

MSET CONFERENCE SEPT
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PNC CENTER, TROY MI

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EXCESSIVE DAYTIME SLEEPINESS

**MOST COMMON CAUSE IS SLEEP
DEPRIVATION:**

**FROM BEING A TEENAGER WHO IS
NIGHT OWL, JET LAG, WORKING
AND STUDYING AT THE SAME
TIME, WORKING 2 FULL TIME
JOBS, RECENT LOSS ETC, SHIFT
WORK DISORDER ETC**



MEDICATIONS

 THEY ARE THE SECOND MOST COMMON CAUSE. MOST MEDICATIONS HAVE POTENTIAL TO MAKE YOU DROWSY EVEN THOSE WHICH ARE MEANT TO KEEP YOU AWAKE SUCH AS ADDERALL, PROVIGIL , NUVIGIL



MEDICATIONS: CONTINUED

- ANTICONVULSANTS ARE MOST NOTORIOUS TO MAKE YOU DROWSY EXCEPT PERHAPS VALPROATE AND ETHOSUXIMIDE
- ANTIDEPRESSANTS: ALL OF THEM MAKE YOU DROWSY-REMERAN MOST AND LEXAPRO LEAST- OTHERS IN BETWEEN



HEAVY MEAL, ALCOHOL ETC

 MAY POTENTIATE THE
EFFECT OF SEDATION

MEDICATIONS (CONTINUED)

- ANTIPSYCHOTICS-MAJORITY OF THEM MAKE YOU DROWSY
- WAKEFULNESS PROMOTING AGENTS MAY ACTUALLY MAKE YOU IRRESISTIBLY DROWSY WHEN THEIR EFFECT IS TAILING OFF
- BENZODIAZEPINES, SLEEP AIDS, ANTIHISTAMINES, OTC MEDS



SLEEP APNEA

- FAR MORE COMMON THAN NARCOLEPSY AND OCCURS IN 2 PERCENT OF ALL WOMEN AND 4 PERCENT OF ALL MAN.
- IT USUALLY PRESENTS AS HYPERMORPHIA ALTHOUGH SOMETIMES, ESPECIALLY, CENTRAL APNEA, PRESENTS AS INSOMNIA



OSA IN CHILDREN

- MAY NOT CAUSE INSOMNIA OR
HYPERMOMNIA BUT ADD OR
ADHD

NARCOLEPSY

- CONSISTS OF IRRESISTIBLE DESIRE TO NAP OR SLEEP AT ODD TIMES OR THE SO CALLED SLEEP ATTACKS
- THAT MAY BE THE SOLE FEATURE OF NARCOLEPSY OR IT MAY HAVE ONE OR MORE AUXILIARY FEATURES



AUXILIARY FEATURES

- HYPNAGOGIC HALLUCINATIONS
- HYPNAPOMPIC HALLUCINATIONS
- SLEEP PARALYSIS
- CATAPLEXY
- AUTOMATIC BEHAVIOR

HYPNAGOGIC HALLUCINATIONS

- OCCUR AT SLEEP ONSET, VIVID, MOVIE LIKE, LESS SPECIFIC, MORE COMMON, MAY OCCUR EVEN WITHOUT NARCOLEPSY




HYPNAPOMPIC HALLUCINATIONS

- OCCUR IN AM BEFORE WAKING UP
- LESS COMMON
- MORE SPECIFIC



SLEEP PARALYSIS

 MAY OCCUR AS A ISOLATED SYNDROME ESPECIALLY IN MEDICAL STUDENTS AND DOES NOT ALWAYS INDICATE NARCOLEPSY

CATAPLEXY

- PARTIAL OR COMPLETE LOSS OF BODY TONE FOLLOWING A STRONG EMOTIONAL EXPERIENCE SUCH AS LAUGHING, CRYING ETC
- THIS IS DIAGNOSTIC OF NARCOLEPSY ALTHOUGH PRESENT ONLY IN 60-90 PERCENT OF ALL PATIENTS



