MEDICINE - CNS
NEET - SS

CONTENT

APPROACH TO NEUROLOGY CASE

Overview of the steps

00:02:17

1. Pathology
2. LMN v/s UMN
3. Specific Pathology
4. Associated features like fever or constitutional symptoms, weight loss, palpations, chest pain, skin rashes, joint pains and swelling, cough and breathlessness

Assessing the pathology

The approach :

1. Onset : Acute/sub-acute/chronic of symptoms.
2. Duration : Days/ hours/ months/ years
3. Progression : Progressive/ improving/ recurrent

Order of examination of nervous system :

- Higher mental functions : Cognitive symptoms.
- Cranial nerves
- motor system + coordination and cerebellum including gait
- Sensory

Acute onset :

Hyper acute : e.g. when patient tells yesterday morning by 9 am when I was writing with pen at, suddenly I felt weakness in upper limb.

Vascular causes and seizures present with hyper acute.

Acute : e.g. morning when I got up I had paraesthesia of

Leave Feedback

right hand and then it worsened and reached shoulder by 1hour. And by afternoon, right upper limb weakness. And by, evening weakness worsened. By next day morning complete weakness.

Classical acute presentations :

1. Vascular : LMN weakness with pain
2. Demyelination like in GBS
3. Trauma
4. Bleed into a tumour

Sub-acute : Progressed over days to months.

1. Demyelinating
2. Thrombotic stroke or multi infarct stroke
3. Nutritional or metabolic
4. Tumour : malignant

Chronic :

1. Degenerative.
2. Genetic or hereditary : Spino cerebellar ataxia.
3. Benign tumours : over years.

Duration :

Symptom of 2 or 3 days : acute.

Years : Degenerating or genetic disease.

Progression :

- Worsening

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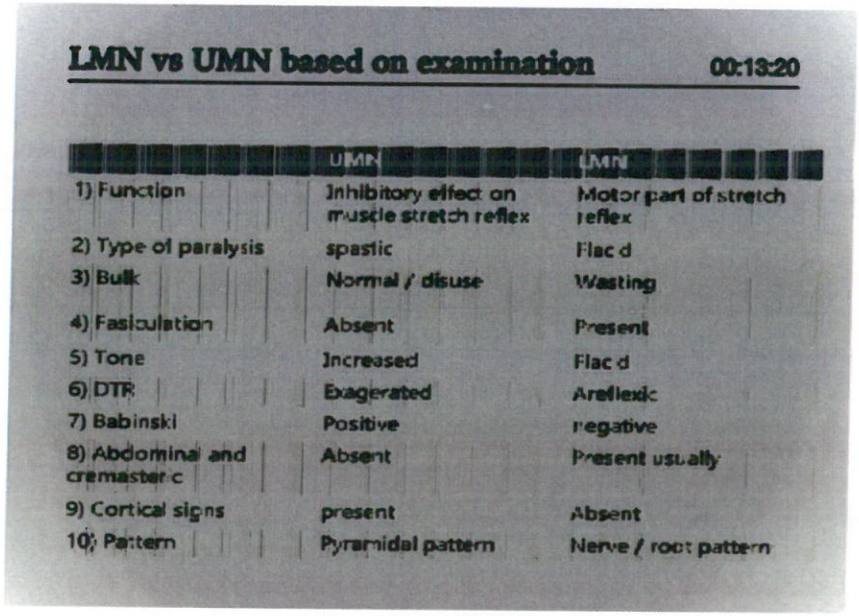
- Improving
- Recurrent illness : demyelination.

LMN v/s UMN

Higher mental function can be remembered as : AIME LOSS handedness

- Appearance, Intelligence, memory, emotional status.
- Level of consciousness, orientation, speech and handedness.
- +/- Lobar functions and mmsc.



LMN vs UMN based on examination 00:13:20

	UMN	LMN
1) Function	Inhibitory effect on muscle stretch reflex	Motor part of stretch reflex
2) Type of paralysis	spastic	Flac d
3) Bulk	Normal / disuse	Wasting
4) Fasiculation	Absent	Present
5) Tone	Increased	Flac d
6) DTR	Exagerated	Areflexic
7) Babinski	Positive	negative
8) Abdominal and cremaster c	Absent	Present usually
9) Cortical signs	present	Absent
10) Pattern	Pyramidal pattern	Nerve / root pattern

	LMN	UMN
Higher motor functions	-	+/-
Cranial nerves	+ and LMN type	+ and UMN type

Active space

motor : 1. Bulk 2. Tone 3. Power 4. Reflexes 5. Gait 6. Co-ordination 7. Involuntary movements	Atrophy Decreased Plexus/Nerve/ Polyradiculopathy Hypo or Areflexia High stepping gait Cerebellum normal Polymini myoclonus, segmental myoclonus	Disuse atrophy Rigidity/spasticity Pyramidal Pattern Exaggerated reflexes Circumduction gait Cerebellum affected +/- myoclonus, dystonia, tremors
Reflexes : Superficial – Plantar & abdominal. DTR	Normal. Unless the segment is affected Decreased	Babinski positive , plantar Abdominal absent Brisk/exaggerated
Sensory	Depends on small or large fibres	Seen in spinal cord injury : funicular, circumferential pain. Ankle jerk is checked.

Ankle jerk :

- In large fibre involvement (peripheral neuropathy) : lost.
- In posterior column involvement : normal.

Pyramidal Pattern : seen in UMN.

Upper limb :

- Wrist extension : weak.
- Supination > Pronation : weak.
- Elbow extension is weak.
- Shoulder abduction is weak.

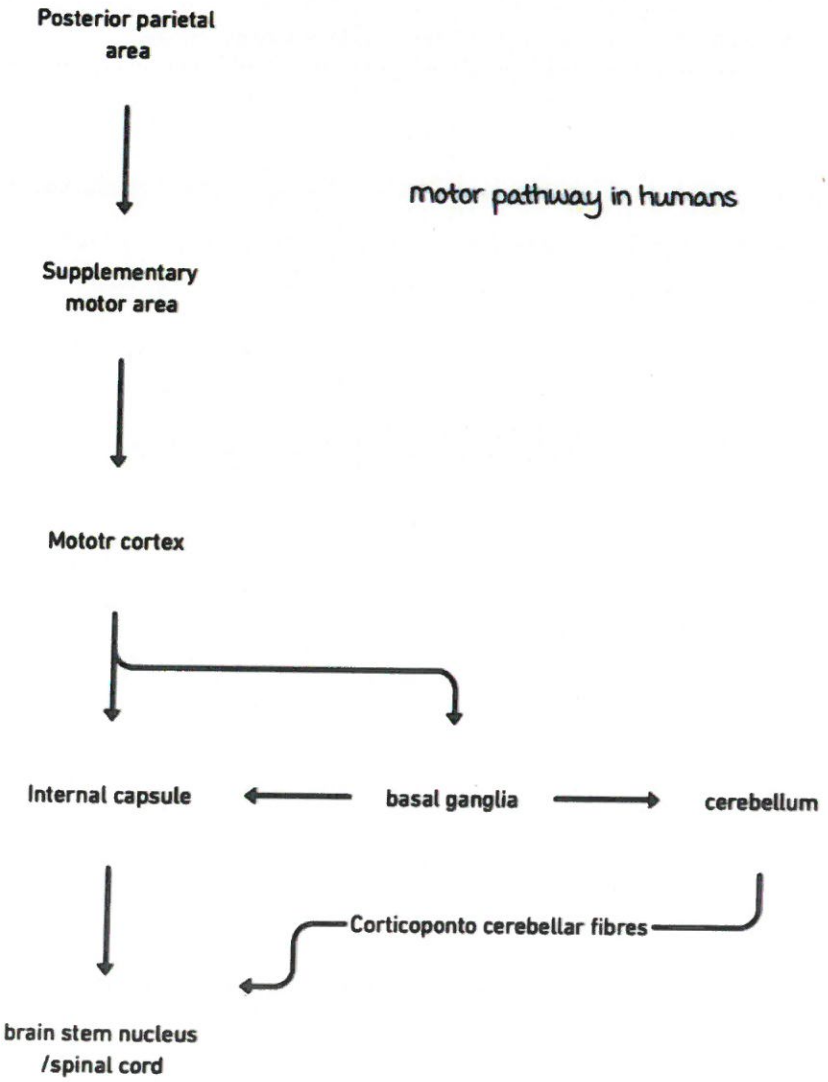
Lower Limb :

- Hip flexion, knee flexion and ankle dorsiflexion is weak.
- Adductor spasticity is present
- Abduction of hip is weak.

Motor features : UMN and LMN 00:31:48

motor :

- Distal or proximal muscle weakness.
- Symmetrical or asymmetrical.
- Nerve pattern/ plexus pattern/pyramidal pattern.
- Any sign of spasticity : Foot clearance from ground is more affected in UMN. Tripping, heaviness and falls is seen in UMN. Wasting, fasciculation's are seen in LMN.
- Reflex.
- Involuntary movements.
- Cerebellum and ataxia.
- Stance and gait : UMN v/s LMN.



motor pathway in humans

Active space

Leave Feedback

UMN approach : Summary

00:40:43

UMN

Cortex
- LOC
- Seizure
- Motor weakness pattern
- Lobar signs
- Language and cognition
- Visual field

Brain stem
- Crossed hemiplegia
- Cranial nerve

Spinal cord
- Sensory level
- Bladder
- Sparing of face
- Back pain / tract pain
- LMN + UMN

Subcortical
- Coronaradiata
- Internal capsule
- Thalamus
- Basal ganglia lesion

In motor cortex : maximum representation is for face, lips and hands. Hence, pattern of weakness will be facio-brachial predominantly, dexterity loss and distal weakness.

Corona radiata : If there is a lesion 1 cm in corona radiata, it will affect only few fibres. 1 cm lesion in internal capsule. it will have dense weaknes as many fibres will be affected.

