Prevalence of Sleep Disorders in Treatment-resistant Depression

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Aknowledgments

Thanks to Megan Glen-Lewis and dr. Leif Brauteseth

Actual Title….

Is a sleep disorder responsible for MDD patients not responding to standard antidepressant treatment algorithms?

Background

Megan’s B.Tech thesis and project:

Prevalence of OSA in Treatment Resistant Depression

State hospital patients

Dr. Leif supplied everything

Background

Open label study

Patients presenting at Rob Ferreira Hospital, Nelspruit, Psychiatric OPD

Patients identified on clinical history, validated by dr Leif Brauteseth

Inclusion Criteria

Any MDD patient who had not responded to standard antidepressant treatment

Clinical history of snoring

Complaining of specific sleep disorder symptoms

Positive responses to 5 standardized sleep screening questionnaires

Included even with:

- Psychiatric co-morbidity
- Hypertension
- Type II DM

Exclusion Criteria

Newly diagnosed

Abnormal organic work-up

HIV

Medically ill

Other obvious uncorrected abnormalities

Study Population

- All patients were screened by medical officers in OPD, then referred to psychiatrist
- All subjects were clinically depressed, according to DSM IV criteria, as evaluated by psychiatrist

Total study cohort: n=30

- Male: n=12
- Female: n=18

Investigations

Full Clinical History

Detailed Psychiatric Evaluation

Detailed Sleep History

5 Standardized Sleep Screening Questionnaires

(Leeds Sleep Evaluation, StopBang, ISI, RLS, ESS)

HADS (Hospital Anxiety and Depression Scale)

$QIDS_{(SR)}$ (Quick Inventory of Depressive Symptoms)

Polysomnogram

CPAP Titration if needed

Results - Subjective

QIDS$_{(SR)}$ Questionnaire n=30:

ALL study cohorts were clinically evaluated as “clinically depressed”

6.6% - No Depression = 2
67% - Mild Depression = 20
6.6% - Moderate Depression = 2
12% - Severe Depression= 4
6.6% - Very Severe Depression = 2

74% reported either “no” or “mild” depression

Results - Subjective

HADS Questionnaire n=30

- **Depression**
- 16% - Non Case = 5
- 17% - Borderline Case = 5
- 67% - Case = 20
- **84% reported significant symptoms of Depression**

- **Anxiety**
- 33% - Non Case = 10
- 17% - Borderline Case = 5
- 50% - Case = 15
- **67% reported significant symptoms of Anxiety**

Results - Subjective

HADS Questionnaire n=30

- **Depression**
- **84% reported significant symptoms of Depression**
- 16% had “no insight” into their depressive symptomatology
- **Anxiety**
- **67% reported significant symptoms of Anxiety**
- 33% had “no insight” into their anxiety symptomatology

Subjective Impressions

$QIDS_{(SR)}$ & HADS Questionnaires

- **ALL study cohorts were clinically evaluated as “clinically depressed”**

HADS

- **16% had “no insight” into their depressive symptomatology**
- **33% had “no insight” into their anxiety symptomatology**

$QIDS_{(SR)}$

- **74% had little insight into the SEVERITY of their Depression**

HADS vs QIDS$_{(SR)}$

Both Scales measure different aspects of MDD - can't compare directly

Patients possibly just do not make any association between sleep problems and daytime symptoms

Patients obviously don’t understand that ALL Sleep Problems constitute a “24 Hour Issue”

Results - AHI Ranges

– AHI 0 to 5	13%	n=4
– AHI 6 to 9	17%	n=5
– AHI 10 to 14	3%	n=1
– AHI 15 to 29	37%	n=11
– AHI 30 or more	30%	n=9

- **83% had an AHI 8 or more (n=25)**
- **70% had an AHI 10 or more (n=21)**
- **67% had an AHI 15 or more (n=20)**

NB: RERAs and associated arousals were not included here

Results - LSEQ

- Leeds Sleep Evaluation Questionnaire
- For the first set of questions please make a mark anywhere on the line which shows how you feel like this:

- More difficult than usual _____|_____ Easier than usual

How would you describe the way you currently fall asleep in comparison to usual?

