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Gender Differences in Executive Control in Schizophrenic Patients

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INTRODUCTION

Cognitive deficits in schizophrenia, especially those related to prefrontal cortex functions (PFC), influence the functional outcome of the disease [1]. There is evidence that schizophrenic males and females show different patterns of cognitive deficits [e.g. 2, 3], although controversial results are found [4]. Sex hormone status, especially estrogen [5] seems to play a role in modulating cognition [6]. Furthermore hyperprolactinemia affects behavior [7] and is a common side-effect of some atypical neuroleptics. The aim of this study was to evaluate different modalities of working memory (WM) and executive control (EC), both functions of the PFC, between genders in schizophrenic patients and normal controls and relate them to hormones and psychopathology. The importance of studying gender differences in PFC cognition in schizophrenia is that it may bring adittional insight in the treatment of gender-specific deficits.

METHODS

Subjects:
40 schizophrenic inpatients (20 female and 20 males), partially remitted and taking atypical neuroleptics in monotherapy, as well as 20 male and 20 female healthy controls matched (within sexes) for age and education were included.

Experimental Battery
We used a battery of computerized tests assessing auditory (to reproduce a sequence of high and low tones), visual, and spatial WM and a dual task for assessing EC developed by the Department of Child and Adolescent Psychiatry of the University of Heidelberg. For a schematic representation of the tests see Figure 1. In order to control for general concentration and attention a paper pencil test (D2 letter cancellation test [8]) was applied.

Modulatory Variables
Hormones (estrogen and prolactin), extrapyramidal symptoms (EPS Scale), and current psychopathological status (BPRS, SANS, SAPS) were evaluated.

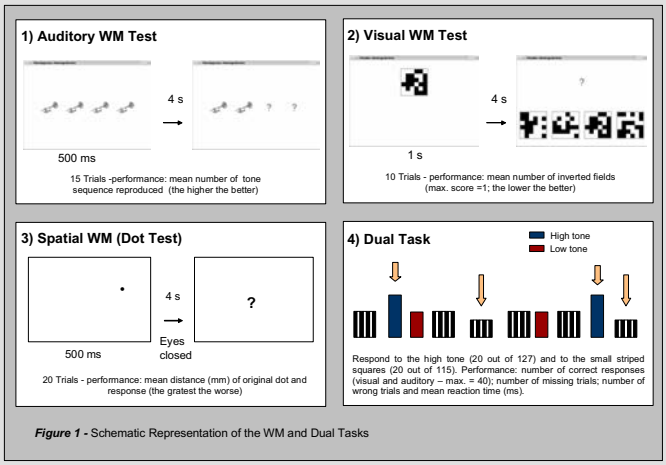

Figure 1 - Schematic Representation of the WM and Dual Tasks

RESULTS

1) Demographic Data: Patients and controls were well matched for age between and within sexes. Patients had a significant lower IQ [9] scores than controls (F(1,68)=18,71; p< .001), but no gender interaction was found (See Table 1).

	Male Patients		Female Patients		Male Controls		Female Controls	
	N=20	SD	N=20	SD	N=20	SD	N=20	SD
Age (years)	**32,30**	7,11	**34,20**	7,16	**32,90**	7,83	**33,90**	9,55
Education (school years)	**11,50**	1,73	**11,25**	1,74	**11,5**	1,64	**11,35**	1,63
Verbal IQ	**110,53**	13,32	**105,06**	12,08	**121,28**	11,67	**120,56**	14,16
Auditory WM	**6,17**	1,74	**6,13**	2,77	**6,95**	1,75	**7,09**	1,43
Spatial WM	**12,08**	2,42	**12,83**	4,56	**10,45**	2,50	**9,68**	1,94
Visual WM	**6,68**	3,45	**6,79**	4,18	**4,23**	3,22	**4,72**	3,38
Single-Auditory (%)	**95,26**	7,54	**86,94**	20,87	**98,75**	3,58	**98,50**	4,62
Single-Visual (%)	**97,89**	5,09	**90,56** *	11,74	**99,25**	2,45	**98,75**	2,22
Single-Auditory (ms)	**373,42**	33,30	**394,17**	70,44	**339,15**	31,09	**354,10**	47,97
Single-Visual (ms)	**414,89**	46,15	**455,94**	57,89	**402,40**	42,22	**415,50**	31,81
Dual (%)	**88,40**	10,55	**78,93** *	15,95	**96,19**	3,49	**96,54**	3,45
Dual (ms)	**432,26**	50,23	**464,39**	71,74	**413,00**	38,36	**430,50**	24,91
D2-Score (KL)	**135,47**	52,37	**117,83**	39,65	**193,20**	62,35	**181,30**	36,69