Thalamus : Fluctuation sensorium will be present.

Basal ganglia : Parkinsonian phenomena, hyperkinetic movement disorders.

Active space

LMN approach : Summary 00:46:00

LMN

Anterior horn
- Pure motor
- Wasting
- Fasciculation
- Reflex loss

Radicle
- Asymmetry
- Radicular pain
- Radicular motor and sensory loss
- Reflex loss isolated

Plexus
- Asymmetry
- proximal plus distal
- Sensory + motor

Peripheral nerve
- Distal predominant
- Nerve pattern sensory motor loss
- Stocking and glow
- Loss of reflex
- +/- wasting

NMJ
- Symmetrical
- Proximal+ distal
- Face and pharyngeal + neck
- Fatigability
- Normal reflex

Muscle
- PROXIMAL > DISTAL
- Symmetrical
- Pure motor
- Normal reflex

Active space

APPROACH TO UMN DISORDERS

UMN Structures :

- Cortex.
- Sub cortex.
- Brainstem :

  Crossed hemiplegia : Ipsilateral cranial nerve palsy + contralateral hemiplegia.

  Cranial nerves symptoms.

  Vertigo : Also seen in insular cortex involvement.
- Spinal cord :

  Sensory level.

  Bladder involvement (depending on level of spinal cord involved).

  Tract pain.

Cortex 00:03:30

Loss of Consciousness : Classical pressenattion

Seizure : Orgin is cortex

Cortex predominantly is grey matter .

Different lobes of cortex :

Frontal :

- medialfrontal cortex containing anterior singulum.

  medial involvement.

  Lack of enrgy / apathy.

  Akinetic muteism
- Dorsolateral prefrontal cortex :

  Executive dysfunction.

  Not able to do Planned & sequential activitiy
- Orbitofrontal area :

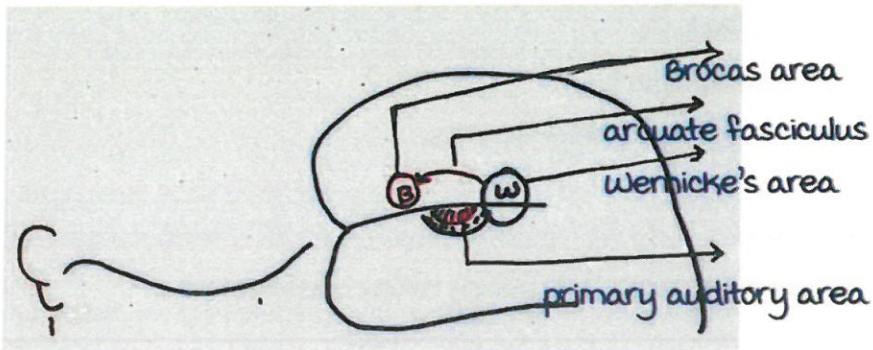
  Personality problem.

  Disinhibition.
- motor cortex :

when retina/optic nerve /optic chiasma involved : Pupillary reflect affected

Language 00:16:43

Language is the basic concept of communication through writing, speaking, gesture etc.
motor output of languages is speech using larynx, pharynx.
Sound falls on ears → Heschl's gyrus identifies → Tone of sound
(primary auditory area)
↓
Wernicke's area & temporal parietal area → Comprehension
(contains internal dictionary Lexicon)
↓
Arcuate fasciculus
↓
Brocas area → Produces reply by activating motor neurons
↓
Produce syntax grammar fluency
↓
Supplementary motor area (planning and programming)
↓
motor cortex
↓
Descends to brainstem cranial nerve nucleus
↓
Speech output



Active space

Weakness predominantly involves face + upper limb.
Distal > proximal.
Dextrective loss.
Loss of fine activities : Pyramidal dysfunction.

Parietal :
Function : Calculation, language, temporal apraxias, proprioception.

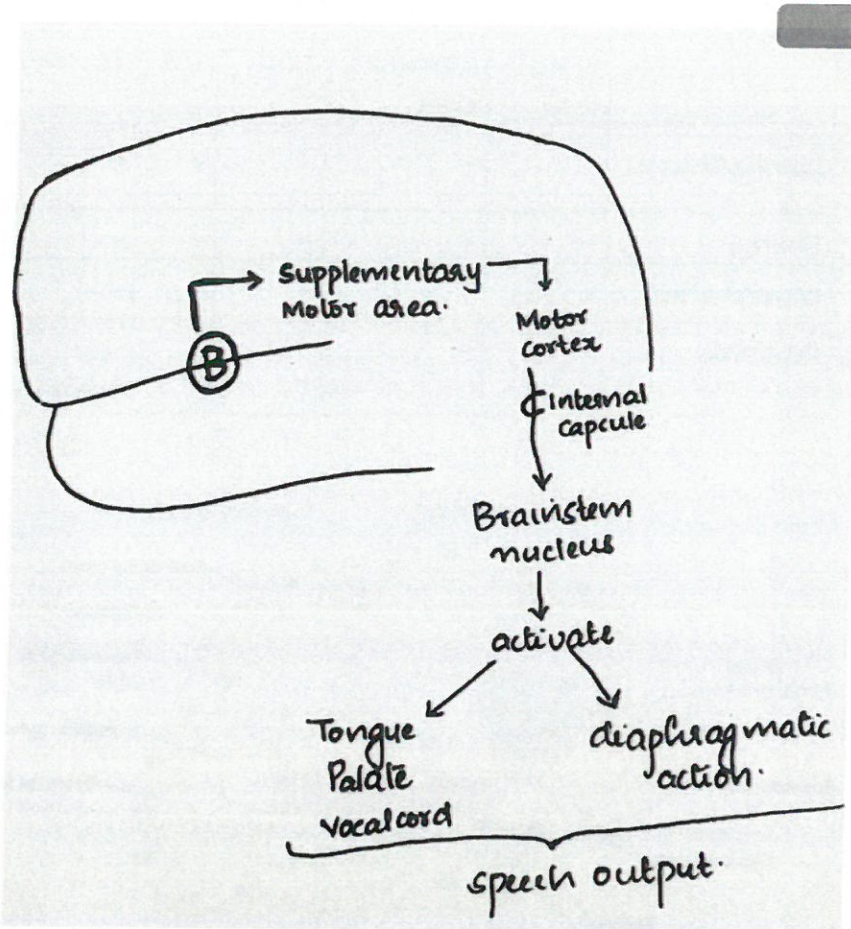
Left parietal :
Involved in calculation & language apraxia.
Dominant.
Lesion of angular gyras produce Gerstman's syndrome (finger agnosia, agraphia, acalculia).

Right parietal :
Dressing apraxia.
Constructional apraxia.
Neglect.
Geographical.

Temporal : 2 parts :
Lateral :
Auditory area.
Wernickes area.
Visual processing.
medial :
memory.
Olfaction.
Limbic part.
most epileptogenic area.

Occipital :
Occipital blindness : Pupillary reflex unaffected

Retina → fibres cross chiasma → lateral geniculate body(LGB)
Pupillary fibres before reaching LGB descends to mid brain to form pupillary reflex.

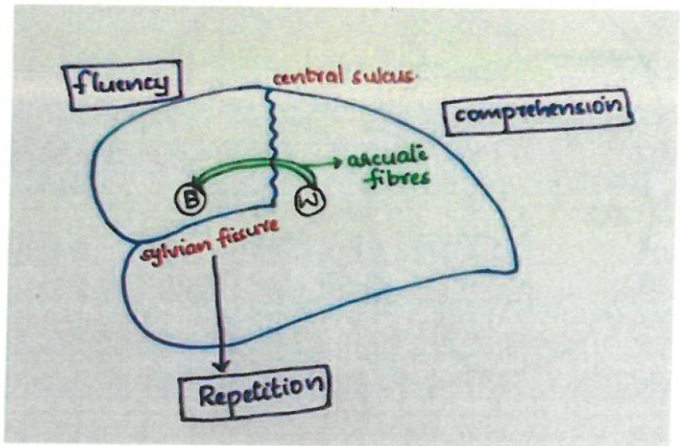


Intentional activation system cannot activate Broca's area causing akinetic mutism (no movement, no talk).

Right > left side :

- Limbic reward system gives emotional intonation.
- Prosody (rhythmic sound of speech).

Rest of language concept lies in left side.

