Effects of Electroconvulsive Therapy on Pituitary Hormones in Depressed Patients

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ABSTRACT:
Effects of electroconvulsive therapy on pituitary hormones in depressed patients

Objective: The exact mechanism of the action of electroconvulsive therapy (ECT) has yet to be established. In this study, we aimed to test the hypotheses that ECT may cause acute alterations in pituitary hormones and that these hormonal responses to ECT may change throughout repeated ECT sessions.
Methods: Nineteen depressed inpatients (8 males, 11 females; mean age ± SD= 44.77 ± 10.59 years) were undergone to 7 ECT sessions under general anaesthesia using propofol (1mg/kg). During the first and seventh ECTs, blood samples were collected 1 min before (baseline) and 2 min after propofol, immediately after ECT, and 30 and 60 min after ECT for measurements of serum prolactin (PRL), adrenocorticotropin (ACTH), cortisol, growth hormone (GH), follicle-stimulating hormone (FSH), and luteinizing hormone (LH).
Results: The results of the study confirmed that ECT had highly selective stimulatory effects on the release of PRL, ACTH and cortisol, but not on GH, FSH and LH. The hormonal responses to ECT did not change throughout ongoing ECT procedures, and did not differ between males and females.
Conclusions: Whether there is a causal relationship between these neuroendocrine responses and the therapeutic effect of ECT is remain uncertain.

Key words: electroconvulsive therapy, pituitary, depression, neuroendocrine, prolactin, adrenocorticotropin.

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INTRODUCTION

Electroconvulsive therapy (ECT) has proved to be one of the most effective treatments of depression and is probably even more effective than drug therapy (1). However, its exact mechanism of action has not yet been established. Major neurobiological effects implicated in the antidepressant action of ECT are mainly: (a). the action of ECT on the monoamine neurotransmitter systems, norepinephrine, serotonin, and dopamine, (b). its neurotrophic action, (c). the anticonvulsant effect of ECT (2). ECT-induced hormonal changes have been measured in depressive patients in order to elucidate brain function, depression pathophysiology and the therapeutic action mechanism of ECT (3). Hormonal responses to ECT may reflect the hypothalamic stimulation by direct local electrical activity, by seizure activity, or by the aggregate of neurotransmitter activity mediating hypothalamic and pituitary hormonal release (4). Since the hypothalamic-pituitary system is controlled by various monoaminergic neurotransmitter systems, which may be involved in the pathophysiology of depression, the investigation of the pituitary hormones in plasma before and after ECT may shed light on the action mechanism of ECT in depression.

Previous studies have shown that ECT produces a marked increase in the plasma concentrations of prolactin (PRL) (4,5,6,7,8), thyroid stimulating hormone (9,10), adrenocorticotropin (ACTH) and cortisol (6,7,9,11) a number of minutes after ECT procedure, generally reducing to normal levels within hours, though not all studies agree on this. Plasma growth hormone (GH), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) levels have shown little or no change with ECT in previous studies (4,6,11). It has been reported that some attenuation may be

Table 1. Clinical variables and Δ hormonal values of the patients during the first and last ECTs

	ECT 1 (n=19)		ECT 7 (n=19)	
	Mean	SD	Mean	SD
Age (years)	44.77	10.59		
Duration of illness (months)	64.00	93.50		
Number of episodes	4.77	4.95		
HAM-D score	21.22	4.31	10.21	2.76
ΔPRL (ng/ml)	26.28	11.97	24.04	13.63
ΔACTH (pg/ml)	54.86	86.62	38.17	32.23
Δcortisol (nM)	15.60	7.90	19.53	25.13
ΔGH (mIU/L)	1.69	3.20	0.82	2.68
ΔFSH (mIU/ml)	3.92	11.90	13.16	22.32
ΔLH (mIU/ml)	3.54	9.57	7.80	6.63

HAM-D: Hamilton Rating Scale for Depression

observed in these hormonal responses throughout repeated ECTs in some studies (5,6,9,12), while some others have not found such an attenuation (4,11,13).

