

Depression & fMRI



Identify MRI signature in humans shared by all members of drug classes using three approaches:

1. Direct pharmacoMRI signature
2. Indirect pharmacoMRI signature
3. PharmacoMRS metabolomic signature

Free of neurochemical tramlines

A collaboration with Bill Deakin, Steve Williams and Ian Anderson, University of Manchester

Solutions to drug development: Translation to patients, Phase I→II



- Healthy volunteer drug-models
(e.g. ketamine psychosis, tryptophan depletion)
- Trait extreme – models of illness
(e.g. high schizotypy; neuroticism)
- Susceptible genotypes & haplotypes
(e.g. 5HTT; COMT; neuroligin)

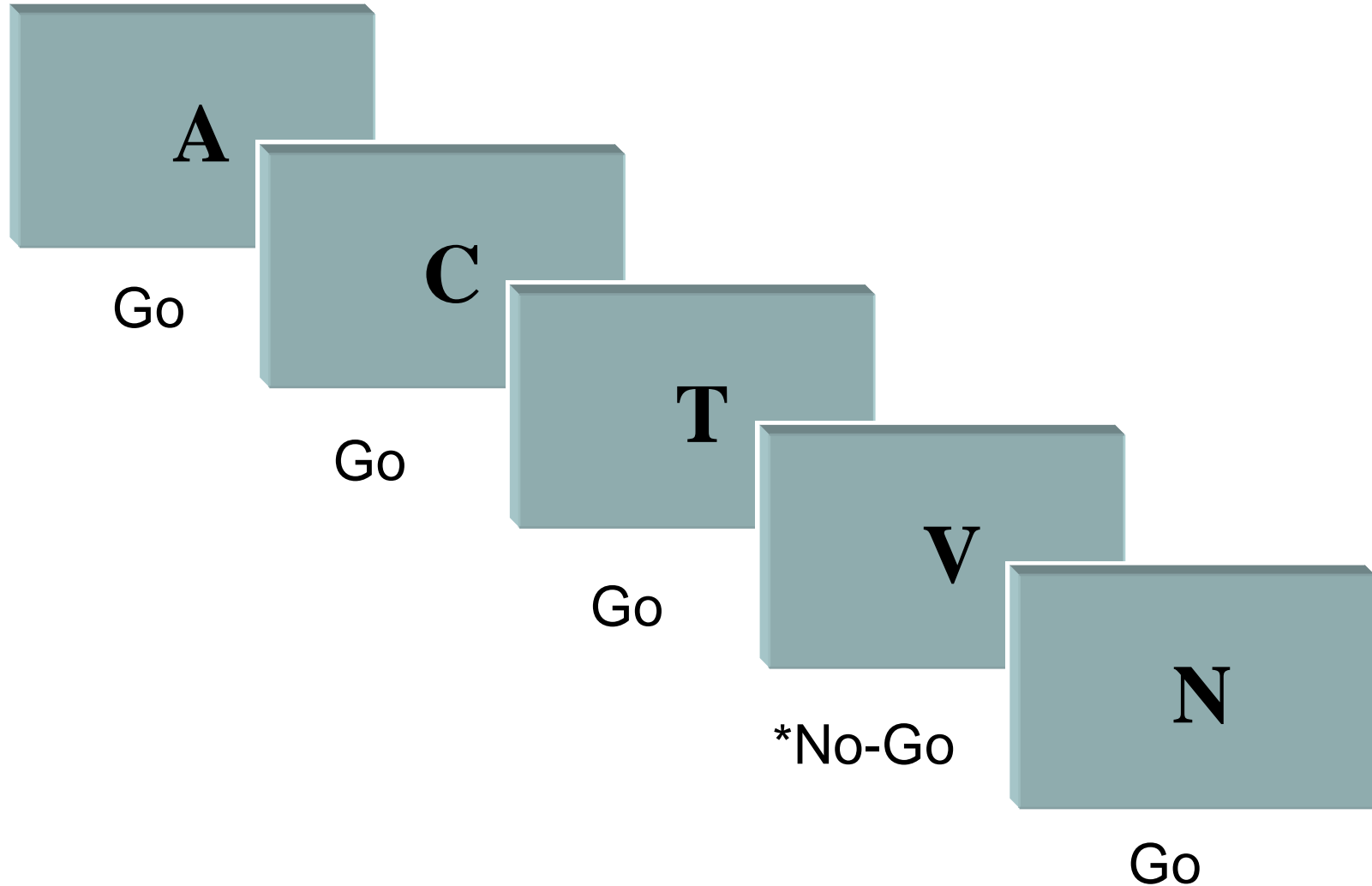
Depression



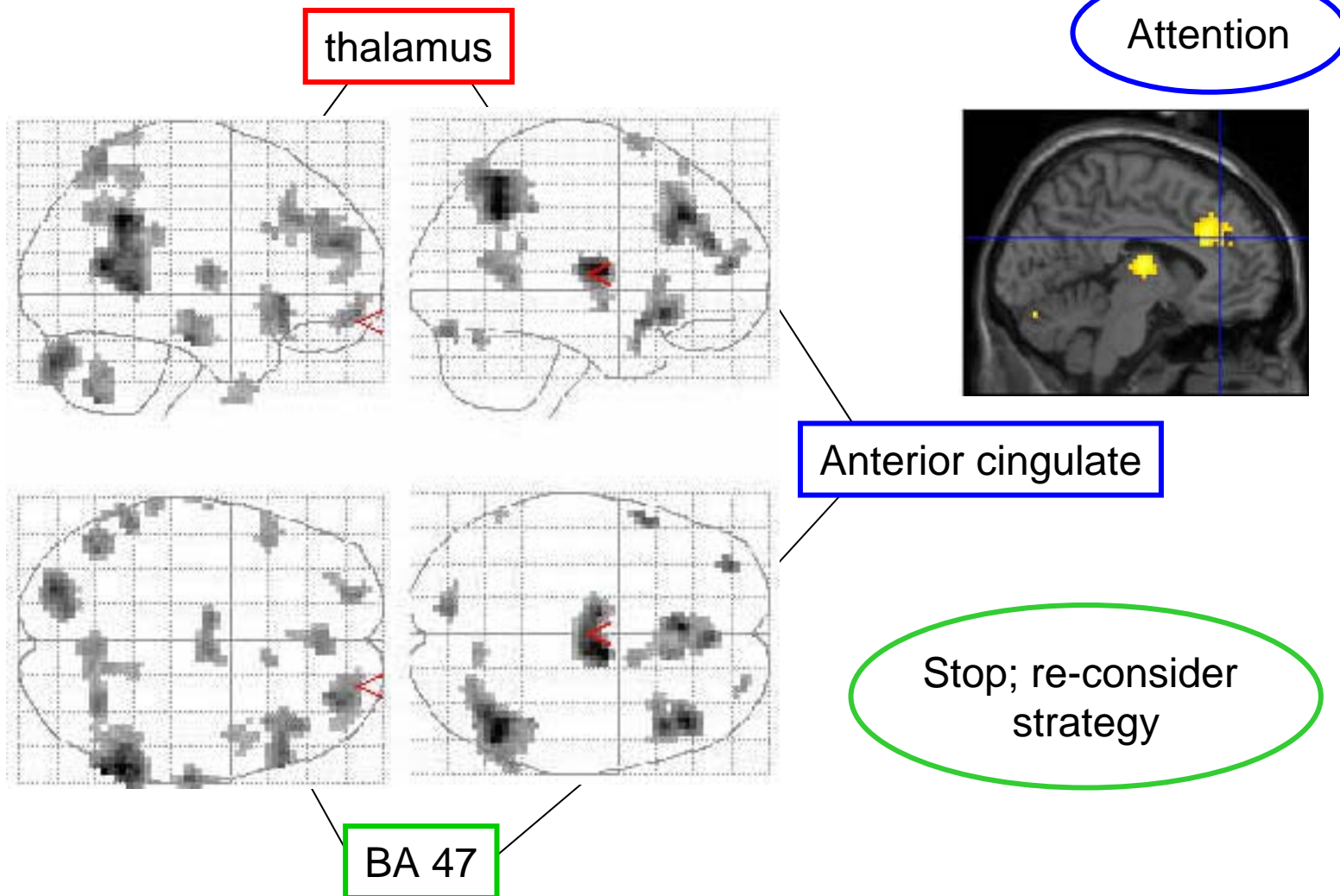
- Indirect pMRI signature

- Drug modulation of relevant cognitive and emotion processing
- Citalopram modulation of go/no-go & fear responses
- Effects on go/no-go shared by mirtazepine

Imaging Behavioural Inhibition Go/No-Go Task



Reproducible Main-Effect of No-Go Activation

