Università di Brescia

Dipartimento di Scienze Cliniche e Sperimentali

Dottorato di Ricerca in
«Intelligenza Artificiale in Medicina e Innovazione nella Ricerca clinica e metodologica»

Coordinatore: Prof. Domenico Russo

Study of Cortical Dynamics Associated with Inhibitory Control During a Countermanding Task

SANA AL HARMAIN

41°

Supervisor: Giovanni Mirabella

Agenda

1. Background and Motivation

2. Literature Review

3. Objectives of the Study

4. Data Familiarization and Renalaysis of Work

5. Future Studies and Proposed Methodology

6. Expected Outcomes and Conclusions

7- References

1. Background and Motivation:

What Are Executive Functions?

Executive functions (EFs) are the top-down mental processes that allow us to override automatic responses and act in a goal-directed, deliberate manner (Diamond, 2013).

Core Executive Functions

01
Inhibitory control
Self-control & interference control

02
Working memory
Holding & manipulating information

03
Cognitive flexibility
Set shifting & mental adaptability

Building Higher Order Executive Functions

Reasoning · Problem solving · Planning Higher-order executive functions

1. Background and Motivation

Voluntary movement is not merely about initiation but the ability to stop or withhold a planned action is equally fundamental to adaptive human behaviour (inhibition).

Inhibition is a **pillar of cognitive control.** Inhibitory control refers to the **capacity to suppress prepotent or automatic responses** in favour of goal-directed behaviour.

It is a cornerstone of **executive function**, shaping how adults regulate attention, action, and decision-making in everyday life (Diamond, 2013). .

At the **neural level**, inhibitory control is associated with activity in the **prefrontal cortex** and its connections with **subcortical structures**, with electrophysiological markers i.e., particularly the N200 and P300 ERP components, or beta-band oscillations serving as reliable indices of inhibitory processing in adults.

2. Literature Review:

Inhibitory control:

Enables flexible and adaptive behaviour by suppressing actions when environmental or internal conditions change

The opportunity to execute an action must be continuously evaluated i.e., when costs outweigh benefits, movements must be suppressed. [Bari & Robbins, 2013; Diamond, 2013; Mirabella, 2014]

Laboratory measurement

Stop-signal task (SST) is the most widely used paradigm to examine inhibitory control.[Bari & Robbins, 2013; Mirabella, 2021; Verbruggen et al., 2019]

Neural substrates

Mirabella proposes that inhibitory control arises from a distributed sensorimotor network involving frontal cortical and basal ganglia circuits. Rather than relying on a dedicated inhibitory center, the suppression of actions is embedded within the same neural systems that plan and execute movements. This view emphasizes the close coupling between motor preparation and response inhibition. (Mirabella, 2014)

Clinical relevance:

Understanding inhibitory control is critical for neurological and psychiatric disorders such as Parkinson's Disease, ADHD, OCD, Autism Spectrum Disorder

2. Literature Review:

- The brain continuously faces a fundamental challenge: when to act and when to stop. Mirabella (2014) proposed that action execution and suppression are not independent processes but emerge from the same overlapping neural networks, dynamically reconfigured according to context.

- To study this, researchers use the countermanding task, which allows estimation of the stop-signal reaction time (SSRT) the latent duration of the suppression process (Logan & Cowan, 1984). Using reaching movements, Mirabella et al. (2006, 2008) confirmed this logic and showed that anticipating a possible stop signal slows reaction times but improves motor programming.

- Imaging and lesion studies then identified the stopping network: right IFG damage specifically prolonged SSRT (Aron et al., 2003), while the STN and pre-SMA were established as downstream nodes via the hyperdirect pathway (Aron & Poldrack, 2006; Aron et al., 2007), yet whether motor cortices were active participants or passive targets remained unresolved.

- Federico & Mirabella (2014) showed behaviorally that the inhibitory system automatically prioritises stopping over moving, with stop-signal frequency biases producing faster SSRTs at the cost of longer reaction times

- Mattia et al. (2012) confirmed this in humans via ECoG, isolating single-trial stop-ERPs selectively in M1 (BA4), PMA (BA6), and BA9 with onsets preceding SSRT end by ~83 ms, satisfying the causal criterion.

- Babiloni et al. (2016) further showed that these same regions display greater alpha/beta desynchronization and gamma synchronization during movement execution than observation, positioning BA4 and BA6 as a dual-function hub for both motor control and action understanding.

- Together these findings converge on one conclusion: the IFG–STN–pre-SMA circuit initiates the stop command, but M1 and PMA are where movement cancellation is ultimately implemented so acting and stopping are two functions of the same flexible system (Mirabella, 2014)

2. Literature Review:

So the question is:

Which motor cortex areas are particularly involved when a movement is stopped?

Since Scalp EEG showed an N200/P300 signal during stopping, But scalp EEG could not localize the exact brain regions where the complex emerges.

Methods:

Researchers recorded the Electrocorticogram activity (ECoG) directly from the cortical surface of 5 epilepsy patients with implanted electrodes. Patients performed a reaching stop-signal (countermanding) task

Main Findings

A characteristic ERP signal appeared when movements were successfully stopped

Signals were found mainly in: Primary motor cortex (M1), Premotor cortex (PMA), Brodmann area 9 (BA9)

The signal appeared before the stop process finished suggests these regions actively contribute to movement inhibition

3. Objectives:

1. To reanalyse ECoG recordings (Mattia et al., 2012) and reproduce their results for understanding the data and the findings.

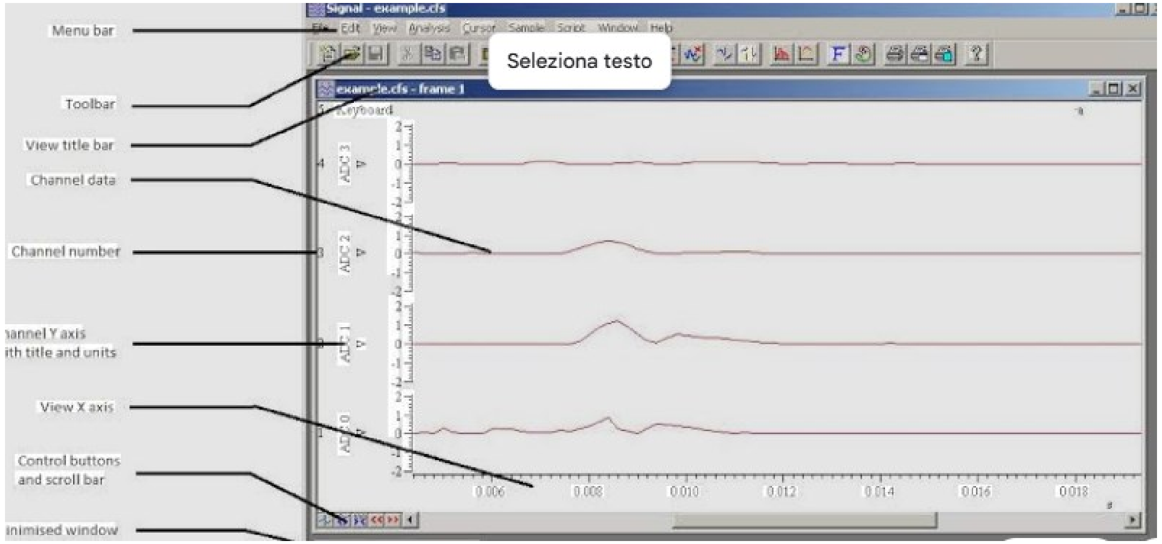
2. To investigate the spatiotemporal dynamics of alpha, beta, and gamma oscillatory rhythms in primary motor, premotor, and dorsal fronto-median cortices during movement inhibition in the stop-signal task, by comparing successful-stop, unsuccessful-stop, and no-stop trials, and to determine which frequency band changes first and whether its onset precedes the end of the stop-signal reaction time.