In this study, we aimed to test the hypotheses that ECT may cause acute alterations in pituitary hormones and that these hormonal responses to ECT may change throughout consecutive ECT sessions.

METHOS

Subjects

Nineteen depressed inpatients (8 males, 11 females; mean age±SD= 44.77±10.59 years) who were considered suitable for ECT were included in the study. Eight had bipolar I disorder-depressive episode, and 11 major depressive disorder (recurrent) according to the DSM-IV criteria (14) (Table 1). The patients had been drug-free for two weeks, and had no neurological, metabolic, cardiologic, renal or endocrine disorders according to their history, and physical and laboratory evaluations. None had received ECT within the previous six months. None of the bipolar patients had rapid-cycling disorder. The 17-item Hamilton Rating Scale for Depression (HAM-D) was used to rate the severity of the depression of the patients before the 1st and 7th ECTs (15) (Table 1).

Procedure

Each patient was undergone 7 ECT sessions under general anaesthesia, three times a week. The ECT procedure consisted of the administration of propofol (1 mg/kg), an anaesthetic agent not considered to have any opioid or glucocorticoid properties, and succinylcholine (0.5 mg/kg), and oxygenation. ECT was given between 09.00 and 11.00 a.m. after an overnight fast and with the electrodes placed in the bitemporal position. The current was sinusoidal and the stimulus intensity was standardised at 700 mA for 5 sec. Seizures were monitored by the cuff method.

Blood samples were collected 1 min before (baseline) and 2 min after propofol, immediately after ECT (when the seizure ended), and 30 and 60 min after ECT with an indwelling catheter inserted into an antecubital vein. In all patients, blood samples were taken during the first and last (7^{th}) ECT. The blood samples for measurements of PRL, ACTH, cortisol, GH, FSH, and LH were centrifuged immediately in cold conditions at 20.000-23.000 rpm for 15 min and then stored at –20°C until analysed. Serum ACTH, cortisol, GH, FSH, and LH concentrations were measured by commercially available immunoradiometric assay kits (IRMA, Immunotech, Beckman Coulter Company, France) and PRL by automated chemiluminescence system (ACS: 180, Bayer). For PRL, the sensitivity was 0.3 ng/ml and the intra- and inter-assay coefficients of variation were 2.8 and 1.2%, respectively. The sensitivity for serum ACTH was 2 pg/ml, and the intra- and inter-assay coefficients of variation were 2.9 and 4.8%, respectively. The sensitivity with 95% probability for serum cortisol was 10nM, and the intra- and inter-assay coefficients of variation were 3.1 and 5.5%, respectively. For GH, the sensitivity was 0.10 mIU/L and the intra- and inter-assay coefficients of variation were 1.5 and 14.3%, respectively. For FSH, the sensitivity was 0.3 mIU/ml, and the intra- and inter-assay coefficients of variation were 1.7 and 2.8%, respectively. For LH, the sensitivity was 0.07 mIU/ml, and the intra- and inter-assay coefficients of variation were 4.5 and 0.7%, respectively.

This study was approved by the local ethics committee and all subjects gave their written informed consent after full understanding of the study.

Data analysis

The data were analysed by ANOVA with repeated measures, followed by Greenhouse-Geisser's correction for each hormone. Hormonal values were taken as the dependent variable, whereas ECT session (1st and 7th ECTs) and time (baseline, after anaesthetic, immediately after convulsion, 30 and 60 min after convulsion) were taken as within-subjects factors. Gender was taken as between-subjects factor in this analysis. Wherever a significant difference was found, post-hoc paired samples t test was used to compare hormonal values at different times or at different therapy sessions. Moreover, for each treatment session, ΔPRL, ΔACTH, Δcortisol, ΔGH, ΔFSH, and ΔLH were calculated for each patient by subtracting the pre-ECT baseline hormonal value from the maximal hormonal concentration after ECT (either immediately, 30 or 60 min after the termination of the seizure). By considering averaged Δ hormonal value as the primary dependent factor, paired samples t test analysis was used to compare the responses of the hormones to the first and last (7th) ECTs for each one. The correlations between clinical and hormonal variables were investigated using Pearson's correlation test.