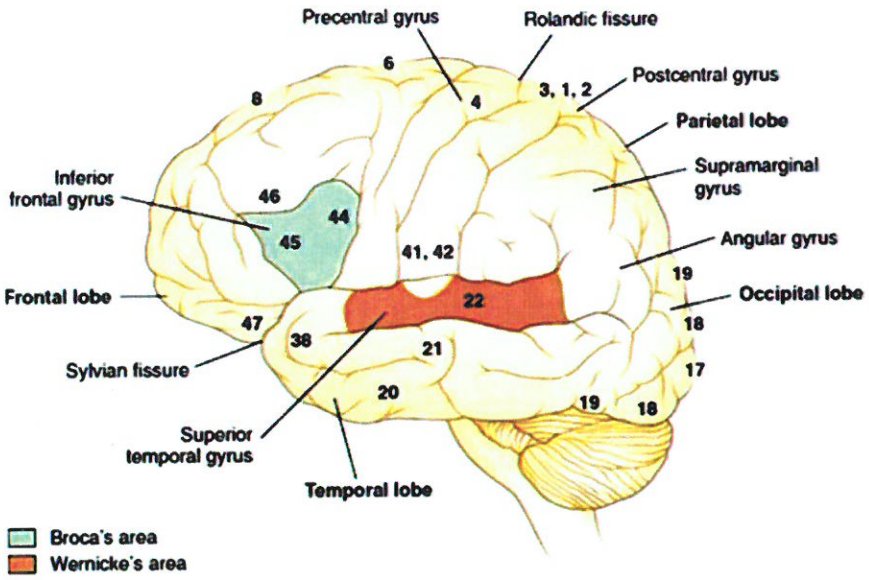


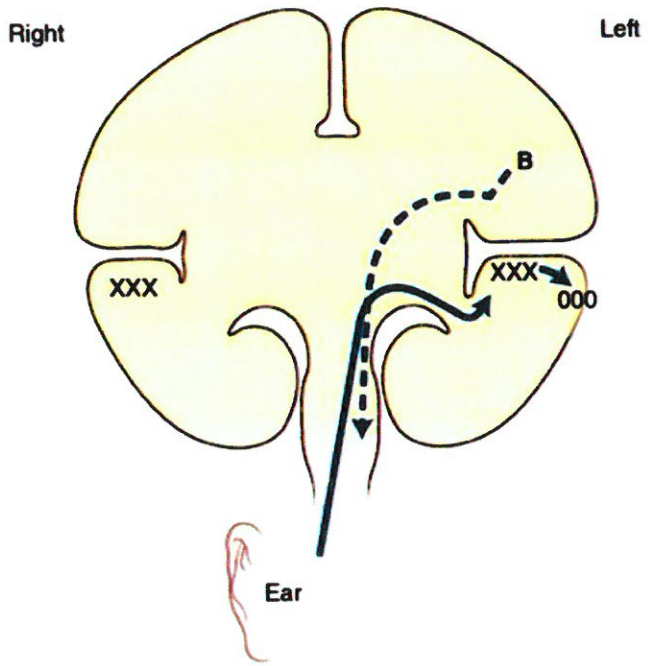
Any lesion anterior to central sulcus → Fluency lost.

Any lesion posterior to central sulcus → Comprehension lostany

Any lesion involving Perisylvian circuit → Repetition lost.

	Broca's area	Wernicke's area	TCM	TCS	TC mixed
Naming/Anomia	-	-	-	-	-
Fluency	-	+	-	+	-
Comprehension	+	-	+	-	-
Repetition	-	-	+	+	+, echolalia.





Active space

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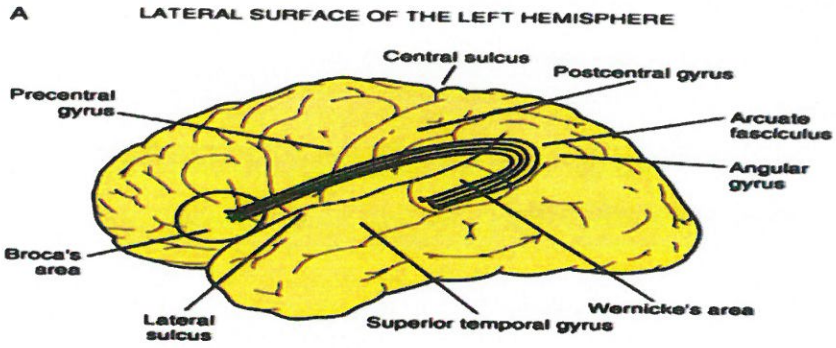
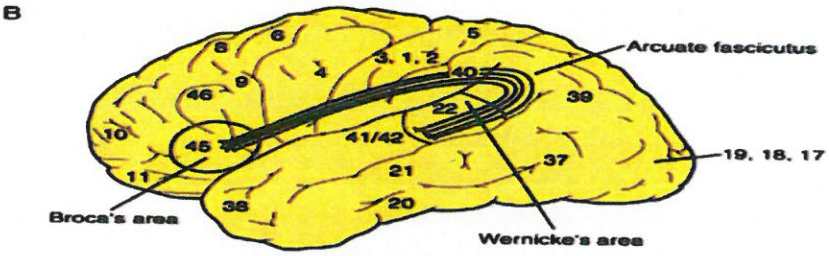
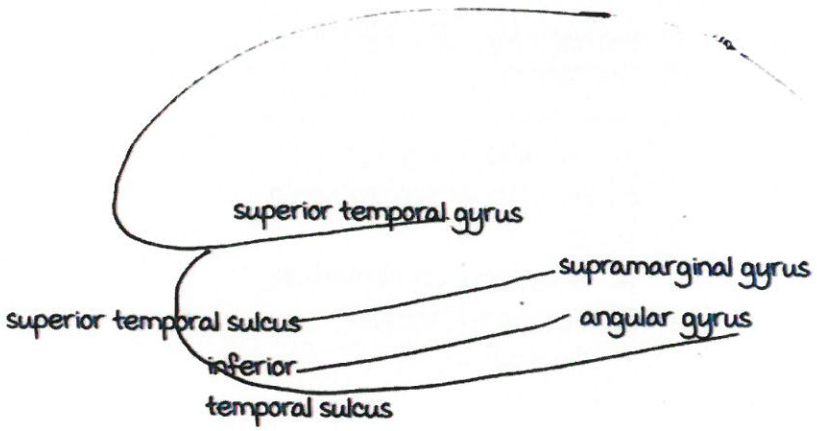






Supramarginal gyrus is involved in phoning, processing of language. Angular gyrus :

Is involved with naming.

Associated with anomia+ Gerstman syndrome.

Localisation of Gerstman syndrome :

Left /Dominant angular gyrus

Speech

00:35:35

Grammar/ syntax

Paraphrasing error :

Literal : Change in sound.

Example : Pencil said as pen'til'.

Active space

Semantic : Change in idea.

Example pencil identified as knife.

Name :

Unusual things given to identify (as otherwise from memory can identify).

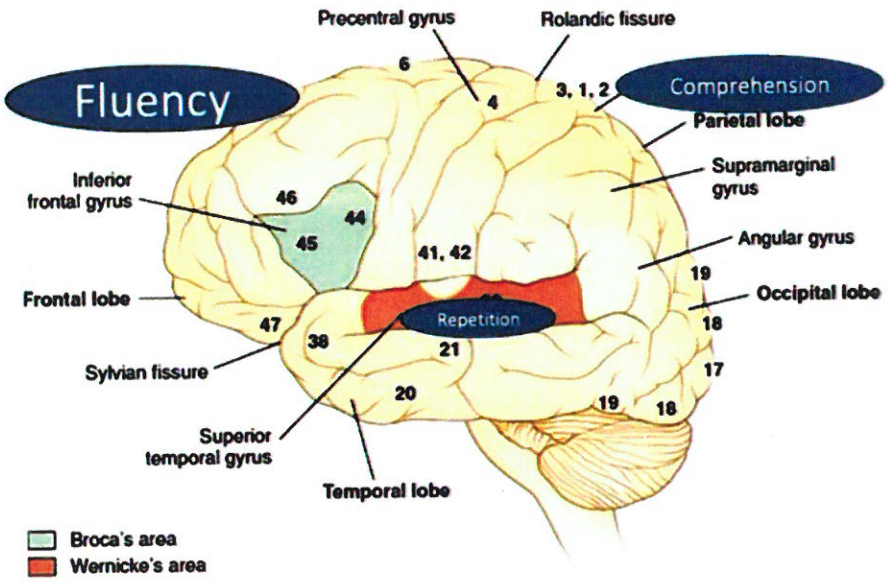
Like :

Small needle of clock.

Tip of pen.

Writing : Assess fluency, grammar, concept of language.

1. Spontaneous speech
   a. Informal interview
   b. Structured task
   c. Automatic sequences
2. Naming
3. Auditory comprehension
4. Repetition
5. Reading
   a. Reading aloud
   b. Reading comprehension
6. Writing
   a. Spontaneous sentences
   b. Writing to dictation
   c. Copying



Anomic aphasia :

Lesion in left angular gyrus.

Associated with Gerstman syndrome.

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Left temporal/ left-sided lesion (diffuse):

Seen in Alzheimer's disease.

Degenerative aphasia.

Conduction aphasia:

Arcuate fasciculus involved.

Repetition grossly affected.

Superior temporal /Inferior parietal dysfunction.

Pure word deafness:

Unable to identify words but able to identify tones, sound.

Auditory comprehension severely affected but can read, write, language circuit normal.

Disconnection syndrome: Due to disconnection of Heschl's gyrus from surrounding Wernicke's area.

Can see (Occipital connected to language) or read and comprehend.

TABLE 13.5 Bedside Features of Anomic Aphasia

Feature	Syndrome
Spontaneous speech	Fluent, some word-finding pauses, circumlocution
Naming	Impaired
Comprehension	Intact
Repetition	Intact
Reading	Intact
Writing	Intact, except for anomia
Associated signs	Variable or none

Aphasia is acquired and dysphasia is congenital defect of language.

TABLE 13.6 Bedside Features of Transcortical Aphasias

Feature	Isolation syndrome	Transcortical motor	Transcortical sensory
Speech	Nonfluent, echolalic	Nonfluent	Fluent, echolalic
Naming	Impaired	Impaired	Impaired
Comprehension	Impaired	Intact	Impaired
Repetition	Intact	Intact	Intact
Reading	Impaired	+ Intact	Impaired
Writing	Impaired	+ Intact	Impaired

Cortical vs subcortical aphasia :
Anterior subcortical aphasia mimics Broca's aphasia (fluency loss) but not as severe as Broca's aphasia.

Caudate :
Severe dysarthria. Initiation defect.

Thalamus :
Comprehension predominant. mimics Wernicke's aphasia.
Fluctuation (alteration) : Periods of normal and abnormal language.

Crossed aphasia :
Right handed person with left dominance for language.
But here defect aphasia due to right hemispheric defect.

Anarthria : Dysfunction of local apparatus like pharynx, larynx.
Dysarthria :
Inability to articulate .
Neurogenic cost of dysarthria is classical .
speech : motor muscle involving activity.

Lesion 00:49:03

Active space

Lesion of corticobulbar fibres :

Lesion of corticobulbar fibres → B/L → Spastic dysarthria.
Diaphragm pushes air out → Larynx with vocal cord → Vocal cord adjusted to position for change in sound → Oral cavity structures like palate, tongue →Produces different intonation.

