Influence of the temporal distribution of electric pulses on transcallosal single unit responses

Alessandro E.P. Villa
Inserm U318 & Neuroheuristic Research Group, Université Joseph-Fourier Grenoble 1, France
<Alessandro.Villa@ujf-grenoble.fr> <www.neuroheuristic.org>

Yoshiyuki Asai
Institute for Human Science and Biomedical Engineering, National Inst. of Adv. Industrial Science and Technology
AIST Tsukuba Central 6, Tsukuba, Ibaraki, 305-8566 Japan
<yoshiyuki.asai@aist.go.jp>

Jose P. Segundo
Department of Neurobiology, UCLA, Los Angeles, CA 90095-1763, USA
<segundo@ucla.edu>

ABSTRACT

Deep Brain Stimulation with pulse trains has been successful when treating Parkinson's Disease, dystonia, epilepsy and possibly other conditions; train timings [***Timing**: instants when pulses occur*] involved 80-150/s averages and always pacemaker patterns [***Pattern**: train dispersion and sequence of intervals close to their average duration*]. Occasionally, however, benefits were partial or absent. Presynaptic timing and pattern sensitivity in individual neurons reflect characteristic features (membrane time constant, refractoriness, synaptic after-effects) of the involved neurons (Segundo, 1986). Our subsequent work will adjust cortical stimuli to these as reported for the involved neurons, thus exploring the question more physiologically. We examined in anesthetized rats how differently timed stimuli to one temporal cortex (area Te1) affected spike trains in the controlateral homotopic field it drives transynaptically.

Four Wistar rats of either sex (250-350 g body weight) were used in this study in compliance with European Union guidelines for the care and use of laboratory animals and after receiving governmental veterinary approval. The subjects were anesthetized with an i.p. injection of Equithesin at a dose corresponding to 130 mg/kg chloral hydrate and 30 mg/kg of pentobarbital; supplemental doses were provided when necessary. Bipolar electrical stimulations were applied through microelectrodes 800 microns below the pia and separated by 1-2 mm. Stimuli consisted of 500-1200 trains of pulses (100 microseconds, <500 microA, 342 ms), separated by 4 s. Stimulation rates were 25, 50, and 125 pulses/s; patterns were either pacemaker, *accelerando* (intervals decreasing monotonically) or *decelerando* (intervals increased). Blocks (separated by 2 minutes) of 100 trains each and in pseudo-random order were delivered. Multiple microelectrodes recorded spike trains from several neurons simultaneously.

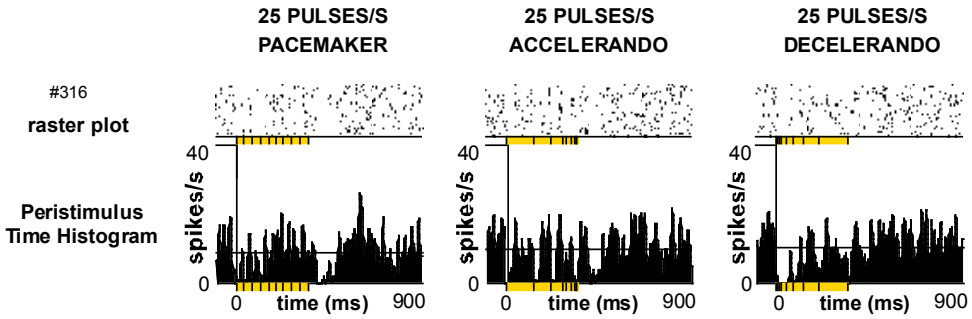

Fig. 1. Effect of different patterns of transcallosal electrical stimulation on a single unit recorded in the rat temporal cortex.

The main statistic was the peristimulus time histogram triggered by the stimulus shock to one temporal cortex and of the firing rate of the spike trains in the corresponding contralateral cortex. We analyzed 64 single units that were well isolated throughout the experimental protocol. Confirming earlier observations, transcallosal responses were predominantly rate decreases, usually extending 200 ms or more beyond stimuli offset. Very often different patterns at the same rate elicited significantly dissimilar outcomes (e.g., Figure 1); so did different rates at a particular pattern. In addition to the effect on the rate of discharges, we studied whether the pattern of stimulation modified the correlated firing of pairs of single units during the interval that followed the offset of the stimulation. We analyzed 57 pairs of units recorded from the same electrode tip. We observed a wide range of effects but the most interesting were the cases with clearly disjoint effects on the rates of discharges and on the cross-correlograms. Peristimulus effects on the firing rate could be strong with little effect on the functional interaction. Conversely, the stimulus pattern could provoke limited rate effects but noticeable changes on the synchronization of firing of cell pairs observed after the offset of the stimulus (e.g., Figure 2).

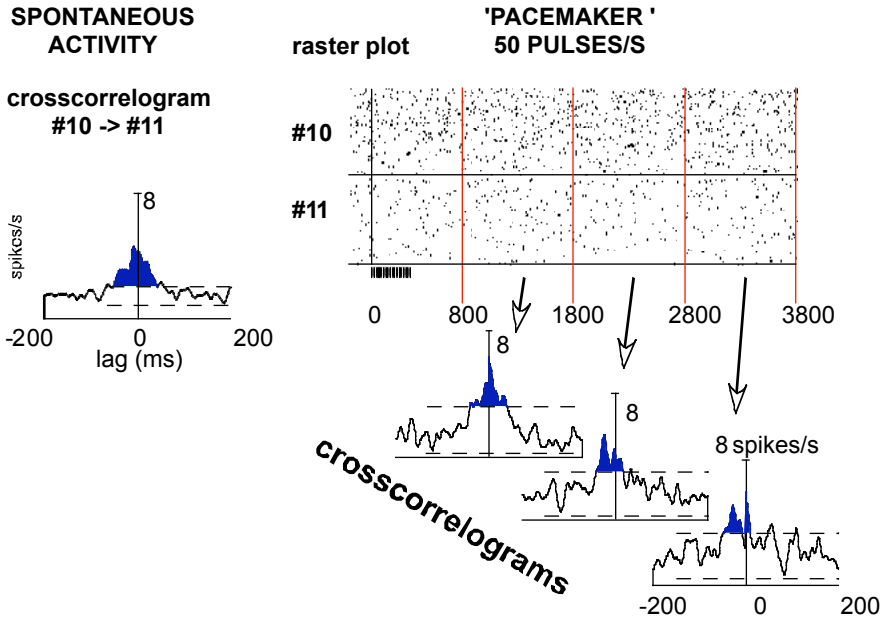

Fig. 2. Example of the effect of transcallosal electrical stimulation on the crosscorrelation of two cortical single units recorded from the same electrode tip. Notice the effect extending seconds after the stimulus offset.

The results presented clear evidence that the pattern of cortical stimulation with electrical pulse trains provoked transcallosal neuronal responses that are not limited to effects on the firing rate and that may extend order of seconds at least after the stimulus offset. We do not pretend to present a thorough investigation of the effects of transcallosal electrical stimulation but these results emphasize the importance of timing in the patterns of stimulation and suggest that differently patterned stimuli should be tested in patients where conventional procedures have not been entirely satisfactory.

Acknowledgements: The authors wish to thank Dr. Jan L. Eriksson for his participation to the recording sessions. This research was partly supported by Canon Foundation in Europe and partly by the Japanese Society for the Promotion of Science.

REFERENCES

Segundo, J.P. (1986) What can neurons do to serve as integrating devices? *Journal of Theoretical Neurobiology*, **5**: 1-59.