

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

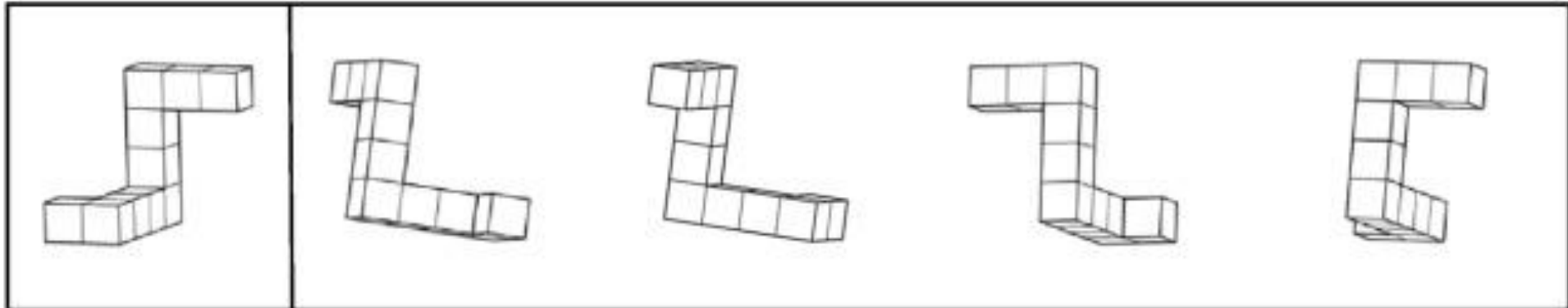
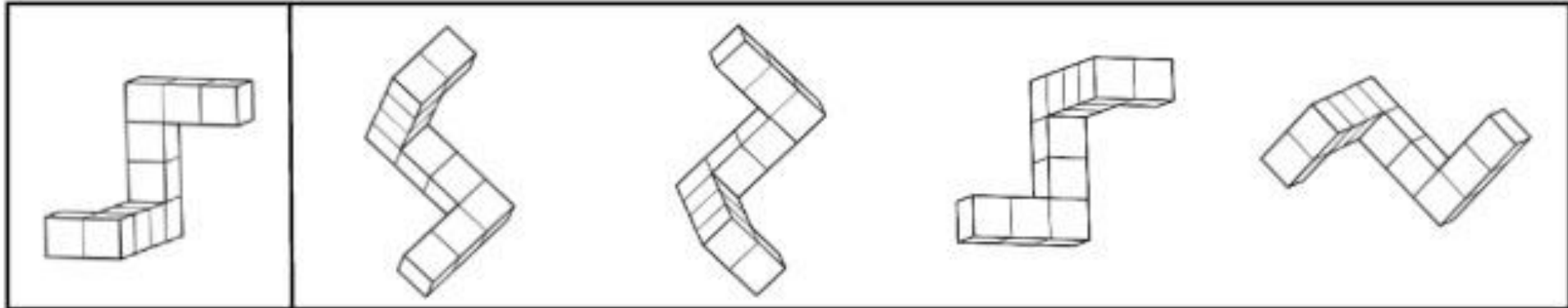
Mood
Post-Traumatic Stress
Substance Use
Aggression