Sound is modulated by pharyngeal and oral apparatus.
Difficulty in both phases of vocal code movement & adjusting with vocal cord apparatus.

Vocal cord to be moved requires more air that have to be pushed by diaphragm imparting explosive character.
Pyramidal tract cut → Increased tone.
Tongue & oral cavity → Spasm → Cannot produce syllables separately → Difficulty in both phases.
Normal dexterity is lost & smooth movement affected.
Less clear, explosive character.

Lesion of LMN cranial nerve / brainstem nucleus :

Flaccid dysarthria.
Less volume.
Entire muscle flaccid.

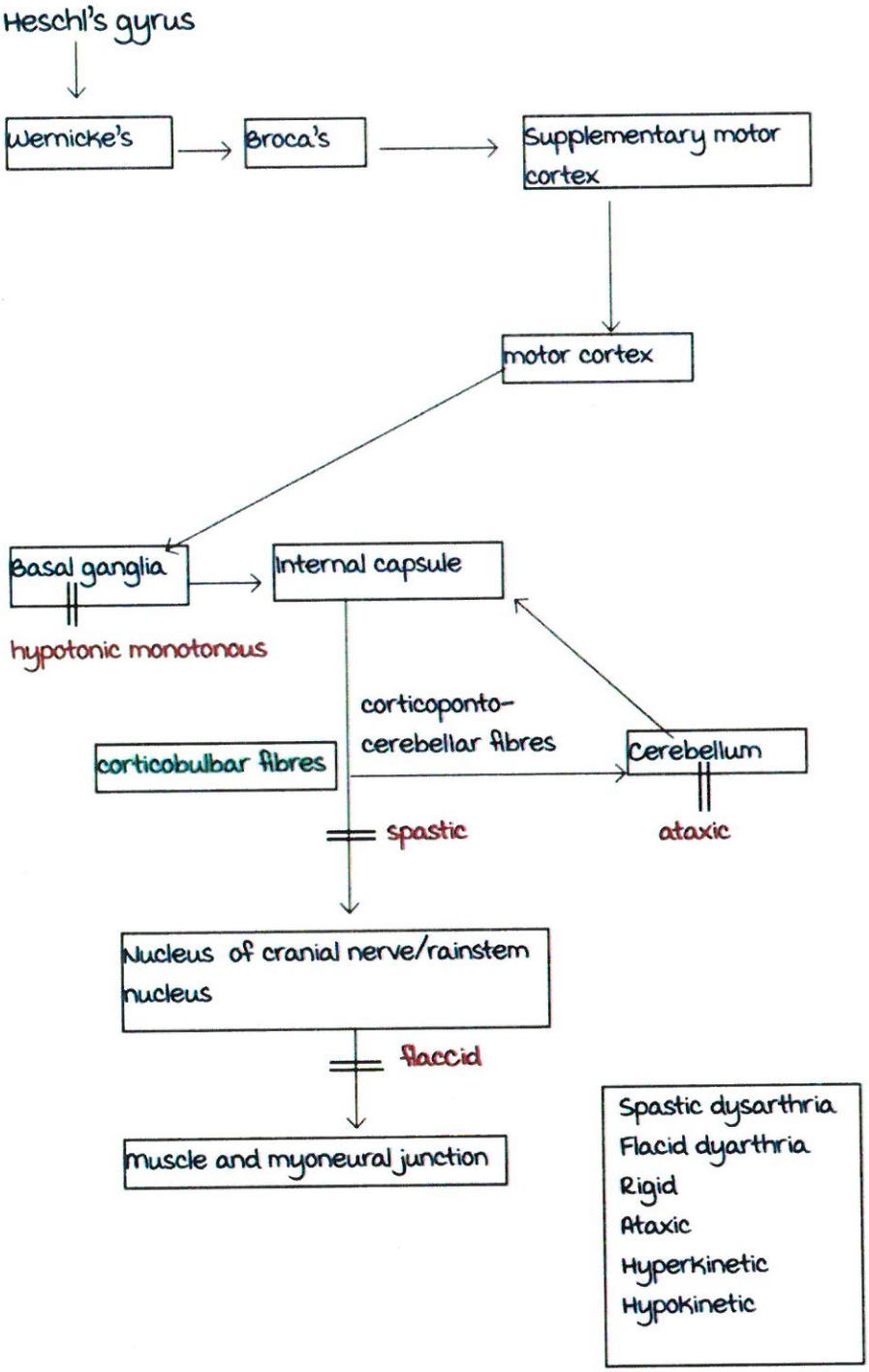
Cerebellar lesion :

Dysmetria : Cannot do finger nose test.
Ataxic dysarthria : Example : Pa-ta-ka. (All letters have fixed gap . Rhythmic gap will override as rhythmic activation by cerebellum not present but will be able to tell letter with separation like scanning of space).
Staccato speech :
Cerebellar dysarthria + lesion in descending (pyramidal) fibres.
Spastic ataxic dysarthria.
In Frederick's ataxia, lesion is in descending fibres of C-spine.

Lesion of basal ganglia :

Function of basal ganglia : Agonist-antagonist tone is maintained.
If lesion → monotonous tone as vocal cord cannot alternate

agonist and antagonist tone.
Also called as rigid dysarthria (increase in rigidity).
Hyperkinetic dysarthria : Chorea with speech.



Flaccid dysarthria :
Breathy, nasal indistinctly pronounced consonants.
Nasal twang.
Nasal regurgitation.
Hoarseness.

Active space

Spastic dysarthria :

B/L Corticobulbar tract lesion.

Harsh strained reduced rate, low pitch ,consonant errors.

Pseudobulbar signs.

Ataxic /scanning :

Scanning : Irregular rythum , slow cadence of speech excessively equal stress on every syllables.

Staccato : Spastic ataxic.

Hypokinetic : Decreased monotonous loudness and pitch.

Hyperkinetic : marked variation in rate ,loudness and timing with distortion of vowels, harsh voice quality and occasional , sudden stoppages of speech.

Muteness

00:59:12

Total lack of motor output (language is normal).

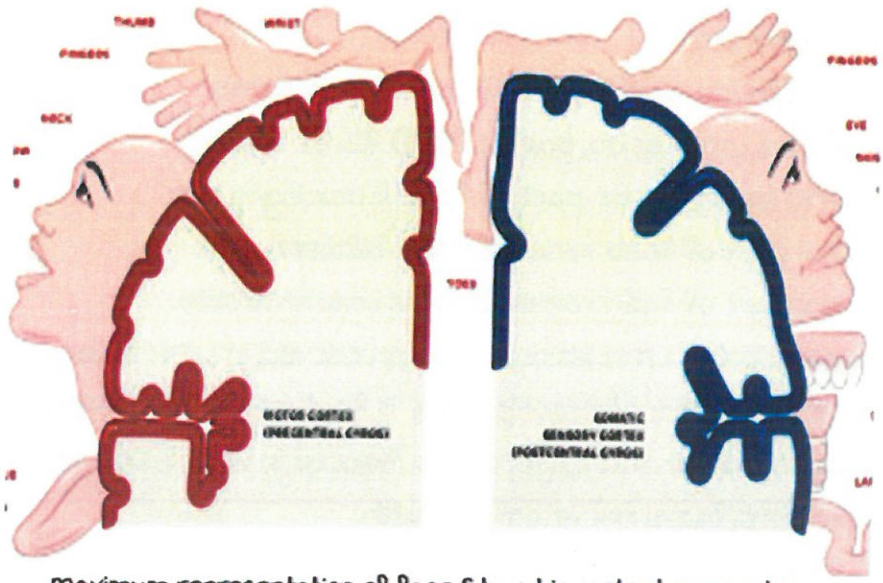
Cause :

Frontal – Akinetic mutism.

Extrapyramidal.

Non neurological disorders of larynx and pharynx.

Psychogenic – Catatonia.



Maximum representation of face & hand in motor homongulus.

Visual field

01:00:42

Temporal :

Superior Quadrant Anopia.

Called as Pie on Sky.

Parietal :

Inferior Quadrant Anopia.

Called as Pie on floor.

Decerebrate versus decorticate posturing :

Red nucleus is located in mid brain.

Rubrospinal tract orginates from red nucleus.

All extrapyramidal → produce extension except Rubrospinal fibre causing flexion of upperlimb.

Lesion above red nucleus :

Rubrospinal tract intact.

Upperlimb in flexion , Lowerlimb in extension → Decorticate posture.

Lesion below red nucleus :

Extension of upper limb and lower limb → Decerebrate posturing.

UMN versus LMN :

In UMN lesion, upper part of face is preserved.

In severe UMN lesion, partial (50%) fibres is lost.

In LMN lesion, upper part of face frowning is lost.

Upper part of face receives from bilateral side.

Lower part of face received from unilateral side.

Taste is lost in LMN lesion, but is preserved in UMN lesion.

Emotional volitional dissociation is a feature of UMN lesion.

Both emotional and volitional is affected in LMN lesion as from pons facial nerve carries both.

In volitional (voluntary) to smile :

Cortex → Internal capsule → Pontine nucleus.

Active space

Autonomic smile :

Frontal lobe → thalamus → pons.

Emotional fibres are unaffected.

Patient on spontaneous smile no deviation is seen but involuntary smile deviation can be appreciated.

Bell's phenomenon :

Is a normal phenomenon.

On closing eyes → orbicularis oculi and elevators of eyeballs are activated at same time → eyeballs move upward.

It is exaggerated in LMN lesion as more power required to close eyeball hence more power provided to elevators.

Bulbar vs pseudobulbar :

Bulbar : LMN lesion affecting cranial nerves where bilateral CBT to brainstem nucleus is damaged.

Pseudobulbar :

UMN lesion (B/L corticobulbar fibres).

