

Relationships between morphological, physiological and behavioral traits associated with the age-dependent development of stress-sensitive arterial hypertension in the ISIAH rats

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Motivation and Aim: Hypertension is one of the most significant risk factors for many cardiovascular diseases. At different stages of arterial hypertension development, various pathophysiological processes can play a key role in the manifestation of the hypertensive phenotype and comorbid conditions. Accordingly, it is thought that when diagnosing and choosing a treatment strategy for arterial hypertension, it is necessary to take into account age, stage of disease development, comorbidities and the influence of emotional and psychosocial factors. However, this approach to treatment selection is hampered by incomplete knowledge of the details of the age-related associations between numerous features that may contribute to the manifestation of the hypertensive phenotype. Therefore, we carried out a study to analyze the age dependent changes in relationships between morphological, physiological and behavioral traits in two groups of hybrid F2(ISIAHxWAG) male rats of different ages.

Methods and Algorithms: The study used two groups of F2(ISIAHxWAG) hybrid males aged 3 (n=103) and 6 months (n = 126), obtained by crossing hypertensive ISIAH rats (simulating stress-sensitive form of arterial hypertension) and normotensive WAG rats. Using a group of hybrid rats allows us to obtain the full range of variability between normal and hypertensive phenotypes. The data set we obtained for these two groups of rats includes data on morphological, physiological and behavioral traits, many of which show interstrain differences and represent the key features in the development of the hypertensive phenotype. Using the principal component method, the relationships between 21 traits were analyzed. The results of previous studies have shown that behavioral traits of rats in the open field test and morphometric traits contributed to different components [1]. Taking this into account, in the present work, the analysis of behavioral and morphometric traits was carried out separately.

Results: The most significant results were obtained when analyzing the set of behavioral and physiological characteristics for rats of both ages taken together. It has been shown, that the development of stress-sensitive hypertension in ISIAH rats is accompanied not only by an age-related (FDR<5 %) persistent increase in basal blood pressure, but also by a decrease in the response to stress and an increase in anxiety: the age indicator was positively and significantly correlated only with second principal component (PC2). The

main contribution to PC2, accounting for 15.4 % of the total variance, was made by the characteristics of hypertensive status, with a positive contribution from basal blood pressure, which suggests that the development of hypertensive status is the main age-related parameter by which the groups of F2(ISIAHxWAG) males differ. The negative contribution of an increase in blood pressure during stress to PC2 corresponds to a decrease in glucocorticoid stress response with age, which is consistent with data obtained in earlier studies. A number of behavioral characteristics also correlated with PC2: a negative contribution was noted for locomotor activity, and a positive contribution was found for parameters such as displaced activity (grooming) and the latency period. That is, in this case we are dealing with behavioral parameters that characterize the conflict of several motivations: anxiety, fear and exploration. Consequently, the second component, associated with the age of rats, can be characterized as a factor of behavioral caution (indecisiveness) and anxiety, which increases with age and the development of sustained hypertension [2]. Analysis performed for the two age groups separately showed that the plasma corticosterone concentration at rest and its increase during short-term restraint stress in a group of young rats did not have a straightforward relationship with the other analyzed traits. However, in contrast to young rats, such associations were found in older animals, suggesting that glucocorticoid adrenal function may modulate a range of behavioral traits associated with emotionality in later life.

Conclusion: The study revealed age-dependent relationships between the key features that determine the manifestation of hypertension in ISIAH rats. Our results may be useful for developing the specific protocols of the treatment strategies for stress-sensitive hypertension, taking into account the age of patients.

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References

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