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A Fuzzy Model and Tool to Analyze SIVD Diseases Using TMS

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***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 and to measure the positive effect, if any, of a repetitive TMS on their motor performances. A tool is also presented to support the mentioned analysis.

***Keywords*—**TMS, SIVD, Electromiography , 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, Alzhaimer'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 model to identify the pathology and to evaluate the therapy of the patients affected by Subcortical Ischemic Vascular Dementia (SIVD). The model is based on the signals associated to the muscular movements in the subjects stimulated by TMS. The paper points out all the aspects involved, from the problem statement to the proposed signal processing methodology and supporting tool to the results obtained.

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This endeavour needs an interdisciplinary team integrating medical and engineering competences. 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 Demency. 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., foots, 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. 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.1 and fig.2

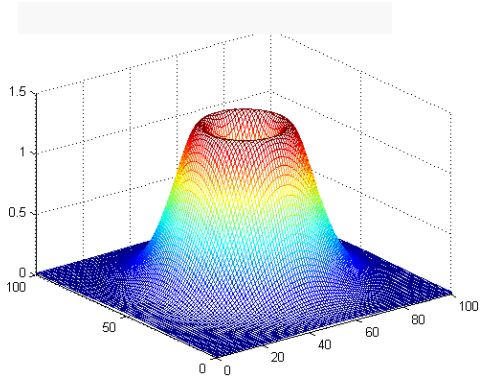

Fig 1. – Magnetic field generated by a circular coil

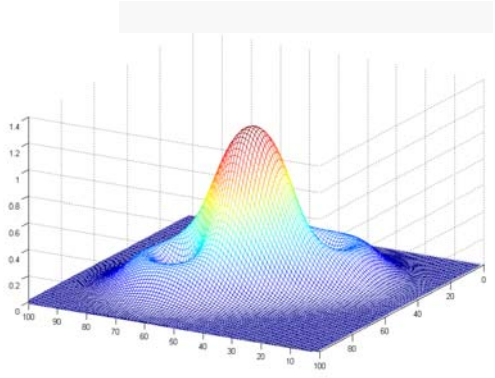

Fig.2 - Magnetic field generated by double coil

The left or the right part of the limb will be excited depending on the direction of the current in the coil. The muscle movements are involuntary and are caused by a magnetic field whose intensity depends on the subject under stimulation. In order 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 subjects, the thumb movement is so feeble that it could be confused with a possible thumb trembling affecting the subject. In such cases an electromyography (EMG) able to detect the arising of small thumb movements due to the magnetic field 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.2 shows how the instruments are used for a correct trans-cranial magnetic stimulation. In particular the cortex is stimulated using the Magstim 200 and the EMG instrument is used to monitor and store the muscular response due to the magnetic pulse.

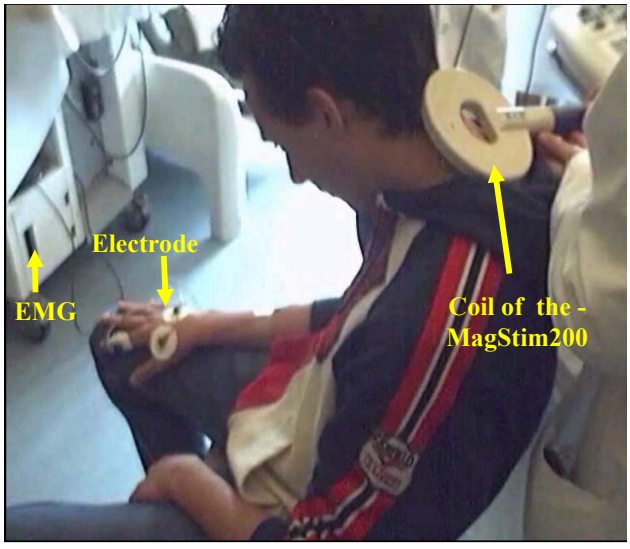

Fig.3 - Transcranial magnetic stimulation

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 how the muscles respond to the magnetic stimulations, the tests have been conducted according to the following protocol:

1. Phase "Bi-Stim-Before": two stimulations are administered 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 administered 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 an 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 a typical response for ISI = 1ms.

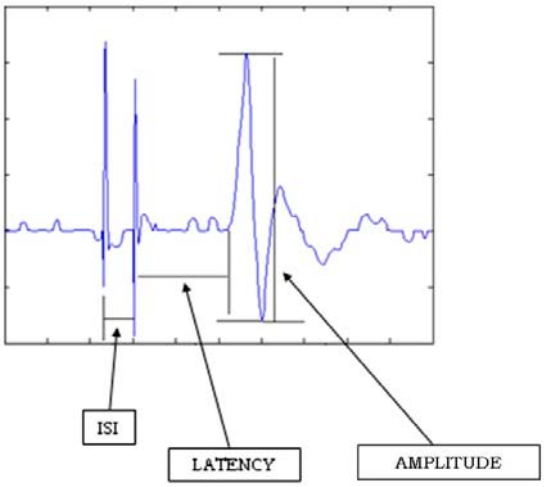

Fig.4 – Typical EMG track

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 Xi and Yi, (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.

