Functional interactions between MCHergic and serotonergic neurons. An *in vivo* electrophysiological study

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BACKGROUND AND AIM

Melanin-concentrating hormone (MCH) containing neurons of the postero-lateral hypothalamus (PLH), project to the serotonergic dorsal (DR) and median raphe nuclei (MR), where MCHergic receptors were identified. In addition serotonergic neurons of these nuclei project towards PLH.

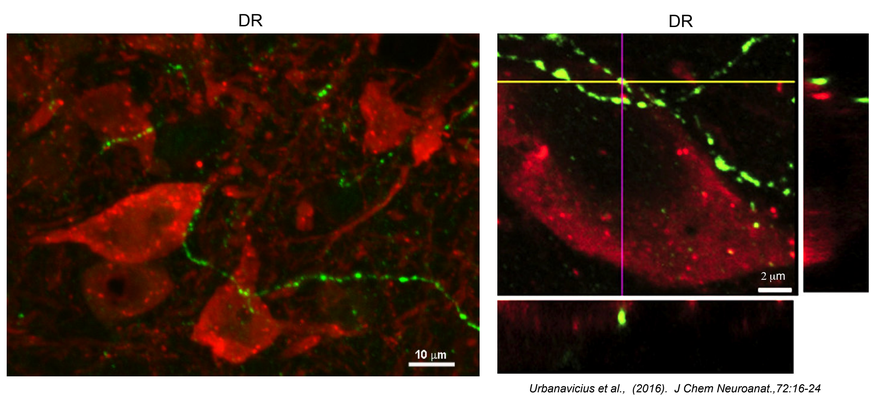
When applied into the DR and MR, MCH produces a pro-depressive effect and increases REM sleep, which is considered a marker of depression. Furthermore, the serotonergic antidepressive Fluoxetine (FLX) decreases MCH levels in the cerebro-spinal fluid, suggesting that MCH promotes a pro-depressive state, and that the DR/MR underlies this behavioral effect.

MATERIALS AND METHOD

In this study we analyzed the effects of intraventricular or juxtacellular application of MCH and MCH-1 receptor (MCHR-1) antagonists on the firing rate of DR/MR neurons. We also investigated the effect of the juxtacellular application of FLX on PLH neurons. Unit recordings of DR/MR and PLH were performed in rats anesthetized with urethane. Recorded neurons were labeled with neurobiotin, and MCH or serotonin were detected by means of immunofluorescence.

Background

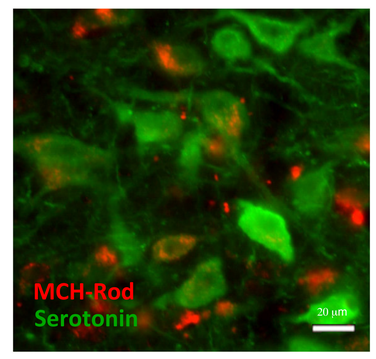
MCHergic neurons project to the DR and MR nuclei