4. Data Familiarization and Replication of Work:

ORIGINAL RESEARCH ARTICLE
published: 29 June 2012
doi: 10.3389/fneng.2012.00012

Stop-event-related potentials from intracranial electrodes reveal a key role of premotor and motor cortices in stopping ongoing movements

M. Mattia[1], S. Spadacenta[2,3], L. Pavone[2], P. Quarato[2], V. Esposito[2], A. Sparano[2], F. Sebastiano[2], G. Di Gennaro[2], R. Morace[2], G. Cantore[2] and G. Mirabella[2,4]*



128-AC-channel Beehive Millenium monitoring system

Participants:

- Five right-handed subjects with intractable epilepsy, who underwent temporary implantation of subdural electrode grids participated in the present study

Electrode and ECoG Acquisition:

- All patients but one had 64-contact grids; one had a 48-contact grid.
- Data acquisition relied on a 128-AC-channel Beehive Millenium monitoring system with sampling rate of 400Hz.
- All recording contacts were **referenced** to an electrode placed outside the skull (either at Fpz or on the mastoid bones**).**

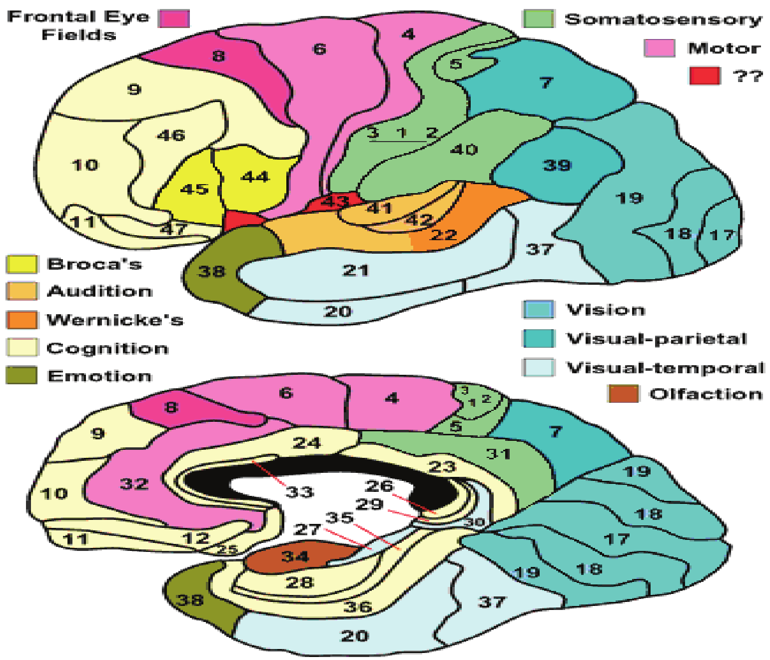
4. Data Familiarization and Replication of Work:

Electrode Localization:

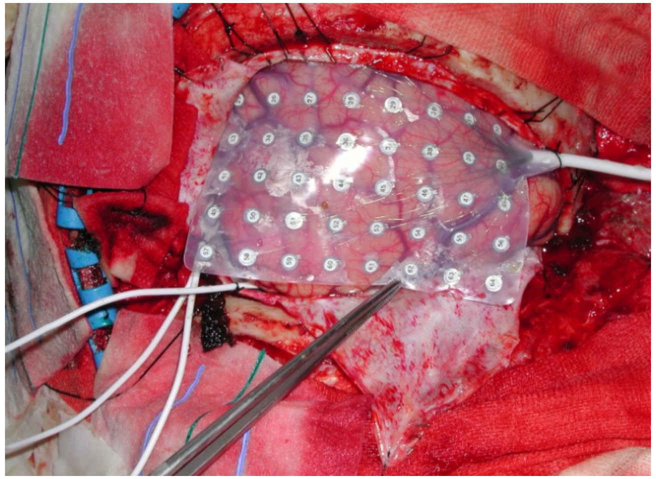
GRID_SIZE = [8 8] [Columns Rows].

GRID_START = 1: Top-left; 2: Top-right; 3: Bottom-right; 4: Bottom-left.

