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EFFECT OF CAFFEINE ON INDUCED SLEEP AND SLEEP BEHAVIOUR IN ALBINO WISTAR RATS.

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ABSTRACT

Aim/Background. Caffeine is the most widely consumed psychoactive substance in the world. As a component of tea, coffee, and soft drinks, caffeine is the most commonly ingested methyl xanthine. This research work was designed to evaluate the effect of caffeine on induced sleep and sleep behaviour in rat. **Method.** 16 Wister rats were used for this research, which were divided into four groups with four rats in each group. Group 1 served as control, group 2, 3 and 4 were given 1.0mg/kg, 1.5mg/kg and 2.0mg/kg of caffeine extract respectively after sleep had been induced. The research work was an acute experiment which lasted for about 1hour, 30 minutes. After induction of sleep and administration of different doses of caffeine extract, there was gradual inhibition of sleep by the extract, which was dose-dependent. The data derived showed that the caffeine has influence on the sleep centre, which was dose-dependent, when compared to the control. **Results**. The *caffeine* extract increased the time for the onset of sleep (i.e. makes the time longer), and reciprocally reduced the time for the onset of wake. Which implies that caffeine to a great extent can inhibit or block the pathway of sleep. It shows the inhibiting property of caffeine which is dose dependent. 1g/ml, 1.5g/ml and 2g/ml of caffeine administered to the rats showed 575%, 400% and 325% in onset of sleep respectively, and 42%, 18% and 21% in onset of wake respectively. Therefore as the doses of the caffeine increased, the time for the onset of sleep decreased when compared to the control group. It also revealed that as days of administration of caffeine elapsed, there was a general reduction in the weights of the rats although in a short-term analysis. **Conclusion**. The caffeine extract conclusively, had a significant inhibitory effect on sleep and also reduced the weights of the rats.

KEYWORDS: Sleep, Caffeine, onset of wake, onset of sleep, rats, sleep behaviour.

INTRODUCTION

Sleep is operationally defined as a specific behaviour during which the organism adopts a recognizable posture (usually characterized by the relaxation of the antigravity musculature), during which the responsiveness to external stimuli is decreased and which is regulated by a homeostatic process whereby the deprivation of sleep subsequently leads to a sleep rebound, in Homeotherms, distinct polygraphic patterns characterize the sleep episodes [1] While the homeostatic process maintains the duration and intensity of sleep within certain boundaries, the circadian rhythm determines its timing [2] Sleep is not a unitary process, but is composed of at least two substrates, each named after its main distinctive features. One is characterized by the presence of rapid eye movements (REMs) despite global muscular tonus abolition and is therefore often referred to as REM sleep and could also be described as paradoxical sleep [3] (PS) because the phasic activity of the eye muscles and the high-frequency pattern of the electroencephalographic (EEG) recording give to REM sleep some resemblance to the awake state. [4]

In animals, a further distinguishing feature of PS is the recording of Ponto-geniculo-occipital (PGO) waves, i.e. prominent phasic bioelectrical potentials that occur in isolation or in bursts just before and during PS [5] PGO waves are closely related to rapid eye movements [6] and are recorded the most easily in the pons [3] the lateral geniculate bodies [7] and the occipital cortex [5] hence their name. In humans, functional equivalence of animal PGO waves has been suggested [8, 9, 10] a hypothesis recently reinforced by the finding of rapid eye movements correlation with geniculate body and occipital cortex blood flow during REM sleep but not during wakefulness [4] The other main sleep type is known as non REM (NREM) sleep. In primates, NREM sleep is divided into several stages, corresponding to increasing sleep depth [11] Stage 2 sleep corresponds to

light sleep and is characterized by K complexes and sleep spindles.

While sleep deepens, the amount of slow oscillations increases leading to stages 3 and 4 sleep, or slow wave sleep (SWS). In carnivores such as cats or dogs, NREM is subdivided into light and deep SWS; and in rats or mice only one NREM stage is usually defined. This categorization of sleep stages is however somehow arbitrary. There is physiologically a continuum in the cellular activities subtending the NREM sleep stages [12] This continuum is better characterized by spectral analysis that allows specifying slow (<1Hz) and delta (1-4Hz) rhythms, that probably correspond to specific discharge patterns observed at the cellular level [13, 14] Sleep is also characterized by a number of specific neurotransmitter and neurochemical changes [15, 16] which profoundly modify cellular functions and interactions throughout the brain. All through the night, the NREM and REM sleep periods alternate following an ultradian cycle, SWS invariably preceding REM sleep in healthy subjects. In humans, the ultradian cycle is about 90-100min, but it is important to note that SWS is most abundant during the first half of the night (up to 80% of the sleep time), while in the second half of the night, the proportion of REM sleep dramatically increases [17]

Despite our increasing understanding of the semiology, the mechanisms and the regulation of sleep [17] its function remains elusive. Among several hypotheses [18, 19] it was suggested that sleep is involved in the processes of brain plasticity for memory consolidation. Brain plasticity, i.e. the capacity of the brain to modify its structure and function along time [20] could support several functions during sleep [21, 22, 23, 24, 25, 26, 27]

