INFLUENCE OF ASPIRIN ON THE CONTINGENT NEGATIVE WAVE IN HEALTHY SUBJECTS

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A study was made of the alterations of the parameters of the slow brain potential, the contingent negative wave, under the influence of aspirin in healthy individuals, using the double blind method. The early and late wave of the CNW were investigated. A statistically significant decrease in the early CN wave was obtained after the ingestion of aspirin, and an increase in the late wave after the ingestion of aspirin and placebo. A central effect of aspirin, affecting the noradrenergic and dopaminergic brain systems, is hypothesized to explain the changes described.

The contingent negative deviation, or contingent negative wave (CNW), is a slow brain potential which arises in a situation of waiting [1, 11]. The CNW has been widely used recently in the study of the activity of the central nervous system and in the assessment of the action of various pharmacological preparations [1, 2, 5-9]. In particular, J. Schoenen has demonstrated [8, 9] that the early component of the CNW is significantly increased in patients with migraine. The taking of β-blockers decreased its amplitude in patients with migraine; this was accompanied by clinical improvement. At the same time, the remedial effect of the prophylactic ingestion of the calcium channel blocker, flunarizine, did not alter the parameters of the CNW [8]. A study of the correlations between the therapeutic effect of other pharmacological agents used in the prophylaxis of migraine and changes in the parameters of the CNW is of interest.

Aspirin, which is widely used in migraine, yields a good therapeutic effect [3, 10]. However, the precise mechanism of its action has not been fully elucidated. While there are many studies on the peripheral effects of aspirin, the central mechanisms of the action of acetylsalicylic acid have been studied inadequately [4, 10]. The assessment of the influence of aspirin on the parameters of the CNW is an objective method of the study of its central action, and may promote a better understanding of the brain mechanisms involved in the pathogenesis of migraine.

The aim of the present investigation was the study of the influence of aspirin on CNW parameters in healthy subjects.

Sixteen healthy right-handed volunteers were selected for the investigation (seven men, nine women, average age 21 ± 3.85 years). The subjects received instructions to refrain from smoking, consumption of alcohol, coffee, pharmacological preparations of any kind for 24 hours before the investigation. Each subject received placebo once and aspirin once in randomized order using the double blind method. The investigation always began at 1700 h. The recording of the CNW was done before and 60 min after the ingestion of 1000 mg of aspirin or placebo.

The usual method of recording the CNW was used in the study [1, 11]. The subjects sat comfortably in chairs in a darkened room. Two acoustic signals of medium intensity were presented to them through earphones: the first, S1, is the warning signal; the second, the S2, after 3 sec, is the imperative signal. After hearing the signal the subject had to press the button turning off the S2 as quickly as possible. Each pair of stimuli was presented every 5-25 sec.

Two active electrodes were mounted symmetrically at a distance of 2 cm from the midline of the head along the auricular vertical (C3 on the left, C4 on the right, according to the Jasper 10-20 system); the reference electrodes were placed on the mastoid processes. The electrooculogram was recorded from the right eye to eliminate artefacts. The averaging of the first 20 responses with minimal electrooculogram artefacts when the button was disengaged by the right hand.

The following CNW parameters were measured: the early wave, defined as the average amplitude in the 550-750 msec interval after the S1, and the late wave, representing the average amplitude 200 msec before the imperative S2 [2].


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Fig. 1. Amplitude of the CNW before (white columns) and after (black columns) the ingestion of aspirin (I) or placebo (II). Significant differences are denoted by an asterisk.

The statistical analysis of the data was done by a one-factor analysis of variance (ANOVA) and the Student t test. The data on the influence of aspirin or placebo on the CNW parameters are shown in Fig. 1. A significant decrease in the early component of the CNW was found after the ingestion of aspirin. The prescription of placebo did not lead to significant changes in the early component of the CNW. An increase in the late component of the CNW was found after the ingestion of both aspirin and placebo. However, this change was significant only in the right lead after the ingestion of aspirin, and was minimal and insignificant after the ingestion of placebo. When the two baseline recordings of the CNW were compared using the t test, significant differences were not obtained. Statistically significant differences were not detected in any of the series of experiments in the analysis of the interhemispheric asymmetry.

A significant decrease in the early component of the CNW after the ingestion of 1000 mg of aspirin was established as a result of the investigation. The interrelationship between the early component of the CNW and the activating systems of the brain, in particular, the mesencephalic reticular activating formation, has been discussed in preceding papers [6, 12]. In addition, the leading role of noradrenergic activation in the genesis of the early wave is discussed [9]. The decrease in the early component of the CNW that we have observed after the ingestion of aspirin may be explained by the inhibiting influence of the latter on the brainstem activating systems and a decrease in noradrenergic activation. If the influence of aspirin on the activating systems were generalized, a decrease in the late component of the CNW should also be expected. However, we observed a significant increase in it in the right hemisphere. The genesis of the late wave of the CNW has been associated with activity of the dopaminergic brain systems [2, 5]. Thus, the results obtained may be interpreted from the perspectives of the selective inhibition by aspirin of local noradrenergic activating systems of the brain. The varied influence of aspirin on the noradrenergic and dopaminergic neurotransmitter system may be discussed. The phenomenon of the increase in the late component of the CNW only in the right hemisphere after the ingestion of aspirin suggests the necessity of further study of interhemispheric asymmetry of the CNW.

Taking note of the increase in the early wave in migraine patients in the inter-attack period and its decrease after the ingestion of aspirin in healthy volunteers, it may be hypothesized that the prophylactic effect of aspirin in migraine is associated with its central action, in particular with a decrease in noradrenergic activation. Preliminary results of the investigation in our laboratory of migraine patients in the inter-attack period also demonstrated a decrease in the early component of the CNW after the ingestion of 1000 mg of aspirin; this may serve as one more argument confirming this hypothesis. The comparative investigation of the CNW dynamics before and after the ingestion of aspirin in migraine patients and healthy subjects will be continued.

REFERENCES