OCD IN OWLS AND LARKS: CIRCADIAN RHYTHMS, SLEEP, AND OCD SYMPTOMS DURING TREATMENT

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HARVARD MEDICAL SCHOOL







- ADVANCING THE SCIENCE + PRACTICE OF EXPOSURE THERAPY AND ITS BEHAVIORAL AND BIOLOGICAL COMPLEMENTS
- Increasing the effectiveness of treatment for Obsessive-compulsive disorder (OCD) and Related conditions
 - IOCDF YOUNG INVESTIGATOR AWARD



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Active Studies



Ecological Momentary Assessment

We are piloting the use of EMA methods in order to collect fine-grained data to better understand patients' inner experiences, predict behavior, and create more opportunities for clinical intervention.



Barriers to Exposure and Response Prevention

We are studying numerous putative factors that contribute to treatment refractorine ss using novel assessment instruments. Such factors include willingness, repetitive negative thinking, motivational factors, and issues around self-concept.



Computerized Cognitive Trainings

We are currently studying computerized cognitive tasks and their potential to retrain the brain's initial response to triggers (cognitive bias modification, CBM) from habits of avoidance and misappraisals to approach and healthier appraisals.



Genetics and OCD

We are examining the relationship between OCD and genetics to determine if there are factors that lead certain individuals to experience OCD.



Identity and OCD

Investigation of the relationship between marginalized identity status and symptoms/treatment response.



Sleep and OCD

Investigations of the relations between sleep, circadian rhythms, and OCD symptoms using ecological momentary assessment (EMA) and psychobiological methods.



Family
Accommodation in
OCD

Investigations of family accommodation using novel assessments with multiple reporters.

AGENDA

Sleep Behavior/Circadian Rhythms & Symptoms of OCD.

Sleep Behavior and Circadian Rhythms & Treatments for OCD

How Do Sleep/Circadian Rhythms Interact with Treatment?

How Can Treatment Integrate Sleep/Circadian Rhythms?

WHAT IS SLEEP?

Wakeful Brain Learning patterns

Obtaining food/water/reward

Respond to environment

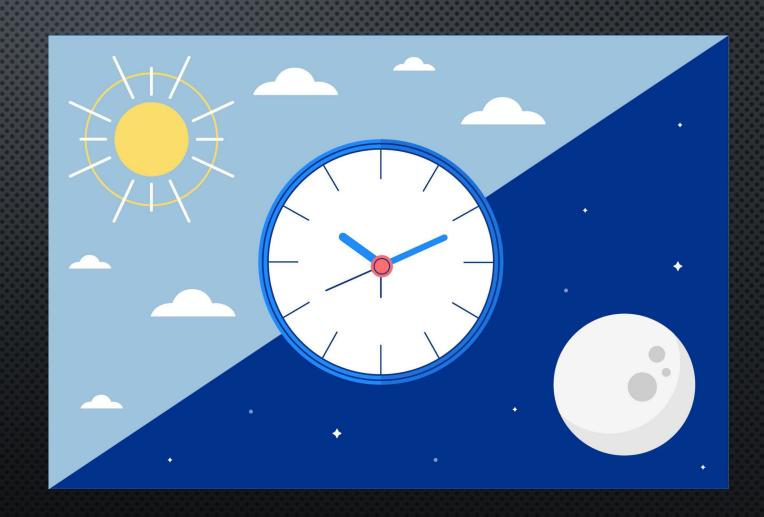
Sleeping Brain
"Solidify" learning

"Clean up" from neuron activity

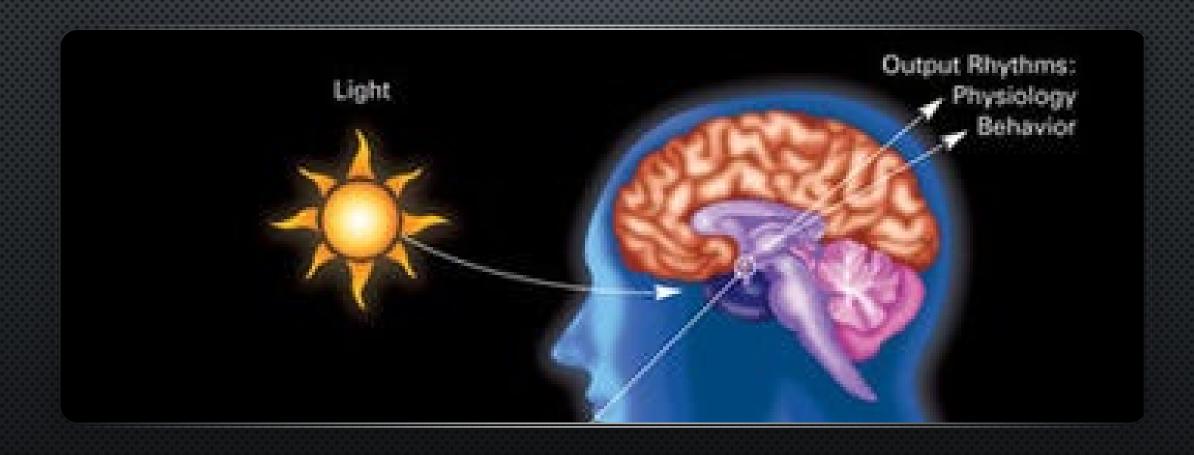
Non-responsive

WHAT ARE CIRCADIAN RHYTHMS?

CIRCA – DIAN
 (ABOUT) (A DAY)



WHAT ARE CIRCADIAN RHYTHMS?



WHICH MODE?

