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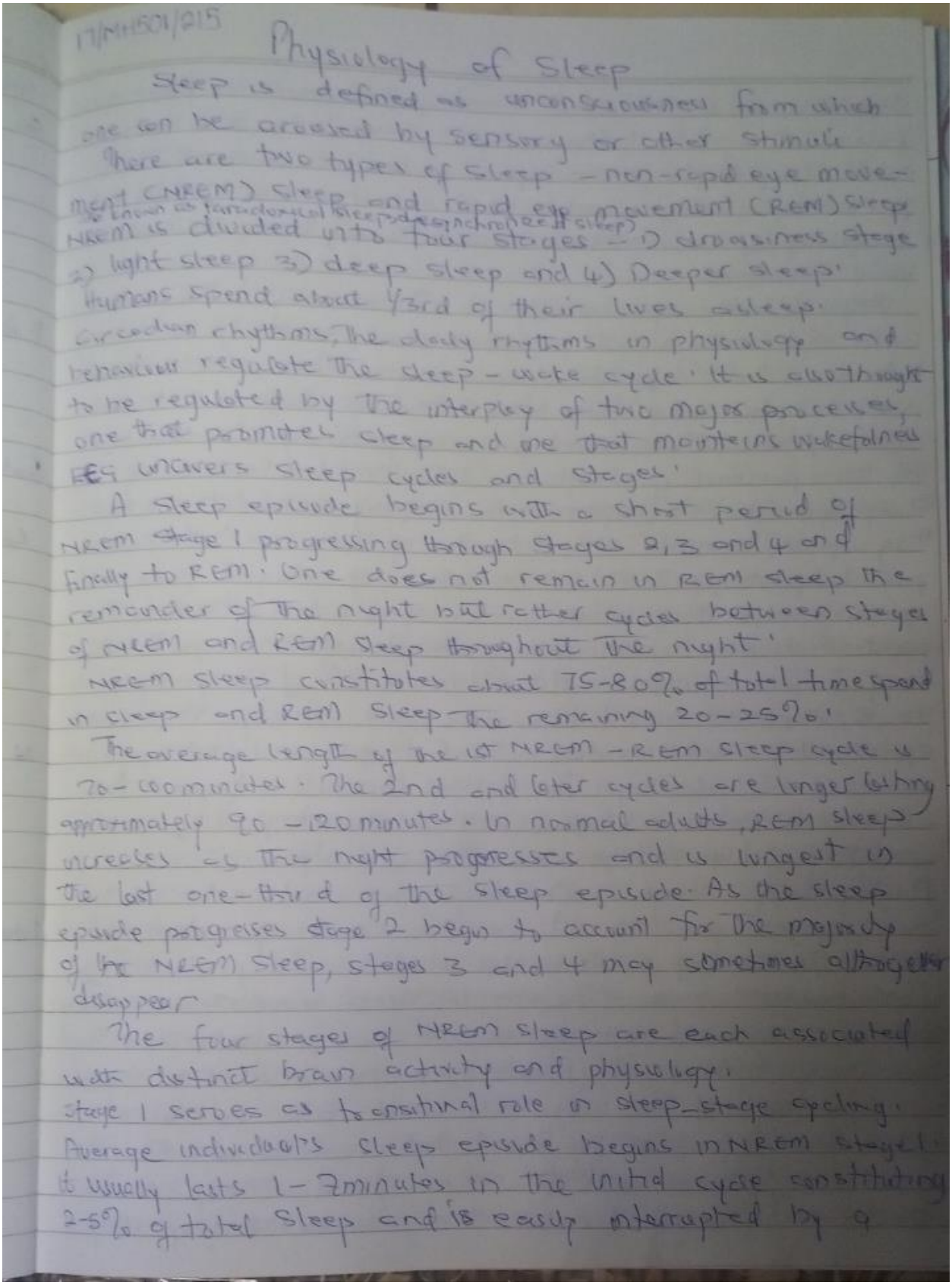

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Physiology of Sleep

Sleep is defined as unconsciousness from which one can be aroused by sensory or other stimuli. There are two types of sleep - non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep (known as paradoxical sleep or desynchronized sleep). NREM is divided into four stages - 1) drowsiness stage 2) light sleep 3) deep sleep and 4) Deeper sleep. Humans spend about 1/3rd of their lives asleep. Circadian rhythms, the daily rhythms in physiology and behaviour regulate the sleep-wake cycle. It is also thought to be regulated by the interplay of two major processes, one that promotes sleep and one that maintains wakefulness. EEG recovers sleep cycles and stages.

A sleep episode begins with a short period of NREM stage 1 progressing through stages 2, 3 and 4 and finally to REM. One does not remain in REM sleep the remainder of the night but rather cycles between stages of NREM and REM sleep throughout the night.

NREM sleep constitutes about 75-80% of total time spent in sleep and REM sleep the remaining 20-25%.

The average length of the 1st NREM - REM sleep cycle is 70-100 minutes. The 2nd and later cycles are longer lasting approximately 90 - 120 minutes. In normal adults, REM sleep increases as the night progresses and is longest in the last one-third of the sleep episode. As the sleep episode progresses stage 2 begin to account for the majority of the NREM sleep, stages 3 and 4 may sometimes altogether disappear.

The four stages of NREM sleep are each associated with distinct brain activity and physiology.