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):

Lx_i and Ly_i
$MaxFx_i$ and $MaxFy_i$
$MinFx_i$ and $MinFy_i$
Ax_i and Ay_i
Px_i and Py_i

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

$Lx_i \sim Ly_i$
$MaxFx_i \sim MaxFy_i$
$MinFx_i \sim MinFy_i$
$Ax_i \sim Ay_i$
$Px_i \sim Py_i$

On the contrary, ill subjects show lower values with respect to the previous ones and some significant variations as shown in the fig.5 and fig.6.

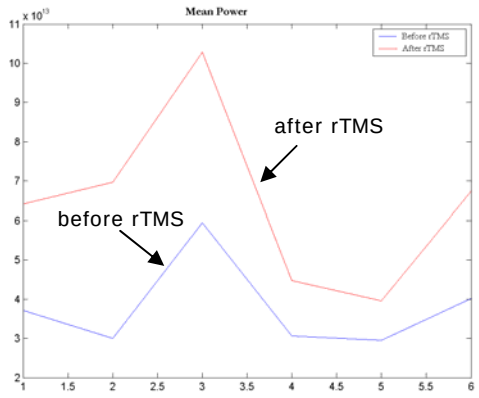

Fig.5 – Comparison between the mean power after and before rTMS for ill subject

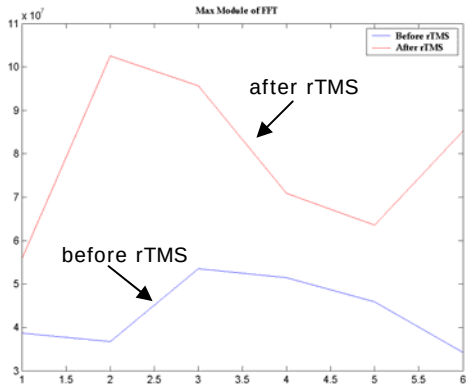

Fig.6 – Comparison between the max module of the FFT after and before rTMS for ill subject

The experiments confirm that, after the rTMS phase, all the subjects affected by Subcortical Ischemic Vascular Dementia (SIVD) show an improvement of their motor performances as pointed out in the following Table I.

TABLE-I
VARIATION OF THE SELECTED PARAMETERS AFTER RTMS.

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

The arrows indicate if their value increases or decreases.

Therefore the amount of the variation could be used as a measure of the efficacy of the therapy and as indicator to stop the therapy when there are no variations and to resume the therapy when after some time (usually about three months) the subjects exhibit a significant performance decay.

However, our problem is not only to evaluate the conditions to continue, to stop or to resume the therapy, but also to identify what combinations of the variations of the selected parameters may characterize the subjects affected by SIVD and, possibly, if such variations may characterize the *disease degree* of the patients. This will be done by the fuzzy model presented in the next section.

V. Signal Classification Using Fuzzy Logic

Fig.7 outlines how the Mamdani system based on fuzzy logic [5] is used to identify the disease of the subject. Its inputs are:

Lx_i Ly_i $MaxFx_i$ $MaxFy_i$, $MinFx_i$ $MinFy_i$ Ax_i Ay_i Px_i Py_i

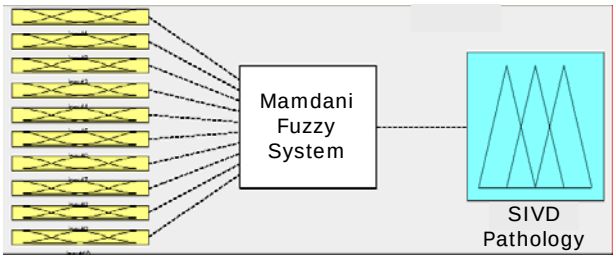

Fig.7 - Fuzzy analyzer of the muscular responses

Each input consists of six values. The membership functions [5] related to Latency and maximum module of FFT are shown respectively in fig.8 and fig.9. They respectively consist of three fuzzy values (i.e., low, middle, high),and of five fuzzy values (i.e., low, mid-low, middle, mid-high, high).

The amplitude membership functions are similar to the one dealing with the latency, whereas the membership functions of the minimum module of FFT are similar to the one dealing with the maximum module of FFT. Latency and amplitude have been characterized by only three fuzzy values since we have noted that the response of the system changes little with their variations.