REGULATED BY TWO PROCESSES

- 1. HOMEOSTATIC DRIVE
- 2. CIRCADIAN DRIVE

MODULATED BY ANOTHER

1. AROUSAL



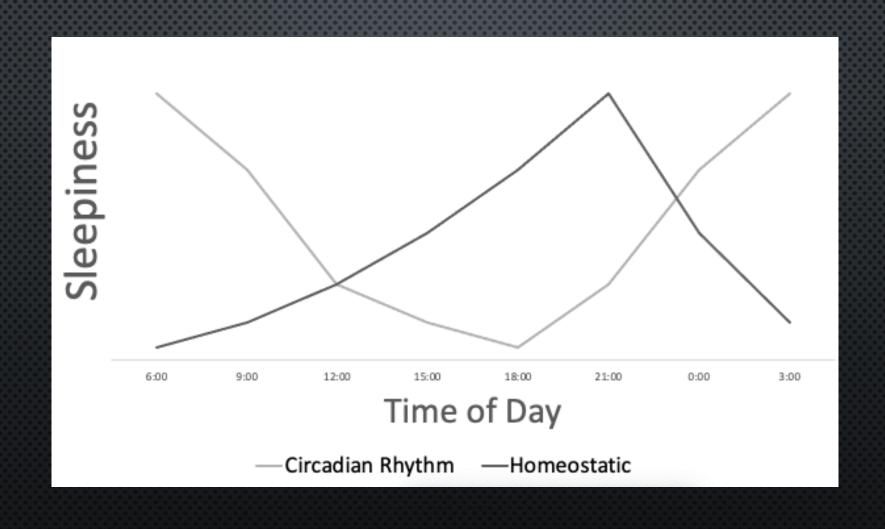
HOMEOSTATIC SLEEP DRIVE



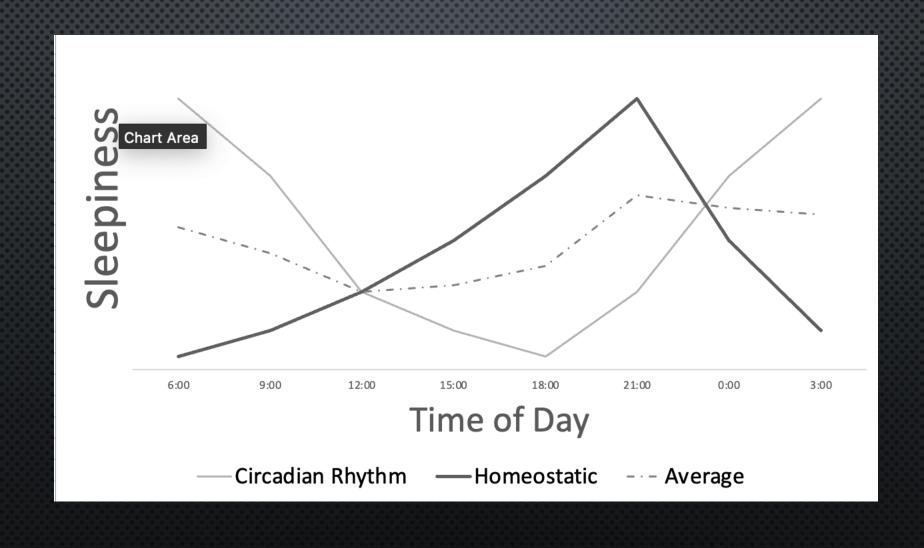
CIRCADIAN RHYTHMS



TWO-PROCESS MODEL OF SLEEP REGULATION



TWO-PROCESS MODEL OF SLEEP REGULATION

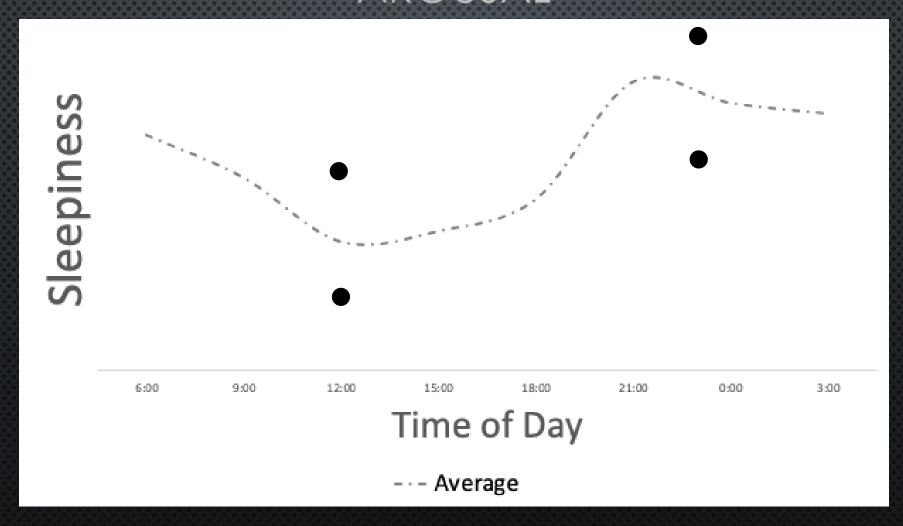


AROUSAL

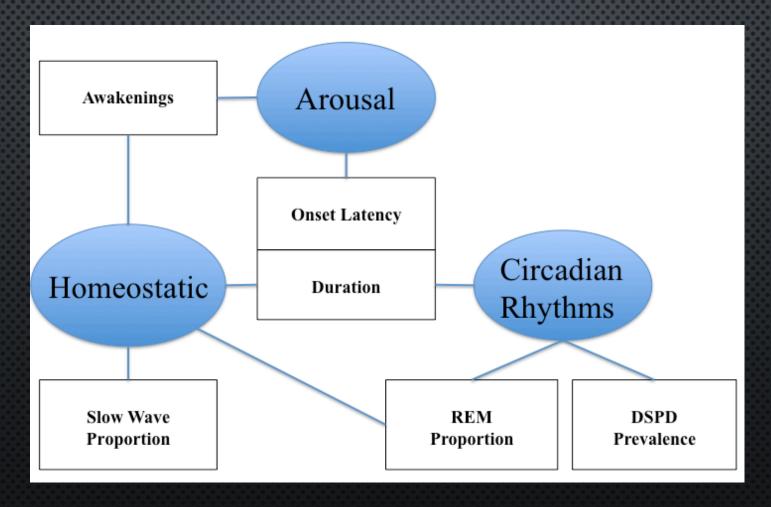
- AROUSAL IS A "CONTINUUM OF SENSITIVITY OF THE ORGANISM TO STIMULI, BOTH EXTERNAL AND INTERNAL."
 - FACILITATES INTERACTION WITH THE ENVIRONMENT IN A CONTEXT-SPECIFIC MANNER (E.G., UNDER CONDITIONS OF THREAT, SOME STIMULI MUST BE IGNORED WHILE SENSITIVITY TO AND RESPONSES TO OTHERS IS ENHANCED, AS EXEMPLIFIED IN THE STARTLE REFLEX),
 - Can be evoked by either external/environmental stimuli or internal stimuli (e.g., emotions and cognition)
 - THREATS
 - NTEREST

