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PHOBIC ANXIETY DOES NOT AFFECT PLASMA LEVELS OF THYROID STIMULATING HORMONE IN MAN

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SUMMARY

(1) The effect of anxiety on plasma levels of thyroid stimulating hormone (TSH) is not clear, despite a number of relevant studies. (2) Nine human subjects with severe phobias had blood samples taken for TSH assay every 20 min during five sessions of 3-hr duration each. (3) Severe anxiety, induced by treating the subject's phobia with *in vivo* flooding, did not influence plasma TSH levels in any consistent way, nor could a specific TSH response to anxiety be identified in any individual subject.

Key Words—Anxiety; thyroid stimulating hormone; thyrotropin; phobia; stress.

INTRODUCTION

THE EFFECT of emotional arousal on thyroid function is a subject of continuing interest, perhaps in part because of speculation regarding the role emotional factors may play in precipitating thyrotoxicosis (Weiner, 1977). The specific question of how anxiety might affect plasma levels of thyroid stimulating hormone (TSH) is unanswered, despite a number of relevant studies. In rabbits, the stress of blood sampling decreases TSH. If, however, the animals are pretreated with dexamethasone, the same stress significantly increases TSH (Leppaluoto, 1972). In rats, cold increases TSH, but forced exercise and immobilization both decrease TSH (DuRuisse *et al.*, 1978). In humans, making a first parachute jump (Noel *et al.*, 1976) and anticipating strenuous exercise (Mason *et al.*, 1973) both increase circulating TSH. TSH also is increased in the first few min of treadmill exercise, but a few hr after such exercise the concentration falls below baseline (Sowers *et al.*, 1977). Motion sickness induced by the Coriolis effect causes decreased TSH, while simple rotation does not (Habermann *et al.*, 1978). Gastroscopy and elective abdominal surgery also suppress TSH (Sowers *et al.*, 1977). The suggestion has been made that 'psychological stress' associated with these stimuli may account for the TSH changes (Mason *et al.*, 1973; Noel *et al.*, 1976). The present study is part of a series carried out over several years in which the protocol has remained the same (flooding therapy in phobic patients) while the hormones studied have varied; other anxiety-related endocrine responses in most, but not all, of the subjects in this study have been reported previously. Anxiety associated with flooding therapy was correlated with plasma growth hormone increases in most subjects (Curtis *et al.*, 1979), but plasma cortisol responses were small and occurred only in subjects treated in the morning (Curtis *et al.*, 1976a, 1978). Plasma prolactin levels were not changed by anxiety (Nesse *et al.*, 1980).

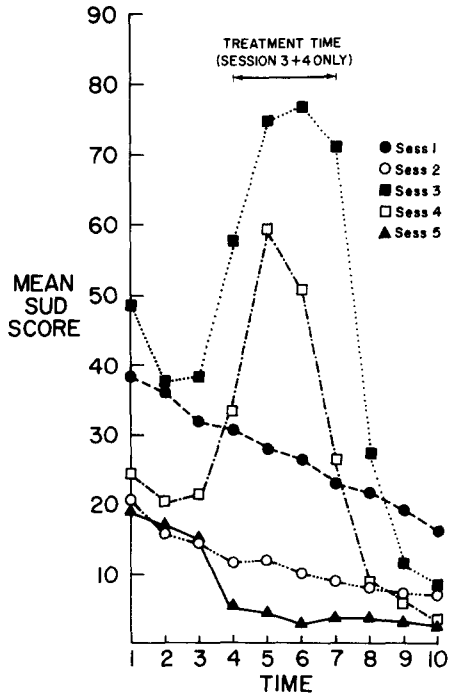

FIG. 1. Mean of all subject's SUD (subjective units of distress, see text) scores at each time of each session (n = 9).

