Decision-making in depression

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KPPP, Hospital of Psychiatry, University of Zürich
DSM IV Major Depressive Disorder

- depressed mood
- anhedonia
- oversleeping / *undersleeping
- weight gain / weight loss
- psychomotor retardation
- fatigue
- guilt / worthlessness / helplessness
- indecisiveness, concentration difficulties
- suicidality

- duration & impairment
DSM IV Major Depressive Disorder

• depressed mood

▷ anhedonia
  • oversleeping / *undersleeping
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• indecisiveness, concentration difficulties
  • suicidality
    • Duration & Impairment
MIDAS

TABLE 1. Sensitivity, Specificity, OR, PPV and NPV of Alternative Symptom Criteria for Major Depressive Disorder ($N = 1523)^{a}$

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<thead>
<tr>
<th>Symptom</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>OR</th>
<th>PPV %</th>
<th>NPV %</th>
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</thead>
<tbody>
<tr>
<td>Depressed mood</td>
<td>92.9</td>
<td>82.4</td>
<td>61.2</td>
<td>86.3</td>
<td>90.6</td>
</tr>
<tr>
<td>Diminished interest/pleasure</td>
<td>80.6</td>
<td>87.8</td>
<td>29.7</td>
<td>88.7</td>
<td>79.1</td>
</tr>
</tbody>
</table>

McGlinchey et al., 2006
Correlations between subjective and overt anger ($r_{20} = 0.34; p < 0.001$) as well as somatic and psychic anxiety ($r_{20} = 0.39; p < 0.001$) were significant.

### RESULTS

Table 1 presents the psychometric performance of each of the alternative symptoms. As evidenced from the ORs representing the overall ability of symptoms to differentiate MDD from non-MDD, diminished drive was the strongest of the alternative symptoms examined, outperforming all of the current diagnostic criteria in the DSM-IV excepting depressed mood, diminished interest or pleasure, and diminished concentration or indecisiveness.

When combined into one compound criterion, diminished drive or loss of energy was endorsed by nearly all MDD patients, and produced an OR differentiating MDD from non-MDD that was higher than all other diagnostic criteria except depressed mood.

Compared with the DSM-IV diagnostic criteria of MDD, the compound criterion of helplessness and hopelessness differentiated MDD from non-MDD more strongly overall than about half of the existing criteria. Likewise, when taken as individual symptoms, helplessness and hopelessness each performed more strongly than about half the DSM-IV symptoms.

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<th>OR</th>
<th>PPV %</th>
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<td>61.2</td>
<td>86.3</td>
<td>90.6</td>
</tr>
<tr>
<td><strong>Loss of energy or diminished drive</strong></td>
<td>97.6</td>
<td>55.3</td>
<td>50.1</td>
<td>72.3</td>
<td>95.0</td>
</tr>
<tr>
<td>Loss of energy</td>
<td>87.2</td>
<td>68.4</td>
<td>14.8</td>
<td>76.8</td>
<td>81.8</td>
</tr>
<tr>
<td>Diminished drive</td>
<td>88.2</td>
<td>69.9</td>
<td>17.3</td>
<td>77.8</td>
<td>83.2</td>
</tr>
<tr>
<td>Diminished interest/pleasure or diminished drive</td>
<td>94.2</td>
<td>66.4</td>
<td>32.2</td>
<td>77.0</td>
<td>90.6</td>
</tr>
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<td>80.6</td>
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*Primary (SCID) and secondary (SADS) symptoms in bold.*

McGlinchey et al., 2006

**TABLE 1.** Sensitivity, Specificity, OR, PPV and NPV of Alternative Symptom Criteria for Major Depressive Disorder ($N = 1523$)
Table 5
Prevalences of lifetime interference, help seeking, and use of medication for minor depression and major depression

<table>
<thead>
<tr>
<th></th>
<th>Interference&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Saw MD&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Saw other&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Took medication&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Any of the four</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (S.E.)</td>
<td>% (S.E.)</td>
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<td>% (S.E.)</td>
<td>% (S.E.) (n)</td>
</tr>
<tr>
<td>Minor depression</td>
<td>18.1 (1.1)</td>
<td>24.5 (1.3)</td>
<td>12.1 (1.0)</td>
<td>10.0 (0.9)</td>
<td>42.0 (1.5) (810)</td>
</tr>
<tr>
<td>Major depression 5–6</td>
<td>29.7&lt;sup&gt;b&lt;/sup&gt; (1.4)</td>
<td>27.8 (1.4)</td>
<td>18.0&lt;sup&gt;b&lt;/sup&gt; (1.2)</td>
<td>15.8&lt;sup&gt;b&lt;/sup&gt; (1.1)</td>
<td>49.7&lt;sup&gt;b&lt;/sup&gt; (1.5) (664)</td>
</tr>
<tr>
<td>Major depression 7–9</td>
<td>52.3&lt;sup&gt;b&lt;/sup&gt; (1.7)</td>
<td>35.3&lt;sup&gt;b&lt;/sup&gt; (1.6)</td>
<td>21.5&lt;sup&gt;b&lt;/sup&gt; (1.4)</td>
<td>20.3&lt;sup&gt;b&lt;/sup&gt; (1.4)</td>
<td>68.2&lt;sup&gt;b&lt;/sup&gt; (1.6) (606)</td>
</tr>
</tbody>
</table>

Average (mean) number of 30-day work loss and work cutback days associated with 12-month minor depression and major depression

<table>
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<tr>
<th></th>
<th>Employed</th>
<th>Homemakers</th>
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<tr>
<td></td>
<td>Work loss days</td>
<td>Work cutback days</td>
</tr>
<tr>
<td></td>
<td>(S.E.)</td>
<td>(S.E.)</td>
</tr>
<tr>
<td>Minor depression</td>
<td>0.17 (0.11)</td>
<td>0.79 (0.23)</td>
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<tr>
<td>Major depression 5–6</td>
<td>0.17 (0.04)</td>
<td>0.99 (0.20)</td>
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<tr>
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<td>0.48&lt;sup&gt;a&lt;/sup&gt; (0.13)</td>
<td>2.75&lt;sup&gt;a&lt;/sup&gt; (0.34)</td>
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The course of depression

Table 5.—Adjusted and Unadjusted Attributable Risks for First-Onset Major Depression at Wave II

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<thead>
<tr>
<th>Psychiatric Disorder</th>
<th>Unadjusted Attributable Risk</th>
<th>Adjusted Attributable Risk</th>
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<tbody>
<tr>
<td>Dysthymia</td>
<td>0.050</td>
<td>0.077</td>
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<td>Panic disorder</td>
<td>0.039</td>
<td>0.007</td>
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<tr>
<td>Somatization</td>
<td>0.017</td>
<td>0.006</td>
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<td>Alcohol abuse</td>
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<td>0.020</td>
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<td>Other drug abuse</td>
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<td>0.000</td>
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<td>0.049</td>
<td>0.011</td>
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<td>Schizophrenia</td>
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<td>Depressive symptoms</td>
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Horwath et al., 1992 - ECA

Iacoviello et al., 2010
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Horwath et al., 1992 - ECA

Table 3
Frequency of Symptom Presentation in the Prodromal and Residual Phases (N = 331 Episodes)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prodromal frequency</th>
<th>Residual frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressed mood</td>
<td>95</td>
<td>79</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>42</td>
<td>40</td>
</tr>
<tr>
<td>Weight loss</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>Increased appetite</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Weight gain</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>Initial insomnia</td>
<td>29</td>
<td>30</td>
</tr>
<tr>
<td>Middle insomnia</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Early waking</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td>Hypersomnia</td>
<td>23</td>
<td>22</td>
</tr>
<tr>
<td>Decreased energy</td>
<td>38</td>
<td>35</td>
</tr>
<tr>
<td>Decreased interest or pleasure</td>
<td>82</td>
<td>75</td>
</tr>
<tr>
<td>Self-blame</td>
<td>51</td>
<td>55</td>
</tr>
<tr>
<td>Decreased concentration</td>
<td>78</td>
<td>75</td>
</tr>
<tr>
<td>Indecision</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Suicidality</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Psychomotor agitation</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Psychomotor retardation</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Crying more frequently</td>
<td>34</td>
<td>31</td>
</tr>
<tr>
<td>Inability to cry</td>
<td>4</td>
<td>2</td>
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<tr>
<td>Hopelessness</td>
<td>195</td>
<td>201</td>
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<tr>
<td>Worrying/Brooding</td>
<td>104</td>
<td>118</td>
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<tr>
<td>Decreased self-esteem</td>
<td>195</td>
<td>199</td>
</tr>
<tr>
<td>Irritability</td>
<td>85</td>
<td>72</td>
</tr>
<tr>
<td>Dependency</td>
<td>45</td>
<td>46</td>
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<tr>
<td>Self-pity</td>
<td>24</td>
<td>28</td>
</tr>
<tr>
<td>Somatic complaints</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Decreased effectiveness</td>
<td>38</td>
<td>37</td>
</tr>
<tr>
<td>Helplessness</td>
<td>35</td>
<td>28</td>
</tr>
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Iacoviello et al., 2010
The course of depression

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Carney et al. 1965
- endogenous vs neurotic
- ECT response

Kendler et al., 1992
- atypical
- mild typical
- severe typical
- in terms of vegetative symptoms

Parker et al., 1994
- Melancholia

Lamers et al., 2010
- Severe melancholic
- Severe atypical
- Moderate severity
What is depression?

- Low expected reward
  - depressed mood
  - anhedonia
  - guilt / worthlessness / helplessness
  - suicidality

- Low energy
  - fatigue
  - psychomotor retardation
  - oversleeping / undersleeping
  - weight gain / weight loss

- Cognition
  - indecisiveness, concentration difficulties

- Duration & Impairment
External causes

- Loss events
- Severe stress
- Chronic stress
- Social defeat

- But: 30% acausal

Kendler et al., 1999, 2000

Kendler et al., 2000
Decision-making in psychiatry

- Gaining prominence
- Applied broadly

- Central concepts: valuation

- What explanations do these models afford?
  - Wrong problem
  - Wrong inference
  - Wrong data
Decision-making in depression

- Emotional components
- Cognitive components
- Neuromodulatory components
No primary impairment

- diminished interest or pleasure in response to stimuli that were previously perceived as rewarding

What is “stimuli”?
- sucrose preference test
  - standard animal assessment of anhedonia, Willner 1997
- Dichter et al., 2010
  - no difference between MDD & HC
  - no effect of psychotherapy (BA)
- Olfaction (Klepce et al., 2010)
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Or is there?