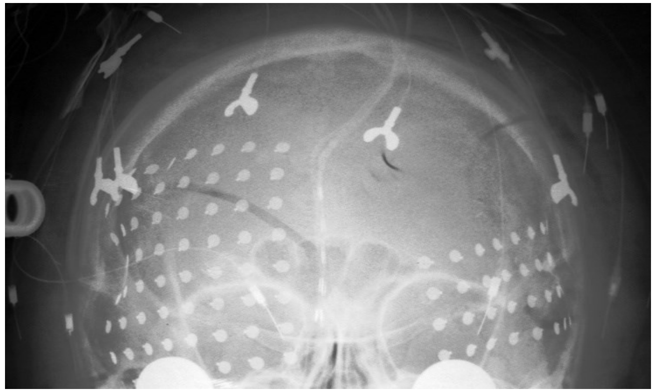
GRID_CLOCKWISE = 1



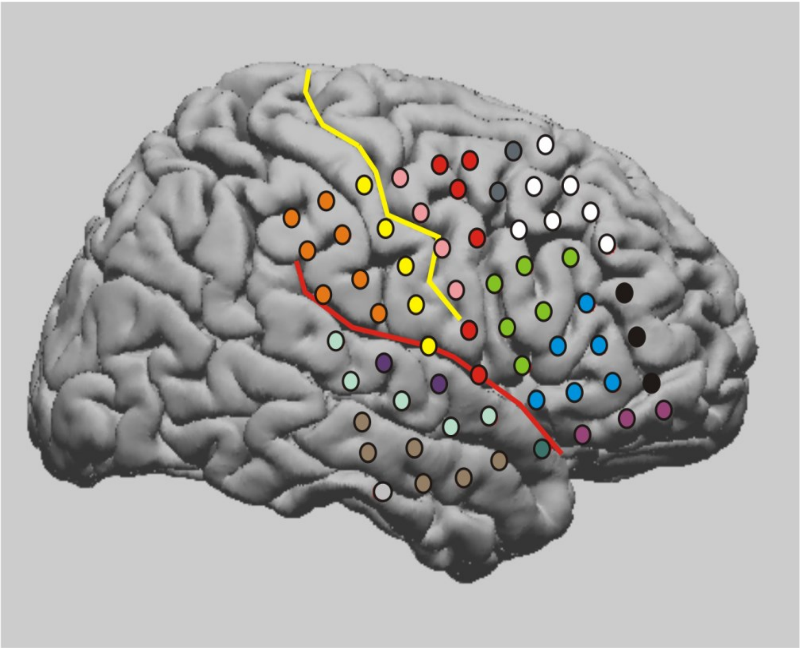
Surgery



CT after implantation



Localization



BA 40 BA 1/2/3 BA 4 BA 6 BA 9
BA 22 BA 41/42 BA 44 BA 45 BA 46
BA 20 BA 21 BA 38 BA 47 BA 8

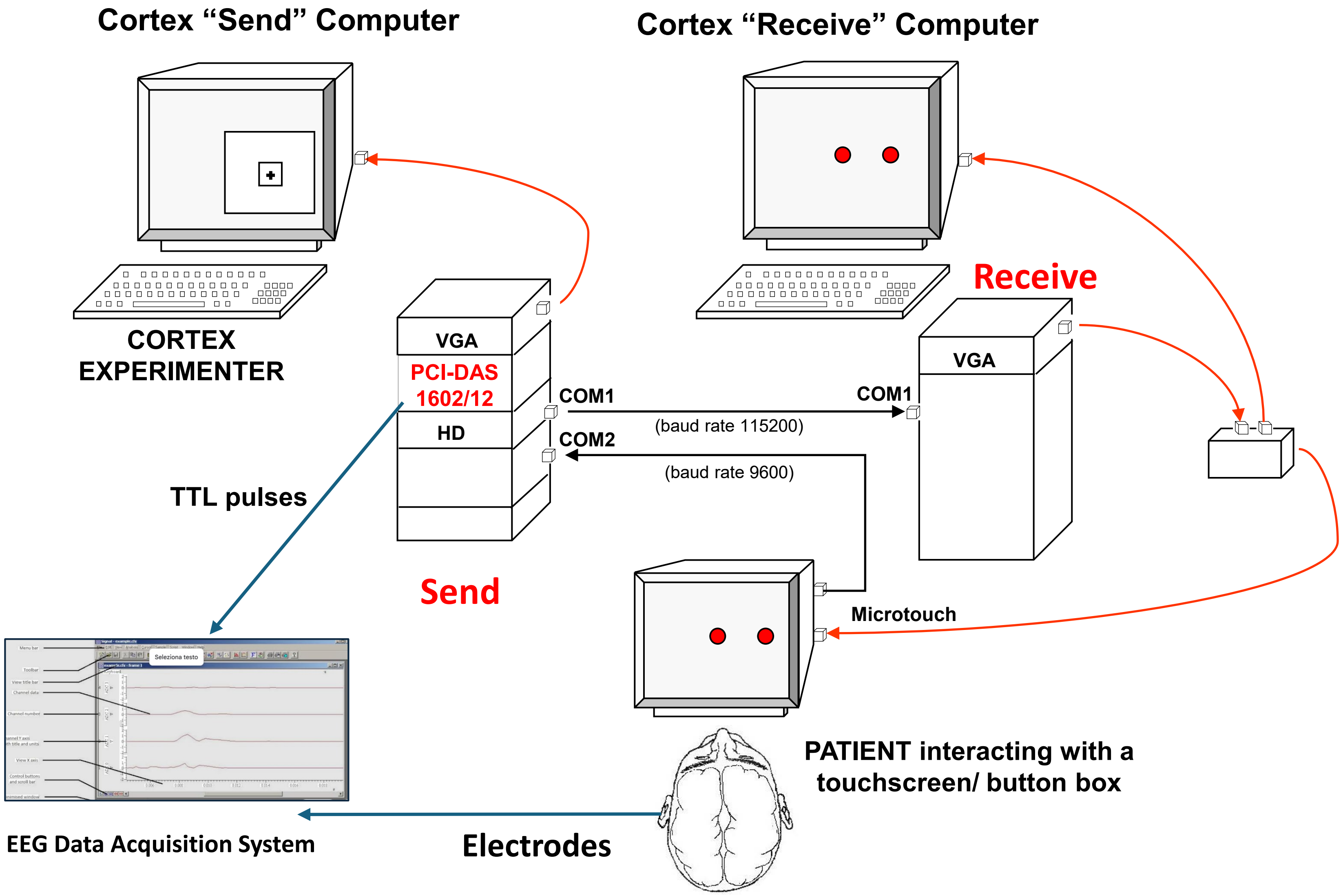
4. Data Familiarization nad Replication of Work-Apparatus:

Cortex Behavioral Control System

Patients were lying on their beds, in front of a PC on which visual stimuli, consisting of red circles against a dark background were presented.

CORTEX, was used to control stimulus presentation and collect behavioral responses.

