## Somesthetic cortex reactivity during sleeping and waking in the rat

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*Summary.* The cortical S1 responsiveness was studied by unique and coupled stimuli of non-maximal intensity applied to somesthetic radiations. The reactivity is highest during sleep with slow waves, lowest during active waking, intermediate during non-active waking and rapid sleep. The recovery of responsiveness presents an exactly opposite form and begins at a long interstimulus delay (> 150 msec).

In order to know more about the influences which govern the state of the central nervous structures during the sleeping-waking cycle, and before undertaking the unitary approach, we have studied the responsiveness of somesthetic S1 cortex.

*Method.* Stimulatory electrodes were implanted in the somesthetic radiations in 9 Wistar rats. Submaximal constant current stimuli of 0.1 msec duration and approximatively 50 μA intensity, were delivered and the correspondingly evoked potentials were recorded from the somesthetic cortex S1. Spontaneous activities were recorded in the frontal and the occipital cortex which, with electromyogram and oculogram, enable the determination of 7 stages of sleep and waking: 1. AW: active waking (with theta activity); 2. NA: waking without theta activity; 3. SW: slow wave; 4. SP: frontal spindle; 5. IS: intermediate sleep[1] characterized by spindles and theta (SW, SP, IS taken together are called slow sleep); 6. R1: rapid sleep without eye movement; 7. R2: eye movements of rapid sleep. The recovery cycle was tested by a second stimulus at different latencies (between 17 and 350 ms). Each stage of behaviour has been analyzed by averaging 65 responses. The positive wave 4 amplitude has been quantified for the 1st and 2nd evoked potentials. The interstate differences have been statistically studied by Student's t-test.

*Results.* First evoked potential. Figures 1 and 2. The response amplitude is minimum in waking with theta activity (AW), increases significantly ($p < 0.05$) in waking without theta activity (NA) and attains the maximum value in SW (with a significant increase at $p < 0.005$ compared to NA). A decrease was observed in other sleep states (SP, IS, R1, R2), all significantly different from SW ($p < 0.02$) but without a significant difference between them.

Recovery cycle. Figure 3. At short interstimuli delay (ID), the different components of the 2nd response (sometimes

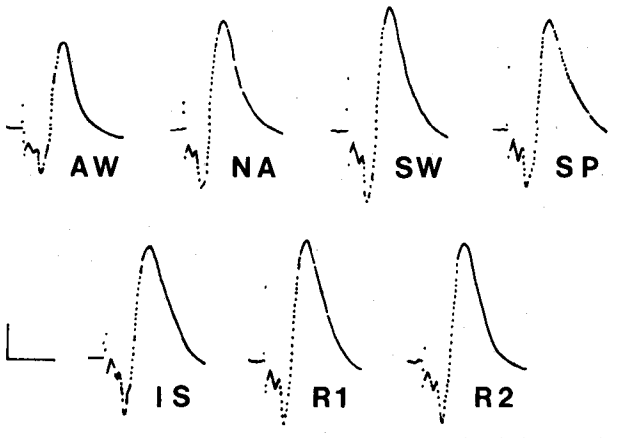


Fig. 1. Cortical evoked potentials induced by stimulation of the somesthetic radiations in the various stages of sleeping and waking. Each potential is the results of 65 averaged responses (positivity downwards). Abbreviations for all the figures: AW: waking with theta activity; NA: waking without theta activity; SW: slow wave; SP: frontal spindle; IS: intermediate sleep; R1: rapid sleep without eye movement; R2: eye movements of rapid sleep. Calibration: 200 μV; 10 msec.

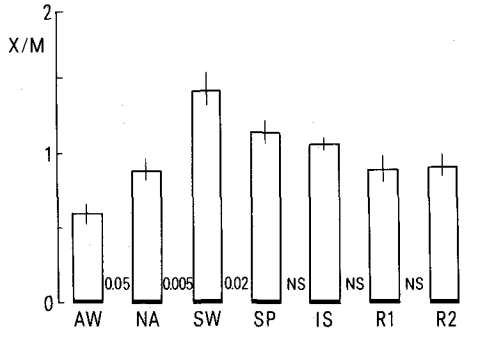


Fig. 2. Cortex S1 responsiveness (mean +SD). X/M: evoked potential wave 4 amplitude relative to the interstate mean.