The system has been trained by data regarding both healthy people and persons affected by subcortical vascular dementia. Consequently its output is characterized by the two membership functions shown in fig.10.

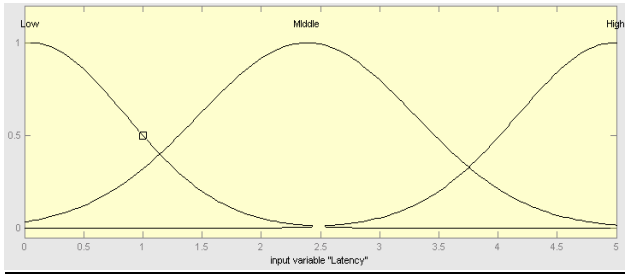

Fig.8 - Membership functions for the latency

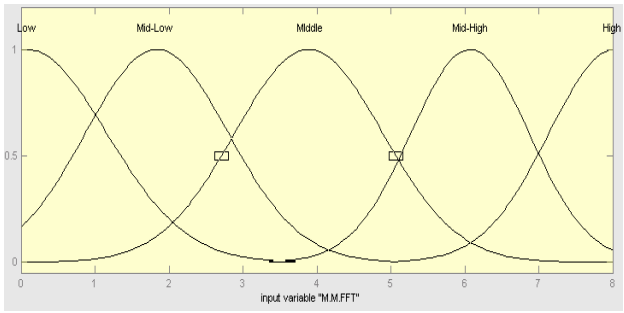

Fig.9 – Membership functions for the max module of FFT

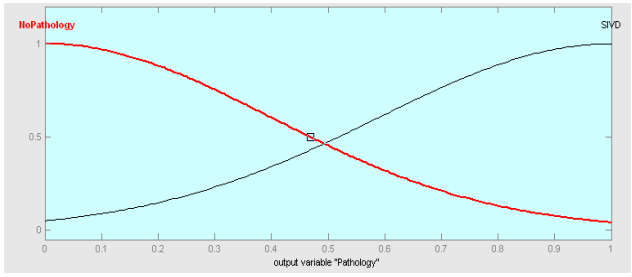

Fig.10 – Membership functions for the output

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

1. *If (Px is low) and (Py is low) then (Pathology is No Pathology)*
2. *If (Px is middle) and (Py is high) then (Pathology is SIVD)*

3. *If (MaxFx is low) and (MaxFy is low) then (Pathology is No Pathology)*
4. *If (MaxFx is middle) and (MaxFy is mid-high) then (Pathology is SIVD)*
5. *If (MaxFx is middle) and (MaxFy is high) then (Pathology is SIVD)*
6. *If (MaxFx is middle) and (MaxFy is high) then (Pathology is SIVD)*
7. *If (MinFx is low) and (MinFy is low) then (Pathology is No pathology)*
8. *If (MinFx is low) and (MinFy is low) then (Pathology is No pathology)*
9. *If (MinFx is mid-low) and (MinFy is mid-high) then (Pathology is SIVD)*
10. *If (MinFx is mid-low) and (MinFy is mid-high) then (Pathology is SIVD)*
11. *If (Px is middle) and (MaxFy is high) then (Pathology is SIVD)*
12. *If (Px is middle) and (MaxFy is high) then (Pathology is SIVD)*
13. *If (Ax is low) and (Ay is high) then (Pathology is No pathology)*

Such fuzzy rules are used by the tool to classify a new case. Since the diagnosis, i.e., *Pathology is SIVD*, is characterized by a membership degree, we can use this number as a measurement of the *disease degree*. Let us note that some in depth consideration about this way of defining the disease degree is surely useful, but it is for further study.

Table II shows that the percentage of success is very high. The classification errors deal with cases that are either not healthy or SIVD, but affected by Alzheimer and this disease that influence the classification of both healthy people and SIVD patients.

TABLE II
EXPERIMENTAL RESULTS

Pathology	% of success
SIVD	90 – 95 %
No pathology	90 %

To support all the outlined diagnostic and therapy phases a tool has been developed whose interface is shown in fig.11. Such a tool allows us to load the tracks of a subject before and after the repetitive stimulation and to evaluate if there are disease symptoms that arise when there is some difference between such tracks.

In order to have some hints about the pathology affecting the subject, the mentioned rules identified by the proposed fuzzy model may be activated by pressing the button pathology of the user interface. 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.

The tool may be also used to increase or decrease the number of the inputs by activating the section "fuzzy logic" of the user interface in search of other relevant rules. In the former case, the user may define a new input indicating, according to the interface shown in fig.12, its name and value (e.g., Hilbert module, Low) the type of the related membership function (i.e., triangular, trapezoidal, etc.) and the values that characterize this function (e.g., for the trapezoidal form this is done by indicating the four characteristic values as follows: Range = min, intermediate1, intermediate 2, max).

