Session 2. Poster

THE CONTROL OF THE INITIATION AND THE INHIBITION OF VOLUNTARY MOVEMENTS: EXPERIMENTAL ANALYSIS AND THEORETICAL MODELLING OF THE NEURAL CORRELATES AT THE POPULATION LEVEL

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Context and purpose

The project aims at characterizing the neural correlate of motor decision processes in non-human primates, by identifying signals and decoding procedures suited for providing information on the areas involved at the neural population level, to shed light on the cooperative dynamics of the underlying distributed network.

A distinctive aspect of our approach is the parallel extraction of the single unit activity (SUA), with standard spike-sorting procedures, and the raw signal recorded by the electrode, which we analyze in the Fourier frequency domain. While the so-called MUA (Multi Unit Activity) and LFP (Local Field Potential) frequency bands are frequently investigated, we extend our analysis to much higher frequencies (kHz and beyond), and argue with theoretical grounding that relevant information on the neuronal collective dynamics can be extracted by comparing the spectral time-dependent properties in the different frequency bands.

The combined analysis of single-unit activity and local field potentials recorded from multiple areas presents technical and conceptual challanges, and is presently an active area of research. Theoretical predictions on model networks, which have been and are developed in the project, add another dimension to the data analysis, promising in the long run to provide heuristic tools for guessing the pattern of functional connectivity underlying the observed task-related behaviour. A first example will be mentioned below.

As a long-term perspective of the project, understanding the neural underpinning of motor decision processes is a prerequisite for a principled approach to the design of Brain-Computer Interfaces (BCI, devices and procedures that decode the neural activity related to planning and executing motor acts, e.g. for driving artificial limbs, and/or selectively stimulate selected brain areas, to restore impaired functions). Conceptual and signal-analysis tools we are developing, aimed at the description at the neural population level, promise to be helpful in this respect.

Research summary for the first year

The mechanisms subserving the inhibitory control of movement are in several respects representative of the motor decision processes. We adopted the "countermanding paradigm" introduced by Logan in the '80, in which the subject is asked to execute a (reaching or saccadic) movement when a GO signal is turned on, but to inhibit (abort) such movement if a STOP signal intervenes during the reaction time (Figure 1).