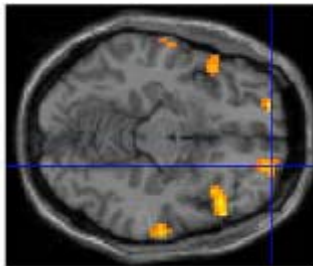
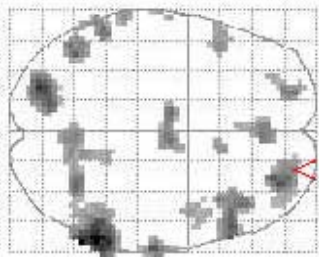
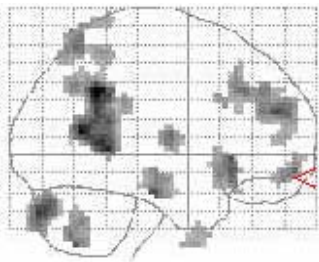


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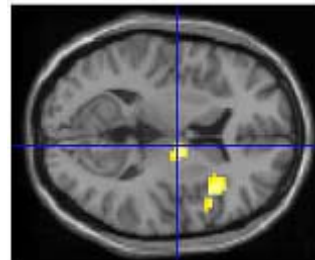
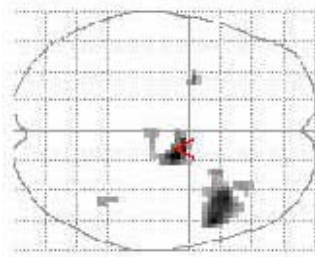
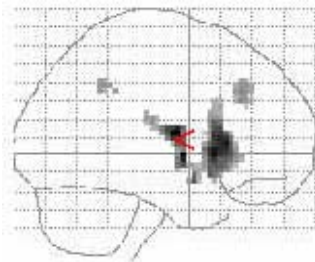
Antidepressants Enhance Thalamo-cortical Components of No-Go Main-effect



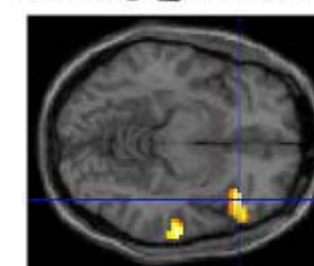
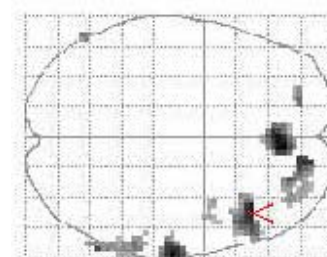
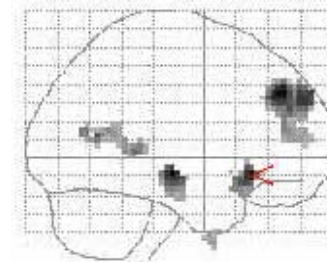
NoGo-Go
main effect