- Reduced “emotional” responses to more complex “affective” stimuli

Bylsma et al., 2008
Or is there?

Reduced “emotional” responses to more complex “affective” stimuli

<table>
<thead>
<tr>
<th>Citation</th>
<th>Year</th>
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<tr>
<td>Greden</td>
<td>1986</td>
<td>63</td>
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</tr>
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<td>Sloan</td>
<td>1997</td>
<td>24</td>
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<td>Allen</td>
<td>1999</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Henriques</td>
<td>2000</td>
<td>18</td>
<td>15</td>
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<td>Gehricke</td>
<td>2000</td>
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<tr>
<td>Sloan</td>
<td>2001</td>
<td>20</td>
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</tr>
<tr>
<td>Rottenberg</td>
<td>2002</td>
<td>72</td>
<td>32</td>
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<tr>
<td>Tsai</td>
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<td>10</td>
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<td>Kaviani</td>
<td>2004</td>
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<td>Dunn</td>
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<td>25</td>
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PER (14) 375 305 $d_{-530}$ $p_{<0.001}$

Bylsma et al., 2008
How about negative stimuli?

3. Results
3.1. Omnibus analyses

We first conducted omnibus analyses of positive and negative emotional reactivity using the fixed effects model. The analysis of positive emotional reactivity (PER) was significant ($p < .0001$) and revealed that PER was reduced in MDD compared to normal controls (see Fig. 1). The effect size for PER was $d = -0.53$, a medium-sized effect by Cohen’s (1988) conventions. Similarly, the omnibus analysis of negative emotional reactivity (NER) was also significant, ($p < .0001$) and revealed that NER was reduced in MDD compared to normal controls (see Fig. 1). The effect size for NER was $d = -0.25$, corresponding to a small effect size. When PER and NER effect sizes were compared in a moderator analysis (with effect type PER versus NER coded as a moderator variable), a significant effect was obtained ($Q = 7.21, p < .01$), reflecting that the PER effect was significantly larger than the NER effect, indicating that MDD individuals exhibited a more pronounced blunting of PER than of NER.
Face processing
Face processing

Citalopram, acute

Harmer et al., 2003

black = Citalopram

Figure 1

Performance in the facial expression recognition task following citalopram (dark bars) or placebo (light bars). Top graph: Percentage of correct responses for each emotion. Asterisks illustrate the statistical significance of simple main effect analyses: * p < 0.05. Lower graph: Reaction time of correct responses for each emotion. Simple main effect analyses revealed a significant facilitation in the speed with which fear (p < 0.05) and happiness (p < 0.02) were detected in the absence of changes in speed to recognize other basic emotions.

Figure 2

Recognition of fear and happiness over the different intensity levels of facial expression used in this task. -, following citalopram; *, following placebo. Top graph: fear recognition. Lower graph: happiness recognition. Asterisks illustrate the statistical significance of simple main effect analyses: * p < 0.05, ** p < 0.001.
Face processing

Citalopram, acute
Harmer et al., 2003

Reboxetine, acute
Harmer et al., 2003b
Shown to increase recognition of happiness with acute administration to euthymic patients with a past history of recognition has been demonstrated following acute SSRI. Administration of a single clinical dose of the antidepressant reboxetine was found to facilitate the processing of positively valenced emotional information in healthy volunteers (Harmer et al., 2003). Our findings suggest that changes in emotional processing may modulate the detection of fearful expressions in depressed patients, with reboxetine increasing and citalopram decreasing fear perception compared to placebo. This result may be related to the fact that citalopram was given acutely in the present study, whereas in this sample, repeated treatment with decreased fear recognition was found after a week (Inoue et al., 1994) and, more recently, in a recent imaging study found that acute citalopram pretreatment reversed the negative biases in perception seen in depressed patients (Harmer et al., 2003).

In summary, acute administration of the SSRI citalopram improved the processing of happy faces, as demonstrated by a significant increase in recognition of happy faces at 2 weeks and persisted to 6 weeks independent of antidepressant used. Increased recognition of happy faces at 2 weeks and was independent of antidepression treatment. The signal detection results suggest that citalopram and reboxetine facilitated the processing of fear-related information as indicated by a significant increase in recognition of fear and anger faces after 2 weeks of treatment with citalopram compared with reboxetine at 2 weeks. The ANCOVA did not demonstrate any significant increase in recognition of disgust, which, as a negative emotion, is reported in healthy volunteers, with citalopram increasing and reboxetine decreasing recognition.

The facial expression task revealed greater recognition of happy faces at 2 weeks and persisted to 6 weeks independent of antidepression treatment. The subjects also performed the Rapid Visual Information Processing test and asked to detect any one of three specified digit sequences (3-5-7), with reboxetine having a greater difference between the improvement in total CORE score from baseline to 2 and 6 weeks compared with placebo. The ANCOVA did demonstrate significant difference between groups (t=3.7, df=22, p=0.001) but again, no change between 2 and 6 weeks. The ANOVA did not demonstrate any significant between-subject effects (medication) at either 2 weeks of treatment for any of the emotions. Comparison between-subject effects (medication) for response bias targets sensitivity results, ANCOVA did demonstrate significant difference between groups (t=3.3, df=22, p=0.003), but again, no change between 2 and 6 weeks. The ANOVA did not demonstrate any significant main or interaction of valence and group was significant (F=5.3, df=1, p=0.02). As shown in Figure 1 (right side), the increase in the percentage improvement in total CORE score from baseline to 6 weeks and the increase in recognition of happy faces at 2 weeks against percentage improvement in total CORE score from baseline to 6 weeks and the increase in recognition of happy faces at 2 weeks is shown.

The increase in the percentage improvement in total CORE score from baseline to 6 weeks and the increase in recognition of happy faces at 2 weeks is shown. Table 2 shows the percentage improvement in total CORE score from baseline to 6 weeks and the increase in recognition of happy faces at 2 weeks. Significant difference between groups (t=3.7, df=22, p=0.001). As shown in Figure 1 (right side), the increase in the percentage improvement in total CORE score from baseline to 6 weeks and the increase in recognition of happy faces at 2 weeks is shown. Table 2 shows the percentage improvement in total CORE score from baseline to 6 weeks and the increase in recognition of happy faces at 2 weeks. Significant difference between groups (t=3.3, df=22, p=0.003).

The role of the amygdala in processing emotional information has been studied in detail. Our findings suggest that changes in emotional processing may modulate the detection of fearful expressions in depressed patients, with reboxetine increasing and citalopram decreasing fear perception compared to placebo. This result may be related to the fact that citalopram was given acutely in the present study, whereas in this sample, repeated treatment with decreased fear recognition was found after a week (Inoue et al., 1994) and, more recently, in a recent imaging study found that acute citalopram pretreatment reversed the negative biases in perception seen in depressed patients (Harmer et al., 2003). The role of the amygdala in processing emotional information has been studied in detail.
Citalopram, acute  
Harmer et al., 2003

Reboxetine, acute  
Harmer et al., 2003b

Cit/Reb, chronic, MDD  
Tranter et al., 2009

Cit, rem MDD  
Baghwar et al., 2004

Remitted MDD
Healthy controls
Face processing

**Citalopram, acute**

Harmer et al., 2003

- Black = Citalopram

**Reboxetine, acute**

Harmer et al., 2003b

**Citalopram, chronic, HC**

Harmer et al., 2004

**Cit/Reb, chronic, MDD**

Tranter et al., 2009

**Cit, rem MDD**

Baghwagar et al., 2004

- Remitted MDD
- Healthy controls
**Face processing**

**Citalopram, acute**  
Harmer et al., 2003
- black = Citalopram

**Reboxetine, acute**  
Harmer et al., 2003b

**Cit/Reb, chronic, MDD**  
Tranter et al., 2009

**ATD, acute, HC never depr**  
Harmer et al., 2003c
- black = ATD

**Cit, rem MDD**  
Baghwagar et al., 2004
- remitted MDD healthy controls
Face reactivity in the amygdala

Single dose citalopram

7 days citalopram

Hariri et al., 2002, Murphy et al., 2009, Harmer et al., 2006, see also Murphy et al., 2013
**Hyperreactivity recovers with treatment**

**Sheline et al., 2001**

*Sertraline, 8 weeks, ca 100mg*

<table>
<thead>
<tr>
<th>Condition</th>
<th>PreTreatment</th>
<th>PostTreatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left Amygdala</strong></td>
<td>-0.1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Right Amygdala</strong></td>
<td>-0.1</td>
<td>0</td>
</tr>
</tbody>
</table>

**ACC and amygdala response (to faces) predicts treatment response**

**Sheline et al., 2001, Fu et al., 2013**
In panic/phobia: fast (50ms stimulus presentation)
In GAD/MDD: slow (only at longer, 500ms)
High-level + need time for elaboration
Sticky aversive info

Siegle et al., 1999, 2002
Predictions for changes in fMRI scanner signal in response to emotional processing and nonemotional processing. A brief summary of the model, described more fully in other papers (Siegle and Hasselmo 2001; Siegle et al.).

Computational simulation allows quantitative integration of assumptions about underlying cognitive and biological systems (Siegle and Hasselmo 2001) and was therefore used to further specify hypotheses.

In our basic hypothesis, we proposed that depressed individuals would show more sustained activation in brain areas involved in emotional processing, particularly flat slopes for negative normed words (t(15) = 3.49, p < .02), compared to control subjects. As shown in Siegle et al., 1999, 2002, this suggests enhanced connections between the affective and nonaffective systems.

The common delayed match to sample, or Sternberg memory trial, was chosen as an appropriate nonemotional processing task. This task involves showing participants stimuli (locally coded in the stimulus units) are presented, and participants are asked whether the fourth number was in the set of the first three. The task was chosen because there is a wealth of evidence that demonstrates the critical role of the amygdala in processing emotional information, and the amygdala is known to be involved in the processing of emotional stimuli.

In the model, the emotional processing units, as an analog of the idea that the amygdala system functions, are responsible for processing emotional stimuli. These layers project to units responsible for making decisions about the information. Activity in the decision units inhibits the emotional processing units, as an analog of the idea that the amygdala activity could inhibit amygdala processing of emotional stimuli.

Figure 1. Model of emotional information processing. A computational neural network model of emotional information processing, with affective and nonaffective features (analog of amygdala system functions) and decision units (analog of the cortex). The model is based on physiological models (LeDoux 1996). In the network, populations of connected neurons are thought to learn associations. By systematically changing the strength of connections between these nodes, the model can be said to learn associations.