- More difficult than usual _____ Easier than usual

- 87% subjective scores of less than 50% (n=26)

Results - ESS

- Epworth Sleepiness Scale
  - Score ≥ 10 is pathological

- 53% (n=16) had an ESS Score of ≥ 10

Results - RLS

No RLS Symptoms	n=9
Some RLS Symptoms	n=21
All 4 Diagnostic RLS Symptoms	n=14

47% of cohort met All 4 Diagnostic RLS Symptoms

Among RLS Symptoms (n=21); 67% Firm Dx RLS

Results - BMI Ranges

- **80% (n=24)** **BMI>25**
- BMI Range **21.6 - 42.2**
- Ave BMI **29,93**

STOP-BANG Sleep Apnea Questionnaire

(Chung F et al Anesthesiology 2008 and BJA 2012)

STOP:

Do you SNORE loudly (louder than talking or loud enough to be heard through closed doors)?	Yes	No
Do you often feel TIRED, fatigued, or sleepy during daytime?	Yes	No
Has anyone OBSERVED you stop breathing during your sleep?	Yes	No
Do you have or are you being treated for high blood PRESSURE?	Yes	No

BANG:

BMI more than 35 kg/m2?	Yes	No
AGE over 50 years old?	Yes	No
NECK circumference > 16 inches (40cm)?	Yes	No
GENDER: Male?	Yes	No

TOTAL SCORE:

High risk of OSA:	Yes 5 - 8
Intermediate risk of OSA:	Yes 3 - 4
Low risk of OSA:	Yes 0 - 2

Results - Stop Bang

- ***Stop Bang Score***
- ***"1"*** ***n*** **= 0**
- ***"2"*** n = **5**
- ***"3"*** n = **8**
- ***"4"*** n = **6**
- ***"5"*** n = **7**
- ***"6"*** n = **4**
- **"7"** n = **0**
- ***"8"*** n = **0**
- 70% of responses were in the “3 to 5” Range

Results - Stop Bang

- BANG portion of the test ??
  - Only 3 of the 4 criteria assessed
    - Omitted to measure Neck Circumference
  - Only 20% were on BP Medications
  - Only 20% had BMI > 35
  - Only 40% were MALE

Study Conclusion

- ~50% had ESS scores > 10
- ~80% - Sleep Disordered Breathing with AHI's above 10 (~70% AHI's > 15)
- ~50% - Restless Legs Syndrome
- Average BMI ± 30
- STOP = 4, All AHI's > 19 (Ave AHI = 25)

Study Conclusion

A high incidence (70-80 %) of this small group of patients has clinically significant OSA, most likely contributing to them not responding to antidepressant drug treatment...

Sleep and Depression

The link between sleep disturbance and major depression is so firm that some researchers have suggested that a diagnosis of depression in the absence of sleep complaints should be made with caution.

Sleep and Depression

Insomnia is common - may be presenting complaint

Sleep architecture is abnormal

Sleep manipulation alters mood

Sleep disturbance may predict treatment outcome

Antidepressants may change sleep architecture

Sleep and Depression

Sleep disturbance symptoms: nature, onset, effect on quality of life (QOL), and further treatment sought. (NAPSAQ-1, 2009)

Nature of sleep and daytime symptoms	%
Sleep disturbance symptoms (n=496)	
Any	97
i) I can't get off to sleep	58
ii) I keep waking up in the night	59
iii) I wake early and can't get back to sleep	61
iv) I sleep for too long	31
Insomnia only (i, ii and/or iii)	69
Hypersomnia only (iv)	10
Mixed insomnia/hypersomnia	21

Sleep disturbance symptoms: nature, onset, effect on quality of life (QOL), and further treatment sought.