Mirtazepine
enhancement



Citalopram
enhancement

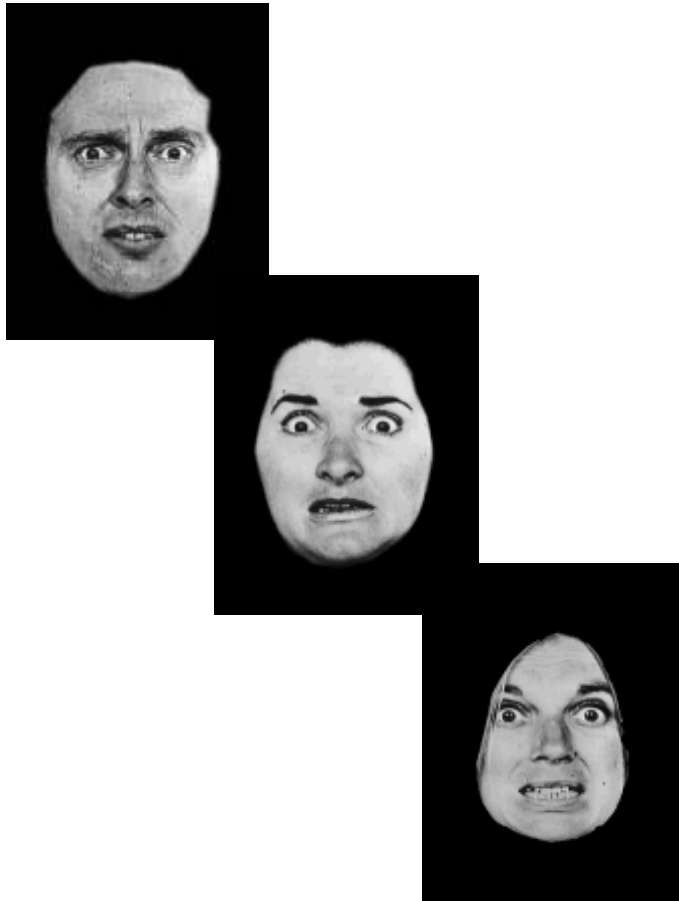


Covert Face Emotion Processing Task

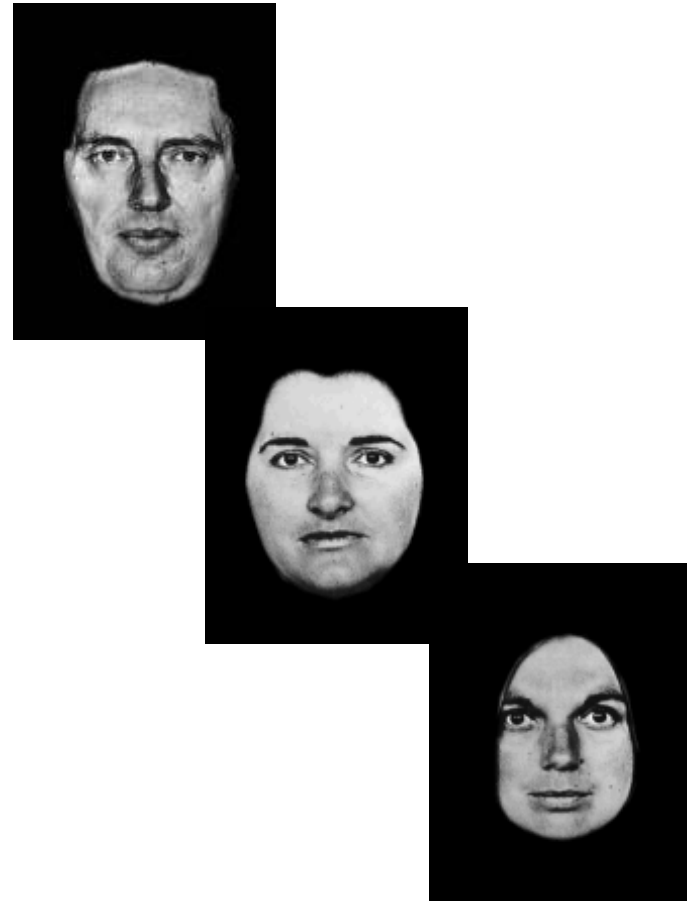


Press 1 if male; press 2 if female

Fear blocks



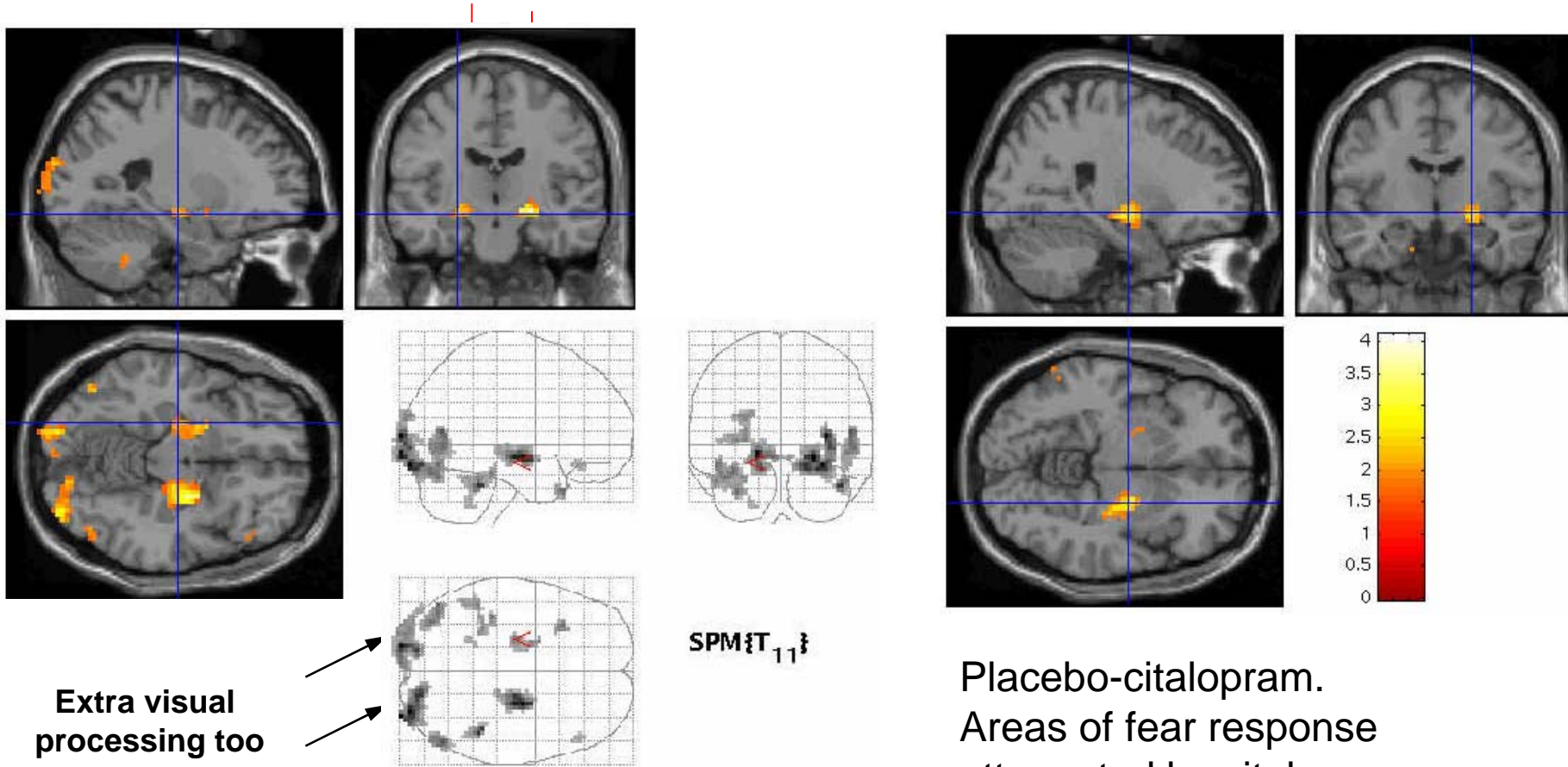
Neutral blocks



Fear: Parahippocampal – limbic Response Suppressed by Citalopram



Bilateral amygdala parahippocampal response



Extra visual processing too

SPM{T₁₁}

Placebo-citalopram.
Areas of fear response
attenuated by citalopram