

A fuzzy system to analyze SIVD diseases using the Transcranial Magnetic Stimulation

A. Faro, D. Giordano, M. Pennisi, G. Scarciofalo, C. Spampinato, F. Tramontana

Abstract – The paper proposes a methodology to process the signals coming from the Transcranial Magnetic Stimulation (TMS) in order to identify the pathology and evaluate the therapy to treat the patients affected by demency diseases. In particular, a fuzzy model is developed to identify the demency of the patients affected by Subcortical Ischemic Vascular Dementia (SIVD) and to measure the effect of a repetitive TMS on their motor performances. A tool is also presented to support the mentioned analysis.

Keywords - TMS, EMG, Fuzzy Logic.

I. INTRODUCTION

Transcranial magnetic stimulation (TMS) is a non invasive diagnostic and therapeutic method without painful effects[1]. The low intensity electrical current produced by such stimulation is not absorbed by the encephalic structures as it arises during the electrical stimulation. After getting over the encephalon, the current reaches without distortion the muscles and the skin receptors and is well tolerated by the subject under test. Since the muscle movements depend on the subject's health conditions, the use of TMS is in principle suitable to discover not only the case in which a subject is affected by some mental diseases [2] (e.g., dementia, Alzheimer's disease, etc.) but also to what extent the subject is affected by such problems and what type of parameters the mental disease has modified with respect to the normal value in order to define some appropriate therapy. A suitable signal processing of the muscular responses is therefore necessary.

In the paper we propose a fuzzy approach to process the signals associated to the muscular movements in the subjects stimulated by TMS in order to identify a model that may be used to identify the pathology and to evaluate the therapy. This endeavour needs an interdisciplinary team integrating medical and engineering competences. Moreover, the experimental part plays an important role for validating the methodology.

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The paper points out all the aspects involved, from the problem statement to the proposed signal processing methodology to the results obtained. Thus, sect.2 presents some generalities about TMS and on how it is usually implemented. Sect.3 describes the protocol followed to test by TMS both healthy people and persons affected by mental diseases and what data and why have been chosen to investigate the Subcortical Ischemic Vascular Dementia. Sect.4 discusses the fuzzy processing we have performed of such data in order to identify a model together with the first experimental results that show the potentialities and limits of the methodology.

II. TMS

TMS may be used to excite the movements of all the muscles even if in the medical practice, it is used to evaluate the responses coming from the limbs (i.e., feets, hands and legs). Usually, a circular magnetic coil is used to cause the muscle movements. As an example, to produce a suitable excitation of the hands, it is enough to put a coil of 9 cm diameter over the hand encephalic area. The stimulator used in this study is the MagStim 200 provided with a circular coil (fig.1). The use of a single circular coil rather than the coil consisting of two circles allows us to stimulate the encephalic region associated to the limb by an uniform magnetic field as shown in fig.2. The left of the right part of the limb will be excited depending on the direction of the current in the coil.



Fig .1 - MagStim200 with Circular Coil

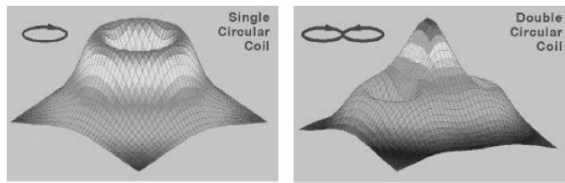


Fig.2 – Magnetic fields produced by circular coils

The muscle movements are involuntary and are caused by a magnetic field whose intensity depends on the subject under stimulation. To evaluate the threshold under which the subject is not excited by the magnetic field, usually the magnetic field intensity is slowly increased until some thumb movement is observed. In some cases the use of a specific instrument (i.e., an electromyograph) is preferred [3]. The muscle responses are measured by superficial electrodes affixed on the skin taking care of ensuring a good contact between the electrodes and the skin. Fig.3 shows graphically how the instruments are used and synchronized for a correct encephalic magnetic stimulation.

