Additional Q&As about Dr. Casarotto's webinar:

Q: How do you interpret the polarity of TEPs - I have seen prominent negativities in some of your examples and other more prominent posititivies in TEPs. In the case of evoked potentials from stimulation of subdural electrodes, CCEPs have typically shown a prominent N1 and N2 peak.

Dr. Casarotto's Answer: *Cortical responses to invasive stimulation have peculiar characteristics as compared to TMS-evoked potentials, mainly because of the different stimulation intensity and by the different type of recording (the signal-to-noise ratio is much higher for CCEPs than for TEPs). N1 and N2 peaks recorded from CCEPs have a different latency as compared to the so-called N1 and P2 components of TEPs (N1 about 100 ms and P2 about 200 ms after stimulation). Thus, I think that it is not easy to directly correlate CCEPs and TEPs components.*

Q: You've shown stim.-intensities using both SO and EF. Why not only the latter (and better!)?

Dr. Casarotto's Answer: *When setting TMS intensity, we usually rely on a real-time estimation of the induced EF (expressed in V/m) provided by the neuronavigation software (included in the Nexstim TMS unit). In the presentation, I reported sometimes the corresponding %MSO simply because many researchers are actually more familiar with it or (more often) are not able to estimate the induced EF in real time. This information, which is anyway valuable, is not enough to ensure an EEG response without artifacts and with high signal-to-noise ratio: that's why, after setting TMS intensity based on the induced EF, we may further adjust (if necessary) the actual TMS intensity based on real-time inspection of EEG responses.*

Q: I don't know I feel the data presented during presentation was from healthy controls but are there additional artifacts one should expect when onewith patients (I.e., stroke patients with large lesions etc.)

Dr. Casarotto's Answer: *Recording TMS-EEG in non collaborative subjects in general and in particular in brain-injured patients surely involves additional problems. In order to maximize the chance of recording a significant EEG response to TMS, it is important to avoid delivering TMS pulses directly on a cortical lesion, because in this case it is unlikely to elicit any neuronal activation. In order to properly avoid lesions, it is particularly important to rely on a navigation software when dealing with brain-injured patients. Skull discontinuity and derivations may further constrain the cortical sites available for direct TMS stimulation.*

Q: Sham protocols and electrical stimulation feel different than active TMS. How can we minimize the impact of sensory components that differ between stimulation conditions?

Dr. Casarotto's Answer: *Currently proposed sham stimulations try to mimic the sensory stimulation possibly associated with TMS, but I agree that they still feel different. I think that the sensation related to coil vibration minimally contributes in amplitude to genuine EEG responses to TMS, unless it is associated with scalp muscle twitch. However, using the GUI it is possible to maximally reduce the unwanted activation of scalp muscles, at least when stimulation is not targeted over very lateral scalp sites. Concerning auditory stimulation, the air-conducted component can be successfully*

reduced by applying proper masking procedures. Bone conduction can still contribute, but to a much lesser extent in my experience. I think that there is room for further improvement on the hardware side of TMS in order to reduce loudness of the coil click and amplitude of coil vibration.

Q: Thank you for the information talk. I understand that the software will be publicly available. Can you confirm my understanding?

Dr. Casarotto's Answer: *Yes, a Matlab-based version of the software code will be made freely available.*

Q: In the Q/A session, you mentioned that you may not get a signal if you are directly over a lesion/infarct. If you are using navigated TMS and you can see where you are stimulating, are there particular places in/near a lesion that you specifically try to either target or avoid to help obtain a better signal?

Dr. Casarotto's Answer: *We typically try to avoid stimulating directly over cortical lesions, because this does not produce any evoked response. In order to properly set the stimulation targets, we always rely on a neuronavigation software that shows in real time where we are stimulating on individual MRI images. It is not easy to predict a priori which stimulation target will provide the "best" EEG response, but we always perform an extensive mapping (e.g. 3-4 cortical sites) over structurally preserved cortical areas.*

Q: It was mentioned during the intro that in your research you look for plastic changes using TMS-EEG. Do you stimulate the same target, in the same orientation, and with the same V/m being received at the target each time and then look for changes in EEG signal? Or is the stimulation intensity and coil orientation modified to manage the signal/artifacts each time?

Dr. Casarotto's Answer: *When looking for longitudinal changes in EEG responses to TMS we do not change stimulation parameters (site, intensity, orientation) across measurement sessions. Usually, a target site whose stimulation does not produce muscle activation, should be devoid of artifacts also when stimulated at different times.*