 2009; Liang et al., 2010). Although the vertex wave has been traditionally interpreted as a byproduct of saliency detection, we recently provided evidence that it directly impacts on motor processing in healthy humans: the amplitude of the positive and negative peaks of the vertex wave is tightly coupled with a concomitant and longer-lasting modulation of an applied isometric force – a phenomenon called cortico-muscular resonance (CMR; Novembre et al., 2018). Remarkably, this CMR is not a stereotyped reflexive response, but strongly depends on the behavioural relevance of sensory information. Thus, this phenomenon likely reflects a neural system subserving purposeful behaviour in response to unexpected environmental events. The VW has been also suggested to be related to the execution of speeded goal-oriented defensive movements, such as hand withdrawal in response to a noxious stimulus (Moayedi et al., 2015). Notably, these motor tasks are either isometric (Novembre et al., 2018) or entail coarse movements requiring the activation of muscles with large motor units (Moayedi et al., 2015), and do not depend on accurate visuomotor transformations. Does the VW also affect the execution of subsequent high-speed and accurate voluntary movements entailing complex visuomotor transformations? This is the question addressed in the five experiments presented in this article.

Fifty-three healthy participants were required to perform a visuomotor task as fast and accurately as possible, while their EEG activity was recorded. We used a number of established measures to describe the temporal and spatial features of the voluntary movement (e.g., Teichner, 1954; Georgopoulos et al., 1981; Wolpert et al., 1995; Andrienko et al., 2008; Ranacher and Tzavella, 2014; Jones, 2015). On the basis of these measures we examined

whether there is a functional link between the VW and such subsequent motor behaviour. We performed an ad-hoc experimental manipulation of the VW amplitude, and also exploited the spontaneous trial-by-trial variability of the VW amplitude. In Experiments 1 and 2 we modulated the VW amplitude using an established paradigm that dissociates stimulus saliency from afferent sensory input (Iannetti et al., 2008; Valentini et al., 2011). In Experiments 3 and 4 we exploited the spontaneous trial-by-trial variability in VW amplitude, thus accessing intrinsic fluctuations in the function of the underlying neural system. In these experiments participants received either somatosensory or auditory stimuli, delivered either individually (Experiments 3 and 4) or in 1 Hz trains of three stimuli (Experiments 1 and 2). Thereby, we also examined the modality-specific vs supramodal nature of the observed effects. Finally, in Experiment 5 we explored the relationship between spontaneous EEG activity and motor behaviour, in the absence of a VW, to test whether the effects found in Experiments 1-4 were due to an EEG signal independent of the VW.

2. Methods

2.1 Ethical approval

Before providing their written informed consent, all participants were informed of the requirements of the study and the sudden sensation elicited by salient auditory and somatosensory stimuli. Participants were free to withdraw at any time. Experiments were conducted by suitably qualified researchers. The experimental procedures adhered to the standards set by the Declaration of Helsinki and were approved by the Ethics Committee of University College London (project number: 2492/001).

2.2 Participants

This study comprised 5 separate experiments. Fifteen subjects (4 women) aged 19-42 years (mean (SD): 25.9 (6.6) years) participated in Experiment 1. Seventeen subjects (7 women) aged 18-37 years (25.2 (6.1) years) participated in Experiment 2. Twenty-one subjects (14 women) aged 19-42 years (25.1 (6.1) years) participated in Experiments 3. Fourteen subjects (10 women) aged 19-42 (24.2 (6.1) years) participated in Experiment 4. Finally, the 32 subjects who took part in Experiments 1 and 2 also participated in Experiment 5. All participants were right-handed. Handedness was assessed using a short self-report questionnaire during the recruitment phase. Participants were asked to report which hand they

use to perform the following activities: writing, throwing and using a computer mouse. Only participants who reported using always the right hand in these activities were included. Participants reporting that they could perform any of these actions with their left hand were excluded from the study. The participants were naïve to the aims of the study and provided written informed consent. All procedures were approved by the UCL ethics committee.

2.3 Sensory stimuli and experimental setup

In all experiments, both behavioural and electroencephalographic (EEG) data were collected. In all experiments except Experiment 5, participants received either somatosensory or auditory stimuli, which were delivered either individually (Experiments 3 and 4) or in 1 Hz trains of three (Experiments 1 and 2). Sensory stimuli were delivered to or near the participants' left hand. Auditory stimuli consisted in a fast-rising tone (rise and fall time 5 ms, frequency 400 Hz, duration 50 ms), delivered through a single loudspeaker (CAT LEB 401) placed on the table in front of the participant's left hand. Somatosensory stimuli consisted in constant current square-wave electrical pulses (200 μs duration; DS7A, Digitimer) delivered transcutaneously through a pair of skin electrodes (0.5 cm diameter, 1 cm inter-electrode distance) placed over the left median nerve at the wrist. In all experiments, the intensity of auditory stimuli was ~85 dB (Pfefferbaum et al., 1979).

In Experiments 1 and 2, where both electrical and auditory stimuli were presented, the intensity of the somatosensory stimuli was adjusted individually by asking each participant to match the perceived intensity of the sensation elicited by auditory stimulation. The procedure for matching the perceived intensities was as follows: we first presented the auditory stimulus to the participants, and explained that they would have to judge the intensity of the sensation elicited by a subsequent somatosensory stimulus in comparison to the sensation elicited by the auditory stimulus. We started by delivering the somatosensory stimulus at an intensity level that we expected the participant would not perceive (5 mA). We then increased the stimulus intensity in steps of 1 mA until the participant reported that the stimulus was perceived. At this point we reminded the participant to report the sensation elicited by the electrical stimulus relative to the auditory one. We continued to increase the stimulus intensity by 1 mA and every 2-3 somatosensory stimuli we also delivered an auditory stimulus (in isolation). Participants would usually report that the sensation elicited by the somatosensory stimulus started to resemble that of the auditory when its intensity was around 20 mA. At this point, somatosensory and auditory stimuli were delivered alternatingly. While

the intensity of the auditory stimulus was kept constant, the intensity of the somatosensory stimulus was changed on the basis of the report: if the participant reported that the sensation of the somatosensory stimulus was less intense, we increased its intensity by 0.2 mA, until the participant reported a comparable sensation. At this point, the intensity of the somatosensory stimulus was decreased by 0.2 mA, until the participant reported that the sensation elicited by the auditory stimulus was more intense (Cornsweet, 1962). The threshold was defined as the intensity of somatosensory stimulation at which 3 consecutive response reversals were observed. As a result, the mean (SD) intensity of somatosensory stimuli was 28.4 (5.9) mA in Experiment 1 and 30.6 (3.3) mA in Experiment 2.

In Experiment 3, where only electrical stimuli were delivered, stimulus intensity was adjusted to match the mean intensity of somatosensory stimuli used in Experiments 1 and 2, unless the subjects felt the stimulus uncomfortable. The mean (SD) intensity of the somatosensory stimuli in Experiment 3 was 23.9 (5.0) mA. Both the intensity and the inter-stimulus interval used, made these stimuli unable to elicit a startle reflex (for a detailed discussion see Novembre et al., 2018).

All experiments took place in a dim, quiet and temperature-controlled room. Participants were seated comfortably with their arms resting on a table in front of them. Their right and left hands were placed symmetrically, ~45 cm from the participant's head, ~25° off the body midline, and ~30° below eye level. Participants performed a visuomotor task with the index finger of their dominant (right) hand using a touchpad (13.4 cm width x 12.9 cm length, Logitech t650) (Figure 1, top left). The visuomotor task is detailed in section 2.3 below. A 17'' monitor (60-Hz refresh rate, resolution 1280 x 1024 pixels [1 pixel = 0.2634 mm]) was placed on the table, ~50 cm in front of them. The height of the monitor was individually adjusted so that the centre of the screen was at eye level. The touchpad was positioned under the participant's right hand. The surface of the touchpad was defined by an *x*-*y* coordinate system with the *x*-axis oriented in the left-right direction and the *y*-axis in the antero-posterior direction. During the experiment, participants were required to keep their right forearm and wrist in contact with the table surface.

Sensory stimuli were delivered using the MATLAB Psychophysics Toolbox (MathWorks; Brainard, 1997). Triggers synchronized with the onset of all stimuli were sent to two computers used for acquiring behavioural and EEG data.

2.4 Experimental paradigm

In all experiments participants had to execute a visuomotor task, which is depicted in Figure 1. The task consisted in producing a single continuous clockwise movement of a cursor displayed on the screen, by sliding the right index finger over the touchpad's surface. Participants were required to start their movement from an initial position (the 'starting position') and pass the cursor through five targets located on the right half of the computer screen. The 'starting position', a gray square with sides of 20 pixels (5.3 mm) was always present at the bottom of the screen, in the middle. The cursor and the targets were blue squares with sides of 10 pixels (2.6 mm) and 15 pixels (3.9 mm), respectively. The size of the side of the starting position square was twice the size of the cursor side, to account for small oscillations of the finger inside the starting position. The distance between two consecutive targets was always 200 pixels (52.7 mm). The targets' position was kept constant throughout the experiment. A line passing through the starting position and Target 3, divided the area circumscribed by the targets into two equal halves, and formed a 30^{o} angle with the midline *y*-axis (Figure 1). We chose both the starting and the target positions with respect to the *x*-*y* axes, as well as the target dimension and the clockwise movement direction, on the basis of several studies examining the effect of these parameters on speed and accuracy of hand movements (e.g., Brown et al., 1948; Corrigan and Brogden, 1948; Begbie, 1959; Mead and Sampson, 1972; Buck 1982; Schaefer et al., 2009), to ensure that subjects could perform a single, fluent, skilled movement.

Each trial started with the cursor positioned at the starting position, within the gray square. After a variable time (10 - 15 s) the gray square turned green, and the five targets simultaneously appeared. This colour change (duration 500 ms) represented the 'go' signal, which instructed subjects to start performing the movement, by moving the cursor through the five targets and returning to the starting position. When the participants returned to the starting position, the five targets disappeared, and the colour of the square at the starting position turned back to gray. This signalled the end of the trial.

Participants were instructed to attend only to the visual 'go' signal, and ignore the preceding auditory and somatosensory stimuli, when present (i.e. in Experiments 1-4). They were also instructed to perform the task as quickly and as accurately as possible. Before each experiment, participants were given time to familiarise themselves with the task and were asked to practice by completing 50 trials.

In Experiments 1 and 2 we tested whether the VW affects the execution of the subsequent voluntary movement, by modulating ad-hoc the vertex wave amplitude using a validated paradigm that dissociates stimulus saliency from afferent sensory input (Iannetti et al., 2008; Valentini et al., 2011). At the beginning of each trial and before participants performed any movement, trains of three auditory and somatosensory stimuli (S1, S2, and S3: a triplet) were delivered with a constant interstimulus interval (ISI) of 1 s (Iannetti et al., 2008). While S1 and S2 always belonged to the same sensory modality (electrical or auditory), S3 belonged either to the same modality as S1 and S2 or to the other modality. This resulted in two experimental conditions: 'no-change' and 'change', respectively. In Experiment 1, triplets consisted of either three identical somatosensory stimuli (SSS; condition 'no-change'), or of two identical auditory stimuli followed by a somatosensory stimulus (AAS; condition 'change'). In Experiment 2, triplets consisted of either three identical auditory stimuli (AAA; condition 'no-change'), or of two identical somatosensory stimuli followed by an auditory stimulus (SSA; condition 'change') (Figure 1). Thus, within experiment, the modality of S3 was identical in the 'no-change' and 'change' conditions. In both experiments, S3 was simultaneous to the 'go' signal of the visuomotor task.