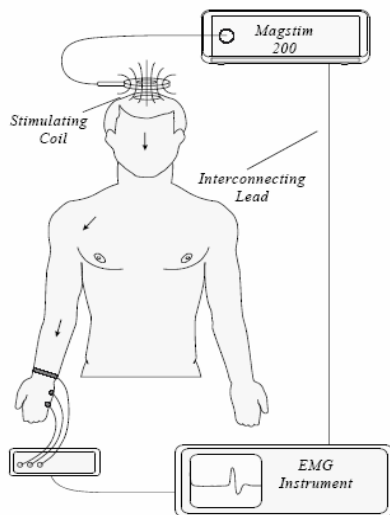


Fig.3 – Transcranial magnetic stimulation

However, as pointed out before, the test conditions, i.e., stimulation power and amplitude of the muscle responses depend on the subject. Moreover it is important to know the time response of the subject to the stimulus in order to find out the most suitable stimulation frequency in case of repeated stimulations. For this reason before stimulating magnetically a subject, she/he has to be exposed to some initial tests in order to determine at least three fundamental parameters that are important for implementing a correct medical protocol. Such parameters are:

- **Threshold:** it can be defined as the power level at which a response can be detected 50% of the time and it can be measured for both facilitated and relaxed muscles.
- **Latency:** it is the time interval between the instant when the stimulation is administered to the subject and the time instant when the muscle starts to move. Latency tends to increase with age and height.
- **Amplitude** of the muscular response: it is the peak-to-peak excursion expressed in volts of the instrument that measures the muscle response.

III. PROTOCOL

To gain some insight about the patient conditions from the muscles response to the magnetic stimulations, the tests have been conducted according to the following protocol:

1. Phase “Bi-Stim-Before”: two stimulations are given to the subject; the first, under the threshold, acts as a conditioning stimulus, the second, above the threshold, acts as the testing stimulus. The muscular responses to be compared with the ones obtained after the repetitive stimulation are taken and stored by an appropriate device, i.e., the ElectroMyoGraph (EMG) shown in fig.3.
2. Phase “rTMS”: a repetitive stimulation is administered to the subject for a certain period of time (e.g., one repetitive stimulation session per day for 15 days)
3. Phase “Bi-Stim-After”: two stimulation are given to the subject; the first under the threshold acts as a conditioning stimulus, the second above the threshold acts as the testing stimulus. The EMG tracks are stored to be compared with the tracks stored before the repetitive stimulation.

Data about muscular responses are collected during the mentioned Bi-Stim phase, varying the delay D between the first and the second stimulus. Six delays have been tested (i.e., 0, 1, 2, 5, 7, 10 ms). For each Inter-Stimulus time Interval (ISI) ten tracks have been stored, for a total of sixty stimulations per subject. Fig.4 shows the a typical response corresponding to $ISI = 1\text{ms}$.

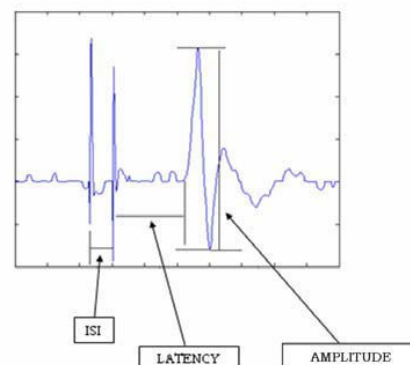


Fig.4 – Typical EMG track

In the rTMS phase the subject receives some stimulation trains whose duration is a few seconds. The train frequency is between 1 and 30 Hz depending on the pathology. A time interval of 30 seconds separates a train from the subsequent one. The stimulation phase has a duration of about 30 minutes per day and it is repeated for 15 days. The amplitude of the stimulation is between 20%-80% of the threshold, i.e., all the trains are under the threshold.

IV. METHODS AND RESULTS

To compare the signals stored before and after the rTMS phase we have decided to compute the average diagram for each ISI thus obtaining six curves X_i and Y_i , (where $i = 1$ to 6). Then we have considered various parameters associated to such curves. The ones that have been found significant for the problem at hand are:

- Latency L
- Maximum module of FFT MaxF
- Minimum module of FFT MinF
- Amplitude A
- Mean Power P

The calculus of the first fourth parameters is straightforward. The fifth parameter (i.e., the one dealing with the average power of the signal) has been evaluated by considering the case $k = 0$ in the following autocorrelation function:

$$c_i(k) = \frac{1}{N} \sum_{n=0}^{N-1} x_i(n) * x_i(n+k)$$

where the label varies from 1 to 6 being six the curves under consideration. Tab.1 shows such six values for a subject affected by Subcortical Ischemic Vascular Dementia (SIVD) computed either before and after the rTMS phase.