The model consists of affective feature unit activity, overtraining + increased feedback + decreased inhibition, original network, and predicted amygdala system BOLD response. The affective feature unit activity is shown in the left panel of Figure 1. The original network shows the activity of the affective feature units over time. The predicted amygdala system BOLD response is shown in the right panel of Figure 1. The predicted BOLD response is derived by convolving affective feature unit activity with a hemodynamic response function. fMRI scans, spaced 4 seconds apart, are on the X axis.

Figure 2. Time courses for traced right and left amygdala regions of interest. The X axis in all graphs represents scan which occurred during an affective valence-identification trial. The last three scans were subjected to hierarchical ANOVA. These revealed a three-way interaction for subject (depressed/never-depressed) × valence (positive, negative, or neutral) × scan (1–9). The height of the BOLD response was fitted to an ex-gaussian waveform in which the height, spread, latency, and tail were allowed to vary. An ex-gaussian is the sum of a gaussian (often used as an idealized physiological signal) and an exponential (often used to model the tail of a physiological signal).

Figure 3. Location and time courses for ANOVA derived amygdala/hippocampal ROI that had time-series similar to those presented above. These particles and associated time series are shown in Figure 3. The coordinates of all ROIs detected in this analysis are listed in Table 1.
Affective feature unit activity

Overtraining + increased feedback + decreased inhibition

Original network

Unit activity

Negative
Positive

Predicted amygdala system

BOLD response

Simulated fMRI scans derived by convolving affective feature unit activity with a hemodynamic response function.
fMRI scans, spaced 4 seconds apart, are on the X axis.

Explanatory information by Depressed Individuals?

WAS SUSTAINED AMYGDALA ACTIVITY STABLE?

Control Subjects

Depressed Subjects

Sustained Amygdala Activity in Depression

F 707

p .022

F 6.6, 12.13

p .04

F 5.1, 14

p .18

F 1.98, 14

p .022

The x axis in all graphs represents scan which occurred 4 sec apart, for a total of 32 sec. The first 4 scans prestimulus (scan 1) baseline, was subjected to hierarchical regressions in which activation to negative stimuli was entered on the first step (R .31, p .13), and no significant effects for right amygdala.

Of particular interest, this analysis revealed bilateral amygdala regions of interest (ROIs) and an hippocampal regions of interest.

In the table, there were a number of other areas detected by voxel ANOVAs (Carter et al 2000) using subject as a random factor, and group, scan, valence, and personal relevance as fixed factors. Random effects analysis per-

reflecting sustained processing of negative emotional stimuli. A criticism rather than working on further specify hypotheses.

Sternberg

WAS SUSTAINED AMYGDALA ACTIVITY STABLE?

Figure 3. Location and time courses for ANOVA derived hippocampal regions of interest.

Exploratory analyses consisted of whole-brain voxel-by-

valence split.
Maintaining positive affect

Decisions in Depression

Heller et al., 2009
So far

- No primary changes (pain, hedonic taste, sucrose)
- Reduced emotional responses +<-
- Attention & memory biased towards negative
  - at conceptual level
  - if allow for elaboration
  - negative conceptual information sticks around longer, positive dissipates away
- Cognitive biases:
  - Negative information is more ‘important’

- Next: learning from reinforcement
  - learning impaired, or outcome insensitive?
Learning & choice

Henriques et al., 1994

Henriques and Davidson, 2000
One measure of the tendency to do this is the response bias. In the study, it was found that participants were more likely to choose the more rewarded stimulus (75% probability) if they correctly identified the "rich" stimulus. Correct identification of the "rich" stimulus was more likely to be rewarded (75% probability) than correct identification of the "lean" stimulus. The dark bars show a hypothetical control group, developing a strong response bias towards the more rewarded stimulus (30% probability) with no punishment, while the rich condition (black bars) refers to the stimulus associated with more frequent reward, and the lean condition (light gray bars) refers to the stimulus associated with less frequent reward.

To test the specificity of these findings and the predictive effects involving Group, a three-way ANOVA was conducted. The ANOVA revealed no significant effects involving Group. To further investigate the relationship between response bias and reward sensitivity, a discriminability measure was calculated as the ratio of the probability of correct responses to the probability of incorrect responses. This measure was found to be significantly higher for participants with high BDI scores compared to those with low BDI scores.

In conclusion, the study provides evidence for the existence of a response bias that is associated with reward sensitivity and predicts future performance. These findings have implications for understanding the role of reward in decision-making processes and could be useful in the development of treatments for mood and anxiety disorders.
Learning or sensitivity?

\[ Q_t(a, s) = Q_{t-1}(a, s) + \epsilon(r_t - Q_{t-1}(a, s)) \]


Text
Learning or sensitivity?

\[ Q_t(a, s) = Q_{t-1}(a, s) + \epsilon(r_t - Q_{t-1}(a, s)) \]

Dopamine


Learning or sensitivity?

\[ Q_t(a, s) = Q_{t-1}(a, s) + \epsilon(r_t - Q_{t-1}(a, s)) \]

Anhedonia

Dopamine


Learning or sensitivity?

\[ Q_t(a, s) = Q_{t-1}(a, s) + \epsilon(r_t - Q_{t-1}(a, s)) \]

Anhedonia

Dopamine


Modelling: first get the task

\[
p(a_t|s_t) = \frac{1}{1 + \exp\left[-\left(\mathcal{W}(a_t, s_t) - \mathcal{W}(\bar{a}_t, s_t)\right)\right]}
\]

\[
\mathcal{W}(a_t, s_t) = \gamma I(a_t, s_t) + \xi Q_t(a_t, s_t) + (1-\xi) Q_t(a_t, \bar{s}_t)
\]

### A

Across all datasets

<table>
<thead>
<tr>
<th>Category</th>
<th>Log Bayes Factor</th>
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</thead>
<tbody>
<tr>
<td>Belief</td>
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<tr>
<td>Action</td>
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</tr>
<tr>
<td>Punishment</td>
<td>400</td>
</tr>
<tr>
<td>Stimulus-Action</td>
<td>600</td>
</tr>
</tbody>
</table>

### B

![Scatter plot: Fraction correct vs log(\(\gamma\))]
Learning or sensitivity?

Huys et al., 2013
Learning or sensitivity?

- Correlation of anhedonia is with reward sensitivity, not learning rate
Learning or sensitivity?

- Correlation of anhedonia is with reward sensitivity, not learning rate
- But: correlations

Huys et al., 2013

Figure 2
Model performance.
A: Model comparison. Group-level log Bayes factors /ΔIBIC for each model relative to model 'Belief' across all datasets. A difference ≥10 in this measure is strong evidence for the model with the lower score.

B: The parameter γ in the model largely captures the probability with which participants made a correct choice. Note that, by design of the task, this explicitly captures the effect of symmetric instructions and perceptual difficulties, rather than the asymmetric effect of rewards.

Reverse orthogonalization did not yield any significant correlations with ϵ.
At least part of the correlation between ρ and ϵ arises because the two parameters can explain similar features of the data, i.e. alterations in one parameter can be compensated for by alterations in the other parameter (see Figure 1). To establish whether the association between AD and the reward sensitivity parameter was due to real features in the data, rather than due to inference issues, we asked whether the correlations with questionnaire measures were statistically significant.

Correlation coefficients between questionnaire measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>BDI</th>
<th>BDI/A</th>
<th>BDA</th>
<th>GDA</th>
<th>GDD</th>
<th>AD</th>
<th>AA</th>
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<tr>
<td>BDI/A</td>
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<tr>
<td>BDA</td>
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<td>0.2</td>
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<td></td>
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<td>GDA</td>
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<td></td>
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<td></td>
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<td></td>
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<tr>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>AA</td>
<td>-2</td>
<td>0.2</td>
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<td></td>
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</tr>
</tbody>
</table>

Figure 3
Correlates of anhedonia.
A: Correlation coefficients for all pairwise correlations between questionnaire measures. All are highly significant (p < .01), except for the correlation between anhedonic depression and anxious anxiety, denoted by a red dot.

B: Hierarchical weighted regression analysis across all datasets, involving all 255 participants with a full set of BDI, BDA and MASQ scores. The plots shows the linear coefficients between anhedonic depression (AD) score and the reward sensitivity and learning rate parameters ρ and ϵ. Each bars shows one linear coefficient; the red error bars indicate ±1 standard error; and the green error bars indicate the 99.4% confidence interval (corresponding to a Bonferroni corrected level p = .05/8). AD is significantly and negatively correlated with the reward sensitivity ρ, but not significantly correlated with the learning rate ϵ.

C: Scatter plot of anhedonic depression against reward sensitivity. Size of dots scale with weight (inference precision).
D: Scatter plot of reward sensitivity vs. learning rate.
E: Significance of correlations across parameter estimates from 70 surrogate data sets. There is an consistent and stably significant correlation between AD and reward sensitivity ρ, but not between AD and learning rate ϵ.

‣ Correlation of anhedonia is with reward sensitivity, not learning rate
‣ But: correlations

Huys et al., 2013
Learning or sensitivity?

- Correlation of anhedonia is with reward sensitivity, not learning rate
- But: correlations
- Fit, generate surrogate data, examine correlations - has the model really captured something about the data?

**Figure 2** Model performance.

**A:** Model comparison. Group-level log Bayes factors \( /Delta1_i BIC \) for each model relative to model 'Belief' across all datasets. A difference \( \geq 10 \) in this measure is strong evidence for the model with the lower score.

**B:** The parameter \( \gamma \) in the model largely captures the probability with which participants made a correct choice. Note that, by design of the task, this explicitly captures the effect of symmetric instructions and perceptual difficulties, rather than the asymmetric effect of rewards.

**Figure 3** Correlates of anhedonia.

**A:** Correlation coefficients for all pairwise correlations between questionnaire measures. All are highly significant \( (p < 0.01) \), except for the correlation between anhedonic depression and anxious anxiety, denoted by a red dot.

**B:** Hierarchical weighted regression analysis across all datasets, involving all 255 participants with a full set of BDI, BDA and MASQ scores. The plots shows the linear coefficients between anhedonic depression (AD) score and the reward sensitivity and learning rate parameters \( \rho \) and \( \epsilon \). Each bars shows one linear coefficient; the red error bars indicate \( \pm 1 \) standard error; and the green error bars indicate the 99.4% confidence interval (corresponding to a Bonferroni corrected level \( p = 0.05/8 \)). AD is significantly and negatively correlated with the reward sensitivity \( \rho \), but not significantly correlated with the learning rate \( \epsilon \).

**C:** Scatter plot of anhedonic depression against reward sensitivity. Size of dots scale with weight (inference precision).