Stage 1 serves as transitional role in sleep-stage cycling. Average individual's sleep episode begins in NREM stage 1. It usually lasts 1-7 minutes in the initial cycle constituting 2-5% of total sleep and is easily interrupted by a

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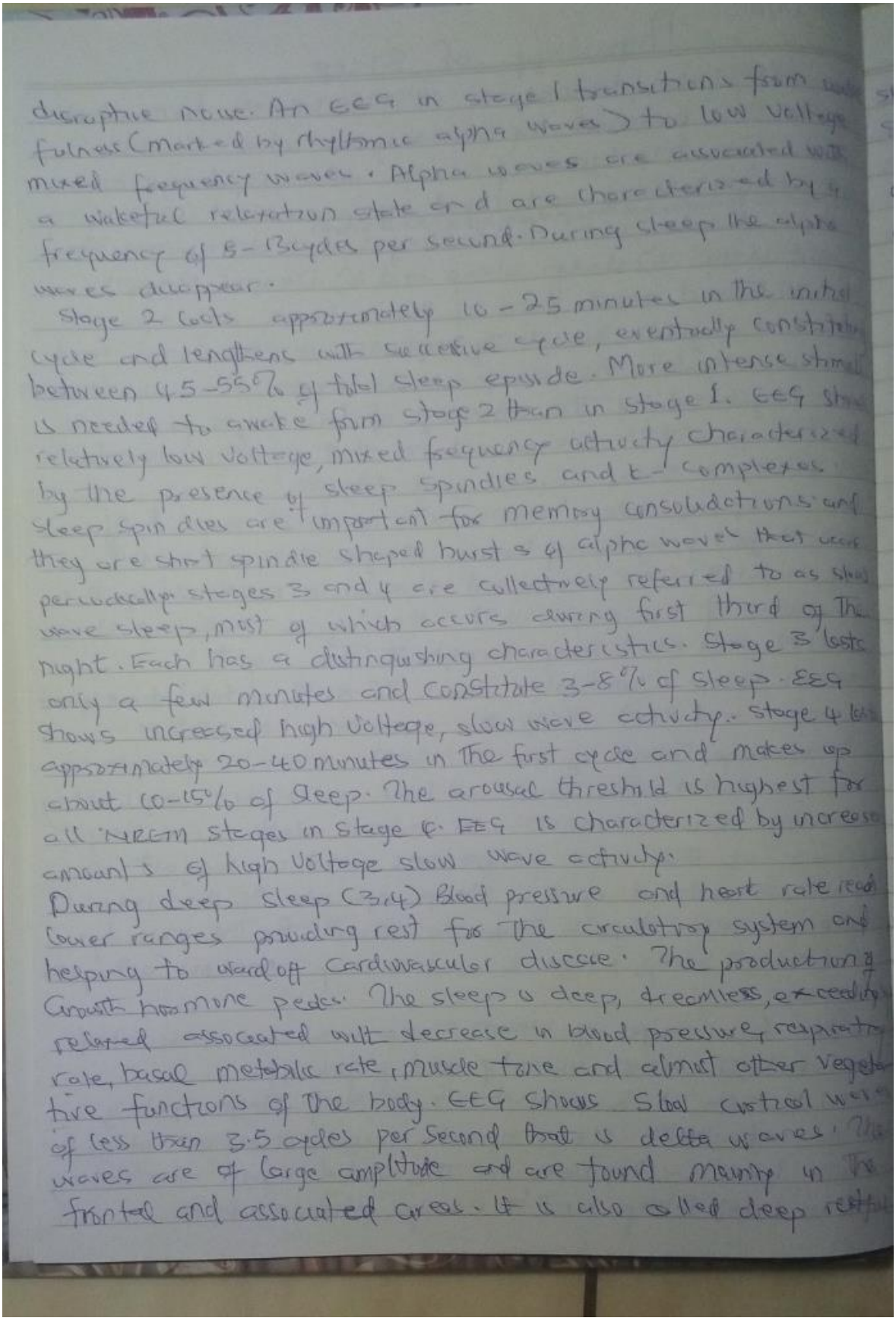

disruptive noise. An EEG in stage 1 transitions from wakefulness (marked by rhythmic alpha waves) to low voltage mixed frequency waves. Alpha waves are associated with a wakeful relaxation state and are characterized by a frequency of 8-13 cycles per second. During sleep the alpha waves disappear.

Stage 2 lasts approximately 10-25 minutes in the initial cycle and lengthens with successive cycle, eventually constituting between 45-55% of total sleep episode. More intense stimuli is needed to awake from stage 2 than in stage 1. EEG shows relatively low voltage, mixed frequency activity characterized by the presence of sleep spindles and K-complexes. Sleep spindles are important for memory consolidations and they are short spindle shaped bursts of alpha waves that occur periodically. stages 3 and 4 are collectively referred to as slow wave sleep, most of which occurs during first third of the night. Each has a distinguishing characteristics. Stage 3 lasts only a few minutes and constitute 3-8% of sleep. EEG shows increased high voltage, slow wave activity. stage 4 lasts approximately 20-40 minutes in the first cycle and makes up about 10-15% of sleep. The arousal threshold is highest for all NREM stages in stage 4. EEG is characterized by increased amounts of high voltage slow wave activity.