	Bulbar	Pseudobulbar
LMN	Nasal twang.	Aspirate on swallow.
	Hoarseness.	-
	Nasal regurgitation.	-
	Flaccid dysarthria.	Spastic dysarthria.
Reflex	Palate : Absent.	Decreased.
	Gag : Absent.	Exaggerated.
	Jaw jerk : Absent/ normal.	Exaggerated (due to mesencephalic nucleus hyperactivation).
emotional	-	Psedobulbar effect.

Bifacial facial nerve is involved in :

1. GBS, porphyria.
2. Leprosy /Lymes/cmv.
3. Sarcoid.
4. Amylodosis.
5. moebius syndrome : 6^{th} + 7^{th}.
6. Bilaterall bells palsy.
7. myasthenia, botulism.
8. FSHD, myotonic dystrophy.

Active space

NEUROBIOLOGY OF SLEEP

Consciousness 00:01:50

Consiousness has 2 parts :

1. Arousal system : Person can respond to external stimulus.
   It is maintained by 2 structures ;
   - Ascending reticular activating system.
   - Thalamus.
2. Content of Consiousness :
   It is maintained by :
   Cortex .
   Thalamus.

Arousal response :

Is a primitive response needed for survival.
Any response for survival comes from the brain stem, sub-cortical structures like thalamus and basal ganglia.
Autonomic survivals for flight and fight response is regulated by the hypothalamic limbic system but orignates from the autonomic nucleus in the brain stem.
The conscious content in a new born baby is minimal. It improves over time with the maturity of the cortex.

Ascending reticular activating system (ARAS) 00:05:18

Reticular activating system are large number of nucleus which is located in the brain stem, predominantly in the pons.
It sends connection upwards to the sub-cortical structures.
This is called as ARAS.
Simultaneously, it sends connection downwards to the spinal cord motor neurons. It goes via the medulla or the pons.
medullary : Lateral and inhibitory.
Pontine : medial and stimulatory.

Thalamus :
It is the gateway to the brain.
All the inputs from the peripheral system travels via the thalamus.
It has multiple nucleus : Anterior nucleus, dorsomedial nucleus, ventrolateral nucleus.
Different inputs come through different nucleus, and these are projected to the cortex.
This is known as thalamocortical pathway.
It is an activating pathway and maintains concsiousness.

The nucleus reticularis thalamus (NRT) :
Specific role.
The only nucleus in thalamus which is inhibitory and does not project the inputs to the cortex.
The inputs are projected to other thalamic nucleus.
As it inhitbits the thalamus; the thalamocortical activation fails, producing sleep or decrease in arousal.
EEG shows synchronisation : The different areas in the brain have similar morphology and frequency (same wave pattern).

ARAD :

1. ARAS inhibit NRT.
   Thalamus activates the cortex.
   As a result of which, the person is awake.
   EEG shows desynchronisation.
2. ARAS also has an extrathalamic pathway.
   This projects to the Basal forebrain and Hypothalamus.

Basal forebrain 00:14:40

In the basal area of the brain near the anterior perforating substance there are certain nucleus (grey matter).
Basal forbrain is the collection of different types of nucleus.
For example: nucleus Accubens, nucleus basalis of meynret, diagonal band of Broca.
There are 3 neurotrsansmitters in the basal forebrain;

- Acetylcholine (most important).
- Adenosine.
- GABA/Glutamate.

Cholinergic neurons in the basal forebrain activate the cortex.
This is significant as in the case of Alzheimer's diesease and dementia, as the basal forbrain gets damaged.
When the basal forebrain neurons are less, the cortical activation is decreased.
This decreased cortical function is portrayed as cognitive impairment or dementia.
Cholinergic drugs (Donepezil, memantine) are used to improve cognitive function.
Hypothalamus secretes a hormone called Orexin.
It plays a major role in awakeness.
It activates the wake promoting regions located in the ARAS.
Simultaneously it acitvates REM off areas.

Arousal system

00:24:10

ARAS : Thalamic and extra thalamic.
Extra thalamic : Activate basal forebrain and posterior hypothalamus.
Hypothalamus produces orexin and histamine.
It containts NRT, Thalamus, ARAS.
NRT inhibits thalamus producing sleep.

Wake promoting systems :
These include :
1. Non-adrenergic (orginates from locus coeruleus).
2. Seratonergic (orginates from Raphae magnus) :
   The raphae magnus nucleus has dorsal raphea and caudal raphae.
   The dorsal raphae will go to the brain for upward circuit and activation.
   The caudal raphae decends to the spinal cord to prodcue motor activity with arousal.
3. Dopaminergic (orginates from ventrolateral periaqueductal

Active space

gray / ventral tegmental area).
From the ventral tegmental area in the midbrain, the neurons will ascend to the cortex to form the mesolimbic and mesocortical pathway. This is formed by dopamine.
The mesocortical goes from the tegmentum to the cortex to activate the cortex. The mesolimbic goes to the limbic areas (behavioural response).
The ventrotegmental pathway is affected in dementia.
The mesocortical and mesolimbic system is involved in the reward pathway.

4. Glutamtatergic (orginates from parabrachial nucleus).
5. Cholinergic (orginates from laterodorsal tegmentum and pedunculopontine nucleus) :
   Activates REM sleep.
   But in general wakefullness.
   Pedunculopontine nucleus is involved in the gait system.
6. Orexinergic : Orexin hypocretin system (secreted from lateral hypothalamus).
   It is a major neurotransmitter involved in wakefullness.
   Orexin production is stimulated by ARAS.
7. Histaminergic neurons (located in the tuberomammillary nucleus of the hypothalamus).
8. Others : REM OFF, SCN (Suprachiasmastic nucleus).

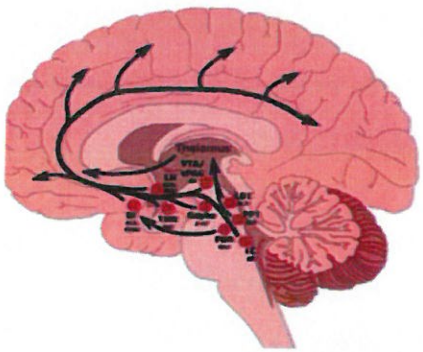
Sleep promoting systems

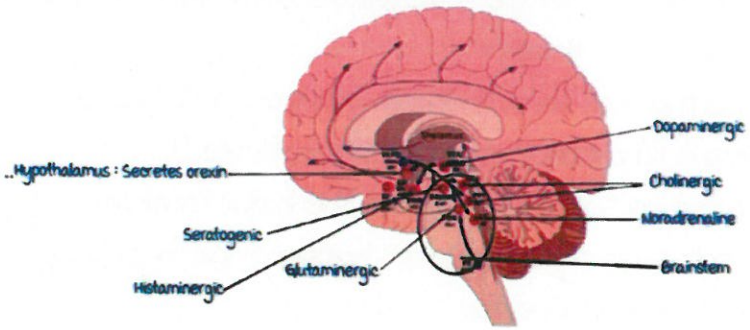
00:30:58

1. Ventrolateral preoptic nucleus (VLPO) of hypothalamus.
   Hypothalamus is involved in sleep and arousal.
   VLPO secretes GABA and galanine.
   Both are inhibitory.
2. Parafacial nucleus (PZ) located in the brain stem.
   It secretes GABA.
3. Others : REM ON, melatonin.
   The sleep promoting areas and wake promoting areas are interlinked.

Active space

Sleep wake switch : Here when the activation of one side is slightly stronge, the weaker side has increased inhibition thus further tipping the balance towards the stronger side.This flipflop switch allows for rapid state transitions.





REM on and off

00:47:52

In wakefullness :

REM on :

There are certain areas called REM on which will switch on REM sleep.

This includes sub-locus cerleus which produces REM sleep.

REM off :

This area will inhibit the REM on area.

Consists of VPLAG and LDT.

Orexin :

Activates the wake promoting area.

The orexin is secreted by the stimulation of ARAS in the hypothalamus.

It inhibits REM.

In cataplexy, orexin is less.

Active space

Leave Feedback

In sleep :

VLPO : When this is activated, it inhibits wake promoting areas, as a result of which ARAS is inhibited and orexin secretion is decreased.

Indirectly and directly it inhibits REM of neurons.

Initial sleep is NREM.

As the sleep progresses, orexin and ARAS activation further decreases leading to REM sleep.

There are 2 swtiches :

1. Sleep-wake switch.
2. NREM and REM swtich.

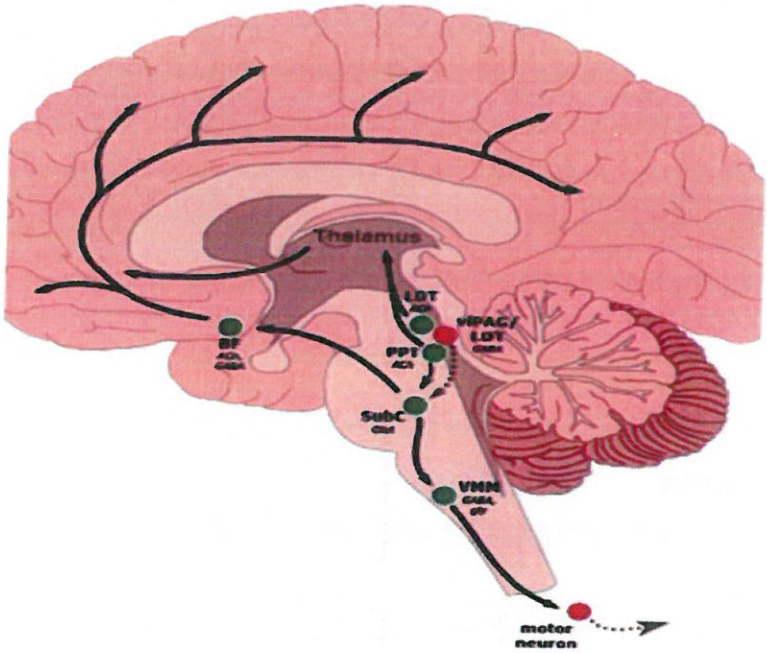
When the REM on centre is activated , REM sleep is initiated which results in 2 things :

1. The REM on will send an input upwards to the basal forebrain (cholinergic neurons are activated).
   When the cortex is activated in the basal forebrain by the cholinergic system causes hypnopompic/hypnagogic hallucinations or dreams.
2. It will send a stimulus to the spinal cord motor neurons either directly or indirectly.
   Inhibition to the spinal cord produces REM atony.
   In cases where atony is absent during REM sleep, the person starts enacting the dreams (as the muscles do not get paralysed).
   This is known as REM sleep behavioural disorder (RBD).
   In cases where the orexin production is decreased, there will be :
   - Decreased sleep latency.
   - Decreased REM latency.
   - Sleep attack / Narcolepsy.

