INTRODUCTION

Neurotensin (NT) is a tridecapeptide widely distributed in brain and peripheral tissues of mammalian species (1). This peptide is closely related to dopaminergic system as well as to other neurotransmitter systems which are involved in the physiopathology of schizophrenia. Behavioural and biochemical effects of centrally administered NT resemble those of systemically administered antipsychotic drugs (2).

Nitric oxide (NO) acts as an intercellular messenger (3). NO may influence the maturation of neurons and synaptogenesis during neuronal development. Therefore, a disturbance in NO release could interfere with the maturation of brain neurons as well as with their functional connections (4). Such alteration at early stages of development could lead to a dysfunctional CNS, which in turn, may exhibit schizophrenia symptoms (5).

We have previously studied cortical synaptosomal membrane Na\(^+\), K\(^+\)-ATPase activity in the presence of NT, to observe that the peptide inhibits this enzyme activity, an effect entirely prevented by high affinity NT receptor antagonist SR 48692 (6). In order to study potential relationship between NO and Na\(^+\), K\(^+\)-ATPase regulation, herein we tested NT effect in membranes isolated from rats early administered with an inhibitor of neuronal nitric oxide synthase (nNOS).

MATERIALS AND METHODS

- Male and female Sprague- Dawley rats maintained in a 12-h light:dark cycle and with access to food and water ad libitum were employed. On postnatal days 3- 5 rat pups were injected (s.c.) with vehicle (saline solution), 10 or 100 mg/kg N-\(\omega\)-nitro-L-arginine (L-NoArg,) (5).
- Procedure for the open field behavioral task: a wooden box with lines dividing the floor into 12 equal squares was used. Rats were gently placed on the posterior left corner of the open field box and allowed to explore for 5 min.
- Synaptosomal membranes were isolated by differential and sucrose gradient centrifugation as previously described in this laboratory (7)
- ATPase activity was measured as described Albers et al.(8).
- \([^3H]\)-ouabain binding assays were carried as described by Antonelli et al. (9).

RESULTS

- Rats were subjected to the open field behavioral task; the number of crosses was counted. A transiently lower locomotor activity and an impediment in learning were observed in rats early administered with nNOS inhibitor.
- The presence of 3.5 x 10\(^{-8}\), 3.5 x 10\(^{-6}\) M NT produced 6%-34% inhibition of Na\(^+\), K\(^+\)-ATPase activity in membranes isolated from 35 days old male and female untreated rats. This peptide concentration range failed to change Na\(^+\), K\(^+\)-ATPase and Mg\(^{2+}\)-ATPase activities in membranes isolated from treated rats. Basal Na\(^+\), K\(^+\)-ATPase and Mg\(^{2+}\)-ATPase activities in cortical synaptosomal membranes from male and female rats early administered with saline (vehicle) or nNOS inhibitor indicated no changes in the mentioned enzyme activities. \([^3H]\)-ouabain specific binding decreased 37% and 53% in young (35 day old) and adult (56 day old) male rat membranes, respectively in the presence of 1.0 x 10\(^{-6}\) M NT. At variance, this peptide concentration decreased 12% \([^3H]\)-ouabain in membranes isolated from control rats of either age.

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CONCLUSIONS
Results presented suggest that inhibition of NO synthesis at early stage of brain development produces a permanent alteration of the neurotensinergic system, which is involved in Na⁺, K⁺-ATPase activity inhibition by neurotensin.

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REFERENCES