Cognitive Differences

Gender Differences in Cognitive Function in Healthy Controls

Gender Differences in Cognitive Function in Schizophrenia

Mental Rotation



Neuropsychological Profile of Schizophrenia

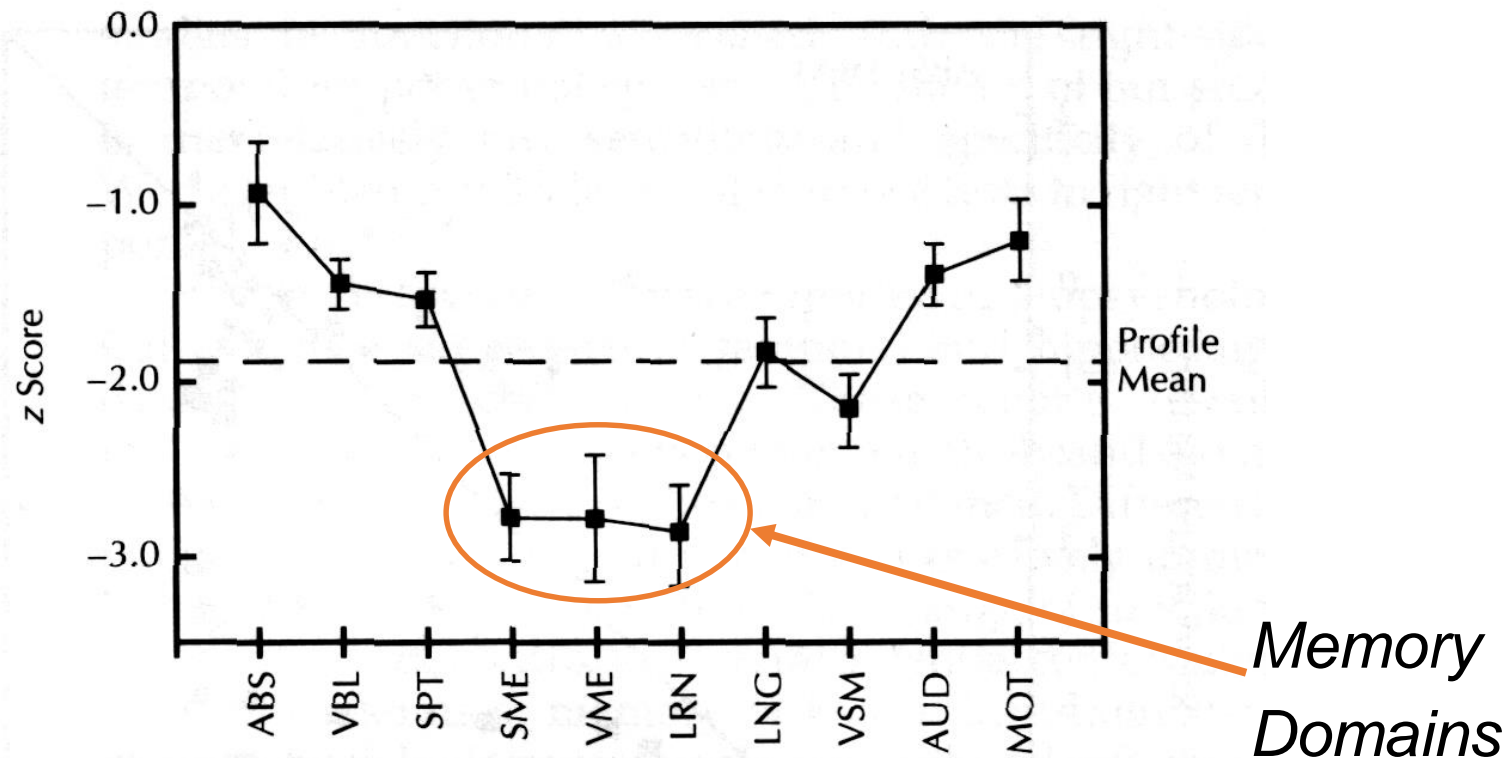


Fig 1.—*Neuropsychological profile (\pm SEM) for patients with schizophrenia ($n = 36$) relative to controls ($n = 36$) whose performance is set to zero (± 1 SD). Functions are abstraction (ABS), verbal cognitive (VBL), spatial organization (SPT), semantic memory (SME), visual memory (VME), verbal learning (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

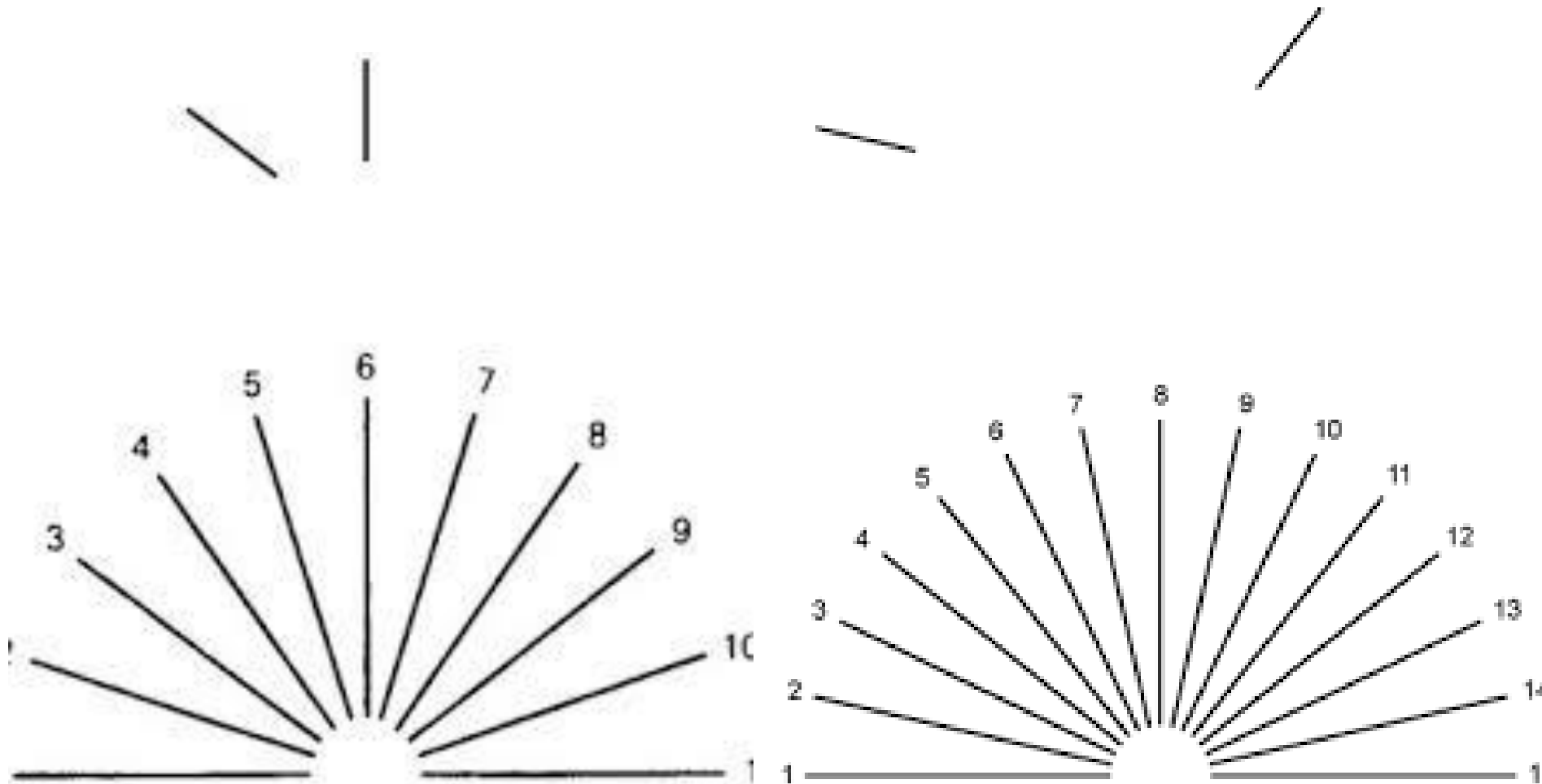
Women > Men (across literature)

