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Psychological and Endocrine Abnormalities in Refugees From East Germany: Part I. Prolonged Stress, Psychopathology, and Hypothalamic-Pituitary-Thyroid Axis Activity

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Abstract. The influence of prolonged psychological stress on hormonal secretion was investigated in 84 East German refugees suffering from psychiatric disorders within 6 weeks of their arrival in West Berlin shortly before or after the fall of the Berlin Wall. Before leaving the German Democratic Republic, these patients had already experienced prolonged stress, which continued after migration. In most cases, the diagnosis was anxious-depressive syndrome with vegetative complaints and symptoms of increased arousal. Their formal *DSM-III-R* diagnoses (American Psychiatric Association, 1987) included adjustment disorders, depressive disorders, and anxiety disorders (the latter including posttraumatic stress disorder). Serum levels of thyroid stimulating hormone (TSH) and thyroid hormones (thyroxine, free thyroxine, triiodothyronine, and reverse triiodothyronine) were measured and compared with those of 20 healthy control subjects. TSH and all thyroid hormone concentrations were significantly reduced in the patient group. Fifty-two of the patients (62%) were in the hypothyroid range but did not show any clinical signs of hypothyroidism. These disturbances in hormonal secretion were not correlated to any psychiatric diagnosis or to the severity of acute or chronic stress. The marked abnormalities in the hypothalamic-pituitary-thyroid axis seen in these refugees differ from those reported in depression and would seem to reflect severe chronic stress rather than specific psychiatric disorders. The underlying neurochemical mechanisms remain to be investigated.

Key Words. Anxiety, depression, posttraumatic stress disorder, thyroid stimulating hormone, thyroid hormones, stress, migration.

Numerous studies have demonstrated that the endocrine system reacts to various stressful psychological and environmental stimuli. Endocrine changes in response to stress depend on various factors, in particular the duration (acute vs. chronic) and the type of stressor (for reviews, see Mason, 1968; Rose, 1984). While many studies have explored endocrinological changes following acute stress, endocrine responses to prolonged psychological stress have rarely been investigated in humans. As far as we know, endocrine responses to migration after prolonged severe psychological stress situations have not yet been systematically studied.

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The German Democratic Republic (GDR), which ruled the eastern part of Germany for four decades, was a totalitarian system that dominated all areas of public life. In 1961, when there was a danger that too many people would leave the GDR, a wall was built between East and West Germany and around West Berlin. From then on, citizens of the GDR could not move freely to or even visit West Germany or other Western countries.

People who were suspected of opposing official state policy or of planning to leave the GDR were usually subjected to arbitrary decisions and maltreatment by state authorities. They were exposed to unpredictable acts of repression and often persecuted by the State Security Police (the so-called STASI). They were persecuted by frequent summonses, interrogations, imprisonment, surveillance at home and at work, social discrimination and degradation, and other measures. No one could be certain that his or her colleagues, friends, or even family members were not secretly passing on information to the STASI. Persons who made an official application to leave the GDR risked losing their jobs immediately or being sent to prison for a period of months or even years. Their children were regularly excluded from high school education and from any advanced occupational training. Pressure was put on these persons to withdraw their applications for permission to emigrate, which were sometimes not accepted for more than 10 years or not at all (Amnesty International, 1989; Peters, 1991; Priebe et al., 1992; Bauer et al., 1993). In 1989, the political situation in Eastern Europe changed, and on November 9, 1989, the Berlin Wall was breached. Around that time, several thousand people left the GDR each week. Most of these people had experienced prolonged stress situations. First, they had been exposed to arbitrariness and harassment by the GDR state authorities. Second, the move itself was frequently difficult (e.g., flight through other East European countries) and associated with emotional distress. Third, the abilities they required to get what they wanted and needed in the West were different from those people had learned in the Communist system (Priebe et al., in press).

The present study was undertaken to investigate the effects of severe, prolonged psychological stress on the hormone secretion of different endocrine axes in 84 refugees who had fled from East to West Germany. We examined persons who had left the GDR shortly before or after the breaching of the Wall and who had sought psychiatric help on an outpatient basis within 6 weeks of their arrival in West Berlin. Part I of this report deals with the patients' histories, sociodemographic data, symptoms, psychiatric diagnoses, and afternoon serum levels of hypothalamic-pituitary-thyroid (HPT) axis hormones. Thyroid stimulating hormone (TSH) and thyroid hormones were measured because many of the patients showed clinical signs of hyperthyroidism, and also because to date no study has investigated the effects of severe prolonged stress on the hormones of the HPT axis.

