

Effects of Sulpiride Treatment on the Hypothalamic Supraoptic and Paraventricular Nuclei

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Abstract: The sulpiride plays an effects on the hypothalamic hypophyseal axis. In this study, we study the effect of sulpiride on the hypothalamic supraoptic and paraventricular nuclei by measurement of the neuronal nuclear volume that is an index of their activity. The results show that many neurons present the nuclear volume similarly to controls but in one rat, M2, the percentage of neurons with lower nuclear volume than the controls indicating a little activity. The comparison between the histogram lines of supraoptic nucleus and paraventricular nuclei shows that in two cases the nuclear volume of the neurons of supraoptic is even more high than the paraventricular, while in a single case with the steady dioestrus, the percentage of neurons with high volume is less high in supraoptic nucleus than paraventricular nucleus indicating that the neurons of the supraoptic nucleus play a decrease activity than the neurons of the paraventricular nucleus in response to the sulpiride treatment. In conclusion, in women before the sulpiride treatment it needs to consider the age, the menstrual cycle and the sexual activity.

Key words: Sulpiride, hypothalamic supraoptic nucleus, hypothalamic paraventricular nucleus, neurons, sexual activity, menstrual cycle

INTRODUCTION

The sulpiride is a drug that used in antidepressant treatment in patients with the depression. Linquette *et al.* (1975) demonstrated that the sulpiride plays an strong antioviulatory effect on the hypothalamic-hypophyseal axis and induces the ovarian resistance to gonadotropins because of hyperprolactinism. Borenstein *et al.* (1977) using electrophysiological tests in cat showed that the hypothalamus represents a preferential target for the action of the sulpiride and sultopiride. Today, no data in literature regards the morpho-functionality of the hypothalamic neurosecretory nuclei. In this study, we want to verify whether the treatment with the sulpiride determinates variations in the neurosecretory activity of the hypothalamic magnocellular nuclei; for this aim, we carried out the measurements of nuclear volume of neurons in the hypothalamic neurosecretory, supraoptic nucleus and paraventricular nuclei since the nuclear volume is a significant morphofunctional parameter indicating their cellular activity.

MATERIALS AND METHODS

The injected solution was prepared by addition. Female rats Wistar (200 g weight) n°6 were treated with sulpiride. The injected solution was prepared adding to

9 mL distilled water 1 phial Dobren (N[(1-ethylpyrrolidin-2-ly)methyl]-2-methoxy-5-sulfamoylbenzamide) 0.0100 g; sodium chloride 0.010; sulfuric acid 0.015; distilled water q.b.). To each female rat a sulpiride dose, 1 mL die⁻¹, v.i. was injected daily after that a vaginal smear was conducted and stained by Shorr's method to determinate the phase of o estral cycle; the treatment was prolonged for 17 days, when the dioestrus phase results constant. Each female rat was sacrificed 1 h after the daily treatment from each specimen, the hypothalamic area was isolated, fixed in Bouin's fluid, dehydrated and embedded in paraffin. Sections, with 8-10 μ thick, were stained with Giemsa or Gomori's methods.

The supraoptic and paraventricular nuclei were outlined and in each nucleus a number 200 of the neuron diameters were measured with an ocular micrometer and objective 30 x Reichert (600 x). In each neuronal nucleus, the major and minor diameters were measured, from which the middle diameter and volume was determined. The nuclear volumes were enclosed in classes with a difference of 0.5.

RESULTS AND DISCUSSION

Control (I2): In the hypothalamic supraoptic nucleus, the volume of the nuclei of the neurons is almost enough