Experiments 1 and 2 consisted of five blocks of 20 trials each. The interval between consecutive blocks was ~5 min. In each block, 10 trials belonged to the condition 'no-change' and 10 trials belonged to the condition 'change'. The order of trials was pseudorandom, with the constraint that no more than 3 trials of the same condition occurred consecutively. The total number of trials of each experiment was 100 (50 per condition). The inter-trial interval (ITI) ranged from 10 to 15 s (rectangular distribution).

In Experiments 3 and 4 we tested whether the VW affects the execution of subsequent voluntary movement, by exploiting the spontaneous trial-by-trial variability in the amplitude of the VW elicited by isolated stimuli delivered at long inter-stimulus intervals. Experiments 3 and 4 consisted of two blocks of 30 trials each. The interval between the blocks was ~5 min. In both blocks, only single stimuli were delivered. In Experiment 3 these were somatosensory stimuli, while in Experiment 4 they were auditory stimuli. The ISI ranged between 10 and 15 s (rectangular distribution). The stimulus onset coincided with the 'go' signal of the visuomotor task.

Experiment 5 was performed to test whether the effects found in Experiments 1-4 were due to an EEG signal independent of the VW. In Experiment 5, participants did not receive auditory or somatosensory stimuli, and they had only to respond (i.e. start the movement) to the 'go' signal. Participants executed the visuomotor task 50 times in total (ITI 10-15 s), separated across two blocks.

2.5 Recording of EEG data and processing

Continuous electroencephalogram (EEG) was recorded using a 32-channel amplifier (SD32; Micromed, Treviso, Italy). 31 Ag–AgCl electrodes were placed on the scalp according to the International 10-20 system and referenced to the nose (Sharbrough et al., 1991). Electrode positions were 'Fp1', 'Fpz', 'Fp2', 'F7', 'F3', 'Fz', 'F4', 'F8', 'T3', 'C3', 'Cz', 'C4', 'T4', 'T5', 'P3', 'Pz', 'P4', 'T6', 'O1', 'Oz', 'O2', 'FC4', 'FC3', 'FCz', 'CPz', 'FT7', 'FT8', 'CP3', 'CP4', 'TP7', 'TP8'. Electrode impedances were kept below 5 kΩ. Signals were amplified and digitized at a sampling rate of 2048 Hz. The remaining channel of the EEG amplifier was used to record the electrooculogram (EOG), using a pair of surface electrodes, one placed below the right lower eyelid and the other placed lateral to the outer canthus of the right eye.

EEG data were pre-processed using Letswave (www.nocions.org; Mouraux and Iannetti, 2008). Continuous EEG data were first band-pass filtered at 0.5-30 Hz (Butterworth, fourth order), then segmented into epochs relative to stimulus onset, and baseline corrected using the prestimulus interval from -0.2 to -0.05 s. Specifically, in Experiments 1 and 2, EEG data were segmented into 3.2 s long epochs (-2.2 to +1 s relative to S3 onset), and baseline correction was performed with respect to S1. In Experiments 3, 4 and 5, EEG data were segmented into 1.2 s long epochs (-0.2 to +1 s).

Artifacts due to eye blinks or eye movements were removed using a validated method based on Independent Component Analysis (ICA; Jung et al., 2000). In all datasets, independent components related to eye movements had a large EOG channel contribution and a frontal scalp distribution. In addition, epochs with amplitude values exceeding ±100 μV (i.e. epochs likely contaminated by artifacts) were rejected.

In Experiments 1 and 2, epochs belonging to the same experimental condition were averaged, thus yielding two average waveforms for each condition ('no-change', 'change'), for each subject. In Experiments 3 and 4 there were no experimental conditions, therefore across-trial

averaging yielded one waveform for each subject. Single-subject average waveforms were used to generate group-level waveforms. In Experiments 1-4 the peak amplitude of the N and P waves of the average waveform at Cz was extracted for each subject. N and P waves were defined as the most negative and positive deflections after stimulus onset (Hu et al., 2014).

2.6 Recording of behavioural data and extraction of movement parameters

Throughout all experiments, the cursor's *x* and *y* positions were recorded with a 60 Hz sampling rate using a custom-written data acquisition script in MATLAB (Mathworks Inc.) and stored for offline analysis. To generate an average trajectory for each subject and experimental condition, cursor positions between each pair of consecutive targets were resampled to 100 positions, separately for each trial (Wolpert et al., 1995). This resampling procedure resulted in the overall trajectory being composed of 600 positions. These 600 positions were averaged across trials, thus obtaining one average trajectory for each subject and condition.

For each single trial, we extracted five established parameters describing the cursor movement in its spatial and temporal aspects, relative to the starting position and the targets (e.g., Teichner, 1954; Georgopoulos et al., 1981; Wolpert et al., 1995; Andrienko et al., 2008; Ranacher and Tzavella, 2014; Jones 2015). Thus, it was necessary to define the cursor position, which was determined with respect to the plane (i) perpendicular to the line connecting the centers of each target, and (ii) passing through that target (i.e. plane perpendicular to the direction of the movement) (Figure 1, bottom panel). The movement parameters are detailed below:

1) The *Movement Onset Time (MOT)* was defined as the time elapsed between the onset of the 'go' signal and the first time point (t_r) at which the cursor was outside a circle of radius r centered around the starting position (r = 15 pixels [3.9 mm]).
2) The *Total Movement Time (TMT)* was defined as the time elapsed between movement onset (t_r) and the time point at which the cursor re-entered the same circle centered around the starting position (t_s).
3) The *Path* was defined as the length of the trajectory from the position when the cursor passed through the circle centered around the starting point to the position when the cursor re-entered the same circle.

4) The *Overall Accuracy* was defined as the mean accuracy across the five targets. The accuracy at each target *n* was calculated as the Euclidean distance between the position of the cursor at target *n* and the actual position of target *n*, irrespectively of side.
5) The *Overall Speed* was defined as the *Path* divided by the *Total Movement Time*.

2.7 Statistical analyses

Statistical comparisons were performed using SPSS 24.0 (SPSS Inc. Chicago). Linear mixed effects (LME) modelling was performed using MATLAB (The MathWorks, Inc.).

Trials were excluded from statistical analyses on the basis on the following three criteria. (1) Trials whose MOT differed >3 SD from the group average MOT. (2) Trials whose trajectory differed >3 SD from the subject average trajectory (Pogosyan et al., 2009). (3) Trials with movement or other artifacts in the EEG signal. When a trial was removed on the basis of behavioural performance, the EEG counterpart was also removed. Similarly, trials which were excluded on the basis of the quality of EEG signal, were also excluded from behavioural analysis.

The criterion that was applied to exclude trials on the basis of MOT resulted in all trials with MOT shorter than 100 ms and longer than 1500 ms not being included in the analyses. The lower MOT limit is compatible with the 'irreducible minimum reaction time' (Woodworth and Schlosberg, 1954) or the 'mean residue' (Green and Luce, 1971; Luce, 1986), reflecting some minimally-needed sensory or motor time, which has been estimated to be around 80-100 ms (Luce, 1986; Green and Luce, 1971; Pascual-Leone et al., 1992).
The difference between the trajectories of a trial *n* and the average trajectory across all trials was calculated for each of the 600 points (as described in the previous section 2.6); the 600 differences were finally averaged together, to obtain a difference value for each trial.
The percentage of trials excluded for each experiment on the basis of the MOT criterion, as well as of all 3 criteria combined, was as follows. MOT criterion: 2.4% [Exp 1]; 1.4% [Exp 2]; 4.3% [Exp 3]; 4.5% [Exp 4]; 1.4% [Exp 5]; all criteria combined: 8.0% [Exp 1]; 8.3% [Exp 2]; 16.2% [Exp 3]; 15.1% [Exp 4]; 12.0% [Exp 5].

2.7.1 Effect of stimulus repetition on VW peak amplitude (Experiments 1 and 2)

To ascertain that in Experiments 1 and 2 the repetition of identical stimuli at 1 Hz caused a reduction of the amplitude of the VW (Iannetti et al., 2008; Rankin et al., 2009; Valentini et

al., 2011), we performed the following analyses. For the condition in which a train of three identical stimuli was delivered (i.e. SSS in Experiment 1 and AAA in Experiment 2) we performed repeated measures ANOVAs on the amplitude of the N and P peaks of the average waveforms elicited by S1, S2 and S3. When we found a significant main effect, pairs of stimuli were compared using paired t-tests. For the condition in which a train of two identical stimuli were followed by a third different stimulus (i.e. AAS in Experiment 1 and SSA in Experiment 2), the amplitudes of the N and P peaks elicited by S1 and S2 were compared using paired t-tests.

2.7.2 Effect of modality change on movement parameters and VW peak amplitude (Experiments 1 and 2)

To assess the effect of modality change on task performance, movement parameters were analyzed using a mixed-effects ANOVA, with within-subjects factor 'condition' (two levels: no-change, change) and between-subjects factor 'experiment' (two levels: Experiment 1, Experiment 2) to determine whether the effect differed between the two experiments. Significant 'experiment' x 'condition' interactions were further explored with paired t-tests. The threshold of significance was Bonferroni corrected for multiple comparisons. The same analyses were conducted to assess the effect of modality change on the amplitude of the N and P peaks of the VW elicited by S3.

We also tested whether participants with larger N and P peak amplitudes in the 'change' condition also showed a bigger change in their motor performance, selectively for the movement parameters that showed an effect of modality change in either experiment. To this end, we calculated Pearson's r correlation coefficient between the difference in vertex wave amplitude between conditions and the corresponding difference in movement parameters.

2.7.3 Exploring the trial-by-trial relationship between movement parameters and spontaneous variability of VW peak amplitude (Experiments 1-4)

We tested whether the trial-by-trial variability in the peak amplitude of the N and P waves of the event-related potential (ERP) elicited by S3 in Experiments 1 and 2, as well as of the N and P waves elicited by the single sensory stimuli in Experiments 3 and 4, was related to the variability of the movement parameters. To extract the single-trial peak amplitude of the N and P waves, we first identified, in each participant, the peak latency of the N and P waves on the across-trial average waveform. Single-trial amplitudes were subsequently extracted as the

most negative value (for the N wave) and the most positive value (for the P wave) within a 60 ms time window centered at each peak (Figure 2).

Since we were interested in testing this relationship *regardless of condition* (the between-condition effects have already been accounted for through the analyses described in section 2.7.2), in Experiments 1 and 2 trial-by-trial values of both ERP and movement data were transformed to z-scores within subject and condition. Subsequently, for each of the Experiments 1 and 2, all trial-by-trial ERP and movement data from all conditions (i.e. no-change and change) and subjects were pooled. In Experiments 3 and 4 where no separate conditions were present, all trial-by-trial values were transformed to z-scores within subject and condition. We calculated Pearson's r correlation coefficient between both N and P peak amplitudes and the movement parameters that showed an effect of modality change in either of Experiments 1 or 2.