RESULTS

PRL:

Very similar response patterns in the first and last ECTs were obtained in PRL. In both ECTs, a significant increase in PRL was found immediately after ECT compared to the pre-ECT values; this increase became more prominent during 30th min after ECT ($F=33.13$; $df=4,64$; $p<0.001$) (Table 2, Figure 1). PRL levels became closer to pre-ECT values at the

Table 2. Hormonal variables of the patients during the first and last ECTs

		ECT 1 (n=19)		ECT 7 (n=19)	
		Mean	SD	Mean	SD
PRL (ng/ml)	before propofol	14.77	17.01	10.88	5.58
	after propofol	14.84	16.34	11.33	5.26
	just after ECT	28.40 a	18.54	25.60 a	14.22
	30 min after ECT	39.11 a	12.33	30.80 a	15.06
	60 min after ECT	21.00	11.48	22.10	9.63
ACTH (pg/ml)	before propofol	24.24	9.93	25.91	10.87
	after propofol	22.99	11.66	31.27	16.75
	just after ECT	57.17 b	42.93	60.22 b	43.73
	30 min after ECT	65.95 b	86.47	48.00 b	20.36
	60 min after ECT	33.28 b	20.27	31.50	12.58
Cortisol (nM)	before propofol	18.50	6.72	18.45	4.85
	after propofol	17.60	5.56	22.22	14.22
	just after ECT	20.28	6.46	29.98	28.24
	30 min after ECT	32.16 c	8.39	34.33 c	17.37
	60 min after ECT	24.67 c	11.71	26.78	15.73
GH (mIU/L)	before propofol	1.92	4.79	1.64	2.10
	after propofol	2.17	4.35	1.42	1.16
	just after ECT	2.05	4.07	1.21	0.99
	30 min after ECT	1.31	2.21	0.59	0.41
	60 min after ECT	1.58	2.00	2.17	1.94
FSH (mIU/ml)	before propofol	39.36	38.43	45.34	29.98
	after propofol	41.00	36.73	46.02	33.38
	just after ECT	38.87	36.94	50.16	35.82
	30 min after ECT	38.72	32.71	49.78	30.32
	60 min after ECT	31.02	30.45	50.65	35.27
LH (mIU/ml)	before propofol	29.60	25.31	26.51	16.28
	after propofol	31.39	22.93	25.61	16.38
	just after ECT	29.69	24.13	32.58	16.38
	30 min after ECT	25.54	14.84	28.35	16.85
	60 min after ECT	27.62	20.51	33.38	17.06

a: Significantly higher than pre-ECT values ($F=33.13$; $df=4, 64$; $p<0.001$)
b: Significantly higher than pre-ECT values ($F=8.72$; $df=4, 64$; $p<0.005$)
c: Significantly higher than pre-ECT values ($F=9.41$; $df=4, 64$; $p<0.005$)

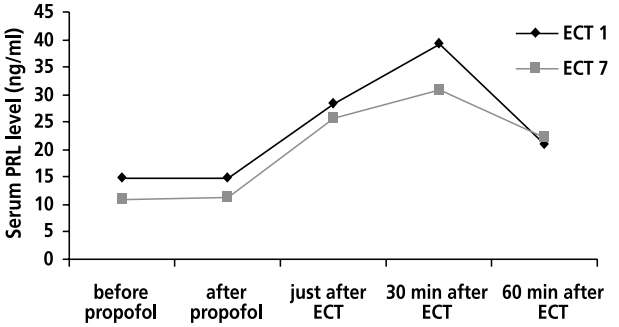

Figure 1. Serum PRL responses to ECT of the patients during the first and last ECTs

60th min No significant difference was found between the PRL responses to the first and last ECTs (F= 0.97; df=4,64; p>0.05) or between males and females. Nor was significant difference found in ΔPRL values between the two ECT sessions (t=0.75; p>0.05) (Table 1).