	Mean Power	Amplitude (Voltage PP)	Latency	Max module FFT	Min module FFT
After rTMS	↑	↑	↓	↑	↓

Table 1 – Variation of the selected parameters after a repetitive stimulation. The arrows indicate if their value increases or decreases after rTMS.

As pointed out before, in general we have the following values for each subject (where labels x and y stay for “before” and “after” rTMS, and $i = 1$ to 6):

$$\begin{aligned} &L_{x_i} \text{ and } L_{y_i} \\ &\text{MaxF}_{x_i} \text{ and } \text{MaxF}_{y_i} \\ &\text{MinF}_{x_i} \text{ and } \text{MinF}_{y_i} \\ &A_{x_i} \text{ and } A_{y_i} \\ &P_{x_i} \text{ and } P_{y_i} \end{aligned}$$

The comparison of all the above parameters for the healthy subjects shows that there is no variation, i.e.,

$$\begin{aligned} &L_{x_i} \sim L_{y_i} \\ &\text{MaxF}_{x_i} \sim \text{MaxF}_{y_i} \\ &\text{MinF}_{x_i} \sim \text{MinF}_{y_i} \\ &A_{x_i} \sim A_{y_i} \\ &P_{x_i} \sim P_{y_i} \end{aligned}$$

On the contrary, ill subjects show lower values with respect to the previous ones and some significant variations. Usually, the variations shown in the previous Tab.1 indicate an improvement of the motor performances of these subjects. Therefore the amount of the variation may be used as a measure of the efficacy of the therapy, to stop the therapy when there are no variations and to resume the therapy when after some time (usually about three months) such subjects show a significant performance decay. However, our problem is not only to evaluate the conditions to continue, stop or resume the therapy, but also to evaluate the disease degree of the patient. This will be done by developing a fuzzy model presented in the next section.

V. SIGNAL CLASSIFICATION USING FUZZY LOGIC

Fig.5 shows the system based on fuzzy logic [5] able to identify the disease of the subject. Its inputs are:

$$L_{x_i} \ L_{y_i} \ \text{MaxF}_{x_i} \ \text{MaxF}_{y_i}, \ \text{MinF}_{x_i} \ \text{MinF}_{y_i} \ A_{x_i} \ A_{y_i} \ P_{x_i} \ P_{y_i}$$

Each input consists of six values. The membership functions [5] related to the inputs are shown in fig.6. The system has been trained by data regarding both healthy people and persons affected by subcortical vascular dementia.

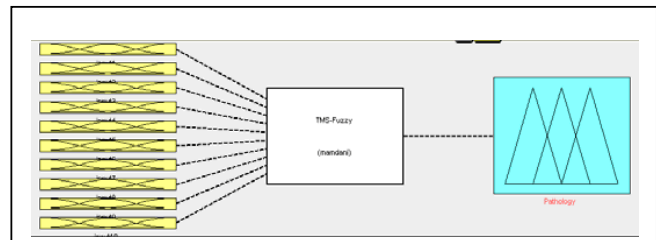


Fig.5 – Fuzzy analyzer of the muscular responses

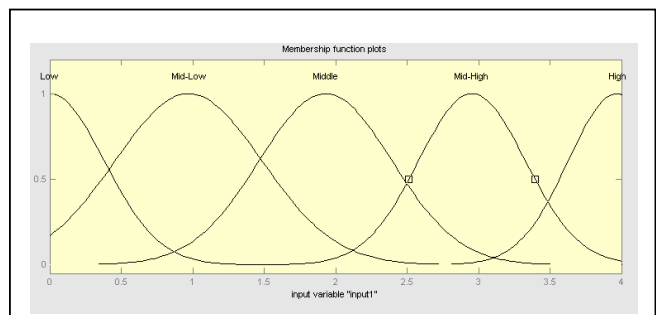


Fig.6 – Membership Functions of the inputs

After the training phase the system has generated a set of rules such as the following ones:

- If (P_x is low) and (P_y is low) then (No Disease)
- If (P_x is medium) and (P_y is high) then (Disease is SIVD)
- If ($MaxF_x$ is low) and ($MaxF_y$ is low) then (No Disease)
- If ($MaxF_x$ is medium) and ($MaxF_y$ is high) then (Disease is SIVD)
- If ($MinF_x$ is low) and ($MinF_y$ is low) then (No Disease)
- If ($MinF_x$ is medium-low) and ($MinF_y$ is medium-low) then (Disease is SIVD)

Such fuzzy rules are followed by the fuzzy system to classify a new case. Tab.2 shows that the percentage of success is very high. The classification errors deal with cases that are not healthy or SVD, but affected by Alzheimer.