2.7.4 Exploring the trial-by-trial relationship between movement parameters and the entire ERP waveform: point-by-point analysis (Experiments 1-5)

To test whether the trial-by-trial variability in EEG amplitude across the entire time course was related to the movement parameters, we used linear mixed effects modelling (LME). This approach takes into account all trials from all participants and conditions simultaneously, whilst accounting for the effects of those factors. To obtain a balance between the number of trials contaminated by movement-related activity and the length of the explored time-window, the LME analysis was conducted on the time-window 0-400 ms. This time-window ensured that less than a quarter of all trials were contaminated by movement (1st quartile of MOT values = 406 ms).

First, we tested for an effect of *trial number* on the movement parameters, and regressed such an effect out if we found one. This prevented us from entering correlated variables as regressors into the later LME. We searched for such effects through a preliminary LME, in which we modelled the trial-by-trial parameter values $\boldsymbol{P}$ as

Equation 1

$$\boldsymbol{P} = \beta_{tp}\boldsymbol{T} + \boldsymbol{u_{tp}S} + \boldsymbol{\varepsilon_p}$$

Where $\boldsymbol{P}$ is a vector specifying the movement parameter for each trial and each subject. $\boldsymbol{T}$ is a design matrix specifying the trial number of each trial, and β_{tp} is the estimated size of the

effect that $\boldsymbol{T}$ has on $\boldsymbol{P}$. $\boldsymbol{S}$ is the random-effects design matrix accounting for the subject number, and $\boldsymbol{u_{tp}}$ is a vector defining the random effects of each subject on the movement parameter (i.e. the mean parameter value per subject). Finally, $\boldsymbol{\varepsilon_p}$ is a vector of the residuals. If we found an effect of trial number $\boldsymbol{T}$ on the movement parameter $\boldsymbol{P}$, we computed a de-correlated movement parameter $\boldsymbol{P'}$ as

Equation 2

$$\boldsymbol{P'} = \boldsymbol{P} - \beta_{tp}\boldsymbol{T} - \boldsymbol{u_{tp}}\boldsymbol{S}$$

We then modelled the EEG response at each timepoint *t* in the window from stimulus onset until +0.4s, for each movement parameter and at each electrode *e*, as

Equation 3

$$\boldsymbol{V} = \beta_{cv}\boldsymbol{C} + \beta_{pv}\boldsymbol{P} + \beta_{tv}\boldsymbol{T} + \boldsymbol{u_{sv}}\boldsymbol{S} + \boldsymbol{\varepsilon_v}$$

Where $\boldsymbol{V}$ is a vector specifying the (EEG) voltage for each trial and subject. $\boldsymbol{C}$, $\boldsymbol{P}$ and $\boldsymbol{T}$ are design matrixes coding for the main effects of condition, movement parameter, and trial number, respectively. If we found an effect of $\boldsymbol{T}$ on $\boldsymbol{P}$, we used $\boldsymbol{P'}$ instead of $\boldsymbol{P}$ (see Equation 2). β_{cv}, β_{pv} and β_{tv} are the estimated main effects that those factors have on the EEG response $\boldsymbol{V}$. As in equation 1, **S** is the random-effects design matrix accounting for the subject number, and $\boldsymbol{u_{sv}}$ is a vector defining the random effects of each subject on the EEG response. Finally, $\boldsymbol{\varepsilon_v}$ is a vector of the residuals.

This method resulted in a p-value for each timepoint, each electrode and each LME parameter. Cluster-based permutation testing (Maris and Oostenveld, 2007) was used to account for multiple comparisons across time points on the data measured at electrode Cz. Clusters were based on temporal consecutivity, with at least two consecutive timepoints with $p<0.05$. The test statistic of each cluster corresponded to the sum of all t values of the timepoints composing it. Once these clusters were identified, permutation testing was used to assess their significance. Specifically, 1,000 random permutations of the data were used to generate a random distribution of cluster test statistics. This random distribution was finally used to define a threshold ($p=0.05$) against which the test statistic of the actual clusters were assessed. Thus, only timepoints surviving these two thresholds (consecutivity in time and random permutation) were considered significant. This test was performed separately for each LME parameter and in each experiment. This resulted in a p-value for each timepoint, electrode and LME parameter.

Such LME analysis and cluster-based permutation testing was performed both separately for each experiment, and on data pooled from all experiments. To pool the data, ***P*** and ***V*** were transformed to z-scores within subject, experiment and condition.

3. Results

3.1 Effect of stimulus repetition on VW peak amplitude (Experiments 1 and 2)

In the 'no-change' conditions (SSS in Experiment 1 and AAA in Experiment 2), rm-ANOVA showed a strong effect of stimulus repetition on both the N ($F=60.8$, $p<0.0001$, $\eta_p^2 = 0.902$ [SSS]; $F= 41.4$, $p<0.0001$, $\eta_p^2 = 0.722$ [AAA]) and the P peaks ($F=7.9$, $p=0.006$, $\eta_p^2 = 0.373$ [SSS]; $F=51.9$, $p<0.0001$, $\eta_p^2 = 0.682$ [AAA]) of the VW. Pairwise comparisons showed that (1) the S1-ERP was always larger than the S3-ERP ($p<0.05$, all comparisons), and (2) the S1-ERP was larger than the S2-ERP ($p<0.05$) in all comparisons except when comparing the P wave of condition SSS ($p=0.561$) (Figure 3).

In the 'change' conditions (AAS in Experiment 1 and SSA in Experiment 2), paired t-tests showed that the N peak was larger in the S1-ERP than the S2-ERP ($p<0.05$), whereas the P peak was larger in AAS ($p<0.0001$) but not in SSA condition ($p=0.913$) (Figure 3).

3.2 Effect of modality change on movement parameters and VW peak amplitude (Experiments 1 and 2)

For both the N and P waves, the two-way ANOVA revealed strong evidence for a main effect of the factors 'condition' ($F=44.2$, $p<0.0001$, $\eta_p^2 = 0.596$ [N wave]; $F=40.4$, $p<0.0001$, $\eta_p^2 = 0.574$ [P wave]), and 'experiment' ($F=5.7$, $p=0.024$, $\eta_p^2 = 0.159$ [N wave]; $F=9.0$, $p=0.005$, $\eta_p^2 = 0.231$ [P wave]), and no interaction ($F=2.3$, $p=0.138$, $\eta_p^2 = 0.072$ [N wave]; $F=1.4$, $p=0.242$, $\eta_p^2 = 0.045$ [P wave]) (Figure 3). The main effect of condition confirms the well-known ERP dishabituation when streams of identical stimuli entail a change of stimulus modality (Valentini et al., 2011). The main effect of 'experiment' verifies the amplitude difference between the responses elicited by somatosensory and auditory stimuli observed in Figure 3.

For both Movement Onset Time and Accuracy, the mixed-effects ANOVA revealed a strong main effect of 'condition' ($F=25.1$, $p=0.000055$, $\eta_p^2 = 0.432$ [MOT]; $F=14.5$, $p=0.001$, $\eta_p^2 = 0.295$ [Accuracy]), no main effect of 'experiment' ($F=0.06$, $p=0.942$, $\eta_p^2 = 0.033$ [MOT];

F=0.02, p=0.888, η_p^2 = 0.011 [Accuracy]), and no interaction (F=0.31, p=0.594, η_p^2 = 0.000028 [MOT]; F=0.60, p=0.457, η_p^2 = 0.032 [Accuracy]), thus indicating that the effect of modality change (i.e. saliency manipulation) was not different between the two experiments. For Speed and Total Movement Time, mixed-effects ANOVAs revealed no main effect of 'condition' (F=1.06, p=0.312, η_p^2 = 0.034 [Speed]; F=0.09, p=0.768, η_p^2 = 0.003 [TMT], respectively), no main effect of 'experiment' (F=0.07, p=0.795, η_p^2 = 0.002 [Speed]; F=0.31, p=0.584, η_p^2 = 0.010 [TMT], respectively), and a weak suggestion of an interaction between the two factors (F=4.9, p=0.034, η_p^2 = 0.142 [Speed]; F=5.2, p=0.030, η_p^2 = 0.148 [TMT]). This interaction was followed up with two post-hoc t-tests, which did not show evidence of an effect of modality change either in Experiment 1 (t=0.3085, p>0.05 [Speed]; t=0.1487, p>0.05 [TMT]) or in Experiment 2 (t=0.1208, p>0.05 [Speed]; t=0.2068, p>0.05 [TMT]). All comparisons were adjusted for multiple comparisons using Bonferroni correction. Finally, for Path, mixed-effects ANOVA revealed no main effect of 'condition' (F=0.35, p=0.557, η_p^2 = 0.012) and 'experiment' (F=0.98, p=0.331, η_p^2 = 0.032), and a strong interaction between the two factors (F=12.04, p=0.002, η_p^2 = 0.286). This interaction was also followed up with post-hoc t-tests, which did not show evidence of an effect of modality change either in Experiment 1 (t=1.278, p>0.05) or in Experiment 2 (t=1.922, p>0.05) (Figure 4).

Therefore, the change of modality affected the N and P wave amplitudes of the S3-ERP and two movement parameters, Movement Onset Time and Overall Accuracy, consistently in both Experiment 1 and 2. Despite this, there was no evidence for a between-subjects relationship between the magnitude of change in any of those two movement parameters and the amplitude difference of either the N or the P waves (Table 1).

3.3 Trial-by-trial relationship between movement parameters and VW (Experiments 1-4)

In Experiments 1, 2 and 4 there was strong evidence of a trial-by-trial positive correlation between the peak amplitude of the P wave and the Movement Onset Time (Table 2; correlations were corrected for multiple comparisons using Bonferroni correction, significant correlations are marked with an asterisk). Thus, a trial with a large peak P amplitude was more likely to entail a longer Movement Onset Time, and vice versa. There was no evidence for any other correlations (Table 2).

3.4 Exploring the trial-by-trial variability between movement and EEG signal: point-by-point analysis (All experiments)

In all experiments, the trial-by-trial variability between movement and EEG signal was explored using an LME model. In Experiments 1 and 2, the effects of factors 'condition' (no-change, change), 'Movement Onset Time' and 'Accuracy' were tested. In Experiments 3, 4, and 5, only 'Movement Onset Time' and 'Accuracy' were tested, as these experiments did not entail a change of modality of a repeated stimulus. In all experiments 'trial number' was included as a separate factor, to control for the variance associated with time-dependent effects. All p-values in the following paragraphs refer to cluster p values.

In Experiments 1, 2, 3, and 4 there was a clear effect of 'trial number' on EEG amplitude, in the N and P time windows (Figure 5). In the N time window (66-115 ms, $p<0.001$ [Exp 1]; 84-140 ms, $p<0.001$ [Exp 2]; 79-150 ms, $p<0.001$ [Exp 3]; 81-142 ms, $p<0.001$ [Exp 4]), the model revealed a positive correlation, and in the P window (172-315 ms, $p<0.001$ [Exp 1]; 159-301 ms, $p<0.001$ [Exp 2]; 194-340 ms, $p=0.001$ [Exp 3]; 160-296 ms, $p<0.001$ [Exp 4]) the model revealed a negative correlation (Figure 5 also displays point-by-point p values). Thus, both waves became smaller as trial number increased. T-value scalpmaps show that the effect of trial number at the time points where this was strongest, was centrally distributed. In Experiment 5, in which no auditory or somatosensory stimuli were delivered, there was a very weak effect of 'trial number' (170-190 ms, $p=0.046$).

