

How is synaptic transmission in the orbitofrontal cortex modulated by the monoamine neurotransmitters?

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Introduction

The orbitofrontal cortex (OFC) is part of the prefrontal cortex, an area of the brain that has been implicated in cognitive defects that are present in psychiatric disorders such as schizophrenia and bipolar disorder.

Work by the Psychobiology research group has characterised synaptic transmission in another part of the prefrontal cortex, the medial prefrontal cortex (mPFC). [2] Field potentials (FP) can be used as a measure of synaptic transmission in brain tissue.

Aims

- Determine optimum electrode positioning to elicit a response, and characterise the FP.
- Examine how the monoamine neurotransmitters, dopamine (DA), serotonin (5HT) and noradrenaline (NA) modulate the FP.
- Characterise which receptors mediate these responses.

Methods

- Coronal brain slices (400µm) from male Lister-Hooded rats were mounted in an interface chamber, kept at 36°C, and perfused with artificial cerebrospinal fluid (aCSF).
- Recording and stimulating electrodes were positioned in the OFC according to topographical studies. [3]
- On finding a FP, signal polarity was reversed to distinguish a true FP from a stimulus artefact.

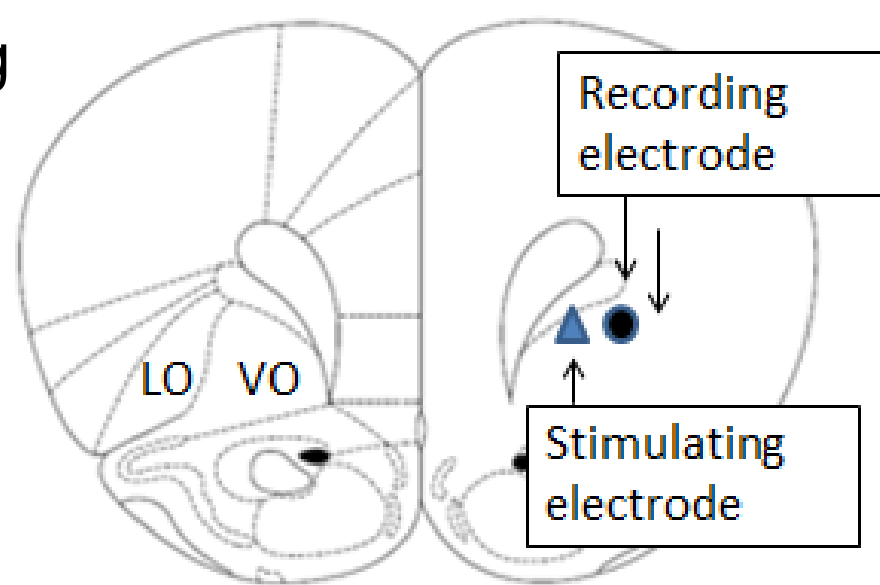


Figure 1. Optimum electrode positioning (VO, Ventral Orbital. LO, Lateral orbital.)