Nature of sleep and daytime symptoms	%
Associated daytime symptoms (n=491)	99
I can't concentrate	81
I feel exhausted and lethargic	80
I have no energy	77
I feel very sleepy	41
I nap during the day	40

Sleep disturbance symptoms: nature, onset, effect on quality of life (QOL), and further treatment sought.

Nature of sleep and daytime symptoms	%
Extra treatment sought (n=341)	69
Prescribed sleeping pills	48
Over-the-counter sleeping aids	29
Extra visits to the doctor	24

Sleep disturbance symptoms: nature, onset, effect on quality of life (QOL), and further treatment sought.

Nature of sleep and daytime symptoms	%
Effect on QOL (n=495)	
Not at all	2
A little	10
Moderately	29
A lot	35
Very much	24
Onset of sleep problems (n=483)	
A long time before my depression	16
About the same time as my depression	68

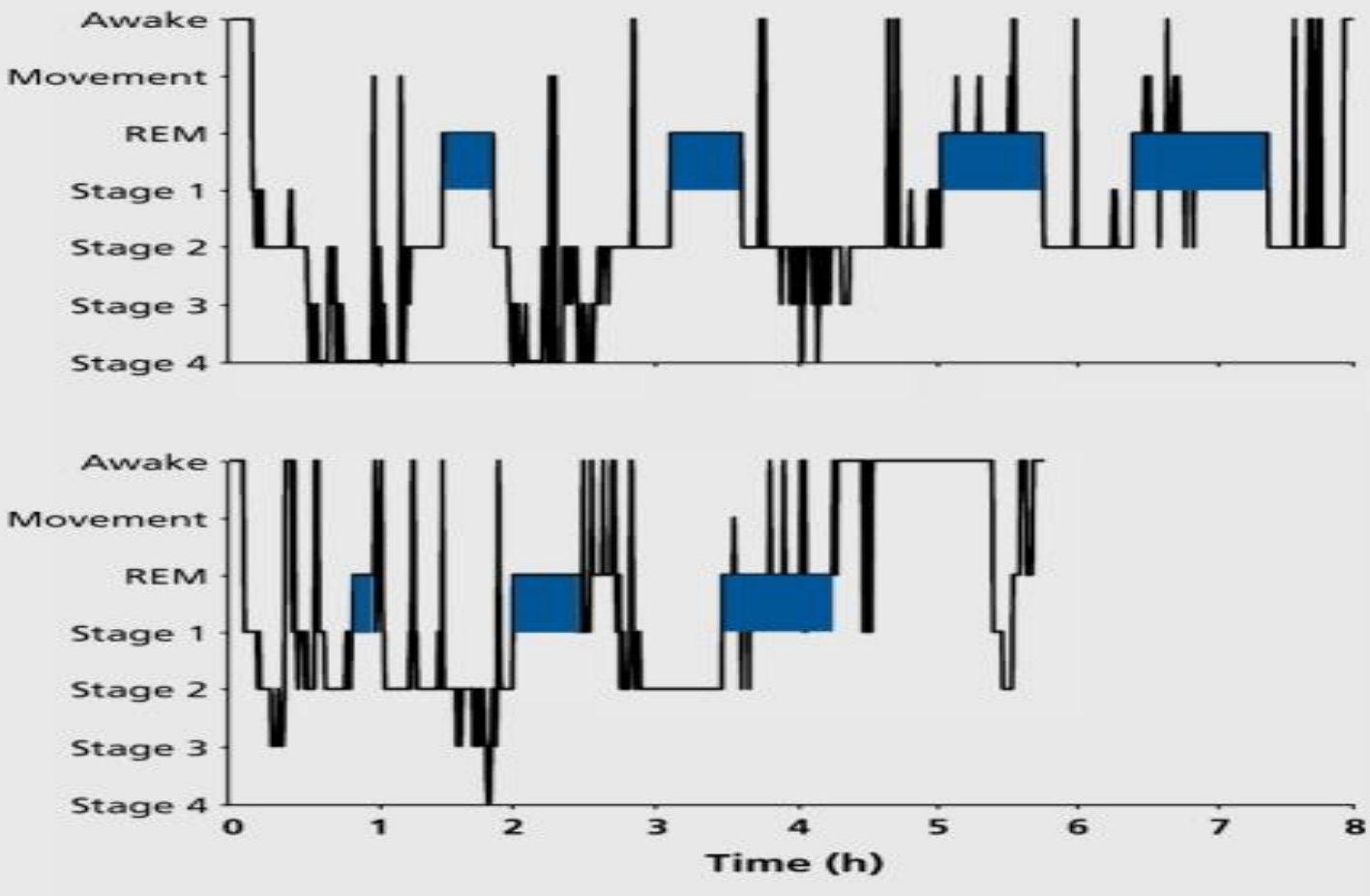
Physiological Factors

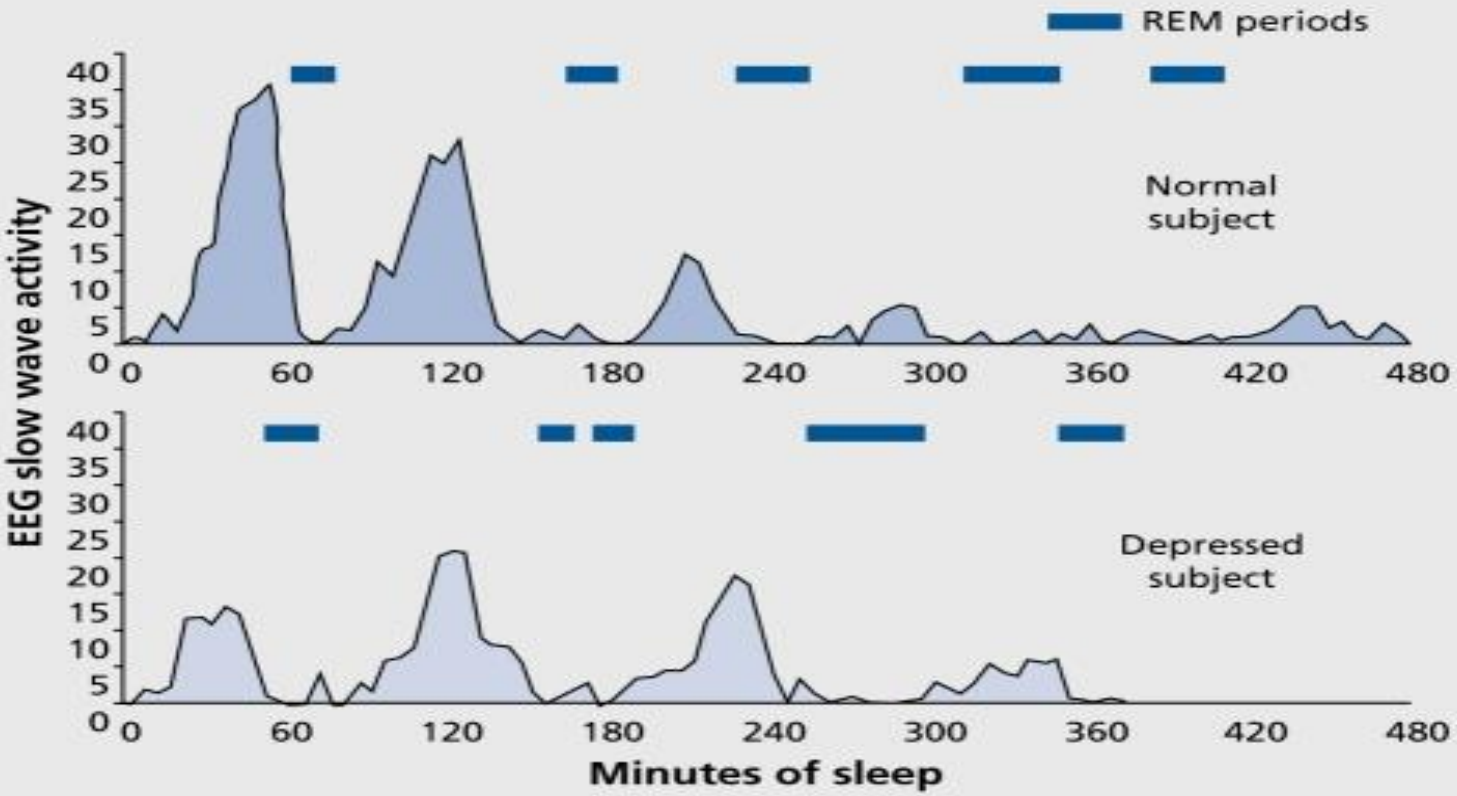
Sleep continuity is often impaired

Sleep onset latency increased, TST reduced