**D:** Scatter plot of reward sensitivity vs. learning rate.

**E:** Significance of correlation across parameter estimates from 70 surrogate datasets. There is a consistent and stably significant correlation between AD and reward sensitivity \( \rho \), but not between AD and learning rate \( \epsilon \).

Huys et al., 2013
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Learning or sensitivity?

- Correlation of anhedonia is with reward sensitivity, not learning rate
- But: correlations
- Fit, generate surrogate data, examine correlations - has the model really captured something about the data?
- Not that they can’t learn, but don’t care.
Chase et al., 2009

- slower learning rates from rewards & losses, and less sensitive to outcomes overall
- even when partial out BDI score
But...

- Chase et al., 2009

- slower learning rates from rewards & losses, and less sensitive to outcomes overall
- even when partial out BDI score
fMRI - learning or reward?

- MID task (Knutson, Schiff...)

![Diagram of MID task](image)
Anticipation

Outcome

- No NAcc
  - R MPFC (BA 32)
  - L Insula (BA 47)
  - R Putamen
  - L Putamen
  - L Superior Frontal Gyrus (BA 6)
  - L Insula (BA 13)
  - L Postcentral Gyrus (BA 3)
  - L Inferior Parietal Lobe (BA 40)

Knutson et al., 2008
Anticipation

Outcome

• No NAcc

  R MPFC (BA 32)
  L Insula (BA 47)
  R Putamen
  L Putamen
  L Superior Frontal Gyrus (BA 6)
  L Insula (BA 13)
  L Postcentral Gyrus (BA 3)
  L Inferior Parietal Lobe (BA 40)

Knutson et al., 2008

Pizzagalli et al., 2009
Model-based fMRI - TD learning

- Pavovian task
  - correlate of reward PE, water outcome

MDD vs HC

Gradin et al., 2008

MDD vs HC

VTA increased

VS reduced
Model-based fMRI - TD learning

- Pavlovian task
  - correlate of reward PE, water outcome

MDD vs HC

med vs unmedicated

Gradin et al., 2008
Correlates with anhedonia?

A significant VTA activation was observed in the MDD group and patients had a significantly stronger TD signal (larger positive TD-LRC) than unmedicated or medicated controls. Consistent with this, more severe MDD, defined by Hamilton, BDI and Spielberger ratings, had the strongest VTA TD signals (Fig. 5). A significant hippocampal deactivation was present in unmedicated controls, the magnitude of which was significantly less in patients. Consequently, the apparently increased hippocampal activity in MDD was due to a blunted deactivation (Fig. 4).

A weaker TD signal (larger positive TD-LRC) was associated with more severe MDD, as defined by Hamilton rating (Fig. 5). A significant rAC deactivation was present in unmedicated controls, the magnitude of which was significantly less in MDD. Again consistent with this, more severe MDD defined by Spielberger rating was associated with a weaker TD signal (larger positive TD-LRC). More severe MDD defined by Snaith–Hamilton anhedonia score was associated with significantly stronger amygdala TD signals (larger positive TD-LRC). No significant correlations were found for control data.
Reward tasks in MDD
Reward tasks in MDD

- Meta-analysis of reward processing tasks in fMRI w/ MDD
Reward tasks in MDD

- Meta-analysis of reward processing tasks in fMRI w/ MDD

![Brain regions with increased activation in MDD compared to healthy controls](image)

**Table 3**
Results from the global ALE analyses of reward-related processing in MDD (results from 22 studies, FDR corrected $p < 0.05$).

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>Side</th>
<th>BA</th>
<th>Site of maximum ALE</th>
<th>Volume (mm$^3$)</th>
<th>Maximum ALE value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Areas of decreased activation</strong> (178 foci from 30 experimental contrasts)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Caudate</td>
<td>L</td>
<td>−6</td>
<td>18</td>
<td>1800</td>
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<td>8</td>
<td>1800</td>
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<td>1192</td>
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<tr>
<td>Thalamus</td>
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<td>14</td>
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<td><strong>Areas of increased activation</strong> (118 foci from 20 experimental contrasts)</td>
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<tr>
<td>Cuneus</td>
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<td>−4</td>
<td>1104</td>
<td>0.014</td>
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<tr>
<td>Cuneus</td>
<td>L</td>
<td>18</td>
<td>−6</td>
<td>1104</td>
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<td>0</td>
<td>0.010</td>
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ALE, activation likelihood estimation; BA, Brodmann area; L, left; R, right; (x y z), Talairach coordinate.
Reward tasks in MDD

Meta-analysis of reward processing tasks in fMRI w/ MDD

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Zhang et al., 2013
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Zhang et al., 2013
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  - BA9 vs sgACC inverse corr

Zhang et al., 2013
Learning at different conceptual levels

First session

Cancer
4 s
Max 6 s
1–5 s
Cancer estimation?
+ 1–3 s
Actual likelihood cancer 30%
+ Estimation error

Second session

Update

Cancer
Cancer estimation?
+ Actual likelihood cancer 30%
+

Time

O1
O2
O1
D1
Choose between the two targets

... -O_1-O_2-O_3-D_3-O_2-O_3-O_2-O_4-D_2- ...

Desirable information
Undesirable information

Absolute mean update

Healthy controls
MDD patients

Update bias
(absolute mean update desirable minus undesirable)

8 DI scores

Sharot et al., 2011, Korn et al, 2014, Stankevicius et al., 2014
Learning at different conceptual levels

**First session**
- Cancer
- Cancer estimation?
- Max 6 s
- 1–5 s
- 2 s
- 1–3 s
- Actual likelihood cancer 30%

**Second session**
- Cancer
- Cancer estimation?
- Actual likelihood cancer 30%

Estimation error

Desirable information
Undesirable information

**Figure 1**

**Learning at different conceptual levels**
- Cancer estimation
- Actual likelihood cancer 30%

**Figure 2**

**Updating behavior**
- \( t^{15.44} (3.60) \)
- \( t^{0.56} (0.32) \)
- \( t^{6.71} (5.30) \)

**Table 2**

<table>
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<tr>
<th>Subject</th>
<th>Desirable information</th>
<th>Undesirable information</th>
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<td>Optimists (N = 30)</td>
<td>0.4</td>
<td>0.8</td>
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<tr>
<td>Controls</td>
<td>0.5</td>
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**Supplementary Results**

- **Desirable information**
- **Undesirable information**

- \( \eta^{2} = 0.15 \)
- \( \eta^{2} = 0.11 \)

- **Main effect of desirability**
- **Group (MDD/controls)**

- **Supplementary Figure 1a**

- **Supplementary Figure 1b**

- **Supplementary Figure 2**

- **Sharot et al., 2011, Korn et al, 2014, Stankevicius et al, 2014**

- **Decisions in Depression**

- **Computational Psychiatry Course, UCL, May 28th 2014**

- **Quentin Huys, TNU/PUK**
So far

- No primary changes (pain, hedonic taste, sucrose)
- Reduced emotional responses +<-
- Attention & memory biased towards negative
  - at conceptual level
  - if allow for elaboration
  - negative conceptual information sticks around longer, positive dissipates away

- Learning from reinforcement / fMRI reward/loss
  - overall unclear whether learning is impaired or results can be explained by insensitivity to outcomes
  - caudate and ACC appear most robustly involved

- “Interpretations”
Decision-making in depression

- Emotional components
- Cognitive components
- Neuromodulatory components
Cognitive biases

- **Extreme thinking**
  - dichotomous - black/white
  - unrealistic expectations - unless perfect it’s useless

- **Selective attention**
  - disqualifying the positive
  - over-generalization

- **Relying on intuition**
  - jumping to conclusions
  - emotional reasoning

- **Self-reproach**
  - self-blame, self-criticism
  - taking things personally

Westbrook et al., 2011
Hopeless attributions are a risk factor for developing depression

Table 3
Frequency of Symptom Presentation in the Prodromal and Residual Phases (N = 331 Episodes)

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<th>Symptom</th>
<th>Prodromal frequency</th>
<th>Residual frequency</th>
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<tr>
<td>Depressed mood</td>
<td>95</td>
<td>79</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>42</td>
<td>40</td>
</tr>
<tr>
<td>Weight loss</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>Increased appetite</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Weight gain</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>Initial insomnia</td>
<td>29</td>
<td>30</td>
</tr>
<tr>
<td>Middle insomnia</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Early waking</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td>Hypersomnia</td>
<td>23</td>
<td>22</td>
</tr>
<tr>
<td>Decreased energy</td>
<td>38</td>
<td>35</td>
</tr>
<tr>
<td>Decreased interest or pleasure</td>
<td>82</td>
<td>75</td>
</tr>
<tr>
<td>Self-blame</td>
<td>51</td>
<td>55</td>
</tr>
<tr>
<td>Decreased concentration</td>
<td>78</td>
<td>75</td>
</tr>
<tr>
<td>Indecision</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Suicidality</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Psychomotor agitation</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Psychomotor retardation</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Crying more frequently</td>
<td>34</td>
<td>31</td>
</tr>
<tr>
<td>Inability to cry</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Hopelessness</td>
<td>195</td>
<td>201</td>
</tr>
<tr>
<td>Worrying/Brooding</td>
<td>104</td>
<td>118</td>
</tr>
<tr>
<td>Decreased self-esteem</td>
<td>195</td>
<td>199</td>
</tr>
<tr>
<td>Irritability</td>
<td>85</td>
<td>72</td>
</tr>
<tr>
<td>Dependency</td>
<td>45</td>
<td>46</td>
</tr>
<tr>
<td>Self-pity</td>
<td>24</td>
<td>28</td>
</tr>
<tr>
<td>Somatic complaints</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Decreased effectiveness</td>
<td>38</td>
<td>37</td>
</tr>
<tr>
<td>Helplessness</td>
<td>35</td>
<td>28</td>
</tr>
<tr>
<td>Decreased initiation of voluntary responses</td>
<td>19</td>
<td>23</td>
</tr>
</tbody>
</table>

Iacoviello et al., 2010
Implicit vs explicit attributions

- Acute consequence
  - implicit: IAT self-worth
  - explicit: CSQ

![Graph showing the relationship between vulnerability and distress scale scores](image-url)
Implicit vs explicit attributions

- Acute consequence
  - implicit: IAT self-worth
  - explicit: CSQ
- Chronic consequence
  - @ 5 weeks only CSQ survives to predict BDI response to acute life stressor
Implicit vs explicit attributions

- **Acute consequence**
  - implicit: IAT self-worth
  - explicit: CSQ

- **Chronic consequence**
  - @ 5 weeks only CSQ survives to predict BDI response to acute life stressor