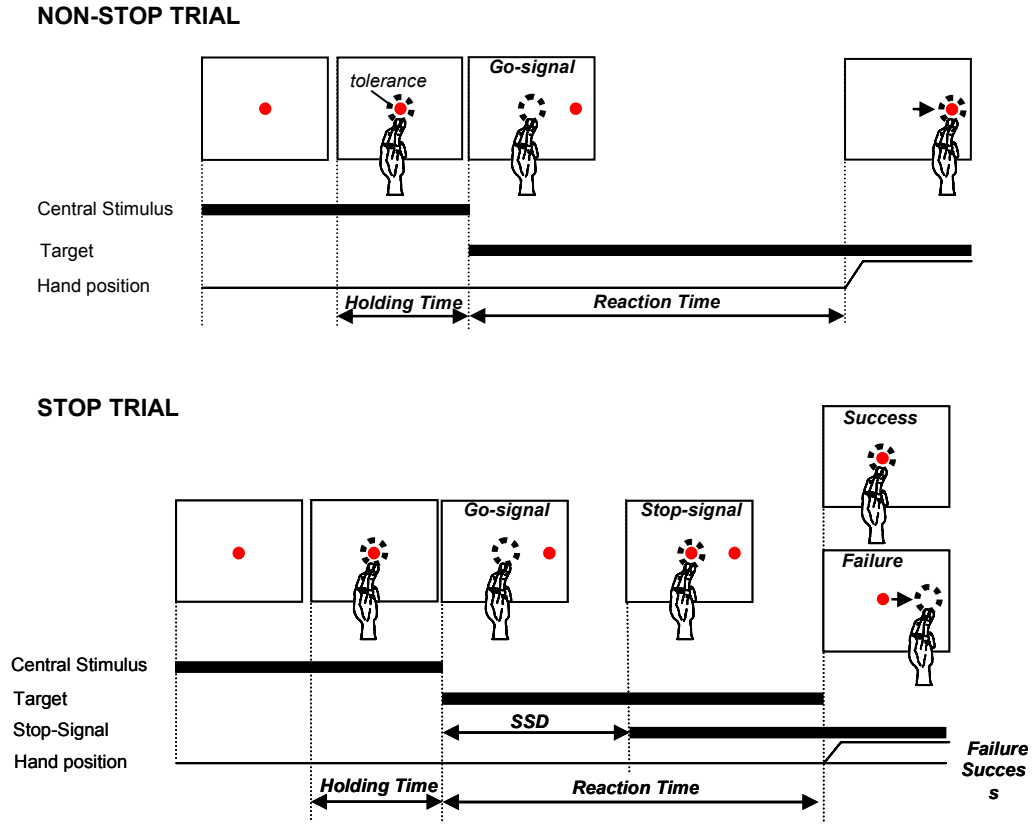

Figure 1. The Countermanding paradigm.
STOP trials and NON STOP trials are randomly intermixed. In NON STOP trials after a go signal the subject has to react as quickly as possible to reach a peripheral target. In STOP trials the subject is requested to withhold the movement whenever a stop signal follows the go signal with one of four possible delays (*stop signal delay*, *SSD*)

The countermanding protocol allows to estimate the 'Stop Signal Reaction Time' (SSRT), which is clearly not directly observable. While the case of saccadic movement inhibition has been thoroughly studied in recent years, little is known on the neural correlates of the motor inhibition for the reaching countermanding.

A monkey (*Macaca mulatta*) was trained to perform a reaching countermanding task. The monkey is sitting in front of a touch-screen, and instructed to reach visual targets, which appear in different positions on the screen. In 25% trials (STOP trials), randomly intermixed with 75%

NON-STOP trials, a stop signal was presented, with a variable delay (SSD, Stop Signal Delay) from the GO signal.

Variable SSD are introduced both for making the task less predictable for the monkey, and for spanning a significant range of monkey's performances, in order to measure the 'inhibition function', which is needed to infer the SSRT (short SSD are easy, long SSD are hard).

Neural activity was recorded from seven movable electrodes in a region covering the Dorsal Premotor areas in the frontal lobe, as well as more prefrontal areas. In parallel with the single unit activity, using standard filtering and sorting, the raw signal was also recorded with a 24 kHz sampling rate, and analysed off-line.

Figure 2 reports the main result derived from the analysis of SUA. For all the SSD the SUA for STOP and NON-STOP trials diverge before the end of the SSRT, which suggests that the recorded activity can be causally related to the reaching movement inhibition.

