A model of synaptic transmission in the orbitofrontal cortex- modulation by monoamines

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Introduction

- Neurocognitive dysfunction plays a central role in the pathology of psychiatric disorders such as schizophrenia. [1]
- The orbitofrontal cortex (OFC) mediates reversal learning in the rat [2], a feature of neurocognitive function .
- Synaptic transmission in the OFC is currently uncharacterised.
- Strength of synaptic transmission can be measured using an electrically evoked field potential (FP).

Aim

To develop a model of synaptic transmission in the orbitofrontal cortex of the rat and to examine its modulation by monoamine neurotransmitters.

Method

Preparation

- 400µm slices of rat orbitofrontal cortex were mounted in an interface chamber, warmed to 36º and perfused with oxygenated aCSF.

Induction of FP

- Stimulating and recording electrodes were placed in layer III and current response was then determined.
- The FP was then allowed to stabilise (<10% variation)

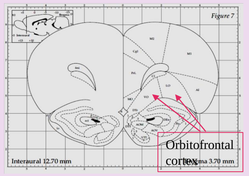


Figure 1: Diagram of coronal section of rat brain showing the OFC (Paxinos and Watson, 1996)

Drugs

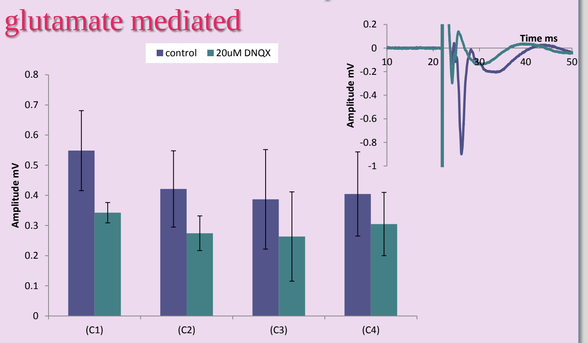
- All drugs were applied via perfusion
- 5-HT, NA and DA were applied for 10 minutes at increasing concentrations.
- antagonists (prazosin (100nM), yohimbine (20µM), propranolol (100µM, 30µM and 1µM) timolol (100nm)) were applied for 10 minutes followed by immediate application of a cocktail of antagonist + 60µM NA

Analysis

- Data was taken from the last 300 seconds of each drug application and analysed using a 2 way ANOVA with repeated measure.

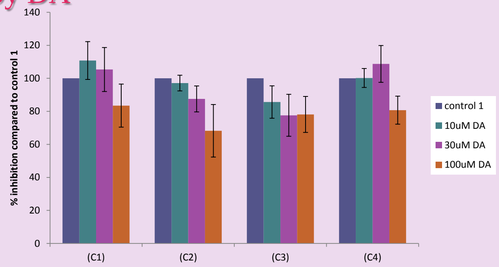
References
[1]Wobrock et al. World Journal of Psychiatry (2008)
[2]McAlonan et al. Behavioural Brain Research (2003)

Results: I The OFC field potential is glutamate mediated



- After application of 20µM DNQX for 10 min, all components of the FP were smaller.

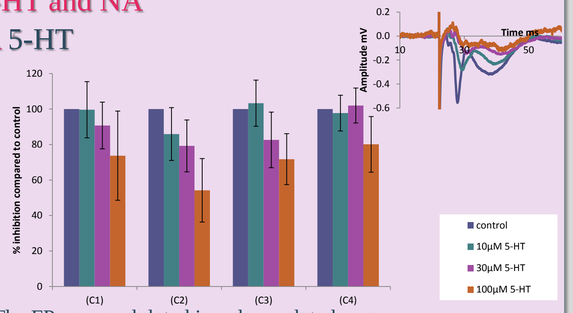
II The OFC field potential is not modulated by DA



- Application of DA for 10 minutes at each increasing concentrations did not modulate the FP.
- No significant interactions between DA and components.

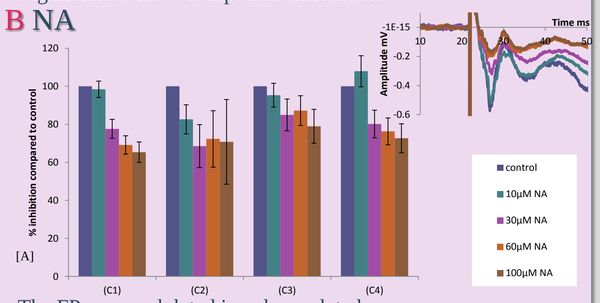
III. The OFC field potential modulated by 5-HT and NA

