

Eficacitatea terapiei pe baza de lumina in tratamentul tulburarilor afective

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- Specificantul „Cu Pattern Sezonier” –acesta poate fi aplicat patternului episoadelor depresive majore din tulburarea bipolară I, tulburarea bipolară II sau tulburarea depresivă majoră recurentă. Elementul esențial îl constituie debutul și remisiunea episoadelor depresive majore în anumite perioade caracteristice ale anului. În cele mai multe cazuri, episoadele încep toamna sau iarna și se remit primăvara. Mai rar, pot exista și episoade depresive recurente, vara.
- Episoadele depresive majore care survin în pattern sezonier se caracterizează adesea prin anergie notabilă, hipersomnie, mâncat excesiv de mult, plus ponderal și dorința de a mânca hidrați de carbon. Nu este clar dacă patternul sezonier este mai frecvent în tulburarea depresivă majoră recurentă ori în tulburările bipolare. În cadrul grupului tulburărilor bipolare, însă, patternul sezonier pare a fi mai probabil în tulburarea bipolară II decât în tulburarea bipolară I. La unii indivizi, debutul episoadelor maniacale sau hipomaniacale poate fi, de asemenea, în raport cu un anumit sezon. Strălucirea luminii din spectrul vizibil utilizată în tratament poate fi asociată cu comutări în episoade maniacale sau hipomaniacale.
- Prevalența patternului sezonier de tip hibernal pare a varia cu latitudinea, etatea și sexul. Etatea este, de asemenea, un predictor puternic al sezonității, persoanele mai tinere fiind expuse unui risc mai mare de episoade depresive hibernale. Femeile constituie 60%-90% dintre persoanele cu pattern sezonier, însă nu este clar faptul dacă sexul feminin este un factor de risc specific în plus față de riscul asociat cu tulburarea depresivă majoră recurentă. Deși acest specificant se aplică apariției sezoniere de episoade depresive majore complete, unele cercetări sugerează că un pattern sezonier poate ilustra tabloul clinic la unii indivizi cu episoade depresive hibernale recurente care nu satisfac criteriile pentru un episod depresiv major.

Criteriile pentru specificantul „Cu Pattern Sezonier”

A. Există o relație temporală regulată între debutul episoadelor depresive majore din tulburarea bipolară 1 sau tulburarea bipolară II, ori tulburarea depresivă recurentă, și o anumită perioadă a anului (de ex., apariția regulată a episodului depresiv major toamna sau iarna). Notă: Nu se includ cazurile în care există un efect evident al stresorilor psihosociali în raport cu sezonul (de ex., a fi în mod regulat fără serviciu în fiecare iarnă).

B. Remisiuni complete (sau schimbare din depresie în manie sau hipomanie) survin, de asemenea, într-o anumită perioadă a anului (de ex., depresia dispare primăvara).

C. În ultimii 2 ani, au survenit două episoade depresive majore, ceea ce demonstrează relațiile temporale sezoniere definite la criteriile A și B, și nu au survenit nici un fel de episoade depresive majore nonsezoniere în cursul aceleiași perioade,

D. Episoadele depresive majore cu caracter sezonier (așa cum au fost descrise mai sus) depășesc substanțial ca număr episoadele depresive majore fără caracter sezonier care au putut surveni în cursul vieții individului.

_Fototerapia (terapia cu lumina) reprezinta expunerea la lumina mai intensa decat lumina becului, dar nu la fel de intensa ca lumina soarelui.

Metoda

- Studiu de metaanaliza realizat de doctori din cadrul departamentului de psihiatrie al Universitatii Carolina de Nord
- S-a folosit platforma PubMed, cautandu-se studii dupa anumiti termeni cheie precum: fototerapie, tulburare afectiva sezoniera, tulburare afectiva bipolară, tulburare de somn, ritm circadian