After the training phase and subsequent testing, the user may decide if it is suitable to substitute the old rules by the new ones. All the different rule sets are always available for the user so that she/he may resume an old set of rules by activating the sub-section Rules of the section Fuzzy Logic.

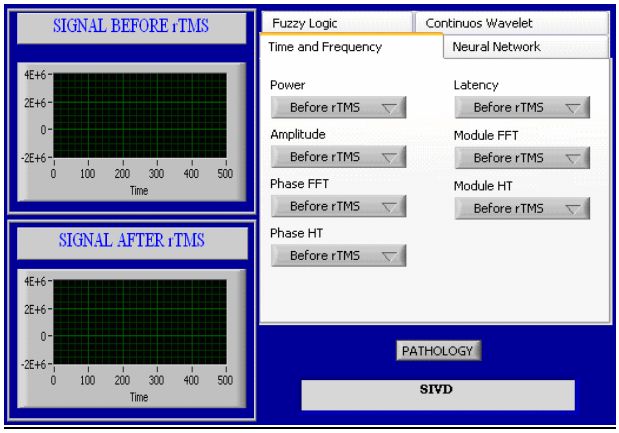

Fig.11 - Interface of the developed software

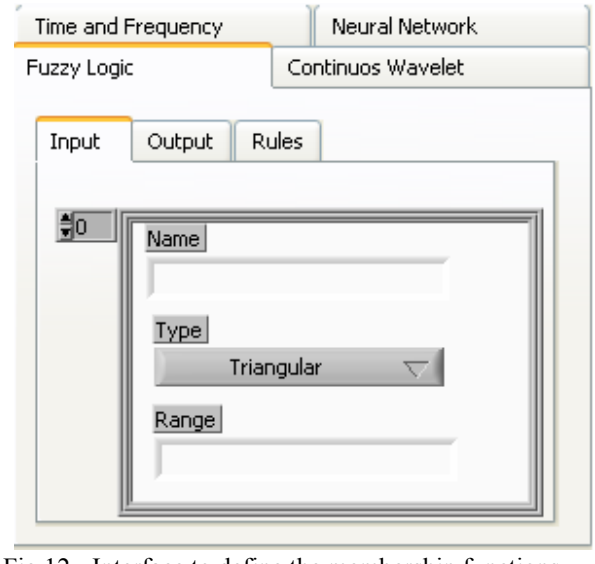

Fig.12 - Interface to define the membership functions of the inputs and the outputs, and to choose the fuzzy rules

VI. Conclusions

The use of TMS for the diagnosis of mental diseases and the treatment of the patients affected by such problems is in an initial stage. The proposed methodology aims at giving an objective basis to both the diagnosis and the therapy by allowing us not only to evaluate very precisely if the patient is affected or not by some mental disease but also the "degree" of his/her mental disease in the sense explained in sect.4.

Moreover, improvements of the patient's performance after the treatment may be measured not only by testing his/her capacity of movement as is currently done in the clinical practice, but by analyzing more precisely 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 following the same methodology used to build the model for SIVD patients, it is possible to identify also the models and related parameters that characterize other mental diseases. However, at the moment the analysis is devoted only to cardiovascular subcortical diseases since we have not enough data about patients affected by other pathologies.

Another important field of research is to find to what extent the model is able to discover if the mental disease is or not in an initial stage, to start some timely therapy. This could be inferred by the disease degree if the value of the membership degree to a certain pathology given by the model is reliable not only for medium-high values (e.g., from 0.5 to 1) but also for small values (e.g., from 0 to 0.5).

To study the problem of also diagnose the disease in its early stage, we have developed an alternative method based on neural networks since the first tests performed by using a small set of data have shown that the neural network classification is about 3% more precise than the one proposed in the paper for patients whose mental disease is in an advanced stage and, hopefully, it will be better also to classify patients with a low disease degree.

However, let us note that this does not mean that the fuzzy approach can be substituted by the mentioned neural network classification because a) the fuzzy rules remain still valid to appreciate the degree of the identified mental disease and b) knowledge of the rules that mainly determine the diagnosis may be useful to support some personalized therapy. As a consequence, for an effective evaluation of the possible disease of the patient under test, the tool will be extended to allow the specialist to use jointly both the fuzzy rules and the neural networks.

The use of the continuous wavelet transforms of the EMG tracks will be also integrated in the tool to further increase its diagnostic performances. The results of the experimentation of the extended tool for choosing the parameters and the rules to be used for analyzing various types of pathologies at different stages is for further study.

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