A 5-HT



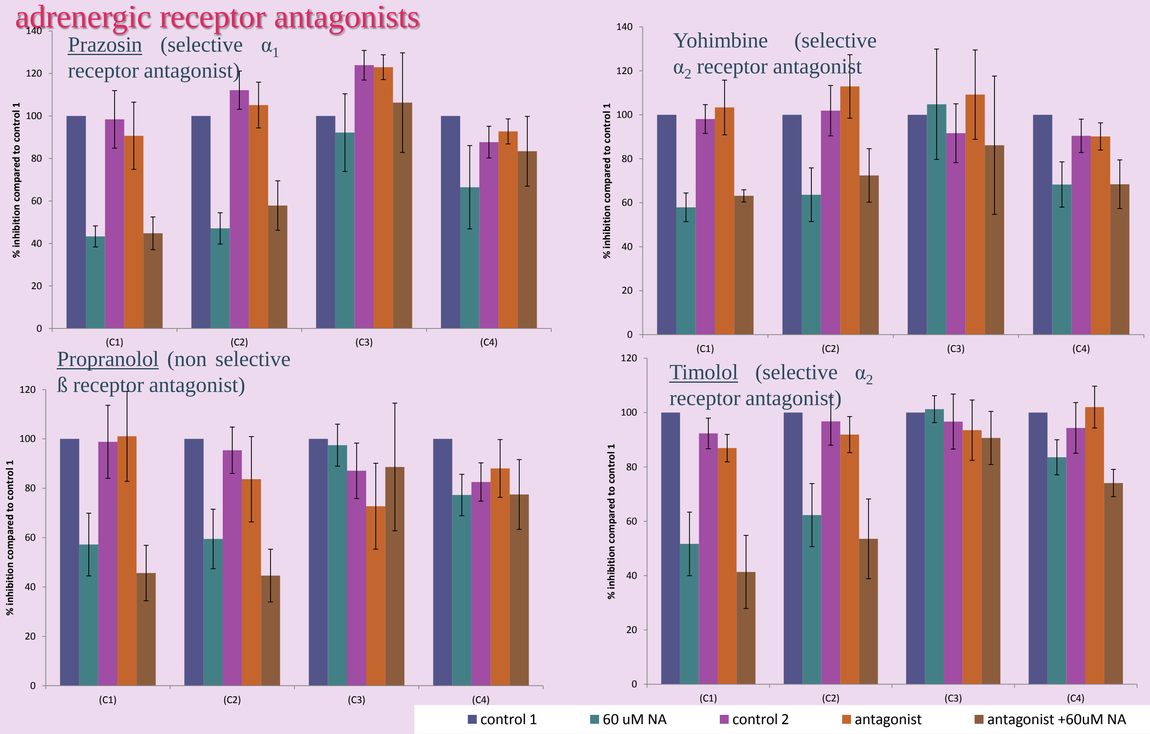
- The FP was modulated in a dose related manner
- Significant 5-HT x component interaction

B NA



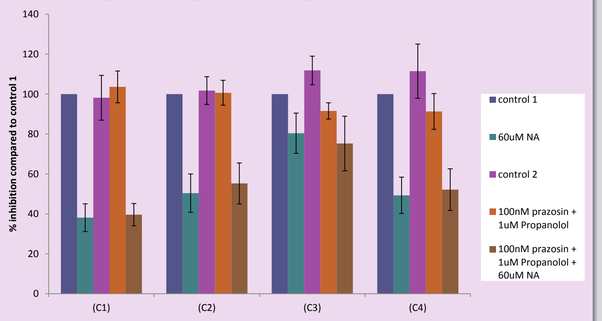
- The FP was modulated in a dose related manner
- Significant NA x component interaction

IV. The effect of NA was not blocked by selective α_1, α_2, and β_1, and non selective β adrenergic receptor antagonists



- No significant difference between application of NA alone, and application with antagonist + NA.
- Higher concentrations of propranolol (30µM and 100µM) had a local anaesthetic effect on the FP, reducing all components.

V. The effect of NA was not blocked by a cocktail of a non selective β and selective α_1 adrenergic receptor antagonist



- No significant difference between NA x component interactions with NA alone, and NA + cocktail of antagonists (1uM Propranolol + 100nM Prazosin)

Conclusions

The results firstly show that the OFC field potential is glutamate mediated and secondly that it is modulated by both 5-HT and NA, but not DA. The effect of NA was not blocked by selective α1, α2, and β1, and non selective β adrenergic receptor antagonists or a cocktail of a non selective β and selective α1 adrenergic receptor antagonist. Possible further studies could look at trying to mimic the response using NA agonists, or investigating the 5-HT response further.