In Experiments 1 and 2, LME also revealed strong evidence for an effect of 'condition' on the EEG signal at Cz, in the N time window (59-137 ms [Exp 1]; 72-140 ms [Exp 2], $p<0.001$ in both experiments) and in the P time window (145-328 ms [Exp 1]; 147-305 ms [Exp 2], $p<0.001$ in both experiments) (Figure 5, also displaying point-by-point p values). Both waves were larger when the modality of S3 was different from that of S1 and S2. This effect of condition confirms the result observed when the effect of modality change on VW peak amplitude was examined (Figure 3; section 3.2). T-value scalpmaps show that also this effect was centrally-distributed.

In Experiments 1, 2 and 4, there was strong evidence for an effect of 'Movement Onset Time' on the EEG signal, in a time window overlapping with the latency of the P wave: centred at 227 ms post-stimulus, and lasting approximately 150 ms (150-360 ms, $p<0.001$ [Exp 1]; 140-280 ms, $p<0.001$ [Exp 2]; $p=0.9990$ [Exp 3]; 165-265 ms, $p<0.001$ [Exp 4]) (point-by-point p

values are shown in Figure 5). Within these time windows, Onset Times were longer when the EEG amplitude was more positive. These results are consistent with what we observed when relating the trial-by-trial variability of the P *peak* amplitude with Onset Times, but, importantly, show that the effect is not necessarily centred around the peak of the P-wave (see Discussion).

Crucially, this same effect was also clearly observable in Experiment 5, again in a time window roughly corresponding to the latency of the P wave (232-332 ms; $p<0.001$) (exact point-by-point p values are shown in Figure 5). Importantly, in Experiment 5 no auditory or somatosensory stimuli were delivered, and therefore no VW was elicited. The result of Experiment 5 indicates that the positive relationship between EEG amplitude and movement onset is independent of the presence of a clear VW.

When all experiments were combined there was a clear effect of 'trial number' on EEG amplitude in the N (68-146 ms) and P wave (157-332 ms) time windows ($p<0.001$ for both) (point-by-point p values are shown in Figure 5). Additionally, the strong evidence for an effect of Movement Onset Time on the EEG signal, in a time window overlapping with the latency of the P wave (137-317 ms, $p<0.001$) was observed.

In all experiments, LME did not show any effect of the factor 'Accuracy' on the EEG waveforms.

4. Discussion

Following the recent observation of a direct link between the biphasic vertex wave and the modulation of isometric force and rapid defensive movements, in this study we tested whether the vertex wave is also functionally linked to voluntary hand movements to perform a complex visuomotor task. We obtained three main results. (1) The increase of vertex wave amplitude caused by an ad-hoc manipulation of its amplitude was paralleled by an increase in accuracy and a reduction in onset time of the voluntary movement. (2) The *negative* relationship between vertex wave amplitude and movement onset, however, was not present when considering the spontaneous trial-by-trial variability in vertex wave amplitude. Instead, single-trial analysis revealed that the P amplitude was *positively* related to the speed of movement onset. (3) This trial-by-trial correlation was driven by a long-lasting EEG

negativity independent from the occurrence of the P vertex wave, although overlapping in time with it.

Stimulus saliency affects movement onset time and accuracy

In Experiments 1 and 2 we used a validated paradigm to modulate stimulus saliency and the amplitude of the ensuing brain responses while keeping the intensity of the afferent volley constant (Iannetti et al., 2008; Valentini et al., 2011). We confirmed that (i) repeating the same stimulus at short and constant ISIs (1 Hz) results in habituation of the elicited ERPs, and (ii) introducing a change in stimulus modality produces a clear response dishabituation (Figure 3). These findings corroborate the supramodal nature of the EEG vertex potentials consequent to the detection of salient stimuli (Liang et al., 2010; Valentini et al., 2011). Importantly, the change in stimulus modality also resulted in a consistent modulation in two out of the five parameters used to describe the voluntary movement performed by the participants (Figure 1): movement onset, which had shorter latency (ΔMOT: -44.6 (4.8) ms [Exp 1]; -44.0 (5.6) ms [Exp 2]), and accuracy in passing through the five targets, which was improved (ΔError: -1.5 (2.2) pixels [Exp 1]; -0.8 (1.5) pixels [Exp 2]). That is, the increased stimulus saliency improved performance on the motor task, in two aspects that are differentially dependent on sensory feedback: onset time, which is virtually feedback-independent, and accuracy, which instead strongly depends on continuous sensory input. The fact that the movement onset and accuracy were the only two parameters consistently affected by the stimulus properties suggests that participants followed the instructions received, as these were the two movement features that participants were required to maximise. This is consistent with evidence that human subjects fine-tune their task-relevant strategies by modifying the gain of particular feature dimensions (e.g., Pfefferbaum et al., 1983; Folk et al., 1992; Found and Müller 1996; Schubotz and von Cramon, 2001; Aasen and Brunner, 2016), a process which has been labelled ‘intentional weighting’ (Memelink and Hommel, 2013). Finally, as was the case for the EEG modulations, these behavioural effects were also supramodal: there was a similar reduction in movement onset time and increase in movement accuracy regardless of whether the stimulus modality changed from auditory to somatosensory (Exp 1) or from somatosensory to auditory (Exp 2).

Spontaneous trial-by-trial variability reveals a positive relationship between P wave and movement onset

The observation that the contextual increase of stimulus saliency resulted in both an increase in N and P peak amplitude and an improved performance in the motor task suggests a potential link between these two features. Therefore, we hypothesized that a large peak amplitude of the N and/or P waves would be related to a faster and more accurate subsequent movement. To test this hypothesis, we correlated the spontaneous variability of the vertex wave and of motor performance, without the possible interaction of saliency-related effects present in Experiments 1 and 2 (Table 2). Inter-trial variability is being increasingly exploited as a rich source of information regarding behavioural performance. Under this framework, variability is not considered only as biological noise but also as an operative feature that shapes the function of the system, its computations and its outcome (e.g., Harris & Wolpert, 1998; McIntyre et al., 2000; Todorov and Jordan, 2002; Davids et al., 2003; van Beers et al., 2004; Churchland et al., 2006; Lee et al., 2016). Thus, we correlated the N and P peak amplitude of the responses recorded in Experiments 3 and 4 with the two movement parameters (i.e. Movement Onset Time and Accuracy) that were consistently affected by experimental conditions in Experiments 1 and 2. We observed a *positive* correlation between the amplitude of the P wave and Movement Onset Time (Table 2). This observation was intriguing, as it indicated a clear relationship between the ERP and motor processing, but in the opposite direction compared to that observed in Experiments 1 and 2 following saliency modulation. In other words, the relationship between P wave amplitude and MOT reverses when the *between-conditions* and *trial-by-trial* correlations are examined (Figures 4 and 6). Interestingly, an independence between average and trial-by-trial variability is described in theories of motor control (Todorov and Jordan, 2002; Todorov, 2004). Furthermore, the trial-by-trial positive relationship between P wave amplitude and MOT was also detected using the LME analysis of Experiments 1 and 2, after the condition effects were modeled out (Figure 5).

Thus, the hypothesis that a large peak amplitude of the N and/or P waves is related to a faster and more accurate subsequent movement was not supported, and an alternative interpretation was required.

Trial-by-trial relationship between P wave and movement is caused by an underlying process independent of the VW

We reasoned that this relationship observed at trial-by-trial level could have emerged as a consequence of an additional neural process independent of the P wave, but overlapping in

time. Indeed, such positive correlation was present regardless of both the modality of the stimulus eliciting the VW (Experiments 1, 2 and 4) and the saliency-dependent modulations of VW amplitude (Experiments 1-2), as revealed by the LME analysis. This positive correlation was still evident when data of Experiments 1-4 were combined, by removing the between-conditions and the between-experiment variability and retaining only the spontaneous trial-by-trial variability. This reasoning was the rationale for conducting Experiment 5, in which no sudden stimuli eliciting a vertex wave were delivered, but the same visuomotor task was performed.

As in Experiments 1, 2 and 4, in Experiment 5 the inter-trial EEG variability was also positively correlated with the variability of Movement Onset Time in a time window overlapping that of the P wave, despite the crucial fact that in Experiment 5 no somatosensory or auditory stimuli were present, and thus no ERP was elicited (Figure 5). This result indicates that the positive correlation between EEG amplitude and movement parameters is independent of the presence of an evoked response, and that the process causing this correlation merely occurred during the P wave.

What could the nature of such a process then be? A pertinent candidate process is attention, which is an important determinant of the fluctuations of both reaction times (e.g., Boulinguez and Nougier, 1999; Baldauf and Deubel, 2010; Hesse et al., 2012) and evoked potentials (e.g., Mangun, 1995; Hillyard and Anllo-Vento, 1998). Examining the N1-P2 waves of the ERP evoked by auditory stimuli (which are largely equivalent to the negative and positive vertex waves recorded in our experiments; Liang et al., 2010), Näätänen, Hillyard and their colleagues have shown that increased attentiveness results in larger peak amplitude of the negative wave and smaller amplitude of the positive wave (Hillyard et al., 1973; 1978; Näätänen et al., 1978; Näätänen and Michie, 1979; Näätänen, 1982; Näätänen and Picton, 1987; Woldorff and Hillyard, 1991; Michie et al., 1990, 1993). This modulation was explained with the occurrence of a broad, low-frequency negative EEG deflection.

This broad negativity is differently labelled across the ERP literature: ‘Processing Negativity (PN)’ (Näätänen et al., 1978; Näätänen and Michie, 1979; Näätänen, 1982), ‘Negative Difference (Nd)’ (Hansen and Hillyard, 1980), ‘N2 Posterior Component’ (with two subcomponents: N2pc [N2-posterior-contralateral] and N2pb [N2-posterior-bilateral]; Luck and Kappenman, 2011) and ‘Posterior Contralateral Negativity (PCN)’ (Woodman and Luck,

1999, 2003; Wolber and Wascher, 2005; Jolicoeur et al., 2008), to name a few (for an extensive review on this topic see Luck and Kappenman, 2011). Here, for simplicity, we refer to it as 'Processing Negativity (PN)' following the nomenclature of Näätänen. Although the PN latency, duration, and scalp topography vary greatly across experiments and cognitive tasks (as highlighted by Hansen and Hillyard, 1980, and Woldorff and Hillyard, 1991), the PN almost always encompasses the P peak of the ERP elicited by stimuli of different modalities. Therefore, in the context of our results, the occurrence of such PN could explain the smaller P amplitude in the fastest trials, i.e. in trials in which participants were likely to be more attentive to the task (e.g., Posner et al., 1980; Schneider et al., 2013). The occurrence of PN could clearly be inferred from the LME results (Figure 5), as well as from showing that the average waveform of the 'slow' trials was more positive than the average waveform of the 'fast' trials at the time interval corresponding to the latency of P wave (Figure 7). The fact that the PN is locked to stimulus onset and not to movement onset (Figure 7) rules out that the PN is a readiness potential (Kornhuber and Deecke, 1964, 1965; Deecke et al., 1969; Shibasaki et al., 1980).