ACTH:

During the first ECT, a significant increase was observed immediately after ECT compared to pre-ECT values, and this increase became more pronounced at 30th min after ECT. Although at 60th min after ECT this surge in ACTH became less pronounced, the statistical difference between that of 60th min and pre-ECT values continued (F=8.72; df=4,64; p<0.005) (Table 2, Figure 2). During the last ECT, the most

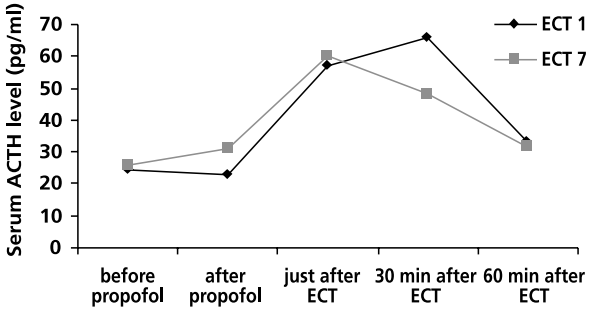

Figure 2. Serum ACTH responses to ECT of the patients during the first and last ECTs

pronounced increase was observed immediately after ECT. At 30 min after ECT, ACTH level was somewhat reduced, however, it still remained significantly higher than pre-ECT values. At 60 min after ECT, ACTH level was reduced to the pre-ECT levels (F=8.72; df=4,64; p<0.005).

There was no difference between ACTH responses to ECT during the first and last ECTs (F=0.0; df=4,64; p>0.05), and no gender effect was observed. With regard to ΔACTH, no significant difference was found between the values in the first and last ECTs (t=0.74; p>0.05) (Table 1).

Cortisol:

In the first ECT, the values of cortisol 30 and 60 min after ECT were found to be significantly higher than those of pre-ECT. The value at 30th min was also significantly higher than the values immediately after ECT and 60th min (F=9.41; df=4,64; p<0.005) (Table 2, Figure 3). It was observed that the highest cortisol values were at 30th min after ECT.

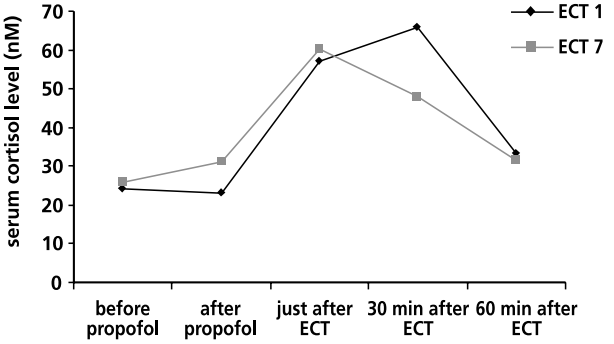

Figure 3. Serum cortisol responses to ECT of the patients during the first and last ECTs

In the seventh ECT, the most marked increase in cortisol levels was again 30 min after ECT. This value was significantly higher than pre-ECT values and than that of 60th min (F=9.41; df=4,64; p<0.005).

There was no significant difference between the cortisol responses to the first and last ECTs (F=1.77; df=4,64; p>0.05), and between those of male and female patients. Neither were Δcortisol values significantly different in the first and last ECTs (t=0.65; p>0.05) (Table 1).

GH:

We found no significant alterations in GH throughout both the ECTs (F=0.75; df=4,64; p>0.05) (Table 2), and there was no significant difference either in the GH responses to the first and last ECT (F=0.40; df=4,64; p>0.05), or ΔGH values during the first and last ECTs (t=1.17; p>0.05) (Table 1). Furthermore, gender was not found to have any effect on GH responses to ECT.

FSH and LH:

During both ECT sessions, no significant

difference was found between the pre- and post-ECT levels of serum FSH and LH ($F=0.69$; $df=4,64$; $p>0.05$; and $F=2.52$; $df=4,64$; $p>0.05$, respectively) (Table 2). There were no significant differences between the hormonal responses to the first and last ECTs ($F=3.80$; $df=4,64$; $p>0.05$; and $F=0.08$; $df=4,64$; $p>0.05$, respectively), and in the ΔFSH and ΔLH values between the first and last ECTs ($t=1.48$; $p>0.05$; and $t=1.47$; $p>0.05$) (Table 1). No gender effect was detected on these responses, either.