NIH RDoC, https://www.nimh.nih.gov/research-priorities/rdoc/constructs/arousal.shtml

AROUSAL



AROUSAL AND REGULATORY SYSTEMS



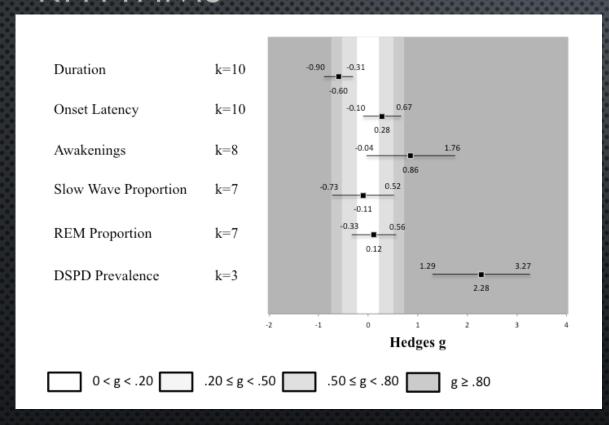
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Differences in sleep behavior and circadian rhythms are associated with symptoms of OCD.

OCD SYMPTOMS AND SLEEP/CIRCADIAN RHYTHMS

- SLEEP DISTURBANCE ASSOCIATED WITH OCD SYMPTOMS IN NCS-R, CONTROLLING FOR DEPRESSION (Cox & Olatunji, 2016)
- DELAYED BEDTIMES ASSOCIATED WITH INCREASED INTRUSIVE THOUGHTS IN NON-CLINICAL SAMPLE (SCHUBERT & COLES, 2015)
- Delayed bedtimes associated with OCD symptoms in undergraduates, controlling for negative affect (Coles, Schubert, & Sharkey, 2012)

OCD SYMPTOMS AND SLEEP/CIRCADIAN RHYTHMS



- More Reviews:
 - PATERSON ET AL., 2013
 - Cox, Jessup, & Olatunji, 2018
 - Cox & Olatunji, 2020

(Reproduced from Nota, Sharkey, & Coles, 2015)

OCD AND SLEEP/CIRCADIAN RHYTHMS

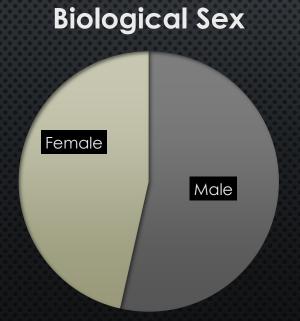
- WEAK CORRELATIONS BETWEEN INSOMNIA/HYPERSOMNIA + OCD SYMPTOMS IN A SAMPLE OF 773
 PATIENTS (LITVIN ET AL., 2022).
 - High-prevalence of delayed sleep phase in samples taken at inpatient units for OCD (18 - 42%; Mukhopadhyay et al., 2008; Turner et al., 2007)
- ADULTS WITH OCD DISPLAYED DELAYED CIRCADIAN RHYTHMS COMPARED TO HEALTHY CONTROLS, AND DELAYED CIRCADIAN RHYTHMS PREDICTED HIGHER OCD SYMPTOMS. 40% MET CRITERIA FOR DSWPD (Cox & Olatunji, 2022).
- 42% OF THOSE WITH OCD MET THE CRITERIA FOR DSWPD (COLES ET AL., 2020)

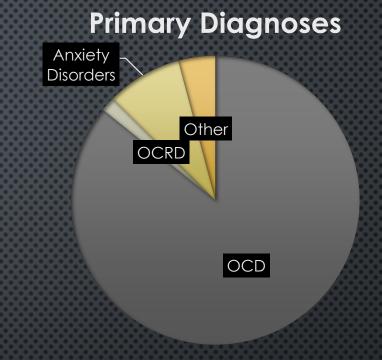
OCD AND SLEEP/CIRCADIAN RHYTHMS

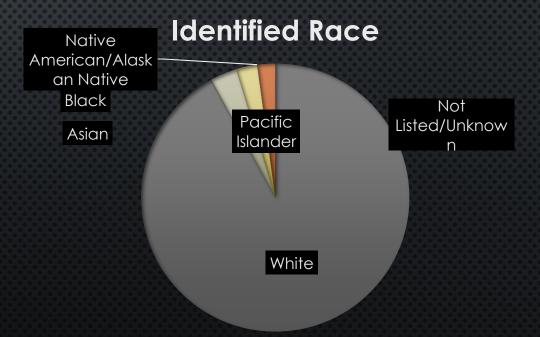
• LATER BEDTIMES PREDICTED INCREASES IN OCD SYMPTOMS IN THOSE WITH OCD, EVEN WHEN CONTROLLING FOR DEPRESSIVE SYMPTOMS (SCHUBERT ET AL., 2020).

OCDI SAMPLES

- 18 YEARS OR OLDER (M = 29.0 YEARS, SD = 11.1 YEARS)
 - DATA COLLECTED DURING THE FIRST 8 WEEKS WERE INCLUDED IN THESE ANALYSES.
 - Data collected each Friday afternoon, Questions are about preceding week