METHOD

Details of methods and procedures have been reported previously (Nesse *et al.*, 1980). In brief, the nine subjects were healthy, medication-free adults who met DSM-III criteria for simple phobia and who scored 4 or 5 on the five-point Gelder and Marks Phobia Severity Scale (Gelder & Marks, 1966). Each subject came to the laboratory for five separate sessions of 3 hr each. Every 20 min blood was drawn via an indwelling butterfly needle and the subject rated his or her anxiety level for the previous 20 min on a 0 – 100 Subjective Units of Distress scale. Subjects sat quietly and read except for the middle hr of the third and fourth sessions when the phobia was treated with flooding *in vivo,* which consisted of prolonged close exposure of the subject to the actual object of the phobia (Curtis *et al.*, 1976b). Three women and one man were studied in the morning, at the crest of the circadian plasma cortisol cycle. Four women and one man were studied in the evening, at the nadir of the cortisol cycle. Plasma TSH concentrations were determined by radioimmunoassay. The between-assays coefficient of variation was 15.1%, with a mean TSH of 8.2 μU/ml and n = 15.

RESULTS

The subjective responses of the subjects have been reported in detail elsewhere (Curtis *et al.*, 1976b). In summary, the subjects reported little or no anxiety except (a) mild to moderate anxiety at the start of the first session and during the hr preceding treatment in sessions three and four, and (b) severe anxiety during the 1-hr treatment period in sessions three and four (Fig. 1). Most subjects reported that the anxiety during flooding treatment was as intense as any they had ever experienced. These reports were supported by observations of weeping, tremor, goose flesh and other signs of intense anxiety.

TABLE I. TSH LEVELS—SUMMARY OF ANALYSIS OF VARIANCE FOR MORNING SUBJECTS

	SS	df	MS	F	p
Subjects	69.16	3	23.05	1.06	n.s.
Sessions	65.04	4	16.26	<1	n.s.
Times	43.95	9	4.88	<1	n.s.
Sub × sess	261.79	12	21.82	7.36	<0.001
Sub × time	69.45	27	2.57	<1	n.s.
Sess × time	198.98	36	5.53	1.87	<0.01
S × S × T	319.68	108	2.96		

TABLE II. TSH LEVELS—SUMMARY OF ANALYSIS OF VARIANCE FOR EVENING SUBJECTS

	SS	df	MS	F	p
Subjects	243.86	4	60.97	3.34	<0.05
Sessions	119.22	4	29.81	1.63	n.s.
Times	20.44	9	2.27	1.30	n.s.
Sub × sess	292.16	16	18.26	10.46	<0.001
Sub × time	61.44	36	1.71	<1	n.s.
Sess × time	56.71	36	1.58	<1	n.s.
S × S × T	251.32	144	1.75		

TSH data for the morning and evening subjects were analyzed by separate three-way analyses of variance (ANOVA), with sessions and times as fixed variables and subjects as a random variable (Tables I and II). The only significant main effect was for subjects in the evening group ($p < 0.05$). The F ratios for main effects of times and sessions were far below the values needed for statistically significant effects.

The only interaction effect that was strongly positive in both groups was sessions × subjects ($p < 0.001$, for both morning and evening groups). The possibility that this represented an experimental effect in some subjects was explored by performing a two-way ANOVA (sessions × times) for each individual subject. Though five of the nine subjects showed significant differences between sessions, only one subject showed a possible experimental effect. Session three plasma TSH for this subject was higher than all other sessions, but a graph of this subject's plasma TSH concentration at each time in each session showed an initially high TSH, which decreased to a value close to the mean for the other sessions 20 min after treatment began, and then increased during the third hr of the session. Because the session as a whole showed high TSH concentrations, yet TSH was lowest at the time when anxiety was maximal, this seems unlikely to be a treatment effect. The only other significant interaction was for sessions × times in the morning subjects only ($p < 0.01$). Two-way ANOVAs for sessions × subjects at each individual time showed the sessions to be different from each other only at $T = 1$ and $T = 7$. Graphs of session means at each time showed no effect that could be attributed to the treatment.