Urbanavicius et al., (2016). J Chem Neuroanat.,72:16-24

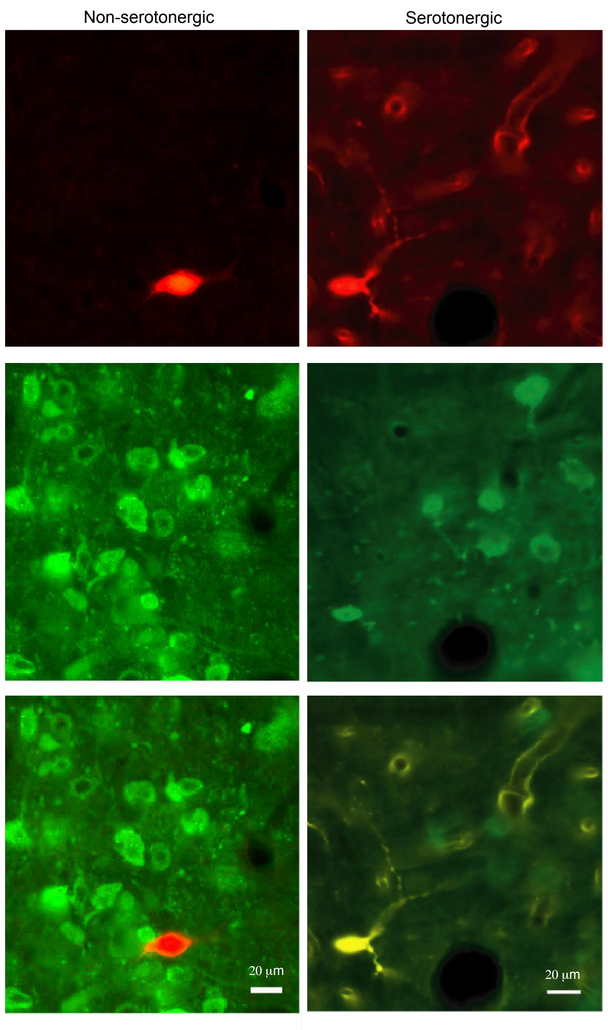
Urbanavicious,In preparation

MCH-rodamine microinjected into the lateral ventricle is incorporated by DRN and MR neurons

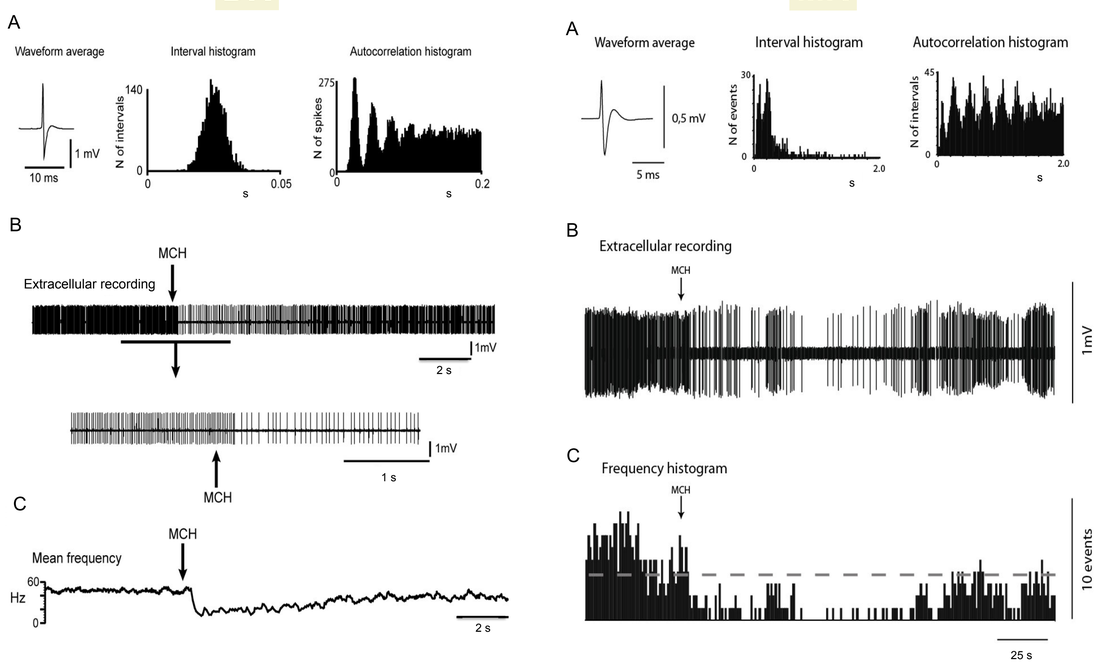


Results

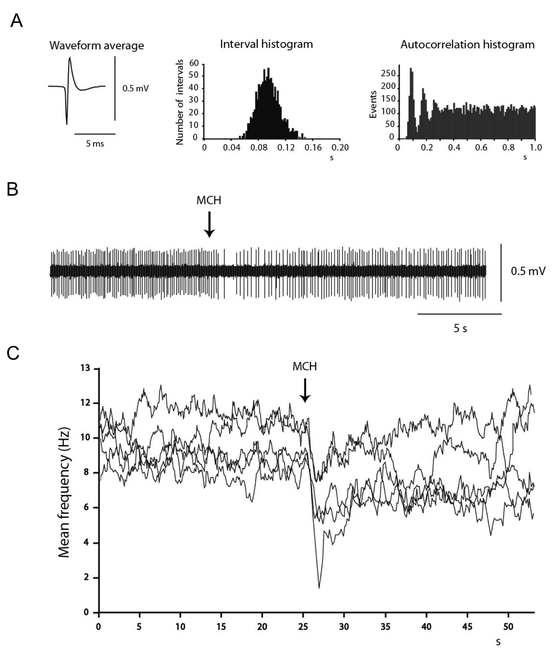
1- Serotonergic and non-serononergic neurons were identified