Caffeine is the most widely consumed psychoactive substance in the world [28] As a component of tea, coffee, and soft drinks, caffeine is the most commonly ingested methyl xanthine. Caffeine consumption per capita in the United Kingdom, Sweden, and Finland is estimated to be between 100 and 400 mg per person per day, with peak consumption, where caffeine intake comes predominantly from tea and coffee, respectively. Peak plasma caffeine is reached between 15 and 120 minutes after oral ingestion in humans at doses of 5 to 8 mg/kg. The caffeine half-life for these corresponding doses ranges from 0.7 to 1.2 hours in rodents, 3 to 5 hours in monkeys, and 2.5 to 4.5 hours in humans.[29]

COLLECTION OF EXPERIMENTAL ANIMALS

Sixteen (16) healthy wistar albino rats (140-250g), of mixed sex were used for this study, and were bred and housed in the pre-clinical animal house, college of Medicine, University of Port Harcourt, Nigeria. The animals were kept and maintained under Laboratory conditions of temperature, humidity and light; and were allowed free access to food (standard pellet) and drinking water ad- Libitum.

The experimental protocols and procedures used in this study were approved by Ethical Committee, University of Port Harcourt, Rivers State, Nigeria and conform to the guideline of the care and use of animals in research and teaching (NIH Publication No. 85-93, revised 1985).

ACCLIMATIZATION OF ANIMALS

After identification, the animals were weighed and housed in a wire mesh cage under standard conditions (Temperature 25-29°C, 12 Hours light/darkness cycle), for four (4) weeks so as to acclimatize with the environmental condition of the University of Port Harcourt. The study was generally conducted in accordance with recommendations from the 1983 declaration of Helsinki on guiding principles in the care and use of animals.

EXPERIMENTAL DESIGN 0F ADMINISTRATION

The experimental animals (albino wistar rat) were divided into four groups of four rats per group.
The weight of all the animals in all the groups were measured periodically.

GROUPS AND DOSAGES OF CAFFEINE ADMINISTERED

The caffeine was administered orally all animals in all the groups were given caffeine orally morning and evening of different concentration as enumerated below.
GROUP ONE: Feed and water (control)
GROUP TWO: 0.1g/ml of caffeine
GROUP THREE: 0.15g/ml of caffeine
GROUP FOUR: 0.2g/ml of caffeine

Note: Thiopental at 40mg/kg (was administered to all the rats in all the groups to induce sleep on them after which they were given the caffeine in different doses as stated above.

ADMINISTRATION OF CAFFEINE DOSAGES

Group One (Control)

The animals in this group were not fed with caffeine; they were given free access to feed and tap water throughout the course of the experiment.

Group Two

The animals in this group were fed with 0.1g/ml of caffeine for fourteen days that is, two weeks morning and evening. To be précised, 8am in the morning and 5pm in the evening. The 0.1g/ml solution of caffeine was formed by the mixture of 10ml of normal saline and 1g of caffeinated coffee.

Group Three

The animals in this group were fed with 0.15g/ml of caffeine for fourteen days that is, two weeks morning and evening. To be précised, 8am in the morning and 5pm in the evening. The 0.15g/ml solution of caffeine was formed by the mixture of 10ml of normal saline and 1.5g of caffeinated coffee.

Group Four

The animals in this group were fed with 0.2g/ml of caffeine for fourteen days that is, two weeks morning and evening. To be précised, 8am in the morning and 5p.m in the evening. The 0.2g/ml solution of caffeine was formed by the mixture of 10ml of normal saline and 2g of caffeinated coffee.

