Background

- Many questions have been raised in the literature about the validity of current diagnostic categories, with much focus on the bipolar/schizophrenia distinction. This is complicated because both illnesses have affective and psychotic features and may share genetic vulnerabilities.
- A history of psychosis is reported to be associated with greater severity of cognitive deficits in patients diagnosed with Bipolar I disorder (BD; Bora, Yucel, & Pantelis, 2010; Balanzá-Martinez, et al., 2010; Brissos et al., 2011) and may serve as an important distinguishing variable.
- This study investigated heterogeneity in Bipolar I disorder based on the chronicity of psychosis (0: no history of psychosis, 1: one episode, 2: two or more episodes, 5: chronic).
- P300 event-related potential (ERP) amplitude and latency were obtained from standard Go/NoGo task.
- Study hypotheses:
  1. Bipolar patients with two or more episodes of psychosis (BD psychosis+) will demonstrate physiological deficits in P300 (e.g. smaller amplitude and/or delayed latency) compared to Bipolar I patients with one or no episode of psychosis (BD psychosis-).
  2. P300 amplitude and latency information will support categorical distinction between BD psychosis+ and BD psychosis-.

Method

Participants: 15 BD psychoses+, 27 BD psychoses- and 25 healthy controls (HC) matched for age, sex, and years of education, but did not match for age of onset (Table 1).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>BD psychoses+</th>
<th>BD psychoses-</th>
<th>HC</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>41.17 (17.30)</td>
<td>42.56 (16.68)</td>
<td>41.00 (7.28)</td>
<td>.44</td>
</tr>
<tr>
<td>Education (yrs)</td>
<td>15.39 (2.74)</td>
<td>15.09 (3.26)</td>
<td>15.16 (3.19)</td>
<td>.28</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Age of onset (yrs)</td>
<td>14.35 (15.16)</td>
<td>16.63 (10.15)</td>
<td>16.07 (1.01)</td>
<td>.22</td>
</tr>
<tr>
<td>Go response</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

EEG Recording

- F3, Fz, F4, C3, Cz, C4, P3, Pz used with 512 Hz sampling rate.
- Referenced to Fz.

Data Analysis

- Repeated-measure ANOVAs with age of onset as covariate for accuracy rate, reaction time (RT), and P300 amplitude and latency difference between BD psychosis+ and BD psychosis-
- Factor: Task (Go, NoGo), Presentation (PST) = Left visual field (LVF), Right visual field (RVF), Cau = Caudality (Frontal, central, parietal); Lat = Hemisphere Laterality (Left, midline, Right), and Group (BD psychosis+, BD psychosis-)

Discriminant function analysis (DA) was performed to investigate how accurately P300 amplitude and P300 latency information classify BD psychosis+ and BD psychosis-.

- Support Vector Machines (SVMs) (Vapnik, 1995) were used to train a classifier that separated between BD patients with high psychosis chronicity (BD psychosis+) and those with low psychosis chronicity (BD psychosis-).
- Each SVM model was trained using subsets of the P300 amplitude and latency features and evaluated using a leave-one-out cross-validation scheme to obtain a statistically unbiased estimate of performance on new patients.
- The subsets are chosen to explore the discriminant information present in the Go and NoGo trials as well as in the amplitude and latency features.
- Linear SVMs were used and the SVM parameter was chosen using leave-one-out cross-validation on the training data.

Area under the receiver operating curve (AUROC) was used to test model discrimination. The AUROC is a standard measure used to assess the performance of a binary classifier, and can be interpreted as the probability that the classifier will assign a higher score to a randomly chosen positive example than to a randomly chosen negative example.

Conclusion

- P300 latency difference in BD psychosis+, BD psychosis- were investigated with 100 trials (42 Go, 18 NoGo) were used. Go : NoGo = 70% : 30%.
- Go (response) and NoGo (withhold) stimuli were presented either on the left or right side of the screen.
- Participants were instructed to respond when the Go stimulus was presented.
- EEG was recorded from 32 scalp electrodes (F3, Fz, F4, C3, C4, P3, Pz, P4) with 512 Hz sampling rate.
- P300 event-related potential (ERP) amplitude and latency were obtained from standard Go/NoGo task.
- Study hypotheses:
  1. Bipolar patients with two or more episodes of psychosis (BD psychosis+) will demonstrate physiological deficits in P300 (e.g. smaller amplitude and/or delayed latency) compared to Bipolar I patients with one or no episode of psychosis (BD psychosis-).
  2. P300 amplitude and latency information will support categorical distinction between BD psychosis+ and BD psychosis-.

Visual Go/NoGo Task (Figure 1)

- 60 trials × 4 blocks
- 15 trials/4 blocks, 18 NoGo
- 30% Go (response) and NoGo (withhold) stimuli were presented either on the left or right side of the screen.

EEG Recording

- F3, Fz, F4, C3, C4, P3, Pz with 512 Hz sampling rate.
- Referenced to Fz.

Data Analysis

- Repeated-measure ANOVAs with age of onset as covariate for accuracy rate, reaction time (RT), and P300 amplitude and latency difference between BD psychosis+ and BD psychosis-
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Area under the receiver operating curve (AUROC) was used to test model discrimination. The AUROC is a standard measure used to assess the performance of a binary classifier, and can be interpreted as the probability that the classifier will assign a higher score to a randomly chosen positive example than to a randomly chosen negative example. An AUROC of 0.5 signifies that the classifier does not separate between the two classes, while a value of 1 signifies perfect separation. Typically good classifiers are ones that achieve an AUROC of 0.8 or greater, while fair classifiers achieve AUROCs of 0.7-0.8, poor ones 0.6-0.7, and bad ones below 0.6.

Results

Conclusions

- Psychosis in BD may be associated with distinct neurophysiological processes, which suggests that psychosis may be an important diagnostic feature.
- Delayed latency in BD psychosis+ especially when the stimulus was projected to the left hemisphere (RVF presentation) suggests that patients diagnosed with Bipolar I disorder with multiple episodes of psychosis may benefit from treatments assisting them to correctly evaluate stimuli and make fast responses that require left hemispheric resources.
- The SVM analysis shows that P300 amplitude features are useful in building diagnostic models for separating BD psychosis- from BD psychosis+ with an AUROC of 0.77.
- SVM analysis utilizing other P300 features (P300 latency, P300 amplitude, and Go/NoGo amplitude) did not yield significant results, with all AUROCs being 0.55 and below.

Table 2. Repeated-measure ANOVA group-related interaction effects with age of onset as covariate (n=50) (a = .05)

<table>
<thead>
<tr>
<th>Group</th>
<th>Low</th>
<th>High</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>P300 amplitude</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Go</td>
<td>.67</td>
<td>.67</td>
<td></td>
</tr>
<tr>
<td>NoGo</td>
<td>.87</td>
<td>.87</td>
<td></td>
</tr>
<tr>
<td>P300 latency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Go</td>
<td>.59</td>
<td>.59</td>
<td></td>
</tr>
<tr>
<td>NoGo</td>
<td>.05</td>
<td>.04</td>
<td></td>
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</tbody>
</table>

References