Enhanced electrical activity of supraoptic neurones following systemic melanocortin administration

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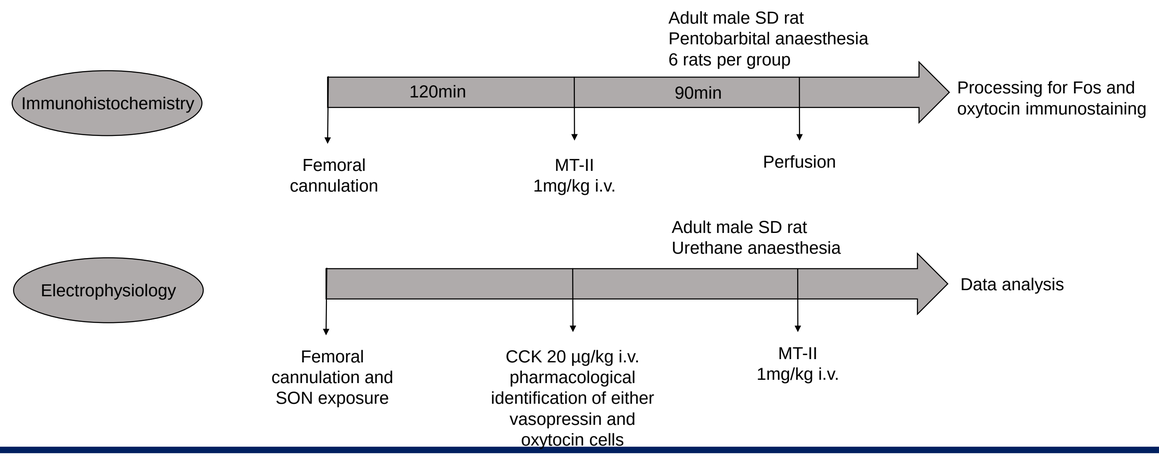
Introduction

Melanocortins stimulate the central oxytocin systems which regulate social behaviours[1]. Alterations in central oxytocin has been linked to neuropsychiatric disorders such as autism and anxiety, and melanocortins have been proposed for therapeutic treatment. Naturally occurring melanocortins including alpha-melanocyte stimulating hormone (α-MSH) potently stimulate oxytocin release from the dendrites of oxytocin cells, but inhibit their electrical activity[2]. α-MSH has a poor penetrance through the blood-brain barrier. Here we investigated whether Melanotan-II (MT-II), a synthetic melanocortin agonist, affects the electrical activity of supraoptic (SON) oxytocin and vasopressin neurons when given intravenously.

