



Pretreatment changes in neural response to emotional stimuli predict clinical response to SSRI treatment in depression

Godlewska BR¹, Browning M², Norbury R^{1,3,4}, Igoumenou A⁵, Cowen PJ¹, Harmer CJ²

¹Psychopharmacology Research Unit, University Department of Psychiatry, University of Oxford, Oxford, UK

²Psychopharmacology and Emotion Research Laboratory, University Department of Psychiatry, University of Oxford, Oxford, UK

³Department of Psychology, Whitelands College, University of Roehampton, UK

⁴Oxford Centre for Magnetic Resonance Research (OCMR), JR Hospital, Oxford, UK

⁵Barnet Enfield and Haringey Mental Health NHS Trust, UK

Background:

❖ Despite years of research, no clinically useful biomarker predictors of medication treatment response in depression have been identified - treatments are still ‘trial and error’, with clinical response being assessed after 4-6 weeks of therapy.

❖ Biomarker identification would be of huge practical value as it would allow more tailored treatment approaches, with earlier responses and a dramatic decrease in the burden of depression.

❖ Previous studies revealed potential candidates, among which the baseline activity of the anterior cingulate cortex (ACC) is one of the most consistently identified biomarkers of future antidepressant treatment response.

❖ People are constantly subjected to emotional stimuli. While many of them may be perceived outside of awareness, they still get processed by neural networks and influence subjective emotional parameters, such as mood.

❖ Treatment response may be influenced by how the brain responds to these non-conscious stimuli in the early stages of treatment (1).

Objective:

Exploration of **neural markers predicting clinical response** after 6 weeks of **antidepressant** treatment - the time when clinical decisions related to treatment response are first made -
in response to a task involving unconscious reactions to **emotional information** presented **below the awareness** level in the form of sad and happy facial expressions

Materials and methods:

❖ Volunteers: 32 depressed patients with DSM-IV Major Depressive Disorder (18F:14M), 20-52 years old, treated with 10mg escitalopram for 6 weeks

❖ Clinical response: a reduction in HAM-D of 50% or more from baseline after 6 weeks of treatment

❖ fMRI scanning was performed at baseline, before treatment started

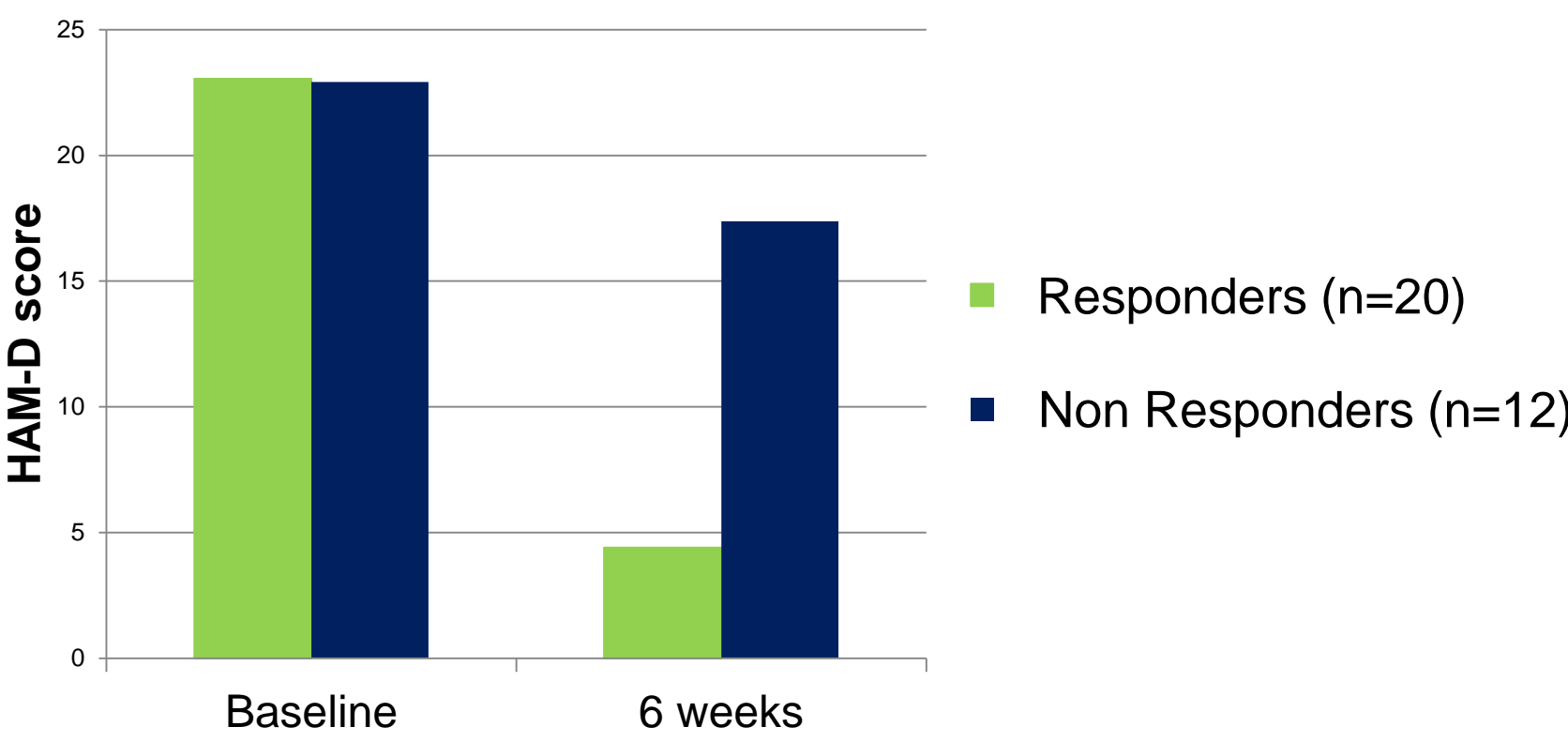
❖ Task consisted of viewing sad and happy facial expressions shown for 30ms, under awareness level, and masked with a neutral facial expression for 70ms, participants were asked to report the gender of the face