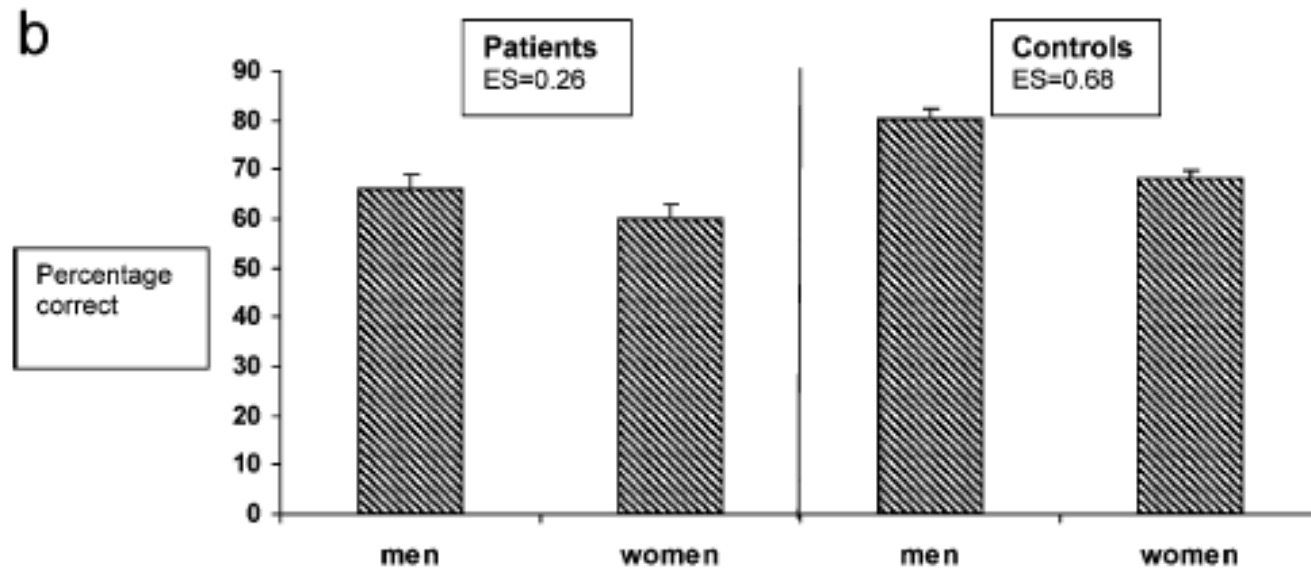
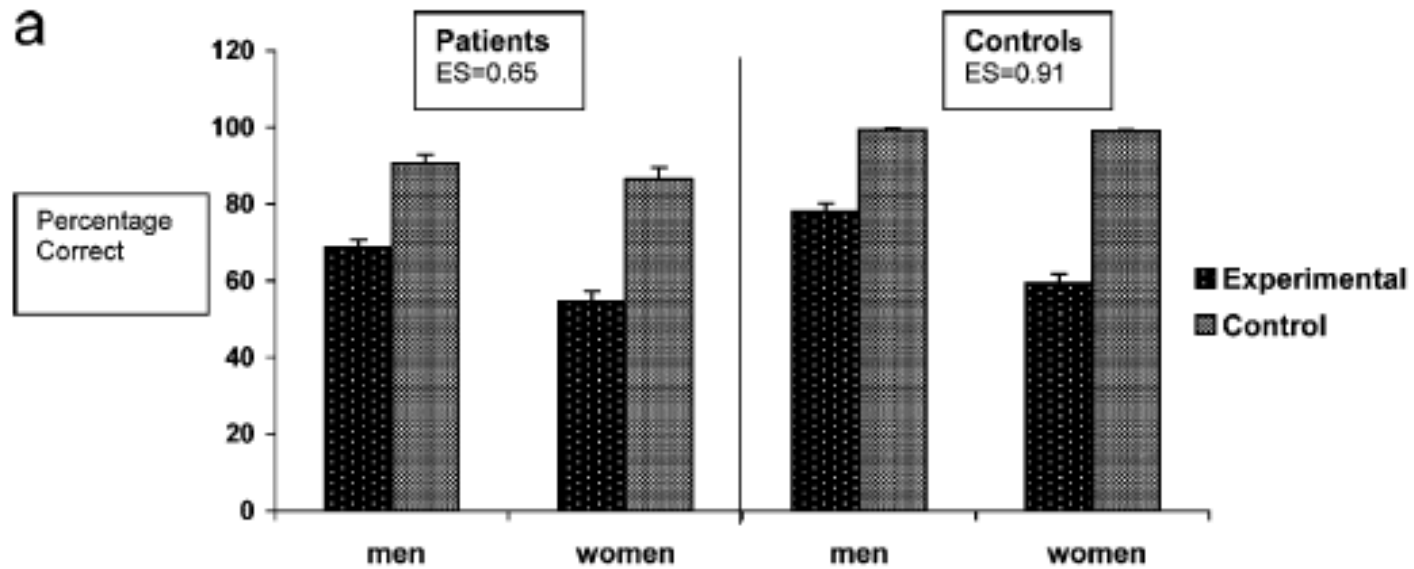
- On measures of attention, language and executive functioning
- On the Digit Symbol subtest
- On all NP measures except attention
- For verbal learning and memory

