P.574 Augmentation of pharmacotherapy by sleep deprivation with sleep phase advance in treatment-resistant depression: changes of cortisol, IL-10, and IL-1β

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Introduction:

Total sleep deprivation (TSD) is a method of chronotherapy for depression which can be strengthened by sleep phase advance (SPA). TSD influences circadian rhythms, cortisol secretion and inflammatory cytokines what may have an impact on the allostatic load in affective disorders [1,2]. Single sleep deprivation affects the immune system differently than chronic sleep disturbances and acts otherwise in healthy people, depressed patients with or without improvement. We proposed that the TSD with SPA could serve as an augmentation strategy of pharmacotherapy in treatment-resistant depression (TRD).

The aim of the study:

To assess the efficacy of integrated therapy (TSD with SPA) in patients with TRD receiving antidepressant and mood-stabilizing drugs, and to delineate biological factors of allostatic load connected with such effectiveness.

Methods used:

- ➢ Drug resistance -lack of adequate response to appropriate courses of at least two antidepressant drugs
- ✓ The most commonly used medicines: venlafaxine and quetiapine
- ✓ Efficacy assessed using the 17-item Hamilton Depression Rating Scale (HDRS)
- ✓ The baseline mean score on HDRS: 21±6 points
- ✓ TSD with SPA during maintaining pharmacotherapy according to the scheme (Fig. 1)

Fig. 1. Timeline encompassing the time of sleep and wakefulness during therapy

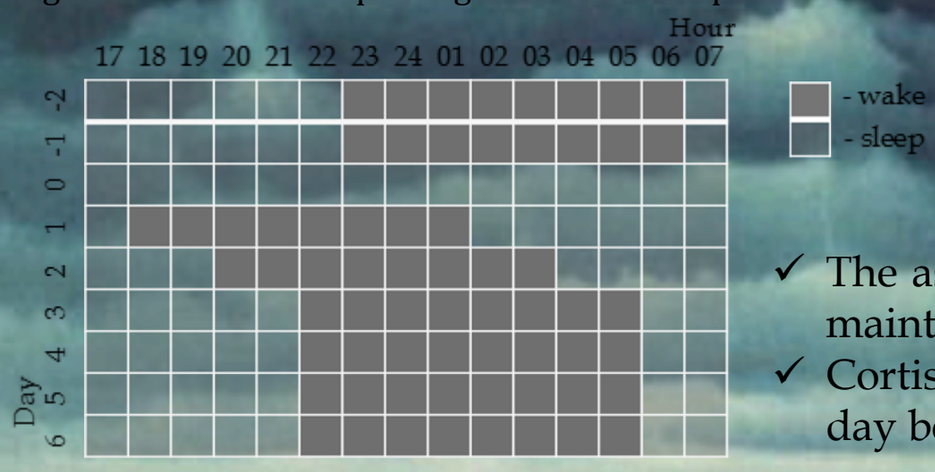

Table 1. Characteristics of the studied sample of patients with TRD

Variable	Statistics
N- number of subjects	21 (100%)
Age (years)	22-69 (49±14)
Gender	
Female	12 (57%)
Mele	9 (43%)
Diagnosis	
Bipolar disorder	10 (48%)
Major depressive disorder	11 (52%)
Total duration of illness (years)	2-31 (9±8)
Duration of depressive episode (months)	4-36 (10±9)

- ✓ The assumed criterion for clinical improvement- a reduction of ≥50% in the HDRS, maintained up to the14th day of the therapy
- ✓ Cortisol, IL-1β, IL-1RA, IL-6, IL-10, TNF-α, sTNF-R2 and IFN- γ measured on the day before, and on 1st, 7th and 14th day after the TSD by ELISA

Results:

The mean score on the HDRS on 14th day in the whole group was 12±9 points. Improvement on the 1st day after TSD in 12 out of 21 patients (57%) was observed and maintained during the entire study in 10 subjects (48%).

Table 2 Serum levels of biological markers studied on the day before, and on 1st, 7the and 14th day after total sleep deprivation

Day	Cortisol (ng/ml)		IL-10 (pg/ml)		IL-6 (pg/ml)		IL-1β (pg/ml)		IL-1RA (pg/ml)		IFN-γ (pg/ml)		TNF-α (pg/ml)		sTNF-R2 (ng/ml)	
	R	N-R	R	N-R	R	N-R	R	N-R	R	N-R	R	N-R	R	N-R	R	N-R
-1	212 ± 76 (201)	257 ± 65 (260)	38 ± 9 (38)	38 ± 5 (38)	601 ± 184 (639)	584 ± 230 (551)	315 ± 99 (309)	353 ± 61 (357)	54 ± 19 (50)	52 ± 15 (54)	49 ± 51 (36)	28 ± 25 (16)	25 ± 23 (19)	23 ± 25 (14)	2.6 ± 1.0 (2.2)	2.1 ± 0.4 (2.1)
1	229 ± 119 (192)	192 ± 55 (204) *	36 ± 4 (37)	44 ± 9 (42) * ▪	587 ± 152 (600)	695 ± 159 (679)	331 ± 100 (302)	385 ± 57 (389)	58 ± 10 (57)	57 ± 26 (55)	17 ± 6 (16)	29 ± 27 (21)	23 ± 9 (24)	26 ± 16 (24)	2.7 ± 0.6 (2.7)	2.7 ± 0.7 (2.4) *
7	185 ± 52 (194)	223 ± 65 (237)	43 ± 9 (43)	39 ± 5 (41)	661 ± 171 (594)	647 ± 103 (677)	387 ± 140 (370)	361 ± 73 (373)	59 ± 23 (55)	57 ± 14 (61)	17 ± 10 (14)	79 ± 82 (55)	27 ± 25 (24)	16 ± 11 (18)	2.7 ± 0.9 (2.3)	2.4 ± 0.6 (2.6)
14	170 ± 61 (178) ^	216 ± 49 (221) ^	47 ± 9 (50) ^	38 ± 7 (39) ▪	668 ± 202 (634)	649 ± 205 (595)	394 ± 96 (377) ^	380 ± 97 (357)	66 ± 25 (61)	53 ± 19 (52)	33 ± 54 (14)	69 ± 77 (33)	28 ± 24 (27)	13 ± 8 (14)	3.0 ± 1.2 (2.9)	2.3 ± 0.4 (2.3) ^

Values are given as mean ± SD (median). R- responders (n=10), N-R- non-responders (n=11); Difference vs responders group ▪ $p<0.05$ (Mann-Whitney test); Difference vs day -1 ^ $p<0.05$ (Wilcoxon test); Difference vs previous measurement * $p<0.017$ (Wilcoxon test with Bonferroni correction)

Conclusions:

We demonstrated the efficacy of the TSD and SPA augmentation of pharmacotherapy in half of the patients with TRD. The main biochemical factors related to clinical response included status of cortisol and increase in IL-10 and IL-1β levels. Chronotherapeutic methods of depression treatment influencing these neurobiological processes can diminish the allostatic load [3]. However, further research is needed to better understand the efficacy of chronotherapeutic methods and their therapeutic mechanisms in treatment-resistant depression.

References:

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