- **Evolution over time**

  ![Graph](image1.png)
  ![Graph](image2.png)

Haeffel et al., 2007, Haeffel 2011
Implicit vs explicit attributions

- **Acute consequence**
  - implicit: IAT self-worth
  - explicit: CSQ

- **Chronic consequence**
  - @ 5 weeks only CSQ survives to predict BDI response to acute life stressor

- **Evolution over time**
  - -> explicit interpretations determine long-term outcome
  - -> both implicit and explicit determine immediate outcome

---

Haeffel et al., 2007, Haeffel 2011
Emotion regulation

- Interpretation precedes emotion

![Diagram of emotion regulation](Image)

Gross, 2002
Habitual emotion regulation strategy

Table 6
Longer Term Implications of Reappraisal and Suppression for Well-Being (Study 5)

<table>
<thead>
<tr>
<th>Emotion regulation strategy</th>
<th>Reappraisal</th>
<th>Suppression</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Depression</strong>&lt;sup&gt;F&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td>-.23*</td>
<td>.25*</td>
</tr>
<tr>
<td>CES-D</td>
<td>-.25*</td>
<td>.23*</td>
</tr>
<tr>
<td>Zung</td>
<td>-.29*</td>
<td>.27*</td>
</tr>
<tr>
<td>Life satisfaction&lt;sup&gt;E&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>.30*</td>
<td>-.34*</td>
</tr>
<tr>
<td>Self-esteem&lt;sup&gt;E&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>.30*</td>
<td>-.39*</td>
</tr>
<tr>
<td>Optimism&lt;sup&gt;C&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>.25*</td>
<td>-.25*</td>
</tr>
<tr>
<td><strong>Well-being</strong>&lt;sup&gt;F&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Environmental mastery</td>
<td>.41*</td>
<td>-.23*</td>
</tr>
<tr>
<td>Autonomy</td>
<td>.29*</td>
<td>-.22*</td>
</tr>
<tr>
<td>Personal growth</td>
<td>.27*</td>
<td>-.28*</td>
</tr>
<tr>
<td>Purpose in life</td>
<td>.25*</td>
<td>-.34*</td>
</tr>
<tr>
<td>Self-acceptance</td>
<td>.35*</td>
<td>-.38*</td>
</tr>
<tr>
<td>Positive relations with others</td>
<td>.23*</td>
<td>-.46*</td>
</tr>
</tbody>
</table>

Note. Standardized beta coefficients. Capital superscripts (e.g., C, E) denote sources of measures. During the analysis, items were centered, and the table reports only the betas. *p < .05.
Habitual ER strategy

- Habitual suppression vs reappraisal - alters amygdala reactivity to aversive IAPS images

SLEA from correlation with ADS/Depression (fig. 1)

Reappraisal Group
- cue blank + picture

Suppression Group
- cue blank + picture

1st eigenvariate signal time courses

pos. neg. neut.

Expect. Present.

Expect. Present.

Abler et al., 2010
Depression and emotional control

Error Analysis.
We looked for group differences in the contrast of correct-trial processing versus error-trial processing. An area in the dorsal cingulate region (BA 32 and 24, Talairach z/H11005 33–45) showed significantly increased activation for error versus correct trials, but this effect did not differ by group. Only one area, in the pregenual cingulate, showed an interaction between trial type and group. In this region, both groups showed deactivation for correct trials and both increased activation (lost deactivation) on errors; however, the depressed group increased activation more sharply than the control subjects.

Posterror Analysis.
All correct trials were classified as either postcorrect (following a correct trial) or posterror (following an error trial). We found two areas in right and left DLPFC (Figure 4 and Table 3) that showed significant group differences in the contrast to of postcorrect versus posterror processing. Both areas showed the same pattern. Both control subjects and depressed patients showed a mode of deactivation on postcorrect trials. However, for the posterror trials, the control subjects increased activation significantly (into the positive range), consistent with recruiting stronger cognitive control, while the depressed patients did not change.

Correlational Analyses.
We conducted correlational analyses to look for similarities in fear-related activation between right DLPFC and left amygdala. We found a significant negative correlation between activity in these regions only in the depressed patients and then only in the attend condition, not in the ignore condition, r/H11005/H11002 .726, p/H11005 .000.

Figure 1. Example of a stimulus screen used in the emotional conflict task.

Figure 2. Areas in the left amygdala (A) and right dorsolateral prefrontal cortex (B) showing a significant three-way interaction of attention/emotion/group. Graphs show percent change in signal magnitude for the fear-minus-neutral contrast in each region. Error bars show standard errors of the mean.

Figure 3. Areas in the subgenual anterior cingulate (A) and superior rostral anterior cingulate (C) show significant group differences across all conditions. Areas in pregenual cingulate (B) show significant differences in a group/attention interaction, where control subjects had less deactivation in the attend-to-faces conditions (left side of graph), while depressed patients had less deactivation in the ignore-faces conditions (right side of graph). Graphs show percent change in signal magnitude for each region. Error bars show standard errors of the mean.

Figure 4. Areas in left (A) and right (B) dorsolateral prefrontal cortex showing significant group differences in the posterror effect: interaction of trial type (postcorrect versus posterror)/group. Graphs show percent change in signal magnitude for each region. Error bars show standard errors of the mean.
Depression and emotional control

- Figure 1: Example of a stimulus screen used in the emotional conflict task.
- Figure 2: Areas in the left amygdala showing a significant three-way interaction of attention modes.
- Figure 3: Areas in left DLPFC and left amygdala. We found a significant negative deactivation in the ignore-faces conditions (right side of graph), while depressed patients had less deactivation in the ignore-faces conditions (right side of graph) compared to the control group.
- Figure 4: Correlational Analyses. We conducted correlational analyses to look for similarities in fear-related activation between right and left DLPFC and left amygdala. We found a significant negative deactivation in the ignore-faces conditions (right side of graph), while depressed patients had less deactivation in the ignore-faces conditions (right side of graph) compared to the control group.

Error bars show standard errors of the mean.
### Mean Pretreatment, Posttreatment, and 6-Month Follow-Up Scores for BDI and HRSD for Four Samples of Participants in Each Treatment Condition

<table>
<thead>
<tr>
<th>Depression and measure</th>
<th>BA</th>
<th>AT</th>
<th>CT</th>
<th>$F(df$s) and $p$</th>
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<tbody>
<tr>
<td>Total sample ($n = 149$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>56 29.3 (6.6)</td>
<td>43 29.1 (6.6)</td>
<td>50 29.8 (6.3)</td>
<td>$F(2, 148) &lt; 1, \text{ ns}$</td>
</tr>
<tr>
<td>Post</td>
<td>56 9.1 (7.9)</td>
<td>43 10.6 (9.3)</td>
<td>50 10.1 (9.6)</td>
<td>$F(2, 145) &lt; 1, \text{ ns}$</td>
</tr>
<tr>
<td>6 months</td>
<td>50 8.5 (7.6)</td>
<td>39 9.3 (8.2)</td>
<td>47 10.3 (8.6)</td>
<td>$F(2, 132) &lt; 1, \text{ ns}$</td>
</tr>
</tbody>
</table>

(Cognitive therapy

### Table: Mean Pretreatment, Posttreatment, and 6-Month Follow-Up Scores for BDI and HRSD for Four Samples of Participants in Each Treatment Condition

<table>
<thead>
<tr>
<th>Depression and measure</th>
<th>BA</th>
<th>AT</th>
<th>CT</th>
<th>$F(df$s) and $p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sample ($n = 149$)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
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</tr>
<tr>
<td>Post</td>
<td>56 9.1 (7.9)</td>
<td>43 10.6 (9.3)</td>
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<td>$F(2, 145) &lt; 1, \text{ ns}$</td>
</tr>
<tr>
<td>6 months</td>
<td>50 8.5 (7.6)</td>
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<td>$F(2, 132) &lt; 1, \text{ ns}$</td>
</tr>
</tbody>
</table>

(Jacobson et al., 1998)
Cognitive therapy

- Identify automatic thoughts
- Modify them

Mean Pretreatment, Posttreatment, and 6-Month Follow-Up Scores for BDI and HRSD for Four Samples of Participants in Each Treatment Condition

<table>
<thead>
<tr>
<th>Depression and measure</th>
<th>BA</th>
<th>AT</th>
<th>CT</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>M(SD)</td>
<td>n</td>
</tr>
<tr>
<td>Total sample (n = 149)</td>
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<td></td>
</tr>
<tr>
<td>BDI</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Pre</td>
<td>56</td>
<td>29.3 (6.6)</td>
<td>43</td>
</tr>
<tr>
<td>Post</td>
<td>56</td>
<td>9.1 (7.9)</td>
<td>43</td>
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<tr>
<td>6 months</td>
<td>50</td>
<td>8.5 (7.6)</td>
<td>39</td>
</tr>
</tbody>
</table>

Jacobson et al., 1998
Cognitive therapy

- Identify automatic thoughts
- Modify them
- Is it the active ingredient?

**Correlations Between Early Mechanism Change and Late Depression Change in Each Treatment**

<table>
<thead>
<tr>
<th>Mechanism measure</th>
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<td>EASQ</td>
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<tr>
<td>Uncontrollable</td>
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<tr>
<td>Internal</td>
<td>.27</td>
<td>.14</td>
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<tr>
<td>Stable</td>
<td>.45**</td>
<td>.03</td>
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<tr>
<td>Global</td>
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<td>.22</td>
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<tr>
<td>PES</td>
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<td>Frequency</td>
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<tr>
<td>Pleasure</td>
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<td>-.25</td>
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<tr>
<td>DAS</td>
<td>.26</td>
<td>-.02</td>
</tr>
</tbody>
</table>

Jacobson et al., 1998
Bad data: helplessness

Master

Yoked

Control

Green arrow pointing downward
Notions of control

A

Probability

outcomes

B

1

0.5

probability

0

1 2 3 4 outcomes

1 2 3 4 actions

C

1

0.5

probability

0

1 2 3 4 outcomes

1 2 3 4 actions

reinforcement

Huys and Dayan, 2009
With the assumption that a large fraction of the rewards in panel B is controllably achievable (reward. (figures D and E. Here, all outcomes, and thus all actions, carry sizeable reinforcements. (Fig. 6. reinforcement gives it greater psychological refinement. In animal models, control tends to be defined in terms of high level rewards in interpersonal relationships. Similarly, helplessness in humans is typically characterised in terms of high level rewards in interpersonal relationships. The notion of controllable reward fraction allows us to capture the aspect of helplessness that is directed towards controllable outcomes that matters; but rather only controllable outcomes which are closer to the notion of controllable outcome achievability, which is closer to ideas in psychology, and entropy, which relates more to ideas in psychology, and
Modelling learned helplessness

Decisions in Depression

However, given the low-control prior over the test environment. For each action negative. (prior over processes that could be used to express similar underlying literatures contain methods such as correlated Dirichlet the machine learning and Bayesian reinforcement learning put set size). We also considered the case of only a single uniform and a delta function (and, partly because of this, and arbitrary mathematical formulations. For example, at achievability.