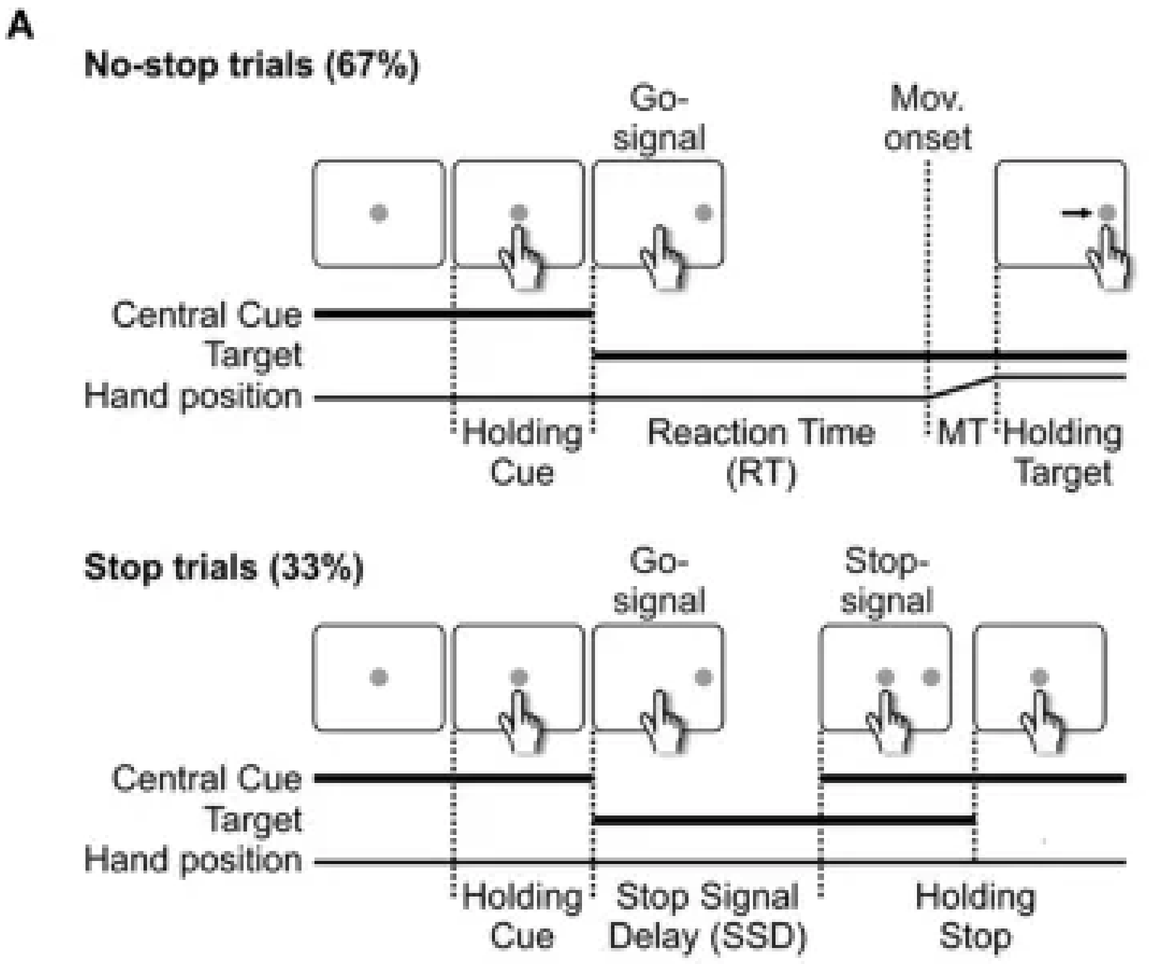
Salient behavioral events (start of the trial, go-signal onset, stop-signal onset, finger detach, end of trial) were sent to the ECoG data system acquisition via TTL pulses.



4. Data Familiarization and Replication of Work-Task Paradigm:

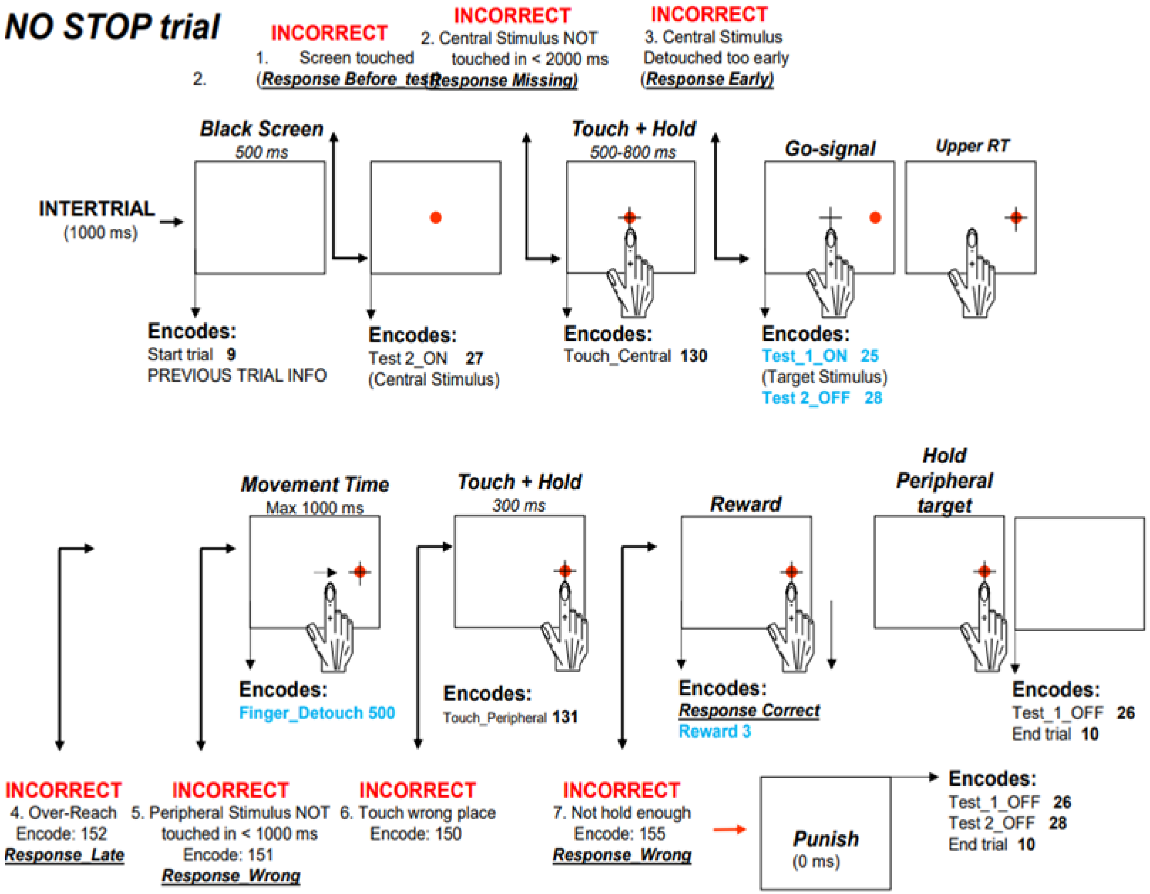
Behavioral Task and Single-Trial Estimate Events:

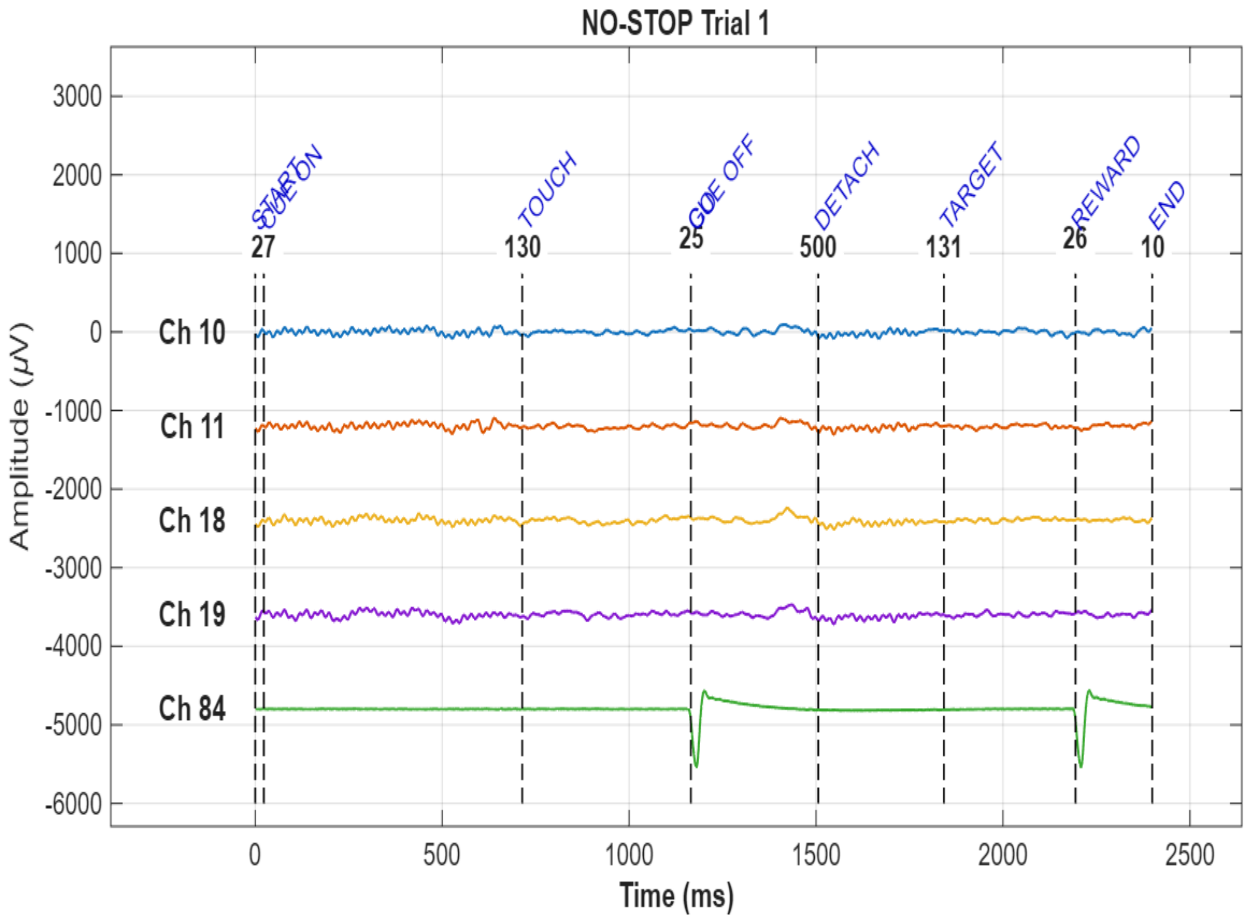
- **(A)** Sequence of screen displays (white boxes) and subject responses (hand positions) during no-stop (top) and successful-stop (SS, bottom) trials of the countermanding task.



4. Data Familiarization and Replication of Work-Task Paradigm:

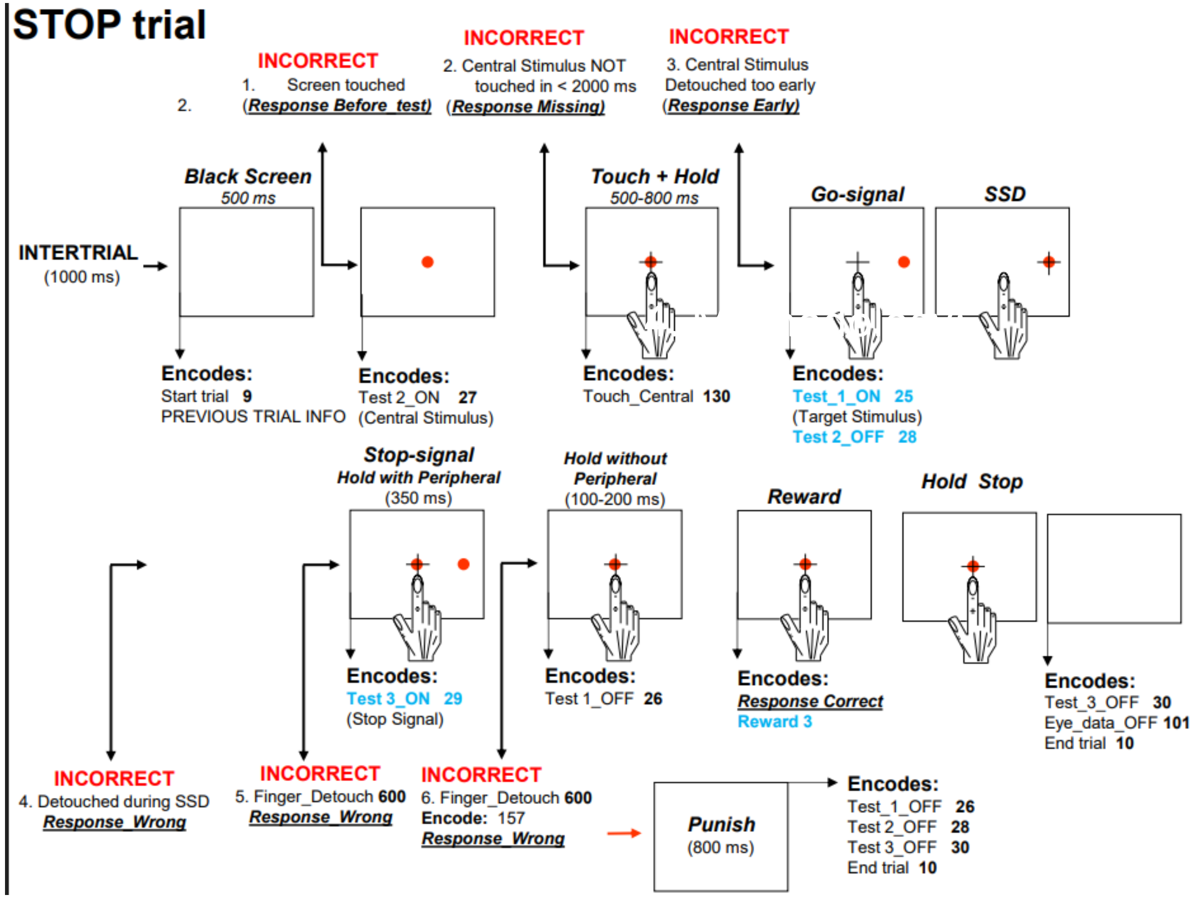
How Cortex Encodes Events and Alignment of ECoG and Behavioral Event