During deep sleep (3,4) Blood pressure and heart rate reach lower ranges providing rest for the circulatory system and helping to ward off cardiovascular disease. The production of Growth hormone peaks. The sleep is deep, dreamless, exceedingly relaxed associated with decrease in blood pressure, respiratory rate, basal metabolic rate, muscle tone and almost other vegetative functions of the body. EEG shows slow cortical waves of less than 3.5 cycles per second that is delta waves. These waves are of large amplitude and are found mainly in the frontal and associated areas. It is also called deep rest

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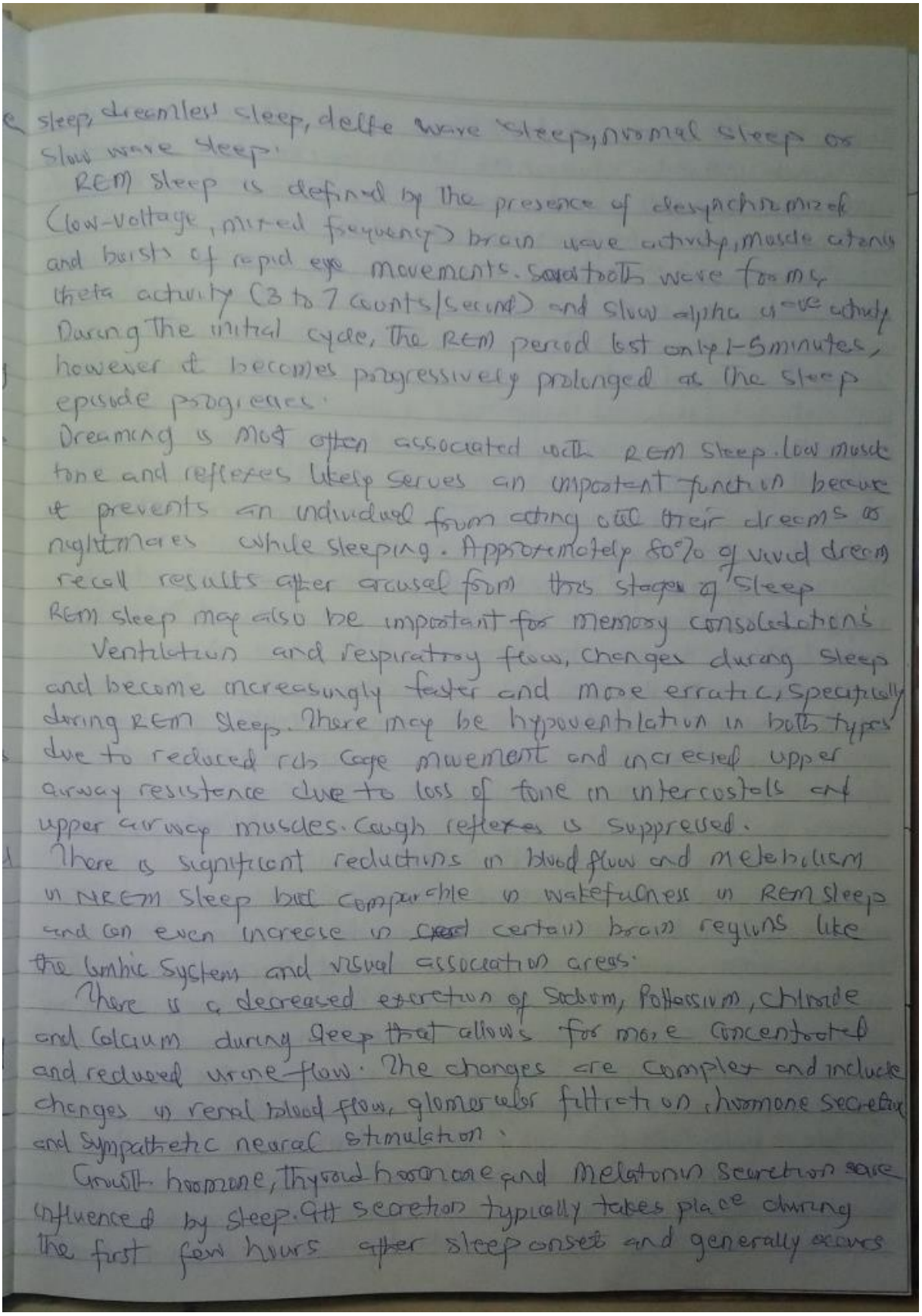

sleep, dreamless sleep, delta wave sleep, normal sleep or slow wave sleep.

REM sleep is defined by the presence of desynchronized (low-voltage, mixed frequency) brain wave activity, muscle atonia and bursts of rapid eye movements. Sawtooth wave forms, theta activity (3 to 7 counts/second) and slow alpha wave activity. During the initial cycle, the REM period last only 1-5 minutes, however it becomes progressively prolonged as the sleep episode progresses.

Dreaming is most often associated with REM sleep. Low muscle tone and reflexes likely serves an important function because it prevents an individual from acting out their dreams or nightmares while sleeping. Approximately 80% of vivid dream recall results after arousal from this stages of sleep. REM sleep may also be important for memory consolidations.

Ventilation and respiratory flow, changes during sleep and become increasingly faster and more erratic, specifically during REM sleep. There may be hypoventilation in both types due to reduced rib cage movement and increased upper airway resistance due to loss of tone in intercostals and upper airway muscles. Cough reflexes is suppressed.

There is significant reductions in blood flow and metabolism in NREM sleep but comparable in wakefulness in REM sleep and can even increase in certain brain regions like the limbic system and visual association areas.