It is interesting to note that when the PN is described, it is often associated to the specific cognitive function examined in the experiment, with an impressive breadth of assigned functions, including distractor suppression (Luck and Hillyard, 1994), deviancy detection (Bubic et al., 2010), stimulus classification (Garcia-Larrea, et al., 1992), stimulus saliency and relevance (Fellrath et al., 2014), visual awareness (Kaernbach et al., 1999), working-memory (Eimer, 1996; Eimer and Kiss, 2010), parallel and serial processing in visual search (Wolber and Wascher, 2003), and change detection (Koivisto and Revonsuo, 2003; Koivisto and Grassini, 2016).

However, our results and a critical assessment of the literature suggest a non-specific interpretation of the PN, as already stated by Näätänen (1990): "[PN] was not produced by a modulation of any exogenous ERP component but was rather a new component emerging during selective attention". Indeed, we observed that the trial-by-trial positive correlation between EEG amplitude and onset of voluntary movement occurring at approximately 200-300 ms is present independently of (1) the sensory modality of the stimulus eliciting the overlapping ERP response (Experiments 1, 2, 4), (2) context-dependent changes in stimulus saliency (i.e. it is observed both when the stimuli are delivered in triplets or individually, as well as when response is dishabituated because of a change in stimulus modality;

738 Experiments 1-4), and, most importantly, (3) the presence of any clear ERP elicited by
739 sudden stimuli (Experiment 5). Thus, this process most likely reflects a general attentional
740 mechanism aimed to optimise the execution of subsequent task-relevant behaviour, whatever
741 the task and the behavior might be. This observation should prompt caution when interpreting
742 correlations between ERPs and behavioural measures, which could be spuriously determined
743 by ERP-independent attentional effects.
744
745 *What is the relation between the VW and the motor system?*
746 Overall, these results show a minimal dependence between the variability of the VW and the
747 performance of a *subsequent* and high-precision voluntary movement. At a superficial glance,
748 this might seem at odds with the tight coupling between the VW and the modulation of the
749 force exerted by human participants in a simple isometric task (Novembre et al., 2018).
750 However, there are two substantial differences between the two tasks. First, the temporal
751 relationship between the VW and the activation of the motor system: in Novembre et al.
752 (2018) the isometric force was exerted *throughout* the presentation of the stimulus eliciting
753 the VW, while in the present experiment the VW occurred *before* the movement was even
754 initiated, and the movement outlasted the VW by approximately 2 seconds. This temporal
755 separation might have prevented an effect of VW on all measured motor parameters (Figures
756 1, 4). This temporal separation might also explain why the most robust effect of VW was a
757 change in MOT, a parameter that reflects the immediate outcome of the planning phase of the
758 movement that probably occurred concomitantly to the VW (Figure 1, top right). Second, the
759 present task was dramatically more complex: it entailed a movement of the index finger,
760 largely dependent on visuospatial input received long after the VW ended (Figure 1). Thus,
761 while an immediate effect of the VW on the motor system is undeniable, and possibly
762 important for presetting the system for subsequent movements not requiring high precision
763 (Moayedi et al., 2015; Novembre et al., 2018), it is likely that in the current design the VW
764 occurred too early to have a detectable effect on movement kinematics. Indeed, movement
765 execution relies heavily on continuous online adjustments based on sensory feedback (Miall
766 and Wolpert 1996) (see the lack of effect on Path, Overall Speed, Total Time Movement) and
767 thus movement kinematics were less amenable to be modulated by the preceding VW. Also,
768 it is possible that the VW does not affect subsequent high precision movements at all. A final
769 alternative explanation is that the effect of PN on motor behavior is stronger than the effect of
770 the VW, and thus obscures it. Further experiments exploring the possible effects of the VW
771 *during* the execution of visuomotor tasks entailing high-precision visuomotor transformations

772 (such as compensatory tracking or pursuit tracking of a continuously moving target, Weir et
773 al., 1989; Miall et al., 1993; Heenan et al., 2011) will be needed to clarify this issue.
774
775 Altogether, these results show a weak link between the VW amplitude and the execution of
776 subsequent voluntary movements requiring both speed and accuracy. Importantly, they
777 highlight the necessity of considering goal-related but stimulus-independent EEG activities as
778 alternative explanations when attempting to relate the amplitude of stimulus-evoked EEG
779 responses with perceptual and behavioural performance.

Author contributions

All experiments were performed at the IannettiLab at the Department of Neuroscience, Physiology and Pharmacology of University College London. MK and GDI designed the experiments. MK collected the data. MK and RJB analysed the data. All authors participated in interpreting the data and drafting the paper. MK and GDI wrote the paper. All persons designated as authors qualify for authorship, and all those who qualify for authorship are included as authors. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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References

Aasen IE & Brunner JF (2016). Modulation of ERP components by task instructions in a cued go/no-go task. Psychophysiology 53, 171-185.

Andrienko NV, Andrienko GL, Pelekis N & Spaccapietra S (2008). Basic Concepts of Movement Data. In: Giannotti F., Pedreschi D. (eds) Mobility, Data Mining and Privacy. Springer, Berlin, Heidelberg

Bancaud J, Bloch V & Paillard J (1953). Contribution E.E.G. a` l'étude des potentiels évoqués chez l'homme au niveau du vertex. Revue Neurologique 89, 399–418.

Baldauf D & Deubel H (2010). Attentional landscapes in reaching and grasping. Vision Res 50, 999-1013.

Begbie GH (1959). Accuracy of aiming in linear hand-movements. Q J Exp Psychol 11, 65-75.

Boulinguez P & Nougier V (1999). Control of goal-directed movements: the contribution of orienting of visual attention and motor preparation. Acta Psychol (Amst) 103, 21-45.

Brainard DH (1997). The Psychophysics Toolbox. Spat Vis 10, 433-436.

Brown JS, Knauft EB & Rosenbaum G (1948). The accuracy of positioning reactions as a function of their direction and extent. Am J Psychol 61, 167-182.

Bubic A, Bendixen A, Schubotz RI, Jacobsen T & Schröger E (2010). Differences in processing violations of sequential and feature regularities as revealed by visual event-related brain potentials. Brain Res 1317, 192-202.

Buck L (1982). Location versus distance in determining movement accuracy. J Mot Behav 14, 287-300.

Churchland MM, Afshar A & Shenoy KV (2006). A central source of movement variability. Neuron 52, 1085-1096.

Cornsweet T (1962). The Staircase-Method in Psychophysics. Am J Psychol 75, 485-491.

Corrigan RE & Brogden WJ (1948). The effect of angle upon precision of linear pursuit movements. Am J Psychol 61, 502-510.

Davids K, Glazier P, Araújo D & Bartlett R (2003). Movement systems as dynamical systems. Sports Med 33, 245-260.

Deecke L, Scheid P & Kornhuber HH (1969). Distribution of readiness potential, pre-motion positivity, and motor potential of the human cerebral cortex preceding voluntary finger movement. Exp Brain Res 7, 158-168.

Eimer M (1996). ERP modulations indicate the selective processing of visual stimuli as a result of transient and sustained spatial attention. Psychophysiology 33, 13–21.

836 Eimer M & Kiss M (2010). An electrophysiological measure of access to representations in
837 visual working memory. Psychophysiology 47, 197-200.
838 Fellrath J, Manuel AL & Ptak R (2014). Task relevance effects in electrophysiological brain
839 activity: early, but not first. Neuroimage 101, 68-75.
840 Folk CL, Remington RW & Johnston JC (1992). Involuntary covert orienting is contingent
841 on attentional control settings. J Exp Psychol Hum Percept Perform 18, 1030-1044.
842 Found A & Müller HJ (1996). Searching for unknown feature targets on more than one
843 dimension: Investigating a "dimension-weighting" account. Atten Percept Psychophys 58,
844 88-101.
845 Garcia-Larrea L, Lukaszewicz A & Mauguiere F (1992). Revisiting the oddball paradigm.
846 Non-target vs. neutral stimuli and the evaluation of ERP attentional effects.
847 Neuropsychologia 30, 723-741.
848 Georgopoulos AP, Kalaska J & Massey JT (1981). Spatial trajectories and reaction times of
849 aimed movements: effects of practice, uncertainty, and change in target location. J
850 Neurophysiol 46, 725-743.
851 Green D & Luce RD (1971). Detection of auditory signals presented at random times: III.
852 Percept Psychophys 9, 257-268.
853 Hansen JC & Hillyard SA (1980). Endogeneous brain potentials associated with selective
854 auditory attention. Electroencephalogr Clin Neurophysiol 49, 277-290.
855 Harris CM & Wolpert DM (1998). Signal-dependent noise determines motor planning.
856 Nature 394, 780-784.
857 Heenan ML, Scheidt RA & Beardsley SA (2011). Visual and proprioceptive contributions to
858 compensatory and pursuit tracking movements in humans. In Engineering in Medicine and
859 Biology Society, EMBC, 2011 Annual International Conference of the IEEE, pp. 7356-7359.
860 Hesse C, Schenk T & Deubel H (2012). Attention is needed for action control: further
861 evidence from grasping. Vision Res 71, 37-43.
862 Hillyard SA & Anllo-Vento L (1998). Event-related brain potentials in the study of visual
863 selective attention. Proc Natl Acad Sci USA 95, 781-787.
864 Hillyard SA, Hink RF, Schwent VL & Picton TW (1973). Electrical signs of selective
865 attention in the human brain. Science 182, 177-180.
866 Hillyard SA, Picton TW & Regan D (1978). Sensation, perception and attention: analysis
867 using ERPs. In: E. Callaway, P. Tueting and S.H. Koslow (Eds.), Event-related Brain
868 Potentials in Man, pp. 223-321. Academic Press, New York.

Hu L, Cai MM, Xiao P, Luo F & Iannetti GD (2014). Human brain responses to concomitant stimulation of Aδ and C nociceptors. J Neurosci 34, 11439-11451.

Iannetti GD, Hughes NP, Lee MC & Mouraux A (2008). Determinants of laser-evoked EEG responses: pain perception or stimulus saliency? J Neurophysiol 100, 815-828.

Jolicoeur P, Brisson B & Robitaille N (2008). Dissociation of the N2pc and sustained posterior contralateral negativity in a choice response task. Brain Res 1215, 160-172.

Jones RD (2015). Measurement and analysis of sensory-motor performance: Tracking tasks. In J. D. Bronzino & D. R. Peterson (Eds.), *The biomedical engineering handbook: Medical devices and systems*. (4th ed.), pp. 31-1 to 31-37. Boca Raton, FL: CRC Press.

Jung TP, Makeig S, Humphries C, Lee TW, McKeown MJ, Iragui V & Senjnowski TJ (2000). Removing electroencephalographic artifacts by blind source separation. Psychophysiology 37, 163-78.

Kaernbach C, Schröger E, Jacobsen T & Roeber U (1999). Effects of consciousness on human brain waves following binocular rivalry. Neuroreport 10, 713-716.

Koivisto M & Grassini S (2016). Neural processing around 200ms after stimulus-onset correlates with subjective visual awareness. Neuropsychologia 84, 235-243.

Koivisto M & Revonsuo A (2003). An ERP study of change detection, change blindness, and visual awareness. Psychophysiology 40, 423-429.

Kornhuber HH & Deecke L (1964). Hirnpotentialänderungen beim Menschen vor und nach Willkürbewegungen, dargestellt mit Magnetbandspeicherung und Rückwartsanalyse. In Pflugers Archiv-European Journal of Physiology (Vol. 281, No. 1, p. 52). Springer-Verlang.