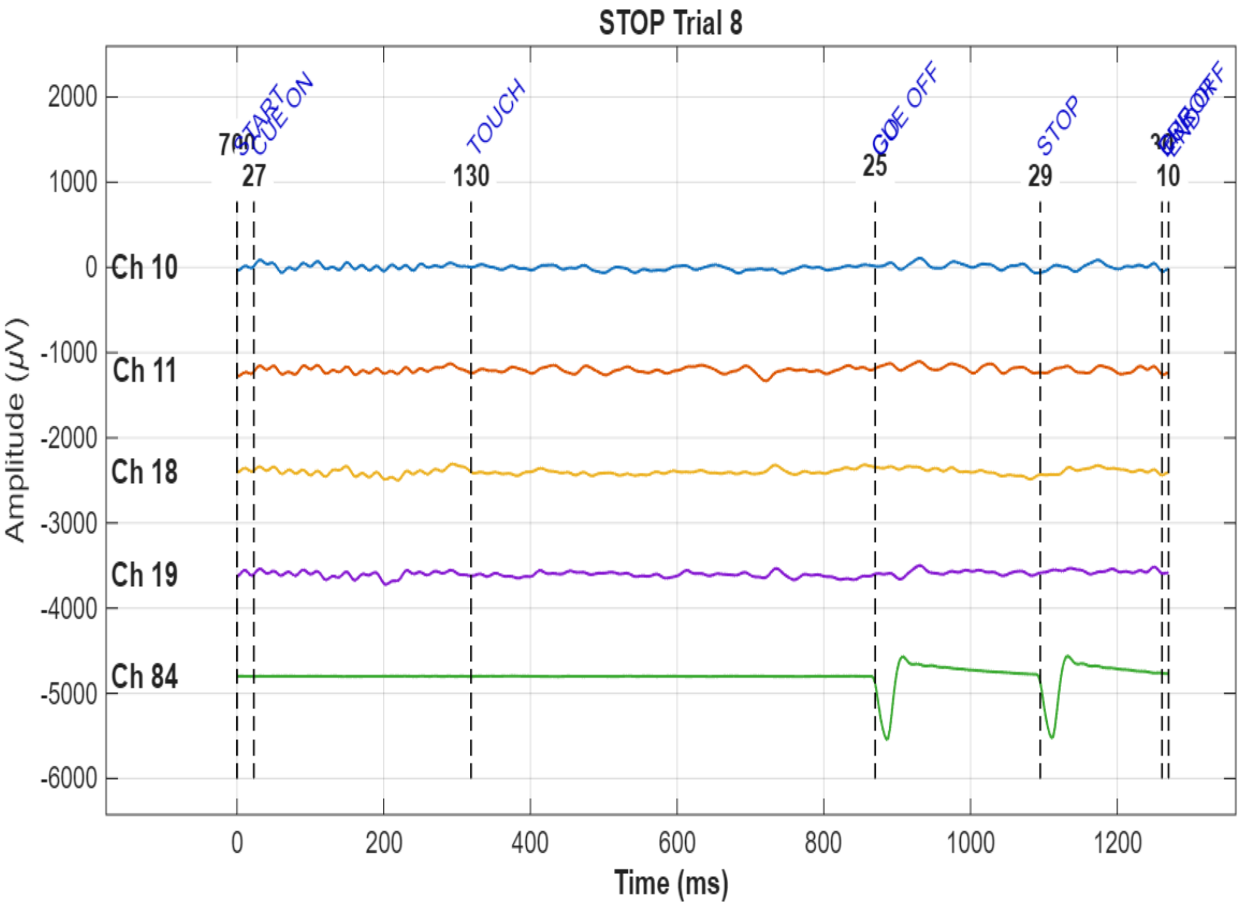




4. Data Familiarization and Replication of Work-Task Paradigm:

How Cortex Encodes Events and Alignment of ECoG and Behavioral Event

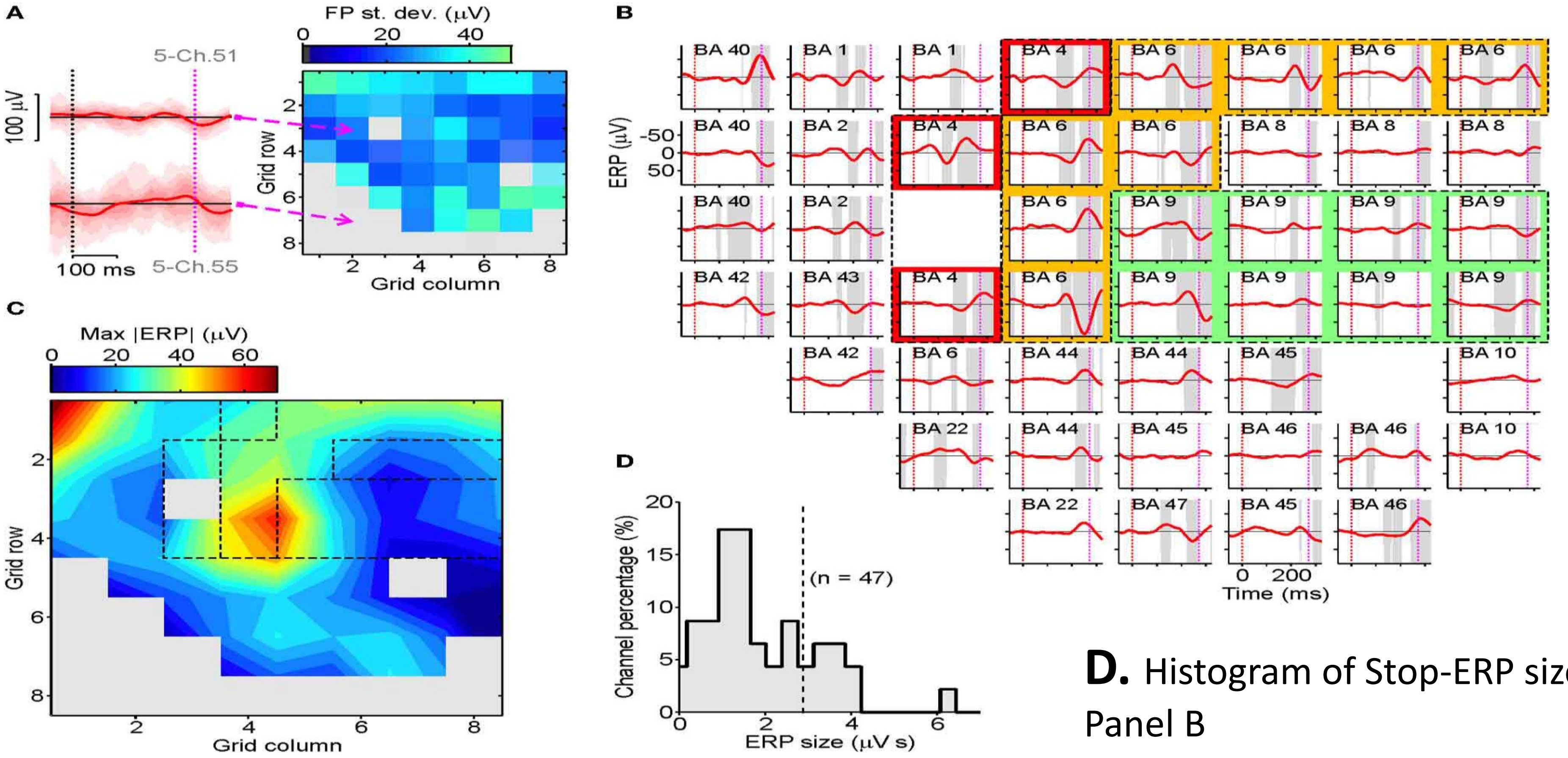




4. Data Familiarization and Replication of Work-Findings (Mattia et. al.) :

A. Map of SD of Field Potentials (FP) in SS Trials

B. Average realigned Stop ERPs of SS trials Corresponding to selected channels



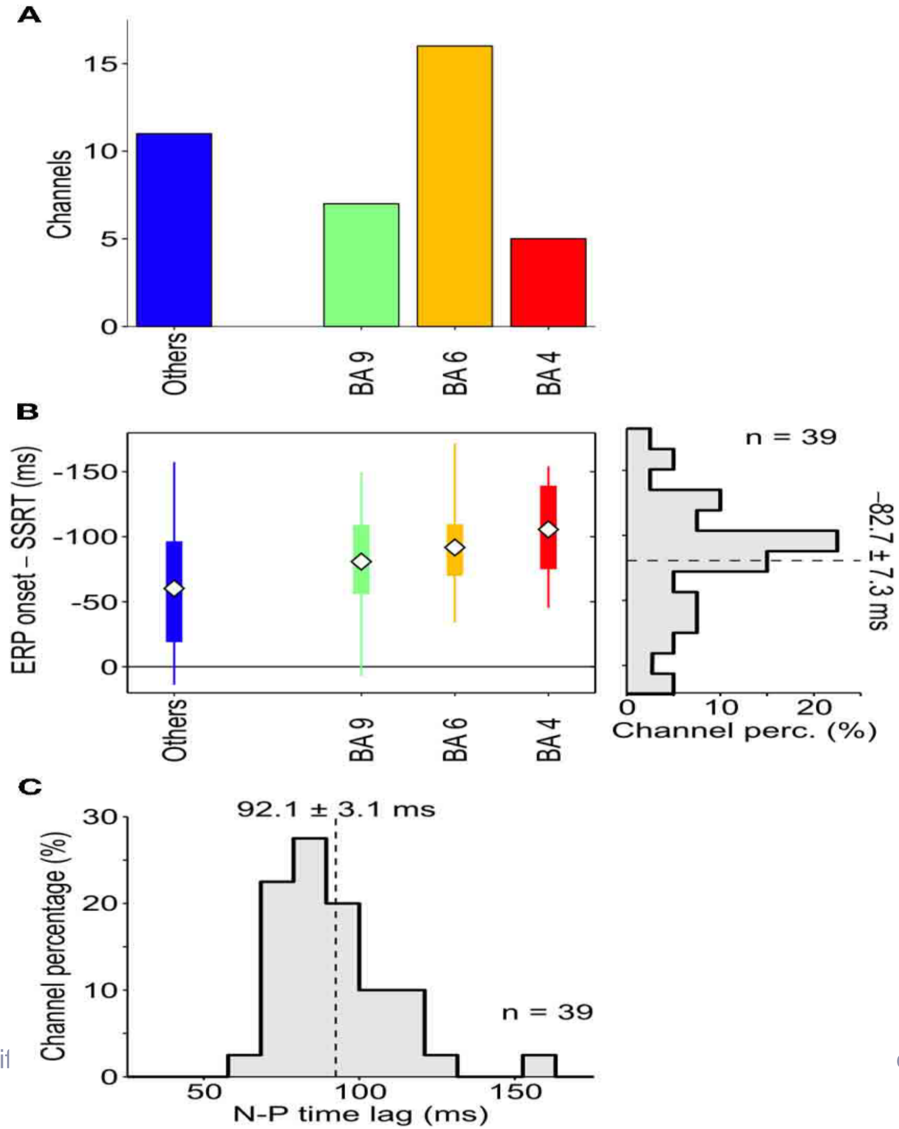
C. Smooth Contour map of the maximum absolute stop ERP amplitudes

D. Histogram of Stop-ERP sizes of Panel B

Spatiotemporal distribution of stop-ERPs in successful-stop (SS) trials.

4. Data Familiarization nad Replication of Work-Findngs (Mattia et. al.) :

Number of channels showing large enough average stop-ERPs (*n* = 39) grouped by Brodmann area.



A. Number of channels showing large enough stop-ERPs (n=39) grouped by Brodmann Areas.

B. Box plot of stop-ERPs onsets measured with respect to end of SSRT across all selected channels.

C. Distribution of time lags between positive and negative peaks across stop_ERPs.

5. Future Studies:

Investigation of Oscillatory Dynamics during Stop-Signal task, to map the spatiotemporal profile of alpha, beta, and gamma oscillatory dynamics across motor, premotor, and prefrontal cortices during Stop and No-Stop trials in the stop-signal task, and to determine whether the onset of these oscillatory changes precedes the end of the stop-signal reaction time to ensure the causality or involvement of the motor cortices.

Hypothesis:

Building on Mattia et al. (2012), who demonstrated that stop-ERPs in primary motor (BA4), premotor (BA6), and dorsal fronto-median (BA9) cortices precede the end of the stop-signal reaction time, we hypothesize that these same areas will show frequency-specific oscillatory changes during successful movement cancellation, specifically beta desynchronization, alpha desynchronization, and gamma suppression, and that beta desynchronization will show the earliest onset among all frequency bands, preceding the end of the SSRT, indicating a causal oscillatory mechanism of inhibitory control. This oscillatory profile will be clearly dissociable from the no-stop trial profile, where gamma synchronization and alpha desynchronization reflect active motor execution.