In turn adds a critical extra feature to straight of outcome entropy, and the notion of achievable rewards three notions of control we presented. The different no-

ments avoidable, control renders the world more pleasant,

5. Discussion

values.

Master rats choose to escape, but it will increase the prob-

shock strength will not increase the probability that the bars) increases faster with increasing reinforcer strength after controllable (H) than uncontrollable (G) reinforcement.

Increasing the size of the punishment in the test environment has more drastic effects on the advantage of action 1 over the other actions after exposur

worst possible outcome). The best action (action 1) has smaller expected reward after exposure to uncontrollable reinforcement (solid line) than after

To focus on the concepts, we used rather impoverished

Simply put, by making rewards exploitable and punish-

Q

A

v

0

0.2

0.4

0.6

0.8

1

0

0.5

1

χ

χ

A

B

C

D

E

F

G

H

Q value

Q(1)−Q(2)

0.1 0.5 1 2 5

|R|_{max}

0.1 0.5 1 2 5

|R|_{max}

0.1 0.5 1 2 5

|R|_{max}

Huys and Dayan, 2009
Hopelessness and uncontrollability?

Fig. 1. Achievable outcomes: A representative reinforcement notion (A) in this figure legend, the reader is referred to the web version of this article). In the left bar chart, all actions preferentially produce the same chocolate bar (even for chocophobic subjects). We thus expect the subjects to have one predominant need in the environment. If there is more than one action, the relationship between the outcomes of the different actions is important. In these bar charts, each column represents the outcome distribution of one action. There are four actions, each with four outcomes. Consider the leftmost bar chart. All actions preferentially lead to one and the same outcome, like a vending machine which produces the same chocolate bar most of the time, whichever button is pressed. For the middle bar chart, each action tends to lead to a different outcome. The rightmost bar chart shows a case in between, where the vending machine reliably leads more deterministically to one outcome (having low entropy) than if it leads to many different outcomes with similar probabilities (and thus has high entropy). In terms of the notion of control, we use the number of possible outcomes (the outcome set size) as a suitable proxy for the entropy (see Section 1).

The entropy measure considers an action that yields all possible outcomes randomly. In this case there is little controllably achievable reward. (For interpretation of the references to color in the right bar chart, then all but the reward-carrying outcome can be reliably evoked; the one chocolate bar that is desired is most likely produced by a single action that is chosen preferentially.) There is extensive control over rewards in both these cases. However, if the reinforcement is as indicated by the red bar in the right bar chart, then all but the reward-carrying outcome can be reliably evoked; the one chocolate bar that is desired is most likely produced by a single action that is chosen preferentially. In the middle bar chart, each action tends to lead to a different outcome. The rightmost bar chart shows a case in between, where the vending machine reliably leads to one and the same outcome, like a vending machine which produces the same chocolate bar most of the time, whichever button is pressed. For the middle bar chart, each action tends to lead to a different outcome. The rightmost bar chart shows a case in between, where the vending machine reliably leads to one and the same outcome, like a vending machine which produces the same chocolate bar most of the time, whichever button is pressed. For the middle bar chart, each action tends to lead to a different outcome. The rightmost bar chart shows a case in between, where the vending machine reliably leads to one and the same outcome, like a vending machine which produces the same chocolate bar most of the time, whichever button is pressed. For the middle bar chart, each action tends to lead to a different outcome. The rightmost bar chart shows a case in between, where the vending machine reliably leads to one and the same outcome, like a vending machine which produces the same chocolate bar most of the time, whichever button is pressed.
Consequences of beliefs about control
Consequences of beliefs about control

Huys et al., 2008
Consequences of beliefs about control

**Exploration vs Exploitation**

- **High control**
- **Low control**

Choose blue slot machine

Choose orange slot machine

\[ Q(a_{\text{known}}) - Q(a_{\text{unknown}}) \]

Predictive Distributions

Reward

\[ P(\text{reward} | a_{\text{known}}) \]

**Huys et al., 2008**
Consequences of beliefs about control

Huys et al., 2008
Consequences of beliefs about control

Exploration vs Exploitation

Predictive Distributions

Huys et al., 2008
Consequences of beliefs about control

Predictive Distributions

High control

Low control

P(reward | a_{known})

Reward

0 0.1 0.2 0.3 0.4 0.5 0.6 0.7

0 1 2 3 4 5

Exploration vs Exploitation

P(reward | a_{known})

Predictive Distributions

High control

Low control

Outcomes

Probability

0 0.5 1

0 1

Huys et al., 2008
Consequences of beliefs about control

Predictive Distributions

P(reward | a_{known})

<table>
<thead>
<tr>
<th>Reward</th>
<th>1</th>
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<th>4</th>
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<td></td>
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Exploration vs Exploitation

Q(a_{known}) - Q(a_{unknown})

<table>
<thead>
<tr>
<th>Tree depth</th>
<th>1</th>
<th>2</th>
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<td>1</td>
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</tbody>
</table>

Choose blue slot machine
Choose pink slot machine

High control
Low control

Huys et al., 2008
Choice probability as function of prior belief

- Bellman equation

\[ Q(a, s) = \sum_{s'} T_{s,s'}^a [R_{s,s'}^a + \arg\max_{a'} Q(a, s')] \]

- Dirichlet prior
  - on entropy of each machine \( a \)

\[ T_{s,s'}^a = P(r|N_t, a, \alpha) \]

Huys et al., 2008
Choice probability as function of prior belief

- **Bellman equation**

\[ Q(a, s) = \sum_{s'} T_{s, s'}^a [R_{s, s'} + \operatorname{argmax}_{a'} Q(a, s')] \]

- **Dirichlet prior**
  - on entropy of each machine \( a \)

\[ T_{s, s'}^a = P(r | N_t, a, \alpha) \]

- **Value of each machine by evaluating tree weighted by belief-dependent outcome probabilities**

\[ Q_t(a | N_t, \alpha) = \sum_r p(r | N_t, a, \alpha)[r + \operatorname{argmax}_{a'} Q_t(a' | N_{t+1}(r), \alpha)] \]

Huys et al., 2008
Casino Task

Imagine you are in a Casino.
With lots and lots of rooms.
Casino Task

In each room, you can choose between slot machines.

You will go through 100 different rooms.

In each room, you get to choose 8 times.

Huys et al., 2008
Casino Task

3 choices to go
Anhedonia or helplessness?

\[ p(a|N_t, \alpha, \beta) = \frac{e^{\beta Q(a; N_t, \alpha)}}{\sum_{a'} e^{\beta Q(a'; N_t, \alpha)}} \]

Anhedonia? Helplessness?

\[ \alpha = \theta_\beta BDA + \theta'_\alpha BHS + \cdots \]
\[ \beta = \theta'_\beta BDA + \theta_\alpha BHS + \cdots \]
Helplessness as normative generalisation

Level III: World
- \(c\)
- \(\sigma^2_c\)

Level II: Situation
- Control: \(\alpha_s\), \(\beta_s\)
- Transition Tendency: \(\theta_{s,a}\)

Level I: Action
- \(a \in A\)

State
- \(S_t\)
- \(S_{t+1}\)

To model \(\theta_{s,a}\) for \(s \in S\) and \(a \in A\), a rational agent may have to learn \(\alpha_s\) and \(\beta_s\). To allow for the transfer of knowledge between states, a further level is needed: in addition to its control, the agent becomes sure that the transition probabilities \(\theta_{s,a}\) are all drawn from the same distribution: a Dirichlet \(\mathcal{D}(\alpha_s, \beta_s)\) and an Inverse-Gamma distribution \(\mathcal{IG}(\beta_s, \alpha_s)\) for \(\alpha_s\) and \(\beta_s\) parameters. The model in Figure 1 can be used to investigate how this generalization is affected by \(c\), \(\sigma^2_c\), and the variability of \(c\) across situations (low \(c\) vs. high \(c\)).

Anne Lieder, Elke Goodman and Quentin Huys, 2013
Helplessness as optimal inference

To answer this question, we simulated decision making by a sampling algorithm used in a hierarchical Bayesian model shown in Figure 1. The rat's decision of transition probabilities was modelled as the hierarchy shown in Figure 4. Specifically, we assumed that the rat simulates five outcomes of each action, a_i, and chooses the action with the highest average utility, s, a_i \sim P(j | S_t, A) for which P(s = 1 | A) = a_i(s, A) = \alpha_i + \beta_i \cdot \ln(\frac{a_i}{1 - a_i})

The plots on right show our model captures this effect of uncontrollable shocks on the probability to escape faster than rats with no prior exposure to shock. Our results indicate that a normative account of generalization of action-outcome contingencies is sufficient to account for many learned helplessness effects, (iv) mastery effects, (v) impaired learning that differentiates stressors as either controllable or uncontrollable, (vi) the interaction between helplessness and task requirements. This suggests that the generalization of experienced control may be sufficient to explain helplessness as optimal inference.

