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PREDICTION of THE MEMORY RELATED SIDE EFFECT of THE ELECTRO CONVULSIVE THERAPY (ECT)

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SUMMARY

We have monitored the fluctuations in plasma zinc concentrations after the first ECT. Then we investigated if the magnitude of these changes have a predictive value for the ECT induced impairment in memory. Subjects who showed the increase of plasma zinc concentration between 15 and 30 minutes after the first ECT were at risk for memory impairment 24 hrs after the fifth ECT. The specific profile of the changes in plasma zinc concentration appeared in the memory impaired population may be related to the underlying pathology directly or it is an indirect phenomenon for the brain and/or blood brain barrier homeostasis disturbed by electricity.

ELEKTRO-KONVULSİV TEDAVİ İLE HAFIZA KUSURU ORTAYA ÇIKMA OLASILIĞININ ÖNCEDEN TAHMİNİ

ÖZET

İlk ECT sonrasında plasma çinko seviyesinde ortaya çıkan dalgalanmaları takip ettik. Bu dalgalanmaların büyüklüğü ile ECT'ye bağlı hafıza kusurları arasında bir ilişki olup olmadığını inceledik. Birinci ECT'den 15 ve 30 dakika sonra plazma çinko seviyesi yükselen olgularda beşinci ECT'den 24 saat sonra test edilen hafıza performanslarında bozukluk olduğunu gördük. ECT'ye bağlı hafıza kusuru gözlenen populasyondaki spesifik plazma çinko profili hafıza kusuruna yol açan patoloji ile doğrudan bağlantılı olabileceği gibi, beyin veya kan beyin bariyerindeki homeostasisin elektrisite nedeniyle bozukluğunu yansıyor olabileceği yorumuna ulaştık.

The length and significance of the period for which memory is permanently or transiently lost or new memories can not be made is at the core of medical investigation, ethical debate and political action related to ECT.

It has been demonstrated that acute effect of electrical stimulation leads a release of previously incorporated zinc from the tissue, and an uptake from the extracellular compartment *(Wallwork, 1987)*. We assume that the same result can be seen in response to the electro convulsive therapy in the hippocampus which has a critical role on the memory related functions (Horwath and et al 1989) and contains a large concentration of zinc.

The experimental studies concerning homeostatic changes after blood Brain Barrier (BBB) disturbances suggest that the periodic measurements of plasma Zinc level procedure may be used for following the events during reversible opening of the BBB to particles in conscious or anaesthetized people with no troublesome sequelae *(Blair and et al 1990)*.

We hypothesized that the ECT related reversible changes in BBB *(Mander and et al 1987)* may lead fluctuations in plasma zinc level reflecting the changes in zinc content of the hippocampal tissue, and the rate of this parameter may be used as a biological marker for predicting the possible side effects of electroconvulsive treatment on the memory related functions of the brain.

We studied 25 physically healthy patients (mean age +/- 32.5, max age 47, min age 18, 13 male, 12 female), with histories of DSM-IIIR catatonic schizophrenia (N#11), bipolar manic episode (N#7), and major depression (N#7). All the patients were drug free for at least 3 weeks before the cure was started. And none of them has been on an additional therapy during and 24 hrs after the ECT course. No one of the subject were anesthesised for ECT. Electrodes

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TABLE I: FLUCTUATİONS OF THE PLASMA ZİNC LEVELS AFTER THE FİRST ECT, AND MEMORY CHANGES AFTER THE FİFTH ECT.

CLINICAL CHARACTERISTICS				MEMORY PERFORMANCE		Plasma Zn Levels %micgL MEASURED DURING THE FIRST ECT			
ID#	AGE	SEX	DSM-IIIR CODE	BASELİNE	24 Hrs after Fifth ECT	Pre	5min	15 min	30min
1	28	M	295.2	1	2	45	50	50	50
2	30	M	296.4	1	2	85	85	80	80
3	38	M	296.4	1	2	70	70	70	40
4	36	M	296.3	1	3	120	70	80	90
5	26	M	295.2	0	1	90	85	80	70
6	22	F	295.2	2	3	80	75	80	90
7	29	F	296.3	1	2	100	75	750	60
8	39	M	296.3	1	2	70	60	50	45
9	29	F	295.2	2	2	80	90	80	75
10	38	F	295.2	2	2	95	70	90	90
11	35	M	296.3	2	2	40	40	40	40
12	36	M	296.4	2	2	110	100	95	95
13	35	F	296.3	2	2	90	95	90	90
14	45	F	295.2	3	2	90	60	60	60
15	23	F	295.2	3	2	90	60	60	60
16	28	F	296.4	3	1	85	90	90	95
17	35	F	295.2	2	1	130	135	110	130
18	32	M	295.2	3	2	60	60	60	65
19	42	F	295.2	3	2	50	70	60	70
20	32	M	296.3	3	2	80	90	70	80
21	44	M	296.3	2	1	120	110	110	120
22	23	F	295.2	2	1	90	70	60	70
23	32	M	296.4	3	1	90	90	70	70
24	38	M	296.4	3	2	90	90	85	85
25	18	M	296.4	3	2	80	90	75	80