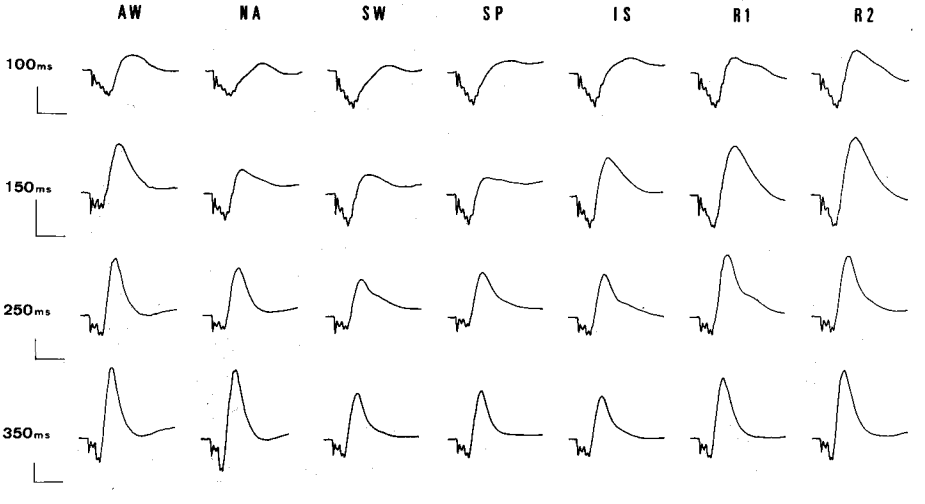


Fig. 3. Recovery cycle of somesthetic cortex S1. At 100 and also 150 msec latencies, the major positive component occurs with an abnormal long delay. At 250 and 350 msec, its latency is the same as for the conditioned stimulus, even if the amplitude is still lower (see text). The state depending variation is very different from that of the 1st evoked potential (each evoked potential is the result of 32 averaged responses. Positivity downwards). Calibration: 200 μV; 10 msec.

of large amplitude) were of too long latencies to be taken into account. The recovery time of the response begins at 150 msec of ID, first in waking and rapid sleep. At 400 msec, the response attains 100% of the conditionant response amplitude in waking without theta (NA); the responses are still of lower amplitude in the states of slow sleep (SW, SP, IS) pointing to a longer recovery time for these states of sleep.

*Discussion.* From a general point of view, our results are in good agreement with those obtained in the cat by stimulation of the somesthetic radiations[2-6]. Nevertheless, there is no facilitation during R2 as observed in the cat by direct visual cortex stimulation[7]. This is probably linked to the absence of cortical phasic activities during rapid sleep in the rat[8]. The study of the 2nd evoked potential, also in agreement with the results obtained in the cat[2,9], shows a long-lasting cortical recovery process. The order of recovery (first in waking, then in rapid sleep and latter in slow sleep), unlike the 1st response, can be explained by the fact that the cortical inhibitory processes are as important as the *initial excitation is significant*[10]. Interesting processes probably linked to cortical[11,12] and sub-cortical[13] influences must occur to explain the curious evolution of the 2 evoked potentials and have to be studied first by antidromic stimulation of pyramidal tract and then by single unit approach.


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## Endothelial injury by nicotine and its prevention[1]


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*Summary.* Nicotine administered i.v. or p.o. in doses above 0.0125 mg/kg to the rat caused a highly significant increase in circulating anuclear carcasses of endothelial cells estimated by an original method. This effect of nicotine was completely prevented by a prior oral administration of the flavonoids hydroxyethylrutosides (HR) or Mono-7-HR.


Smoking is generally accepted to be one of the main risk factors of coronary heart disease. Nevertheless, the mechanism of its damaging influence on blood vessels is far from clear. From this point of view, nicotine is the most conspicuous among the noxious tobacco products; but besides its vasoconstricting activity, no direct damaging effect has been shown conclusively.

A very sensitive experimental as well as clinical method has now been developed in our laboratory to demonstrate the endothelial injury[2]. The method is based on counting circulating anuclear carcasses of detached endothelial cells. In principle, 1 ml of platelet-rich plasma is mixed with 0.2 ml of 2.34 M adenosine-5'-diphosphate (Calbiochem) and mechanically shaken for 10 min. Plasma is centrifuged at 395×g for 20 min to remove platelet aggregates. The supernatant is centrifuged at 2100×g for 20 min and the sediment suspended in 0.1 ml physiological saline. From this suspension a Bürker's chamber is filled and the cells counted under phase contrast microscope in two ruled platforms corresponding to 0.9 µl each. The counting is repeated once more and the mean from 4 platform countings is taken as the result. The results are expressed in terms of the element count in the volume of 1 platform after the correction for dilution. The elements were identified mor-

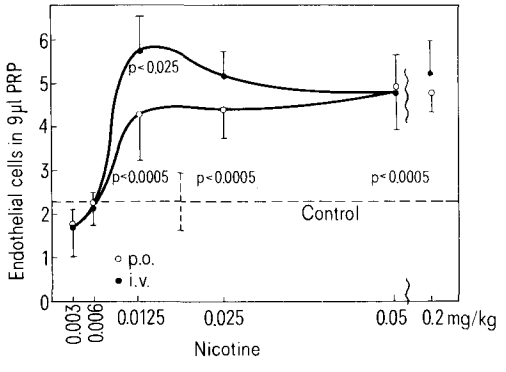


Fig. 1. The dose-dependence of the endothelial cell count increasing effect of nicotine in rats. Means (n = 10) ± SD are indicated. Control: saline i.v.

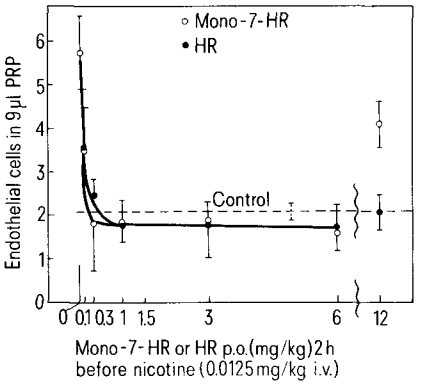


Fig. 2. The inhibition of the nicotine effect on endothelaemia by mono-7-hydroxyethylrutoside (Mono-7-HR) and by a mixture of hydroxyethylated rutosides (HR).