



Published in final edited form as:

*Schizophr Res.* 2010 July ; 120(1-3): 234–235. doi:10.1016/j.schres.2009.12.009.

## Cognitive differences between men and women: a comparison of patients with schizophrenia and healthy volunteers

Julia Longenecker<sup>1</sup>, Dwight Dickinson<sup>1,2,\*</sup>, Daniel R. Weinberger<sup>1</sup>, and Brita Elvevåg<sup>1</sup>

<sup>1</sup>Clinical Brain Disorders Branch, National Institute of Mental Health, NIH, Bethesda, Maryland, USA

<sup>2</sup>Department of Psychiatry, University of Maryland School of Medicine, Baltimore, Maryland, USA

### Abstract

Gender modulates cognition such that women display advantages in certain domains while men excel in others tasks. Similar patterns have been seen in patients with schizophrenia. We derived six cognitive factor domain scores from a cognitive battery and examined gender-based cognitive differences in patients with schizophrenia and controls. There were strikingly different effects of gender in patients as compared to controls. The large sample size and broad range of tests in our study add important findings to the neuropsychological literature of schizophrenia, which serve to reinforce some aspects of past research on gender differences in cognition, while questioning others.

### Keywords

Schizophrenia; Gender; Cognition

---

Dear Editor,

Gender modulates cognition with women displaying advantages in verbal memory and processing speed and men in visuospatial tasks (Collaer & Hines, 1995). Patients with schizophrenia have shown similar patterns (Jimenez, Mancini-Marie, & Mendrek, 2009; Rubin, Haas, Keshavan, Sweeney, & Maki, 2008). However, these clinical findings have been based on small samples ( $n < 100$ ) and select tests. Therefore, we examined gender differences in cognitive performance in (i) a large sample of patients and controls; and (ii) using a comprehensive test battery - from the “NIMH Sibling Study” (Egan, et al., 2000).

Our analyses focused on six cognitive domain composite scores. The composites were based on factor analysis of the Sibling Study dataset and are expressed as z-scores calculated using healthy volunteer means and standard deviations (Dickinson, et al., in review). The domains assessed and variables utilized were: 1) verbal memory (WMS-R Logical Memory -immediate and delayed recall, Verbal Paired Associates – immediate recall, and California Verbal Learning Test - total words recalled); 2) working memory on the N-back (1-, 2-, and 3-back; Goldberg, et al., 2003); 3) visual memory (WMS-R Visual Reproduction - immediate and 30 minute delayed recall); 4) processing speed (WAIS-R Digit Symbol, Trails A & B); 5) card sorting/executive functioning (Wisconsin Card Sorting Test - percent perseverative errors,

---

\*Corresponding author: CBDB/NIMH/NIH, MSC 1377, 10 Center Drive 7SE-5350, Bethesda, MD 20892-1377, Telephone: (301) 451-2123; Fax: (301)480-4678, dickinsond@mail.nih.edu.

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

categories obtained, and number correct) and; 6) working memory span (WMS-R Digit Span Forward and Backward, WAIS-III Letter-Number Sequencing). Individuals with scores in all six domains were retained in these analyses, including 374 healthy volunteers (218 females; 156 males) and 240 schizophrenia patients with DSM-IV schizophrenia diagnoses (57 females; 183 males). All participants were between 21 and 55 years old and had a current IQ of 70 or more. Written informed consent was obtained from all participants after complete description of the study.

First, we examined healthy volunteers in order to determine whether women were superior in verbal and processing speed domains and men in visuospatial domains. There was an effect of gender across all factors ( $F(6, 367)=3.65, p<0.005$ ; see Figure 1). Post hoc t-tests revealed the only significant, domain-specific gender difference was that women performed more poorly in the N-back working memory domain ( $t(372)=3.4, p<0.001$ ). This may relate to prominent visuospatial elements in this version of the task.