5. Future Studies:

To quantify the event-related changes of ECoG power, we will calculate the so-called event-related desynchronization/synchronization. The ERD/ERS is defined as the percentage decrement/increment in the instant power density during a given event period as compared to the instant power density during a pre-event period.
The formula was the following:

$$ERD/ERS(\%)=(E-R)/R\times 100$$

where **E** indicates the power density during the event period and **R** indicates the power density during the pre-event period. (ERD/ERS; Pfurtscheller and Aranibar, 1979; Pfurtscheller and Neuper, 1994; Pfurtscheller et al., 1997)

5. Proposed Methodology for Future Studies:

1. SPATIAL MAPPING

ERD/ERS computation across electrodes (SS trials)
↓
Separate by frequency bands:
Alpha | Beta | Gamma
↓
Topographic cortical maps

2. REACTIVE ELECTRODE SELECTION

Per Brodmann Area (BA):
- Alpha/Beta → max ERD
- Gamma → max ERS
↓
Select "most reactive electrode" per BA

3. ONSET TIMING ANALYSIS (CAUSALITY)

Permutation-based time statistics
↓
First significant deviation from baseline
= ONSET TIME
↓
Compare ONSET vs SSRT
- Before SSRT → causal role
- After SSRT → consequence

4. FREQUENCY BAND ORDERING

Compare onset across all frequency bands:
↓
Determine temporal sequence (which band activates first?)

5. SPATIAL HIERARCHY ANALYSIS

Compare brain regions:
Premotor
vs Motor cortices
↓
Test:
- Top-down sequence OR
- Parallel activation

6. UNSUCCESSFUL STOP-TRIAL ANALYSIS

Compare beta ERD onset and amplitude between SS and US trials to test for delayed oscillatory signatures of failed inhibition.

6. Expected Outcome and Conclusion:

Expected Outcomes:

No-stop trials are expected to show prominent alpha and beta desynchronization with gamma synchronization in BA4, BA6, and BA9, reflecting active motor execution. In successful-stop trials, beta desynchronization is expected to show the earliest onset among all frequency bands, preceding the end of the stop-signal reaction time indicating a **causal role** in movement cancellation. Gamma synchronization, prominent during no-stop trials, is expected to be suppressed during successful stopping reflecting cancellation of motor output. In unsuccessful-stop trials, beta desynchronization is expected to appear but with a **delayed and reduced** onset compared to successful-stop trials, reflecting a stop process that was engaged too late to cancel the movement.

Conclusion:

This study extends the foundational work of Mattia et al. (2012) from the time domain into the frequency domain, providing the first spatiotemporal spectral profile of inhibitory control using ECoG in the stop-signal task. By examining alpha, beta, and gamma oscillatory dynamics in BA4, BA6, and BA9 across successful-stop, unsuccessful-stop, and no-stop trials, the study aims to determine whether beta desynchronization precedes the SSRT end, establishing a causal oscillatory mechanism of movement cancellation. The findings will dissociate causal from consequential oscillatory dynamics, clarify the temporal ordering of frequency bands during stopping, and deepen our understanding of how motor cortices implement inhibitory control.

7. References:

- Aron, A. R., Behrens, T. E., Smith, S., Frank, M. J., & Poldrack, R. A. (2007). Triangulating a cognitive control network using diffusion-weighted magnetic resonance imaging (MRI) and functional MRI. *Journal of Neuroscience, 27*(14), 3743–3752.
- Aron, A. R., Fletcher, P. C., Bullmore, E. T., Sahakian, B. J., & Robbins, T. W. (2003). Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. *Nature Neuroscience, 6*(2), 115–116.
- Aron, A. R., & Poldrack, R. A. (2006). Cortical and subcortical contributions to stop signal response inhibition: Role of the subthalamic nucleus. *Journal of Neuroscience, 26*(9), 2424–2433.
- Babiloni, C., Del Percio, C., Vecchio, F., Sebastiano, F., Di Gennaro, G., Quarato, P. P., Morace, R., Pavone, L., Soricelli, A., Noce, G., Esposito, V., Rossini, P. M., Gallese, V., & Mirabella, G. (2016). Alpha, beta and gamma electrocorticographic rhythms in somatosensory, motor, premotor and prefrontal cortical areas differ in movement execution and observation in humans. *Clinical Neurophysiology, 127*(1), 641–654.
- Bari, A., & Robbins, T. W. (2013). Inhibition and impulsivity: Behavioral and neural basis of response control. *Progress in Neurobiology, 108*, 44–79.
- Diamond, A. (2013). Executive functions. *Annual Review of Psychology, 64*, 135–168.
- Federico, P., & Mirabella, G. (2014). Effects of probability bias on reaction times and on stop signal reaction times of reaching movements. *Experimental Brain Research, 232*(4), 1293–1307.
- Logan, G. D. (1994). On the ability to inhibit thought and action: A users' guide to the stop signal paradigm. In D. Dagenbach & T. H. Carr (Eds.), *Inhibitory processes in attention, memory and language* (pp. 189–239). Academic Press.
- Logan, G. D., & Cowan, W. B. (1984). On the ability to inhibit thought and action: A theory of an act of control. *Psychological Review, 91*(3), 295–327.
- Mattia, M., Spadacenta, S., Pavone, L., Quarato, P., Esposito, V., Sparano, A., Sebastiano, F., Di Gennaro, G., Morace, R., Cantore, G., & Mirabella, G. (2012). Stop-event-related potentials from intracranial electrodes reveal a key role of premotor and motor cortices in stopping ongoing movements. *Frontiers in Neuroengineering, 5*, 12.
- Mirabella, G. (2014). Should I stay or should I go? Conceptual underpinnings of goal-directed actions. *Frontiers in Systems Neuroscience, 8*, 206.
- Mirabella, G. (2021). Inhibitory control and impulsive behavior: Lessons from the stop-signal paradigm. *Frontiers in Neurology, 12*, 658467.
- Mirabella, G., Pani, P., & Ferraina, S. (2006). Inhibitory control of reaching movements in humans. *Experimental Brain Research, 174*(2), 240–255.
- Mirabella, G., Pani, P., & Ferraina, S. (2008). Context influences on the preparation and execution of reaching movements. *Cognitive Neuropsychology, 25*(7), 996–1010.
- Swann, N., Tandon, N., Canolty, R., Ellmore, T. M., McEvoy, L. K., Dreyer, S., DiSano, M., & Aron, A. R. (2009). Intracranial EEG reveals a time- and frequency-specific role for the right inferior frontal gyrus and primary motor cortex in stopping initiated responses. *Journal of Neuroscience, 29*(40), 12675–12685.
- Verbruggen, F., Aron, A. R., Band, G. P., Beste, C., Bissett, P. G., Brockett, A. T., Brown, J. W., Chamberlain, S. R., Chambers, C. D., Colonius, H., Congdon, E., De Jong, R., Forstmann, B. U., Georgiev, D., Heckhausen, J., Hervey, A. S., Huster, R. J., Jahfari, S., Langford, Z. D., ... Boehler, C. N. (2019). A consensus guide to capturing the ability to inhibit actions and impulsive behaviors in the stop-signal task. *eLife, 8*, e46323.

Università di Brescia

Thank you for Your Attention !

Artificial Intelligence in Medicine and Innovation in Clinical Research and Methodology

sana.alharmain@unibs.it