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THE BIOLOGICAL EFFECTS OF EXTERNAL MAGNETIC STIMULATION ON PARKINSON 'S DISEASED PATIENTS

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Abstract: The aim of this study was to investigate the influence of external transcranial magnetic stimulation (TMS) in parkinson 's diseased (PD) patients using a whole-head 122-channel magnetometer and Fourier statistical analysis. The examined group consisted of 30 patients (22 males and 8 females; mean age 65 years: range 49-80 years). External transcranial magnetic stimulation in the order of pico Tesla (TMS) was applied on the above patients with proper field characteristics, which were obtained prior to TMS (magnetic field amplitude: 1-7.5pT, frequency: the α-rhythm of the patient: 8-13 Hz). The MEG recordings after the application of TMS shown a rapid attenuation of the high abnormal activity followed by an increase of the α-rhythm (8-13 Hz). The patients' responses to the TMS were a feeling of relaxation and partial or complete disappearance of tremor, muscular ache and levodopa induced dyskinesias as well as rapid reversed visuospatial impairment, which were followed by a corresponding improvement and normalization of the MEGs.

Keywords: 122-channel magnetometer, Parkinson's disease, external magnetic stimulation

Introduction

Sandyk et al. [1] reported that parkinson 's disease (PD) is associated with neurochemical disturbances, which include reduced brain serotonin, norepinephrine, GABA and several neuropeptides which may be related to motor fluctuations. Since the pineal gland melatonin hormone also regulates such activities it has been suggested that these side effects in PD patients are related to disruption of the pineal gland melatonin functions [2-4]. The pineal gland is known to be a magnetosensitive organ in the brain of mammals and humans [5,6]. Therefore, since the application of external magnetic fields has been shown to alter the rate of melatonin production and its circadian release in both animals and humans it has been suggested to investigate their effects in PD patients [7].

Materials and Methods

Thirty PD patients (22 males, 8 females; mean age 65 years: range 49-80 years) were referred to our laboratory by practicing neurologists. All patients had diagnosed independently to suffer from idiopathic PD with no history of other neurological disease. Patients had normal routine serum biochemical studies, as well as normal CT or MRI scans. Informed consent for the methodology and the aim of the study was obtained from all patients prior to the procedure. All patients were initially placed on levedopa/ carbidopa (Sinemet 25/250)(1 tablet twice daily), but due to progressive deterioration in their motor disability the dosage was increased to 3 ½ tablets/day (1/2 tablet every 2 hours). They remained on this dosage for more than 8 years. Biomagnetic measurements were performed using a whole-head Neuromag 122 MEG system in a magnetically shielded room with gradient noise 5fT/(cmHz$^{1/2}$) for the 95% of the channels and max noise 10fT/(cmHz$^{1/2}$). The sampling frequency was 256Hz and filtered with cut – off frequencies between 0.3 to 40Hz. The time taken for each recording was between 2-10 secs. Afterwards, external transcranial magnetic stimulation in the order of pico Tesla (TMS) was applied with proper field characteristics, which were obtained prior to TMS using an electronic device (magnetic intensity: 1-7.5 pT; frequency: the α-rhythm of the patient: 8-13 Hz) [8,9]. The coils of this device were placed on the patient's scalp and weak magnetic fields, were applied for total 6 minutes (2 minutes over each of the following areas: left and right temporal regions, frontal and occipital regions, and over the vertex). This device consists of a generator that produces square waves of low frequencies magnetic field in the range from 2-13 Hz to a group of coils of 1cm diameter. The coils are enclosed between two parallel plane surfaces in such a way that their axis is situated perpendicular to these surfaces. The time between the first MEG and the MEG obtained after the application of the TMS was about an hour. To confirm that the responses to TMS were reproducible, the patients were instructed to apply TMS with the same characteristics nightly at home. Since this resulted in the same reaction to the one obtained in our laboratory and since this effect was sustained for a period more than a month, we preliminarily concluded that the application of the TMS is a non-invasive, safe and efficacious modality in management of PD patients.