In a parallel examination of the patient sample, there was also an overall effect of gender ( $F(6, 233)=2.40, p<0.05$ ), but women performed better in most domains. Post hoc tests identified significant advantages in verbal memory ( $t(238)=-2.06, p<0.05$ ) and processing speed ( $t(238)=-2.34, p<0.05$ ). Additionally, visual memory ( $t(238)=-1.94, p=0.053$ ) and card sorting/executive functioning ( $t(238)=-1.91, p=0.057$ ) showed trends toward superior performance by women.

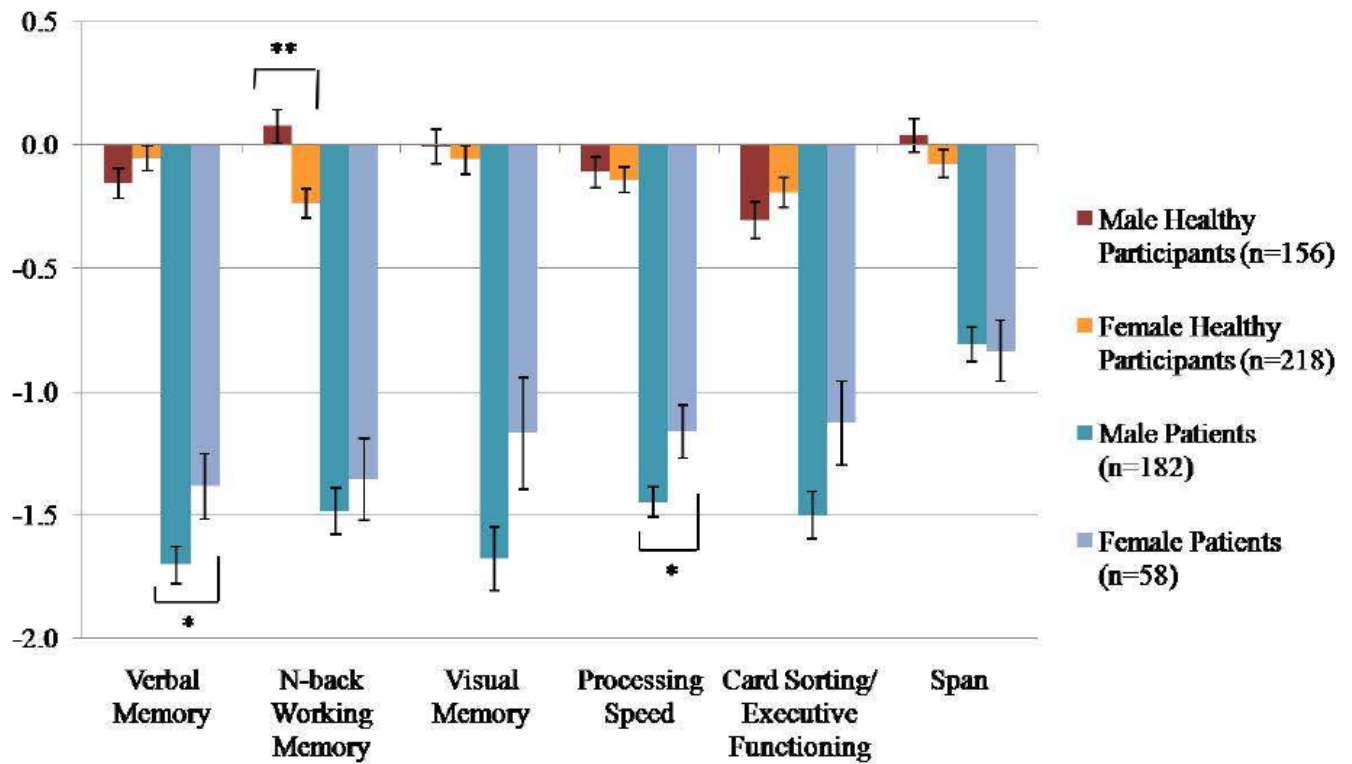
The male advantage in the N-back working memory domain was absent in patients (underlying a significant interaction of gender and diagnosis in this factor ( $F(1, 603)=4.63, p<0.05$ )). The individual N-back conditions employ parametrically varying cognitive abilities -1-back is comparable to a continuous performance task with low working memory requirements, 2-back requires constant updating and puts a greater load on working memory, and 3-back further tests these capacities. To understand the gender-by-diagnosis interaction in this domain in more detail, we performed separate ANOVAs for the two diagnostic groups, with gender as a between groups factor and N-back condition as a within groups factor. While healthy volunteers showed no interaction of gender and N-back condition ( $F(2, 736)=1.22, p=.29$ ), the interaction was significant for patients ( $F(2, 470)=3.25, p<0.05$ ). Contrary to intuition, male patients' impairment relative to controls actually decreased as task demands increased ( $F(2, 358)=26.68, p<0.001$ ), while female patients' performance was stable across the conditions ( $F(2, 112)=1.31, p=0.27$ ).