There is a decreased excretion of Sodium, Potassium, Chloride and Calcium during sleep that allows for more concentrated and reduced urine flow. The changes are complex and include changes in renal blood flow, glomerular filtration, hormone secretion and sympathetic neural stimulation.

Growth hormone, thyroid hormone and Melatonin secretion are influenced by sleep. GH secretion typically takes place during the first few hours after sleep onset and generally occurs

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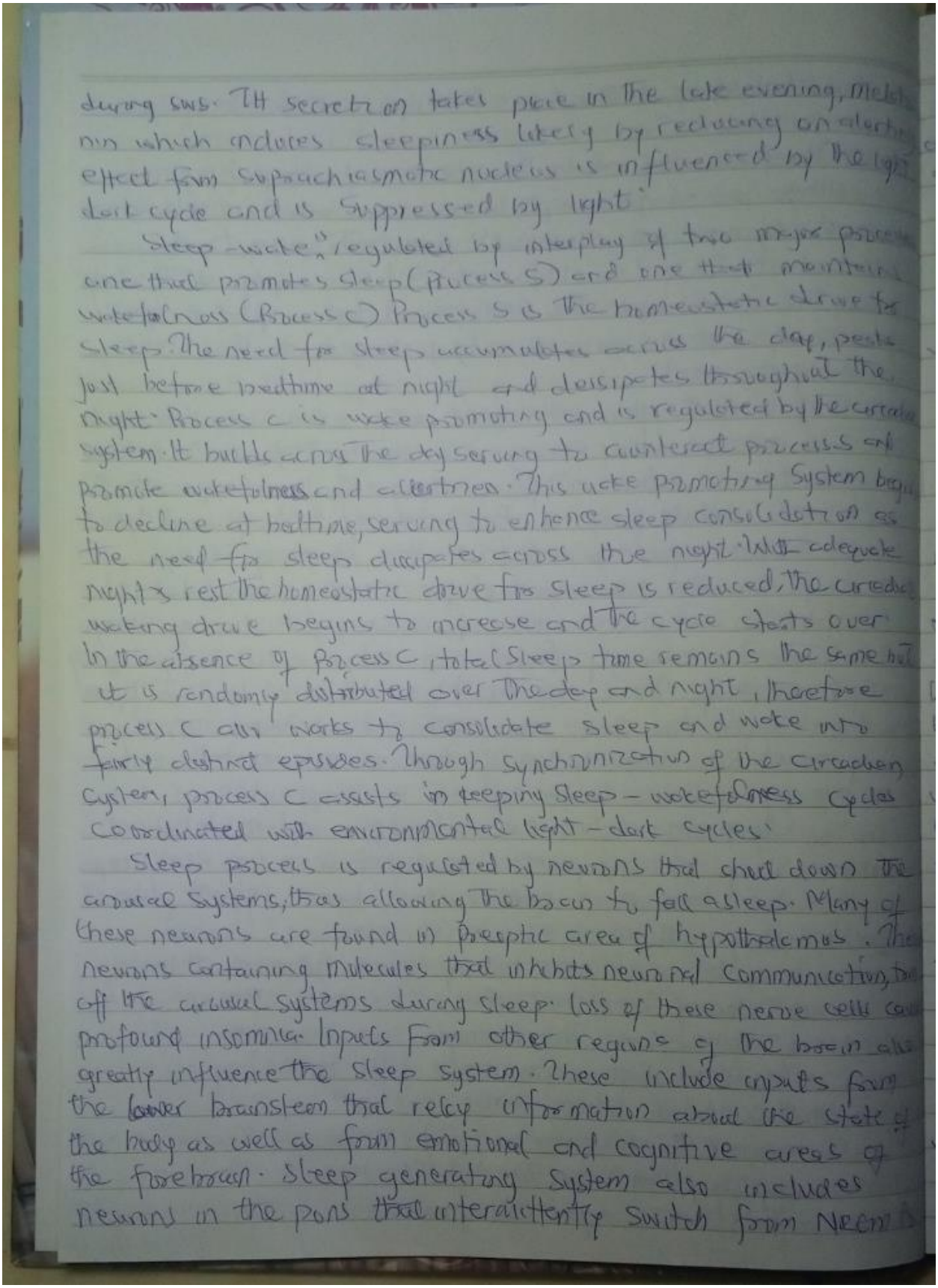

during sws. TH secretion takes place in the late evening, Melat
nin which induces sleepiness likely by reducing an alertn
effect from suprachiasmatic nucleus is influenced by the ligh
dark cycle and is suppressed by light.

Sleep-wake" regulated by interplay of two major proces
one that promotes sleep (Process S) and one that maintains
wakefulness (Process C) Process S is the homeostatic drive for
sleep. The need for sleep accumulates across the day, peaks
just before bedtime at night and dissipates throughout the
night. Process C is wake promoting and is regulated by the circadia
system. It builds across the day serving to counteract process S and
promote wakefulness and alertness. This wake promoting System begi
to decline at bedtime, serving to enhance sleep consolidation as
the need for sleep dissipates across the night. With adequate
night's rest the homeostatic drive for sleep is reduced, the circadia
waking drive begins to increase and the cycle starts over.
In the absence of Process C, total Sleep time remains the same but
it is randomly distributed over the day and night, therefore
process C also works to consolidate sleep and wake into
fairly distinct episodes. Through synchronization of the circadian
System, process C assists in keeping Sleep - wakefulness cycles
coordinated with environmental light - dark cycles.

