Negative Self-Schemas are Associated with Variation in the Serotonin Transporter-Linked Polymorphic Region (5-HTTLPR)

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Background

Negatively-biased information processing and the *5-HTTLPR*

- Negatively-biased processing of information can be a risk factor for depression.[1]
- Negative self-schemas (negative views of the self) make it easier to view negative terms as self-referent.
- A common deletion polymorphism in a promoter region for the gene that codes for the serotonin transporter (*5-HTTLPR*) results in short (*S*; vulnerable) and long (L) variants of the gene.[2]
- The *5-HTTLPR* has been associated with biased attention.[3] It may result in sustained negative affect and depressogenic cognitions.[2] It thus may influence the development of negative cognitive schemas.

The Self-Referent Encoding Task (SRET)

- The SRET can be used to measure schema strength.
- It is an affective decision-making task that has participants answer whether positive and negative words apply to them.[4]
- The number of self-referent words recalled is one proxy for negative schema. Another is the diffusion model.[5] We used the diffusion model to analyze the reaction time data, resulting in the drift rate (ease of categorizing words), a comprehensive measure of schema strength.

Our Hypotheses

- Individuals with short alleles of *5-HTTLPR* will exhibit more negative schema strength—more negative drift rates to negative words.
- This negative schema strength will be associated with memory bias, with drift rates indicating more negative schemas being associated with greater recall of self-referential negative words.

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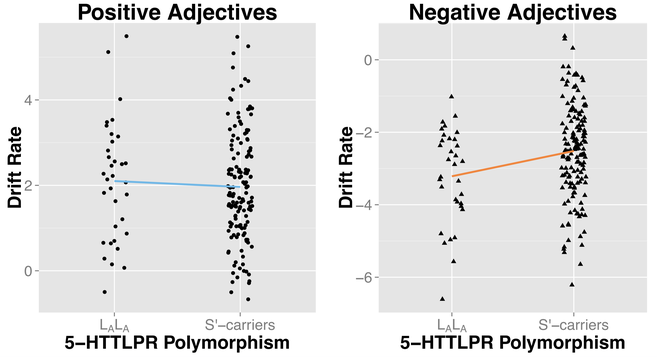
3. Beevers, C. G., Wells, T. T., Ellis, A. J., & McGeary, J. E. (2009). Association of the serotonin transporter gene promoter region (5-HTTLPR) polymorphism with biased attention for emotional stimuli. *Journal of Abnormal Psychology*, 118(3), 670–681.
4. Derry, P. A., & Kuiper, N. A. (1981). Schematic processing and self-reference in clinical depression. *Journal of Abnormal Psychology*, 90, 286.
5. Ratcliff, R. (1978). A theory of memory retrieval. *Psychological Review*, 85(2), 59.

Results & Discussion

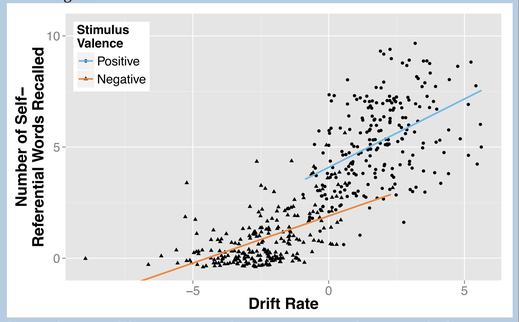
Association between 5-HTTLPR and drift rate for both positive and negative words on the SRET. The *5-HTTLPR* x stimulus valence interaction was significant, $b = .83$, $SE = .35$, $t = 2.38$, $p = .017$. Model $R^2 = .76$, $N = 183$.



Left: the lack of relationship for positive adjectives between *5-HTTLPR* and drift rate. Points in both graphs are jittered to demonstrate the spread of data.

Right: S′-carriers of the *5-HTTLPR* polymorphism (on the right) show a less-negative drift rate, indicating more difficulty categorizing negative words as not self-referential.

Association between drift rate for positive and negative words and recall for self-referential words of each valence on the self-referent encoding task.

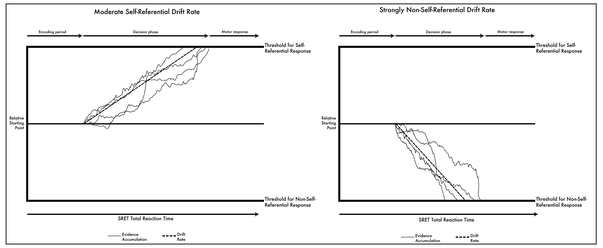


Jittered points. There is a significant interaction between drift rate and valence, $b = .31$, $SE = .12$, $t = 2.69$, $p = .007$. More negative scores indicate ease categorizing words as not self-referent; more positive scores ease categorizing words as self-referent. More difficulty categorizing negative adjectives as not self-referential was associated with increased recall for self-referential negative words; the reverse is true for positive words. Regression lines show the correspondence between drift for both positive (circles) and negative words (triangles) and recall for self-referential words of that valence.

- Sample was free of psychopathology to focus on the genetic linkage to cognitive bias, but this study should be replicated in a depressed sample.
- These results reinforce previous associations between the *5-HTTLPR* polymorphism and negative cognitive bias. Those who had vulnerable copies of the polymorphism showed a negative, but not positive, bias.
- It is likely that other genes also play a role in biased cognitive processing, rather than just the *5-HTTLPR* alone. Genome-wide or cumulative genetic approaches may be useful for future research.
- This sample is relatively small for a candidate gene approach. As such, we are currently replicating this study.
- The diffusion modeling approach is useful for operationalizing cognitive schemas. Precise measurements of cognitive phenomena are vital in order to find generalizable and reproducible results.
- We believe taking a comprehensive approach to understanding depression vulnerability by measuring processes across levels of analysis will foster the development of comprehensive models of depression vulnerability and may ultimately help us to better understand the etiology of depression.

Method

- $N = 183$ (106 female, mean age 25.12 (4.30)) adults without psychiatric illness, with self-report of depression in the healthy range.
- Genetics from saliva samples were analyzed at the lab of the second author. L_G fragments of *5-HTTLPR* were treated as equivalent to S. The L_AL_A group had two copies of the L_A allele; the S′-carrier group consisted of individuals who carried the S or L_G allele.
- Fast-dm[6] was used to implement the diffusion model, which deconstructs reaction time for two-choice decision tasks into components of cognitive processing. Drift rate was the primary outcome measure. Other components were not associated with *5-HTTLPR*.



Diffusion model drift rate. Representations of a subset of trials from hypothetical results. The time taken to reach the threshold across all trials is used to determine drift rate. Each individual generated two drift rates, one pertaining to decision making for positive adjectives and one for negative adjectives.

- Left: a moderate, self-referential drift rate.
- Right: a strong, non-self-referential drift rate.

6. Voss, A., & Voss, J. (2007). Fast-dm: A free program for efficient diffusion model analysis. *Behavior Research Methods*, 39(4), 767–775.

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