Results 2: The 5 components of the field potential

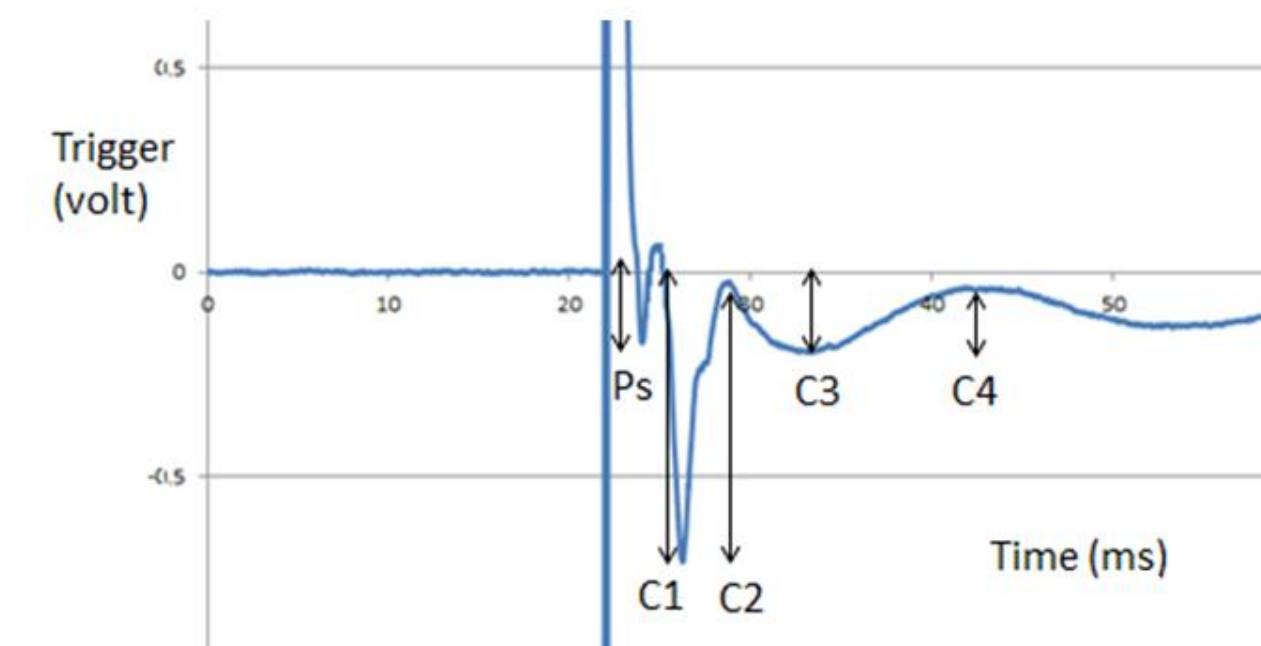


Figure 2. An average of 6 control field potentials in aCSF.

- As in the mPFC, the field potential had 5 components.
- Ps, the presynaptic component, was not always present.
- C1 had a short latency, suggesting a monosynaptic response.
- C3 and C4 were thought to be polysynaptic components due to their longer latencies.

Results 4: There is no significant effect of DA on the field potential

- Dopamine (DA) in 3 different concentrations was applied to a stabilised field potential.
- There was no consistent significant inhibitory effect of DA.
- The D1/D5 receptor agonist SKF similarly had no consistent effect on any component.