Results

Table I shows each patient's clinical report and their response to TMS. All the patients have diagnosed to suffer from idiopathic tremor, rigidity, and dyskinesia PD on the basis of clinical observations and routine EEG recordings. The patients were divided into two subgroups according to the degree of their responsiveness to TMS. The first subgroup included patients who exhibited only partial response (PR) to TMS (i.e., their tremor or muscular ache or dyskinesias recurred within 12 months after TMS and partial appearance of α-rhythm with low amplitude in their EEG). The second subgroup included patients who demonstrated a favorable response (FR) to TMS (i.e., they were free from the above symptoms for at least one year after TMS and the appearance of α-rhythm with high amplitudes in their EEG) (table I). Table II shows that 12 patients (40%) were classified as partial responders (PR) and the remaining 18 (60%) exhibited a favorable response (FR) to TMS. From the partial responders to TMS, normal EEG (i.e., the appearance of high amplitude of power spectrum in the α- rhythm frequency) was seen only in 5 patients (41.67%). In contrast, 16 out of 18 patients (88.88%) who showed a favorable response to TMS had normal EEG (i.e., the appearance of very high amplitude power spectrum in the α-rhythm frequency). This difference was statistically significant ($p<0.1$,chi-square=2.55). At this point it should be mentioned that the EEG and the MEG diagnosis before and after TMS was based on the appearance of α-rhythm

amplitude in their power spectra amplitude distribution.

Discussion

Exposure of a biological organism or material to external magnetic fields has been reported to induce a variety of effects which result to mutagenic (10), immunological (11), metabolic (12) endocrine (13), behavioral (14) and anticonvulsant responses (15). It was also shown that external magnetic stimulation alter, at cellular level, the properties and stability of biological membranes as well as, their transport characteristics including the intra- and extra cellular distributions and flux of calcium ions (15). Although the striking beneficial effects of the application of the TMS on the clinical picture of the PD patients were well observed, the mode of action of TMS in PD remains an open question. This question is difficult to be answered given the complexity of cellular, systemic and neuroendocrine effects of TMS on biological systems and their potential impact on neurotransmitter functions. Despite all these and independent of their mechanisms of action, this method of magnetic stimulation may be considered an important non-invasive modality in the management of idiopathic PD patients.

Table I.

Individual clinical data for each PD patient (N=30)

SUBJECTS	*AGE*	*AGE START*	*EEG DIAGBMS*	*EEG DIAGAMS*	*MEG DIAGBMS*	*MEG DIAGAMS*	*IMPROVEMENT (YEARS)*
MEN	77	55	P	N	A	A	2
	61	52	P	N	A	N	2
	79	58	N	N	A	N	3
	57	63	P	N	A	A	3
	69	57	P	N	A	A	3
	71	52	P	N	A	N	3
	49	45	P	N	A	N	2
	55	48	P	N	A	N	2
	67	63	P	P	A	N	3
	66	61	N	N	A	N	2
	58	50	P	N	A	N	3
	80	64	P	N	A	N	2
	76	65	P	N	A	N	2
	58	66	A	N	A	N	3
	58	50	N	N	A	N	2
	66	60	P	N	A	A	3
	78	58	N	N	A	N	2
	75	52	P	N	A	A	3
	51	48	P	N	A	N	2
	64	59	P	N	A	N	2
	73	55	P	N	A	N	3
	54	45	A	N	A	N	3
WOMEN	58	47	P	N	A	N	2
	72	67	P	N	A	N	3
	62	55	A	N	A	N	2
	76	61	P	N	A	N	2
	58	50	P	P	A	N	3
	52	50	P	N	A	A	2
	68	58	A	P	A	A	2
	65	49	P	N	N	N	2

A: abnormal; P: partial normal; N: normal diagnosis; DIAGBMS: diagnosis before TMS; DIAGAMS: diagnosis after TMS

Table II.

Classification of the examined PD patients according to their EEG and MEG diagnosis and their response to magnetic stimulation. The results were of statistical significance ($p<0.1$, chi-square=2.55).

Response	*NORMAL EEG*	*ABNORMAL EEG*	*TOTAL*
PR	5	7	12
FR	16	2	18
TOTAL	21	9	30

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