Correlations:

Some significant positive correlations were found between age and basal FSH levels in both treatments ($r=0.50$, $p<0.05$; $r=0.61$, $p<0.005$, respectively), between age and LH levels in both treatments ($r=0.52$, $p<0.05$; $r=0.49$, $p<0.05$, respectively), between the duration of the illness and baseline ACTH level in the first ECT ($r=0.53$, $p<0.05$), between basal LH and FSH levels in both ECTs ($r=0.88$, $p<0.001$; $r=0.80$, $p<0.001$, respectively), between ΔACTH and ΔGH values during the first ECT ($r=0.64$, $p<0.005$), between ΔACTH and Δcortisol values in the first ECT ($r=0.54$, $p<0.05$), and between Δcortisol and ΔPRL in the first ECT ($r=0.77$, $p<0.001$). In addition, a number of significant negative correlations were also found between basal PRL and ΔPRL values in the first ECT ($r=-0.61$, $p<0.005$), and between basal GH and ΔGH values during the last ECT ($r=-0.72$, $p<0.001$).

DISCUSSION

The findings of the present study show that ECT causes remarkable and rapid increases in the serum concentrations of PRL, ACTH, and cortisol, and that repeated ECTs do not result in any alterations on these ECT-induced hormonal responses. These results are in general consistent with those of the previous studies reporting an increase in the serum levels of PRL (5-9,11,13,16), and of ACTH and cortisol (5-7,9,11,17). Moreover, we found that ECT has no effect on the GH, FSH and LH. This finding is also consistent with the data of previous studies (4,5,11). All the findings of the present and previous studies point to the selective effects of the ECT on some certain hormones secreted by the pituitary, and in turn, on brain neurotransmitter systems controlling the hypothalamic-pituitary system.

PRL levels were observed to show some three-fold rise 30 min after ECT in both the first and last (7^{th}) ECTs. We found no change in the PRL response throughout repeated ECTs, similar to the findings of some previous studies (4,13), but in contrast to those of some others (5,9). In previous studies, five to seven-fold increases have been reported in PRL levels after ECT and the average peak time of the PRL rise was 10 to 30 min after ECT (4,7,8,13). Swartz (1997) proposes that blood sampling should be at 20 min to catch the peak PRL (3). Our finding of the lower PRL increase (three-fold) compared to that of the previous reports may be due to the delay in sampling (30 min instead of 15 or 20 min after ECT) in this study.

It has not yet been fully elucidated how ECT actually causes increases in PRL and in some other pituitary hormones. There are two main hypotheses that may account for the effects of ECT on the pituitary hormone release. One suggests that the selective effects of ECT on hormonal release result from the direct action of the spread of electrical currents or the effects of seizure on the neurones that secrete hypothalamic-pituitary hormones. The finding that higher intensities of the ECT stimulus cause higher amounts of PRL increases after ECT may support this hypothesis (18). In addition, the finding that, albeit significantly less than real ECT, cardioversion also causes a PRL rise supports the idea that PRL surge may be a non-specific stress response to electrical stimulation occurring in the absence of a generalized convulsion (7). Nevertheless, in Deakin et al.'s study (1983), the finding that while subthreshold currents did not cause a significant rise in PRL, real convulsions induced by ECT caused PRL surge suggests that it is seizure that elevates PRL following ECT, rather than the current (5). Accordingly, it has been argued by some authors that ECT-induced PRL elevations might be related to seizure activity in the amygdala, which is believed to be involved in the pathophysiology of depression (3).