Methods



MT-II induces Fos expression in the SON

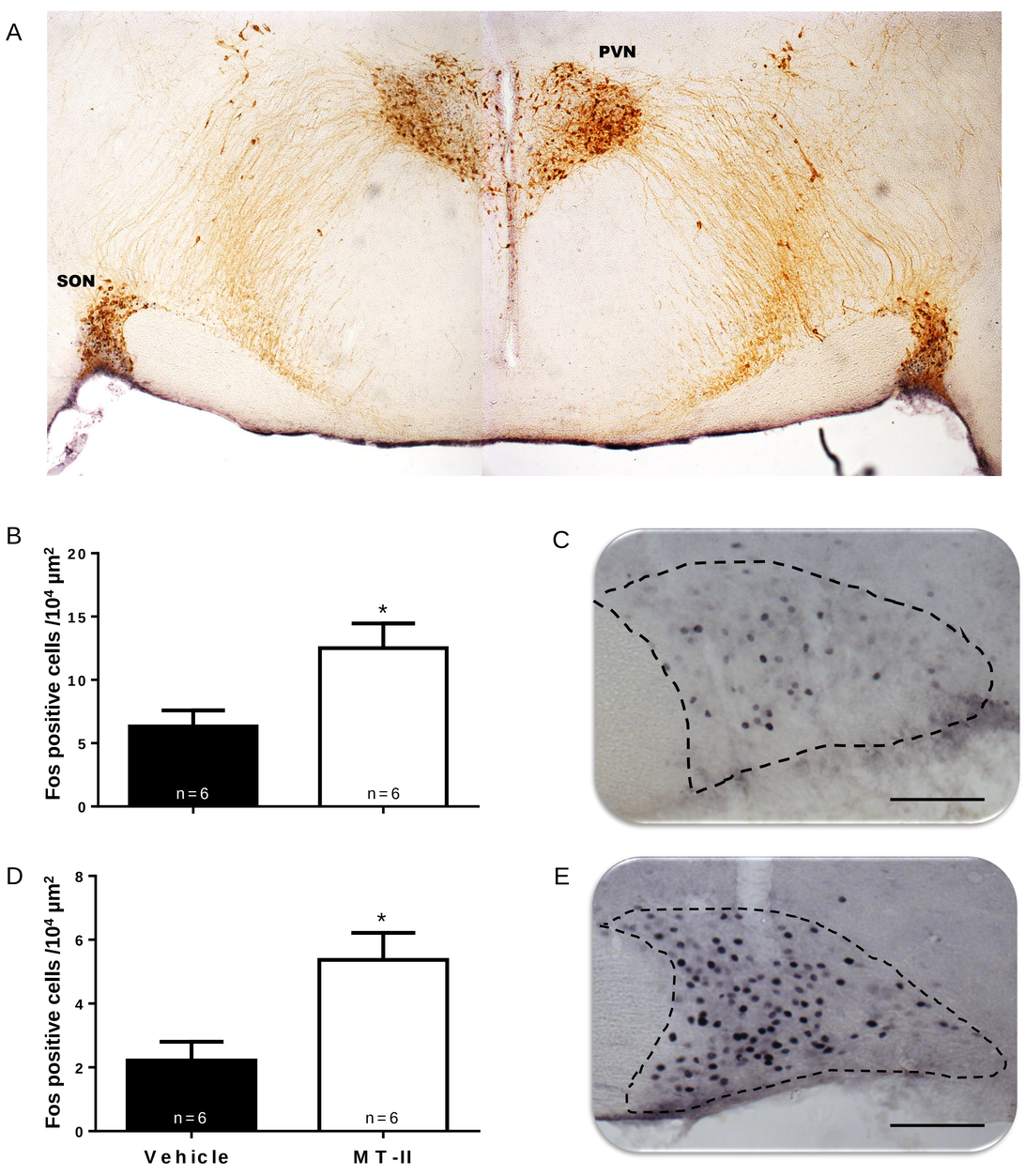


Fig. 1. The SON and paraventricular nucleus (PVN) are the main sites of synthesis of oxytocin and vasopressin in the brain. (A) Coronal section showing immunostaining for Fos (black nuclear) and oxytocin (brown cytoplasm) in the PVN and SON in a control rat. (B) I.v. injections of MT-II increase Fos expression in the SON. (D) Fos expression in oxytocin cells of the SON increase following MT-II administration. (C,E) Fos expression in the SON in vehicle (C) and MT-II (E) treated rats (no oxytocin staining in these sections). Scale bar = 100µm. Means ± S.E.M.; *P<0.05, Mann-Whitney U test.

MT-II enhances electrical activity in oxytocin neurons when given i.v.