The endocrine findings are discussed and related to the clinical data. The results for cortisol, prolactin, luteinizing hormone, follicle stimulating hormone, and testosterone are reported in Part II.

Methods

Patients. Patients who sought treatment in a psychiatric practice offering exclusively

outpatient care within 6 weeks of their arrival in West Berlin and who were found to have a psychiatric disorder by each of two psychiatrists working independently of each other were included in the study. Both psychiatrists agreed on the same diagnosis in 78 of the 84 patients who were finally included in the study (see below). In six further patients, the two raters differed regarding the diagnosis. In these cases, they discussed the symptoms of each individual patient and finally agreed on a common diagnosis. Patients with schizophrenia, bipolar or organic disorders, or substance addictions and those younger than 18 years were excluded. Patients taking antidepressants or any hormonal or psychotropic medication, including oral contraceptives, thyroid hormones, or glucocorticoid hormones, or who were suffering from any serious somatic disease were also not included in the investigation. The interviewer was not involved in the treatment. Participation in the study was voluntary and not associated with any advantages to the patients.

Clinical Ratings and Diagnostic Classification. The patients' histories and current life situations were assessed in a semistructured interview. Psychopathological symptoms were rated on the 21-item Hamilton Rating Scale for Depression (Hamilton, 1960) and the Hamilton Rating Scale for Anxiety (Hamilton, 1959). Criteria for posttraumatic stress disorder (PTDS) were assessed using a symptom checklist based on *DSM-III-R* criteria (American Psychiatric Association, 1987). The patients rated themselves on the von Zerssen Depression Scale, the von Zerssen Complaints Checklist (von Zerssen, 1986), and the State-Trait Anxiety Inventory X1 (State anxiety; Spielberger, 1983). Diagnostic classification using a semistructured interview was made according to *DSM-III-R* (Axes I, II, and V) (American Psychiatric Association, 1987).

Hormone Determinations. Hormonal data were obtained for 84 patients (43 women, 41 men); their mean age was 32.7 (SD = 8.4; range 20-60) years. Twenty healthy volunteers, all members of the staff of the psychiatric clinic, were also tested. All of these control subjects had been known to one of the authors (A.B.) personally for a period of at least 3 years. A history of recent trauma could therefore be excluded in these volunteers. Additional confirmation was also obtained by asking these subjects whether they had suffered traumatic life events within the last 12 months. None of them answered in the affirmative. Five of the control subjects were women, 15 men, and their mean age was 30.8 (SD = 7.5; range 20-45) years. None of them had a history or current symptoms of any psychiatric disease or traumatic experience and none was taking any medication.

Blood samples were collected from the patients on the day of the interview. All blood samples from both patients and control subjects were taken between 2 and 4 p.m. The subjects were seated and the samples were drawn from a single venipuncture between 2 and 4 p.m. The blood was centrifuged at 3000 rpm for 10 minutes. The serum was collected and frozen at -20 °C. The serum concentrations of TSH, thyroxine (T_4), free thyroxine (fT_4), triiodothyronine (T_3), and reverse T_3 (rT_3) were measured in all patients ($n = 84$) and control subjects ($n = 20$). All hormones were determined in duplicate using commercial kits. We used the IRMA kit for TSH and radioimmunoassay (RIA) kits manufactured by Henning, Berlin for T_4, fT_4, and T_3. Reverse T_3 was determined using RIA kits from Serono Diagnostica. Details on the sensitivities of the kits used and the interassay coefficients of variation measured by our laboratory have been published in previous reports (Baumgartner et al., 1988*a*, 1990). All hormone levels were determined in the same assay for both patients and control subjects.

Data Analysis. Where appropriate, the results are expressed as means ± standard deviations (SD). Student's *t* tests (two-tailed) were used to compare the hormone levels of the patients with those of the control subjects. One-way analysis of variance with the factor "subgroup" was calculated to compare the hormone levels in the different diagnostic subgroups. The Newman-Keuls test was applied for individual ranking. For correlations of hormone levels with clinical and sociodemographic variables, we used Pearson's coefficient of correlation. The level of statistical significance was set at p values < 0.05.

Results

Sample and History. The subjects' educational levels were as follows: 10 or more years of education, 76%; university degrees, 11%; other kinds of occupational training, 77%; and no vocational qualifications, 12%. At the time of the interview, 64% were living with a partner and 48% with children.