The second hypothesis regarding PRL surge after ECT claims that the selective effects of ECT on pituitary hormones are due to the selective activation of central neurotransmitter systems that mediate the release of different hormones. Concerning PRL, if this hypothesis is taken into account, one can put forward that a decrease in dopamine or gamma-aminobutyric acid (GABA) activity or an increase in serotonergic activity due to ECT may explain the PRL surge after ECT, because PRL secretion is known to be inhibited by dopaminergic activity and by high concentrations of GABA (6,19), and to be activated by serotonin (20). The explanations related to dopamine and GABA seem to be unlikely because it was observed that ECT, and its animal equivalent electroconvulsive shock (ECS), causes acute increases, rather than decreases, in dopamine and GABA releases (21-23). Thus, the explanation that increased central 5-HT activity caused by ECT may stimulate PRL release from

pituitary gland appears to be more plausible (6,23). In support of this idea, the finding that pretreatment with pindolol attenuates the ECT-induced PRL increase suggests that this neuroendocrine response is a 5-HT_{1A}-mediated event (24).

However, there is still a considerable confusion in the literature as to whether acute ECT gives rise to a transient increase in serotonergic activity or not, although there are sufficient data suggesting that chronic ECT or ECS causes an elevation in the central serotonergic activity due to either presynaptic 5-HT_{1A} autoreceptor down-regulation (25), or to an up-regulation of the postsynaptic 5-HT_{1A} and 5-HT_2 receptors (26-28). Moreover, we cannot easily rule out the explanation that alterations in the dopaminergic activity may account for the acute increase in PRL after ECT, since it has been reported and argued by some authors that plasma PRL rise after ECT may be derived from a transient decrease in the inhibitory dopaminergic input of the hypothalamus to the pituitary lactotrophs caused by the electrical stimulus or the subsequent seizure (28-30). Despite the fact that it has been proposed by some authors that ECT releases a substance which antagonizes dopaminergic neurotransmission such as endogenous opioid peptides (5), the finding that the opiate receptor blockade by naloxone does not alter the release of PRL after ECT does not support a role for endogenous opiates in PRL rise seen after ECT (17). Because thyrotropin-releasing hormone (TRH) also stimulates PRL secretion from the pituitary, another mechanism that can explain, or at least contribute to, PRL surge following ECT may be TRH increase induced by ECT (31-33).

Taken together, although our results confirm the consistent finding of previous studies that ECT causes an acute and transient rise in PRL, its mechanism is not clear. Alterations in serotonergic or dopaminergic activity induced by ECT appear to be most probable candidate mechanisms underlying this effect.

The neurobiological determinants and clinical significance of ECT-induced PRL rise have not been well characterized either. In the present study, no change was found in PRL response to ECT between the first and last ECTs, nor any effects of gender, age, the duration of the disease or the severity of depression on PRL responses were observed. The findings of previous studies do not give any support to the idea that the greater clinical improvement is associated with the greater PRL surge with ECT (4,5,11,13). Whereas in some studies it has been reported that a considerable attenuation may occur in PRL responses to ECT throughout repeated ECTs (5,6), more recent studies have not found this attenuation (4,11,13), which is consistent with our result. All these data suggest that the mechanisms or pathways responsible for the PRL release may not be essential to therapeutic effects of ECT.

In some studies, greater PRL responses to ECT in females have been reported (4,17) and this has been explained by a lower threshold of females or by higher hormonal responses to stress due to their inherent biological vulnerability. However, we did not find such an effect of gender on PRL responses. This inconsistency may be attributed to the small number of our sample or to methodological differences between two studies.

Another finding in the present study of increase in ACTH and cortisol levels in response to ECT is in accordance with those of most previous studies (5-7,9,11,17,18). The mechanism underlying the ACTH and cortisol increases following ECT is not clear either. Firstly, an increase in the hypothalamic hormones inducing ACTH secretion from the pituitary such as corticotropin-releasing hormone (CRH) and arginin vasopressin (AVP) may be considered responsible for this increase. These are all the stress hormones secreted in the stressful situations such as ECT. Nonetheless, the secretion of another stress-related hormone, GH, appears to be unaffected by ECT in our study, and also in many previous studies (4,5,11). This suggests that ECT-induced hormonal increases are not explained only by stress associated with ECT. Rather, it can be said that ECT has selective effects on some particular stress hormones such as AVP, ACTH, cortisol, and PRL. Moreover, the finding of Whalley et al.'s study (1987) that a similar pattern of increases in these hormones did not occur during induction of anaesthesia or surgical operation also supports the idea that hormonal responses to ECT cannot simply be attributed to stress (6).