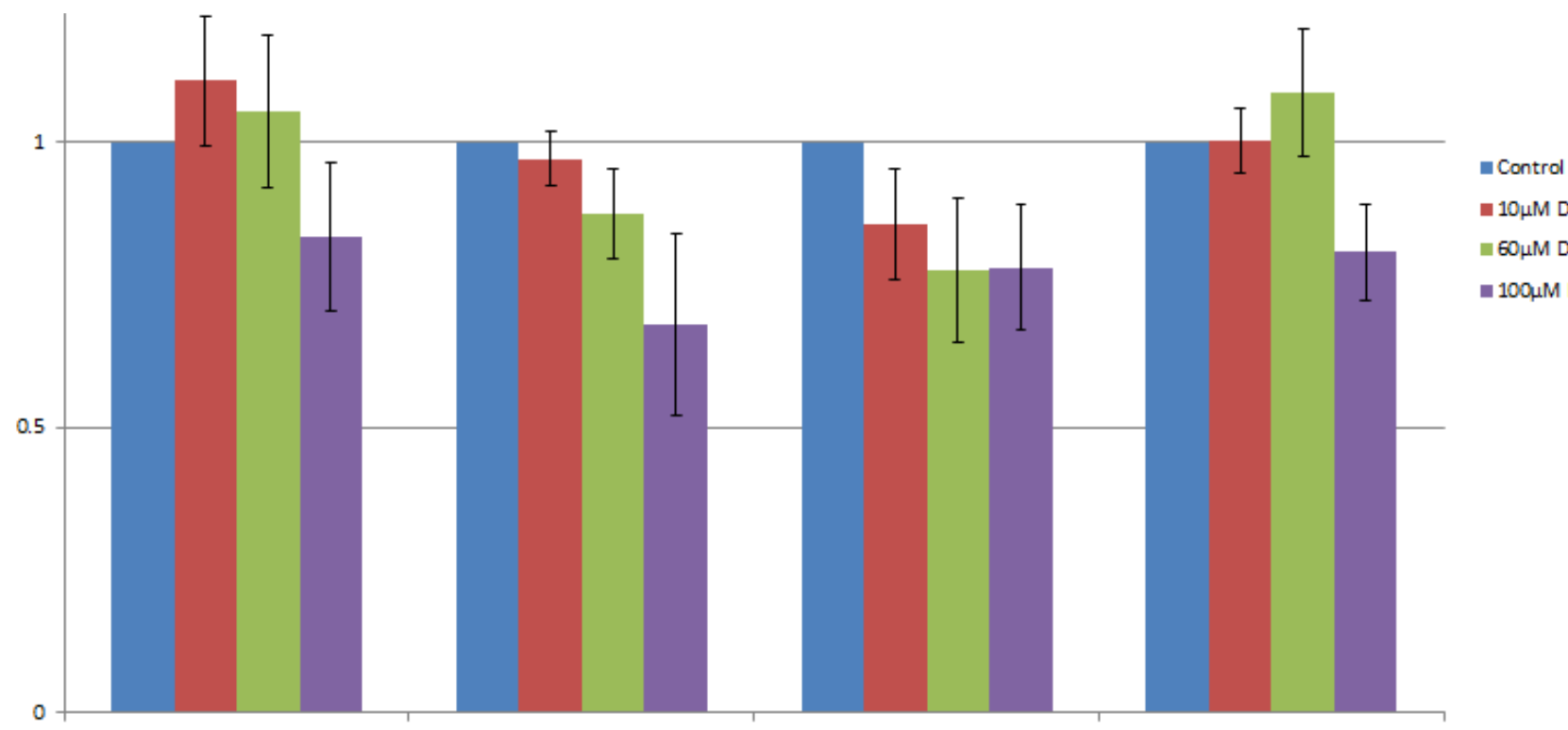


Figure 4: Effect of DA on individual components, as % of control value.