The patients reported that they had made the decision to leave the GDR between several days and 12 years before they were actually able to do so. On average, the time between decision and departure was 22.1 months (SD = 21.9). Nearly all patients (97%) reported that they felt subjectively repressed by the political system in the GDR and that this was the reason for leaving their country.

Twenty-three (27%) patients had been imprisoned for political reasons. The duration of imprisonment varied between 4 and 160 weeks (mean = 40.8 weeks, SD = 15.1). Between 2 months and 2 years had elapsed between the time of release from prison and the migration (mean = 12 months). Patients reported psychological torture in prison and fears because it was uncertain when they would be released. In prison, the patients had never known what had happened to their relatives, were never certain whether cell mates were STASI informers or not, and never knew when they might be moved to a different cell or prison or be released. The climate in prison was described as hostile and mistrustful. The most stressful conditions identified were solitary confinement (between 14 and 180 days); interrogations conducted by STASI agents in a repressive manner that went on for several hours, frequently at night, over a period of several weeks; and regular turning on and off of the cell lighting or constant lighting at night. The diagnoses of patients who had been imprisoned were as follows: major depression ($n = 4$), dysthymia ($n = 3$), adjustment disorders ($n = 6$), and PTSD ($n = 10$).

Twenty-three patients (27%) had been forced by the state authorities to do jobs that were clearly beneath their level of qualification in the GDR. Twenty-eight patients (32%) had fled to other eastern European countries on their way to West Berlin. At the time of the study, 75 patients (89%) were without a job, 31 (37%) were living in hostels, 10 (12%) in gymnasiums, 29 (34%) in an apartment together with friends or relatives, and 14 (16%) in a small apartment of their own.

Eighty-seven percent stated that they had suffered from the same symptoms in the GDR as they were having after migration. In 62%, the symptoms had been present immediately before leaving; in 40% continuously for more than 6 months. Fifty-two percent reported that their symptoms had begun at or after the time when they made the decision to leave. Twenty-six (31%) patients had been receiving primary medical care in the GDR because of their psychiatric symptoms; only 13 (15%) had undergone psychiatric treatment; five (6%) had received treatment in a psychiatric hospital.

Symptoms and Diagnoses. The complaints spontaneously reported by more than 15% of the patients included sleep disturbances (83%), nervousness (63%), headaches (42%), sadness (38%), aggressiveness (30%), repeated crying (30%), exhaustion (26%), perspiration (24%), agoraphobia (19%), loss of appetite (18%), poor concentration (17%), and backache (17%). More complaints were marked on the von Zerssen Complaint List. The symptoms rated as moderate or severe by $\geqslant 50\%$ of the

patients were: inner restlessness (92%), irritability (89%), a tendency to become exhausted quickly (85%), brooding (83%), insomnia (83%), a feeling of weakness (67%), heavy perspiration (63%), headaches (58%), trembling (54%), an excessive need of sleep (52%), and weight loss (50%).

The scores on the clinical and self-rating scales showed—on the average—moderate symptoms of depression and anxiety. The mean scores were 14.8 (SD = 4.7) on the Hamilton Rating Scale for Depression, 15.9 (SD = 6.0) on the Hamilton Rating Scale for Anxiety, 16.5 (SD = 8.3) on the von Zerssen Depression Scale, 57.7 (SD = 9.7) on the State-Trait Anxiety Inventory (X1), and 45.2 (SD = 11.3) on the von Zerssen Complaint List. On the Global Assessment of Functioning Scale (according to Axis V of *DSM-III-R*), the current level of functioning varied between 45 and 75 (mean = 61.3, SD = 6.4). The highest level in the past year ranged from 50 to 90 (mean = 71.8, SD = 10.5).

Table 1 summarizes the 16 different *DSM-III-R* diagnoses. Adjustment disorders (n = 33), depressive disorders (n = 28), PTSD (n = 12), and anxiety disorders (n = 11) were diagnosed most frequently. In addition, 17 patients received two Axis I diagnoses: seven patients were found to fulfil the criteria for an adjustment disorder, three patients had a somatoform disorder not otherwise specified (NOS), two patients were diagnosed as having alcohol abuse, and two as having a depressive disorder NOS. Generalized anxiety disorder, social phobia, and primary insomnia were each diagnosed in one patient.

