Neurobiological and temperamental assessment in the offspring of bipolar patients with different degrees of lithium response.

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Excellent lithium responders (ELR)

Patients in whom lithium concentrations exceed complete remission of manic and depressive episodes for 10 or more years

ERL make up about 1/5 of lithium treated patients

Response to lithium is associated with clinical features of an anergic course, bipolar facet history and low psychomotor comorbidity

ERL constitute a phenotype for pharmacoepidemiological studies due to significant genetic background

The aim of the study

To find possible differences in neurobiological:

- BDNF - brain derived neurotrophic factor
- MAPP-9 - matrix metalloproteinase-9
- A-6 - serotonin 6
- TNF-a - tumor necrosis factor alpha

and temperamental:

- TEMPS-A - Temperament Scale of Almqvist, Pisa, Paris, and San Diego Highscore
- O-LIFE - Oxford-Liverpool Inventory of Feelings and Experiences

The markers of hypothalamus-gastric antral and immune system suggested as biological indicators of illness (Roy et al., 2010).

Bipolar offspring

Ten-fold increased risk of developing BD, depression, and anxiety, and up to half may show any psychiatric disorders (Owen et al., 2000).

Offspring with mood disorders demonstrate clinical and neurobiological characteristics similar to their parents, including a familial factor of response to lithium (Petterson et al., 2011).

The markers of hypothalamus-gastric antral and immune system suggested as biological indicators of illness (Roy et al., 2010).

Neurobiological and temperamental related to parental lithium response have not been studied so far.

BDNF

- BDNF levels are decreased during depressive and manic episodes with tendency to increase after treatment (Curcio et al., 2008).
- Decrease in serum BDNF as a marker of later stage of bipolar disorder (Byrne et al., 2009).
- ERL have normal BDNF levels and cognitive functions (Byrne et al., 2010).

Assays performed using enzyme-linked immunosorbent assays (ELISA) and QuantiKine System.

Subjects studied

- 50 persons
- 27 females, 23 male, aged 17.5-45.18 years
- the offspring of 36 long-term lithium treated patients (9-10 years, mean 20.9 years).
- In which response to lithium was evaluated by the Almqvist and three categories scale (excellent lithium responders - ERL, partial responders, non-responders).
- 13 offspring of ERL and 37 of remaining groups.

The differences in age and proportion of females

Clinical assessment

Significantly higher percentage of patients treated for mood disorders in ERL offspring.

46% of ERL offspring (6/13) treated (one for bipolar I disorder, four for bipolar II disorder and one for major depressive episode)

16% in the remaining groups (6/37) (four for bipolar II disorder and two for depressive episodes)

TEMPS-A and ERL offspring

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<thead>
<tr>
<th>Group</th>
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<th>ERL offspring</th>
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<tr>
<td>Healthy</td>
<td>n=50</td>
<td>n=9</td>
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<tr>
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<td>n=13</td>
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</tr>
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O-LIFE and ERL offspring

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Temperament and ERL offspring

TEMPS-A

- ELR offspring obtained significantly higher scores on each of the temperament scales, except for hypomania scale.
- Healthy ERL offspring had significantly lower scores on hypomanic and anxious temperament and lower depressive and anxiety temperament than ERL offspring with mood disorders.

O-LIFE

- ELR offspring had significantly higher scores on each of the temperament scales, except for hyperysis.
- Healthy ERL offspring had significantly lower scores on hypomanic, anxious, and depressive temperament than ELR offspring with mood disorders.

Conclusions

- ERL offspring showed higher frequency of clinical mood disorders.
- A tendency to higher BDNF and lower IL-6 levels is familial.
- Hypomanic temperament and low cognitive disorganisation may be protective against emergence of mood disorders in ELR.
- Higher MAPP-9 levels in ERL offspring strongly correlate with more depressive episodes.

References