The REM on neurons are inhibited by REM off.

REM off is indirectly under the control of VLPO and orexin system.

Active space



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NEUROBIOLOGY OF SLEEP II

Circadian rhythm / Process C 00:01:15

It maintained mainly by suprachiasmatic nucleus (SCN) of hypothalamus.
It inhibits superior cervical ganglion.
The superior cervical ganglion usually produces noradrenergic input to the pineal gland.
Pineal gland produces melatonin which in turn stimulates sleep.
When light falls on the eyes (retina), the retinohypothalamic tract will activate the SCN (wake promoting area) which inhibit the superior cervical ganglion.
As a result, wake response is activated.

On the contrary, in the dark the SCN is not activated, melatonin is produced and induces sleep via venterolateral preoptic nucleus.
The normal circadian rythym has melatonin surge at 3-5 am (maximum surge) and 3-5pm (mild stimulation).

Homeostatic processes 00:05:37

As the arousal time increases, sleep debt will increase.
This is will cause increase secretion of adenosine (secreted in the basal forebrain) which will activate venterolateral preoptic area which will induce sleep.

Other factors like temperature, or core temperature, sleep, appetite, mood chnages also modulate the SCN.
mood modulation is controled by the dorsal raphae of serotinergic system.
mood asscciated insomnia can be treated with Gaba-agonists like benzodiazepines or serotinergics.

Active space

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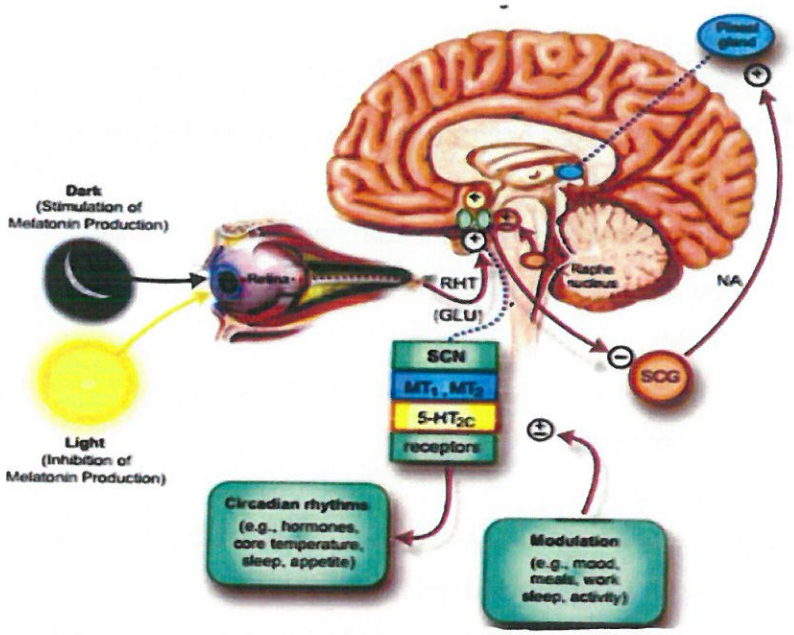

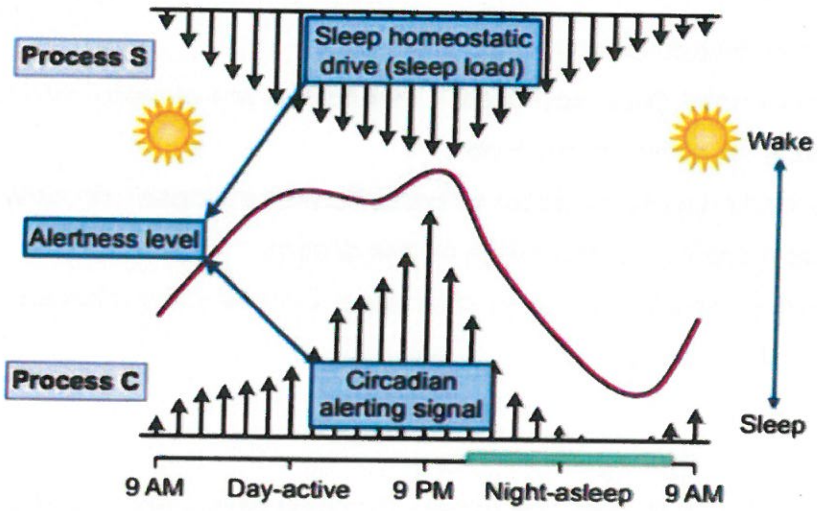

Homeostatic process (process S) :
maintains the length and depth of sleep.
N1, N2, N5 maintained by process S.
Circadian rythyms (process C) :
Internal organisation, timing and duration of daily sleep/wake cycle.

NREM sleep

00:11:54

The sleep is induced by the venterolateral pre-optic (VLPO)

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activation.
VLPO is under the activation of circadian rythym or homeostatic process.
The wake promoting areas like orexin will inhibit the VLPO.
Orexin activate REM off.
When the VLPO is activated it will inhbit ARAS (wake promoting areas) and REM OFF neurons. This is the Sleep wake switch.
When ARAS is not active, orexin concentration decreases and NRT is uninhibited.
Synchronised EEG.
As a result, it produces NREM sleep and slowly switch REM sleep. This is the NREM-REM swtich.
After a while when the wake promoting system is stronger it will inhibit VLPO and result in wakefullness.

REM ON activation :
When REM ON is activated it inhibits the spinal motor neurons causing atonia in the limbs.
Acending glutamatergic to basal forebrain causes dreams.
REM atonia, no enactaion of the dream.
80% of dreams occur in REM sleep. (can be remembered once awake).

1. Orexin dysregulation :
- Orexin activates the wake promoting areas and REM OFF.
- Latency of REM sleep decreased.
- Sudden sleep while walking - Sleep attack.
- Sleep Paralysis.
- Seen in narcolepsy cataplexy syndrome.

2. Abscence of atonia in REM.
- Enacting dreams. (REM behavioural disorders).

Dreams

00:19:51

80% dreams occur in REM.
REM :
- Basal forbrain activation.

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- Highly emotionally charged complex and bizzare dreams.
- RBD.

NREM : realistic and rational.

Awakening from REM : generally oriented.

Awakening from NREM : Disoriented and confused.

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00

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SLEEP CYCLE

Sleep cycle

00:00:25

One sleep cycle lasts for 90–100 minutes.

There are 4–6 cyles per sleep.

It is initially NREM which then progresses to REM.

1st two cycle N3 predominates.

Last 3rd of sleep is dominated by REM.

80% dreams in REM.

It can be classified into :

N1.

N2.

N3.

REM sleep.

It can be recognised on a polysonography.

While a person is awake, there will be alpha waves 8–13 hz frequency (posterior).

Once the person is drowsy the alpha wave freqeuncy decreases.

1. Then it progresses to N1, where alpha is <50% in one Epoch (30sec) +/- vertex waves, beta or theta waves.
2. N2 phase is charecterised by K complex and spindle.
   <20% slow waves.
   Vertex may continue.
3. N3 is known as slow wave sleep. Here delta waves are seen and the amplitude is >75 microvolt & <2 Hz frequency in each Epoch.
   It occupies >20 %.
   Vertex may be present.
4. REM :
   Rapid eye movements.
   Saw tooth waves.
   Chin EMG tone is minimal.

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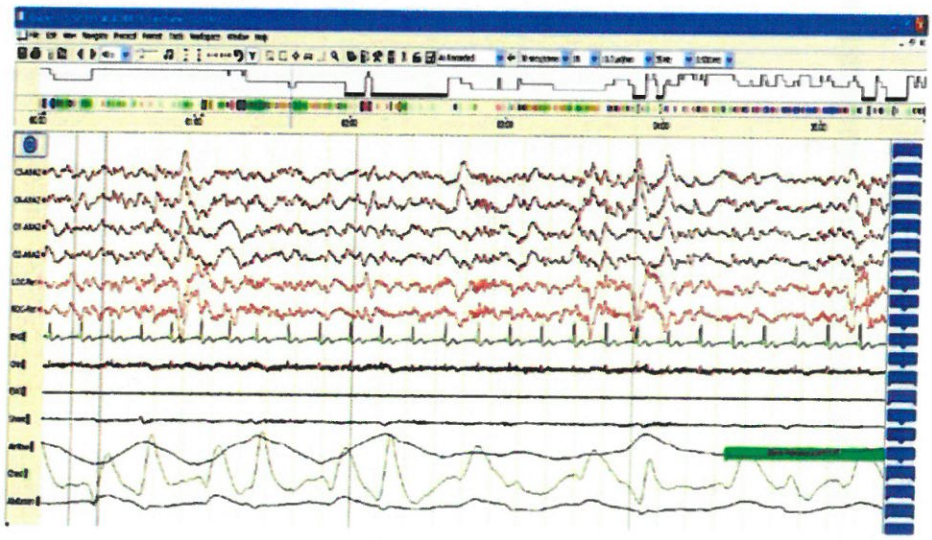
Sleep Stage Nomenclature		
	R&K	AASM
Wake	Stage W	Stage W
NREM	Stage 1 Stage 2 Stage 3 Stage 4	Stage N1 Stage N2 Stage N3
REM	Stage REM	Stage R

AASM = American Academy of Sleep Medicine[2]; NREM = non-rapid eye movement; R&K = Rechtschaffen and Kales A[1]; REM = rapid eye movement; stages 3 and 4 are combined into stage N3.