Kornhuber HH & Deecke L (1965). Hirnpotentialänderungen bei Willkürbewegungen und passiven Bewegungen des Menschen: Bereitschaftspotential und reafferente Potentiale. Pflügers Arch ges Physiol 284, 1-17.

Lee J, Joshua M, Medina JF & Lisberger SG (2016). Signal, noise, and variation in neural and sensory-motor latency. Neuron 90, 165-176.

Liang M, Mouraux A, Chan V, Blakemore C & Iannetti GD (2010). Functional characterisation of sensory ERPs using probabilistic ICA: effect of stimulus modality and stimulus location. Clin Neurophysiol 121, 577-587.

Luce RD (1986). Response times: Their role in inferring elementary mental organization. Oxford University Press.

Luck SJ & Kappenman ES (Eds.) (2011). The Oxford handbook of event-related potential components. Oxford University Press.

902 Luck SJ & Hillyard SA (1994). Spatial filtering during visual search: evidence from human
903 electrophysiology. J Exp Psychol Hum Percept Perform 20, 1000-1014.
904 Mangun GR (1995). Neural mechanisms of visual selective attention. Psychophysiology 32,
905 4-18.
906 Maris E & Oostenveld R (2007). Nonparametric statistical testing of EEG- and MEG-data. J
907 Neurosci Methods 164, 177-190.
908 McIntyre J, Stratta F, Droulez J & Lacquaniti F (2000). Analysis of pointing errors reveals
909 properties of data representations and coordinate transformations within the central nervous
910 system. Neural Comput 12, 2823-2855.
911 Mead PG & Sampson PB (1972). Hand steadiness during unrestricted linear arm movements.
912 Hum Factors 14, 45-50.
913 Memelink J & Hommel B (2013). Intentional weighting: a basic principle in cognitive
914 control. Psychol Res 77, 249-259.
915 Miall RC, Weir DJ & Stein JF (1993). Intermittency in human manual tracking tasks. J Mot
916 Behav 25, 53-63.
917 Miall RC & Wolpert DM (1996). Forward models for physiological motor control. Neural
918 Network 9, 1265-1279.
919 Michie PT, Bearpark HM, Crawford JM & Glue LC (1990). The nature of selective attention
920 effects on auditory event-related potentials. Biol Psychol 30, 219-250.
921 Michie PT, Solowij N, Crawford JM & Glue LC (1993). The effects of between-source
922 discriminability on attended and unattended auditory ERPs. Psychophysiology 30, 205-220.
923 Moayedi M, Liang M, Sim AL, Hu L, Haggard P & Iannetti GD (2015). Laser-evoked vertex
924 potentials predict defensive motor actions. Cereb Cortex 25, 4789-4798.
925 Mouraux A & Iannetti GD (2008). Across-trial averaging of event related EEG responses and
926 beyond. Magn Reson Imaging 26, 1041-1054.
927 Mouraux A & Iannetti GD (2009). Nociceptive laser-evoked brain potentials do not reflect
928 nociceptive-specific neural activity. J Neurophysiol 101, 3258-3269.
929 Näätänen R (1982). Processing negativity: An evoked-potential reflection. Psychol Bull 92,
930 605-640.
931 Näätänen R (1990). The role of attention in auditory information processing as revealed by
932 event-related potentials and other brain measures of cognitive function. Behav Brain Res 13,
933 201-228.
934 Näätänen R, Gaillard AWK & Mantysalo S (1978). Early selective attention effect on evoked
935 potential reinterpreted. Acta Psychol (Amst) 42, 313-329.

936 Näätänen R & Michie PT (1979). Early selective-attention effects on the evoked potential: a
937 critical review and reinterpretation. Biol Psychol 8, 81-136.
938 Näätänen R & Picton T (1987). The N1 wave of the human electric and magnetic response to
939 sound: a review and an analysis of the component structure Psychophysiology 24, 375-425.
940 Novembre G, Pawar VM, Bufacchi RJ, Kilintari M, Srinivasan MA, Rothwell JC, Haggard P
941 & Iannetti GD (2018). Saliency detection as a reactive process: unexpected sensory events
942 evoke cortico-muscular coupling. J Neurosci 38, 2385-2397.
943 Pascual-Leone A, Brasil-Neto JP, Valls-Sole J, Cohen LG & Hallett M (1992). Simple
944 reaction time to focal transcranial magnetic stimulation: comparison with reaction time to
945 acoustic, visual and somatosensory stimuli. Brain 1151, 109-122.
946 Pfefferbaum A, Ford J, Johnson R, Wenegrat B & Kopell BS (1983). Manipulation of P3
947 latency: speed vs. accuracy instructions. Electroencephalogr Clin Neurophysiol 55, 188-197.
948 Pfefferbaum A, Ford JM, Roth WT, Hopkins WF & Kopell BS (1979). Event-related
949 potential changes in healthy aged females. Electroencephalogr Clin Neurophysiol 46, 81-86.
950 Pogosyan A, Gaynor LD, Eusebio A & Brown P (2009). Boosting cortical activity at beta-
951 band frequencies slows movement in humans. Curr Biol 19, 1637-1641.
952 Posner MI, Snyder CR & Davidson BJ (1980). Attention and the detection of signals. J Exp
953 Psychol 109, 160-174.
954 Ranacher P & Tzavella K (2014). How to compare movement? A review of physical
955 movement similarity measures in geographic information science and beyond. Cartogr Geogr
956 Inf Sci 41, 286-307.
957 Rankin CH, Abrams T, Barry RJ, Bhatnagar S, Clayton DF, Colombo J. Coppola G, Geyer
958 MA, Glanzman DL, Marsland S, McSweeney FK, Wilson DA, Wu CF & Thompson RF
959 (2009). Habituation revisited: an updated and revised description of the behavioral
960 characteristics of habituation. Neurobiol Learn Mem 92, 135-138.
961 Schaefer SY, Haaland KY & Sainburg RL (2009). Dissociation of initial trajectory and final
962 position errors during visuomotor adaptation following unilateral stroke. Brain Res 1298, 78-
963 91.
964 Schneider WX, Einhäuser W & Horstmann G (2013). Attentional selection in visual
965 perception, memory and action: A quest for cross-domain integration. Phil Trans R Soc B
966 368, 20130053.
967 Schubotz RI & von Cramon DY (2001). Functional organization of the lateral premotor
968 cortex: fMRI reveals different regions activated by anticipation of object properties, location
969 and speed. Brain Res Cogn Brain Res 11, 97-112.

970 Sharbrough F, Chatrian GE, Lesser RP, Lüders H, Nuwer M & Picton TW (1991). American
971 Electroencephalographic Society guidelines for standard electrode position nomenclature. J
972 Clin Neurophysiol 8, 200–202.
973 Shibasaki H, Barrett G, Halliday E & Halliday AM (1980). Components of the movement-
974 related cortical potential and their scalp topography. Electroenceph Clin Neurophysiol 49,
975 213-226.
976 Teichner WH (1954). Recent studies of simple reaction time. Psychol Bull 51, 128-149.
977 Todorov E (2004). Optimality principles in sensorimotor control. Nat Neurosci 7, 907-915.
978 Todorov E & Jordan MI (2002). Optimal feedback control as a theory of motor coordination.
979 Nat Neurosci 5, 1226-1235.
980 Valentini E, Torta DM, Mouraux A & Iannetti GD (2011). Dishabituation of laser-evoked
981 EEG responses: dissecting the effect of certain and uncertain changes in stimulus modality. J
982 Cogn Neurosci 23, 2822-2837.
983 Van Beers RJ, Haggard P & Wolpert DM (2004). The role of execution noise in movement
984 variability. J Neurophysiol 91, 1050-1063.
985 Walter WG (1964). The convergence and interaction of visual, auditory, and tactile responses
986 in human non-specific cortex. Ann N Y Acad Sci 112, 320–361.
987 Weir DJ, Stein JF & Miall RC (1989). Cues and control strategies in visually guided tracking.
988 J Mot Behav 21, 185-204.
989 Wolber M & Wascher E (2003). Visual search strategies are indexed by event-related
990 lateralization of the EEG. Biol Psychol 63, 79-100.
991 Woldorff MG & Hillyard SA (1991). Modulation of early auditory processing during
992 selective listening to rapidly presented tones. Electroencephalogr Clin Neurophysiol 79, 170-
993 191.
994 Wolpert DM, Ghahramani Z & Jordan MI (1995). Are arm trajectories planned in kinematic
995 or dynamic coordinates? An adaptation study. Exp Brain Res 103, 460-470.
996 Woodman GF & Luck SJ (1999). Electrophysiological measurement of rapid shifts of
997 attention during visual search. Nature 400, 867-869.
998 Woodman GF & Luck SJ (2003). Serial deployment of attention during visual search. J Exp
999 Psychol Hum Percept Perform 29, 121-138.
1000 Woodworth RS & Schlosberg H (1954). Experimental psychology, Rev. ed. Oxford,
1001 England: Holt.

Tables

Table 1. Between-subject correlation between the change-induced modulation of N and P waves peak amplitude and movement parameters (Experiments 1 and 2)

	N-wave amplitude		P-wave amplitude	
	r	p	r	p
Movement Onset Time (Exp 1)	-0.3278	0.2330	-0.1272	0.6514
Movement Onset Time (Exp 2)	-0.2690	0.2965	0.02514	0.5433
Overall Accuracy (Exp 1)	0.3927	0.1477	-0.4108	0.1283
Overall Accuracy (Exp 2)	-0.3730	0.1404	0.1938	0.4560
Overall Speed (Exp 1)	0.1083	0.7010	0.5793	0.0236
Overall Speed (Exp 2)	-0.0328	0.9007	-0.1415	0.5881
Total Movement Time (Exp 1)	-0.2615	0.3465	-0.2374	0.3943
Total Movement Time (Exp 2)	0.2279	0.3790	0.2836	0.270
Path (Exp 1)	-0.4643	0.0813	0.4004	0.1391
Path (Exp 2)	0.1270	0.6270	-0.1282	0.6240

Table 2. Trial-by-trial correlation between spontaneous variability of N and P waves peak amplitude and movement parameters (Experiments 1-4)

	N-wave amplitude		P-wave amplitude	
	r	p	r	p
Movement Onset Time (Exp 1)	-0.0195	0.4702	0.1040	**0.0001***
Movement Onset Time (Exp 2)	0.0399	0.1154	0.1337	**<0.00001***
Movement Onset Time (Exp 3)	0.0122	0.660	0.060	0.0304
Movement Onset Time (Exp 4)	-0.0205	0.5390	0.1358	**<0.00001***
Overall Accuracy (Exp 1)	-0.0005	0.9843	0.0254	0.3471
Overall Accuracy (Exp 2)	-0.0057	0.8229	0.0322	0.2040
Overall Accuracy (Exp 3)	0.0004	0.9887	-0.0275	0.3404
Overall Accuracy (Exp 4)	0.0372	0.2641	-0.0035	0.9155