REM-sleep latency shortened - reduced amount of SWS

REM-density increased


Awake
Movement
REM
Stage 1
Stage 2
Stage 3
Stage 4
Awake
Movement
REM
Stage 1
Stage 2
Stage 3
Stage 4
0
1
2
3
4
5
6
7
8
Time (h)


REM periods
Normal subject
Depressed subject
EEG slow wave activity
Minutes of sleep
0
5
10
15
20
25
30
35
40
0
60
120
180
240
300
360
420
480

Physical Factors

OSA

?CSA

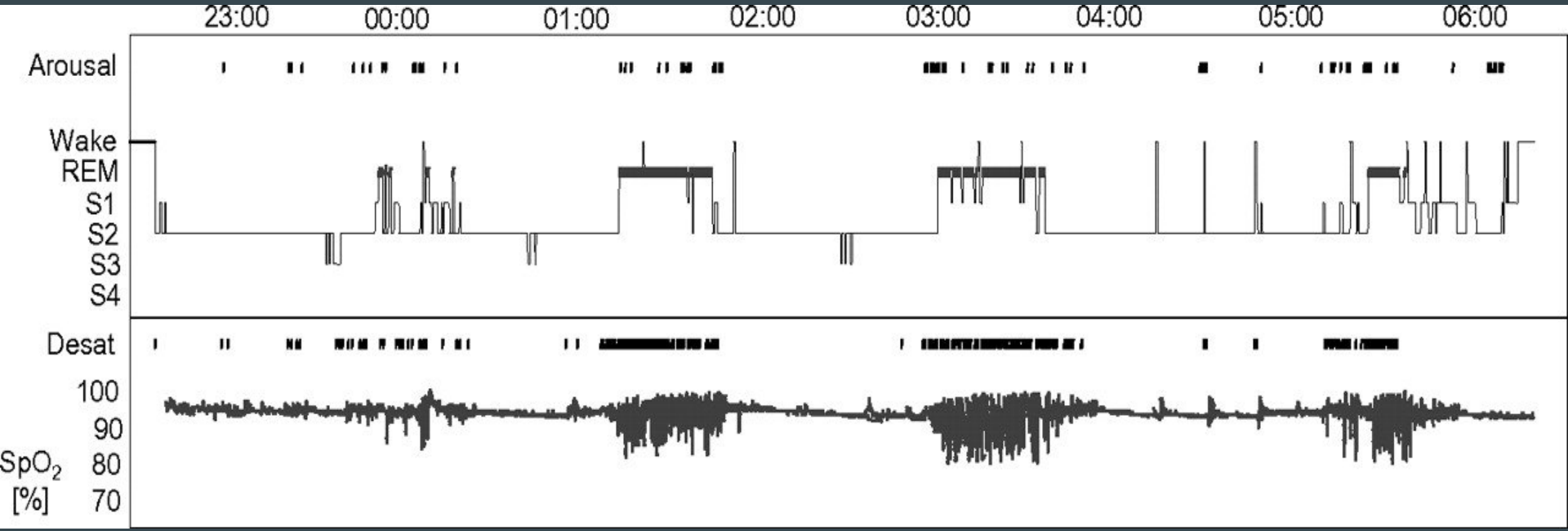
RLS

UARS

PLMD

All may / will contribute to some degree of “insomnia”:

- frequent arousals
- REM-sleep related
- Initiating sleep


23:00
00:00
01:00
02:00
03:00
04:00
05:00
06:00
Arousal
Wake
REM
S1
S2
S3
S4
Desat
100
90
SpO2
80
[%]
70

Sleep Med. 2008 Aug;9(6):675-83

Hypersomnolence, insomnia and the pathophysiology of upper airway resistance syndrome.

Gold AR, Gold MS, Harris KW, Espeleta VJ, Amin MM, Broderick JE.

Severity of hypersomnolence decreased over the continuum from severe to mild OSA/H

A model fit to the OSA/H patients to predict severity of hypersomnolence significantly underestimated hypersomnolence in UARS patients, which was comparable in severity to that of patients with mild OSA/H

The frequency of sleep-onset insomnia increased over the continuum from severe to mild OSA/H and increased further in UARS

Prevalence of Insomnia Symptoms in Patients With Sleep-Disordered Breathing

Barry Krakow, MD, Dominic Melendrez, PSG-T, Emily Ferreira, James Clark
Chest: 2001;120(6)

231 patients with SDB diagnoses

115 patients reported no insomnia complaints (SDB-only patients)

116 patients reported clinically meaningful insomnia complaints (SDB-plus patients)

Compared to SDB-only patients, SDB-plus patients reported significantly worse mean sleep characteristics consistent with insomnia, including sleep latency (17 min vs 65 min), total sleep time (7.2 h vs 5.6 h), and sleep efficiency (92% vs 75%)

SDB-plus patients experienced significantly more psychiatric disorders, cognitive-emotional symptoms, and physical and mental symptoms that disrupted or prevented sleep

SDB-plus patients also reported greater use of sedative and psychotropic medications and had significantly more primary complaints of insomnia, restless legs or leg jerks, and poor sleep quality despite having relatively similar referral rates for sleep apnea or complaints of loud snoring

The symptoms and signs of upper airway resistance syndrome: a link to the functional somatic syndromes

Gold A et al. Chest 123(1):87-95 · January 2003

The percentage of women among the patients with sleep-disordered breathing ($p = 0.001$) and the prevalence of sleep-onset insomnia ($p = 0.04$), headaches ($p = 0.01$), irritable bowel syndrome ($p = 0.01$), and alpha-delta sleep ($p = 0.01$) was correlated with decreasing severity of AHI group.

They concluded that patients with UARS, mild-to-moderate OSA/H and moderate-to-severe OSA/H differ in their presenting symptoms/signs.

The symptoms/signs of UARS closely resemble those of the functional somatic syndromes

Relevance to MDD

Hamilton Rating Scale for Anxiety and Depression (HAM-D)

Multiple item questionnaire used to provide an indication of depression, and as a guide to evaluate recovery

Published by Max Hamilton in 1960, revised in 1966, 1967, 1969 and 1980

The questionnaire is designed for adults and is used to rate the severity of their depression by probing mood, feelings of guilt, suicide ideation, insomnia, agitation or retardation, anxiety, weight loss, and somatic symptoms

17+4 Questions

Should not be used as diagnostic instrument

Conclusion

Subjective and objective sleep disturbance in depression is prevalent

Careful history taking is key to identifying possible sleep disorder-related causes in TRD patients

More successful management of sleep disturbances in depression can improve quality of life in these patients and reduce an important factor in depressive relapse and recurrence

Thank you for your attention