Example 1



Examples

Example 2-cataplexy



Example 3

Example 3 cataplexy



Cataplexy in animals

Cataplexy in a dog



Cataplexy in a cat




CATAPLEXY

frequently affects individuals who have narcolepsy

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AUTOMATIC BEHAVIOR

 IS LEAST APPRECIATED BUT PRETTY COMMON FEATURE IN WHICH YOU MAY BE ON A AUTO PILOT AND DO A FUNCTION WITHOUT REMEMEBERING IT LIKE DRIVING 10 MILES AND TAKING AN EXIT WITHOUT REMEMEBERING ANYTHING IN BETWEEN



NOCTURNAL SLEEP

- IS UNIFORMLY POOR AND CHOPPY IN NARCOLEPTICS AND NEVER NORMAL
- DAYTIME NAPS ARE REFRESHING

CHILDREN

- 10 PERCENT PATIENTS ARE BEFORE PUBERTY
- HARD TO DIAGNOSE IN THIS AGE GROUP UNLESS SUSPECTED
- NO CLEARCUT CRITERIA EXIST IN LITERATURE ABOUT PSG AND MSLT RESULTS IN CHILDREN
- SHOULD ALWAYS BE SUPECTED AS DIFFERENTIAL DIAGNOSIS IN THOSE WITH ADHD AND SEIZURES



ADULTS

- 90 PERCENT CASES ARE IN ADULTS
- MOSTLY SYMPTOMS BEGIN AT PUBERTY DUE TO A COMBINATION OF GENETIC PRESSURE FROM SOME HLA GENES SUCH AS HLA DR2 (HLA DR 15) AND DQ W1 (HLADQB1*0602) AND AN ENVIRONMENTAL INSULT SUCH AS HEAD TRAUMA EVEN WHEN IT IS MINOR INDUCING AN AUTOIMMUNE DESTRUCTION IN HYPOTHALAMUS




PATHOGENESIS

- THIS LEADS TO 90 PERCENT REDUCTION IN OREXIN-A OR HYPOCRETIN 1 PRODUCING CELLS IN LATERAL AND POSTERIOR HYPOTHALAMUS
- OREXIN IS A 33 AMINO ACID PEPTIDE WITH CYSTEINE AT POSTION 6, 7, 12 AND 14



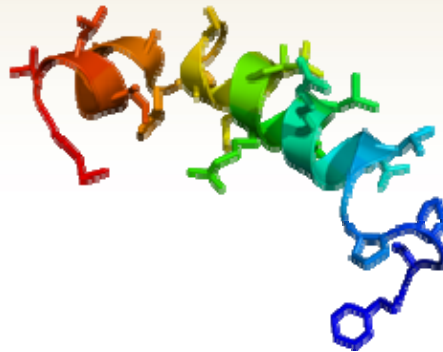
OREXIN-A OR HYPOCRETIN 1

 IT MAINTAINS WAKEFULNESS BY MODULATING NEUROTRANSMITTERS NAMELY NE, DOPAMINE, A CH AND HISTAMINE BY BINDING TO THE G RECEPTOR ON THE OUTSIDE OF THE CELL AND INDUCING TRANSDUCTION