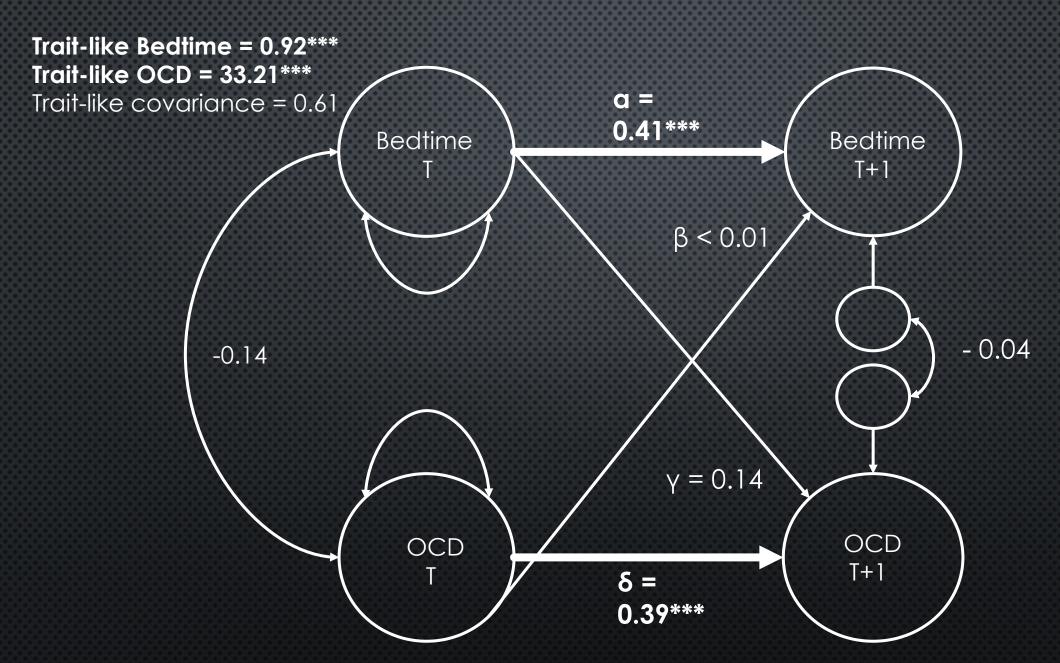


Admission YBOCS-SR Total 26.9 DSP NDSP

$$t(139) = -2.46, p = .02$$

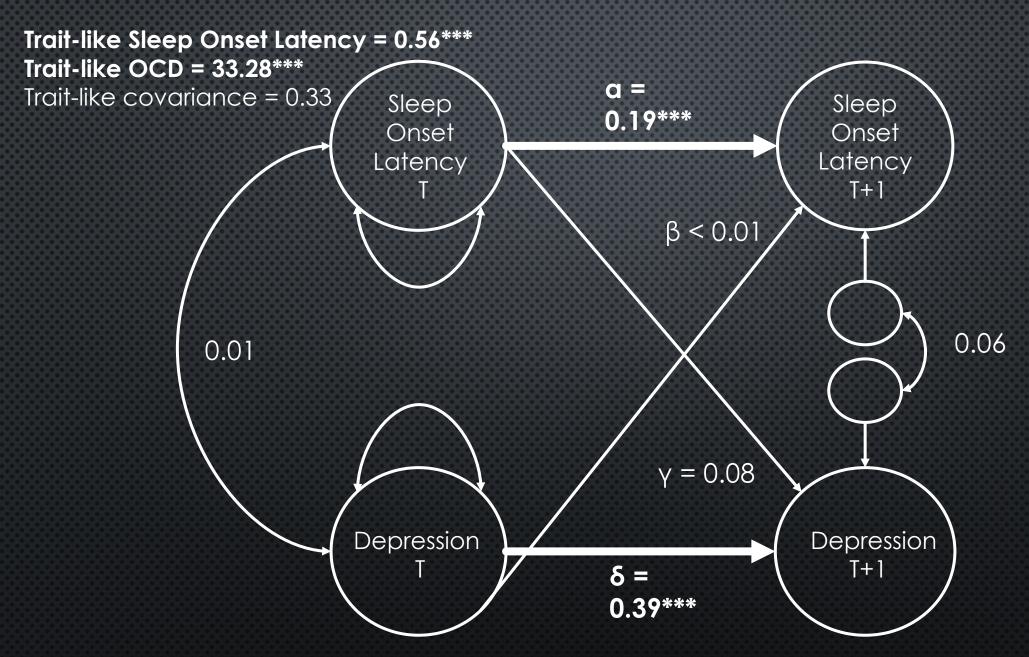
Admission YBOCS-SR Total 24.6 No Insomnia Insomnia

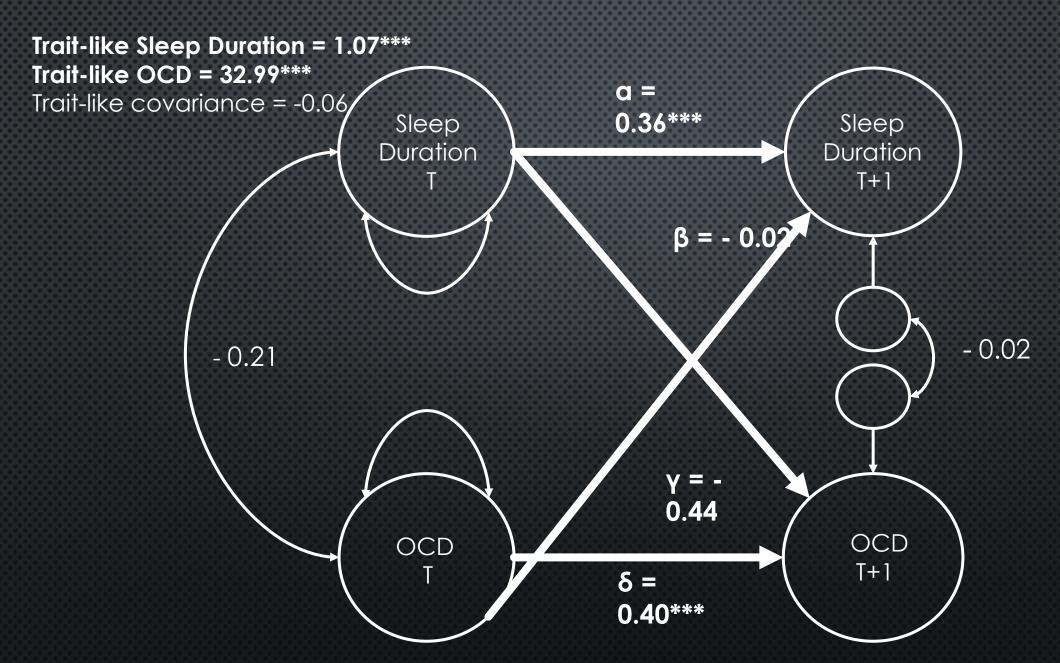
$$t(139) = 0.50, p = .62$$



* p < .05, ** p < .01, *** p < .001

(Nota, in preparation)





* p < .05, ** p < .01, *** p < .001

(Nota, in preparation)

Differences in sleep behavior and circadian rhythms are associated with response to existing treatments for OCD.