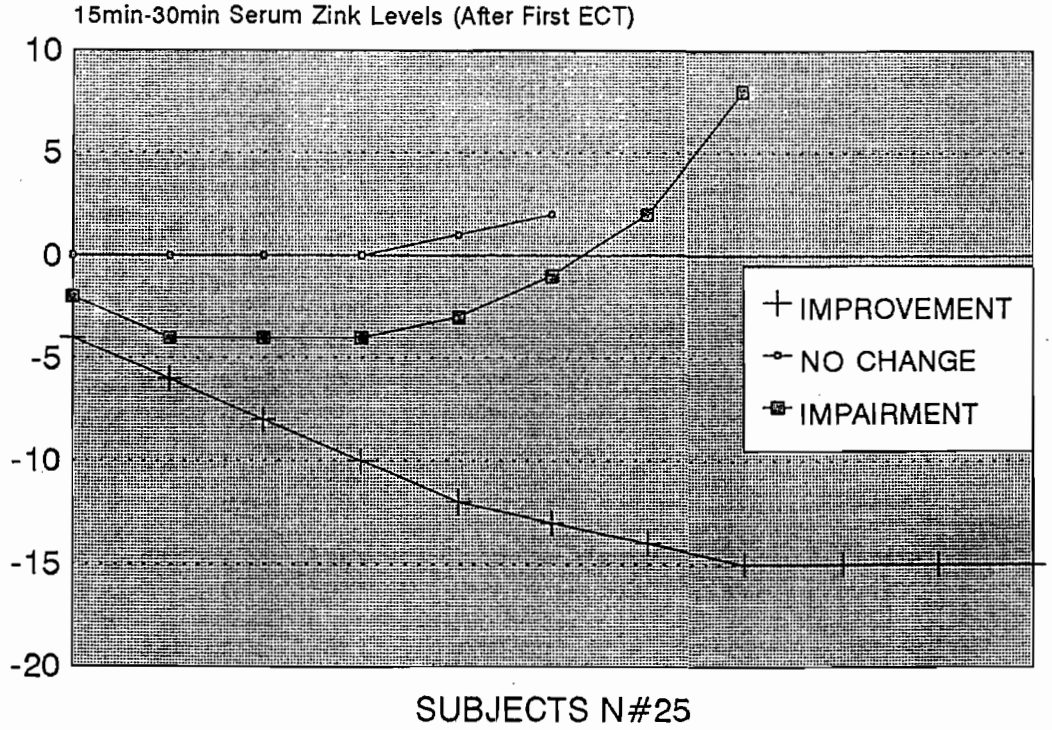
were placed bilaterally on both frontotemporal locations. Oxygenation was maintained throughout. The current type was sinewave (Duopulse MK-4). The intensity was 100v. The stimuli were given for 2 seconds. Motor convulsions were lasted approximately 20 to 40 seconds for the subjects. Patients were interviewed on two occasions. The first interview took place 30 minutes before the first ECT done. After this interview, they were informed of the nature of electroconvulsive treatment and their agreement was obtained. Second interview took place 24 hrs after the fifth ECT. Patients were screened for memory impairment having them learn three unrelated words, and recalling after 5 minutes *(Folstein and et al 1975)*. After overnight fasting, ECT was induced at 9.00 a.m. three times a week with the same intervals for each patient. Blood samples were collected before the ECT course and 5min, 15min, 30min after the first ECT and before, 5min, 15min, and 30min after the fifth ECT. Sera were analyzed in duplicates for Zn by atomic absorption spectrometry using a Perkin Elmer model 360 spectrometer. Results were given microgram per 100ml. Results for individual patients are described in Table I.

We have subtracted the first scores of the MMS from the scores obtained after the fifth ECT. Then we made three subgroups, 1. IMPAIRMENT; if the results were negative, 2. NO CHANGE; if the result were zero, 3. IMPROVEMENT; if the result were positive.