Criterii de selectie

- Varsta 15-65 ani in dorinta de a stabili un tratament adecvat standard
- Studii randomizate, controlate placebo
- Doza minima:
 - tratamentul cu lumina puternica: minim 4zile x 3000 lucsi-ora; placebo: maxim 300 lucsi
 - tratament dawn simulation (simularea diminetii): crestere treptata a intensitatii luminii de la 0 la 300 lucsi intr-o perioada de 1,5-2 ore.; placebo: o cretere < 5 lucsi si/sau <15 minute

Selectia studiilor

- Initial 173 studii
- In urma aplicarii criteriilor de excludere: 21 studii

TABLE 1. Randomized, Controlled Trials of Bright Light and Dawn Simulation in the Treatment of Mood Disorders

Treatment, Diagnosis, and Study	Duration of Trial (days)	Experimental Group				Control Group				Effect Size
		Condition	Illuminance (lux)	Time (hours/day)	Number of Patients	Condition	Illuminance (lux)	Time (hours/day)	Number of Patients	
Bright light Seasonal affective disorder										
Avery et al., 2001 (9)	42	White light	10,000	0.5	33	Red light	0.5	1.5	31	0.09
Eastman et al., 1998 (10)	24	White light	6,000	1.5	49	Deactivated negative air ionizer		1.5	22	0.19
Michalon et al., 1997 (11)	14	White light	2,500	2.0	15	Red light	<300	2.0	14	1.53
Rosenthal et al., 1984 (1)	14	White light	2,500	6.0	9	Yellow light	100	6.0	9	2.08
Rosenthal et al., 1985 (12)	7	White light	2,500	6.0	13	Yellow light	≤300	6.0	13	1.19
Rosenthal et al., 1987 (13)	7	White light	2,500	5.0	7	White light	≤300	5.0	7	2.11
Schwartz et al., 1997 (14)	21	White light	10,000	1.5	17	Active light avoidance (dark goggles outdoors)			17	2.01
Terman et al., 1998 (15)	10–14	White light	10,000	0.5	85	Negative ion density (1.0×10 ⁴ ions/cm ³)		0.5	19	1.05

Nonseasonal depression										
Baumgartner et al., 1996 (16)	7	White light	2,500	2.0	19	Red light	50	2.0	15	0.40
Kripke et al., 1992 (17)	7	White light	>2,000	3.0	25	Red light	<50	3.0	26	0.78
Volz et al., 1991 (18)	7	White light	2,500	2.0	22	Red light	50	2.0	20	0.35
Dawn simulation for seasonal affective disorder										
Avery et al., 1992 (19)	7	White light ("gradual dawn")	0–275	2.5	9	White light ("rapid dawn")	0–275	0.2	9	0.25
Avery et al., 1993 (20)	7	White light ("gradual dawn")	0–250	2.0	13	White light ("rapid dawn")	0–0.2	0.5	9	1.16
Avery et al., 1994 (21)	7	White light ("gradual dawn")	0–250	1.5	10	Red light	0–2	1.5	9	1.10
Avery et al., 1998 (22)	7	White light ("gradual dawn")	0–250	1.5	6	Red light	0–2	1.5	6	1.33
Avery et al., 2001 (9)	42	White light ("gradual dawn")	0–250	1.5	31	Red light	0–0.5	1.5	31	0.54
Bright light as adjunctive treatment of nonseasonal depression										
Beauchemin and Hays, 1997 (23) ^a	7	White light	10,000	2.0	8	White light	2,500	0.5	11	1.31
Fritzsche et al., 2001 (24) ^b	14	White light	2,500	2.0	21	Red light	50	2.0	19	0.09
Holsboer-Trachsler et al., 1994 (25) ^c	16	White light	5,000	2.0	14	No light treatment			14	-0.74
Muller et al., 1997 (26) ^c	28	White light	5,000	2.0	14	No light treatment			14	-0.80
Neumeister et al.,	6	White light	3,000	4.0	10	White light	100	4.0	10	0.81

Rezultate

TABLE 2. Significance of Effect Sizes for Studies of Bright Light and Dawn Simulation in the Treatment of Mood Disorders