In the experiment's appetitive choice task, rats were rewarded with food for going into one of two chambers after they had been trained to prefer the other chamber in which a reward would be delivered. Figure 6 shows our model captures that uncontrollable shocks reduced the probability that a rat would first seek rewards. To assess whether our model impairs not only the ability to learn from punishments but also from rewards, we simulated the experiment by [6]. The plots on right show our model accounts for the mastery effect that rats who had been exposed to controllable shocks prior to the task, (Figure 5, left panel), and when they succeeded to escape (Figure 5, right panel). Furthermore, (Figure 5, left panel), and when they succeeded to escape (Figure 5, right panel). Furthermore, subjects failed to escape more often than naive subjects. The three columns correspond to the experimental conditions. The lines are model predictions; diamonds are data points.
Helplessness as optimal inference

Figure 6 shows our model captures that uncontrollable stressors, due to the generalization that the world is uncontrollable, impair not only the ability to learn from punishments (Figure 5, left panel), and when they succeeded to escape shock and the time required to do so [17]: yoked subjects' perceived control broken at random. Under these assumptions, the learning dynamics shown in Figure 4 capture the qualitative effects on the subjects' performance taken action that did (Figure 3A shows the simulated changes in the average utility of each action that learned helplessness induces depression-like states to account for many learned helplessness effects, whereby prior exposure to uncontrollable stress fails to induce helplessness, (iii) that helplessness is induced by uncontrollable stressors and task requirements. This suggests that the generalization of action-outcome contingencies is sufficient to explain helplessness as optimal inference. To answer this question, we simulated decision making and learning in the experiment by [19]. In this simulation, the rat's hierarchical Bayesian model shown in Figure 1. The rat's agent beliefs in the corresponding value of the utility of each action, the average utility, are estimated using Monte-Carlo (MCMC) methods. To sample from the posterior distribution of the agent's beliefs, we simulated how strongly naive subjects, subjects who might consider treating diabetes, performed worse than naive rats across all 10 blocks of experiments. For escapable and inescapable shocks, we performed 1, 2, or 3 lever presses. For uncontrollable shocks, we performed 2 for 2 seconds long, and simulated one decision, one observation with one action that did (\( \pi^a_{t-1} \)) from uncontrollable stress. Mirroring the fact that rats who were exposed to controllable shocks prior to the task, escape faster than rats with no prior exposure to shock, our simulation captures that yoked rats performed worse than naive rats across all 10 blocks of trials.

Hannum et al. (1976) Simulation Results

<table>
<thead>
<tr>
<th>Masters</th>
<th>Yoked</th>
<th>Naive</th>
</tr>
</thead>
<tbody>
<tr>
<td>#Escapes out of 40 trials</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>Escape Latency (sec)</td>
<td>60</td>
<td>40</td>
</tr>
</tbody>
</table>

Discussion

Lieder, Goodman and Huys, 2013
Helplessness - goal-directed decisions

- Matches the neurobiology

![Graphs showing 5-HT levels in inescapable and escapable conditions](image-url)
So...

- **Emotional component**
  - No primary changes (pain, hedonic taste, sucrose)
  - Negative “emotional” biases & decision-making
    - conceptual -> interpretation?

- **Cognitive component**
  - Helplessness
  - Goal-directed “interpretations”

- **Neuromodulators: 5HT**

- **Cognitive Neuropsychological model: emotional biases lead to cognitive biases**
  - How?
SSRIs

- Main treatment modality

![Network diagram of antidepressants](image)

- the more specific the better?

Cipriani et al., 2009
SSRIs

- **Main treatment modality**

- **the more specific the better?**

---

Cipriani et al., 2009
Acute tryptophan depletion

- 80% in patients who have responded to SSRIs. 16% in those who have not.
- AMT: similar for NA -> converse picture

Smith et al., 1999
Acute tryptophan depletion

- 80% in patients who have responded to SSRIs. 16% in those who have not.
- AMT: similar for NA -> converse picture

Smith et al., 1999
Serotonin in MDD: 5HTT
Serotonin in MDD: 5HTT

Caspi et al., 2003

Groups of individuals having different numbers of life events

Caspi et al., 2003
Serotonin and depression

SSRI

<table>
<thead>
<tr>
<th>Effect</th>
<th>inhibit reuptake</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>increase 5HT??</td>
</tr>
</tbody>
</table>

Depression treats causes acute relapse

Smith et al. 1999
Serotonin and depression

SSRI

<table>
<thead>
<tr>
<th>Effect</th>
<th>inhibit reuptake</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>increase 5HT??</td>
</tr>
</tbody>
</table>

Depression treats

Smith et al. 1999
## Serotonin and depression

<table>
<thead>
<tr>
<th>SSRI</th>
<th>5HTTLPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect</td>
<td>inhibit reuptake</td>
</tr>
<tr>
<td></td>
<td>increase 5HT??</td>
</tr>
<tr>
<td>Depression</td>
<td>treats</td>
</tr>
</tbody>
</table>
### Serotonin and depression

<table>
<thead>
<tr>
<th>Effect</th>
<th>SSRI</th>
<th>5HTTLPR</th>
<th>Tryptophan depletion</th>
</tr>
</thead>
<tbody>
<tr>
<td>inhibit reuptake</td>
<td>increase 5HT??</td>
<td>increase 5HT??</td>
<td>reduce 5HT</td>
</tr>
<tr>
<td>inefficient reuptake</td>
<td>increase 5HT??</td>
<td>increase 5HT??</td>
<td>reduce 5HT</td>
</tr>
</tbody>
</table>

Depression: treats causes acute relapse

---

Smith et al. 1999
Serotonin in helplessness

Table 2
Effects of inescapable shock on the number of Fos+ 5-HT cells and Fos+ TH cells.

<table>
<thead>
<tr>
<th>Nuclei</th>
<th>Cage control</th>
<th>Shocks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>DRN</td>
<td>7.8 ± 1.7</td>
<td>76.8 ± 12.6**</td>
</tr>
<tr>
<td>MRN</td>
<td>1.8 ± 1.2</td>
<td>7.8 ± 1.8</td>
</tr>
<tr>
<td>NRM</td>
<td>1.8 ± 0.5</td>
<td>31.3 ± 2.1**</td>
</tr>
<tr>
<td>NRO</td>
<td>0.5 ± 0.3</td>
<td>9.7 ± 1.8*</td>
</tr>
<tr>
<td>NRP</td>
<td>2.3 ± 0.5</td>
<td>9.3 ± 2.5</td>
</tr>
<tr>
<td>LC</td>
<td>49.0 ± 15.2</td>
<td>332.3 ± 31.2***</td>
</tr>
</tbody>
</table>

Values are means ± S.E.M.; n = 4 for cage control; n = 6 for 0, 10, 50 and 100 shocks. *p < 0.05; **p < 0.01; ***p < 0.001 vs. cage control; †p < 0.01; ††p < 0.001 vs. 0 shocks; §p < 0.05; ‡‡p < 0.01; §§§p < 0.001 vs. 10 shocks; by one-way ANOVA and Newman–Keuls multiple comparison test.

Takase et al., 2005

Maier and Watkins, 2005
Behavioural inhibition and 5HT

Release of punishment-suppressed responding  
= anxiolysis

Tye et al., 1977
5HT: Panic and anxiety

Deakin, Graeff, Gray et al.

Panic

Anxiety

5HT: Panic and anxiety

Deakin, Graeff, Gray et al.

**5HT: Panic and anxiety**

Deakin, Graeff, Gray et al.

Soubrié (1986) - not anxiety, but behavioural suppression

Inhibition with aversive expectations?

Cools et al., 2007
ATD abolishes Pavlovian inhibition in humans

Crockett et al., 2012
ATD abolishes Pavlovian inhibition in humans

Crockett et al., 2012

Reward-only (RO) Block
- Incorrect: 0
- Correct: +10

Reward + punishment (RP) Block
- Incorrect: -10
- Correct: +10

Punishment-induced inhibition
(NR_{RT} - NR_{RO})

Crockett et al., 2012
Decisions in Depression

PIT

Table 1. Action outcome contingencies for the different instrumental stimuli

<table>
<thead>
<tr>
<th>Action Context</th>
<th>Outcome</th>
<th>Instrumental Stimuli</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approach</td>
<td>-20 cents</td>
<td>Mushrooms</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>+20 cents</td>
<td>Mushrooms</td>
</tr>
<tr>
<td>Go/Nogo</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Approach Go (good) Go (collect)

Table 2. Trait characteristics and data from neuropsychological background tests

<table>
<thead>
<tr>
<th>Trait</th>
<th>BAL1st</th>
<th>TRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of trials</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of trials</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit span</td>
<td>16.2 (0.6)</td>
<td>18.1 (0.6)</td>
</tr>
<tr>
<td>Number cancelation</td>
<td>227.7 (6.2)</td>
<td>207.5 (5.7)</td>
</tr>
<tr>
<td>NLV</td>
<td>85.8 (1.4)</td>
<td>85.6 (1.8)</td>
</tr>
<tr>
<td>Kirby-large</td>
<td>0.02 (0.01)</td>
<td>0.03 (0.02)</td>
</tr>
<tr>
<td>Kirby-medium</td>
<td>0.03 (0.01)</td>
<td>0.03 (0.02)</td>
</tr>
<tr>
<td>Kirby-small</td>
<td>0.04 (0.01)</td>
<td>0.05 (0.02)</td>
</tr>
<tr>
<td>STAI</td>
<td>30.2 (1.3)</td>
<td>30.5 (1.2)</td>
</tr>
<tr>
<td>HRSD</td>
<td>0.9 (0.2)</td>
<td>0.9 (0.3)</td>
</tr>
<tr>
<td>EPQ-lie</td>
<td>6.2 (0.6)</td>
<td>6.6 (0.7)</td>
</tr>
<tr>
<td>EPQ-neuroticism</td>
<td>2.2 (0.4)</td>
<td>1.9 (0.3)</td>
</tr>
<tr>
<td>EPQ-extraversion</td>
<td>10.0 (0.4)</td>
<td>9.3 (0.6)</td>
</tr>
<tr>
<td>EPQ-psychoticism</td>
<td>2.1 (0.4)</td>
<td>1.2 (0.2)</td>
</tr>
<tr>
<td>BDI</td>
<td>1.1 (0.35)</td>
<td>1.4 (0.36)</td>
</tr>
<tr>
<td>BAS-fun</td>
<td>8.2 (0.3)</td>
<td>8.4 (0.5)</td>
</tr>
<tr>
<td>BAS-drive</td>
<td>7.6 (0.5)</td>
<td>7.5 (0.5)</td>
</tr>
<tr>
<td>BAS-reward</td>
<td>8.9 (0.5)</td>
<td>9.1 (0.5)</td>
</tr>
<tr>
<td>BAS-total</td>
<td>24.7 (1.1)</td>
<td>28.1 (3.1)</td>
</tr>
<tr>
<td>BIS</td>
<td>18.3 (0.8)</td>
<td>17.0 (0.9)</td>
</tr>
<tr>
<td>Barratt-nonplanning</td>
<td>24.4 (1.3)</td>
<td>22.2 (1.7)</td>
</tr>
<tr>
<td>Barratt-motor</td>
<td>18.9 (1.1)</td>
<td>17.6 (1.5)</td>
</tr>
<tr>
<td>Barratt-total</td>
<td>59.4 (3.1)</td>
<td>54.3 (4.1)</td>
</tr>
</tbody>
</table>


Huys et al., 2011

Quentin Huys, TNU/PUK
Conditioned suppression, ATD

**Figure 2.** Behavioral data from the PIT stage as a function of group. Shown are choice data as a function of CS Valence (SP

**Figure 3.** Instrumental learning and generalization to the PIT stage after tryptophan depletion (right graph, TRP

**Discussion**

According to these theories, both serotonin and dopamine have coordinated effects that serve to couple a motivational axis (appetitive versus aversive processing), and an activational axis (enabling versus inhibiting). These axes work in concert to modulate behavior across different contexts. The role of serotonin in appetitive behavior is well understood, but its role in aversive processing is less clear. The results of this study suggest that serotonin depletion attenuates aversive PIT, thus providing evidence for a selective role of serotonin in tying aversive expectations to behavior. This concurs with current theories according to which serotonin serves as a motivational opponent to dopamine.