In statistical analysis, considering distributional characteristics and the selected experimental design, Wilcoxon 2-Sample Test was used to identify predictive value of the changes in plasma zinc concentrations within a time course after the first ECT done. Table-1 summarizes the comparisons between three groups. Concerning the changes in the plasma zinc levels between 15 minutes and 30 minutes after the first ECT, significant differences were found between memory impaired patients and the patients who did not show any change in their memory performance. Same finding was evident between the me-

TABLE II: Wilcoxon Scores (Rank Sums)
Classified by Variable MEMORY CHANGES (Average Scores were used for Ties) Wilcoxon 2-Sample Test
(Normal Approximation, Continuity Correction of .5) T-Test approx. Significance = 0.0132

Zn CHANGE IN TIME	GROUPS	N	Sum of Scores	Expected Under HO	Std Under HO	Mean Score	S	Z	P > Z
(pre-5m)	IMPROVEM	8	64.0	60.0	7.65	8.0	41.0	-.45	0.6474
	NOCHANGE	6	41.0	45.0	7.65	6.8			
(pre-15m)	IMPROVEM	8	66.0	60.0	7.53	8.2	39.0	-.72	0.4657
	NOCHANGE	6	39.0	45.0	7.53	6.5			
(pre-30m)	IMPROVEM	8	69.0	60.0	7.69	8.6	36.0	-1.10	0.2693
	NOCHANGE	6	36.0	45.0	7.69	6.0			
(5m-15m)	IMPROVEM	8	59.5	60.0	7.55	7.4	45.5	0	0.9999
	NOCHANGE	6	45.5	45.0	7.55	7.5			
(5m-30m)	IMPROVEM	8	66.0	60.0	7.58	8.2	39.0	-.72	0.4682
	NOCHANGE	6	39.0	45.0	7.58	6.5			
(15m-30m)	IMPROVEM	8	63.0	60.0	7.39	7.8	42.0	-.33	0.7354
	NOCHANGE	6	42.0	45.0	7.39	7.0			
(pre-5m)	IMPROVEM	8	98.5	80.0	11.96	12.3	98.5	1.50	0.1325
	IMPAIRME	11	91.5	110.0	11.96	8.3			
(pre-15m)	IMPROVEM	8	80.5	80.0	12.01	10.0	80.5	0	0.9999
	IMPAIRME	11	109.5	110.0	12.01	9.9			
(pre-30m)	IMPROVEM	8	98.5	80.0	11.99	12.3	98.5	1.50	0.1336
	IMPAIRME	11	91.5	110.0	11.99	8.3			
(5m-15m)	IMPROVEM	8	57.0	80.0	11.76	7.1	57.0	-1.91	0.0557
	IMPAIRME	11	133.0	110.0	11.76	12.0			
(5m-30m)	IMPROVEM	8	88.5	80.0	12.00	11.0	88.5	0.66	0.5051
	IMPAIRME	11	101.5	110.0	12.00	9.2			
(15m-30m)	IMPROVEM	8	105.0	80.0	11.79	13.1	105.0	2.07	0.0378
	IMPAIRME	11	85.0	110.0	11.79	7.7			**
(pre-5m)	NOCHANGE	6	60.5	54.0	9.81	10.0	60.5	0.61	0.5410
	IMPAIRME	11	9.25	99.0	9.81	8.4			
(pre-15m)	NOCHANGE	6	43.5	54.0	9.80	7.2	43.5	-1.01	0.3080
	IMPAIRME	11	109.5	99.0	9.80	9.9			
(pre-30m)	NOCHANGE	6	62.0	54.0	9.70	10.3	62.0	0.77	0.4395
	IMPAIRME	11	91.0	99.0	9.70	8.2			
(5m-15m)	NOCHANGE	6	38.0	54.0	9.77	6.3	38.0	-1.58	0.1127
	IMPAIRME	11	115.0	99.0	9.77	10.4			
(5m-30m)	NOCHANGE	6	54.0	54.0	9.75	9.0	54.0	0.05	0.9591
	IMPAIRME	11	99.0	99.0	9.75	9.0			
(15m-30m)	NOCHANGE	6	81.0	54.0	9.50	13.5	81.0	2.78	0.0053
	IMPAIRME	11	72.0	99.0	9.50	6.5			*****



Cumulative Changes in Memory Functioning (Baseline minus 24 Hrs. After the Fifth ECT)

mory impaired population and the population who showed an improvement in their memory capacity.

Thus, our results indicate that subjects who show increase of plasma zinc concentration between 15 and 30 minutes after the first ECT are at risk for memory impairment 24 hrs after the fifth ECT.

Although, there is a number of possibility have been suggested, the reason for cognitive impairment as a result of ECT still remains unclear.

Changes of the zinc content in cell membranes may lead to membrane destabilization and altered regulatory functions at receptor and transport sites *(Srinivasan, 1984)*, and/or enzymes (*Kula and et al 1990)*.

(Note: since, the main purpose of this study was establishing a methodology for prediction of cognitive side effects of the ECT, we anticipated that the results would need replications, therefore, we decided to use the simplest memory assessment procedure so that it could be used in any institute on any patient and by any investigator. On the basis of this idea, we have selected the Folstein's Mini Mental State Examination to screen for memory impairments as a result of ECT. Allowing the researcher to repeat the measurements within a short period without any concern about the patients habituation was another advantage of this procedure.)

KAYNAKLAR

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