Diagnosis and Treatment	Number of Studies	Effect Size	95% CI	p (z test)
Seasonal affective disorder				
Bright light	8	0.84	0.60 to 1.08	<0.0001
Dawn simulation	5	0.73	0.37 to 1.08	<0.0001
Nonseasonal depression				
Bright light	3	0.53	0.18 to 0.89	<0.003
Adjunctive bright light	5	-0.01	-0.36 to 0.34	>0.95

FIGURE 2. Effect Sizes in Studies of Treatment of Seasonal Affective Disorder With Bright Light

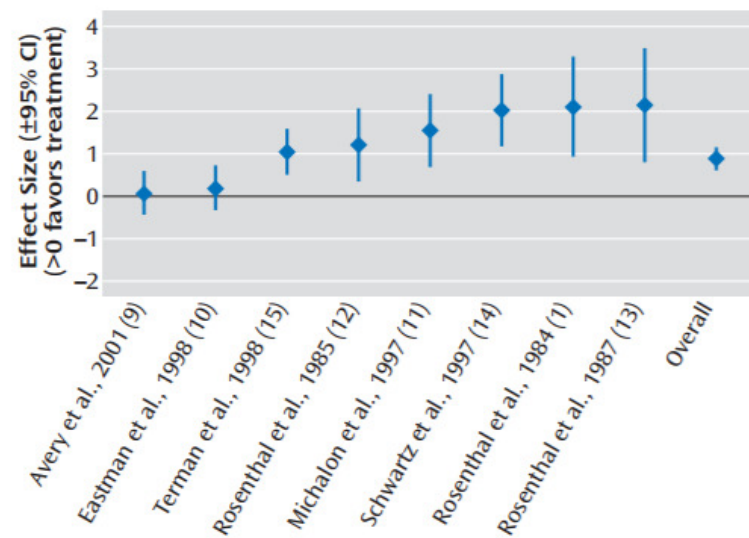


FIGURE 3. Effect Sizes in Studies of Treatment of Seasonal Affective Disorder With Dawn Simulation

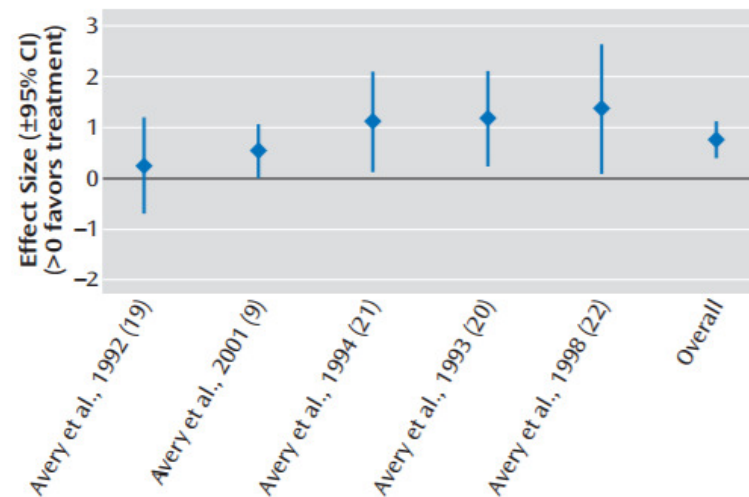


FIGURE 4. Effect Sizes in Studies of Treatment of Non-seasonal Depression With Bright Light

