Through a glass, happily: What can antidepressants tell us about how we see the emotional world?

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"For now we see through a glass, darkly."

1 Corinthians 13:12
Of how we emotionally perceive the world around us.

How depression affects our emotional world.

What antidepressants may actually do.

Of some research done...

to be done...

And what it may mean for you.
The antidepressant market is the third largest by value, with global annual sales of over €21 billion in 2008.

1 in 6 people will experience depression at some time in their lives.

Depression is the leading cause of disability in Europe.

We still under diagnose and under treat depression.

Antidepressants

Five-fold increase in antidepressant prescribing over recent years.

1 in 10 adults treated with antidepressants.

The antidepressant market is the third largest by value, with global annual sales of over €21 billion in 2008.
Standard paradigm of antidepressant action

- Final common pathway
- All antidepressants equal
- Selection of antidepressant on basis of clinical symptoms
- Therapeutic response 2 weeks
- Downstream neurochemical effects
- Antidepressants correct a chemical imbalance
What is depression?

- Depression is a broad and heterogeneous diagnosis
- Spectrum between sadness and depression?

<table>
<thead>
<tr>
<th>Key symptoms</th>
<th>Associated symptoms</th>
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<tbody>
<tr>
<td>• persistent sadness or low mood</td>
<td>• disturbed sleep <em>(decreased or increased compared to usual)</em></td>
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<tr>
<td>• and/or</td>
<td>• decreased or increased appetite and/or weight</td>
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<tr>
<td>• marked loss of interests or pleasure</td>
<td>• fatigue or loss of energy</td>
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<tr>
<td>Duration: 2 weeks for threshold Sxs</td>
<td>• agitation or slowing of movements</td>
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<tr>
<td>2 years for sub-threshold Sxs</td>
<td>• poor concentration or indecisiveness</td>
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<tr>
<td>Impairment: Work, activities, relationships</td>
<td>• feelings of worthlessness or excessive or inappropriate guilt</td>
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<td></td>
<td>• suicidal thoughts or acts.</td>
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Depression and cognition

• Beck’s triad: self (worthless), world (pointless) and future (hopeless).
• Black and white thinking, overgeneralisation.
• Selective memory for negative material.
• Negative bias to interpreting ambiguous stimuli, eg faces.
• Difficulty shifting attention way from negative emotional material.
• Treatments targeting cognition (eg CBT) also effective at treating other symptoms of depression.
Different emotional tasks

• Processing of Emotional Images or sounds
  – the International Affective Pictures Series
  – Confounded by changes in emotion

• Face Processing Tasks
  – Ekman’s faces
  – Do not affect emotion

• Memory and Attention Bias Tasks
  – Story recall
  – Stroop words
Facial expression recognition

Morphed facial expressions (developed by Young et al. 1997)

Harmer et al 2004
Facial recognition in clinical samples

• People with depression show a behavioural bias to emotional faces, being more sensitive to negative faces than positive faces.

• Similar biases seen in people at high vulnerability to depression, and easily triggered by mood induction techniques.

• Limbic areas of the brain, eg the amygdala, show greater activation to negative stimuli and reduced activation to positive stimuli in depression.

• Neural markers more sensitive than behavioural markers.
Healthy volunteer facial expression studies

- Harmer et al 2003: single dose reboxetine increased recognition of happiness
- Harmer et al 2003: single dose citalopram increased recognition happiness and fear
- Harmer et al 2006: 1/52 citalopram decreases recognition of fear

**Table 1** Effects of depression and antidepressants on emotional processing

<table>
<thead>
<tr>
<th></th>
<th>Depression</th>
<th>Citalopram&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Reboxetine&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recognition of negative v. positive facial expressions</td>
<td>↑&lt;sup&gt;b&lt;/sup&gt;</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Speed to name positive v. negative self-descriptors</td>
<td>↓&lt;sup&gt;c&lt;/sup&gt;</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Number of positive v. negative descriptors recalled</td>
<td>↓&lt;sup&gt;d&lt;/sup&gt;</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Amygdala response to masked fearful faces</td>
<td>↑&lt;sup&gt;e&lt;/sup&gt;</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>

<sup>a</sup> Citalopram and reboxetine were administered to healthy participants for 7 days in studies with double-blind, placebo-controlled designs.<sup>21,20,31</sup>
<sup>b</sup> See reference 7.
<sup>c</sup> Further information available from the authors.
<sup>d</sup> See reference 6.
<sup>e</sup> See reference 32.
Primary Care Antidepressant-Preference study

- Criteria: any patient starting a new course of antidepressants
- unified GP referral pathway.
- Psychiatrists: consent, baseline assessment and randomisation.
- Randomise primary care patients to SSRI (citalopram) or NaRI (reboxetine).
- Open label, naturalistic, not a RCT.
- Follow-up by research officer @ 2/52 & 6/52
Effects of antidepressants on emotional processing

![Bar chart showing the effects of antidepressants on emotional processing. The chart compares baseline, weeks 2, and weeks 6 for emotions like anger, disgust, fear, happy, sad, and surprise. The accuracy is measured on the y-axis, and the emotions are on the x-axis. Significant changes are indicated with asterisks (*) for p < 0.05, ** for p < 0.01, and *** for p < 0.001.](image-url)
Increased recognition of happy faces over 2 weeks treatment predicts outcomes at 6 weeks.
Research report

The effect of serotonergic and noradrenergic antidepressants on face emotion processing in depressed patients

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ARTICLE INFO

Article history:
Received 5 November 2008
Received in revised form 26 January 2009
Accepted 27 January 2009
Available online xxxx

Keywords:
Depression
Emotional processing
Citalopram
SSRI
Reboxetine
NaRI

ABSTRACT

Background: In healthy volunteers, exposure to antidepressants increases the recognition of positive face emotions and decreases recognition of negative emotions. It has been proposed that this may underlie therapeutic effects of antidepressants, but to date this has not been tested in clinical populations.

Method: Recognition of facial emotions was measured at baseline (N = 108) and after 2 (N = 59) and 6 weeks (N = 69) of treatment in depressed primary care patients who had been randomised to treatment with either citalopram (SSRI) or reboxetine (NaRI) in an open-label study. Changes in emotional processing were compared to clinical outcome after 6 weeks of treatment.

Results: Significant increases in recognition accuracy of disgust, happiness and surprise occurred by two weeks of treatment with both antidepressants, and did not further change at six weeks.
Early changes in emotional processing predicts clinical response to antidepressants

• Over 8 weeks of treatment:
  – Fu et al 2007: decreased neural activation to sad faces associated with response to AD in MDD.
  – Fu et al 2008: increase neural activation to happy faces associated with response to AD in MDD.
  – Chen et al 2008: AD increased coupling between amygdala and ACC with successful treatment.
• Keedwell et al 2009: decrease neural activation to sad faces associated with response to AD in MDD.
• Harmer et al 2009: increase recognition happy faces after one dose AD predicts 6 weeks clinical outcome.
Depression: Understanding mechanisms and Evaluating Treatments

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Antidepressants and psychotherapy

Catherine Harmer: Cognitive model of antidepressant drug action.

Catrin Eames, Erin Heerey & Debbie Mills
Bangor University
We look at our world through emotionally tinted glasses.

There are systems in our brains that constantly monitor our emotional world.

Depression affects how those systems function, increasing our bias towards negative emotional stimuli.

Antidepressants can normalise the changes seen in the emotional systems of the brain.

These effects can be measured using emotional and social tasks.

Enhancing our perceptiveness of the world around us may be a novel route to treat depression.