Finally, we were interested to establish whether the length of time the patients had been under stress in the GDR was related to the severity of the current symptoms. It is obviously difficult to measure the duration of the stress period exactly. For example, some patients had grown up in families that openly opposed the Communist system and had thus been exposed to maltreatment over a very long period. We defined the stress period as the length of time between the decision to leave the GDR and the actual departure, although this decision may often have been

Table 1. *DSM-III-R* diagnoses (n = 84)[1]

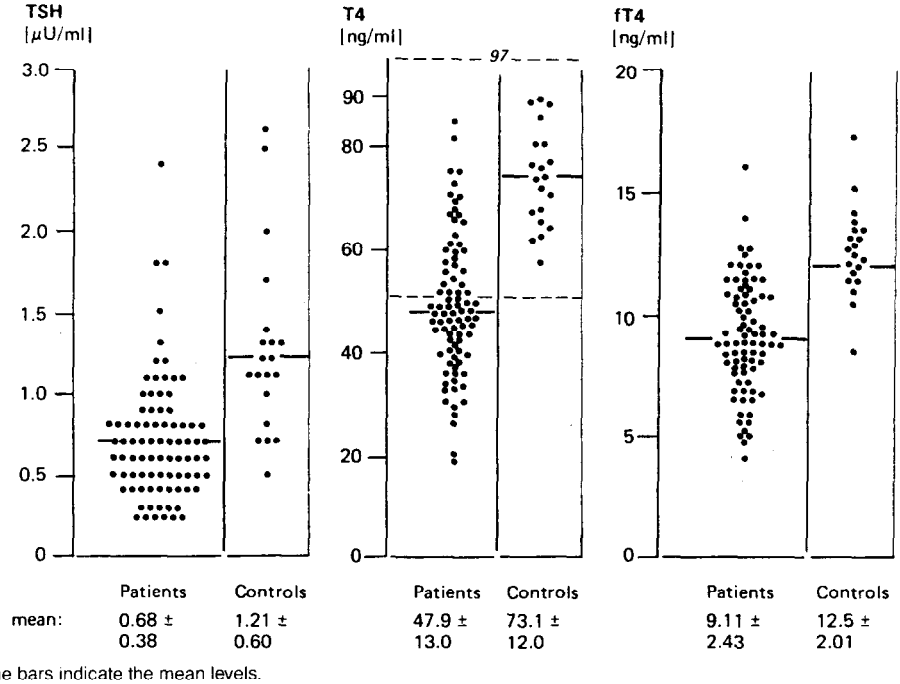
Major depression, single episode	13
Major depression, recurrent	5
Anxiety disorder not otherwise specified	5
Generalized anxiety disorder	2
Agoraphobia without history of panic disorder	1
Social phobia	5
Dysthymia	10
Somatoform disorder not otherwise specified	3
Primary insomnia	1
Alcohol abuse	2
Adjustment disorder with depressed mood	3
Adjustment disorder with anxious mood	8
Adjustment disorder with mixed emotional features	23
Adjustment disorder with physical complaints	6
Posttraumatic stress disorder	12
Depressive disorder not otherwise specified	2

1. Two diagnoses were given in 17 patients (for details, see text).

the result of distress rather than the onset of it. There was a moderate, but significant positive correlation between this period of time and the score on the von Zerssen Complaint List (Pearson's $r = 0.22$, $p < 0.05$). The correlations with other rating scales, including the Global Assessment of Functioning Scale, were not statistically significant.

Hormonal Analysis. Fig. 1 presents the T_4 concentrations of the 84 patients and the 20 healthy control subjects. As illustrated in Table 2, the mean T_4 concentrations of the patients were significantly lower than those of the control group. The normal range was determined by calculating the mean hormone levels ± 2 SD of the control subjects (range = 49.1-97.1 ng/ml; see dotted line in Fig. 1). On the basis of these criteria, 52 (62%) of the patients were hypothyroid. However, they had no clinical signs of hypothyroidism or goiter. As shown in Table 2 and Figs. 1 and 2, the fT_4, T_3, rT_3, and TSH concentrations were also significantly reduced in the patient group.

Fig. 1. Thyroid stimulating hormone (TSH), thyroxine (T_4), and free T_4 (fT_4) concentrations in 84 patients and 20 healthy control subjects



The bars indicate the mean levels.