**Results**

Results show that serotonin depletion attenuates aversive PIT, consistent with the hypothesis that serotonin modulates the inhibitory impact of aversive Pavlovian stimuli. This finding is in line with previous research showing that serotonin depletion reduces aversive Pavlovian stimulus-induced behavioral inhibition.

**Table 2**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAL</td>
<td>0.60</td>
<td>0.20</td>
</tr>
<tr>
<td>TRP</td>
<td>0.58</td>
<td>0.21</td>
</tr>
</tbody>
</table>

**Table 5**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAL</td>
<td>0.62</td>
<td>0.23</td>
</tr>
<tr>
<td>TRP</td>
<td>0.59</td>
<td>0.22</td>
</tr>
</tbody>
</table>

**References**

- Daw et al., 2002
- Cools et al., 2011
- Huys et al., 2011
- Boureau and Dayan, 2011
- Cools et al., 2011
- Daw et al., 2002
Modelling Pavlovian inhibition

Either proceed according to the fixed arrows

OR

inhibit and restart randomly in $I$
Inhibit and restart

Either proceed according to the fixed arrows
OR
inhibit and restart randomly in $I$

Dayan and Huys, 2008
Inhibit if faced with aversive prediction $V$
Inhibit if faced with aversive prediction $V$

\[ \alpha_{5HT} \]

Continuation probability $p_{5HT}(s)$

$V(s)$

Dayan and Huys, 2008
Punishment sensitivity supports optimism

\[ \alpha_{5HT} = 20 \]

Dayan and Huys, 2008
Punishment sensitivity supports optimism

Dayan and Huys, 2008
Serotonin and depression

\[ \alpha_{5HT} = 20 \]
Serotonin and depression

\[ V_{\text{est}} \]  \hspace{1cm} \uparrow \alpha_{5HT} \hspace{1cm} \rightarrow \hspace{1cm} \alpha_{5HT} = 20

Dayan and Huys, 2008
Serotonin and depression

5HTTLPR → increased 5HT tone

V_{est} \rightarrow \alpha_{5HT}

V_{true} \rightarrow \alpha_{5HT} = 20

Dayan and Huys, 2008
Serotonin and depression

5HTTLPR → increased 5HT tone

acute reduction

Dayan and Huys, 2008
Serotonin and depression

5HTTLPR → increased 5HT tone

\[ \alpha_{5HT} \uparrow \]

\[ \alpha_{5HT} = 20 \]

acute reduction

% utility vs \( \alpha_{5HT} = 20 \)

Dayan and Huys, 2008
Serotonin and depression

5HTTLPR → increased 5HT tone

\[ \alpha_{5HT} \]

acute reduction

Dayan and Huys, 2008
5HTTLPR affects Amg-PFC connectivity

Pezawas et al., 2005
pgACC - amygdala connectivity & ER

Our data provide new evidence that the trait-like ability to regulate emotional responses is associated with modulation of the amygdala activity as well as with amygdala-PFC functional connectivity. Specifically, we found that individuals who were better able to down-regulate negative emotion (as measured with enhanced cEMG scores) exhibited greater amygdala-pgACC connectivity when down-regulating negative emotion.

Table 1

<table>
<thead>
<tr>
<th>Brain region (Brodmann area)</th>
<th>Size</th>
<th>t-score</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inferior frontal gyrus (BA 47, 11)</td>
<td>688</td>
<td>3.37</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Inferior semi-lunar lobule, cerebellar tonsil, pyramis</td>
<td>944</td>
<td>3.49</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Anterior cingulate, medial/superior frontal gyrus (BA 32, 9, 10)</td>
<td>1768</td>
<td>3.48</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Inferior, middle temporal gyrus (BA 20, 37)</td>
<td>2248</td>
<td>3.96</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Lentiform nucleus</td>
<td>1352</td>
<td>4.39</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Middle, superior, medial frontal gyrus (BA 8, 9, 6)</td>
<td>17784</td>
<td>5.06</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Image: pgACC - amygdala connectivity & ER

Fig. 4. (A) Top panel depicts PFC clusters showing functional connectivity with amygdala during suppress versus maintain as predicted by cEMG difference scores. (B) Scatterplots between amygdala-PFC connectivity (y-axis; standardized mean beta) for each individual. Error bars indicate the SEM.

Note: Corrected cluster for multiple comparisons at obtai ned 1.3 years earlier. Individuals who were more successful at down-regulating negative emotion (more negative cEMG scores) exhibited greater amygdala-pgACC connectivity when down-regulating negative emotion (as measured with enhanced cEMG scores) specifically, within the pgACC. Conversely, unsuccessful regulators showed more positive coupling between the amygdala and several regions of the PFC including the pregenual anterior cingulate cortex (pgACC), orbitofrontal cortex (OFC), and dorsolateral PFC (dlPFC) when down-regulating negative emotion.

BOLD signal changes by regulating negative emotion were detected in the pgACC, amygdala, and these PFC regions. Among these PFC regions, when examining the main effects of regulatory goal, OFC was not modulated by regulation instructions (fire or maintain) signifying that the OFC was not modulated by regulation instructions (fire or maintain) signifying that the OFC was not modulated by regulation instructions (fire or maintain). Instead, the OFC was modulated by the degree of suppression of negative emotion.
Pruning one’s thoughts

- Could reflexive (serotonergic) inhibition also apply to internal thought processes?
- Pruning to approximate goal-directed problems we can’t solve
Psychochess

3 moves to go
A poor experimental psychologist’s version of chess

A tree search task

Huys et al., 2012
A poor experimental psychologist’s version of chess

A tree search task

Huys et al., 2012
Make a choice...

\[ X = 70 \]
Make a choice...

Optimal choices depend on the depth
There are $S \times D$ optimal paths.

$X = 70$
Approximate planning

-140
-20
+140
-20
-140
+20
+20
-20
-140
-20
-140
-20
Approximate planning

-140
-20
-140
-20
-140
-20

key ‘U’

key ‘I’

+140 +20 -20 -140 -20 -140 -140 -20
Approximate planning

[Graph showing choice fraction predicted by full tree search for Groups 140, with choices to go from 1 to 8.]
Approximate planning

Don’t look all the way to the end

Huys et al., 2012

Approximate planning

Choice fraction predicted by full tree search

Choices to go
Group 140

Huys et al., 2012
Pruning

key ‘U’
key ‘I’
Pruning

key ‘U’
key ‘I’

-140
-20
+20
+20
-20
+140 +20 -20 -140 -20 -140 -140 -20
Pruning

key ‘U’
key ‘I’

-140
-20
+20
+20
-20
+20
-20
-20
-140
-140
-140
-20
+140
+20
-20
-140
-20
-140
-140
-20
Pavlovian pruning

- **Optimality**
  - conserve guarantees
  - difficult & computationally expensive

- **Approximate**
  - trade optimality for speed
Pavlovian pruning

- **Optimality**
  - conserve guarantees
  - difficult & computationally expensive

- **Approximate**
  - trade optimality for speed

- **Pavlovian**
  - reflexively prune on encountering a punishment
Pavlovian?

Pruning

-140
-20
+140
+20
-20
-140
-140
-140
-140
-260
-20
-140
-140
-140
-20
-140
-180
-60
Pavlovian?

Pruning

-140 → -100

+140 +20 -20 -100

+20 -20 -100 -100 -20

+20 -140 -100 -260 -20 -100 -140 -60
Pavlovian?

Pruning

-140

-20

+20

+140

-20

-140

-20

-140

-20

-20

-140

-140

-140

-20

-20

-140

-140

-20

-140

-140

-180

-60
Pavlovian?

Pruning

-140

-20

+140

+20

-20

-140

-20

-140

-20

-20

-20

+20

-140

+140

-260

-20

-140

-180

-60
Optimal sequences containing losses

Lally, Huys and Roiser, in prep.
Optimal sequences containing losses

![Graphs showing fraction of optimal paths chosen with Large Loss and No Large Loss, and with varying depth.](image)
Adaptive pruning model

Probability of transition through large loss

Probability of other transitions

Huys et al., 2012
Adaptive pruning wins

![Graph showing group-level Bayes factor preferences]

- Pruning
- Discounting
- Look-ahead

Group-level Bayes factor

Pruning & Immediate (separate)

Huys et al., 2012
Adaptive pruning wins

Huys et al., 2012
Pruning is Pavlovian

Huys et al., 2012
Pruning is Pavlovian

Maximal loss

% choices predicted by model

Choices to go
Group 140

Huys et al., 2012
Pruning is Pavlovian

Maximal loss

-100

-140

% choices predicted by model

0

0.2

0.4

0.6

0.8

1

Choices to go

Group 100

Group 140

Huys et al., 2012
Pruning is Pavlovian

Maximal loss

-70  -100  -140

% choices predicted by model

Choices to go
Group 70  Group 100  Group 140

Huys et al., 2012
Pruning parameters

- Given the model, can now look at parameters

![Graph showing shallow and deep below large loss and below any outcome for different groups](image-url)

Parameter estimate

Shallow Deep

Huys et al., 2012
Pruning parameters

- Given the model, can now look at parameters

![Graph showing pruning parameters for different groups and depths.](image)
Pruning parameters

- Given the model, can now look at parameters

![Bar chart showing depth vs. groups and pruned parameters](chart.png)

- Shallow
- Deep

Legend:
- Blue: below large loss
- Red: below any outcome

Huys et al., 2012
Minor symptoms of depression increase pruning

- leads to increased pruning

- prediction: in MDD less pruning

More pruning
- more dependence on pruning
- more sensitivity to drops in 5HT?

Huys et al., 2012
Emotional component
- No primary changes (pain, hedonic taste, sucrose)
- Negative “emotional” biases & decision-making
  - conceptual -> interpretation?

Cognitive component
- Helplessness
- Goal-directed “interpretations”

Serotonin

Pavlovian influence on goal-directed thought processes as one influence of emotion on cognition.