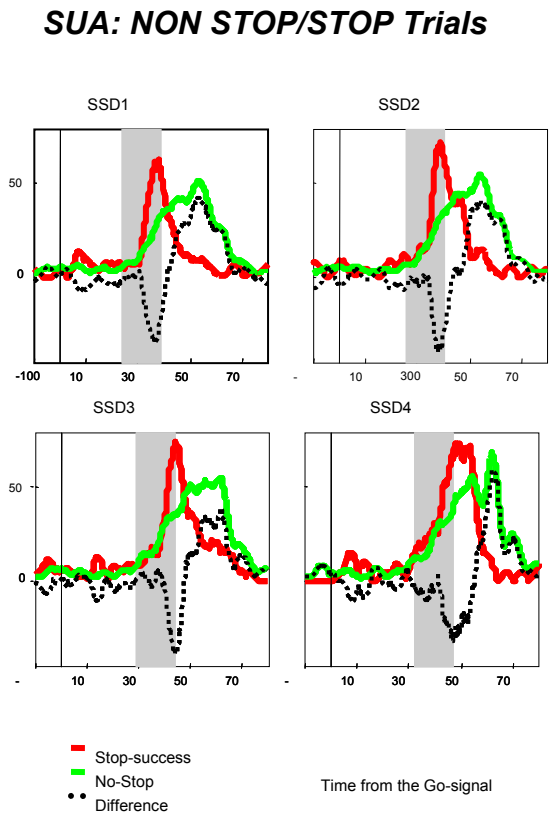

Figure 2. Results on the task-related single-unit activity.
Green solid lines are the PSTH (per-stimulus time histogram) for the NON_STOP trials;
red solid lines are the PSTH for the STOP trials, and the dotted black line is their difference.
All the PSTH are aligned to the GO signal. The four panels correspond to different SSD.
The grey shaded region represent the duration of the SSRT

The analysis of the unsorted raw signal is illustrated in Figure 3.

Panels A and B show two preliminary results meant to illustrate the potential of the approach.