Results 5: The field potential is inhibited by NA

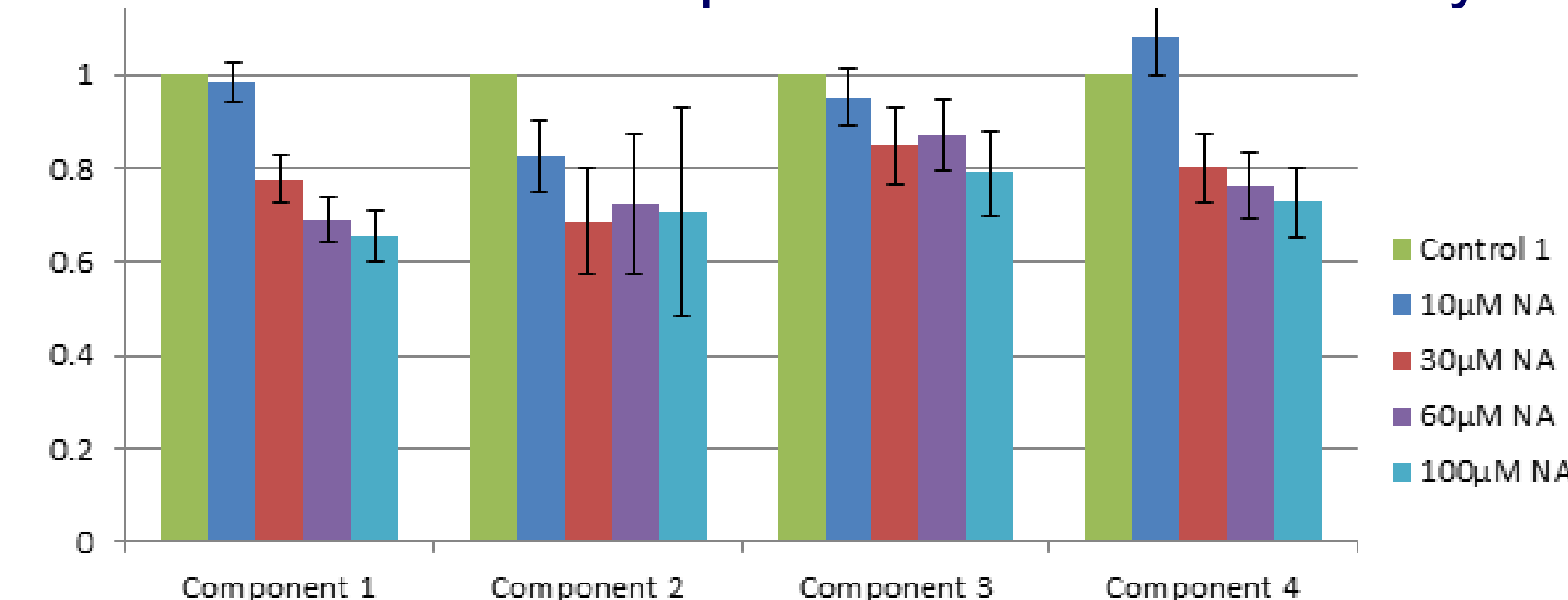


Figure 5: Effect of NA on individual components, as % of control value.

Results 3: The field potential is inhibited by 5HT

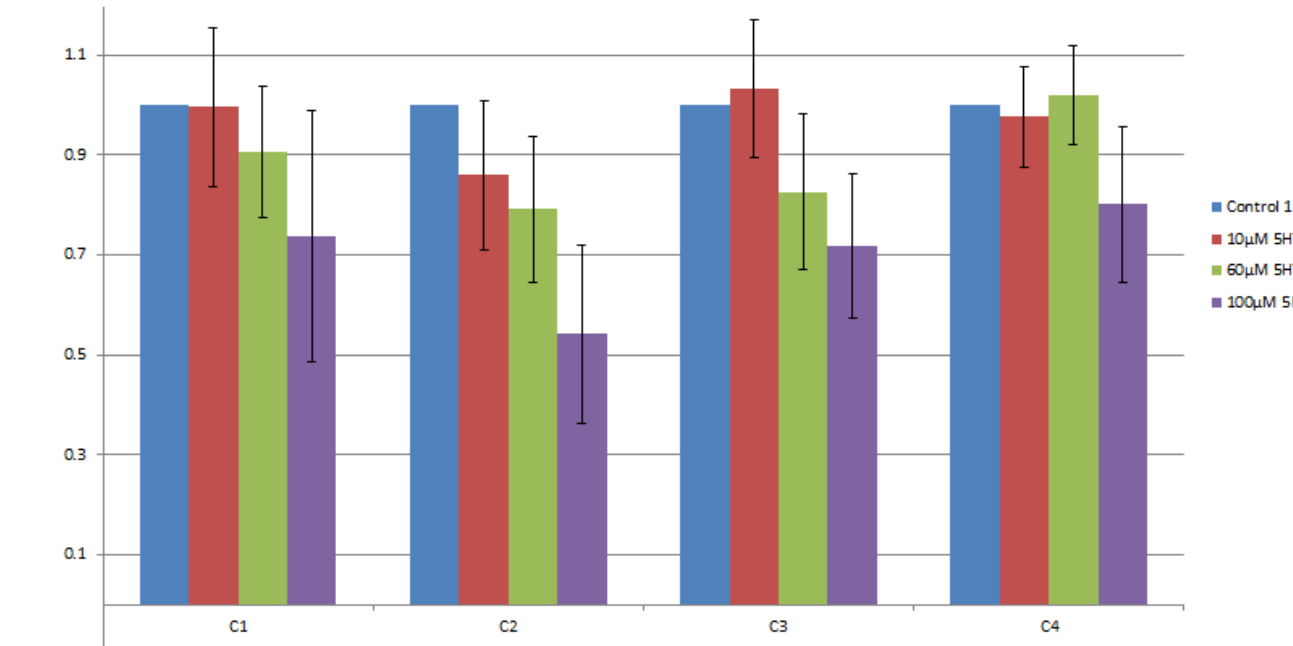


Figure 3: Effect of 5HT on individual components, as % of control value.

- As in the mPFC, there was a significant inhibitory effect of 5HT.
- The effect appears to be dose-related, but further data is needed.
- 100µM 5HT showed consistent and significant inhibition across all components.