❖ MRI data acquired at 3T Siemens TIM TRIO: 256 volumes, voxel resolution of 3x3x3mm, TR/TE/FA=2000ms/28ms/89°

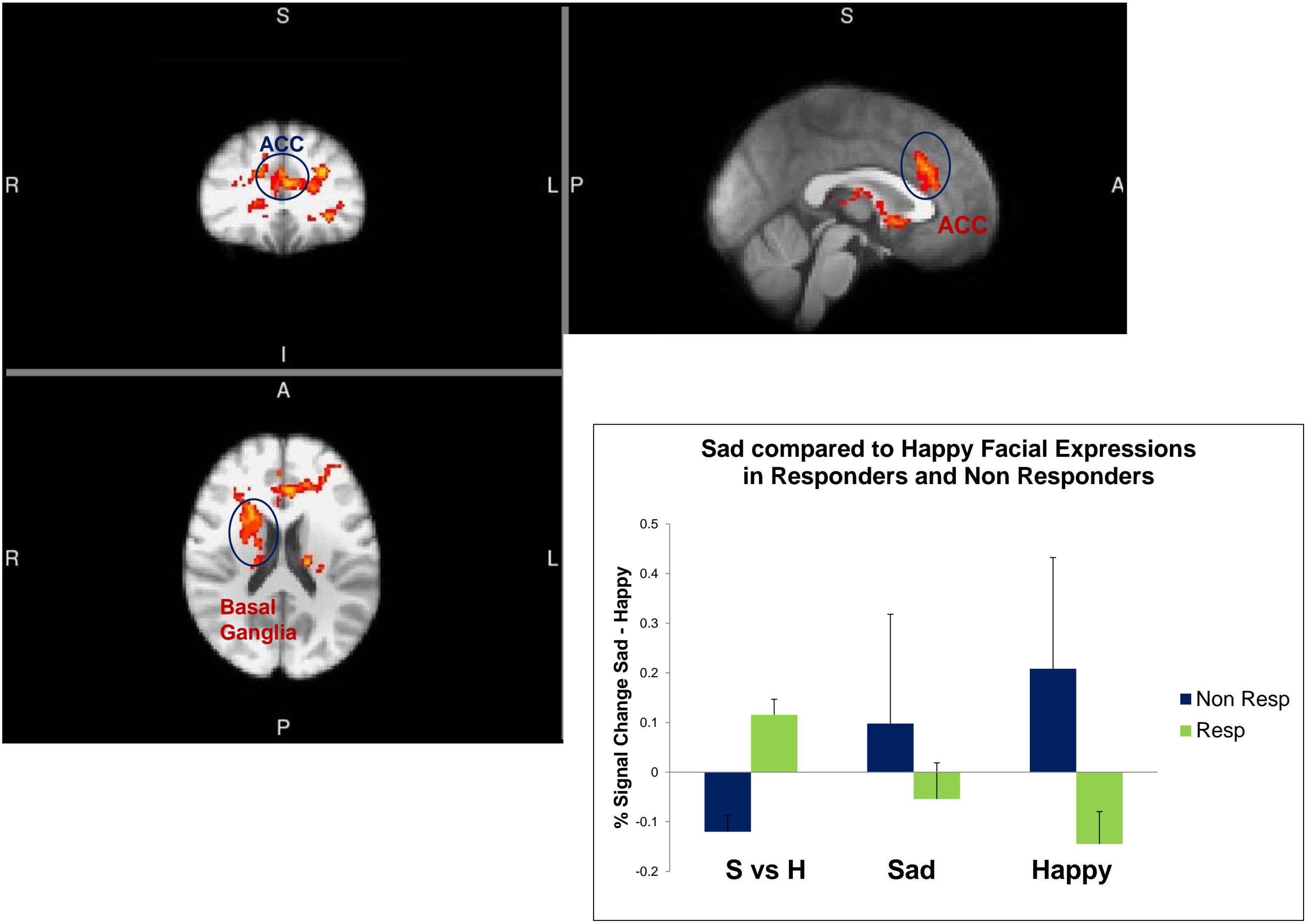
❖ Image preprocessing and analysis performed using FSL v5.0.4.