OCD AND SLEEP/CIRCADIAN RHYTHMS IN TREATMENT

- SLEEP DISTURBANCE (INSOMNIA) IMPROVED IN **4-DAY INTENSIVE ERP TREATMENT FOR OCD**; PRETREATMENT SLEEP DISTURBANCE ASSOCIATED WITH GREATER REDUCTION IN OCD SYMPTOMS AT DISCHARGE (NORDAHL ET AL., 2018)
- 4-DAY INTENSIVE ERP TREATMENT FOR OCD IS EFFECTIVE IRRESPECTIVE OF COMORBID INSOMNIA, INSOMNIA PROBLEMS ARE MODERATELY REDUCED FOLLOWING TREATMENT (HAGEN ET AL., 2021)
- PATIENTS WHO REPORTED BEDTIMES LATER THAN 1AM EXHIBITED LESS SYMPTOM REDUCTION AND WERE SIGNIFICANTLY MORE LIKELY BE "NON-RESPONDERS" TO ERP COMPARED TO THOSE WITH EARLIER BEDTIMES (COLES ET Al., 2021).
- OBJECTIVE AND SUBJECTIVE MEASURES OF DELAYED SLEEP TIMING PREDICT NON-RESPONSE TO RTMS
 <u>TREATMENT</u> FOR OCD (Donse et al., 2017)

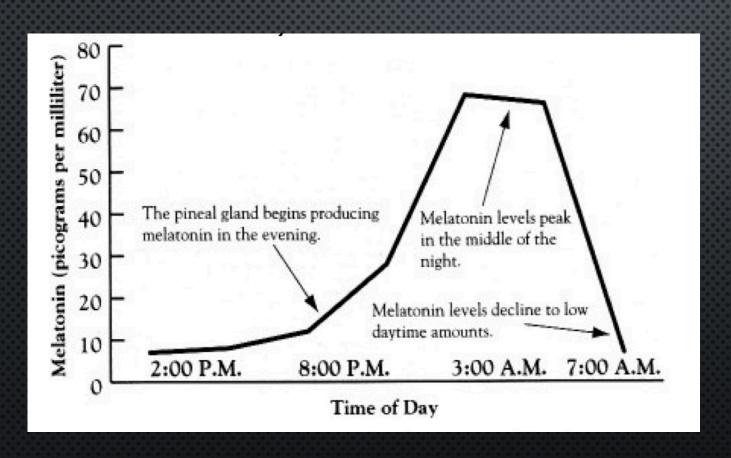
	DSP	NDSP
Discharge YBOCS <u>></u> 16	N = 13	N = 36
Discharge YBOCS <16	N = 10	N = 61

	Insomnia	No Insomnia
Discharge YBOCS <u>></u> 16	N = 8	N = 41
Discharge YBOCS <16	N = 14	N = 57

$$X^2(1) = 2.9, p = .09$$

$$X^{2}(1) = 0.2, p = .64$$

DIM LIGHT MELATONIN ONSET (DLMO)



OCD AND BIOLOGICAL CIRCADIAN RHYTHMS

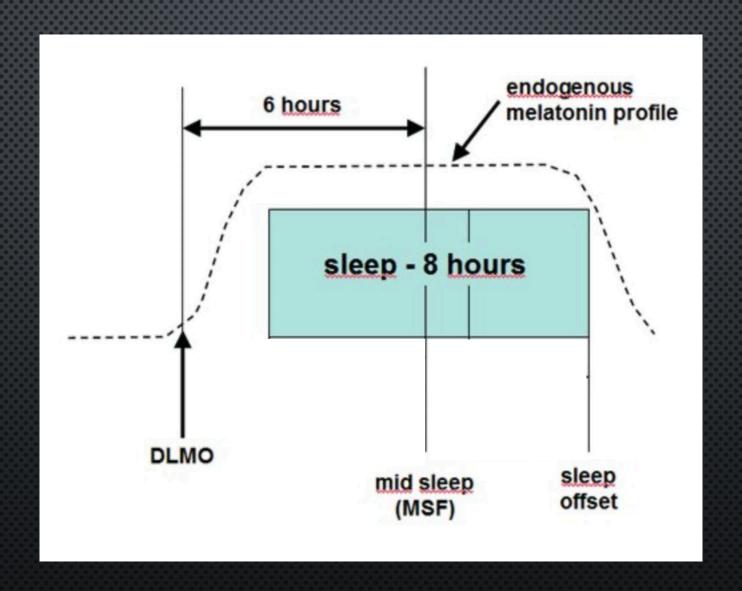
- INDIVIDUALS WITH OCD DEMONSTRATED DLMO 1.5 HRS LATER THAN HEALTHY CONTROLS.
 - NO SIGNIFICANT CORRELATION BETWEEN DLMO/LATER BEDTIME + OCD SYMPTOMS (COLES ET Al., 2020).

DLMO STUDY

TIME	AVERAGE DLMO
Admission	10:38PM
Week 2	9:45PM
Week 4	10:06 PM
Discharge	9:25PM

DLMO STUDY

TIME	AVERAGE SLEEP DURATION	AVERAGE BEDTIME
Admission	7 hours + 17 minutes	11:58PM
Week 2	7 hours + 22 minutes	11:05PM
Week 4	7 hours + 36 minutes	10:46PM



DLMO AND SLEEP MIDPOINT

Participant #1

Participant #2

Participant #3

Participant #4



Long length = good alignment between circadian rhythm & sleep-wake schedule

Short length = poor alignment

Time of night

DLMO AND SLEEP MIDPOINT

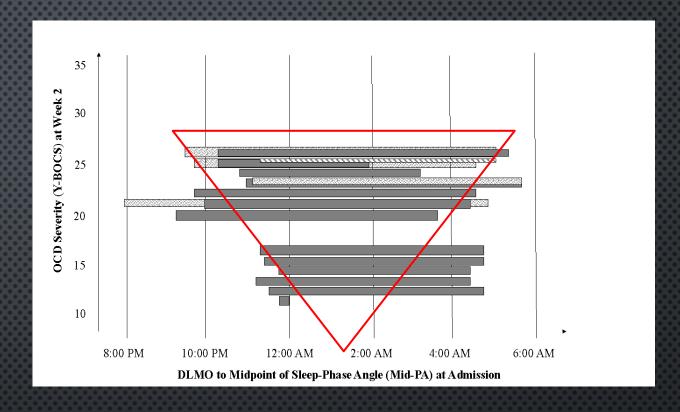


Figure 1. Relation between dim light melatonin onset (DLMO) to midpoint of sleep-phase angle (Mid-PA) at admission and OCD symptom severity at the 2nd week of treatment. Cases were plotted in order of OCD symptom severity.