Cognitive Impairment but Preserved Sexual Dimorphism (Halari et al 2006)

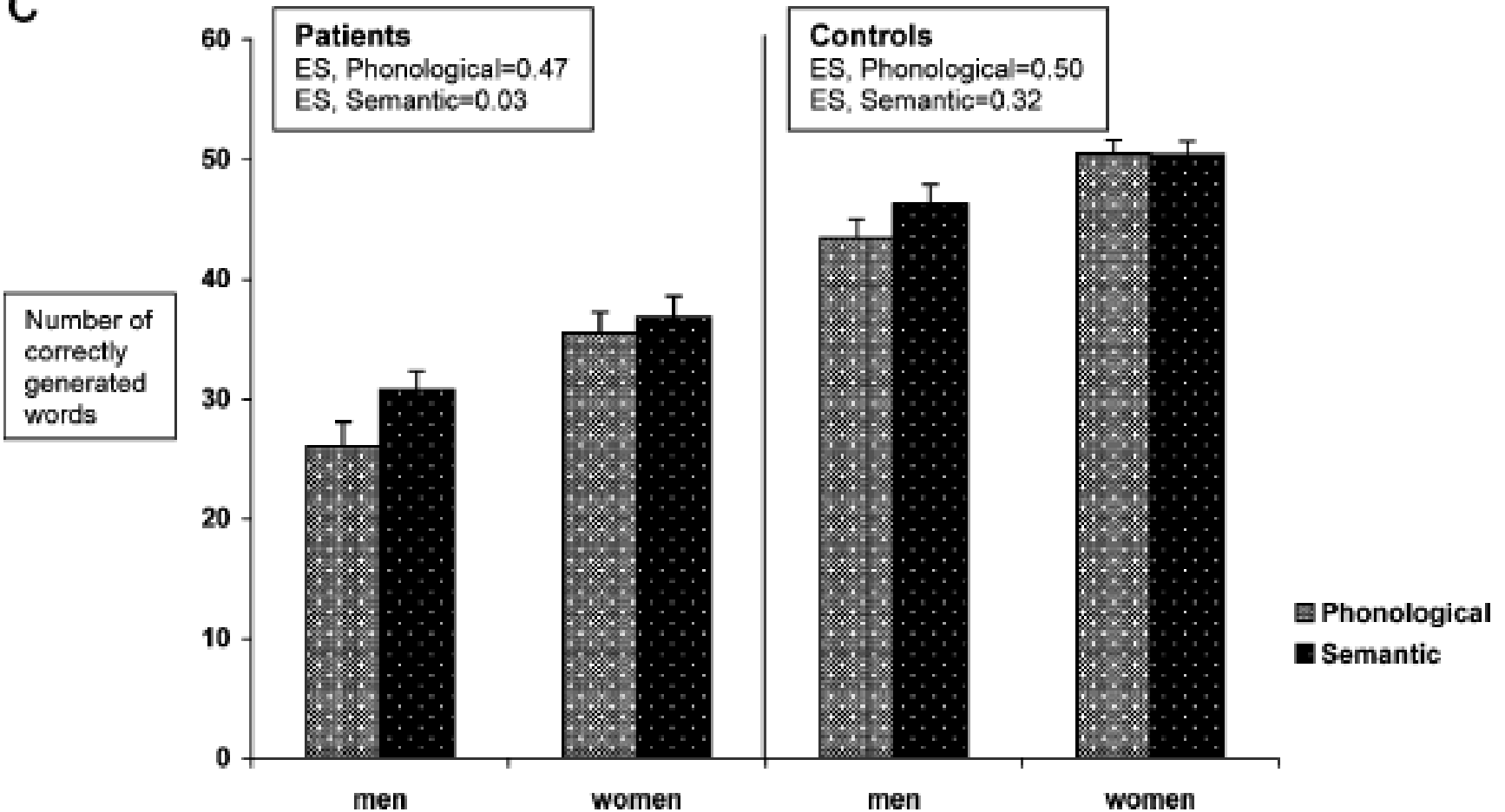
- Hypothesized that (i) men and women with schizophrenia would generally perform worse on all (verbal and spatial) cognitive tasks compared with the control subjects; and
- (ii) sex differences favoring men on the spatial tasks and women on the verbal fluency tasks would be found in both the control and patient groups
- Spatial Tests: Mental Rotation, Judgment of Line Orientation
- Verbal Tests: Phonological and Semantic Fluency