Figures and legends

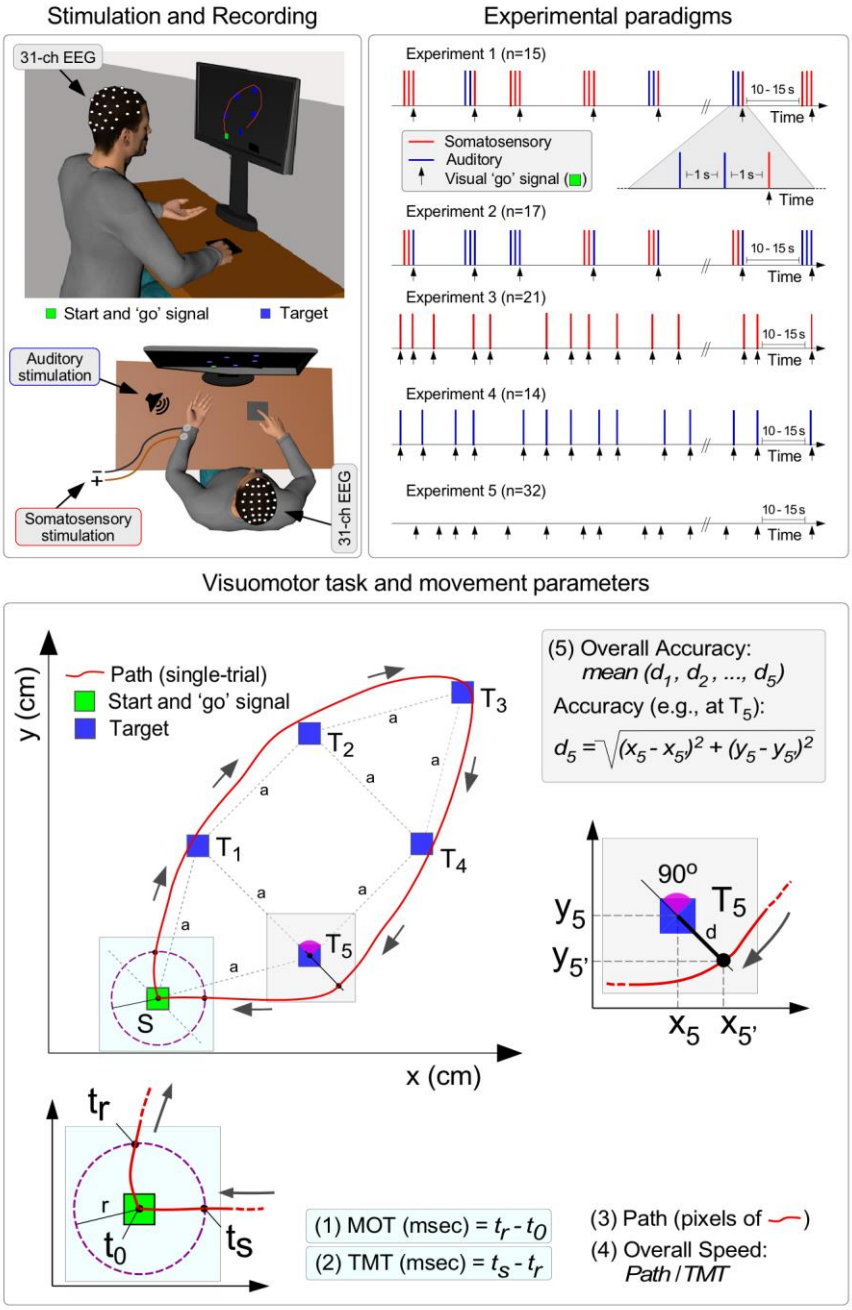

Figure 1. Experimental design, visuomotor task and movement parameters.

Top left. Participants were required to execute a visuomotor task, consisting in performing a single continuous clockwise movement of a cursor displayed on a screen, by sliding the right index finger over a touchpad. *Top right.* Before the subjects performed the movement, task-irrelevant auditory or somatosensory stimuli were delivered using different paradigms (Experiments 1-4, see sections 2.3 and 2.4 for details). In Experiment 5, no stimuli were

delivered. EEG was recorded in all experiments. *Bottom*. Schematic representation of the visuomotor task. For each trial, a number of parameters describing the cursor movement in its spatial and temporal aspects were calculated: *Movement Onset Time (MOT)* was the time elapsed between the onset of the 'go' signal and the first time point (t_r) at which the cursor was outside the circle of radius r centered around the starting position; *Total Movement Time (TMT)* was the time elapsed between movement onset (t_r) and the time point at which the cursor re-entered the circle around the starting position (t_s). *Path* was the length of the trajectory of the cursor; *Overall Accuracy* was the mean accuracy across the five targets (accuracy at each target *n* was calculated as the Euclidean distance between the position of the cursor at target *n* and the actual position of target *n*, irrespectively of side); *Overall Speed* was the *Path* divided by the *TMT*. Arrows indicate the direction of the movement.

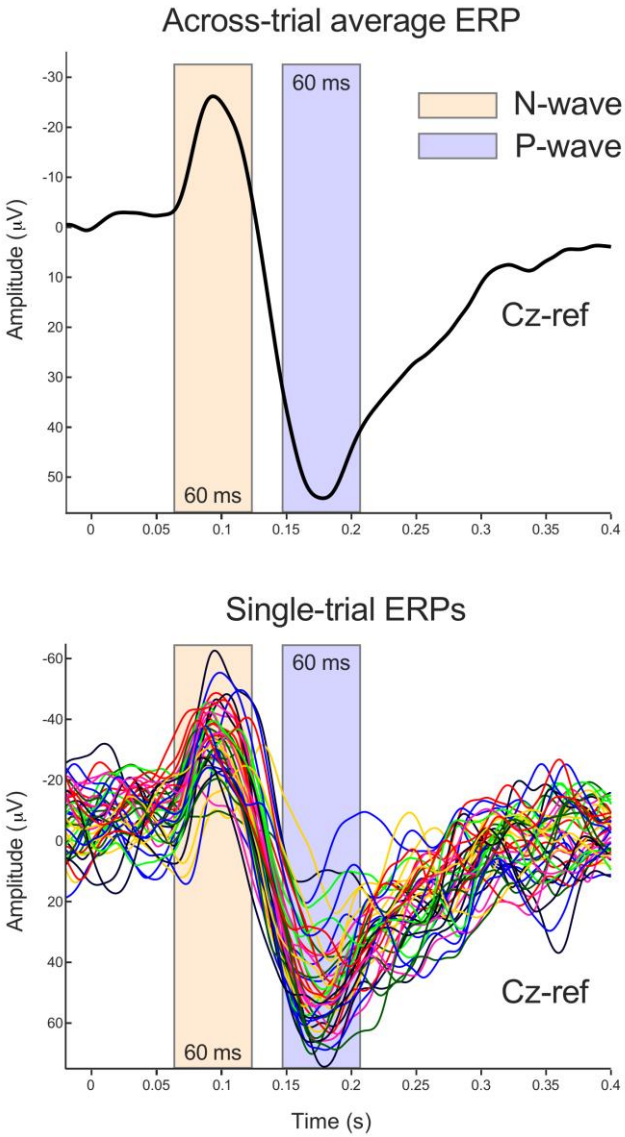

Figure 2. Estimation of single-trial amplitude of the N and P waves.

After calculating the across-trial average ERP at Cz in each participant (top graph), a 60 ms time window centered around each peak was defined (N wave, orange; P wave, blue), and the maximum negative value (for the N wave interval) and positive value (for the P wave interval) were extracted. Data from a representative participant of Experiment 1.

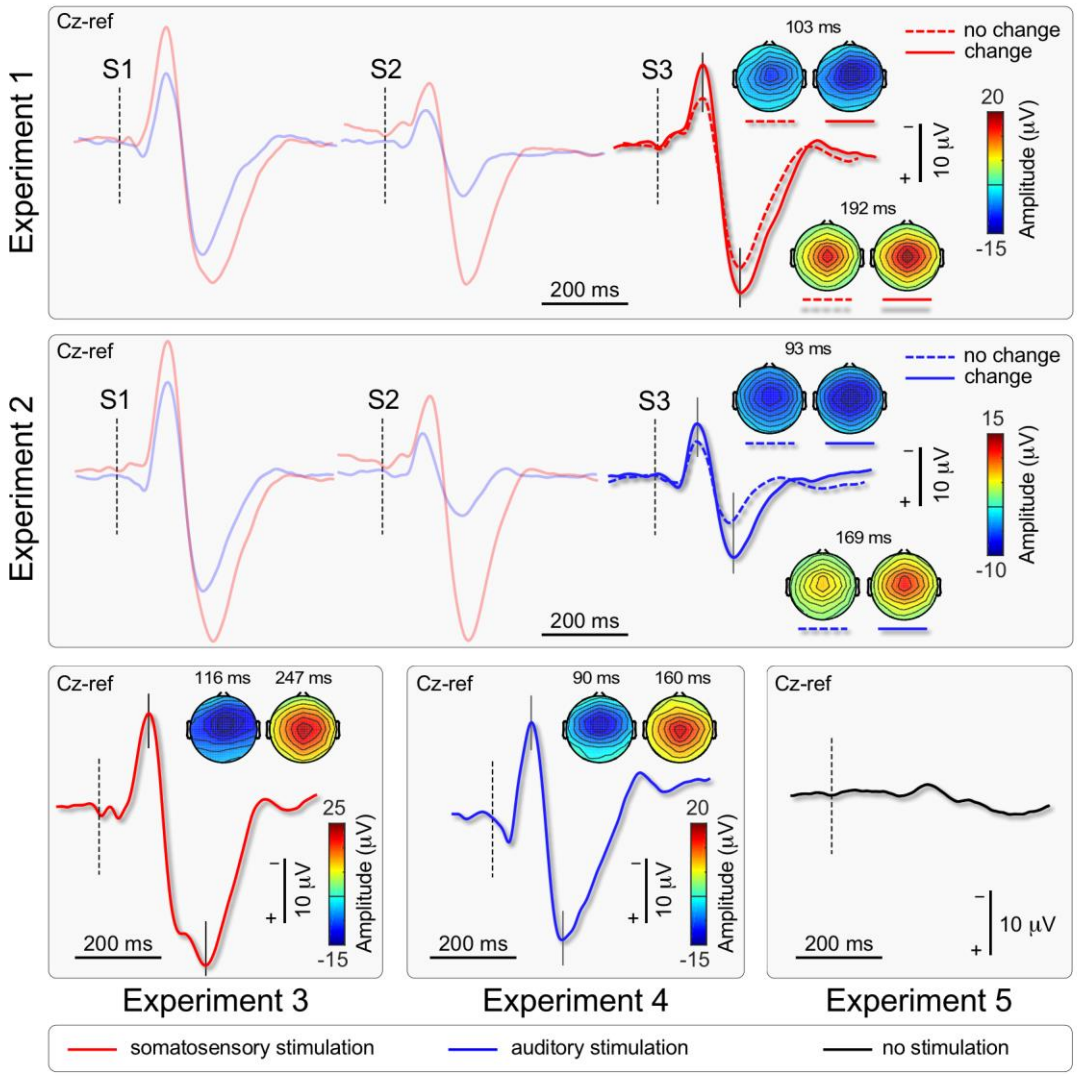

Figure 3. ERP waveforms and topographies.

Thick waveforms show the group-level average vertex waves (VW) elicited by either somatosensory (red) or auditory (blue) stimuli presented simultaneously to the 'go' cue of the visuomotor task. Vertical dashed lines mark stimulus onset. Scalp topographies displayed at the peak of the N and P waves show the typical distribution maximal at the vertex. In Experiments 1 and 2, amplitude of S3-ERPs elicited by physically-identical stimuli was larger when there was a change of modality between S2 and S3. Note also the lack of a clear VW in Experiment 5, in which no somatosensory or auditory stimuli were delivered.