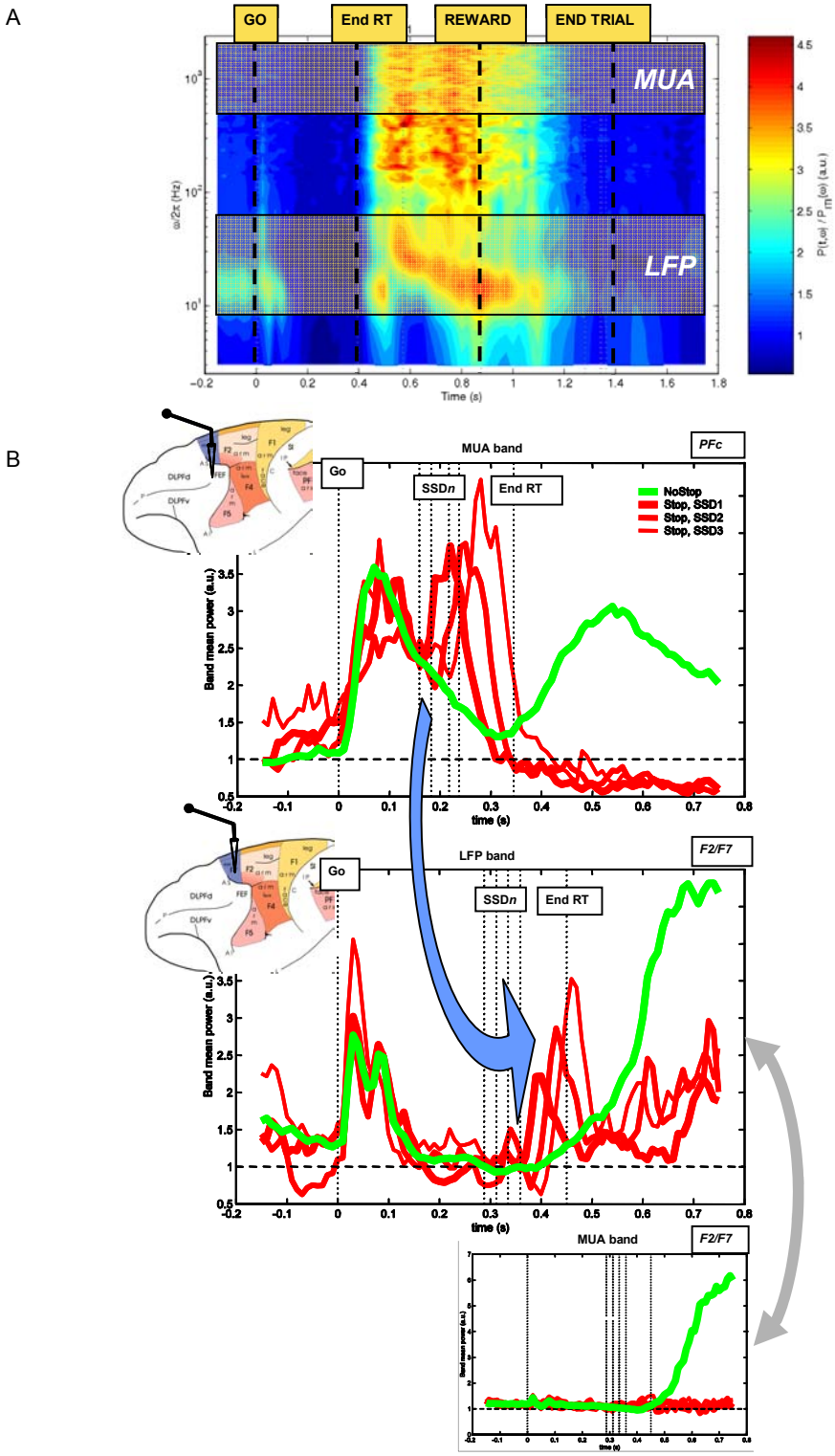

Figure 3. Task-related power modulation at the population level can suggest patterns of functional connectivity. A: Spectrogram of the raw electrode signal aligned to the GO signal relative to Inter-Trial Intervals. The MUA and LFP band are defined. B: Power spectral density, averaged in selected frequency bands, *vs* time, for STOP (red), NON-STOP (green) trials, for the two recording sites shown on the left. Red solid lines with different thickness correspond to different SSDs

The spectrogram in panel A shows a movement-related structure in NON-STOP trials: a marked power decrement just before the movement for all frequencies, followed by a power excess, for high frequencies (greater than 100 Hz), during the movement. A prominent power peak appears around 30 Hz and, as the movement proceeds, drifts towards lower frequencies, down to about 15 Hz when the reward signal occurs. As a working hypothesis, suggested also by our theoretical predictions on the relation between spectral power resonances and characteristic times of spike transmission, we propose that the movement-related power modulation is due to activity of neural populations in the vicinity of the electrode, while other time-dependent features at lower frequencies would be related to more distributed neural signals, as perhaps those due to reward expectation. This would account for the downward frequency shift in power for the no-stop trials.

Panel B shows an evocative relationship observed between the activity recorded from two different sites.

The most noteworthy feature is the hierarchy of power peaks related to the SSD values, expressed in the MUA band for the first site (prefrontal site, top plot), and the analogous sequence of power peaks occurring in the LFP band for the F2-F7 recording site, which appear as a shifted version of the former MUA peaks. No relevant MUA power structure is visible in the F2-F7 recordings, as illustrated by the small bottom plot.

According to the standard interpretation, the mean power in the MUA band is related to the local spiking activity, while the mean power in the LFP band is related to local or distributed synaptically transmitted reverberant activity. Therefore the combined analysis of LFP and MUA could provide information about the local or distributed nature of the synaptic communication between the neural populations involved.

The suggested scenario includes a STOP-related reverberant activity originating from PFc, which would be synaptically propagated to the (anatomically connected) area F2-F7, without significantly affecting the spiking activity of the latter, as witnessed by the absence of relevant MUA power modulation in F2-F7.

Short-term perspectives and outlook

A second monkey is now being trained and the experiments are scheduled for late fall 2006.

The US partner Dr. R.H. Wurtz came to visit the ISS-Roma1 group in the summer 2005; during the visit we could discuss and compare our preliminary results on the reaching countermanding, to the studies on the neural correlates of decision processes for eye movements, explored in a series of works by dr. Wurtz group.

In view of the potential for application to a BCI, less invasive recording devices have of course an appeal. We recently started recording from standard sub-dural grids of electrodes in epileptic patients performing motor or visual tasks; building on that experience, the context for cooperation with the NIH group got strengthened by the decision to add suitably engineered subdural grids to the standard depth electrodes for recording on monkeys, to check if the sole signal from the grid would provide the essential information which, when collected by the depth electrodes, is able to drive a BCI.

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