Judgment of Line Orientation





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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**

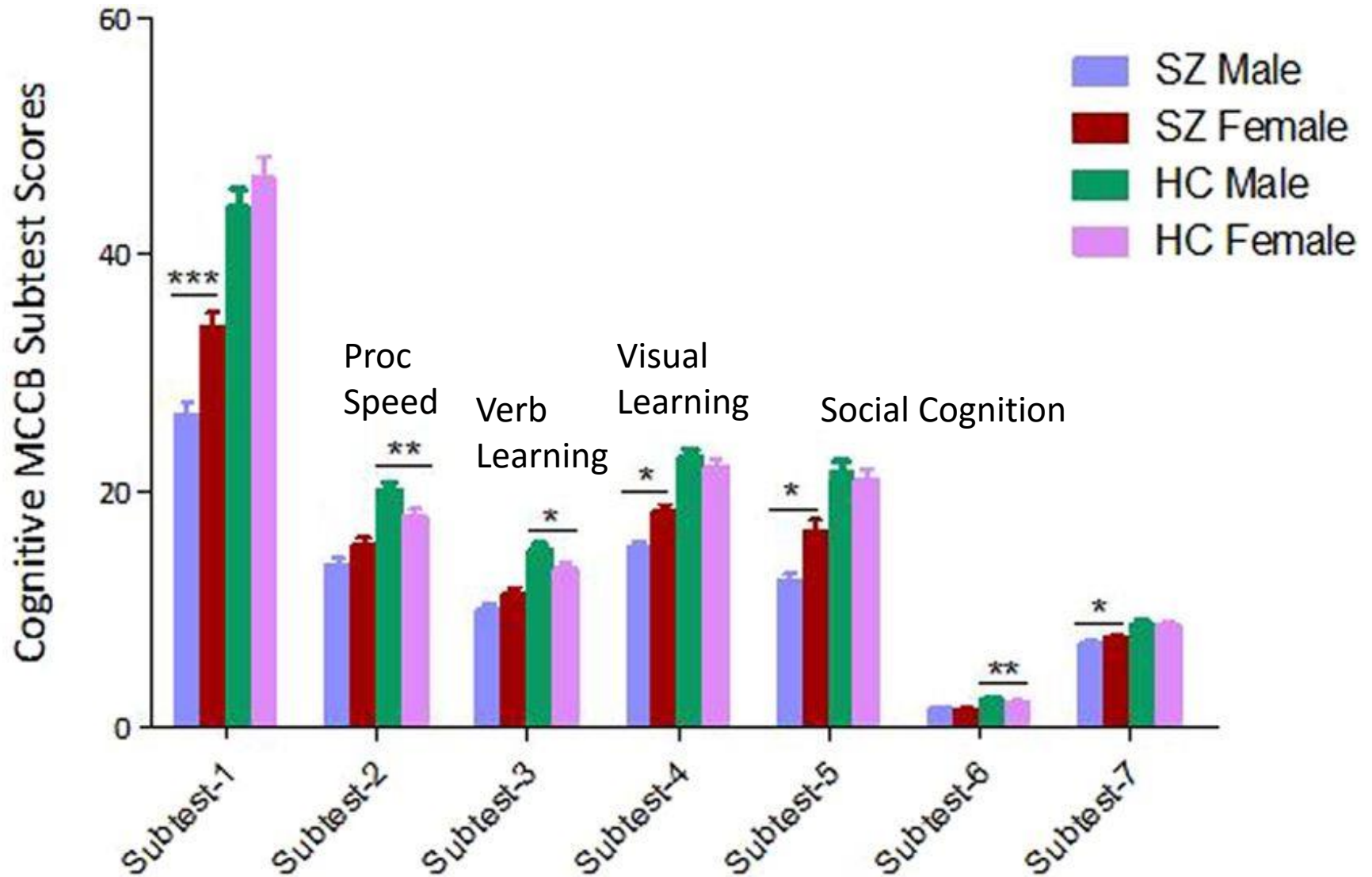
RBANS Scores by Gender

		Schizophrenia		
		Male	Female	F
Total Score	€	86 ± 13	81 ± 10	Group × Gender
Immediate Memory	€	85 ± 15	76 ± 12	2.8 [†]
Visuospatial Ability	€	87 ± 16	85 ± 14	2.1
Language	€	98 ± 12	94 ± 10	1.9