It has consistently been reported that AVP is released rapidly following ECT (7,8,11), while the results with regard to plasma CRH are rare and conflicting (7). Therefore, AVP may be the major factor responsible for the ACTH surge with ECT. Still, one possibility is that electrical stimulation causes hypothalamic CRH and AVP which act synergistically to give rise to ACTH release but without a detectable rise in the CRH in the peripheral blood. In some reports, CRH levels in cerebrospinal fluid (CSF) have been reported to decrease after a course of ECT (33,34). This suggests that, even if ECT might not cause a detectable acute change in the hypothalamic CRH secretion, it may have a normalising effect on the CRH elevation over time, which is reported to exist in depression. The studies of CRH stimulation test before and after ECT also confirm the idea that

ECT normalises hypothalamic-pituitary-adrenal (HPA) axis hyperactivity in depressive patients (35). One may speculate that, if ECT induces acute CRH and AVP secretions, a down-regulation in CRH and AVP activity or in the pituitary response to CRH and AVP occurs with the course of the treatment, and this mechanism may be involved in the treatment of depression by ECT. Nevertheless, in our study the finding of no change in ACTH and cortisol responses to convulsions after the termination of ECT treatment does not support this idea.

Another mechanism that may be put forward to account for ACTH increase following ECT may be the serotonergic activation by ECT (6), since serotonin has a stimulating effect on HPA axis (36,37). We observed very similar rising patterns in ACTH, cortisol, and PRL in response to ECT (Figures 1,2,3), although we did not observe such a rising pattern in GH , FSH, or LH. Additionally, we found positive correlations between the alterations in ACTH, cortisol, and PRL during the first ECT. These observations suggest that there must be a common stimulator of ACTH and PRL during the ECT procedure, which may be somehow related to stress response of the brain. It may be proposed that this common stimulator of these stress hormones during the ECT may be serotonin, which is known to have a stimulating effect on both PRL and ACTH. Whether the acute effects of ECT on neurotransmitters such as serotonin are related to the therapeutic effects of ECT or just an epiphenomenon of seizure activity is not clear.

The finding that GH levels did not change with ECT is consistent with previous studies (4,5,11,38). FSH and LH also did not show any alterations in response to ECT procedure, which is in agreement with previous studies (11). These are the hormones whose concentrations may be altered by numerous factors such as weight, diet, physical activity, stress, sex, menopausal status, and the time of the menstrual cycle. Therefore, their place in the pathophysiology of mood disorders or in the treatment mechanism of ECT is difficult to interpret (39).

We did not observe any alteration on the hormonal responses to ECT throughout the course of treatment. This suggests that ECT-induced pituitary hormonal changes may not be directly related to its therapeutic effect in depression, and may be only an epiphenomenon. However, we still believe that such hormonal changes in response to ECT and relevant monoaminergic alterations have some significance in its action mechanism.

Several important should be considered in interpreting the results of our study. One of the limitations of the study is the small sample size, which is hard to to make inference about all major depressive disorder patients. Another limitation is the lack of a control group exposed to another stress-induced situation such as a surgical operation with anaesthesia, which might have allowed us to exclude the effects of stress and anaesthetic agents on the hormonal responses. Additionally, the quantities of hormones released from the brain itself may be too small to be reliably detected in the bloodstream, and a static assessment of peripheral hormones may not reflect their central function adequately. Likewise, we cannot readily claim that such alterations in pituitary hormones during ECT are in any way related to its therapeutic mechanism in depression.

In conclusion, the data of the study confirm that ECT has highly selective stimulatory effects on the release of PRL, ACTH and cortisol, but not on GH, FSH and LH. The rises in ACTH and PRL may result from the direct induction of the hypothalamic-pituitary structures by the electrical current or the seizure, or be associated with the acute release of serotonin or decrease in dopaminergic inhibitory tone on the pituitary. The hormonal responses to ECT do not alter throughout ongoing ECT procedures, and do not differ between males and females. Whether there is a causal relationship between these neuroendocrine responses and the therapeutic effect of ECT remain uncertain.

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