Regional assessment of Neurochemical Pathology by Magnetic Resonance Spectroscopy in Bipolar Disorder

Thesis

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Psychiatry

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This study is to identify the concentration of NAA, Cho and Cr containing compounds in frontal lobes, hippocampi, and thalami of patients with bipolar, which may enhance our understanding of the neurophysiology. 1H MRS was performed in 25 patients with bipolar disorder and 20 ages matched healthy subjects in the three mentioned cerebral areas and the comparable values of for NAA, Cr, and Cho have been taken and compared with patients with schizophrenia as well. The results of the study were that substantial evidence that the distribution of the metabolite alterations in the brain is significantly different in the 3 groups. Moreover, Brain metabolites are affected by number of episodes, age, age at onset, and severity of the current episode.

Key words: Bipolar mood disorder, 1H MRS, spectroscopy, schizophrenia, NAA, Cr, Cho, Brain metabolites


<table>
<thead>
<tr>
<th>List of contents</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Acknowledgment</td>
<td>1</td>
</tr>
<tr>
<td>List of abbreviations</td>
<td>3</td>
</tr>
<tr>
<td>Introduction and the aim of the work</td>
<td>6</td>
</tr>
<tr>
<td>Review of literature</td>
<td>11-80</td>
</tr>
<tr>
<td><strong>Chapter 1 neurobiology of bipolar</strong></td>
<td>11-44</td>
</tr>
<tr>
<td>I. Where are the bipolar disorder genes?</td>
<td>12</td>
</tr>
<tr>
<td>A. Linkage studies</td>
<td>14</td>
</tr>
<tr>
<td>B. Association studies</td>
<td>15</td>
</tr>
<tr>
<td>C. Neurotransmitter systems</td>
<td>17</td>
</tr>
<tr>
<td>D. Genes involved in intracellular signal</td>
<td>19</td>
</tr>
<tr>
<td>i. Transduction</td>
<td>19</td>
</tr>
<tr>
<td>ii. The mitochondrial hypothesis of bipolar disorder</td>
<td>20</td>
</tr>
<tr>
<td>II. Alteration in brain structure</td>
<td>21</td>
</tr>
<tr>
<td>III. Neurochemical changes</td>
<td>30</td>
</tr>
<tr>
<td>A. Noradrenergic systems</td>
<td>32</td>
</tr>
<tr>
<td>B. Serotonergic system</td>
<td>34</td>
</tr>
<tr>
<td>C. Dopaminergic system</td>
<td>38</td>
</tr>
<tr>
<td>D. Cholinergic system</td>
<td>40</td>
</tr>
<tr>
<td>E. G proteins</td>
<td>43</td>
</tr>
<tr>
<td><strong>Chapter 2 bipolar disorder and schizophrenia</strong></td>
<td>45-63</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>46</td>
</tr>
</tbody>
</table>
List of contents

Bipolar-schizophrenia continuum 48
Comparison of bipolar disorder and schizophrenia 49
  A. Epidemiology 49
  B. Neuroanatomy 50
  C. Genetics 54
  D. Pathophysiology 58

Chapter 3 neuroimaging of bipolar 64-81
I. Neuroimaging in psychiatry 65
II. The emerging role of neuroimaging in psychiatry 65
III. History of neuroimaging 66
IV. Core domains of pathology in bipolar disorder 70
  A. Impaired emotion processing and executive control 70
  B. Neural systems underlying emotion processing and executive control 71
V. Neuroimaging findings in bipolar disorder 72
VI. Neuropathological findings in bipolar disorder 76
VII. Effects in neuroimaging 77
VIII. Emerging technologies 79

Subjects and methods 82

Results 88-116

Discussion 117-135
  I. The epidemiological and descriptive 118
findings of the patients with bipolar disorder

II. The comparisons between patients with bipolar disorder and control

III. The comparisons between patients with bipolar disorder and patients with schizophrenia

IV. The MRS results of the patients with bipolar disorder
   A. Psychotic versus non-psychotic bipolar
   B. Gender differences
   C. Bipolar: number of episodes
   D. Bipolar: family history
   E. Bipolar: age, age of onset and duration of the illness
   F. Bipolar: severity
   G. Bipolar: depression versus mania