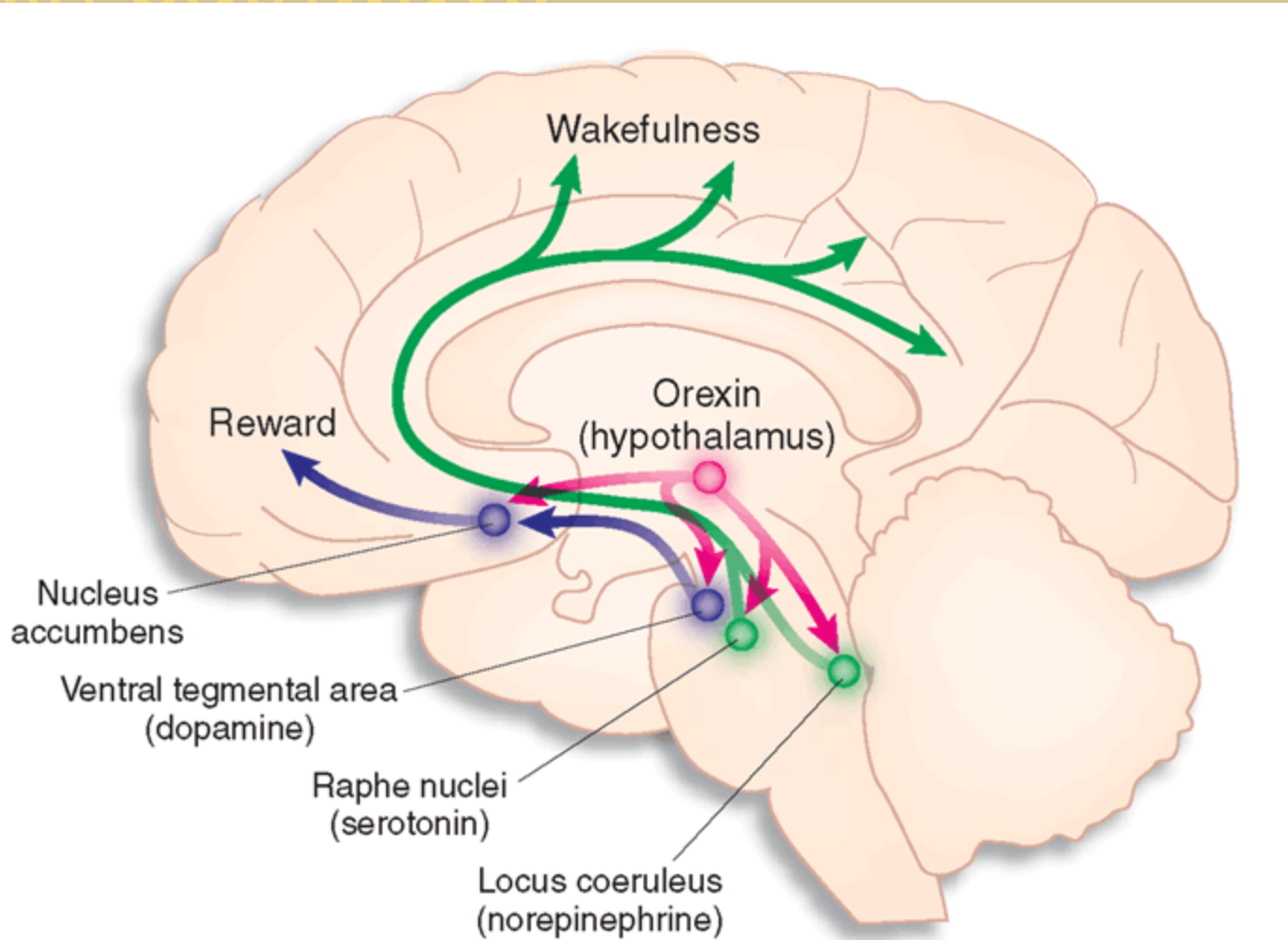


Orexin-A

 Hypocretin-1



Orexin pathways

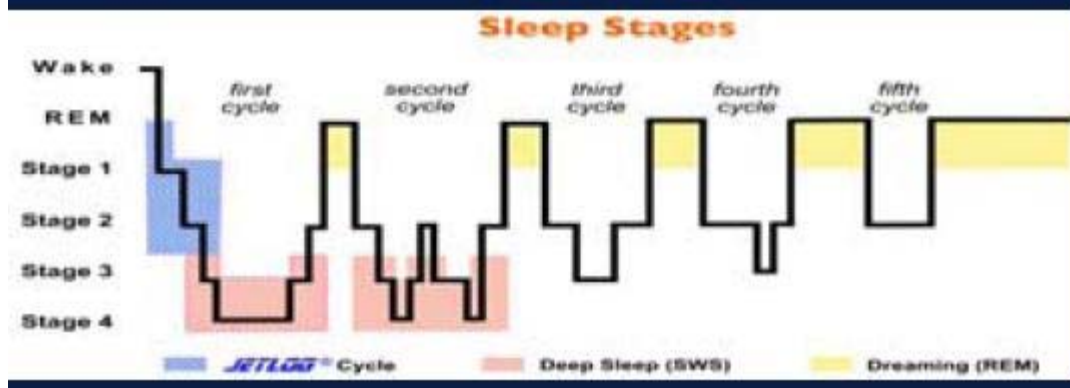
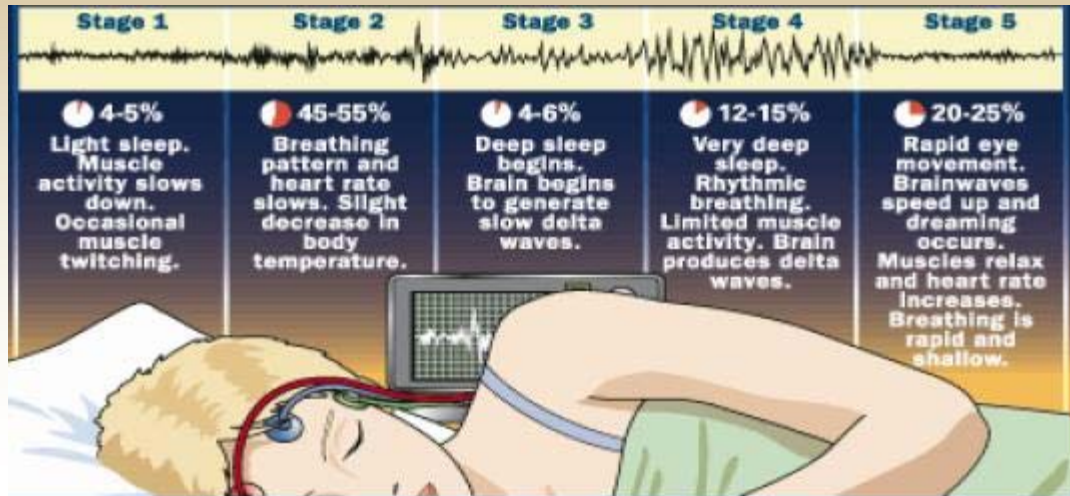


NORMALLY

- THERE ARE 4-6 REM CYCLES IN 6-8 HR NOCTURNAL SLEEP
- FIRST CYCLE IS ONLY 5-10 MIN AND LAST ABOUT 1 HOUR
- THEY OCCUR EVERY 90-120 MIN
- THIS CYLCITY IS DISTURBED IN NARCOLEPTICS



Sleep Stages



THUS

- REM SLEEP MAY INTRUDE ON THE PATIENT AT ANY TIME
- IF IT ITRUDES DURING DAYTIME IT CAUSES SLEEP ATTACK
- IT INTRUDES AT THE BEGINNING OF SLEEP IT CAUSES HYPNAGOGIC HALLUCINATION



AND

- IF IT INTRUDES AT THE END OF SLEEP IT CAUSES HYPNAPOMPIC HALLUCINATIONS
- IF IT INTRUDES WHEN YOU ARE ABOUT TO WAKE UP IT CAUSES SLEEP PARALYSIS IN WHICH YOU BRAIN IS AWAKE BUT BODY IS STILL IN REM SLEEP PARALYSED BY IMPULSES TRAVELLING IN LATERAL RETICULOSPINAL TRACT TO ALPHA MOTOR NEURONES



IF

- IT INTRUDES ON YOU WHEN YOU ARE LAUGHING OR CRYING, YOU DEVELOP CATAPLEXY
- THUS IT IS EASY TO UNDERSTAND ALL SYMPTOMS OF NARCOLEPSY IF YOU MEMORIZE IT LIKE THIS



