Water Intake: Influence on Development of Rat Saline Hypertension

Chronic dietary sodium excess leads to the development of arterial hypertension in many species and a given amount of sodium load is usually more effective when added to drinking water than when added to the food of animals drinking water ad lib. SAPIRSTEIN[1] speculated as early as 1950 that the hypertensinogenic properties of salt loading might be enhanced by associated water restriction, but this hypothesis has really never been tested carefully. We studied this question by selectively controlling and independently varying sodium and water intake in rats.

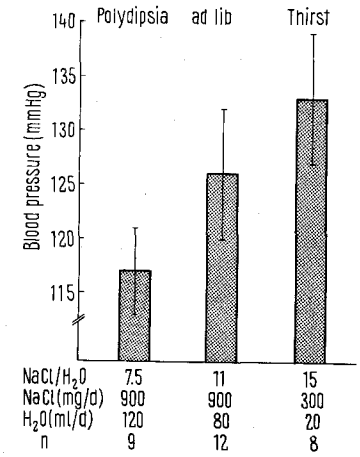
Materials and methods. Thirty-six male Sprague-Dawley rats, with a mean body weight of 130 g and a mean blood pressure of 110 mmHg, were randomly divided into 3 equal groups. During the 7 weeks of experiment, all groups ate low salt purina chow (0.47% NaCl); their fluid intake was recorded daily, their systolic pressure was measured weekly without anesthesia by tail plethysmography, and they were tube fed with 10 ml of fluid twice a day.

Salt and water regimen and systolic pressure at the end of 7 weeks are summarized in the Figure. Animals in group 1 (Polydipsia) were tube fed with 300 mg of NaCl/day/rat for 2 weeks, 600 mg for 3 weeks and 900 mg for 2 weeks. They were allowed to drink distilled water containing glucose 3% and saccharine 0.125%[2]; their average consumption was 120 ml/day/rat at the 7th week. The final blood pressure in this group, 117 mmHg, was not significantly different from the initial value of 114 mmHg. Three deaths were accidental.

Rats in group 2 (ad lib.) were tube fed with the same amount of sodium as group 1. They drank distilled water ad lib; the average daily consumption was 80 ml at the 7th week and the final blood pressure was 126 mmHg.

Rats in group 3 (thirst) were tube fed with 300 mg of NaCl per day, dissolved in 20 ml of distilled water, and deprived of any drinking water. 4 rats had died by the end of the 6th week; the others looked weak and had lost weight. Despite their poor shape and the fact that they consumed 3 times less NaCl than the 2 other groups, their average final blood pressure was the highest at 133 mmHg, significantly different from that of the first (Polydipsia) group. Had these rats not been ill, then blood pressure may conceivably have been higher.

Discussion. These data indicate a positive correlation between blood pressure increment and ratio of NaCl/H20 consumed rather than with actual amount of ingested salt. This phenomenon, which probably stems from renal inability to concentrate and excrete salt loads without adequate water intake, could explain why salt loading regimens which differ in their degree of water restriction also differ in their hypertensinogenic effectiveness. Thirst could prove to be a useful means for potentiating experimental hypertensions other than saline. Furthermore, surveys trying to link salt consumption of human populations with their blood pressure should include data on water ingestion[3].



Systolic blood pressure (mean and 95% confidence interval) of uninephrectomized rats submitted to salt loading for 7 weeks. Values in group (thirst) were significantly higher ($p<0.05$ by variance analysis) than those in group (Polydipsia). Pressure elevation is inversely related to water intake.

Résumé. Après 7 semaines de surcharge saline administrée par gavage, l'augmentation de tension artérielle systolique de 3 groupes de rats uninephrectomisés soumis à différents régimes d'hydratation s'avéra être en meilleure corrélation avec le rapport NaCl/H20 ingéré qu'avec la quantité absolue de sodium ingéré. La soif pourrait possiblement potentialiser d'autres formes d'hypertension expérimentale.

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The Caudate Spindle During Various Sleep Stages

Little is known of the significance of the striatum (caudate nucleus and putamen) with regard to sleep. R. HESS et al.[1] have shown that electrical stimulation of the caudate nucleus in the cat causes akinesia. The behaviour of the animals is, however, distinct from that which follows the induction of sleep by thalamic stimulation, being more like a catatonic stupor, although, to quote these authors, the electroencephalographic pattern is difficult to distinguish from that of spontaneous sleep. HEATH and HODES[2] induced drowsiness and sleep in monkeys and humans by electrically stimulating the head of the caudate nucleus, and similar results were obtained by PARMEGGIANI[3] with cats. HERNÁNDEZ-PEÓN et al.[4] initiated sleep in the cat by the local application of acetylcholine to various brain structures, including the caudate nucleus and putamen. It is interesting to note that the latencies of onset of both

