Contextual prediction in schizophrenia: Multimodal imaging evidence from a semantic priming paradigm

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Introduction

- Language processing deficits in schizophrenia are often characterized by impairments in using relevant contextual information to predict and facilitate the processing of incoming semantic information (Kuperberg 2015; Bosch et al. 2012).
- Indeed, impairments in using contextual information to ‘predict the future’ may be a core abnormality, potentially driving multiple cognitive impairments and symptoms in schizophrenia (Ford & Mathalon, 2012; Fitcher & Frith, 2009; Barch & Ceaser, 2012; Cohen & Savan Schreiber, 1992).
- During normal language comprehension, the effective use of context to predict upcoming words entails a word-by-word ‘integration-activation’ cycle. We must: (a) integrate words within a context to generate a new representation; (b) hold this representation online within working memory; (c) use this working memory representation to feed back to semantic memory to pre-activate what is likely to come next, thereby facilitating semantic processing of incoming words; and (d) integrate the incoming word with the existing context to start a new cycle.
- Because these steps are elaborately dependent on one another, it has been difficult to determine exactly where the breakdown in the predictive use of context occurs in schizophrenia: is the primary abnormality in integrating an incoming word into its preceding context and maintaining this representation online within working memory (Kuperberg et al. 2006)? Or are impaired in the strategic use of any type of top-down information to activate information within semantic memory?
- We have recently developed a relatedness proportion semantic priming paradigm to specifically probe the effects of top-down activation on semantic facilitation, while keeping the demands of integration to a minimum (Lau et al., in press).
- Here we use this paradigm in combination with EEG and fMRI to ask whether patients with schizophrenia are able to use top-down strategies to facilitate semantic processing of an incoming word within 300ms of its onset.

Design

**Low-proportion: 10% related**
- Table – GRASS
- Bride – CAR pencil – WALLET cheddar - CHEESE

**High-proportion: 50% related**
- Table – GRASS
- Bride – GROOM salt – PEPPER cheddar - CHEESE

Previous work: effect of relatedness proportion in young adults

(Lau et al., in press; Lau et al., in preparation)

- Small N400 relatedness effect in the absence of expectation; much larger with increased expectation for a related target
- MEG sensors show stronger dipolar pattern for the relatedness effect in the presence of expectation
- MEG whole-brain source analysis localizes the effect of relatedness in the presence of expectation to left anterior temporal cortex

Methods

Demographic Information

<table>
<thead>
<tr>
<th>Total</th>
<th>Controls</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.4</td>
<td>25.5</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>20/15</td>
<td>20/15</td>
</tr>
<tr>
<td>Education (years)</td>
<td>16.4</td>
<td>16.4</td>
</tr>
<tr>
<td>Smoking status</td>
<td>6/19</td>
<td>6/19</td>
</tr>
<tr>
<td>Blood pressure (mmHg)</td>
<td>115±20/75±10</td>
<td>117±20/75±10</td>
</tr>
<tr>
<td>Head size (mm)</td>
<td>51.8±2.4</td>
<td>51.8±2.4</td>
</tr>
<tr>
<td>fMRI resolution</td>
<td>2.5x2.5x5</td>
<td>2.5x2.5x5</td>
</tr>
<tr>
<td>Subjects with healthy EEG</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Duration of illness, years</td>
<td>33.1±9.2</td>
<td>33.1±9.2</td>
</tr>
</tbody>
</table>

EEG/MEG and fMRI sessions on separate days, using completely different lists (no word repeated across sessions). EEG recorded from 70 electrodes, MEG from 102 x 3 sensors (1 megagnetometer and 2 planar gradiometers in each position). EEG sessions containing ocular artifact (suprathreshold VEOG or MEOG) rejected. SFP applied to remove cardiac artifact from MEG sensors in participants with visible EEG. 20-100 Hz low-pass filter; ERP and EFP baseline connected to activity in -1000ms internal prior to target

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Conclusions

- Patients with schizophrenia do show N400 amplitude facilitation in ERP and a seemingly similar effect in MEG. This suggests that they have the capacity to use top-down strategies to facilitate the semantic processing of upcoming words (cf. Condray et al. 1999, 2003)
- We suggest that patients’ impairments in using context to predict upcoming information are driven primarily by a failure to integrate multiple sources of information, rather than by a fixed inability to use top-down strategies to pre-activate semantic information in memory.
- Future fMRI and MEG analyses will assess whether different parts of the language network contribute differentially to priming and prediction effects in schizophrenia relative to controls

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