Attention	€	89 ± 16	87 ± 18	1.0
Delayed Memory	€	88 ± 16	85 ± 9	1.6

are two-way ANOVAs;

BD, bipolar disorder; F is reported for the m

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



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

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

Gender Differences in Schizophrenia

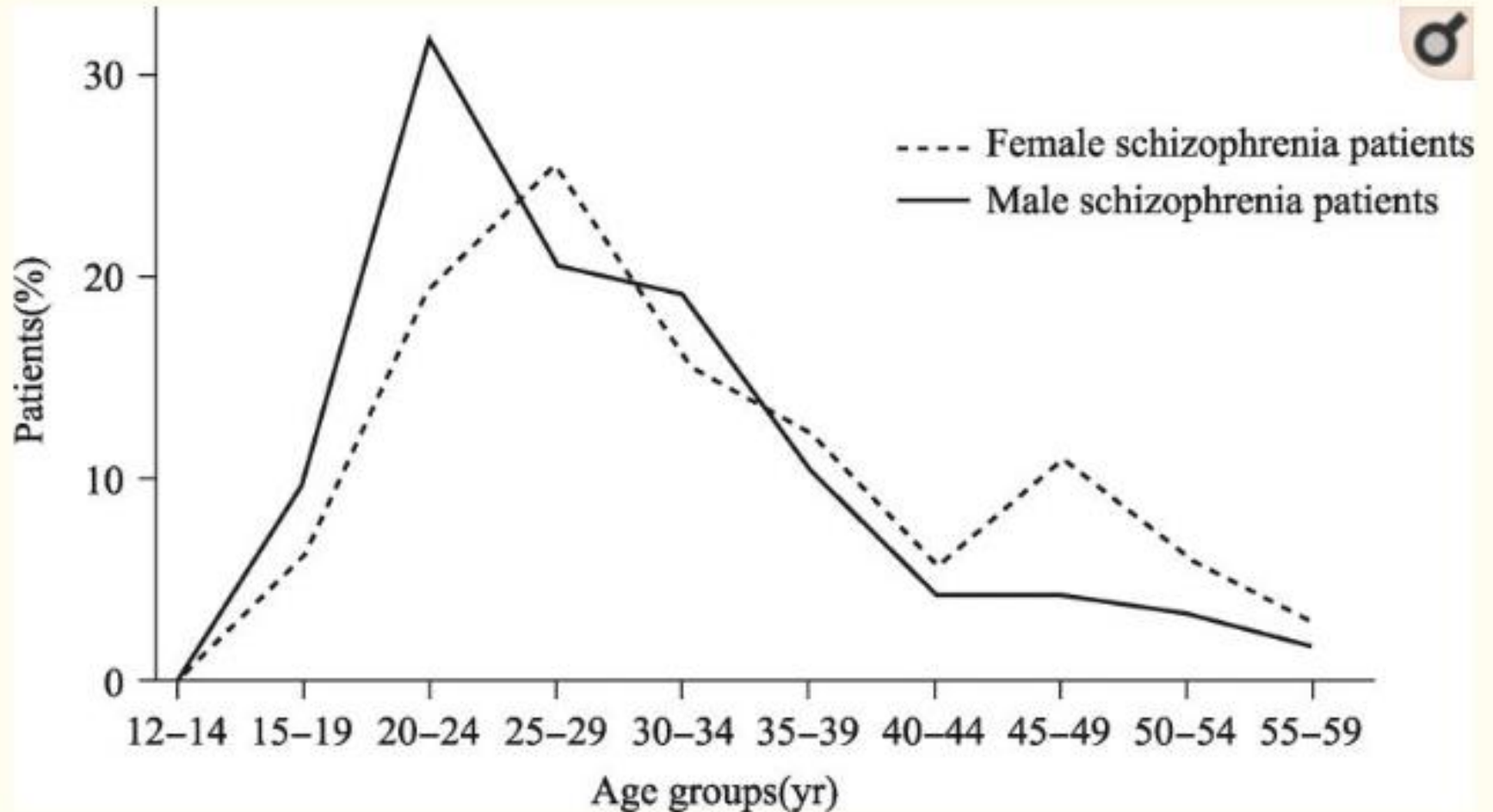
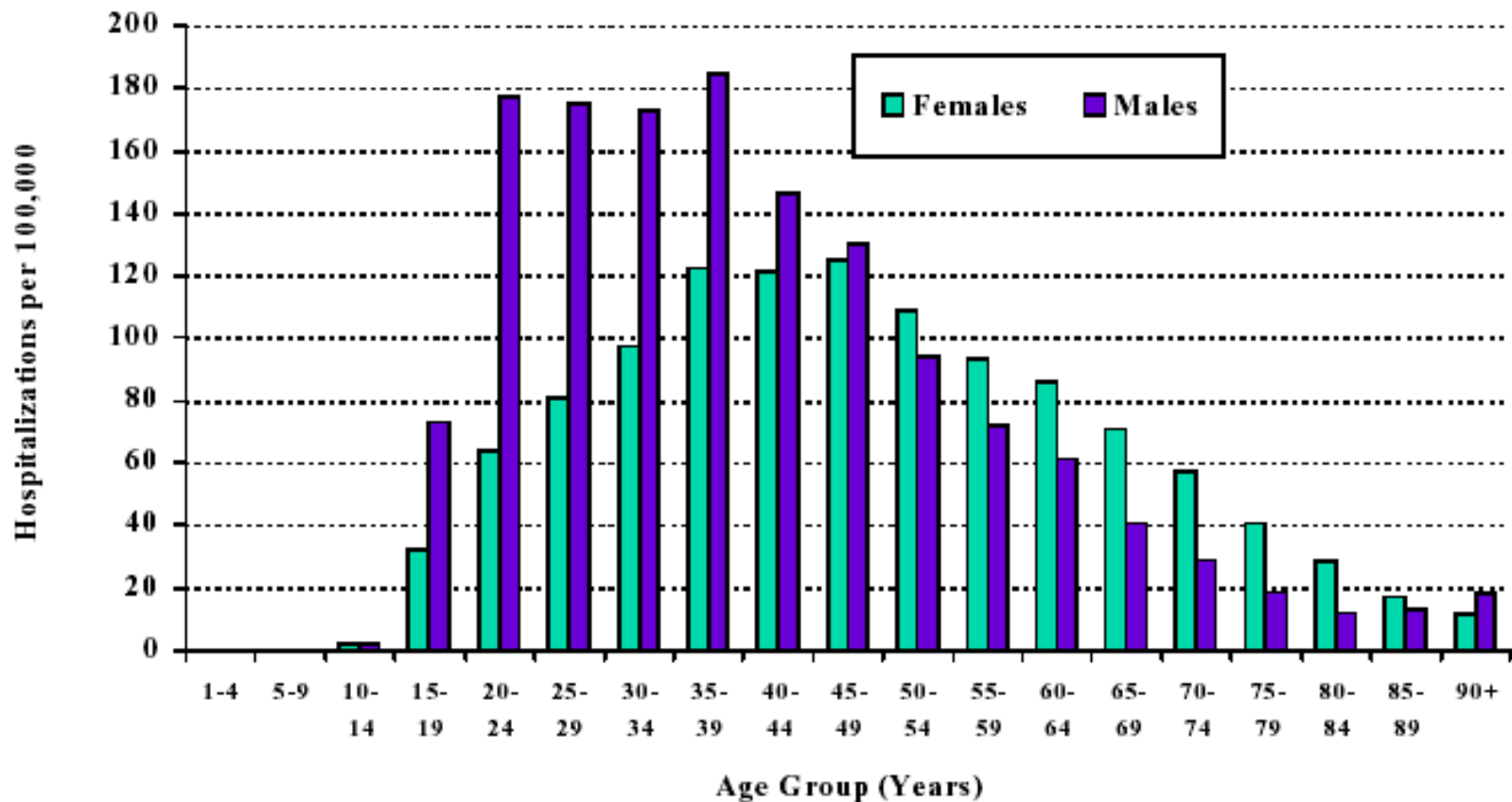