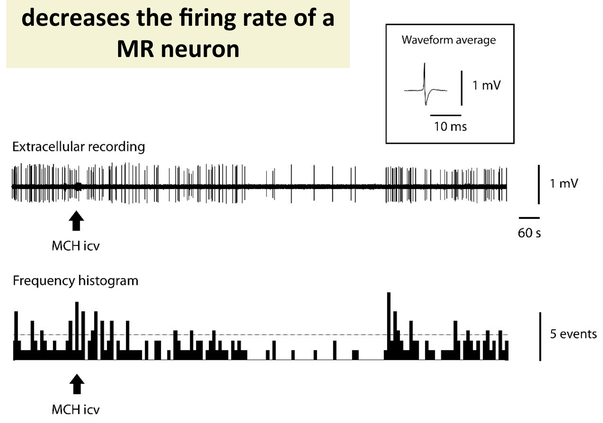
2- Juxtacellular administration of MCH decreases de firing rate of DR and MR neurons



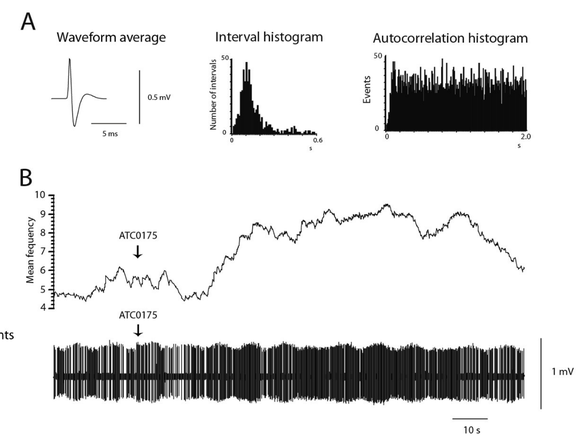
3- Repeated administration of juxtacellular MCH produces a similar effect



4- Microinjection of MCH into the lateral ventricle decreases the firing rate of a MR neuron



5- Juxtacellular administration of MCHR-1 antagonist produces de opposite effect



Summary and conclusion

- In the DR/MR, MCH decreased the firing rate of most of the recorded neurons; some of them had serotonergic phenotypes.
- MCHR-1 antagonist produced the opposite effect.
- In the PLH, FLX decreased the firing rate of 92% of recorded neurons. Some of them were recognized as MCHergic.

These data highlight the robust interactions between MCHergic and serotonergic systems, and support the hypothesis that MCH is a pro-depressive factor.

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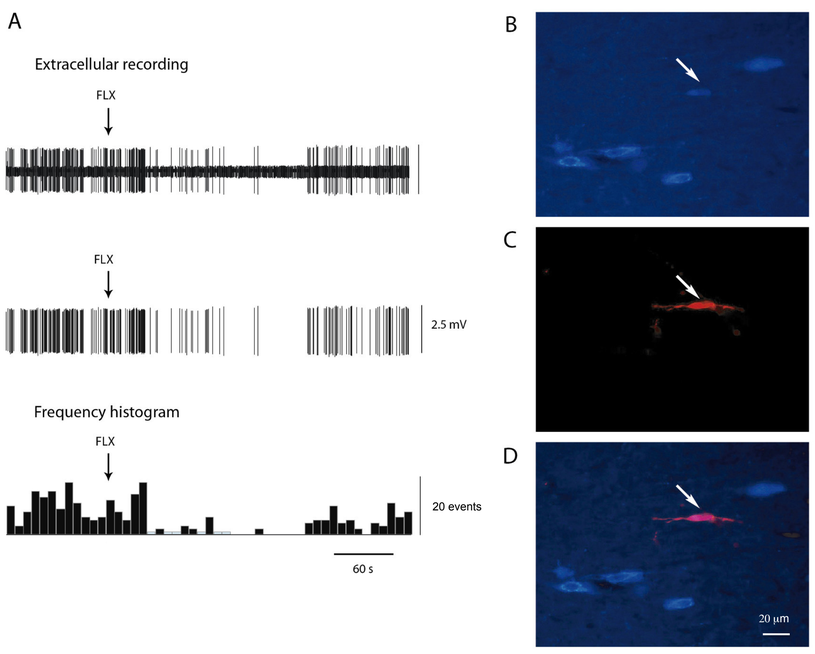
Effect of fluoxetine in MCHergic neuronal activity

6- MCHergic neurons are inhibited by fluoxetine



7- Non-MCHergic neurons are inhibited by fluoxetine