Results 6: The effect of NA is not mediated by α-1 or α-2 receptors

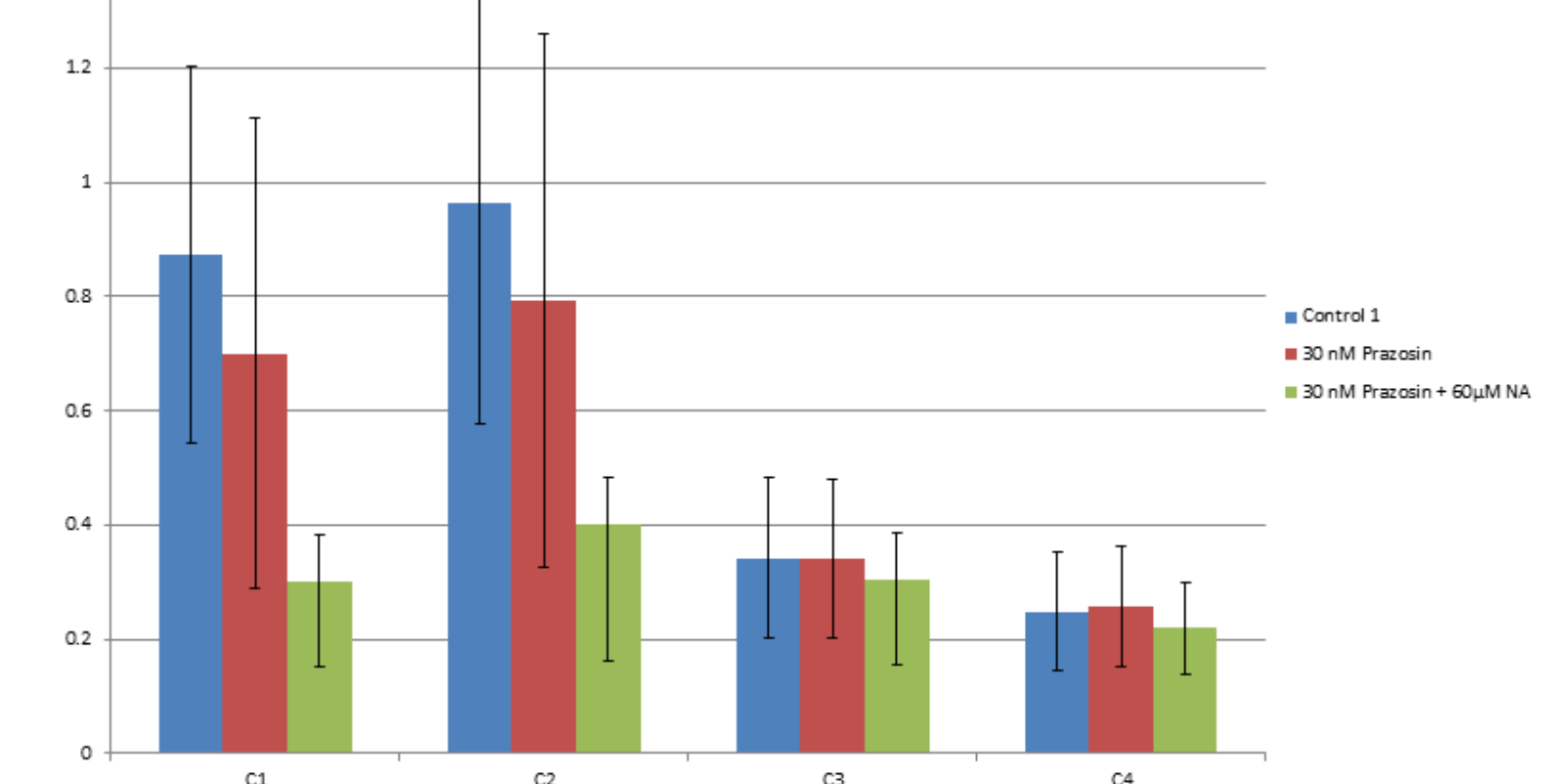


Figure 6. Prazosin does not block the inhibitory effect of NA. Expressed as % of control value

