Depression & Reinforcement Learning

23 / 10 / 2017

Sam Rupprechter
s1520312@sms.ed.ac.uk
Outline

- Depression
- Reinforcement Learning (RL)
- RL Impairments in Depression
- Modelling Theory
Major Depressive Disorder (MDD)
Major Depressive Disorder (MDD)

- Core symptoms:
  - Depressed mood
  - Anhedonia (inability to experience pleasure)
  - Loss of energy
  - Change in weight or appetite
  - Insomnia / Hypersomnia
  - Psychomotor agitation / retardation
  - Concentration difficulties
  - Suicidal thoughts / ideation
Major Depressive Disorder (MDD)

- Categorical view has little basis in biology?
  - Research moves towards dimensional view

- RDoC framework
  - Multiple levels of analysis
    - Neural circuitry, genes, behaviour

- Endophenotypes
  - Anhedonia
  - Neuroticism
Treatment

- Cognitive Behavioural Therapy (CBT)
- Antidepressant medication
  - Selective Serotonin Reuptake Inhibitors (SSRIs)
    - Primary first line treatment
  - Serotonin-Norepinephrine Reuptake Inhibitor (SNRIs)
  - Tricyclic Antidepressants (TCAs)
- Electroconvulsive therapy (ECT), Surgery
  - Very severe, treatment-resistant cases
MDD Theories

• **Cognitive Theory** *(Beck, 2008)*
  - Negative cognitive schemas (CBT targets those)
  - e.g. biased recalling of negative events

• **Learned Helplessness** *(Seligman, 1972)*
Learned Helplessness

Huys et al., 2008; NIPS
MDD Theories

- **Cognitive Theory** (Beck, 2008)
  - Negative cognitive schemas (CBT targets those)
  - e.g. biased recalling of negative events

- **Learned Helplessness** (Seligman, 1972)

- **Stress** → deficits in reinforcement / reward processing (learning) → anhedonia (Pizzagalli, 2014)
  - 70-80% of Major Depressive Episodes preceded by major life event
Impact

• High (lifetime) prevalence (esp. in developed countries)
  – USA: 16.2% (Kessler et al., 2003)
  – UK / Europe: 7-10% (Ayuso-Mateos et al., 2001)
  – Depression rates are rising (e.g. Mojtabai et al., 2016)

• High economic impact (Europe: €92 billion in 2010) (Olesen et al., 2012)

• People are suffering
  – Risk factor for suicide (Olsson et al., 2017)
    • And suicide rates are increasing
  – Cognitive Impairments (e.g. Snyder, 2013)
    • Attention, concentration, executive functioning, working memory, …
  – Impairments in Reinforcement Learning (Chen et al., 2015)
Reinforcement Learning (RL)

- Make a choice
  - Based on “internal values”
- Observe an outcome (reinforcer)
  - Often probabilistic
  - Generates prediction error
- Update internal values
Reinforcement Learning (RL)

- Update values
  \[ V(t + 1) = m \times V(t) + \varepsilon \times (\rho \times r(t) - V(t)) \]

- Decide between two options
  \[ p(a \mid V, \theta) = \frac{1}{1 + \exp(-\beta \times (V_a - V_b))} \]

- (Can be made more sophisticated; e.g. Q-learning)
RL Impairments in MDD

- Signal Detection Task
- fMRI studies
- Computational Modelling

- Iowa Gambling Task (?)
- Reversal Learning (?)
Signal Detection Task (e.g. Pizzagalli et al., 2005)

DEMO

(sort of)
Signal Detection Task (e.g. Pizzagalli et al., 2005)

- One stimulus rewarded more often
  - (healthy) participants become biased towards it
Reminder: Reinforcement Learning (RL)

- Update values
  \[ V(t + 1) = m \times V(t) + \varepsilon \times (\rho \times r(t) - V(t)) \]