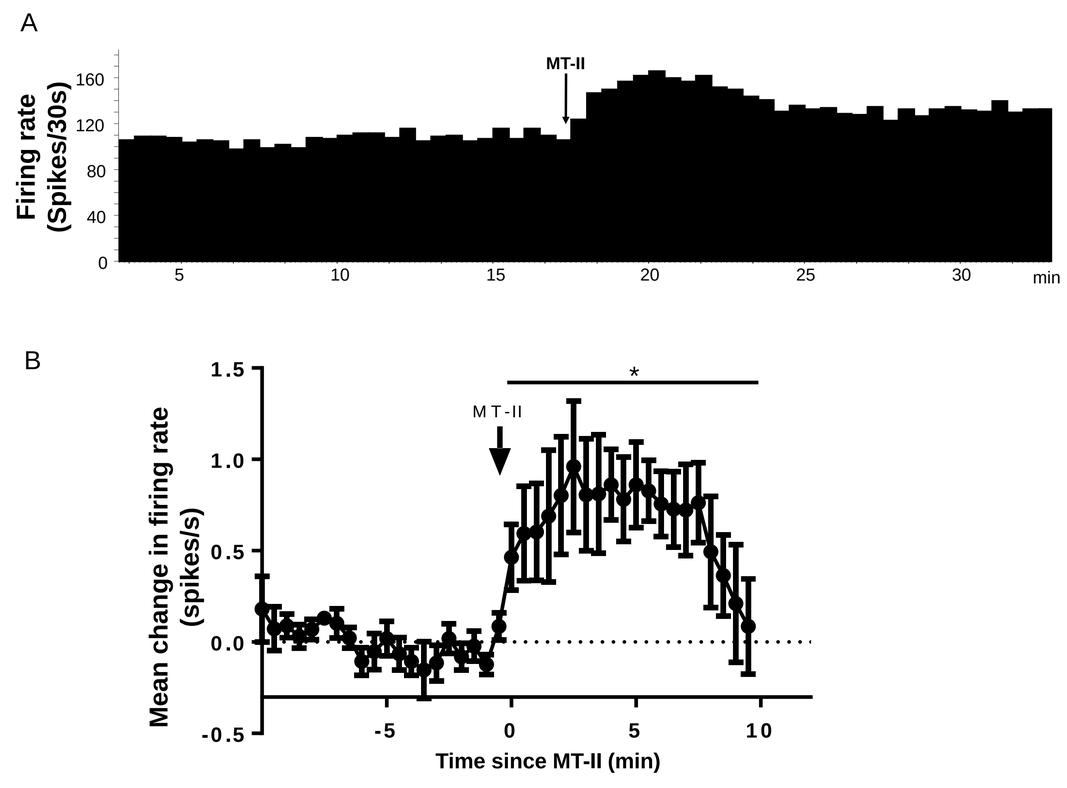


Fig. 2. (A) Typical example of the increase in firing rate in an oxytocin neuron in response to i.v. administration of MT-II. (B) Mean change in firing rate of 8 oxytocin cells after MT-II i.v. in 30-s bins (± S.E.M.; *P<0.05, Wilcoxon Signed Rank test).

MT-II also enhances electrical activity in vasopressin neurons

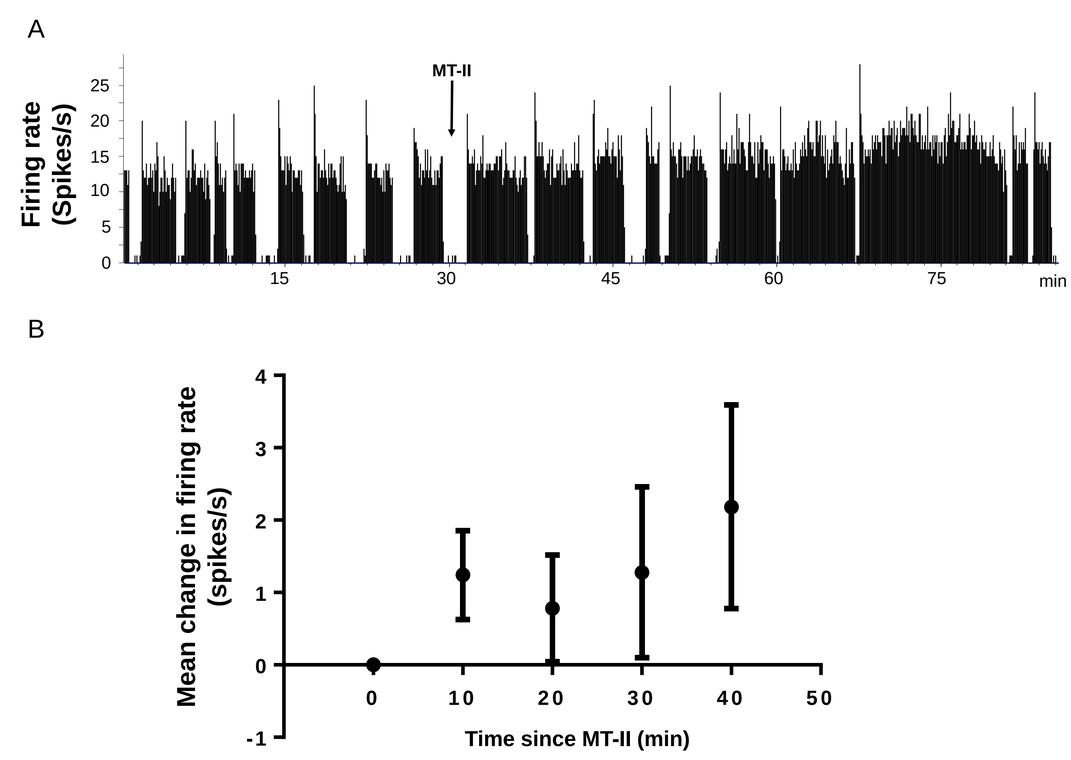


Fig. 3 (A) Typical example of the increase in firing rate in a vasopressin neuron in response to i.v. administration of MT-II. (B) Mean change in 6 vasopressin cells in response to MT-II i.v. in 10-min bins (± S.E.M; Wilcoxon Signed Rank test).

Conclusions

Intravenous (i.v.) administration of MT-II induces neural activation in oxytocin and vasopressin cells of the SON. As oxytocin neurons are electrically inhibited in response to direct application of melanocortin agonists, the actions of intravenous MT-II are likely to be mediated indirectly.

References

1. Modi et al. 2015. Melanocortin receptor agonists facilitate oxytocin-dependent partner preference formation in the prairie vole. *Neuropsychopharmacology* 40: 1856-1865.
2. Sabatier et al. 2003. Alpha-melanocyte-stimulating hormone stimulates oxytocin release from the dendrites of hypothalamic neurons while inhibiting oxytocin release from their terminals in the neurohypophysis. J Neurosci 23:10351-58.

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