Pathology	Success rate
SIVD	90 – 95 %
No pathology	90 %

Tab.2 – Experimental results

To support all the diagnostic and therapy phase a tool has been developed whose interface is shown in fig 7. Such a tool allows to load the tracks of a subject before and after the repetitive stimulation and to compute a cross-correlation in order to find if there are disease symptoms that arise when there is some difference between the tracks. In such cases the fuzzy system is activated in order to have some hints about the pathology affecting the subject. During the therapy the tool may be used to compute the improvement in motor performance after the treatment and the performance decay during the time.

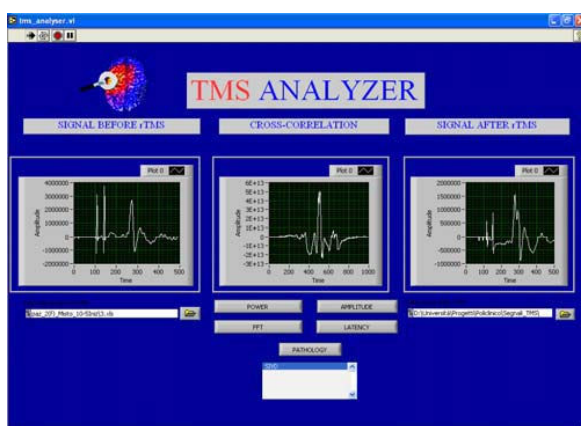


Fig.7 – TMS Analyzer

VI. CONCLUSION

The use of TMS for the diagnosis of mental diseases and the treatment of the patients affected by such problems are in an initial stage. The proposed methodology aims at giving an objective basis to both the diagnosis and the therapy by allowing us not to evaluate very precisely if the patient is or not affected by some mental disease but also it may be suitably extended to identify different stages of the disease.

Moreover, improvements of the patient's performance after the treatment may be measured not only by testing his/her motor ability as currently done in the clinical practice, but more precisely by analyzing how his/her responses to the stimulation vary with respect to the EMG tracks taken at the end of the treatment. The use of the TMS analyzer has allowed us to confirm that the positive effect of the repetitive stimulation tends to disappear in two-three months.

Finally, let us note that, in principle, by the proposed methodology it is possible to control patients affected by various mental diseases. However at the moment the analysis is devoted only to Subcortical Ischemic Vascular Dementia diseases since we have not enough data about patients affected by other pathologies. This means that the identification of the parameters and the rules to be used for analyzing other pathologies is for further study.

References

- [1]. A.T. Barker, R. Jalinous, and I.L. Freeston, "Non-invasive magnetic stimulation of human motor cortex", *Lancet*, I, pp. 1106-1107, 1985.
- [2]. H. Shimamoto, K. Takasaki, M. Shigemori, T. Imaizumi, M. Ayabe, and H. Shoji, "Therapeutic effect and mechanism of repetitive transcranial magnetic stimulation in Parkinson's disease", *J.Neurol.*, vol.248, pp.III48-III5, 2001.
- [3]. C.M. Epstein, "Applications of transcranial magnetic stimulation", In proceeding of the first Joint BMES/EMBS Conference Serving Humanity, Advancing Technology, Oct.13-16, Atlanta (USA), 1999.
- [4]. A. Pascual-Leone, N. J. Davey, J. Rothwell, E.M. Wassermann, B.K. Puri, "Handbook of transcranial magnetic stimulation", Oxford University, 2002.
- [5]. L. A. Zadeh, "Fuzzy Logic and the Calculi of Fuzzy Rules and Fuzzy Graphs", *International Journal of Multiple-Valued Logic*, 1, 1-39, 1996
- [6]. H.-J. Zimmermann. *Fuzzy Sets Theory and its Applications* Boston: Kluwer, 1991.