- Decide between two options
  \[ p(a \mid V, \theta) = \frac{1}{1 + \exp(-\beta \times (V_a - V_b))} \]
MDD Modelling Studies (behavioural)

- Chase et al., 2010
  - Lower learning rates
- Kunisato et al., 2012
  - Lower temperature parameter
- Huys et al., 2013
  - Lower reward sensitivity
- Beevers et al., 2013
  - Higher temperature parameter
- Dombrovski et al., 2010
  - Lower memory [in suicide attempters]
Analysing fMRI Data (with SPM)

Image time-series → Realignment → Normalisation → Template

Kernel → Smoothing

Design matrix → General linear model → Parameter estimates

Statistical parametric map (SPM) → Statistical inference → p < 0.05

Gaussian field theory

http://www.fil.ion.ucl.ac.uk/spm/doc/intro/intro.pdf
Back to MDD

- Model-based fMRI (e.g. Kumar et al., 2008; Gradin et al., 2011)
  - No real behavioural differences
  - Abnormal reward prediction errors
  - Abnormal expected reward values
(Behavioural) Modelling

- How do I actually “fit” a model to data?
  - Try to find “optimal” values for the parameters of the model that our data “most likely”
    (maximize the probability of observed choices)
Maximize the Likelihood

\[ L = p(A \mid V, \theta) = \prod_{a \in A} p(a \mid V, \theta) \]

- Multiplying lots of small numbers is a bad idea… take the log instead!
- Instead of maximizing log likelihood → we usually minimize negative log likelihood

\[ NLL = - \sum_{a \in A} \log p(a \mid V, \theta) \]
Example Experiment

Stankevicius et al., 2014; Further work in progress
Our Model

• Value Update

\[ V_{i}^{t+1} = A \times V_{i}^{t} + r_{i}^{t} \]

• Decision

\[ p(\text{choose fractal } i) = \frac{1}{1 + \exp(-\beta(f(V_{i}) - \phi_{i}))} \]
function nll = neg_log_likelihood(data, theta)
    A = theta(1);
    beta = theta(2);
    X = data.decisions;
    T = data.num_trials;
    r = data.obs_rewards;
    p = data.phis;
    V = zeros(T, 1);
    for i = 1:size(r, 2)
        V = A*V + r(:, i);
    end
    probs = logsig(X .* beta .* (V/4 - p));
    nll = -sum(log(probs));
end
Estimate parameters

• Different options (e.g. gradient descent)
  – We will simply use one of the built-in functions
And in MATLAB

1 \( f = @(x)(\text{neg}\_\text{log}\_\text{likelihood}(\text{data}, x)) \);
2 \( \text{thetas} = \text{fminunc}(f, [0;0]) \);
How good is our estimation?

- **Simulate data** from estimated parameters
  - Does generated data look like the original data?
  - Re-fit parameters to simulated data and compare parameters

- Look at the curvature (Hessian / 2\textsuperscript{nd} order derivative) at the estimated point
  - Returned by fminunc
  - Take inverse to get covariance matrix
Correlated Parameters

• Might cause issues during inference
  – e.g. if two parameters are (highly) negatively correlated
    • Likelihood surface will have a “ridge”
    • We can arbitrarily change one of the parameters and then adjust the second parameter so as to keep the previous “maximum” likelihood (extreme example)
    • What does that mean if we are interested in the actual values of these parameters (e.g. for group comparisons)?
Correlated Parameters

• Parameters might actually be correlated
  – People who learn faster (higher learning rate) might be better at “remembering” what they learned (lower discounting)
Model Comparison

• How do we choose a model (hypothesis)?

• We want a Trade-off
  – Which model fits our data best? (accuracy)
    • Likelihood
  – Which model is the simplest? (complexity)
    • Number of parameters

• Turn to Bayesian model comparison…
Occam’s razor

\[ P(D|H_1) \]

\[ P(D|H_2) \]

Evidence

C_1

D

MacKay, 2003
Bayesian Model Comparison

- ... or rather approximations

$$AIC = 2 \times NLL + 2 \times d$$

$$BIC = 2 \times NLL + d \times \log(n)$$

- Calculate for each model
- Choose model with lowest value
- Note that adding redundant parameters will affect the comparisons
Model Recovery Simulations

Do we have the data we need to answer the questions we are asking?