Results:

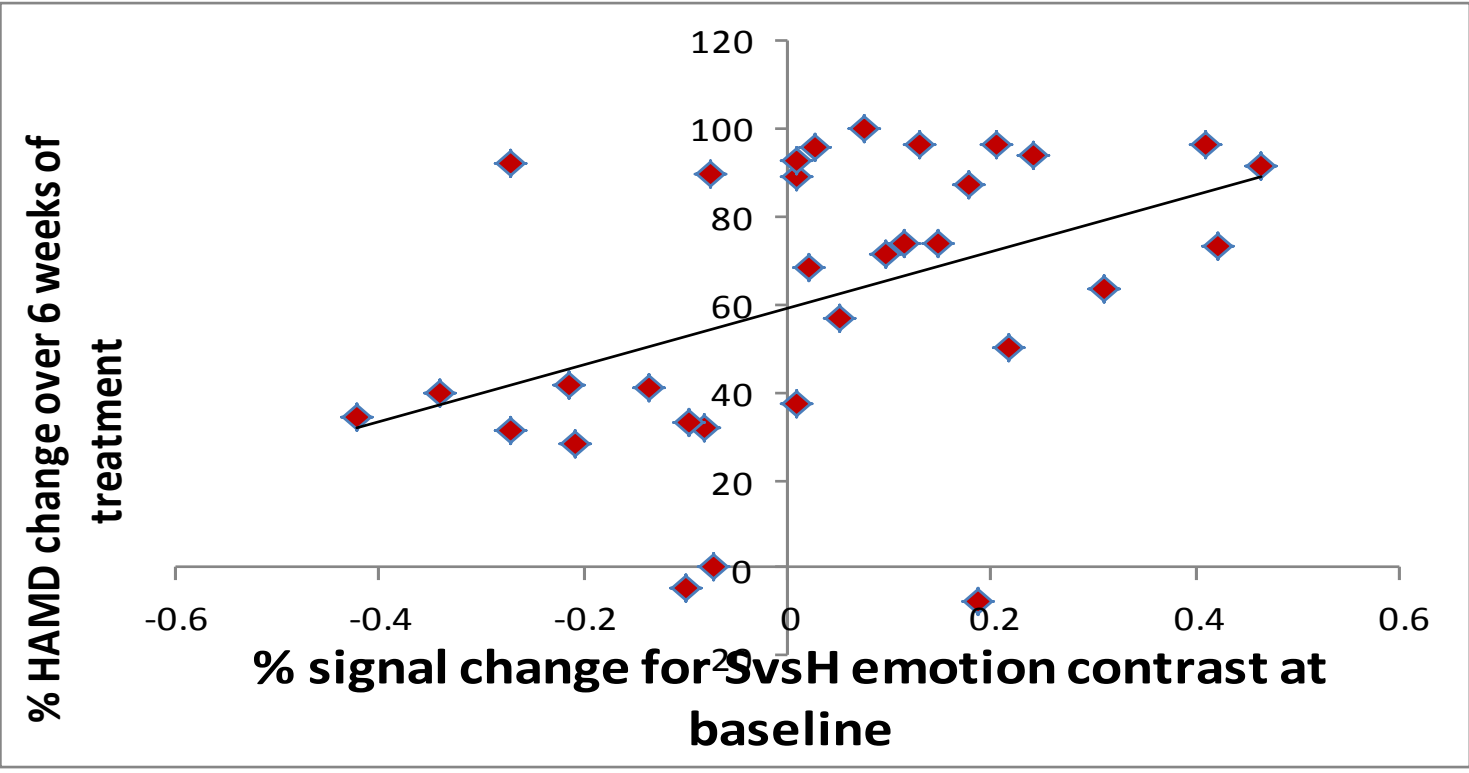
1. After 6 weeks of treatment with escitalopram there were 20 (62.5%) responders and 12 non-responders



2. **Responders** showed **greater neural response to masked sad vs happy facial expressions** in the clusters including the ACC, subcallosal cortex, paracingulate gyrus, bilateral thalamus, and basal ganglia (bilateral caudate, left putamen, left accumbens), before and after controlling for baseline HAM-D scores ($P < .05$, FWE corrected whole brain analysis)



3. The level of activation in the above structures correlated with improvement in depressive scores (0.443, $p = 0.001$)



Conclusions:

❖ Baseline neural response to sad vs happy facial expressions perceived below the level of conscious awareness predicted clinical response to escitalopram after 6 weeks of treatment.

❖ The areas of the brain whose activity was predictive of treatment response included areas crucial for emotional and reward processing, such as the ACC and basal ganglia.

❖ The level of their functional impairment in depression may be related to treatment response.

❖ A response to implicit emotional tasks may provide a useful neural predictor of clinical response to antidepressant treatment in depression.

Reference (1) Victor TA et al., Changes in the neural correlates of implicit emotional face processing during antidepressant treatment in major depressive disorder. Int J Neuropsychopharmacol. 2013;16:2195-208.

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