Sleep process is regulated by neurons that shut down the
arousal systems, thus allowing the brain to fall asleep. Many of
these neurons are found in preoptic area of hypothalamus. The
neurons containing molecules that inhibits neuronal communication, to
off the arousal systems during sleep. loss of these nerve cells ca
profound insomnia. Inputs from other regions of the brain also
greatly influence the sleep system. These include inputs from
the lower brainstem that relay information about the state of
the body as well as from emotional and cognitive areas of
the forebrain. Sleep generating System also includes
neurons in the pons that intermittently switch from NREM

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REM sleep over the course of the night. These neurons send outputs to the lower brainstem and spinal cord that cause muscle atonia, REMS and chaotic autonomic activity that characterize REM sleep. Other outputs are sent to the forebrain including activation of cholinergic pathways to the thalamus to activate the EEG.

Wakefulness is generated by ascending arousal system from the brainstem that activates forebrain structures to maintain wakefulness. These ascending arousal care two major pathways that originates in the upper brainstem. The first takes origin from cholinergic neurons in upper pons and activates parts of the thalamus that are responsible for maintaining transmission of sensory information to the cerebral cortex. The second originates in cell groups in upper brainstem that contains monoamine neurotransmitters (norepinephrine, serotonin, dopamine, and histamine), enters the hypothalamus where it picks up inputs from nerve cells that contain peptides (orexin or hypocretin) and melanin concentrating hormone) These inputs then traverse the basal forebrain where they pick up additional inputs from cells containing acetylcholine and gamma-aminobutyric acid. All these inputs enter cerebral cortex where they diffusely activate the nerve cells and prepare them for the interpretation and analysis of incoming sensory information.

The falling phase of the body temperature at night and increase in heat loss promotes sleep onset and maintenance. There is a gradual increase in body temperature several hours before waking. The brain sends signals the other parts of the body that increase heat production and conservation in order to disrupt sleep and promote waking.

Sleep architecture changes continually and considerable with age. Sleep efficiency declines with age. Newborns sleep about 16-18hrs per day with three types of sleep - quiet sleep (similar to NREM sleep), active sleep (analogous to Rem sleep) and indeterminate sleep. By 2 months infants typically sleeps 14 to 15 hours per day with the majority

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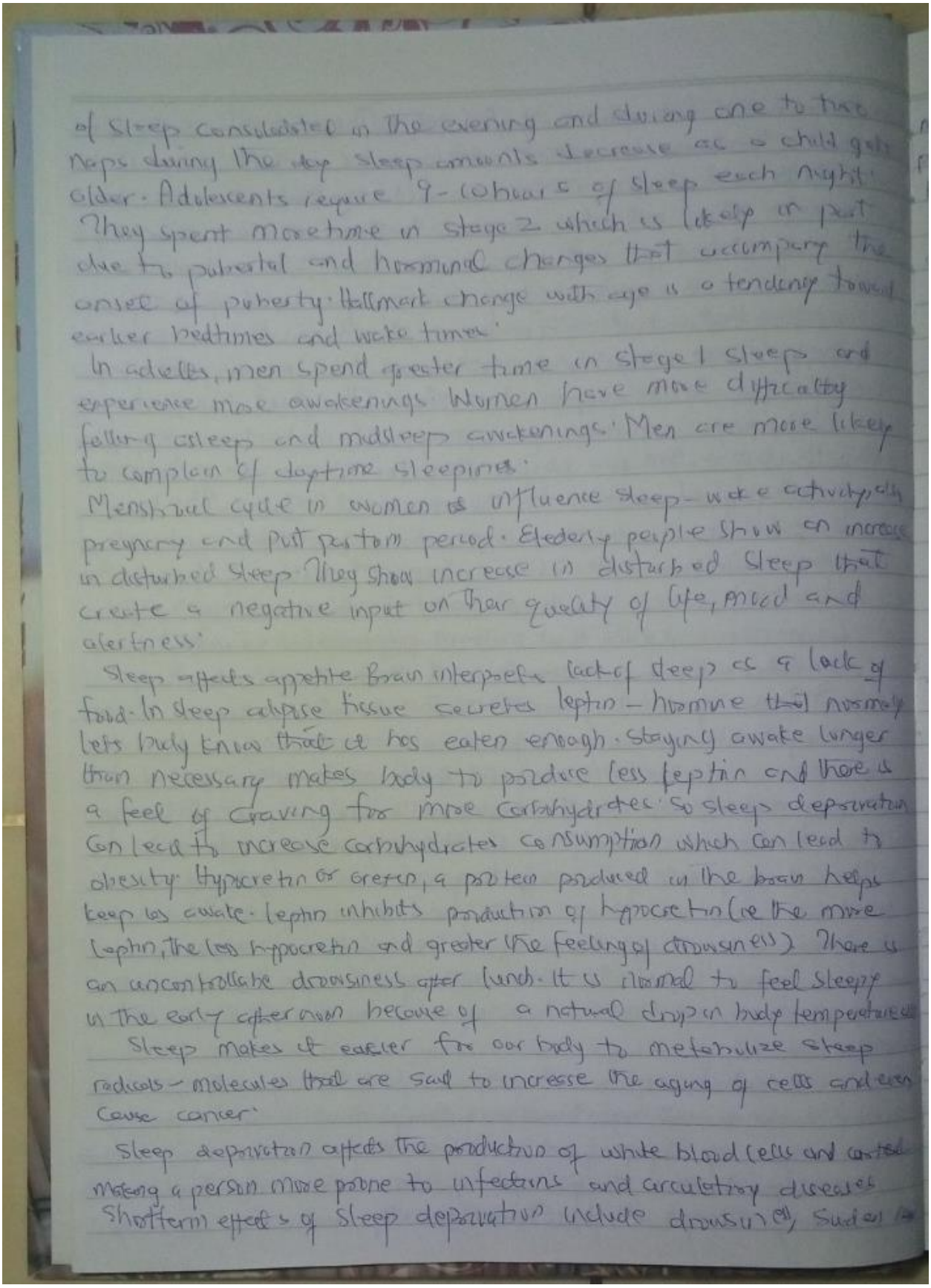