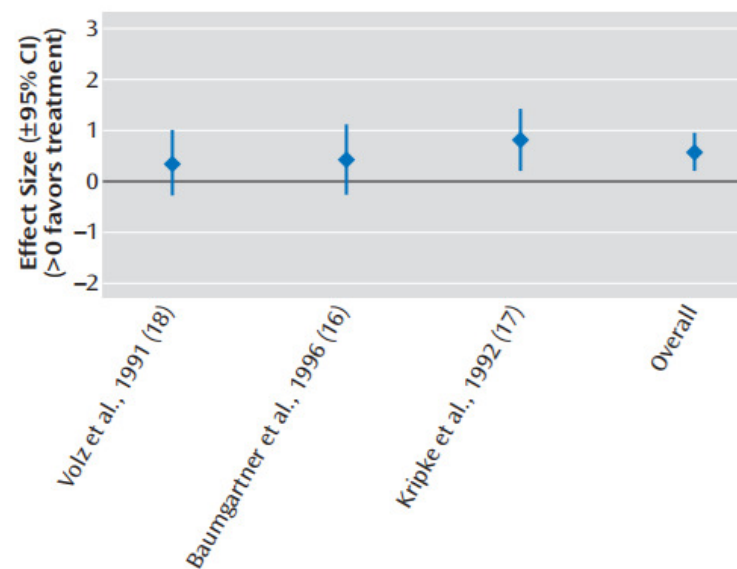
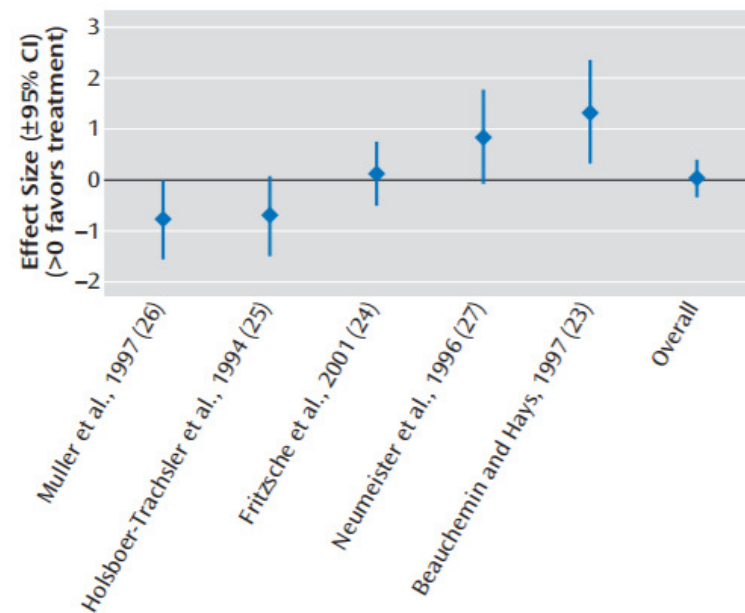


FIGURE 5. Effect Sizes in Studies of Treatment of Non-seasonal Depression With Bright Light as Adjunctive Treatment



Discutii

- Un numar mare de studii nu au indeplinit criteriile de selectie
- Crearea unui placebo corespunzator este dificila in acest tip de terapie
- Nu exista un interes al industriei farmaceutice in a oferi fonduri pentru studiile privind terapia pe baza de lumina
- Trebuie investigata eficacitatea terapiei pe baza de lumina si in grupurile <15 ani si >65 ani

