Working Memory Impairments in Schizophrenia Patients: A Bayesian IRT Analysis

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Background

- **Schizophrenia** - psychiatric disorder characterized by delusions, hallucinations, and thought disorder.

- **Working Memory** - active system for temporarily storing and manipulating information needed in the execution of complex cognitive tasks.

- **Spatial WM** - impaired in schizophrenia
  1. Empirical Evidence: Eye-tracking, hand movement studies
  2. Physical Evidence: Primate studies

- **Object WM** - not previously studied in schizophrenia.
Method

Goal: Compare object and spatial working memory in schizophrenics

1. Is object working memory impaired in schizophrenia patients?
2. If so, is the degree of impairment the same on spatial and object working memory?

- 28 schizophrenics and 33 normal controls participated in memory test with 64 object working memory and 64 spatial working memory items.
Test Schematic

Subject Fixates

500 ms Targets

3,000 ms Retention

Spatial: Is it in the same location as either target? (correct = No)

Object: Is it the same shape as either target? (correct = Yes)
Summary Statistics

<table>
<thead>
<tr>
<th></th>
<th>Spatial % Correct</th>
<th>Object % Correct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenics</td>
<td>86.3</td>
<td>72.7</td>
</tr>
<tr>
<td>Normals</td>
<td>92.5</td>
<td>80.8</td>
</tr>
</tbody>
</table>

1. How can we determine whether schizophrenics are more impaired on spatial or on object working memory when both groups did better on spatial tasks?

2. Not all items had equal difficulty, even within object or spatial tasks. Comparing only percent correct data over all trials ignores available information.
Item Response Theory

Item response theory (IRT) analyzes test-takers’ abilities while also analyzing and taking into account properties of the test items themselves.

- Allows abilities to be compared even when test items have differing levels of difficulty.

Main assumption: the probability of answering each item correctly is a monotonic function of subjects’ latent ability $\theta$.

- The exact function (Item Response Function) is determined by latent properties of the item $\beta$. 
Dichotomous Item Response Model

- $X_{ij}$ represents response of $i$th subject to $j$th test item: $X_{ij} = 1$ if $i$th item correct, 0 otherwise.
- $\theta_i$ represents ability parameter of $i$th subject
- $\beta_j$ represents characteristics of $j$th item
- Assume $X$ depends only on $\theta$ and $\beta$
- Assume independence of measures within and across subjects, given $\theta$
- Model estimates probability of a correct response:
  $$p_{ij}(\theta_i, \beta_j) = P(X_{ij} = 1 | \theta_i, \beta_j)$$
Examples

Two-parameter Logistic Model (2PL)

- \( p_{ij}(\theta_i, \beta_j) = \frac{1}{1 + \exp[-\beta_2 j \theta_i + \beta_1 j]} \)
- \( \beta_1 j \) represents difficulty and \( \beta_2 j \) the discrimination power of \( j \)th item

Three-parameter Logistic Model (3PL)

- \( p_{ij}(\theta_i, \beta_j) = \beta_3 j + \frac{1 - \beta_3 j}{1 + \exp[-\beta_2 j \theta_i + \beta_1 j]} \)
- \( \beta_3 j \) represents pseudo-guessing parameter, the probability the \( j \)th item is guessed correctly.
Maximum Likelihood Estimation

- IRT models pose problems for standard maximum likelihood analysis:
  1. Joint ML estimates of item and ability parameters are not consistent
  2. Marginal ML - treat ability parameters as missing data, use EM to estimate item parameters. Standard errors for ability parameters are then underestimated.

- Bayesian analysis automatically takes uncertainty about all other parameters into account, thereby avoiding these problems (Patz and Junker, 1999).
Bivariate IRT Model

Bivariate ability parameters: \( \theta_i \equiv (\theta_i^o, \theta_i^s) \)

Object items: \( p_{ij}(\theta_i, \beta_j) = \beta_{3j} + \frac{1 - \beta_{3j}}{1 + \exp[-\beta_{2j}\theta_i^o + \beta_{1j}]} \)

Spatial items: \( p_{ij}(\theta_i, \beta_j) = \beta_{3j} + \frac{1 - \beta_{3j}}{1 + \exp[-\beta_{2j}\theta_i^s + \beta_{1j}]} \)

Can model and estimate correlation between \( \theta_i^o, \theta_i^s \)
Bayesian IRT Model: Likelihood