Confusion matrix

- For each model m
  - Generate data from m
  - Fit all models to this data
  - Does model comparison choose m?
  - (repeat steps inside loop multiple times)

<table>
<thead>
<tr>
<th></th>
<th>H1</th>
<th>H2</th>
<th>H3</th>
</tr>
</thead>
<tbody>
<tr>
<td>H1</td>
<td>20</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>H2</td>
<td>0</td>
<td>19</td>
<td>1</td>
</tr>
<tr>
<td>H3</td>
<td>0</td>
<td>1</td>
<td>19</td>
</tr>
</tbody>
</table>
References

- Ayuso-Mateos, J. L.; Vázquez-Barquero, J. L.; Dowrick, C.; Lehtinen, V.; Dalgard, O. S.; Casey, P.; Wilkinson, C.; Lasa, L.; Page, H.; Dunn, G. & others; Depressive disorders in Europe: prevalence figures from the ODIN study; The British Journal of Psychiatry, RCP, 2001, 179, 308-316
- Bakic, J.; Pourtois, G.; Jepma, M.; Duprat, R.; Raedt, R. & Baeken, C.; Spared internal but impaired external reward prediction error signals in major depressive disorder during reinforcement learning; Depression and anxiety, Wiley Online Library, 2017, 34, 89-96
- Beevers, C. G.; Worthy, D. A.; Gorlick, M. A.; Nix, B.; Chotibut, T. & Maddox, W. T.; Influence of depression symptoms on history-independent reward and punishment processing; Psychiatry research, Elsevier, 2013, 207, 53-60
- Huys, Q. J.; Pizzagalli, D. A.; Bogdan, R. & Dayan, P.; Mapping anhedonia onto reinforcement learning: a behavioural meta-analysis; Biology of mood & anxiety disorders, BioMed Central, 2013, 3, 12
References

- Mojtabai, R.; Offson, M. & Han, B.; National trends in the prevalence and treatment of depression in adolescents and young adults; Pediatrics, Am Acad Pediatrics, 2016, e20161878
- O'Doherty, J. P.; Hampton, A. & Kim, H.; Model-based fMRI and its application to reward learning and decision making; Annals of the New York Academy of sciences, Wiley Online Library, 2007, 1104, 35-53
- Offson, M; Blanco, C; Wall, M & others; National trends in suicide attempts among adults in the united states; JAMA Psychiatry, 2017
- Pizzagalli, D. A.; Depression, stress, and anhedonia: toward a synthesis and integrated model; Annual review of clinical psychology, NIH Public Access, 2014, 10, 393
- Seligman, M. E.; Learned helplessness; Annual review of medicine, Annual Reviews 4139 El Camino Way, PO Box 10139, Palo Alto, CA 94303-0139, USA, 1972, 23, 407-412
- Snyder, H. R.; Major depressive disorder is associated with broad impairments on neuropsychological measures of executive function: A meta-analysis and review; American Psychological Association, 2013
Images

- https://www.nimh.nih.gov/images/rdoc/rdoc_logo_nobg_153390_1.png
- https://image.flaticon.com/icons/svg/492/492338.svg
- https://image.flaticon.com/icons/svg/554/554420.svg
- https://image.flaticon.com/icons/svg/164/164996.svg
- https://upload.wikimedia.org/wikipedia/commons/2/2f/Haemodynamic_response_function.svg
- https://upload.wikimedia.org/wikipedia/commons/f/ff/Gradient_descent.svg
- https://upload.wikimedia.org/wikipedia/commons/d/db/Gradient_ascent_%28contour%29.png