of sleep consolidated in the evening and during one to two naps during the day sleep amounts decrease as a child gets older. Adolescents require 9-10hours of sleep each night. They spent more time in stage 2 which is likely in part due to pubertal and hormonal changes that accompany the onset of puberty. Hallmark change with age is a tendency toward earlier bedtimes and wake times.

In adults, men spend greater time in stage 1 sleep and experience more awakenings. Women have more difficulty falling asleep and mid sleep awakenings. Men are more likely to complain of daytime sleepiness.

Menstrual cycle in women influence sleep - wake activity in pregnancy and post partum period. Elederly people show an increase in disturbed sleep. They show increase in disturbed sleep that create a negative input on their quality of life, mood and alertness.

Sleep affects appetite. Brain interprets lack of sleep as a lack of food. In sleep adipose tissue secretes leptin - hormone that normally lets body know that it has eaten enough. Staying awake longer than necessary makes body to produce less leptin and there is a feel of craving for more carbohydrates. So sleep deprivation can lead to increase carbohydrates consumption which can lead to obesity. Hypocretin or orexin, a protein produced in the brain helps keep us awake. Leptin inhibits production of hypocretin (ie the more leptin, the less hypocretin and greater the feeling of drowsiness). There is an uncontrollable drowsiness after lunch. It is normal to feel sleepy in the early afternoon because of a natural drop in body temperature.

Sleep makes it easier for our body to metabolize sleep radicals - molecules that are said to increase the aging of cells and even cause cancer.

Sleep deprivation affects the production of white blood cells and antibodies making a person more prone to infections and circulatory diseases. Shortterm effects of sleep deprivation include drowsiness, Suicidal

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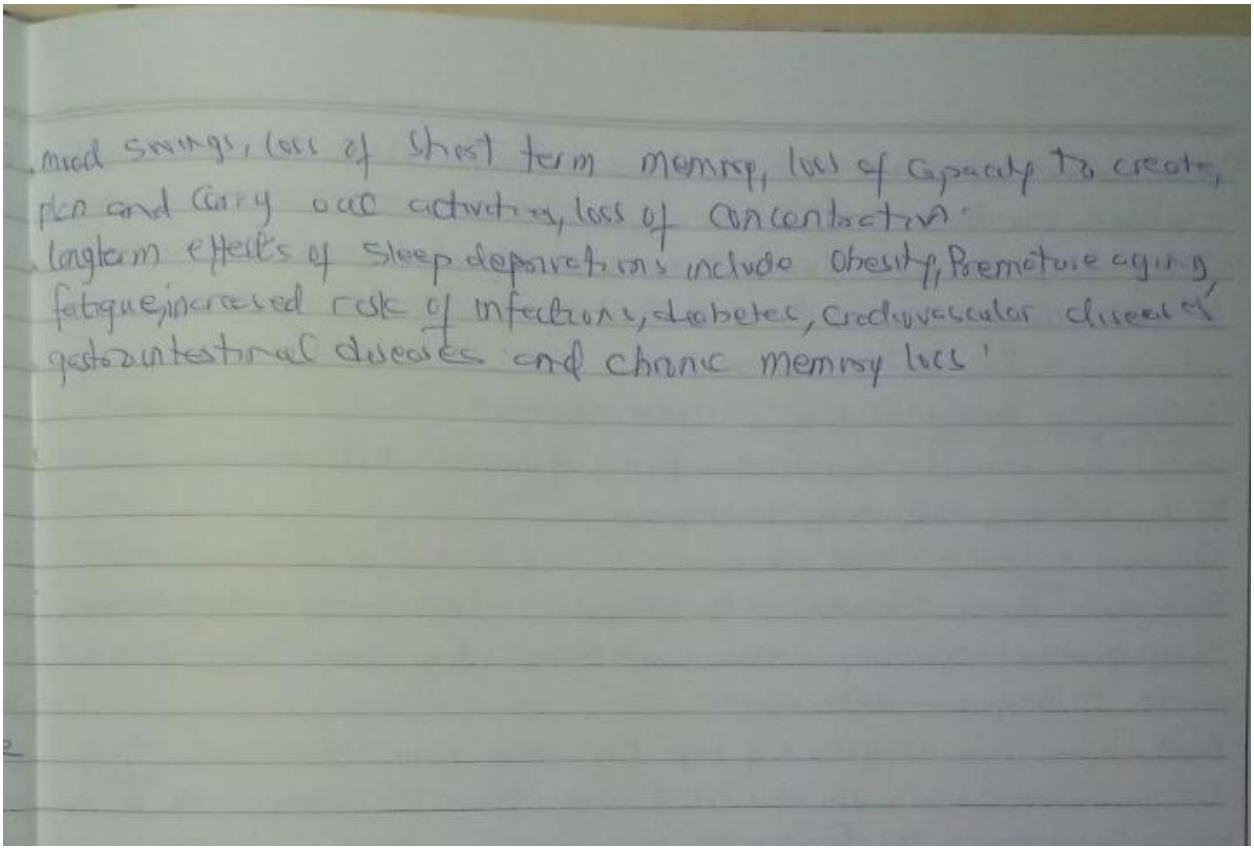