- Normals:
  \[ X_{ij}^N \sim \text{Bern} \left( 0.5 + \frac{0.5}{1 + \exp[-\beta_{2j} \theta_{N,i}^t + \beta_{1j}]} \right) \]
  \[ i = 1, \ldots, 33, \quad j = 1, \ldots, 128 \]

- Schizophrenia Patients:
  \[ X_{ij}^S \sim \text{Bern} \left( 0.5 + \frac{0.5}{1 + \exp[-\beta_{2j} \theta_{S,i}^t + \beta_{1j}]} \right) \]
  \[ i = 1, \ldots, 28, \quad j = 1, \ldots, 128 \]

- \( t = 1 \) for object items and \( t = 2 \) for spatial items
Bayesian IRT Model: Prior Distribution

- **Ability Parameters**

  \[ \theta_{N,i} \sim N_2(\mu_N, \Sigma_N) \quad i = 1, \ldots, 33 \]  
  (Normals)

  \[ \theta_{S,i} \sim N_2(\mu_S, \Sigma_S) \quad i = 1, \ldots, 28 \]  
  (Patients)

- **\( \mu_N[1] = \mu_N[2] = 0 \) and \( \Sigma_N[1,1] = \Sigma_N[2,2] = 1 \) to anchor the model.**

  \* \( \mu_S[1] - \mu_S[2] \) represents difference between schizophrenia patients’ impairment in object, spatial working memory.
• Item Parameters

Object Items \((k = 1, 2, 3)\):
\[
\beta_{1j}^{o,k} \sim N(\eta_1^{o,k}, \tau_1^{o,k}) \quad \beta_{2j}^{o,k} \sim N(\eta_2^{o,k}, \tau_2^{o,k}) : \beta_{2j}^{o,k} > 0
\]

Spatial Items \((k = 1, 2, 3)\):
\[
\beta_{1j}^{s,k} \sim N(\eta_1^{s,k}, \tau_1^{s,k}) \quad \beta_{2j}^{s,k} \sim N(\eta_2^{s,k}, \tau_2^{s,k}) : \beta_{2j}^{s,k} > 0
\]

• All other parameters have diffuse prior distributions
### Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>95% Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\mu_S[1]$</td>
<td>-1.10</td>
<td>(-1.99, -0.38)</td>
</tr>
<tr>
<td>$\mu_S[2]$</td>
<td>-1.17</td>
<td>(-2.03, -0.40)</td>
</tr>
<tr>
<td>$\mu_S[1] - \mu_S[2]$</td>
<td>0.07</td>
<td>(-0.95, 1.08)</td>
</tr>
<tr>
<td>$\Sigma_S[1, 1]$</td>
<td>1.25</td>
<td>(0.37, 2.93)</td>
</tr>
<tr>
<td>$\Sigma_S[2, 2]$</td>
<td>2.55</td>
<td>(0.98, 5.13)</td>
</tr>
<tr>
<td>$\rho_N$</td>
<td>0.13</td>
<td>(-0.47, 0.66)</td>
</tr>
<tr>
<td>$\rho_S$</td>
<td>0.47</td>
<td>(-0.15, 0.90)</td>
</tr>
</tbody>
</table>
Conclusions

- In addition to spatial working memory, object working memory also impaired in schizophrenia patients.
  - The two domains appear to exhibit the same mean degree of impairment.
  - Could be the result of impaired rule-following strategies in schizophrenia patients.
- Some evidence of difference between variances of object and spatial working memory.
  - Possible indication that schizophrenia does not affect the two domains equally.
**Extensions and Future Work**

- Include clinically unaffected first-degree relatives of schizophrenia patients to explore models for the genetic inheritance of schizophrenia.

- Try to replicate results found here in different testing situations.

- Further comparisons of likelihood and Bayesian methods for parameter estimation in IRT models.
Including Relatives

- Motivation: Schizophrenia runs in families but isn’t common enough to be purely genetic
- Goal: Find traits that are impaired in unaffected relatives of schizophrenia patients
  - Do relatives have impaired working memory?
- Method: Mixture Modeling
IRT Mixture Model

\[ X_{ij}^R \sim \text{Bern} \left( 0.5 + \frac{0.5}{1 + \exp[-\beta_{2j} \theta_{R,i}^t + \beta_{1j}]} \right) \]

\[ \theta_{R,i} \equiv (\theta_{R,i}^o, \theta_{R,i}^s) \]

\[ p(\theta_{R,i}) = \pi N_2(\mu_S, \Sigma_S) + (1 - \pi) N_2(\mu_N, \Sigma_N) \]

- Interest in \( \pi \), proportion of unaffected relatives with impaired working memory

- Results inconclusive