Waves of EEG

00:10:12

1. Beta waves : > 13 Hz.
2. Alpha wave : 8-13 Hz.
3. Theta waves : 4-7.99Hz.
4. Delta waves : 0-3.99 Hz.
5. Slow waves : 0.5-2 Hz and amplitude >75 microvolt. Seen in N3 phase of sleep.



Polysonography measures :

EEG.

ECG.

EOG.

EMG : Chin and limb.

Snoring sensor.

Chest movement.

Abdominal movement.

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Air flow sensor.

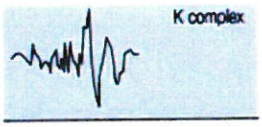
Saturation.

Plethysmography.

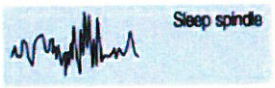
Body position.

Pulse rate.

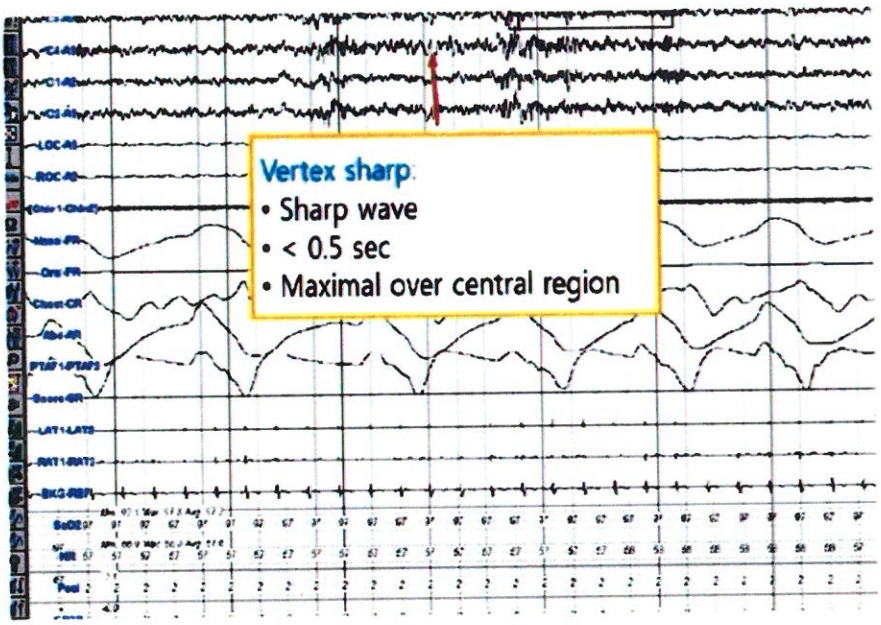
Sharply contoured, negative bursts most in central leads



Negative sharp wave followed by a positive component duration ≥0.5 seconds,maximal in over the frontal regions



burst of 11–16 Hz prominent in central leads last for 0.5–1.5 seconds.



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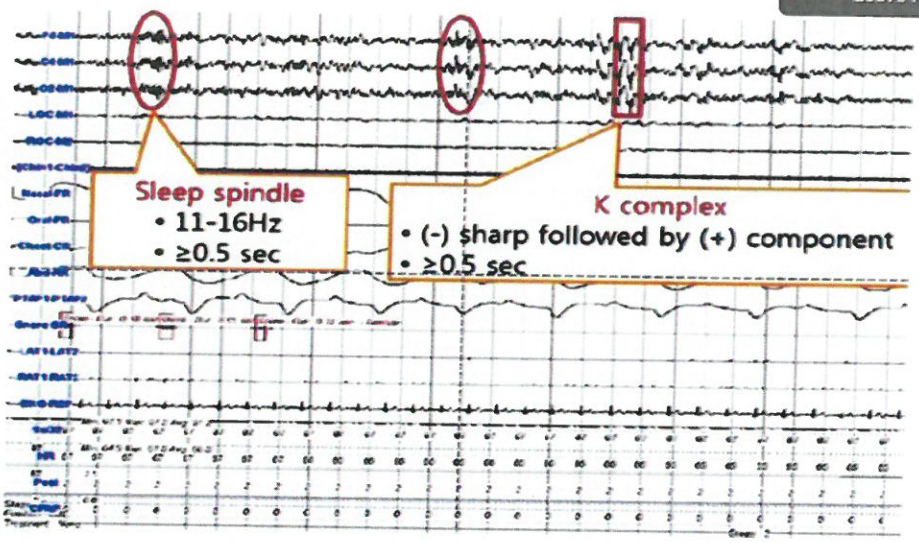

Phases of sleep and its charecterstics 00:19:40

1. NI sleep :
   - <50% alpha.
   - Vertex waves towards end of N 1.
   - EMG decrease, slow rolling eye movement.

2. N2 :
   - 10-12 min after onset.
   - Sleep spindles and K complex.
   - Slow wave appear but <20%.

3. N3 :
   - Slow wave 20-100%.

4. REM :
   - 60-90 min of onset first REM noted.
   - Saw toothed waves : Sharply contoured or triangular.
   - 2-6Hz waves.
   - Maximal in amplitude over the central region.
   - Rapid eye movements (REMs) : EOG.
   - Low chin EMG tone.
   - Transient muscle activity : Superimposed on low EMG tone.

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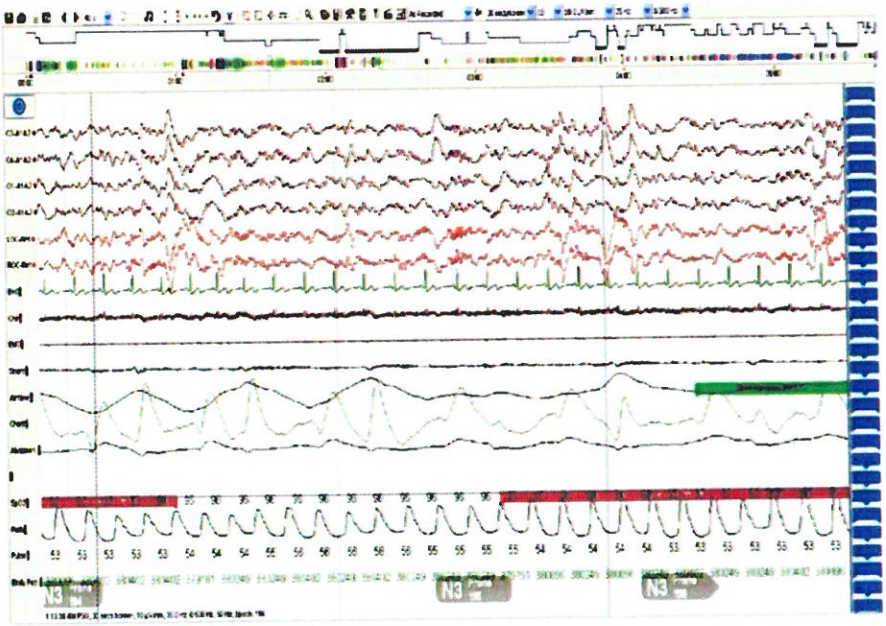