DLMO AND SLEEP MIDPOINT

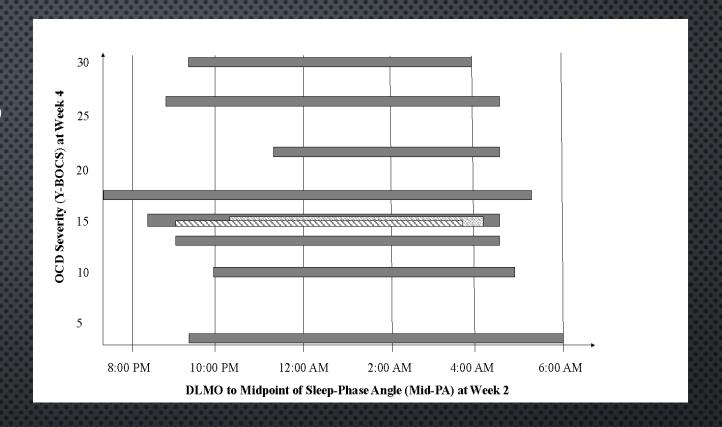


FIGURE 2. RELATION BETWEEN DIM LIGHT MELATONIN ONSET (DLMO) TO MIDPOINT OF SLEEP-PHASE ANGLE (MID-PA) AT 2ND WEEK OF TREATMENT AND OCD SYMPTOM SEVERITY AT THE 4TH WEEK OF TREATMENT. CASES WERE PLOTTED IN ORDER OF OCD SYMPTOM SEVERITY.

CURRENT IMPLICATIONS



Relation between sleep timing and OCD symptoms (including change) is present but without clear mechanism



Without understanding the mechanism(s) of the relation, we cannot be reliable in predictions.

- Theoretical importance of sleep and circadian rhythms' relations with OCD for understanding psychopathology is not yet clear
- Evidence-based treatment recommendations are not yet clear

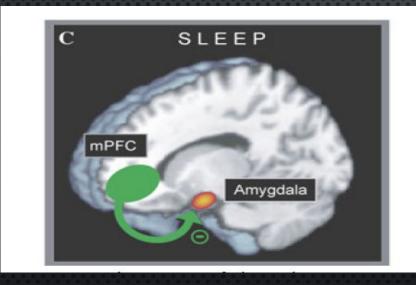
How do sleep and circadian rhythms interact with treatment?

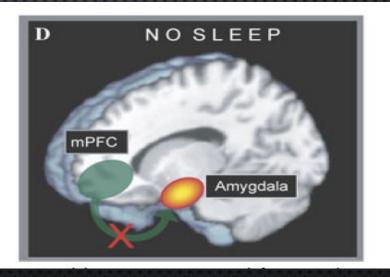
HOW WOULD SLEEP INTERACT WITH TREATMENT

- SHIFTING BEDTIMES EARLIER REDUCED OCD SYMPTOMS IN INDIVIDUALS WHO HAD NOT INITIALLY BENEFITED FROM ERP TREATMENT (COLES & SHARKEY, 2011)
- A CONSISTENT SCHEDULE AND LIGHTS OUT FOR PATIENTS MAY BE BENEFICIAL IN OCD TREATMENT.
 PROGRAMS WITH SCHEDULE CONSISTENCY WERE MORE LIKELY TO HAVE A SIGNIFICANT TREATMENT
 RESPONSE; 78% OF PROGRAMS WITH LIGHTS OUT SHOWED A TREATMENT RESPONSE (COLES & STEWART, 2019).

MECHANISMS\$

- POOR OR INSUFFICIENT SLEEP MAY IMPAIR INHIBITORY CONTROL, WHICH MAY THEN DIMINISH
 THE ABILITY TO INHIBIT INTRUSIVE THOUGHTS AND/OR REPETITIVE BEHAVIORS. (COX, PARMAR,
 & OLATUNJI, 2020)
- THOSE WITH ELEVATED OCD SYMPTOMS AND SHORT SLEEP DURATION EXHIBITED **DECREASED INHIBITORY CONTROL** (NOTA, SCHUBERT, COLES, 2016).
- STUDY SHOWED THAT THE PROSPECTIVE LINK BETWEEN INSOMNIA SYMPTOMS AND OBSESSIONS OVER SIX MONTHS WAS MEDIATED BY FOCUSING <u>ATTENTIONAL CONTROL</u> (COX, COLE, KRAMER, OLATUNJI, 2018).



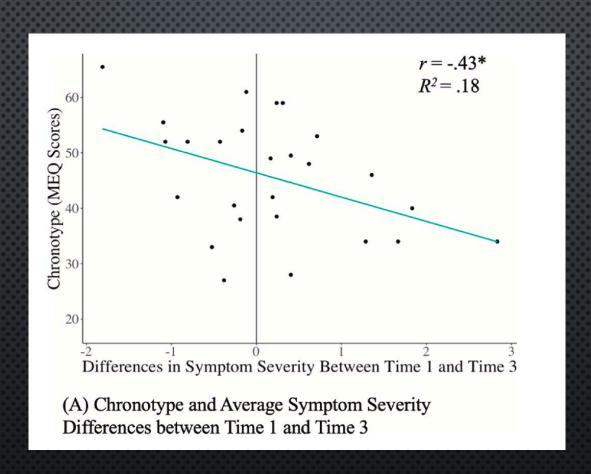


(Reproduced from Yoo et al., 2007)

CURRENT QUESTIONS

- MECHANISMS
 - PSYCHOLOGICAL DISTRESS? (BRIERLEY ET Al., 2021)
 - EMOTION DYSREGULATION? (COX, JESSUP, & OLATUNJI, 2019)
 - CHRONOTYPE AND/OR PHASE-RELATIONSHIP WITH ENVIRONMENT (SCHUBERT ET AL., 2019;
 NAFTALOVICH ET AL., 2021)?
 - ALERTNESS? (KALANTHROFF ET AL., 2017; NAFTALOVICH, TAUBER, & KALANTHROFF, 2020)
- DSPD and OCD INDICATIVE OF VARIANT OF OCD WITH POTENTIALLY DIFFERENT ENDOPHENOTYPE? (Donse et al., 2017)

Interaction between Environment and Person



How can treatment integrate sleep and circadian rhythms?