Table 3 lists the TSH and thyroid hormone concentrations separately for the five different diagnostic subgroups. Analysis of variance did not reveal a significant group effect for any of these hormones. Likewise, the mean hormone levels of the 23 patients who had a history of political imprisonment did not differ from the mean values of the patients who had not been in prison (detailed data not shown).

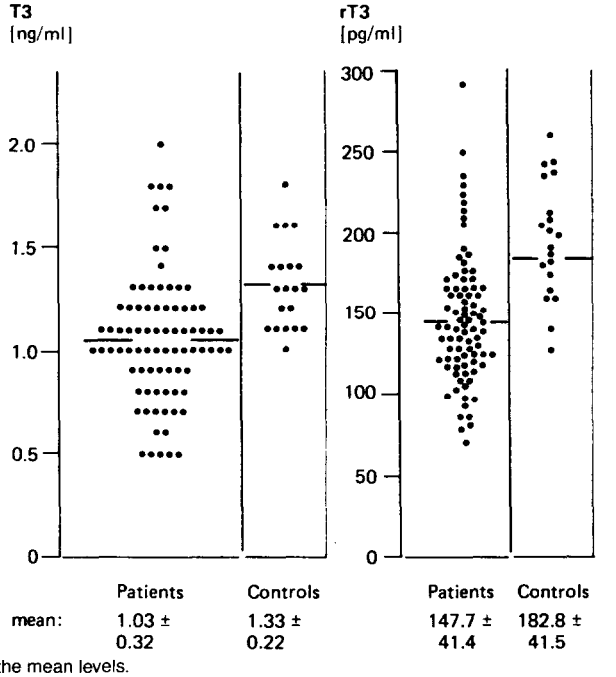
Table 2. Hormone concentrations of patients and healthy control subjects[1]

	Patients ($n = 84$)		Control subjects ($n = 20$)		
Hormones	**Mean**	**SD**	**Mean**	**SD**	***p***
TSH	0.68	0.38	1.21	0.60	0.003
T_4	47.9	13.0	73.1	12.0	< 0.0001
fT_4	9.11	2.43	12.50	2.01	< 0.0001
T_3	1.03	0.32	1.33	0.22	< 0.0001
rT_3	146.7	41.4	182.8	41.5	0.001

Note. TSH = thyroid stimulating hormone. T_4 = thyroxine. fT_4 = free T_4. T_3 = triiodothyronine. rT_3 = reverse T_3.

1. For units of measurement, see text and Figs. 1 and 2.

Fig. 2. Triiodothyronine (T_3) and reverse T_3 (rT_3) concentrations in 84 patients and 20 healthy control subjects



The bars indicate the mean levels.

We also calculated Pearson's coefficients of correlation between TSH and all thyroid hormones on the one hand, and the length of time spent in prison (in months) on the other. However, neither of these correlations showed even a trend toward significance. Likewise, we found no significant correlations between the hormone levels and the duration of time between the decision to leave the GDR and the actual time of emigration, which we considered a suitable value for defining the duration of the stress. Finally, there were no significant correlations between the

Table 3. Mean TSH and thyroid hormone concentrations in all patients, in five different diagnostic subgroups, and in the subgroup of former political prisoners[1]

	All patients ($n = 84$)	Major depressive disorders ($n = 18$)	PTSD ($n = 12$)	Anxiety disorders ($n = 11$)	Dysthymia ($n = 10$)	Adjustment disorders ($n = 33$)	Previously imprisoned patients ($n = 23$)
TSH							
Mean	0.68	0.86	0.83	0.52	0.71	0.62	0.88
SD	0.38	0.55	0.38	0.22	0.46	0.30	0.51
T_4							
Mean	47.9	48.0	45.2	48.9	46.8	47.5	44.3
SD	13.0	10.9	8.9	20.4	6.9	12.2	10.0
fT_4							
Mean	9.11	9.15	8.75	8.77	9.23	9.14	9.30
SD	2.43	2.00	1.67	2.53	1.27	2.21	2.93
T_3							
Mean	1.03	1.10	1.03	1.02	1.05	0.99	1.03
SD	0.32	0.32	0.33	0.43	0.20	0.28	0.31
rT_3							
Mean	146.7	144.8	142.0	158.0	150.2	144.1	149.0
SD	41.4	38.1	24.0	61.1	43.1	40.1	30.2

Note. PTSD = posttraumatic stress disorder. TSH = thyroid stimulating hormone. T_4 = thyroxine. fT_4 = free T_4. T_3 = triiodothyronine. rT_3 = reverse T_3.