- 1. Rosenthal NE, Sack DA, Gillin JC, Lewy AJ, Goodwin FK, Davenport Y, Mueller PS, Newsome DA, Wehr TA: Seasonal affective disorder: a description of the syndrome and preliminary findings with light therapy. *Arch Gen Psychiatry* 1984; 41:72–80
- 2. Terman M, Boulos Z, Campbell SS, Dijk D-J, Estman CI, Lewy AJ: Light treatment for sleep disorders: ASDA/SLTBR Joint Task Force Consensus Report. *J Biol Rhythms* 1995; 10:101–176
- 3. Parry BL, Mahan AM, Mostofi N, Klauber MR, Lew GS, Gillin JC: Light therapy of late luteal phase dysphoric disorder: an extended study. *Am J Psychiatry* 1993; 150:1417–1419
- 4. Wirz-Justice A: Beginning to see the light. *Arch Gen Psychiatry* 1998; 55:861–862
- 5. Spitzer RL, Endicott J, Robins E: Research Diagnostic Criteria: rationale and reliability. *Arch Gen Psychiatry* 1978; 35:773–782
- 6. Williams JBW, Link MJ, Rosenthal NE, Terman M: Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorders Version (SIGH-SAD). New York, New York State Psychiatric Institute, Biometrics Research, 1988
- 7. Lipsey MW, Wilson DB: Applied Social Research Methods: Practical Meta-Analysis, vol 49. London, Sage Publications, 2000
- 8. Hedges LV: Distribution theory for Glass's estimator of effect size and related estimators. *J Educational Statistics* 1981; 6: 107–128
- 9. Avery DH, Eder DN, Bolte MA, Hellekson CJ, Dunner DL, Vitiello MV, Prinz PN: Dawn simulation and bright light in the treatment of SAD: a controlled study. *Biol Psychiatry* 2001; 50:205–216
- 10. Eastman CI, Young MA, Fogg LF, Liu L, Meaden PM: Bright light treatment of winter depression: a placebo-controlled trial. *Arch Gen Psychiatry* 1998; 55:883–889
- 11. Michalon M, Eskes GA, Mate-Kole CC: Effects of light therapy on neuropsychological function and mood in seasonal affective disorder. *J Psychiatry Neurosci* 1997; 22:19–28
- 12. Rosenthal NE, Sack DA, Carpenter CJ, Parry BL, Mendelson WB, Wehr TA: Antidepressant effects of light in seasonal affective disorder. *Am J Psychiatry* 1985; 142:163–170
- 13. Rosenthal NE, Skwerer RG, Sack DA, Duncan CC, Jacobsen FM, Tamarkin L, Wehr TA: Biological effects of morning-plusevening bright light treatment of seasonal affective disorder. *Psychopharmacol Bull* 1987; 23:364–369
- 662 *Am J Psychiatry* 162:4, April 2005 LIGHT THERAPY <http://ajp.psychiatryonline.org>
- 14. Schwartz PJ, Murphy DL, Wehr TA, Garcia-Borreguero D, Oren DA, Moul DE, Ozaki N, Snelbaker AJ, Rosenthal NE: Effects of meta-chlorophenylpiperazine infusions in patients with seasonal affective disorder and healthy control subjects: diurnal responses and nocturnal regulatory mechanisms. *Arch Gen Psychiatry* 1997; 54:375–385
- 15. Terman M, Terman JS, Ross DC: A controlled trial of timed bright light and negative air ionization for treatment of winter depression. *Arch Gen Psychiatry* 1998; 55:875–882
- 16. Baumgartner A, Volz HP, Campos-Barros A, Stieglitz RD, Mansmann U, Mackert A: Serum concentrations of thyroid hormones in patients with nonseasonal affective disorders during treatment with bright and dim light. *Biol Psychiatry* 1996; 40: 899–907
- 17. Kripke DF, Mullaney DJ, Klauber MR, Risch SC, Gillin JC: Controlled trial of bright light for nonseasonal major depressive disorders. *Biol Psychiatry* 1992; 31:119–134
- 18. Volz HP, Mackert A, Stieglitz RD, Muller-Oerlinghausen B: Diurnal variations of mood and sleep disturbances during phototherapy in major depressive disorder. *Psychopathology* 1991; 24:238–246
- 19. Avery DH, Bolte MA, Cohen S, Millet MS: Gradual versus rapid dawn simulation treatment of winter depression. *J Clin Psychiatry* 1992; 53:359–363
- 20. Avery DH, Bolte MA, Dager SR, Wilson LG, Weyer M, Cox GB, Dunner DL: Dawn simulation treatment of winter depression: a controlled study. *Am J Psychiatry* 1993; 150:113–117
- 21. Avery DH, Bolte MA, Wolfson JK, Kazaras AL: Dawn simulation compared with a dim red signal in the treatment of winter depression. *Biol Psychiatry* 1994; 36:180–188
- 22. Avery DH, Bolte MA, Ries R: Dawn simulation treatment of abstinent alcoholics with winter depression. *J Clin Psychiatry* 1998; 59:36–42
- 23. Beauchemin KM, Hays P: Phototherapy is a useful adjunct in the treatment of depressed in-patients. *Acta Psychiatr Scand* 1997; 95:424–427