RESULTS

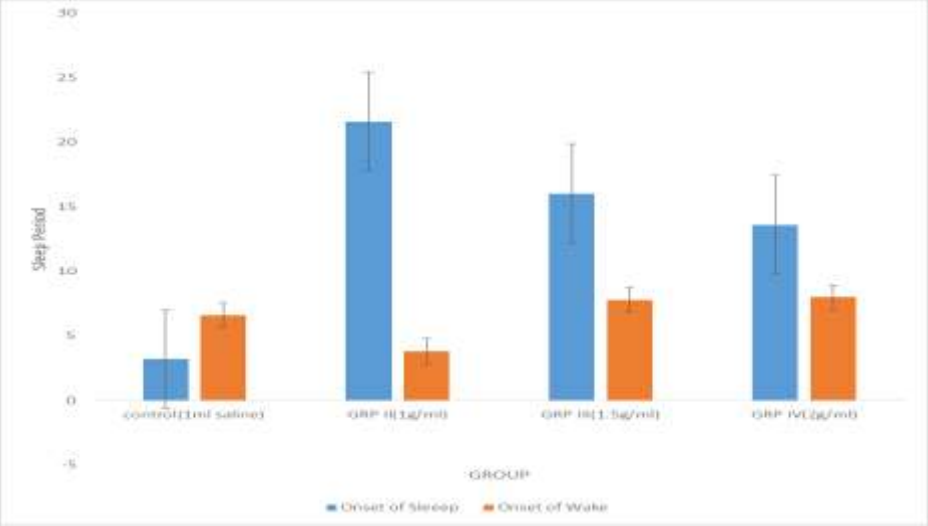

Figure 1: Showing the onset of sleep and onset of wake

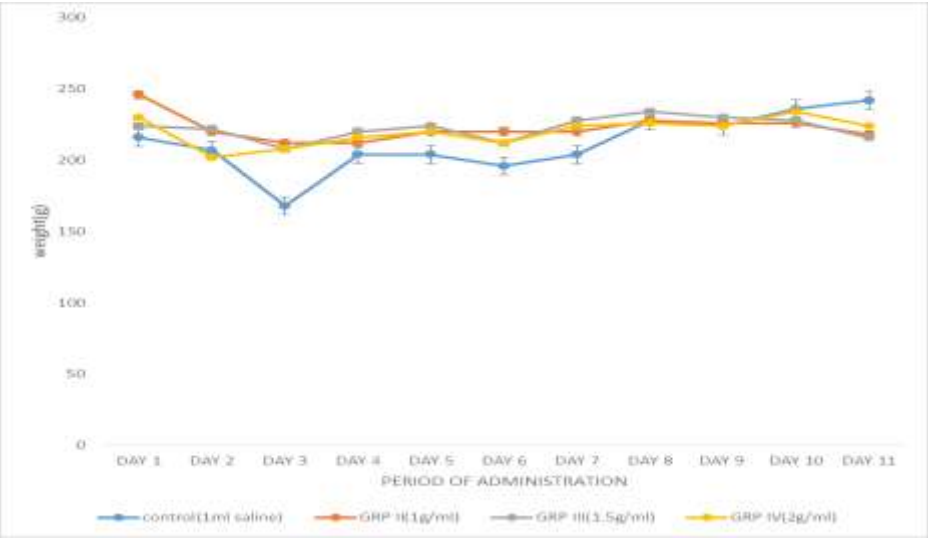

Figure 2: Variations in weights of the rats during administration

DISCUSSION

The previous studies have demonstrated that caffeine has an inhibitory input on the sleep promoting system [30] Excessive sleepiness is thought to result from the lack of maintenance of the arousal threshold, which, ultimately, alleviates the inhibition exerted on the sleep-promoting system during wakefulness [31] From the experimental data gathered in this research work, it has been demonstrated that caffeine extract increased the time for the onset of sleep (i.e. makes the time longer), and reduced the time for the onset of wake. Which implies that caffeine to a great extent can inhibit or block the pathway of sleep. And the action of these extract are seen to be dose dependent.

Table 1 shows the inhibiting property of caffeine which is dose dependent. 1g/ml, 1.5g/ml and 2g/ml of caffeine administered to the rats showed 575%, 400% and 325% in onset of sleep respectively, and 42%, 18% and 21% in onset of wake respectively. The onset sleep/wake chart also shows the various percentages above. Therefore as the dose of the caffeine increases, the time for the onset of sleep decreases when compared to the control group.

Wake-promoting agents reinforce wakefulness by stimulating the release of neurotransmitters involved in the maintenance of the arousal threshold and therefore, counterbalance the inhibitory inputs from the sleep-promoting system to the wake promoting one. [32] Nicotine stimulates the cholinergic neurons in the basal forebrain that lead to cortical activation. Caffeine

participates to the cortical activation by blocking adenosine receptors located on cholinergic neurons in the basal forebrain. Caffeine also blocks adenosine receptors located on GABAergic neurons, thus reinforcing the inhibition exerted on neurons in the preoptic/ anterior hypothalamus that are involved in sleep induction and may indirectly increase dopamine neurotransmission [33]

Modafinil may promote waking via activation of the tuberomammillary nucleus and hypocretin neurons, which leads to an activation of the ascending arousal system. The fact that either amphetamine-like stimulants or modafinil have failed to exert any waking effect on DAT knockout mice suggests that the dopamine system may play a role in the wake-promoting properties of these compounds.[34, 35, 36]

The above theoretical explanation can buttress the fact that caffeine contributes an inhibitory input to sleep when taken since the data gathered from this research showed that caffeine can increase the time of wakefulness and reduce the period of sleep in rats, caffeine therefore can be considered as one of those wake-promoting agents, which work by substantially stimulating the release of neurotransmitters involved in the maintenance of the arousal threshold and thereby inhibits the sleep pathway.

CONCLUSION

From the experimental data gathered from this research work, it can be concluded that caffeine has an inhibitory effect on sleep, thus can increase the period between wakefulness and onset of sleep. But, Understanding how wake-promoting drugs interact with different components of the dopamine system to induce arousal remains a challenge for future research to establish new stimulant treatments.

Therefore, further studies are required to elaborate and establish the molecular mechanism for proper clinical utility.

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