COGNITIVE-BEHAVIORAL TREATMENT

• PRINCIPLES FROM CBT FOR INSOMNIA CAN BE APPLIED ADJUNCTIVELY AND IN AN INTEGRATED FASHION WITH ERP

1. What time did you get into bed?	Sample 4/5/11 10:15 p.m		Consensus Sleep Diary-Core	ep Diary-Core	ID/Name:		
2. What time did you try to go to sleep? 3. How long did it take you to fall astern?	11:30 p.m 55 min.						
3. How long did it take you to fall askeep? 4. How many times did you wake up, not counting your final awakening?	55 min.						
5. In total, how long did these awakerings last?	1 hour 10 min.						
6. What time was your final awakening?	6:35 a.m.						
7. What time did you get out of bed for the day?	7:20 a.m						
8. How would you rate the quality of your steep?	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	Very poor Poor Fair Sood Very good	Verypoor Poor Fair Good Verygood	Very poor Poor Fair Good Very good	Very poor Poor Fair Good Very good	Very poor Poor Fair Good Very good	Uvery poor Poor Fair Good Very good
9. Commerts (if applicable)	I have a cold						

=	9. Comments (If applicable)		•	rate the quality of your steep?	8. HO#	7. Whattime did you get out of bed for the day?	6. What time was your fina awakening?	5. In total, how long did these awakenings last?	4. How many times did you wake up not counting your awakening?	3. How org did it take you to fall askeep?	2. Whattime did youtry to go to steep?	1. What me did you get into bed?	鼍	
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		Very good		Poor	□ Very poor									IL/INAITRE
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STRUCTURE

- EMPLOYMENT DEMANDS
- SOCIAL DEMANDS
- GEOGRAPHY

Structure, Culture, Identities

Arousal and Regulatory Systems

CULTURE

- BELIEFS ABOUT SLEEP'S RELATIVE IMPORTANCE
- NORMS OF THOSE AROUND YOU AND HOW THEY SLEEP
- VALUES INFORM WHAT WILL GRAB AND HOLD OUR ATTENTION

Structure, Culture, Identities

Arousal and Regulatory Systems

IDENTITIES

- AGE (AND GENERATION)
- <u>D</u>ISABILITY STATUS (PHYSICAL)
- **D**IAGNOSIS STATUS (PSYCHOLOGICAL)
- **R**ELIGION (AND SPIRITUALITY)
- <u>E</u>THNICITY (AND RACE)
- **S**EXUALITY
- **S**OCIOECONOMIC STATUS
- IMMIGRATION STATUS (AND INDIGENOUS HERITAGE)
- **N**ATIONALITY (AND CITIZENSHIP)
- **G**ENDER

Structure, Culture, Identities

Arousal and Regulatory Systems

IDENTITIES

- DIAGNOSIS STATUS
 - Depression
 - WORRY
 - OCD SYMPTOM CONTENT
- IDENTITIES INFORM WHAT WILL GRAB AND HOLD OUR ATTENTION

Structure, Culture, Identities

Arousal and Regulatory Systems

- PHENOMENOLOGY
 - AFTERNOON/EVENING OBSESSIONS
 - EVENING/LATE NIGHT DIFFICULTY INHIBITING COMPULSIONS
 - INCREASED AROUSAL AT NIGHT
 - RITUALS DELAYING BEDTIME
 - OBSESSIONS (OR AVOIDANCE OF THEM) DELAYING SLEEP ONSET

- TREATMENT PLANNING
 - Considering motivation
 - RESOURCE-FOCUSED MODELING OF TREATMENT PLAN
 - TEMPORAL PRECEDENCE IS NOT USUALLY USEFUL, MUTUALLY MAINTAINING

- EXPECTATIONS AND EVALUATION OF PROGRESS
 - CAN BE VERY DIFFICULT TO GAIN TRACTION AT FIRST
 - EXPECT TO ITERATE ON TREATMENT PLAN AS A RULE

CBTi Interventions

Sleep Behavior	First Target	Second Target	Third Target	Fourth Target
Sleep Onset Latency	Sleep Hygiene	Sleep Restriction/Stimulus Control	Sleep Cognitions	Regularizing Circadian Rhythms
Wake Time	Sleep Hygiene	Regularizing Circadian Rhythms	Sleep Restriction/Stimulus Control	Sleep Cognitions

Note: CBTi = cognitive behavioral therapy for insomnia (Edinger & Carney, 2014). This table outlines a potential pattern of relative associations for the purpose of initiating individualized model evaluation. Consider all options!

SLEEP HYGIENE

- AVOID:
 - CAFFEINE THROUGHOUT THE DAY. LATER IN THE AFTERNOON PARTICULARLY.
 - GOING TO BED HUNGRY
 - EXCESSIVE LIQUIDS IN THE EVENING
 - EXCESSIVE ALCOHOL USE IN THE EVENING.
 - This can put you to sleep but interferes with processes that should happen during sleep for you to feel rested and alert the next day.
 - TOBACCO BEFORE BED OR DURING THE NIGHT
 - NICOTINE IS A STIMULANT DRUG

SLEEP HYGIENE

MAKE BEDROOM:

- QUIET
- DARK
- COMFORTABLE
- MODERATE TEMPERATURE

Other things that affect sleep (Other approaches and special considerations should be made if you have/take these):

Allergies, bronchitis, asthma

Medications

Sleep apnea, parasomnias, seizure disorders

Bipolar depression, panic disorder

Shift work

SLEEP HYGIENE

• STRESS:

- ACTIVATED STRESS SYSTEMS WORK IN OPPOSITION TO CIRCADIAN RHYTHMS AND HOMEOSTATIC SLEEP DRIVE TO KEEP ONE AWAKE.
- CAN'T "TRY TO RELAX." JUST PRACTICE EXERCISE AND LET RELAXATION DO WHAT IT WILL AT ITS
 OWN PACE
 - PROGRESSIVE MUSCLE RELAXATION
 - DIAPHRAGMATIC BREATHING
 - MINDFULNESS EXERCISES
- PRACTICE RELAXATION AT REGULAR TIME OF DAY, IN BEDROOM IF POSSIBLE

REGULARIZE CIRCADIAN RHYTHMS

- Make a point of having a regular wake-up time
 - EVERY DAY
- CHRONOTHERAPY: CONTROLLED EXPOSURE TO ENVIRONMENTAL STIMULI (E.G., LIGHT, MELATONIN) THAT ACT ON BIOLOGICAL RHYTHMS
- LIGHT THERAPY CAN BE USED TO SYNCHRONIZE OR PHASE SHIFT RHYTHMS
 - Internal synchronization: Timing between core body rhythms (e.g., cortisol, temp) and sleep
 - EXTERNAL SYNCHRONIZATION: TIMING OF THESE RHYTHMS TO THE DAY-NIGHT CYCLE



- EXPECTATIONS AND EVALUATION OF PROGRESS
 - CIRCADIAN RHYTHM INTERVENTIONS
 - ONE WEEK PER HOUR OF SHIFT
 - STIMULUS CONTROL, SLEEP COGNITIONS
 - Two weeks
 - SLEEP RESTRICTION
 - ONE WEEK PER 15 MINUTE CHANGE

SLEEP COGNITIONS



Sleep

- 1. Leave the room temporarily when your mind is active. You can return to the BEDROOM WHEN YOUR THOUGHTS HAVE BECOME MORE MANAGEABLE AND YOU ARE NO LONGER WORRYING.
- 2. Use Constructive Worry if your worries continue to follow you to bed. This will mean setting aside time to do this in the Early Evening.
- 3. Use Thought Records when you are having persistent feelings or thoughts about your sleep problem.

STIMULUS CONTROL

- BED IS ONLY FOR SLEEP
 - NOT TV, READING, TALKING, WORRYING, ARGUING, EATING...
- ESTABLISH REGULAR PRE-SLEEP SIGNALS THAT YOUR BODY CAN ASSOCIATE WITH BEDTIME*
- If you cannot fall asleep within 20 minutes of Getting into BED, Get up and go into another space
 - ENGAGE IN QUIET/BORING/LOW-KEY ACTIVITY UNTIL YOU FEEL DROWSY
- RETURN TO BED AND TRY TO FALL ASLEEP
 - IF NOT SUCCESSFUL, REPEAT PREVIOUS STEP

*If you notice your pre-sleep routine becoming compulsive, mix it up and/or seek consultation

SLEEP RESTRICTION

- SLEEP EFFICIENCY = (TOTAL SLEEP TIME/ TIME IN BED) X 100
 - Want this to be $\geq 85\%$
- Use this metric to limit your time in bed
 - SPECIFICALLY TO SCHEDULE GETTING INTO BED (USUALLY LATER THAN ONE HAS BEEN)
 - AVOID NAPS AND MAINTAIN REGULARIZED WAKE-UP TIME

PSYCHOPHARMACOLOGICAL AND BIOLOGICAL TREATMENTS

- Considerations with antidepressants:
 - SSRIS HAVE BEEN ASSOCIATED WITH DISRUPTIONS IN CIRCADIAN RHYTHMS AND SLEEP (CARDINALI ET AL., 2011; Mayers & Baldwin, 2005).
 - BE COGNIZANT OF THE TIME OF DAY FOR MEDICATIONS.
 - PATIENTS WITH OCD CAN EXHIBIT A HIGHER FREQUENCY OF THE EVENING CHRONOTYPE (KANI ET AL., 2018). INDIVIDUALS WITH AN EVENING CHRONOTYPE MAY EXPERIENCE LESS EFFECTIVENESS FROM SSRIS (McGlashan et al., 2018).

PSYCHOPHARMACOLOGICAL AND BIOLOGICAL TREATMENTS

- RECENT FINDINGS SUGGEST THAT MELATONIN CAN PLAY A UNIQUE, NEUROPROTECTIVE ROLE FOR A VARIETY OF NEUROPSYCHIATRIC DISORDERS, INCLUDING OCD (MAHMOOD ET AL., 2016).
 - MELATONIN SYNTHESIS MAY BE DISTURBED IN THOSE WITH OCD. SOME EXHIBIT REDUCED 24 HOUR-SECRETION OF MELATONIN COMPARED TO HEALTHY CONTROLS WITH A CORRELATION BETWEEN MELATONIN AND OCD SYMPTOM SEVERITY (LANGE ET AL., 2012; MAHMOOD ET AL., 2016)
 - EXOGENOUS MELATONIN COULD BE BENEFICIAL FOR PATIENTS WITH OCD, ESPECIALLY IF THEY STRUGGLE WITH SLEEP DISORDERS (MAHMOOD ET AL., 2016; PATERSON ET AL., 2013).

SOURCES OF ADDITIONAL INFORMATION ABOUT SLEEP AND MENTAL HEALTH

- Principles and Practice of Sleep Medicine (2011) by M. Kryger, T. Roth & W. Dement
- Wulff, K., Gatti, S. Wettstein, J.G., & Foster, R.G. (2010). Sleep and circadian rhythm disruption in psychiatric and neurodegenerative disease. Nature Reviews Neuroscience.
- Special issue of Clinical Psych Review on *Insomnia and Behavioral Sleep Medicine*. Volume 25, Issue 5, Pages 535-706 (July 2005): Edited by R. Manber and A. Harvey
- AMERICAN ACADEMY OF SLEEP MEDICINE (http://www.aasmnet.org/)
- SOCIETY FOR LIGHT TREATMENT AND BIOLOGICAL RHYTHMS (HTTP://WWW.SLTBR.ORG/)
- CENTER FOR ENVIRONMENTAL THERAPEUTICS (HTTP://WWW.CET.ORG/)

QUESTIONS?

- 1. RESEARCH AND METHODOLOGY
- 2. CLINICAL APPLICATIONS

THANK YOU!

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