PREVALENCE

- EQUAL IN MALES AND FEMALES
- 1 IN 3000 AMERICANS
- ABOUT 1/3RD AS COMMON AS MULTIPLE SCLEROSIS
- MAY START SYMPTOMS AT A LATE AGE ESPECIALLY AFTER HEAD TRAUMA OR EVEN STROKE, USUALLY AT PUBERTY



DAYTIME EEG

 USUALLY NORMAL UNLESSSS YOU
ARE LUCKY TO CATCH A SOREMP

OVERNITE NOCTURNAL POLYSOMNNOGRAM

- ALWAYS ABNORMAL
- USUALLY SLEEP EFFICIENCY IS LESS THAN 85 PERCENT
- TOTAL NUMBER OF AWAKENINGS AND STAGE SHIFTS ARE INCREASED
- SOREMP IN ONLY 2 PERCENT BUT IS HIGHLY SPECIFIC



PERCENT OF REM

- IN 24 HRS IS NOT INCREASED
- IT COMES AT ODD TIMES,
HOWEVER AS STATED EARLIER

STAGE 1 PERCENTAGE

- USUALLY INCREASED DUE TO CHOPPINESS IN SLEEP

5 NAP DAYTIME MSLT

- SHOWS SLEEP LATENCY LESS THAN 8 MIN IN MOST PATIENTS
- AND 2 OR MORE SOREMPs
- NEGATIVE IN 15 PERCENT PATIENTS WHEN DONE ONLY ONCE
- 4 MSLTS PICK UP 100 PERCENT OF ALL CASES



Adjunctive Help in Diagnosis

- HLA DR2 AND HAL DQW1
- CSF HYPOCRETIN LEVEL LESS THAN 110 PCG/ML
- REPEAT MSLT X 3
- SOREMP IN PSG
- CLEARCUT HX OF CATAPLEXY

TREATMENT-BEHAVIORAL

- TAKE NAP BEFORE NAP TAKES
YOU-PLANNED MID MORNING OR
MID AFTERNOON NPAS OR BOTH-
MAY NEED TO TALK TO THE BOSS
- KEEPING ACTIVE, COFEE ETC
- SITTING DOWN WHEN LAUGHING
OR CRYING



BEHAVIORAL

- AVOID NIGHT AND AFTERNOON SHIFT OR ROTATING SHIFT
- ADEQUATE NIGHT SLEEP
- AVOID SEDATION AND ALCOHOL



WAKEFULNESS PROMOTING AGENTS

- MODAFINIL OR ITS COUSIN
- ARMODAFINIL
- ADDERALL OR RITALIN OR CONCERTA
- CAFFEINE
- DEXEDRINE
- MAY EXACERBATE AUXILIARY SYMPTOMS



SODIUM OXYBUTATE

- ALSO CALLED XYREM
- ABUSED AS DATE RAPE DRUG
- ACTS BY INCREASING SELTA SLEEP AT NIGHT
- USED TO TREAT CATAPLEXY WHEN IMIPRAMINE, PROZAC OR EFFEXOR FAIL
- ALSO GREAT FOR DAYTIME SLEEPINESS




XYREM-SIDE EFFECTS

- MAY NOT BE SUITABLE FOR MOMS WITH INFANTS AND CHILDREN AS IT INCREASES DEEP SLEEP
- MAY CAUSE INCONTINENCE AND SLEEP WALKING
- MAY INCREASE FALLS AND FRACTURES
- MAY CAUSE LOSS OF WEIGHT



IMPROVING NOCTURNAL SLEEP

 BY KLONOPIN, XYREM,
IMIPRAMINE OR EVEN OTHER
BENZODIAZEPINES MAY PAY
DIVIDEND IN REDUCING THE
DAYTIME SLEEP DEBT



This photo shows 2 existing and one future sleep specialist