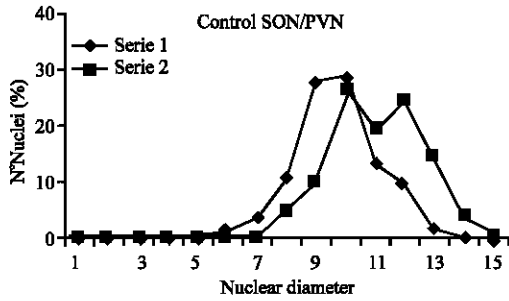


Fig. 1: Control untreated rats. Confront between the curves of the supraoptic nucleus, serie 1, (blue) and paraventricular nucleus, serie 2 (red)

constant, indeed the percentage of neurons with similar volume is high and the volume range is much restricted. In hypothalamic paraventricular nucleus, the neurons have the nuclear volume higher than the nuclear volume of the neurons of the hypothalamic supraoptic nucleus. The comparison between hypothalamic supraoptic and paraventricular nuclei evidences that a percentage greater of the neurons of the supraoptic nucleus presents the lesser and are much constant volume; the neurons of the hypothalamic paraventricular nucleus present a volume greater than supraoptic neurons (Fig. 1). In the sequent, are reported some cases of the sulpiride treated rats.

Case M2: In the hypothalamic supraoptic nucleus, the percentage of the neurons with nuclear less volume values has a narrow range (much limited), the percentage of neurons with middle-high volumes is much elevated and present two peaks, while the percentage of the neurons with large volume is much high than PVN. In hypothalamic paraventricular nucleus, the range of the volumes is extended.

The percentage of neurons less volume is much low, the percentage of the neurons with large volume is high and neurons with much high volume are present. Comparison between the two nuclei evidences that the neurons with high volume are less numerous in SON than in PVN (Fig. 2).

Case S2: In the supraoptic nucleus, the volume range is much limited with an much high percentage of neurons and therefore, the nuclear volume results although constant.

In the paraventricular nucleus, the volume range is less limited and few neurons have a large nuclear volume. The comparison between the two nuclei evidences that in the supraoptic nucleus the neurons present a volume range less extended than paraventricular nucleus (Fig. 3).

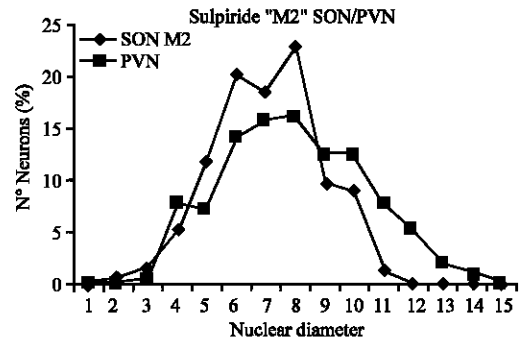


Fig. 2: Sulpiride treated rats. Confront between the curves of the supraoptic nucleus (bleu) and paraventricular nuclei (red)

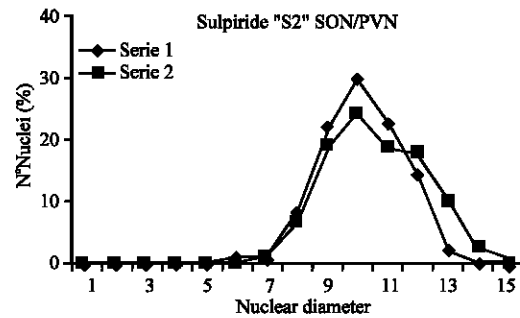


Fig. 3: Sulpiride treated rats. Confront between the curves of the supraoptic nucleus serie 1 (blue) and paraventricular nucleus (red)

Case D2: In supraoptic nucleus, the range-volume is large, the percentage with little volume is low, the percentage with medium-high volume is high. In paraventricular nucleus, the neurons with little volume are absent, the percentage of neurons with medium-high volume is elevated. The comparison between the two nuclei evidences that the percentage of neurons with high volume is less high in supraoptic nucleus than paraventricular nucleus (Fig. 4). The comparison between control rats and treated rat shows that in supraoptic nucleus the percentage of neurons with similar nuclear volume differs little (Fig. 5) and that in paraventricular nucleus in the control rats, the percentage with volume is lightly higher than in the treated rats (Fig. 6).