- 24. Fritzsche M, Heller R, Hill H, Kick H: Sleep deprivation as a predictor of response to light therapy in major depression. *J Affect Disord* 2001; 62:207–215
- 25. Holsboer-Trachsler E, Hemmeter U, Hatzinger M, Seifritz E, Gerhard U, Hobi V: Sleep deprivation and bright light as potential augmenters of antidepressant drug treatment—neurobiological and psychometric assessment of course. *J Psychiatr Res* 1994; 28:381–399
- 26. Muller MJ, Seifritz E, Hatzinger M, Hemmeter U, Holsboer-Trachsler E: Side effects of adjunct light therapy in patients with major depression. *Eur Arch Psychiatry Clin Neurosci* 1997; 247:252–258
- 27. Neumeister A, Goessler R, Lucht M, Kapitany T, Bamas C, Kasper S: Bright light therapy stabilizes the antidepressant effect of partial sleep deprivation. *Biol Psychiatry* 1996; 39:16–21
- 28. Mackert A, Volz HP, Stieglitz RD, Muller-Oerlinghausen B: Effect of bright white light on non-seasonal depressive disorder. *Pharmacopsychiatry* 1990; 23:151–154
- 29. Bech P, Cialdella P, Haugh MC, Hours A, Boissel JP, Birkett MA, Tollefson GD: Meta-analysis of randomised controlled trials of fluoxetine v placebo and tricyclic antidepressants in the short-term treatment of major depression. *Br J Psychiatry* 2000; 176: 421–428
- 30. Terman M, Terman JS, Quitkin FM, McGrath PJ, Stewart JM, Rafferty AB: Light therapy for seasonal affective disorder: a review of efficacy. *Neuropsychopharmacology* 1989; 2:1–22
- 31. Tam EM, Lam RW, Levitt AJ: Treatment of seasonal affective disorder: a review. *Can J Psychiatry* 1995; 40:457–466
- 32. Labbate LA, Lafer B, Thibault A, Sachs GS: Side effects induced by bright light treatment for seasonal affective disorder. *J Clin Psychiatry* 1994; 55:189–191
- 33. Terman M, Terman JS: Bright light therapy: side effects and benefits across the symptom spectrum. *J Clin Psychiatry* 1999; 60:799–808 \
- 34. Gallin PF, Terman M, Reme CE, Rafferty B, Terman JS, Burde RM: Ophthalmologic examination of patients with seasonal affective disorder, before and after bright light therapy. *Am J Ophthalmol* 1995; 119:202–210
- 35. Chan PK, Lam RW, Perry KF: Mania precipitated by light therapy for patients with SAD (letter). *J Clin Psychiatry* 1994; 55:454
- 36. Swedo SE, Allen AJ, Glod CA, Clark CH, Teicher MH, Richter D, Hoffman C, Hamburger SD, Dow S, Brown C, Rosenthal NE: A controlled trial of light therapy for the treatment of pediatric seasonal affective disorder. *J Am Acad Child Adolesc Psychiatry* 1997; 36:816–821
- 37. Sonis WA, Yellin AM, Garfinkel BD, Hoberman HH: The antidepressant effect of light in seasonal affective disorder of childhood and adolescence. *Psychopharmacol Bull* 1987; 23:360–363
- 38. Kobayashi R, Fukuda N, Kohsaka M, Sasamoto Y, Sakakibara S, Koyama E, Nakamura F, Koyama T: Effects of bright light at lunchtime on sleep of patients in a geriatric hospital, I. *Psychiatry Clin Neurosci* 2001; 55:287–289
- 39. Oren DA, Wisner KL, Spinelli M, Epperson CN, Peindl KS, Terman JS, Terman M: An open trial of morning light therapy for treatment of antepartum depression. *Am J Psychiatry* 2002; 159:666–669
- 40. Epperson CN, Terman M, Terman JS, Hanusa BH, Oren DA, Peindl KS, Wisner KL: Randomized clinical trial of bright light therapy for antepartum depression: preliminary findings. *J Clin Psychiatry* 2004; 65:421–425
- 41. Smith ML, Glass JV, Miller TI: *The Benefits of Psychotherapy*. Baltimore, Johns Hopkins University Press, 1980
- 42. Klein DF: Flawed meta-analyses comparing psychotherapy with pharmacotherapy. *Am J Psychiatry* 2000; 157:1204–1211