Average duration in sec of the electrically evoked caudate spindle during sleep and wakefulness (stimulation right caudate; evaluation of the spindles left caudate)

EEG phase		Spindle duration for each subject			No. of evoked spindles received by each subject		
		1	2	3	1	2	3
1	Excitation	0.49	0.31	0.36[a]	100	538	102
2	Quiet	0.68	0.60	0.64	695	532	631
3	Transitional phase	0.91	0.85	1.09[b]	604	539	476
4	Sleep; spindle phase	1.17[a]	1.16[a]	1.19[b]	332	283	583
5	Sleep; slow wave phase	0.34	0.24	0.43[a]	524	752	636
6	Sleep; paradoxival phase	1.18[a]	1.24[a]	1.36	213	159	434

All points of values within each column are significantly different (t-test) from each other ($p < 0.001$), except those pairs marked [a] $p < 0.01$ and [b] not significant.

slow wave sleep (SWS) and paradoxical sleep (PS) were less when application was made in striatal structures than when made in limbic and neocortical structures.

On the other hand, WEISS[5] reported a slight, but significant, reduction in the SWS duration in the rat on stimulation of the caudate nucleus. This discrepancy could possibly be explained by the different stimulation parameters employed in this study. MEYERS[6] remarked, during a short discussion, that no sleep disturbances were seen in patients following unilateral, and in some cases bilateral, extirpation of the head and anterior body of the caudate nucleus.

In view of the findings, it is still an open question whether or not the striatum is directly involved in sleep processes. The current study was carried out to investigate the possibility of a relationship between the duration of caudate spindles[7,8], induced by single electric shocks applied to the caudate nucleus, and the various phase of sleep and wakefulness.

Method. Three female rats (Charles River CD, ca. 230 g) were used in the present study. Platinum needle electrodes were permanently implanted bilaterally in the caudate nucleus, and unilaterally in the dorsal hippocampus. Silver wire electrodes were used for bilateral recordings from the occipital cortex, and the EMG was derived from the neck muscles. The implantation method has been described elsewhere[9]. A period of 15 days was allowed to elapse post-operatively before using the animals. Throughout the experiments the rats were in sound attenuated cages under constant illumination. Rectangular impulses of 9 V and 0.05 msec duration were delivered by a Grass stimulator S4C with an isolation unit SIU 4B to the right caudate nucleus at 10 sec intervals throughout the experiment (from 08.00 h to 16.30 h). The tips of the stimulation electrodes were spaced 1 mm apart. Recordings were made on a Schwarzer electroencephalograph at a paper speed of 15 mm/sec. For the purpose of evaluation, the EEG records were classified into 6 different phases. 1. Excitation: High frequency, low voltage cortical potentials; theta rhythm in the hippocampus. 2. Quiet: Flat, desynchronized activity in all traces. 3. Transitional phase: Higher amplitudes in all traces, with occasional slow elements, and a slight degree of synchronization. 4. Sleep; spindle phase: Characterized by the appearance of spindle groups. 5. Sleep; slow wave phase (SWS): High amplitude, slow waves. The animal lies curled up on its side, or rolled in a ball. 6. Sleep; paradoxical phase (PS): Low voltage, fast activity in the cortex and caudate nucleus intermittently synchronized with the hippocampal theta rhythm. The amplitude in all of the traces is distinctly higher than in phase 1. The animal lies flat, with occasional twitching of the nose and paws. No EMG activity.

The duration of each evoked spindle was measured from a left (contralateral) monopolar caudate trace[10] and designated according to the EEG phase in which it occurred.

Results. The average duration of the electrically evoked caudate spindles in the various EEG phases is presented in the Table. During EEG-phase 1, the spindles are short and have an irregular form. In EEG-phase 2, they are somewhat longer and show a recruiting tendency, although an abrupt finish is often exhibited. The form becomes increasingly regular during EEG-phases 3 and 4 and at the same time, the spindles show an increase in duration. There are no great differences between the spontaneous spindles and those evoked by stimulation.

Spindles could be rarely induced in the slow wave phase (phase 5). The stimulation response is limited mainly to an initial spike followed by a slow wave of roughly 200 msec duration. The few spindles spontaneoulsy arising in this phase were always limited to the cortical derivations, often being present only in the interhemispheric trace.

During the period 30–60 sec preceding PS (classified under phase 4) the evoked spindles show a marked increase in duration reaching a maximum at the onset of PS (Figure). Stimulation falling in this period merely seems to enhance the synchronized background activity, although the spindles again show a recruiting form. Like the spontaneous spindles, they were synchronized in the cortex, caudate nucleus, and dorsal hippocampus.