Our data showed distinct cognitive patterns in healthy volunteers and patients. Healthy males performed better than females on a version of the N-back task that combined spatial and working memory demands. Unexpectedly, healthy females did not outperform healthy males in the verbal and processing speed domains. However, female patients did outperform male patients in these domains. This is consistent with the hypothesis that female patients show less cognitive impairment than males (Goldstein, et al., 1998). Among patients, women were superior to men in four domains, namely verbal memory, processing speed, visual memory, and card sorting/executive functioning. Interestingly, across the three N-back conditions, we found that male patients' performance relative to controls was most impaired on the least demanding condition (i.e., 1-back).

The large sample size and broad range of tests in our study serve to reinforce some aspects of past research on gender differences in cognition, while raising questions about others. Characterizing these cognitive gender differences is a crucial step in understanding how cognition is mediated by neuroanatomical, biological, and genetic traits (Leung & Chue, 2000) and how it may be a contributing factor in treatment efficacy.

## References

- Collaer ML, Hines M. Human behavioral sex differences: A role for gonadal hormones during early development? *Psychological Bulletin* 1995;118(1):55–107. [PubMed: 7644606]
- Dickinson D, Goldberg TE, Gold JM, Egan M, Elvevåg B, Weinberger DR. Cognitive factor structure and invariance in people with schizophrenia, their unaffected siblings, and controls. in review.
- Egan MF, Goldberg TE, Gscheidle T, Weirich M, Bigelow LB, Weinberger DR. Relative risk of attention deficits in siblings of patients with schizophrenia. *Am J Psychiatry* 2000;157(8):1309–1316. [PubMed: 10910796]
- Goldberg TE, Egan MF, Gscheidle T, Coppola R, Weickert T, Kolachana BS, et al. Executive subprocesses in working memory: Relationship to catechol-O-methyltransferase Val158Met genotype and schizophrenia. *Archives of General Psychiatry* 2003;60(9):889–896. [PubMed: 12963670]
- Goldstein JM, Seidman LJ, Goodman JM, Koren D, Lee H, Weintraub S, et al. Are there sex differences in neuropsychological functions among patients with schizophrenia? *American Journal of Psychiatry* 1998;155(10):1358–1364. [PubMed: 9766767]
- Jimenez J, Mancini-Marie A, Mendrek A. The case for not combining men and women in neurocognitive studies for schizophrenia. *Schizophrenia Research* 2009;108(1-3):293–294. [PubMed: 19150221]
- Leung A, Chue P. Sex differences in schizophrenia, a review of the literature. *Acta Psychiatrica Scandinavica Supplementum* 2000;401:3–38. [PubMed: 10887978]
- Rubin LH, Haas GL, Keshavan MS, Sweeney JA, Maki PM. Sex difference in cognitive response to antipsychotic treatment in first episode schizophrenia. *Neuropsychopharmacology* 2008;33(2):290–297. [PubMed: 17392734]



**Figure 1.** Factor z-scores for male and female healthy volunteers and patients with schizophrenia, reported with standard error bars. In healthy volunteers, the effect of gender was significant for the N-back factor. In patients, the effect of gender was significant for the verbal memory and processing speed factors. Z-scores were calculated from healthy volunteers' data, so in any domain '0' is average performance across all healthy volunteers, while a negative value represents less than average performance. Because of the general cognitive impairment associated with schizophrenia, the patients' scores fall in the negative range.

\*p<0.05  
 \*\*p<0.001