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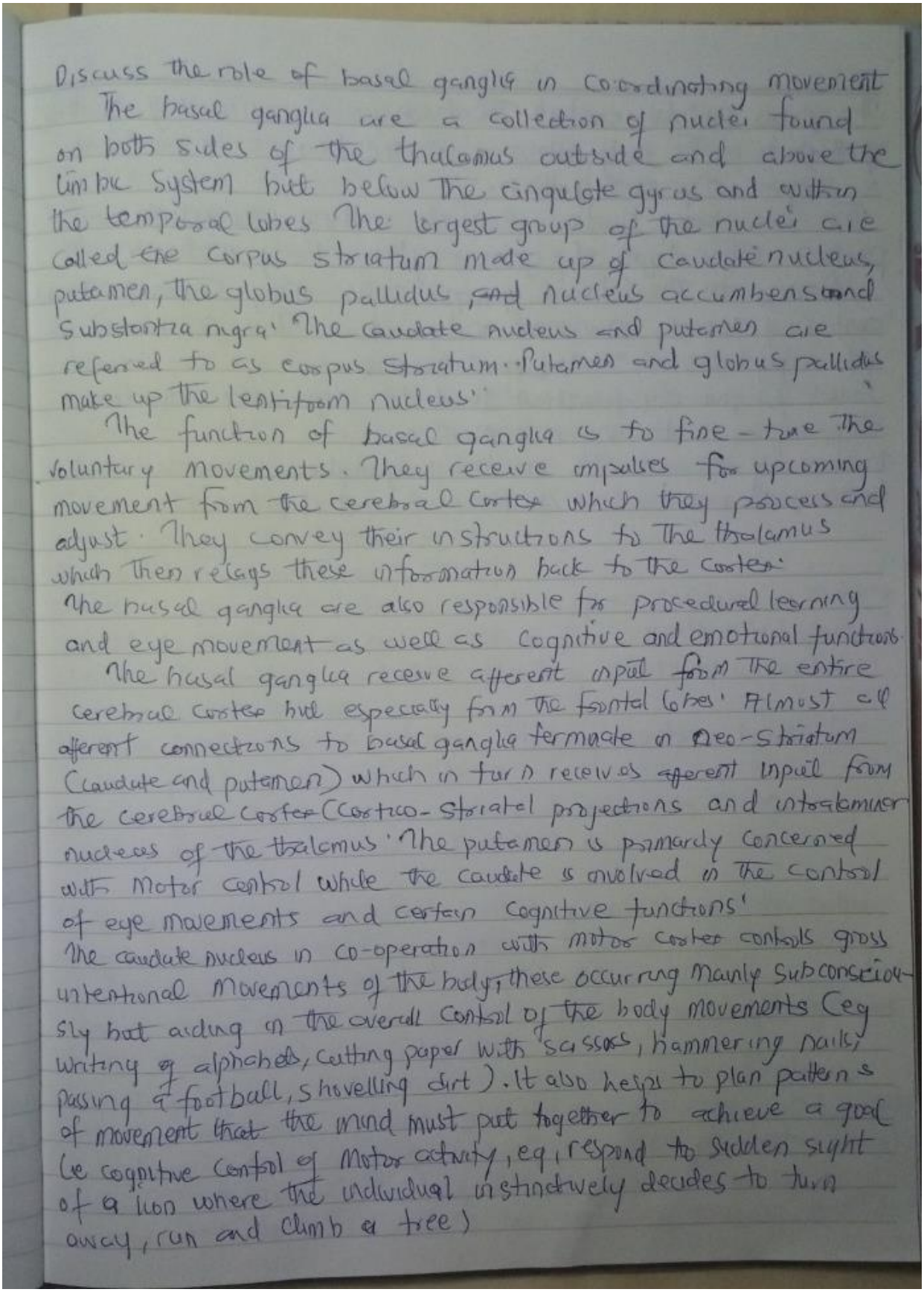

Discuss the role of basal ganglia in co-ordinating movement

The basal ganglia are a collection of nuclei found on both sides of the thalamus outside and above the limbic system but below the cingulate gyrus and within the temporal lobes. The largest group of the nuclei are called the corpus striatum made up of caudate nucleus, putamen, the globus pallidus, and nucleus accumbens and substantia nigra. The caudate nucleus and putamen are referred to as corpus striatum. Putamen and globus pallidus make up the lentiform nucleus.

The function of basal ganglia is to fine-tune the voluntary movements. They receive impulses for upcoming movement from the cerebral cortex which they process and adjust. They convey their instructions to the thalamus which then relays these information back to the cortex.

