

# Chronobiological thyroid axis activity and suicidal behavior in depressed patients

Fabrice DUVAL, Marie-Claude MOKRANI, Felix GONZALEZ LOPERA, Ksenia PROUDNIKOVA, Hassen RABIA, Alexis ERB  
Pole 8/9 - Centre Hospitalier Rouffach France



## Introduction

A substantial body of evidence suggests that TRH acts as a homeostatic modulator in the central nervous system. In depressed patients, TRH hypersecretion leading to downregulation of the TRH receptors of the pituitary thyrotrophs—as evidenced by reduced TSH responses to TRH—may be seen as a compensatory mechanism in order to normalize serotonin (5-HT) activity (Duval et al., 1999). We have hypothesized that a decrease in 5-HT function triggers an increased TRH secretion that secondarily normalizes 5-HT neurotransmission and also maintains normal thyroid hormone levels. Furthermore, we have also recently suggested that this compensatory mechanism is not effective in depressed patients with a history of suicidal behavior (Duval et al 2010), which could play a role in the sustained 5-HT hypoactivity consistently linked to suicidal behavior (Mann and Currier, 2007).

The aim of this study was to investigate the relationship between suicidal behavior and chronobiological thyroid axis activity in a wider population of depressed inpatients than in our previous study.

## Results

**Table 1** : Demographic and biological data

	Controls (n=50)	No Suicide H. (n=107)	Past attempters (n=52)	Recent attempters (n=71)	Controls vs.			No Suicide H. vs.		Recent vs. Past attempters
					No Suicide H.	Past attempters	Recent attempters	Past attempters	Recent attempters	
Age, yrs	40.2 ± 8.3	42.3 ± 11.7	41.5 ± 12.1	37.9 ± 11.5	...	...	...	...	...	...
Gender M/F	20/30	62/45	19/33	28/43	...	...	...	...	...	...
HAM-D17 items		27.0 ± 4.6	27.2 ± 3.5	27.7 ± 3.9	...	...	...	...	...	...
<b>8 AM Values</b>										
TSHB, mU/L	1.15 ± 0.62	1.07 ± 0.50	1.41 ± 0.69	1.24 ± 0.73	...	...	...	0.013	...	...
ΔTSH, mU/L	7.70 ± 3.14	6.18 ± 3.10	7.79 ± 3.54	7.73 ± 4.19	0.033	...	...	0.037	0.048	...
FT4B, pmol/L	12.8 ± 2.3	13.8 ± 3.1	12.2 ± 3.1	11.4 ± 2.9	...	...	4 10 <sup>-6</sup>	0.021	2 10 <sup>-6</sup>	...
FT3B, pmol/L	5.2 ± 0.8	5.2 ± 0.9	4.9 ± 0.8	5.1 ± 1.4	...	...	...	...	...	...
<b>11 PM Values</b>										
TSHB, mU/L	1.09 ± 0.54	0.92 ± 0.45	1.17 ± 0.54	1.03 ± 1.06	...	...	...	...	...	...
ΔTSH, mU/L	11.62 ± 3.85	7.34 ± 2.99	11.60 ± 4.22	9.49 ± 3.95	6 10 <sup>-8</sup>	...	0.022	4 10 <sup>-8</sup>	8 10 <sup>-4</sup>	0.034
ΔΔTSH, mU/L	3.89 ± 1.50	1.18 ± 1.46	3.82 ± 1.81	1.88 ± 2.75	4 10 <sup>-17</sup>	...	6 10 <sup>-6</sup>	1 10 <sup>-13</sup>	...	4 10 <sup>-5</sup>
<b>Post-DST</b>										
Cortisol, nmol/L	42 ± 37	90 ± 109	90 ± 120	79 ± 76	...	...	...	...	...	...

Values are mean±SD. Analysis was by t-test (p values corrected with Bonferroni's method), except for gender (analysis by Fisher exact test). TSHB indicates basal thyrotropin concentration; ΔTSH, peak concentration minus basal thyrotropin concentration; ΔΔTSH, 11 PM- minus 8 AM-ΔTSH; FT4B, basal free thyroxine concentration; FT3B, basal free triiodothyronine concentration; DST, dexamethasone suppression test.

### • Compared to controls :

- 1) **Patients with a recent suicide attempt** showed lower TSH response to TRH (ΔTSH) at 11 PM, lower ΔΔTSH values (differences between 11 PM-ΔTSH and 8AM-ΔTSH), and lower free thyroxine (FT4) levels;
- 2) **Patients with a past suicide attempt** showed no major alteration of the HPT axis activity;
- 3) **Patients without a suicide attempt history** showed both lower 8 AM-ΔTSH and 11 PM-ΔTSH, and lower ΔΔTSH values, but no alteration of circulating thyroid hormone levels.

### • Compared to recent suicide attempters

- 1) **Patients with a past suicide attempt** showed higher 11 PM-ΔTSH and higher ΔΔTSH values;
- 2) **Patients without a suicide attempt history** showed lower 8 AM-ΔTSH and 11 PM-ΔTSH values, lower ΔΔTSH values, and higher FT4 levels.

## Conclusions

Our results suggest that in patients without a suicide attempt history increased hypothalamic TRH stimulation (leading to downregulation of the TRH receptors of the pituitary thyrotrophs—as evidenced by reduced TSH responses to TRH) might be a compensatory mechanism. In patients with a suicide history this compensatory mechanism is not effective. In patients with a recent suicide attempt the evening TSH blunting, associated with reduced FT4 levels, might be indicative of a decreased central TRH activity leading to a reduction in the TSH resynthesis in the thyrotrophs during the day after the morning challenge.

## Methods

Serum levels of thyrotropin (TSH) levels were measured before and after protirelin (TRH; 200 µg intravenously) given at 8 AM and 11 PM, on the same day, in 230 medication-free DSM-IV euthyroid major depressed inpatients and 50 healthy hospitalized controls. In addition, free thyroxine (FT4) and free triiodothyronine (FT3) levels were measured at 8 AM.

On day 2, a dexamethasone suppression test (DST) was performed.

### • Suicide history assessment :

- 71 patients were recent suicide attempters (the suicidal act occurred during the current depressive episode),
- 52 patients were past suicide attempters,
- 107 patients had no history of suicide attempt.

