

Altered neural activation by emotion regulation and reduced startle response in healthy volunteers after subchronic diazepam treatment



UNIVERSITY OF
OXFORD

Julia Gottwald¹, Abbie Pringle², Matthew Warren², Elizabeth Parsons², Catherine J. Harmer²

¹University of Cambridge, Department of Psychiatry, Cambridge, UK, ²University of Oxford, Department of Psychiatry, Oxford, UK

Background

Selective serotonin reuptake inhibitors (SSRIs) are efficacious in both depression and anxiety. A large body of research focuses on their psychological effect, but the discrimination of anxiolytic and antidepressant effects is very difficult.

A potential way of distinguishing between these two effect classes is the comparison of SSRIs with drugs that are clinically useful for anxiety but not depression, such as diazepam, a benzodiazepine.

Aim

Investigation of the neuro-psychological effects of diazepam, which are due to its anxiolytic properties.

Methods

- 36 healthy volunteers (aged 18-34 years) were randomly allocated to receive either diazepam (15mg/day) or placebo for 7 days with a double-blind study design.
- On day 6/7, participants completed an emotion regulation task while undergoing fMRI, using a previously established paradigm [1].
- In addition, the eye-blink response in the emotion-potentiated startle task was measured. The increase of the startle reflex in response to unpleasant conditions is interpreted as the processing of threat-relevant information and perceived fear.

[1] Phan, K.L. *et al.* 2005. Neural substrates for voluntary suppression of negative affect: a functional magnetic resonance imaging study. *Biol Psychiatry* 57, 210–219.

[2] Murphy, S.E. *et al.* 2008. Direct effects of diazepam on emotional processing in healthy volunteers. *Psychopharmacology* 199, 503–513.

Results

EMOTION REGULATION TASK

The whole-brain analysis showed that the ventrolateral prefrontal cortex, S1, and cerebellum were downregulated by diazepam in comparison to placebo when subjects suppressed negative affect.