The basal ganglia are also responsible for procedural learning and eye movement as well as cognitive and emotional functions.

The basal ganglia receive afferent input from the entire cerebral cortex but especially from the frontal lobes. Almost all afferent connections to basal ganglia terminate on Neo-Striatum (caudate and putamen) which in turn receives afferent input from the cerebral cortex (Cortico-striatal projections and intralaminar nucleus of the thalamus. The putamen is primarily concerned with motor control while the caudate is involved in the control of eye movements and certain cognitive functions.

The caudate nucleus in co-operation with motor cortex controls gross intentional movements of the body, these occurring mainly subconsciously but aiding in the overall control of the body movements (eg writing of alphabets, cutting paper with scissors, hammering nails, passing a football, shovelling dirt). It also helps to plan patterns of movement that the mind must put together to achieve a goal (ie cognitive control of motor activity, eg, respond to sudden sight of a lion where the individual instinctively decides to turn away, run and climb a tree)

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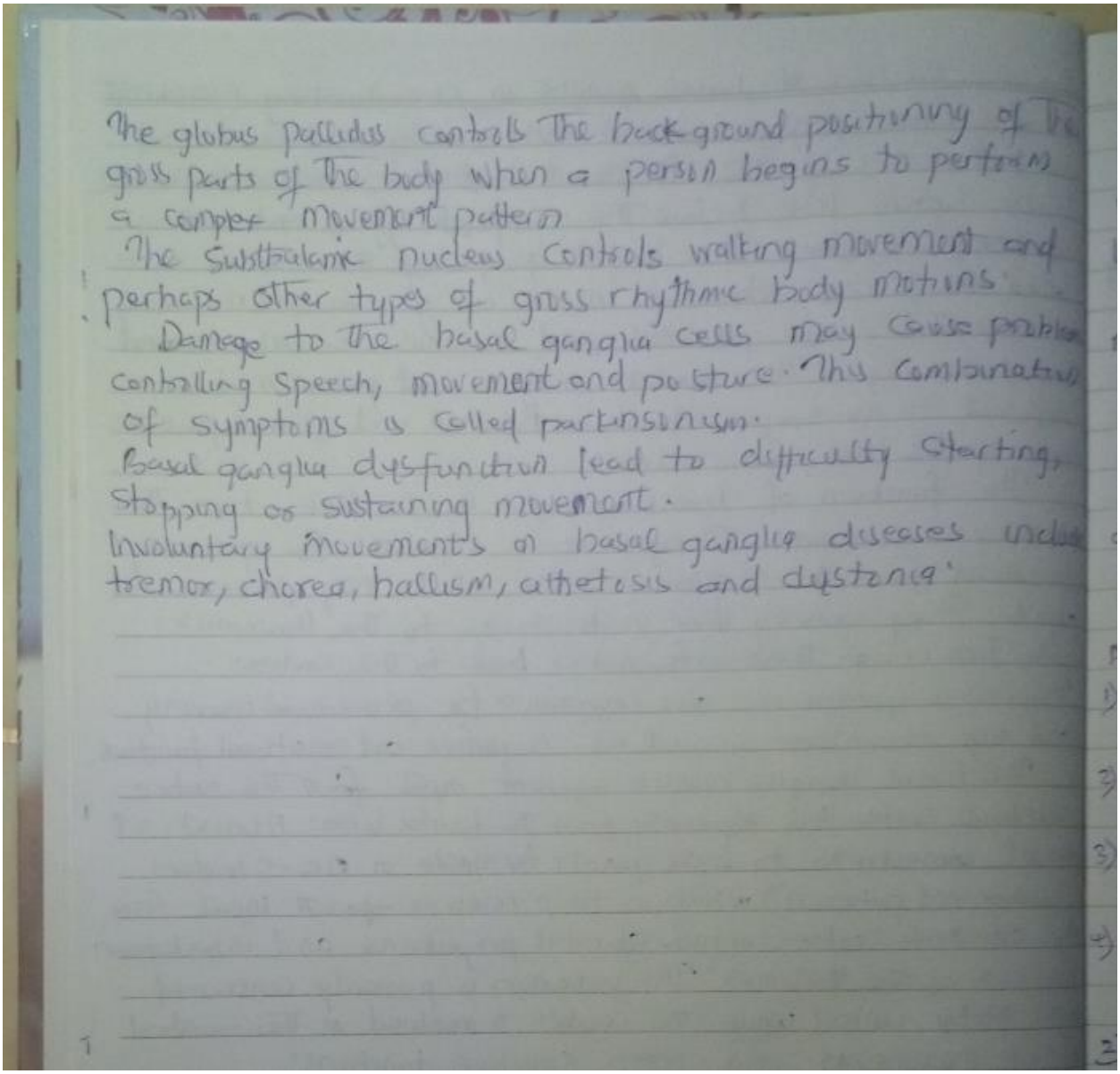

The globus pallidus controls the background positioning of the gross parts of the body when a person begins to perform a complex movement pattern
The subthalamic nucleus controls walking movement and perhaps other types of gross rhythmic body motions.
Damage to the basal ganglia cells may cause problem controlling speech, movement and posture. This combination of symptoms is called parkinsonism.
Basal ganglia dysfunction lead to difficulty starting, stopping or sustaining movement.
Involuntary movements in basal ganglia diseases include tremor, chorea, hallism, athetosis and dystonia.