Gender Differences in Cognition and Clinical Presentation in Schizophrenia

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Features of Schizophrenia

Positive Symptoms
- Delusions
- Hallucinations
- Disorganized Speech

Negative Symptoms
- Affective Flattening
- Alogia
- Avolition
- Anhedonia
- Social Withdrawal

Social/Occupational dysfunction
- Work
- Interpersonal Relationships
- Self-Care
- Education

Cognitive Deficits
- Attention
- Memory
- D/O
- Executive Functions
- Unawareness

Comorbid Syndromes
- Mood
- Post-Traumatic Stress
- Substance Use
- Aggression
Cognitive Differences

Gender Differences in Cognitive Function in Healthy Controls
Gender Differences in Cognitive Function in Schizophrenia
Mental Rotation

[Diagram of various 3D shapes representing mental rotation tasks.]
Fig 1.—Neuropsychological profile ($\pm$ SEM) for patients with schizophrenia ($n = 36$) relative to controls ($n = 36$) whose performance is set to zero ($\pm 1$ SD). Functions are abstraction (ABS), verbal cognitive (VBL), spatial organization (SPT), semantic memory (SME), visual memory (VME), verbal learning (LRN), language (LNG), visual-motor processing and attention (VSM), auditory processing and attention (AUD), and motor speed and sequencing (MOT).

Gender Differences in Cognition

- Variable consensus in the literature

- Lower IQ has reported in men relative to women (Aylward et al 1984)

- Other studies have found no differences in IQ reported in other studies (e.g., Andia et al, 1995)

- On the information subtest of the WAIS

- Better functioning in neuropsychological performance in men than women
Schizophrenia: Gender Differences in Cognition
Women > Men (across literature)

• On measures of attention, language and executive functioning

• On the Digit Symbol subtest

• On all NP measures except attention

• For verbal learning and memory
Cognitive Impairment but Preserved Sexual Dimorphism (Halari et al 2006)

• Hypothesized that (i) men and women with schizophrenia would generally perform worse on all (verbal and spatial) cognitive tasks compared with the control subjects; and
• (ii) sex differences favoring men on the spatial tasks and women on the verbal fluency tasks would be found in both the control and patient groups

• Spatial Tests: Mental Rotation, Judgment of Line Orientation
• Verbal Tests: Phonological and Semantic Fluency
Judgment of Line Orientation
What's on HER mind? Gender Differences in Cognitive Function

**Patients**
- ES, Phonological = 0.47
- ES, Semantic = 0.03

**Controls**
- ES, Phonological = 0.50
- ES, Semantic = 0.32

Number of correctly generated words

- men
- women

- Phonological
- Semantic
Gender Differences in Cognition

• Repeatable Battery for Assessment of Neuropsychological Status (RBANS)

• 5 Domains:
  • Immediate Memory
  • Delayed Memory
  • Language
  • Attention
  • Visuospatial/Constructional

• Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS)

• 7 Domains:
  • Processing Speed
  • Attention/Vigilance
  • Working Memory
  • Verbal Learning
  • Visual Learning
  • Reasoning/Problem Solving
  • Social Cognition
### RBANS Scores by Gender

<table>
<thead>
<tr>
<th>Schizophrenia</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Score</td>
<td>86 ± 13</td>
<td>81 ± 10</td>
</tr>
<tr>
<td>Immediate Memory</td>
<td>85 ± 15</td>
<td>76 ± 12</td>
</tr>
<tr>
<td>Visuospatial Memory</td>
<td>87 ± 16</td>
<td>85 ± 14</td>
</tr>
<tr>
<td>Ability Language</td>
<td>98 ± 12</td>
<td>94 ± 10</td>
</tr>
<tr>
<td>Attention</td>
<td>89 ± 16</td>
<td>87 ± 18</td>
</tr>
<tr>
<td>Delayed Memory</td>
<td>88 ± 16</td>
<td>85 ± 9</td>
</tr>
</tbody>
</table>

*F*-values:
- Group × Gender: 2.8²
- 2.9²
- 2.1
- 1.9
- 1.0
- 1.6

*are two-way ANOVAs;*
Gender differences measured by the MATRICS consensus cognitive battery in chronic schizophrenia patients (from Zhang et al, 2017)
Differences in Clinical Presentation

What we know
More severe form
Negative symptoms
Typical features
Thought withdraw
Audible thoughts
Delusion of reference
Religious delusion

Made volition
Made feelings
Somatic control
Response to voice comment
Delusion control

Less severe form
Atypical features
Depressive symptoms
Thought broadcast
Thought insertion
Voice argument
Morbid jealousy
Sexual delusion
Gender Differences in Schizophrenia

![Graph showing gender differences in schizophrenia patients by age group.](image)
Figure 3-1 Hospitalizations for schizophrenia* in general hospitals per 100,000 by age group, Canada, 1999/2000

* Using most responsible diagnosis only

Source: Centre for Chronic Disease Prevention and Control, Health Canada using data from Hospital Morbidity File, Canadian Institute for Health Information
Brain Changes

- Most studies of gross neuroanatomy show enlarged ventricles and smaller frontal lobes in men relative to women with schizophrenia.
- This finding reflects normal sexual dimorphism.
- In comparison, studies of brain activation suggest a disturbance in normal sexual dimorphism, at least in emotion circuitry.
Potential Explanations of Gender Differences in Schizophrenia

Or, what we don’t know
What causes sex differences in schizophrenia?

• Could be caused by:
  • the disease process itself
  • by genetic and hormonal differences
  • by differences in the maturation and morphology of the brain

• Differing psychological vulnerability between genders based on symptomatology
Biological Protective Factors in Women?

• Estrogen hypothesis” emphasizes the possible neuroprotective effect of estrogen in women

• Relative dopaminergic inhibition by estrogens
  • Mediates impact of DA in its role as regulator of cognitive brain functions

• Relatively bilateral representation of left hemisphere functions in women
  • redundancy”
Other Factors Influencing Gender Differences

- Individual learning experiences
- Culture
- Gender stereotypes
- Biosocial interaction
- Experience
- Education
- Baseline functioning

Fig. 2. Gender differences in social functioning (men, ■; women, □).
Why do we care?

• Impact on treatment
  - Intervention at level of potential risk factors or moderators
  - May drive strategies when trying to enhance quality of life or employment

• Guide clinical and preclinical research

• Enhance our understanding regarding heterogeneity in schizophrenia
References