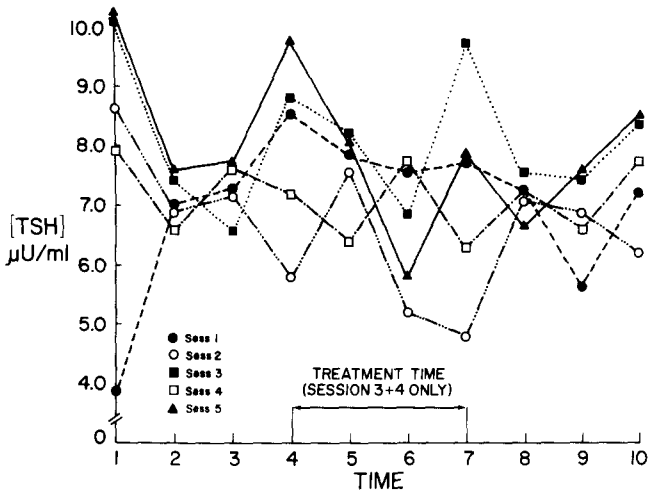

FIG. 2. Mean of all morning subjects' plasma TSH concentration at each session at each time.

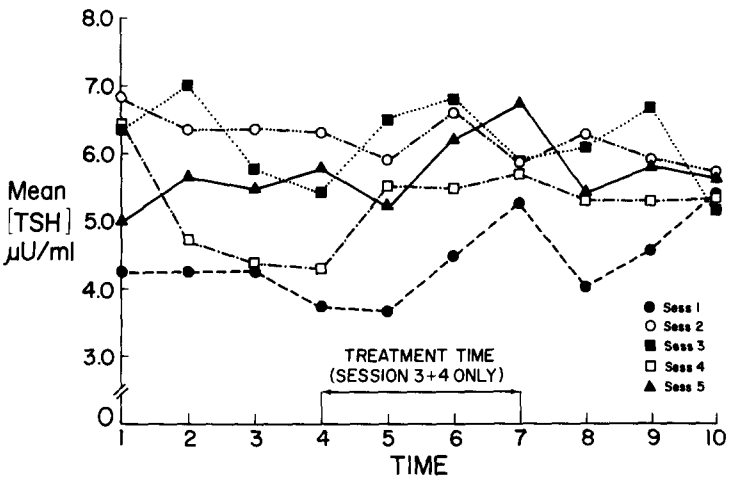

FIG. 3. Mean of all evening subjects' plasma TSH concentration at each session at each time.

To identify trends or individual responses that may not have been statistically significant, graphs of each subject's TSH at each time of each session were examined (Figs. 2 and 3). No instance of TSH response to the anxiety stimulus was found, with the possible exception of one evening subject who showed a small rise in TSH during the middle of session three. Similar increases were observed for all subjects at many other times. Of the 18 treatment hr in the study, only one of these hr had a mean TSH that was the highest of any hr for that subject. Finally, the standard deviations of TSH values for all sessions and subjects were calculated for each specific time. No pattern of increased TSH variation during any specific period was found.

The coefficient of variation for all TSH values for morning subjects was 0.31; for evening subjects the value was 0.37. This amount of variation is approx. the same as that calculated from the data of Chan *et al.* (1978), and it is less than the amount found in other studies (Weeke & Gundersen, 1978). In our study, much of the baseline variation was from differences between subjects and differences between sessions. The rest of the variation most likely resulted from circadian variation (Chan *et al.*, 1978) and from the well-documented rapid fluctuations of plasma TSH which have a cycle of approx. 30 min (Weeke & Gundersen, 1978).

DISCUSSION

The evidence that intense phobic anxiety occurred during flooding treatment is clear, but we found no consistent change in plasma TSH concentrations in response to this anxiety. The possibility that some individual subjects showed a TSH change was considered, but this was rejected after examination of the data for each subject individually. We conclude that even intense phobic anxiety does not change plasma TSH in humans.

The hypothesis that TSH is changed by every kind of psychological stress is contradicted by our findings. We suspect that physiologic and metabolic factors may account for changes in TSH previously attributed to psychological factors. It also is possible that this neuroendocrine system responds differently to different kinds of psychological arousal and that psychological stimuli other than severe phobic anxiety can change plasma TSH concentrations.

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