Early change in emotional processing as a predictor of treatment outcome with antidepressants or psychotherapy

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Antidepressant drug action

- Negative affective biases are a key psychological maintaining factor in depression.

- Recent evidence suggests antidepressant drugs affect these processes very early in treatment.
Early effects of antidepressants on negative bias in depressed patients

Healthy volunteers and acutely depressed patients randomised to receive placebo or antidepressant (reboxetine) in a double blind design. Emotional processing assessed 2h later.
Recognition of happy facial expressions

Effects of depression

- Healthy controls
- Depressed patients

Effects of single dose antidepressant

- Depressed: placebo
- Depressed: reboxetine

Harmer et al 2009
Emotional Memory

Effects of depression

- Number of items recalled
- Effects of single dose antidepressant

- Effects of depression
  - Negative
  - Positive
  - *

- Effects of single dose antidepressant
  - Negative
  - Positive
  - **
Predicting clinical response?
Association with later clinical response

- Improvement in happy recognition following two weeks antidepressant treatment predicted clinical outcome at week 6

FERT: facial expression recognition task;

Tranter et al., 2009
### Can we classify likely responders?

<table>
<thead>
<tr>
<th></th>
<th>Response</th>
<th>No Response</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive EP test</td>
<td>22</td>
<td>15</td>
<td>37</td>
</tr>
<tr>
<td>Negative EP test</td>
<td>1</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>25</td>
<td>48</td>
</tr>
</tbody>
</table>

- 91% of those patients who did not respond on emotional processing measure did not respond to their antidepressant treatment.
- 60% of patients who responded to emotional processing also responded to the antidepressant treatment.
Emotion recognition processing as early predictor of response to 8-week citalopram treatment in late-life depression

Week 1 recognition of happy facial expression predicted later clinical improvement in late life depression (Shiroma et al., 2014)
Prediction of therapeutic gain from emotional processing bias interacted with levels of interpersonal support

- A change in emotional processing with antidepressant drug treatment may be more effective when combined with good interpersonal support/function

(Shiroma et al., 2014)
Summary

- Antidepressants affect the processing of emotional information in depressed patients
- These effects occur early in treatment
- Changes in emotional bias predict later clinical changes in symptoms (in interaction with the environment)
Neural Correlates
Depression is associated with increased amygdala response to negative facial expressions.

Godlewska et al 2012
A 7 day treatment with 10mg escitalopram normalised this amygdala response.
Study design

- Acutely depressed patients: escitalopram (10mg) for 6 weeks

Godlewska et al. *submitted*
Early change in neural processing of fear predicts antidepressant response

Godlewska et al submitted
Summary

- Antidepressant treatments decrease amygdala responses to fear early in treatment and independently from changes in mood.

- Antidepressant effects on neural circuitry involved in emotional processing predict later clinical response.

- Prospective studies are now needed using pre-defined criteria to assess sensitivity and specificity of individual response prediction.
Do psychological interventions have similar effects?

• CBT for depression and anxiety reduces negative processing biases, measured at the end of treatment (Fu et al 2008; Tobon et al 2011)

• But can we see early effects of CBT before therapeutic change as we do with drug treatment?

• 28 patients with DSM-IV panic disorder and agoraphobia, unmedicated during last 6 months, given single session CBT or equivalent experimenter contact
Single-session CBT
Panic disorder and agoraphobia (N=28)
Attentional bias measurement

Vigilance

Fear             Happy

Attential bias: faster responses to detect probe when in same (vs opposite) location to threat face

Reinecke et al., 2012
Symptom changes with single session CBT are expressed with a delay

Agoraphobia (Mobility Inventory)

Score

Waiting Group

CBT Group

Baseline  Post-Treatment Day  4-Weeks Follow-up

Reinecke et al (2013)
Early changes in emotional bias predict later clinical changes.

Threat bias one day after treatment:
- Treatment: [Bar graph showing a lower threat bias compared to waiting.]
- Waiting: [Bar graph showing a higher threat bias compared to treatment.]

Prediction of symptom change during 4-weeks follow-up:
- Agoraphobia change vs. Threat bias (Linear regression graph: $R^2 = 0.44, p = 0.01$.)

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-20 -10 0 10 20 30 40 50 60 70 80

-1.2 -0.8 -0.4 0 0.4 0.8 1.2

-60 -40 -20 0 20 40 60 80

Threat bias change
Agoraphobia change
Threat bias
Towards personalised treatment for depression and anxiety

- Changing psychological processes important in depression and anxiety occurs with both drugs and psychological treatments before changes in clinical state.
- These early changes are predictive of later therapeutic change.
- Using these early changes as a marker of treatment response may allow for improved stratification of treatment in depression.
- Prospective clinical trials are now needed.
Acknowledgements

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