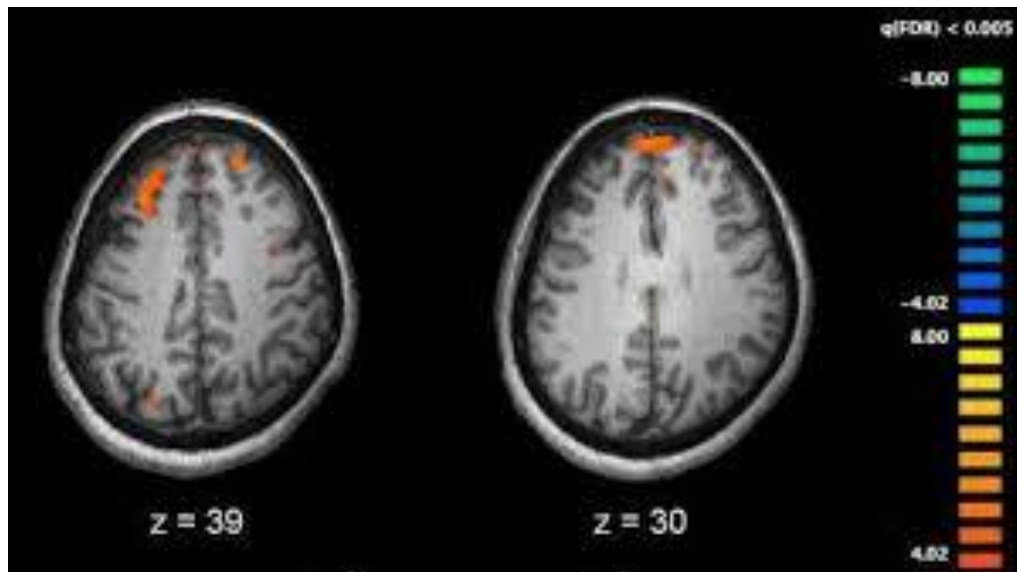
Figure 3-1 Hospitalizations for schizophrenia* in general hospitals per 100,000 by age group, Canada, 1999/2000