* gender vs. group interaction, p<.05

Table 1 - Mean demographic variables and neuropsychological performance and standard deviations (SD) of male and females divided into healthy controls and patients with schizophrenia

2) Neuropsychological Data (see Table 1 and Figure 2): We performed separate multifactorial ANOVAs with group (patients vs. controls) and gender as independent factors and performance for each test as dependent variable. In general, patients performed worse than controls in every neuropsychological test. For controls no differences between genders were found in any of the tests. Differences between genders were not found for any of the WM tasks for patients. However, in the dual task, female patients showed less correct detection of trials than male patients and controls (F(1,73)=4.99; p=.03).Furthermore, analysing the performance of the single visual and auditory subtests of the dual task showed that female patients presented difficulties in discriminating the visual stimuli (F(1,73)=5.44; p=.02). Inclusion of IQ as co-variable did not alter the results.

3) Disease characteristics (see Table 2): no differences in duration of disease and number of episodes was found between sexes, however there was a trend for a later onset of female patients (p=.08). Regarding psychopathology no significant differences were found. Neither there was a difference in extrapyramidal symptoms nor of medication dosage (CPZ equivalents).

	Male Patients		Female Patients	
	N=20	SD	N=20	SD
EPS	**0,20**	0,19	**0,32**	0,28
BPRS	**39,21**	10,23	**35,53**	10,33
SANS	**40,16**	17,32	**29,37**	24,86
SAPS	**17,26**	15,15	**13,68**	16,73
Duration of Disease (y)	**6,83**	6,12	**5,11**	6,44
Number of Hospitaliuzations	**2,75**	1,97	**2,50**	2,40
Age of Onset (years)	**25,35**	5,86	**29,10** *	7,58
CPZ-Equivalent (mg)	**561,50**	504,33	**460,84**	308,56

* Trend p=.08

Table 2 - Mean psychopathological, extrapyramidal symptoms score, Chlorpromazine Dose Equivalence (CPZ-equivalence) for atypical neuroleptics and standard deviations (SD) of patients according to gender

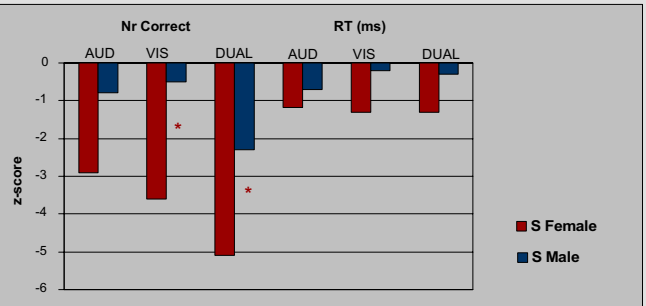

Figure 2 - Z-scores of number of correct trials and reaction time (ms) according to performance of controls (merged for gender) in the single auditory (AUD) and visual (VIS) subtests and in the dual task between male and female patients.

4) Analyses of Hormones: No significant correlation of estrogen on neuropsychological function was found for either female controls or patients. For female patients, a significant association between prolactin levels and performance in the dual task was found (R=.056, p<.05).

DISCUSSION

The present study shows absence of gender differences in different WM modalities and EC function in healthy subjects. For patients, no gender differences were found in WM tests. However EC-Function seems to be more affected in female than in male patients and controls. Moreover, female patients showed worse performance in the simple visual task of the dual task, pointing to an underlying visual selective attention deficit, which may have contributed to the dual task impairment. Visual attention deficits have been shown to be worse in female patients [10]. Sampling biases, like recruiting female patients with early onset, which are described to have a worse prognosis, was not the case in this study [11]. Similarly, there was no difference in psychopathology between sexes, which would be likely to affect cognition. Concerning hormones, there was an association between high prolactin levels and worse performance in the dual task in female patients. No association with estrogen was found for females in either group, contradicting the results in the literature e.g [12, 13].

CONCLUSION

These results point to the presence of gender differences in EC in non-acute schizophrenic patients taking atypical neuroleptics. The worse performance of females is associated with an underlying selective attention deficit in the visual modality. A beneficial influence of estrogen on cognition was not systematically found. However hyperprolactinemia seems to be associated with worse performance in EC in female patients.

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Acknowledgements
This work was supported with a "Investigator Initiated Trial Grant" from the Lilly Centre for Women's Health