1. For units of measurement, see Figs. 1-2.

hormone levels and the acute severity of the symptoms as measured by any of the rating scales mentioned above. The hormone values were not correlated to the ages and the gender of the patients.

There were significant positive correlations between TSH and all the individual thyroid hormones, and also intercorrelations between all the individual thyroid hormones (all p's < 0.05). The only exception was the correlation between TSH and rT_3, which was not significant ($r = -0.03$, $p = 0.38$). In contrast, the correlations between TSH and T_4, TSH and T_3, and T_4 and T_3 were not significant in the healthy subjects. Only the correlations between T_4 and fT_4, and T_4 and rT_3, respectively, were highly significant ($p < 0.05$). Correlations between the hormones of the HPT axis and hormones of other endocrine axes are shown and discussed in Part II of this study. None of the hormone concentrations of the HPT axis showed significant correlations with any psychiatric diagnosis or with the results of the psychopathological rating scales. There were also no significant differences between the hormone values of the patients who had been political prisoners and those of the control subjects.

Discussion

The length and severity of the stress that the patients actually experienced in the GDR may have varied greatly. It is safe to assume, however, that they were exposed to prolonged stress situations, since many of them had been politically persecuted for months or years. The last part of the stress period was characterized by the same life event: all the patients left the GDR and arrived in the West under the historical circumstances of late 1989. On arrival in the West, most of them had neither employment nor anywhere to live, were temporarily housed in large numbers in hostels or gymnasiums, and faced highly uncertain futures. They also had to adjust to a completely different social and economic system.

Following this prolonged period of stress, all of the patients were characterized by a similar syndrome. They all suffered from moderate symptoms of depression and anxiety (as reflected by the scores of the rating scales), which were accompanied by vegetative complaints (e.g., headaches) and symptoms of increased arousal (e.g., irritability and sleep disturbances). This syndrome resembles the psychiatric disorders diagnosed after other forms of political persecution (Kinzie et al., 1984; Mollica et al., 1987; Allodi, 1991). In particular, there are similarities with the mental sequelae of concentration camp imprisonment, although the degree of stress was clearly lower in the sample examined in this study than in Holocaust survivors (Matussek, 1971; Eitinger, 1980).

The syndrome seemed characteristic to us; nevertheless, diagnostic classification according to *DSM-III-R* was often difficult and unsatisfactory. This was reflected by the fact that 10 patients (12%) received a "not otherwise specified" (NOS) diagnosis of some kind. The frequency of the diagnosis of PTSD obviously depends on how narrowly the definitions are interpreted. While 12 patients (14%) were diagnosed as fulfilling all PTSD criteria, other patients did not clearly show the "persistent avoidance of stimuli associated with the trauma or numbing of general responsiveness" (criterion C). Moreover, since it was assumed that the practice of STASI

surveillance and harassment was widespread in the GDR, the criterion of stressor exposure level (criterion A for PTSD) was not fully met for all patients. It was often not possible to diagnose adjustment disorder, because the symptoms had persisted for longer than 6 months (criterion D).

The data suggest that, irrespective of the formal diagnoses, the syndrome as described above was mainly related to prolonged stress resulting from political repression and migration. This assumption is strongly supported by a retrospective study with an unselected sample of persons who fled from the GDR and who showed a marked improvement of symptoms within the first 6 months of living in the West (Priebe et al., 1991).

The concentrations of HPT axis hormones were measured in the patients and compared with the values of 20 healthy control subjects. We found a marked reduction in thyroid hormone concentrations (T_4, fT_4, T_3, and rT_3) in the patient group. Furthermore, the TSH levels of this group were also significantly lower, which is exactly the opposite of what one would expect in hypothyroidism. The levels of fT_4 were also reduced, thus also ruling out the possibility of a disturbance in T_4 protein binding. Lower T_3 concentrations in the patient group ruled out a "low T_3 syndrome" (see Wartowsky and Burman, 1982). Since iodine was added to the drinking water in the GDR, an endemic shortage of iodine cannot have been the cause of the hypothyroidism in our sample. As the patients were well-fed, it is also unlikely that nutritional factors played a role in these thyroid abnormalities. Malnutrition and weight loss also lead to an increase not a decrease in rT_3 concentrations (see Wartowsky and Burman, 1982).