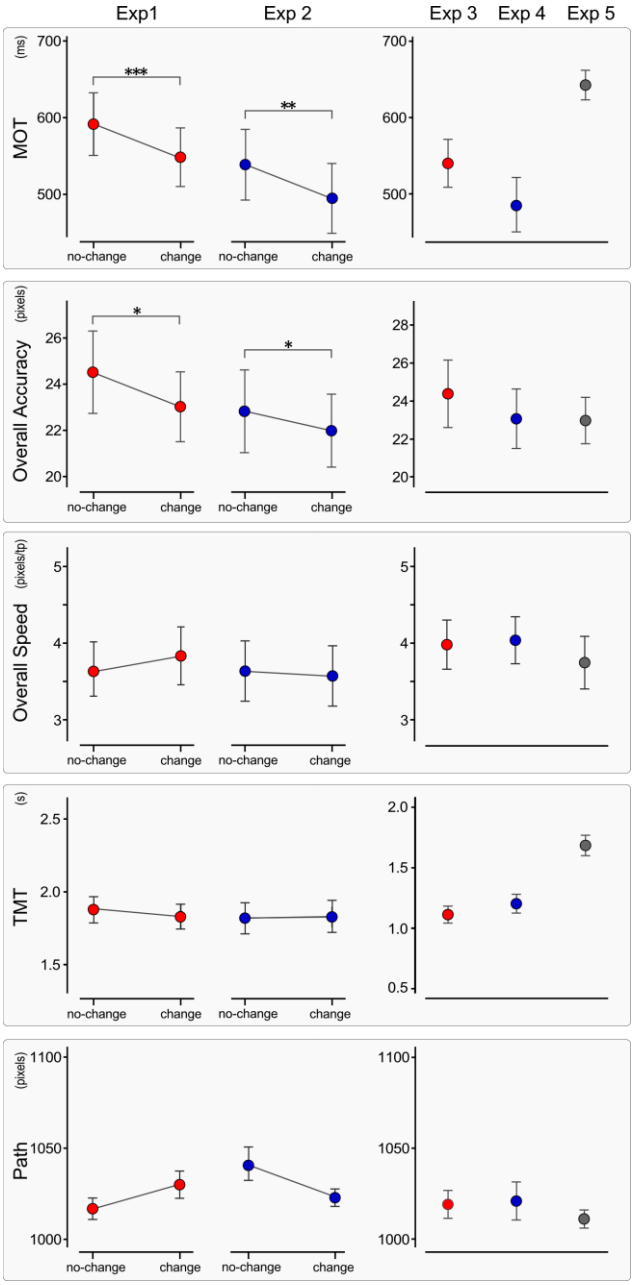

Figure 4. Behavioural results.

Mean values (±SE) of the five explored movement parameters (rows), in all experiments (columns). In Experiments 1 and 2, movement onset time (1st row) and overall accuracy (2nd row) were the only two parameters consistently affected by the modulation of stimulus saliency consequent to the change in stimulus modality. Significant differences between conditions of Experiments 1 and 2 are marked with asterisks (*p<0.05; **p<0.01; ***p<0.001). In Experiments 1-4 the 'go' signal was concomitant to either somatosensory (red) or auditory (blue) stimuli. In Experiment 5 (gray) no auditory or somatosensory stimuli were delivered.

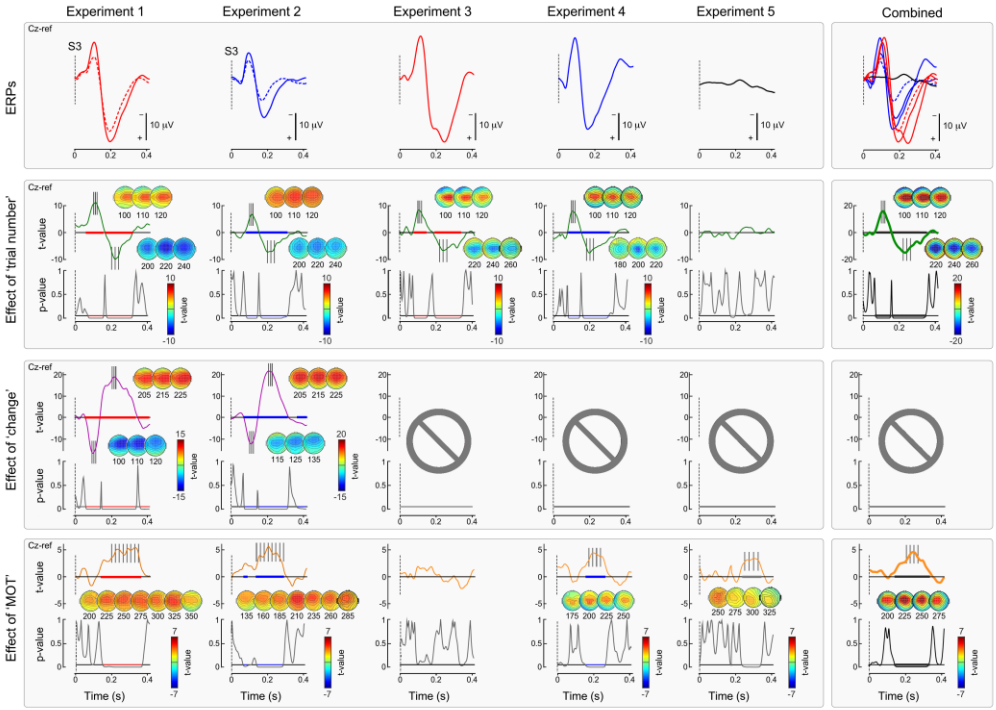

Figure 5. Results of LME analysis.

Top row: Group-level average ERP waveforms for each experiment. *Bottom rows*: Relationship between EEG signal at Cz and factors 'change' (Experiments 1 and 2), and 'MOT' (all experiments), after controlling for an effect of 'trial number' (all experiments), i.e., when such an effect was found, it was regressed out. The strength of the relationship is expressed as t-values (top waveforms of rows 2-4), and its significance as p-values (bottom waveforms of rows 2-4). Scalpmaps show the topographical distribution of t-values at the significant time intervals (highlighted in colours, after correction using permutation testing). In Experiments 1-4, in which stimuli evoking an ERP were delivered, there was strong evidence of a significant effect of trial number on EEG amplitude. Although, the statistical strength of the effect of trial number on the EEG differs slightly in topography between experiments, the observed effect indicates that in all experiments N and P amplitude was reduced as trial number increased. In Experiments 1 and 2, which entailed a change of stimulus modality, there was strong evidence that the modality change resulted in bigger amplitude of both the N and P waves of the S3-ERP. In all experiments except 3, there was strong evidence that a more negative EEG amplitude within a time window approximately corresponding to the time window of the P wave predicted shorter MOT of the subsequent movement. Crucially, Experiment 5 showed that this relationship was present (bottom row 'effect of MOT', 5th graph from the left) even without an evoked response. The far right panels show results from all experiments combined.

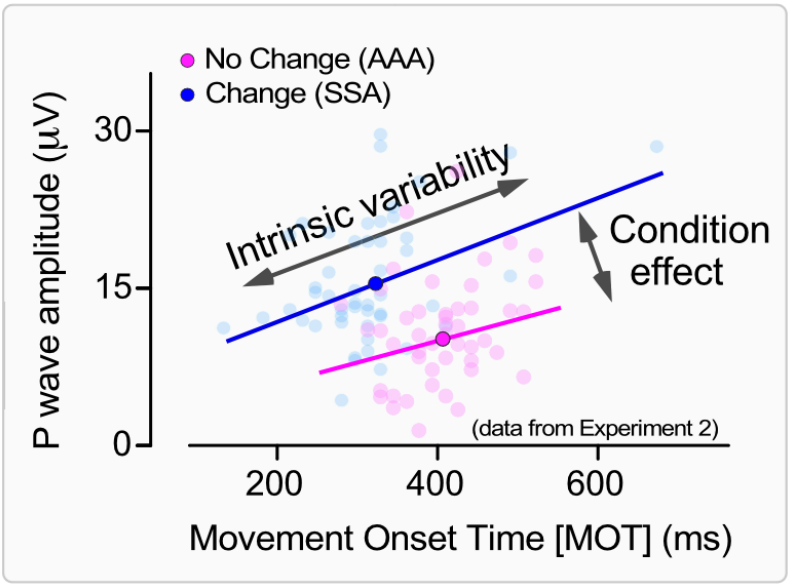

Figure 6. Relationship between P wave amplitude and MOT: Condition effect vs Intrinsic variability.

Dissociation between 'Condition effect' and 'Intrinsic trial-by-trial variability' on the relationship between Movement Onset Time (*x*-axis, ms) and P wave amplitude (*y*-axis, μV). Data from a representative participant of Experiment 2. Each pale dot represents a single trial. The two conditions are colour-coded. The opaque coloured dots represent the average across trials, for each condition. The lines represent the significant linear fit within each condition. Note how when considering the intrinsic trial-by-trial variability there is a positive relationship between P wave amplitude and MOT. In contrast, when considering the condition effect by averaging the response across trials, there is a negative relationship between P wave amplitude and MOT.

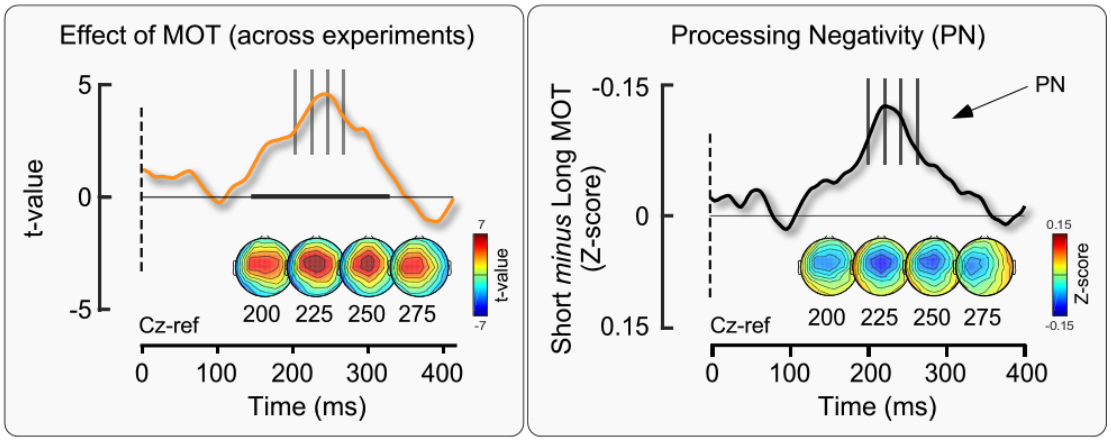

Figure 7. 'PN' wave in trials with short MOT.

The occurrence of PN observed in the LME results (left panel, reproduced from Figure 5) was confirmed by the subtraction of the average waveforms of the 'short MOT' and 'long MOT' trials (right panel). These waveforms were generated by combining the normalised EEG signal from all experiments (1-5), after removing any within-subjects (all experiments), between-conditions (Experiments 1-2) and between-experiments effects variability. The average waveform of the trials with shorter Movement Onset Times was less positive than the average waveform of the trials with longer Movement Onset Times at a time window around 120-400 ms resulting in the observed negativity.