V. Critical appraisal

Summary

Recommendations

References

Appendix

Arabic summary
5-HIAA: 5-hydroxyindoleacetic acid
5-HT1D: 5-hydroxytryptamine (serotonin) receptor 1D
ACC: the anterior cingulate cortex
ADHD: attention deficit hyperactivity disorder
ANOVA: Analysis of Variance
ATD: acute tryptophan depletion
BPD: bipolar disorder
CAT or CT: computerized axial tomography
Cho: choline
CNS: central nervous system
COMT: catechol-o-methyl transferase
Cr: creatine
CSF: cerebrospinal fluid
DA: dopamine
DLPFC: dorsolateral prefrontal cortex
DNA: Deoxyribonucleic acid
DSM: Diagnostic and statistical manual of mental disorders
DTBZ: dihydrotetabenazine
DTI: diffusion tensor imaging
FA: fractional anisotropy
FH: Family history
fMRI: functional Magnetic Resonance Imaging
GABA: γ aminobutyric acid
GI: gyrification index
Glx: glutamate/glutamine
GPCRs: G protein-coupled receptors
GWAS: genome-wide association studies
HAM-D: Hamilton rating scale for depression
HC: Health Control
HPA: hypothalamic-pituitary-adrenal
HRs: high-risk
ICD: International classification of diseases
L-DOPA: L-3,4-dihydroxyphenylalanine
MAO: Monoamine oxidase
MDD: Major depression disorder
MEG: magnetoencephalography
MHPG: 3-methoxy-4-hydroxyphenylglycol
mI: myo-inositol
MRI: magnetic resonance imaging
MRS: Magnetic resonance spectroscopy
NAA: N-acetylaspartate
NE: noradrenergic.
PET: positron emission tomography
ROI: region of interest
SCID-I: Structured Clinical Interview for DSM-IV axis I disorders
sMRI: Structural Magnetic Resonance Imaging
SNPs: single nucleotide polymorphisms
SPECT: single photon emission computed tomography
SPSS: Statistical Package for the Social Sciences
SZ: schizophrenia
TEM: treatment-emergent mania
UPD: Unipolar depression
VBM: Voxel-based morphometry
VLPFC: ventrolateral prefrontal cortex
VMAT2: vesicular monoamine transporter protein
VPA: valproate
WMH: white matter hyperintensities
IQ: An intelligence quotient
INTRODUCTION
AND
THE AIM
OF
THE WORK
Introduction:

Bipolar disorder continues to present complex diagnostic and therapeutic challenges. Originally considered 2 separate diseases (mania and depression), bipolar disorder is now recognized to be a single disorder characterized by different subtypes and degrees of severity (Möller; 2003).

Both disorders, schizophrenia and bipolar disorder - diagnosed according to the prevailing manuals International Classification of Diseases, Tenth Revision (ICD-10) and Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) - reveal striking similarities: (a) lifetime prevalence of about 1% in males and females (independent of culture); (b) early age at onset (between late adolescence and early adulthood); (c) familial aggregation due to genetic influences with very similar recurrence risks of the same disorder among relatives (~10-fold increase in children); and (d) comparable concordance rates for monozygotic and dizygotic twins with heritability estimates of 60-80%. The fact that both disorders are genetically complex with multiple genes operating in concert with nongenetic environmental factors has now gained consensus (Maier, Zobel and Wagner; 2006).
Bipolar disorder and schizophrenia also demonstrate some similarities in neurotransmitter dysfunction. As further indirect evidence of a possible association, many newer atypical antipsychotic agents approved for the treatment of schizophrenia are also proving useful for bipolar disorder (Möller; 2003).
HYPOTHESIS AND AIM OF THE WORK

Hypotheses

Null Hypothesis: there is a continuum from bipolar disorder to schizophrenia; Schizophrenia and bipolar disorder have similar brain metabolite alterations.

Alternative Hypothesis: there are different metabolite alterations between bipolar disorder and schizophrenia. Schizophrenia and Bipolar disorder are two separate disorders.

Aim of the work

The aim of this work is to study the metabolite alterations in the brains of a sample of patients with bipolar disorder and of patients with schizophrenia. It will intend:

- To assess the concentration of NAA, Cho and Cr containing compounds in frontal lobes, hippocampi, and thalami of patients with bipolar disorder.

- To compare ratios of metabolites in patients with bipolar disorder and healthy subjects.
- To compare ratios of our findings regarding metabolites in patients with bipolar disorder and findings of other studies in patients with schizophrenia.

- To study the relationship between ratios of metabolite and clinical variables.