As the reductions in the concentrations of TSH and all the thyroid hormones were equal across all five diagnostic subgroups (Table 3), it seems justified to ascribe these remarkable hormone changes to factors related to chronic stress factors. Our results show an HPT axis impairment and do not match the endocrine pattern usually ascribed to major depressive disorder. The vast majority of investigators have found normal thyroid hormone levels in depression (for a review, see Baumgartner et al., 1988*a*). The endocrine abnormalities found in the present study are therefore more likely to have resulted from severe long-term stress than from a depressive disorder.

Very little is known about the influence of acute stress on the HPT axis and virtually nothing about that of chronic stress. Habermann et al. (1978) found normal T_3 and T_4 levels in helicopter pilots after flying and after motion sickness, but elevated urinary concentrations of T_3 and T_4 after both stressful events. Baumgartner et al. (1988*b*) found no significant differences in baseline TSH, T_4, T_3, or rT_3 levels in medical students during a major examination. Increased TSH concentrations have been found after parachute jumping (Noel et al., 1976), in young men anticipating unfamiliar muscular exercise (Mason et al., 1973), and in rats exposed to acute stress (Dohler et al., 1977). In contrast, decreased TSH levels have been reported after treadmill exercise and surgery (Sowers et al., 1977). Langer et al. (1982) determined depressed basal TSH levels in rats after chronic exposure to immobilization stress. In corroboration of these results, Armario et al. (1987) found that an initial TSH rise induced by acute stress was blunted in chronically stressed rats. To summarize what is known about stress-induced changes in hormones of

the HPT axis, we must emphasize that the results for thyroid hormones are contradictory and that TSH levels seem to rise in acute stress and fall in chronic stress.

Mason et al. (1990) reported somewhat elevated concentrations of T_4 and fT_4 in PTSD patients. Their data are hardly comparable to ours, however, as values in PTSD patients were not compared with values in a healthy control group, the number of PTSD patients was rather small ($n = 9$), no detailed data were given regarding the length and nature of the stressors in the patients, and no statistical analysis was provided. Kosten et al. (1990) found normal mean T_4, fT_4, baseline TSH, and TSH levels after stimulation with thyrotropin releasing hormone (TRH) in 11 patients with PTSD. Details about the length and nature of the trauma were not provided, making comparison with our results difficult.

The origins of the marked declines in all HPT-axis parameters in our chronically stressed patients are currently unknown. A "down-regulation" of pituitary TSH receptors, caused by elevated TRH levels resulting from chronic noradrenergic hyperactivity due to prolonged severe psychological stress, seems conceivable. As regards the neuroendocrine regulation of the HPT axis, a stimulatory action of norepinephrine has been shown in both in vitro and in vivo experiments in animals and in humans (for reviews, see Reichlin, 1986; Spira and Gordon, 1986). Another hypothetical explanation for the decreased T_4/T_3 serum levels would be an increased uptake of T_4/T_3 into the cells. This mechanism could be the reason why the patients' symptoms were similar to those of hyperthyroidism, whereas their laboratory parameters showed a clearly hypothyroid pattern. It is now well known that serum thyroid hormone levels provide—at best—only very indirect information on the physiological intracellular concentration of T_3 (for a review, see Silva and Larsen, 1986). This applies particularly to tissues such as the brain, where the intracellular level of T_3 depends on intracellular deiodination of T_4 (for a review, see Leonard and Visser, 1986). Finally, it is conceivable that chronic stress enhances intracellular deiodination of T_4 to T_3 in tissues such as the pituitary and/or certain areas of the brain. No direct information on the effects of stress on the regulation of 5'II-deiodinase, which catalyzes the deiodination of T_4 to T_3 in these tissues, is yet available. It is well known from animal studies, however, that noradrenergic activity may enhance the activity of these enzymes in various tissues in the rat (e.g., Raasmaya and Larsen, 1989). Moreover, after 24 hours' sleep deprivation, which is certainly a stressful procedure, we recently found enhanced 5'II-deiodinase activity in some areas of the rat brain (Campos-Barros et al., 1993). It is therefore theoretically possible that stress activates intracellular deiodination of T_4 to T_3, leading to a hyperthyroid intracellular state, which is clinically reflected by a hyperthyroid symptomatology. If T_3 production were also enhanced in the pituitary, the result would be an inhibition of TSH secretion and a subsequent down-regulation of all thyroid hormone serum concentrations. All these possibilities are as yet hypothetical and require further investigation.

The depression of the HPT axis seen in the refugees is further discussed in relation to the results for other endocrine axes that are reported in Part II of this study.

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