Discussion. The duration of the evoked caudate spindles in the rat varies according to the state of consciousness. Two peaks are observed. The first arises in the transition from wakefulness to sleep, and occurs in a phase when the mediothalamic excitability (recruiting

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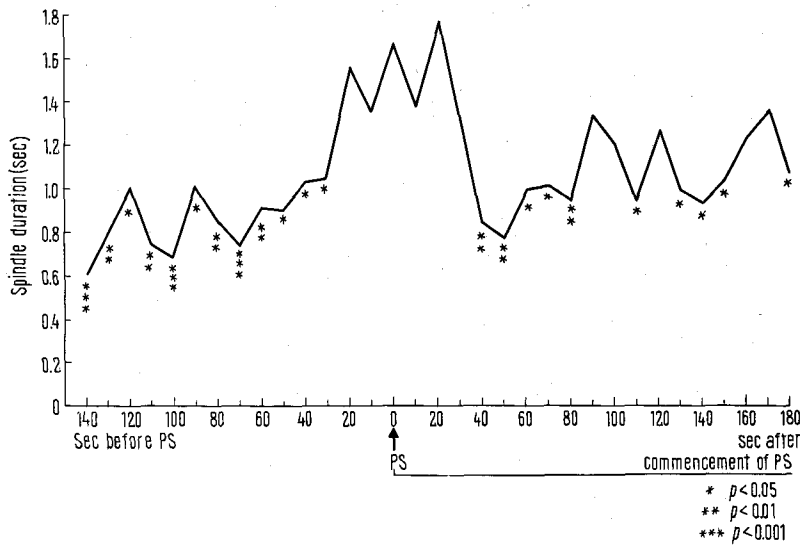

Average evoked spindle duration before and during paradoxical sleep. (Significance levels given for the comparisons between the average evoked spindle durations and this duration at time 0, using the *t*-test.)

response) reaches a maximum[11]. The coincidence of these events may be an expression of the increased tendency towards synchronization and rhythmicity in the areas of the cortex, thalamus, and striatum, three structures whose functional inter-relationship is hardly to be doubted. With increasing duration of the slow wave phase, both the spontaneous and evoked spindles virtually vanish, and the EEG is dominated by slow, high amplitude potentials.

As is shown in the Figure, the second increase in the duration of evoked caudate spindles begins some 30–60 sec before the onset of the typical PS. This is also the point at which the arousal threshold reaches a maximum, and at which the ponto-geniculo-occipital potentials appear[12]. After a further 10–30 sec the hippocampal potentials show an increased frequency with a clearer rhythmicity, and at the same time long, spontaneous, high amplitude spindles appear in all of the caudate and cortical traces. At this point the duration of the evoked spindles reaches a maximum. In this phase there is a greater tendency to rhythmicity and the evoked spindles frequently appear as an amplification of the background activity.

On the other hand, during periods of arousal, as represented in the EEG, spindles cannot be elicited. The explanation for these different responses to stimulation may lie in the function of the ascending reticular formation. During PS this system is strongly inhibited, as is shown by the raised EEG-arousal threshold[12–16], whereas during arousal itself, the ascending reticular system exerts an inhibitory effect on the caudate nucleus, resulting in abolition of the evoked spindles[17].

Zusammenfassung. Bei Ratten wurde über $8^1/_2$ Stunden alle 10 Sek durch elektrischen Reiz eine Kaudatum-Spindel ausgelöst. Die Dauer der einzelnen Spindeln wurde dem EEG-Bild zugeordnet. Bei statistischer Auswertung ergaben sich 2 Maxima für die Spindeldauer, das eine in der Einschlafphase (Übergangsphase + Spindelphase), das zweite beim Übergang vom Slow-wave-Schlaf zum paradoxen Schlaf.

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Norepinephrine-Induced Thermogenesis: Effect of Interscapular Brown Fat[1]

The function of brown adipose tissue (BAT) as a thermogenic effector during cold stress has been well documented[2–4]; however, its role during extended periods of cold exposure has not yet been resolved. In the rat, prolonged cold exposure is followed by adaptive responses among which is the shift from shivering to nonshivering thermogenesis (NST)[5]. Accompanying this transition are trophic changes in BAT resulting in an elevation of the thermogenic capacity of the tissue[2,3]. Notably, much of this heat is applied locally to the thoracocervical spinal cord, the thoracolumbar autonomic structures, and the heart[2,6]. The significance of this distribution is emphasized by the recent demonstration of temperature sensors in the thoracocervical spinal cord[7–9]. That is, the finding that warming of these thermosensitive areas is followed by an inhibition of shivering[7–9] has led to the proposal that during acute cold exposure, heat conveyed from the BAT to the cord may be an important link in controlling the