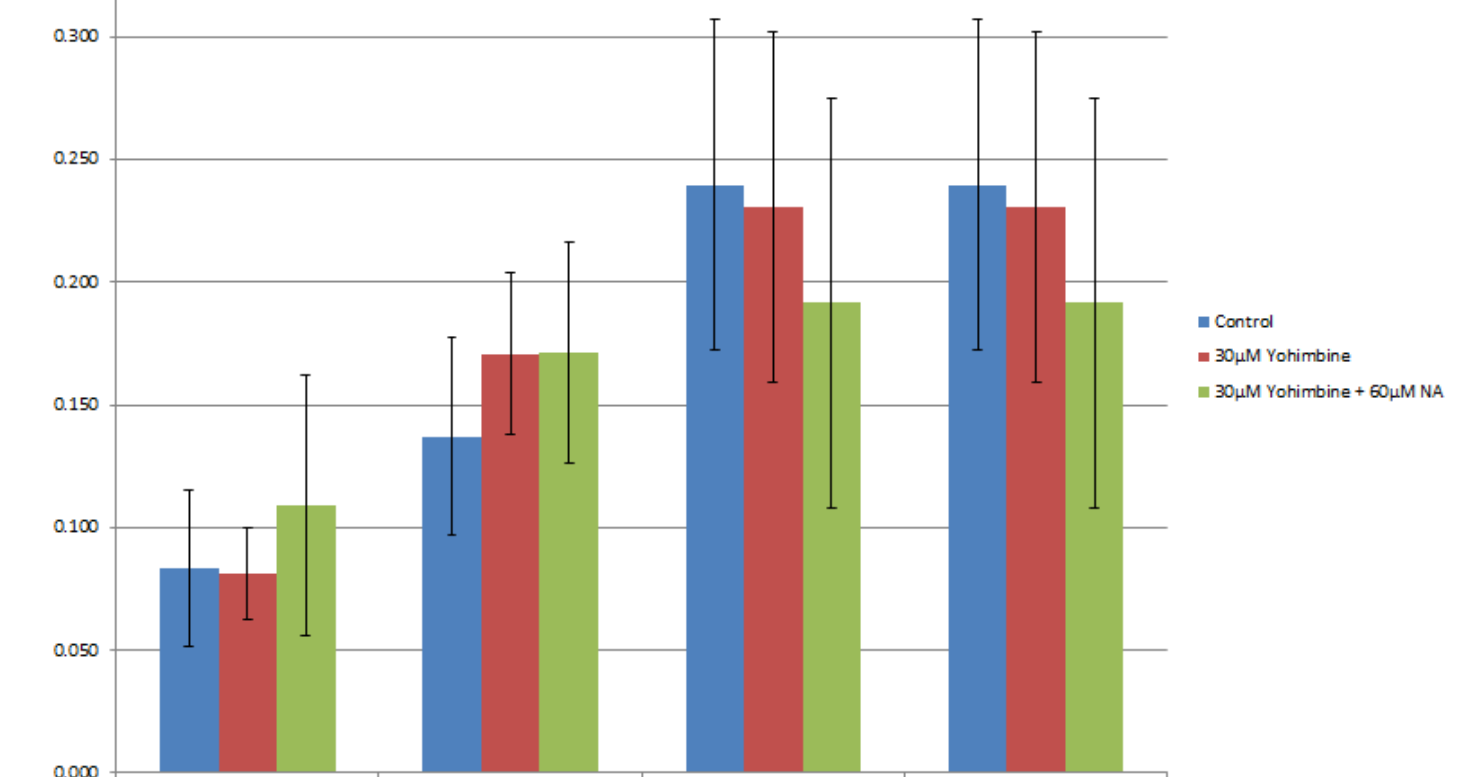


Figure 7. Yohimbine does not block the inhibitory effect of NA. Expressed as % of control value

- Prazosin, (α1 antagonist), and Yohimbine, (α2 antagonist) did not block the inhibition by noradrenaline.
- This shows that the effect of noradrenaline is not mediated by alpha-1 or alpha-2 adrenergic receptors.

Conclusions

- Optimum electrode positions in the lateral orbital orbitofrontal cortex were established.
- The field potential was characterised as having 5 distinct components.
- Serotonin and noradrenaline caused significant inhibition of the FP, and dopamine did not.
- Prazosin and Yohimbine did not block the inhibitory effect of noradrenaline; the mediating receptor is not alpha-1 or alpha-2 adrenergic.
- Further work to determine which receptors mediate the response will be carried out in the laboratory.

References

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Acknowledgments

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