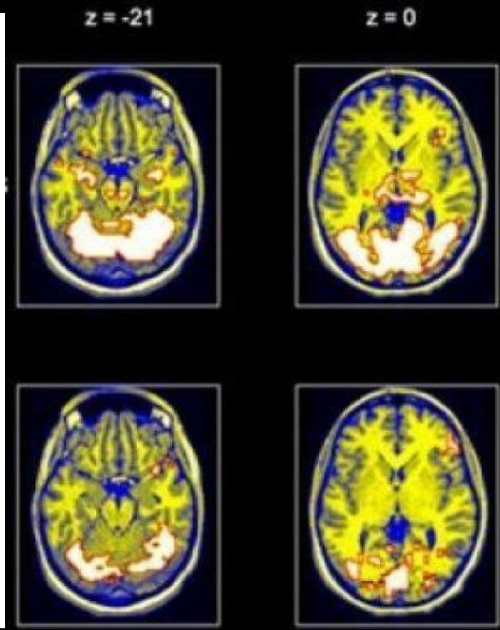
* Using most responsible diagnosis only

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

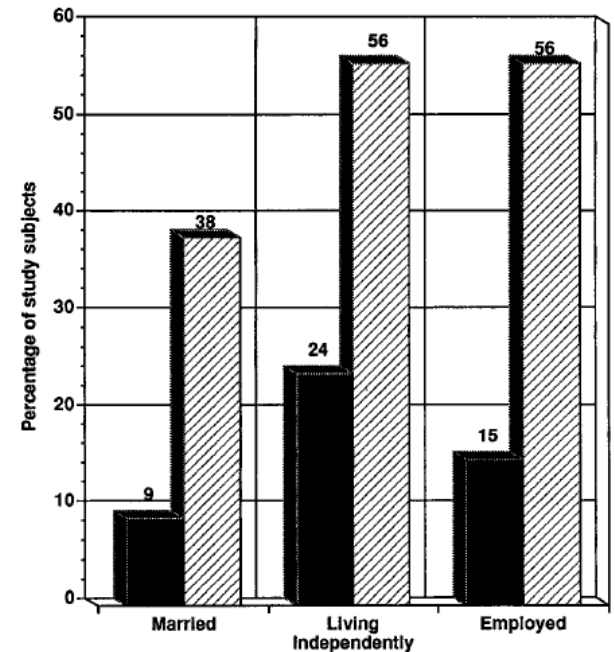


FIG. 2. Gender differences in social functioning (men, ■; women, ▨).

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

Andia AM, Zisook S, Heaton RK et al (1995). Gender differences in schizophrenia. *J Nervous & Mental Disease*, 183(8): 522-528

Aylward E, Walker E, Bettes B (1984). Intelligence in schizophrenia: Meta-analysis of the research. *Schizophr Bull*, 10: 439-459.

Halari R, Mehrotra R, Sharma T et al (2006). Cognitive impairment but preservation of sexual dimorphism in cognitive abilities in chronic schizophrenia. *Psychiatry Res*, 141(2): 129-139.

Han M, Huang X-F, Chen DC et al (2012). Gender differences in cognitive function of patients with chronic schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry*, 39(2): 358-363.

Karilampi U, Helldin L, Archer T (2011). Cognition and global assessment of functioning in male and female outpatients with schizophrenia spectrum disorders. *J Nervous & Mental Disease*, 199(7): 445-448.

References

Perlick D, Mattis S, Stastny P et al (1992) Gender differences in cognition in schizophrenia. *Schiz Research*, 8(1): 69-73

Saykin AJ, Gur RC, Gur RE et al (1991). Neuropsychological function in schizophrenia: Selective impairment in memory and learning. *Arch Gen Psychiatry*, 48(7): 618-624.

Zhang B, Han M, Tan S et al (2017). Gender differences measured by the MATRICS consensus cognitive battery in chronic schizophrenic patients. *Scientific Reports*, 7:11821 (www.nature.com/scientificreports)