The sulpiride is used in clinical therapy as psychotropic (Justin-Besaçon *et al.*, 1967a, b) psychotropic and antidepressive drug and acts on prolactin and gonadotropin secretions in the women clinical observations evidence variable incidence of amenhorrea (Coliche, 1971). The results in rat evidence that the sulpiride treatment determines a notable variability of the oestral cycle but often more long

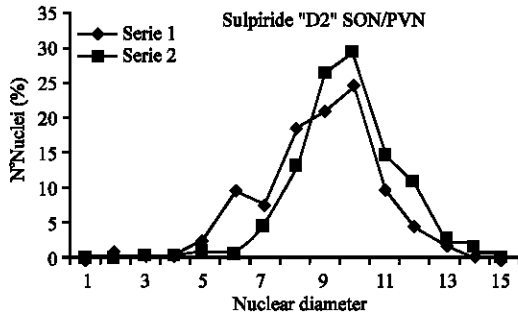


Fig. 4: Sulpiride treated rats. Confront between the curves of the supraoptic nucleus, serie 1(blue) and paraventricular nuclei serie 2 (red)

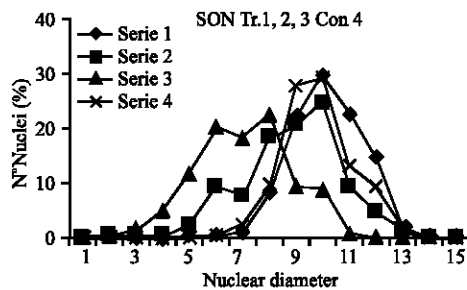


Fig. 5: Supraoptic nucleus. Confront between the curves of the sulpiride treated rats: series 1 (blue), 2 (red), 3 (yellow) and control untreated rats, serie 4 (green)

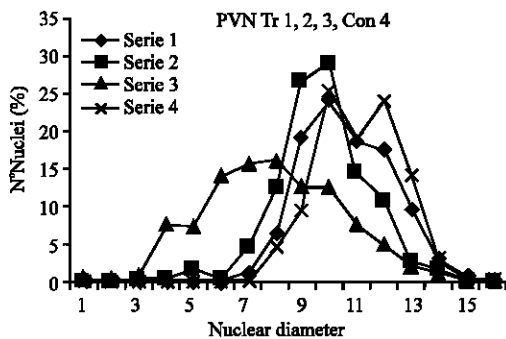


Fig. 6: Paraventricular nucleus. Confront between the curves of the sulpiride treated rats: series 1 (blue), 2 (red), 3 (yellow) and control untreated rats serie 4 (green)

dioestral stage occurs. In this study, since a correlation between the activity of the hypothalamic parvocellular and the oestral cycle occurs, we want study whether in the hypothalamic magnocellular supraoptic and paraventricular nuclei the sulpiride treatment induces in neurons some changes the nuclear volume that can be consider a index of their activity.

In all treated rats cases, the histogram line relative to both the hypothalamic supraoptic nucleus and hypothalamic paraventricular nucleus shows that many neurons present the nuclear volume similarly to controls and only in one case, M2, shows a percentage of neurons with lower nuclear volume than the controls indicating a little activity. The comparison between the histogram lines of supraoptic nucleus and paraventricular nuclei shows that in cases, S2 M2, the nuclear volume of the neurons of supraoptic is even more high than the paraventricular; while in a single case, D2, with the dioestrus, the comparison between the two lines shows that the percentage of neurons with high volume is less high in supraoptic nucleus than paraventricular nucleus indicating that the neurons of the supraoptic nucleus present a decrease activity in response to the sulpiride treatment than the neurons of the paraventricular nucleus. The comparison between the neuronal volumes in the supraoptic and paraventricular nuclei of the treated and controls rats shows that in the paraventricular nucleus the neuronal volume is higher in the controls than in the treated rats, while in the supraoptic nucleus the neuronal volume little differs in the control and treated indicating that the paraventricular nucleus presents activity higher than the supraoptic nucleus by sulpiride treatment.

CONCLUSION

In this study, the treatment with sulpiride surely has effects on the hypothalamic neurosecretory nuclei but with variable incidence in single rat so we thought that also each women for the treatment with sulpiride needs a attention to the age and sexual activity and cycle menstrual.

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