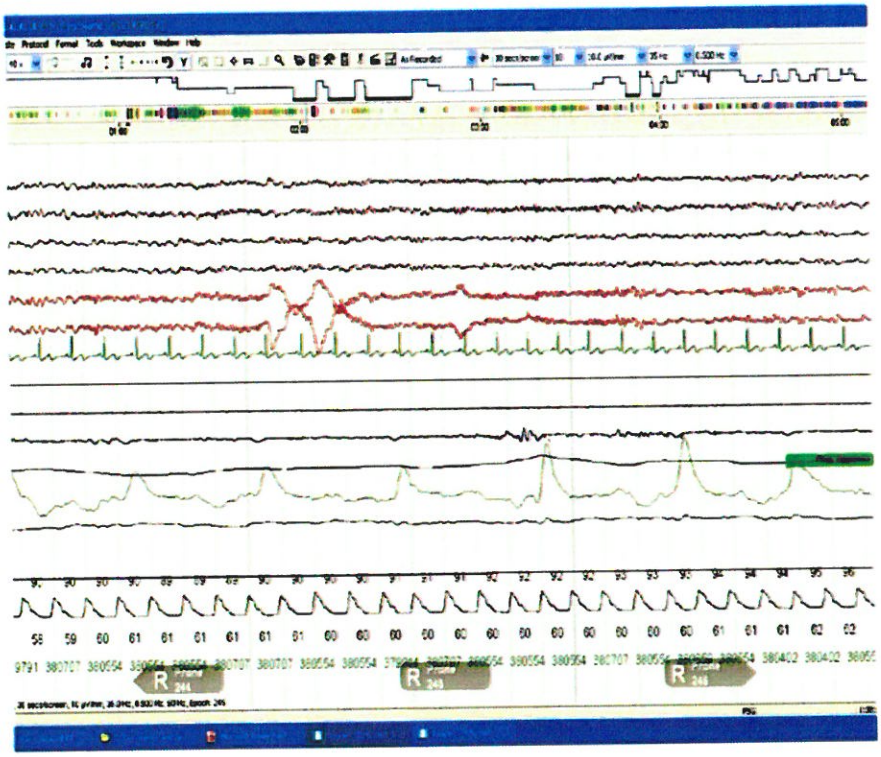

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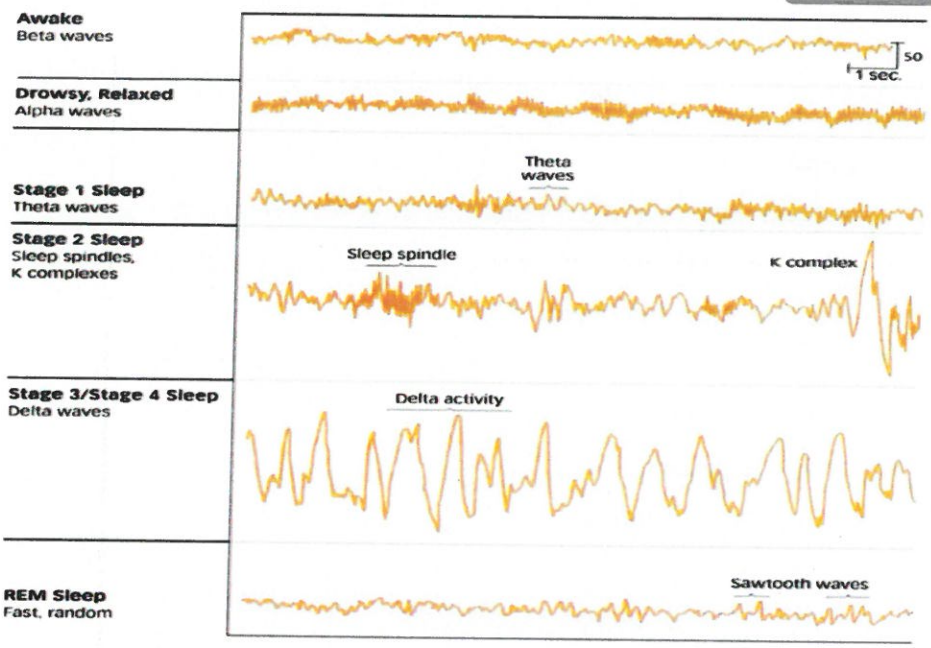
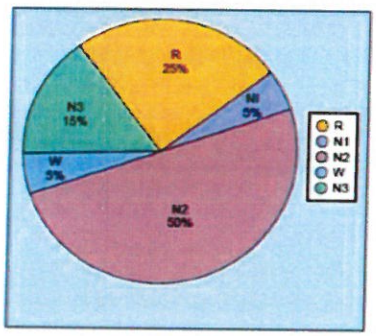
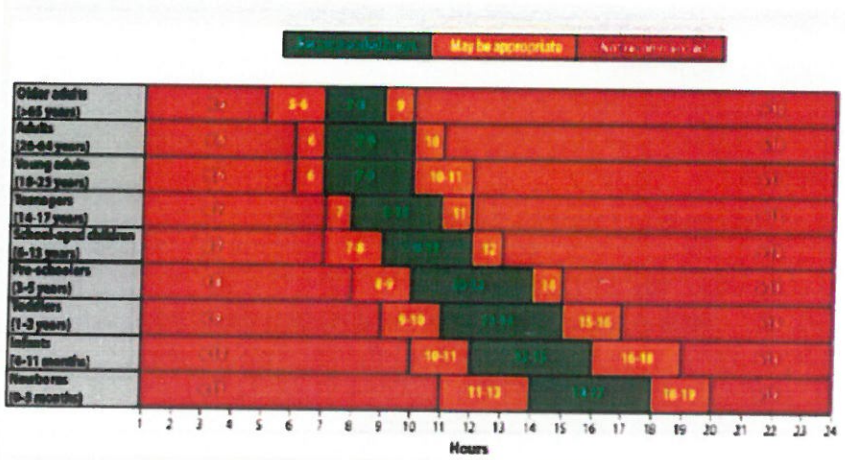




Sleep state	% sleep time
NREM sleep	75–80
N1	3–8
N2	45–55
N3	13–23
REM sleep (stage R)	20–25
Tonic stage	Continuous
Phasic stage	Intermittent



Active space

SLEEP DISORDERS I

Case :

51 year old male, had episodes of awakening from sleep at night. He felt as if his head is exploding and a loud blast happened in his head.

Sleep disorders :

1. Insomnia.
2. Hypersomnia.
3. Parasomnia.
4. Circadian sleep disorders.
5. Sleep associated with movement disorders.
6. Sleep associated with breathing disorders.
7. Other disorders.

Insomnia

00:03:37

Acute insomnia :

<3 months.

Causes :

- Stress.
- Environmental factors.
- Illness.
- Stimulants.

Chronic insomnia :

>3 months.

Causes :

- Idiopathic : starts during childhood.
- Psychogenic. : Patient is anxious about his sleep. This does not include psychiatric disorders.
- Poor sleep hygiene : Patient complains of insomnia despite sleeping adequetly.
- Paradoxical insomnia : very common
- Other chronic disorders :
  1. medical disorders.

2. Neurological disorders.
3. Psychiaatric disorders .
4. Substance abuse.

Insomnia management

00:13:16

Sleep hygiene.
Early hours the person should stay active.
Avoid lying on the bed during the morning time.
Hot water bath and wear comfortable clothes.
Avoid bright light : bright light can activate hypothalamic pathway and inhibit melatonin.
Decrease screen time before sleep.
Reading helps to induce sleep.

Drug treatment :
The sleep promoting areas :

- They are VLPO and PZ (parafascial zone).
- These 2 predominently prodcue GABA.
- Insomnia occurs if there is decrease production of GABA.

Wake promoting centres :

- Awareness is provided by the ARAS.
- ARAS activate extra thalamic and thalamic which inturn activate the hypothalamus and basal forebrain.
- The hypothalamus secretes major 2 hormones.
- Orexin and Histamine (produced by tuberomammary nucleus).

Aim of drug therapy is to

- Increase GABA inhibition :
  1. Benzodiazepines :
  Can be addictive.
  Benzodiazepine Receptor agonist :
  Examples : Eszopiclone, Zolpidem, Zalepon.
  Benzodiazepine agonist :
  Temazepam, Triazolam.

2. Newer drugs that are not addictive like ; zolpidem.
3. Ramelteon : receptor agonist of melatonin.

- Suppress wake promoting centres :
  Suvorexant : orexin antagonist.
  Heterocyclics (anti-histaminergic) : Doxepin, Trazodone.

Hypersomnia

00:20:04

Case :

- 15 year old girl with c/o one episode of right upper limb weakness which spontaneously improved in about 1-2 minutes.
- She changed her school recently due to her poor performance.
- She also has a history of quarrel with one of her friends followed by which her water bottle fell from her right hand.
- Inability to move the hand for a few minutes and then recovered.
- Her teacher often complains that she seems disinterested in her class.
- She was also taken to a psychologist in her school.
- She had frequent history of dropping her pen more frequently from her right hand.
- She found difficulty to follow the class.
- Detailed history revealed she had excessive day time sleepiness and would feel fresh even if its a short nap.
- MRI : Normal.
- EEG : Normal.

Pathophysiology :
Orexin is activated by the ascending reticular formation via the extra thalamic pathway
Orexin activates the wake promoting particulary locus coeruleus.
Simulataneously it also activates REM OFF neurons.
The REM OFF neurons inhibits the REM ON.

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There is overactivation of the wake promoting area.
The VLPO is the major centre of sleep.
VLPO activatation produces NREM sleep.
As the sleep progresses, the inhibition of VLPO on REM OFF is slowly and readily increasing.
The VLPO also inhibits all the wake promoting areas.
After few minutes to hours of sleep the REM OFF is completely inhibited and activation of REM on takes place.

If there is a dysfunctioning orexin ;

- The wake areas do not get activated properly.

REM off is not getting stimulates as a result of which REM on gets activated prematurely. This is known as decrease latency of sleep. (person experiences sudden attacks of sleep).

- Decrease latency of REM sleep or Sleep onset REM period of sleep. This is known as sleep attacks or narcolepsy.

In REM sleep, it goes upwards to the basal forebrain to activate the cholinergic system in the basal forebrain to produce hallucinations or dreams. The cholinergics which are located in the lateral dorsal pontine areas, activate a centre in the medulla called medullary reticular formation. This inhibits the muscles in the lower limbs causing atony. These are the events that occur in REM sleep.

1.If the upward pathway is overactivated it produces hallucinations known as sleep onset hallucinations or hypnogogic hallucinations (before the onset of sleep).
Normally, while a person is walking the ARAS gets activated which inturn activates orexin. This orexin inhibits the REM sleep and prevent REM atonia.

If the downwards pathway is overactivated :
2. Cataplexy can be unilateral or focal or multifocal.
Classiclaly, cataplexy lasts for 1-2 mins.
Triggered by positive emotions :
Emotion activates cholinergic pathyway in the pons ⟶

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activate medullary reticular formation ⟶ produce atony.
⟶ Dysregulation of REM sleep.
3. Sleep paralysis :
Person has a paralysed limb while waking up from sleep.
Lasts for 15-20 mins.
4. Narcolepsy or sleep attacks.
Short refreshing naps.
These four forms the Narcolepsy cataplexy tetrad.

Automatic behavior and disturbed sleep in the Narcolepsy cataplexy syndrome.

Narcolepsy - Cataplexy syndrome 00:33:31

They are 2 types.
Narcolepsy I :
It is associated with decrease hypocretin ; <110pg/m.
Has narcolepsy / cataplexy.
Narcolepsy II :
Here hypocretin is normal.
Only narcolepsy.

Causes :

- Genetic associations :
  1. Hypocretin receptor 2.
  2. HLA factors : HLADQB1 association is 100% in Narcolepsy type I.
  3. Pre-pro hypocretin gene.
- Autoimmune response against the neurons that produce hypocretin.
- Narcolepsy associated stroke.

multiple sleep latency test :
In this test the patient takes multiple short naps.
From the time of lying down to sleep to the onset of sleep is known as latency of sleep. Seen in both types.
Latency of sleep is (normally 10-15) : </=8mins or

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