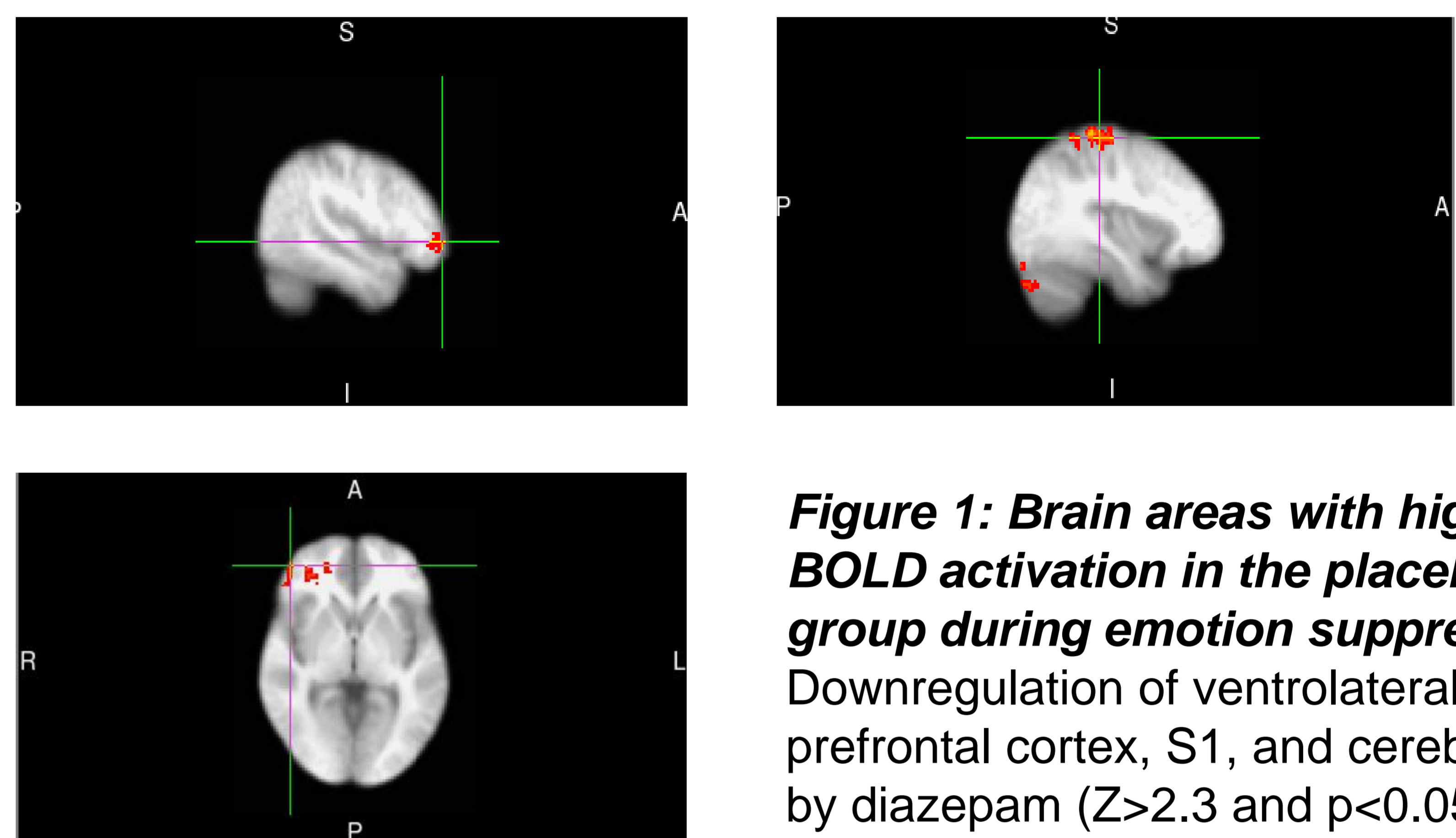


Figure 1: Brain areas with higher BOLD activation in the placebo group during emotion suppression. Downregulation of ventrolateral prefrontal cortex, S1, and cerebellum by diazepam ($Z > 2.3$ and $p < 0.05$).

EMOTION-POTENTIATED STARTLE TASK

The analysis of mean eye-blink amplitudes in this study suggested that the overall startle response was reduced in the diazepam group, consistent with previous findings for acute benzodiazepine effects [2]. These effects might reflect a decreased sensitivity to the anxiogenic component of the startle experiment itself, since they were not specific to the valence of pictures and occurred in the absence of significant sedative effects or changes in mood.

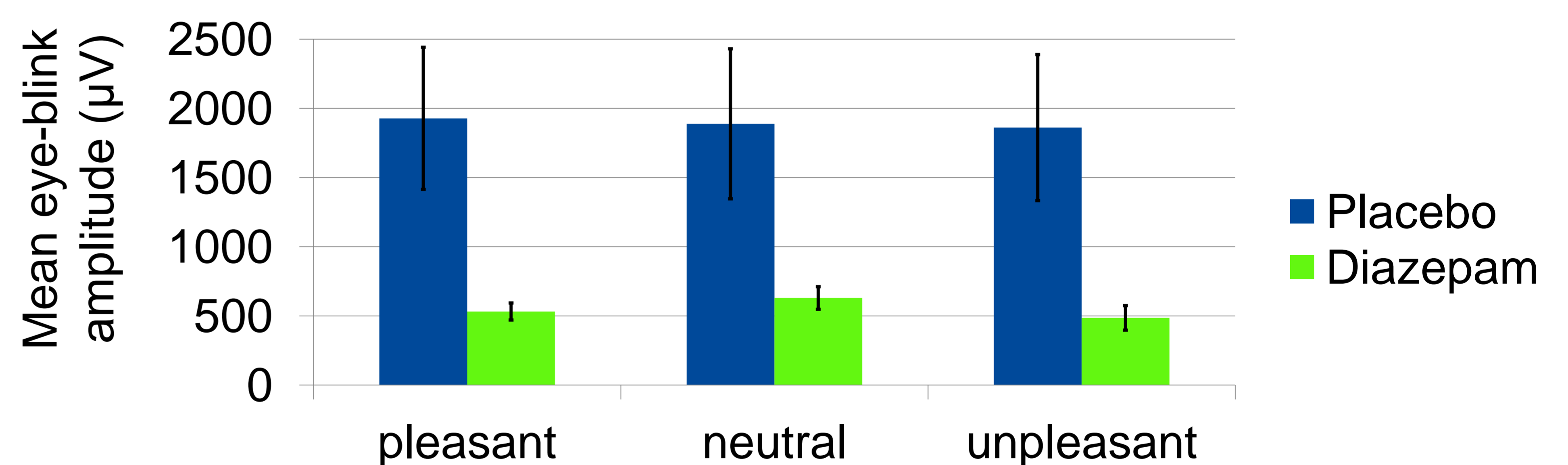


Figure 2: Mean eye-blink response in emotion-potentiated startle task Reduction in the diazepam group. Significant group difference for pleasant and unpleasant pictures (independent samples t-test, $t = -2.698$, $df = 9$, $p = 0.024$ and $t = -2.569$, $df = 10$, $p = 0.029$, respectively).

Conclusions

The overall reduction of startle-response has not been observed for SSRIs and might represent an important difference between the two drug classes. Future research will have to investigate the effect of SSRIs on emotion regulation in a similar task to draw conclusions about different mechanisms of action.