Sex specific differences in the middle cerebral artery blood flow in the first episode of psychosis during neurocognitive testing

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INTRODUCTION:

While men and women affected by schizophrenia share several common features, including the clinical presentation of prodroms, and psychotic symptoms once first episode of psychosis (FEP) develops, as well as the longitudinal course of illness over a longer term period, there are significant differences between women and men with schizophrenia. While FEP usually occurs later in life in women than in men , woman are also more prone to experience affective- depressive symptoms and have higher prevalence of chronic somatic comorbidities but achieve functional recovery more often than men. Men significantly more often exhibit aggressive and antisocial behavior and are more likely to have cognitive deficits and more severe negative symptoms . The processes underlying these sex-related differences in patients with schizophrenia are largely unknown. Studies reported gender based differences at the neuroanatomical and neurofunctional level, as well as at the level of hormonal response. We recently reported significant differences in cerebral blood flow velocity (BFV) in the main intracranial arteries (using the Transcranial Doppler Ultrasonography (TCD)) between resting state and the activated state while performing neurocognitive tasks in FEP compared to healthy controls. As we found significantly more pronounced changes of BFV in the middle cerebral arteries (MCAs) between the resting state and the activated state in controls compared to FEP, we assumed a different intracranial hemodynamics in patients suffering from FEP compared to the healthy population. Considering the reports that showed sex- specific pattern of BFV changes between resting and activated state, while performing neurocognitive tasks, in healthy population, we sought to analyze sex-specific differences in patients with FEP as well.

METHODS:

We enrolled 46 patients with the FEP admitted at the Department of psychiatry, Zagreb University Hospital Centre, Croatia, during 2016-2017 and 41 healthy controls. The primary outcome was BFV in the middle cerebral arteries (MCAs) measured by Transcranial Doppler Ultrasonograhly (TCD) in resting state and during the neurocognitive testing.

RESULTS:

During neurocognitive testing, BFV in both MCAs increases in healthy control and decreases in FEP patients (p<0.001). We observed the significantly different patterns of BFV change between female and male patients with FEP and healthy controls, in both MCAs. In healthy control group increase of BFV during testing was higher in women than in men while in FEP both genders experienced the similar decrease of BFV.

Table 1. Differences between first episode psychosis patients and healthy men and women in change of the middle cerebral artery blood flow velocity at rest and during the neurocognitive testing

	Cerebral blood flow velocity		Δ	$\Delta\%$	p	η^2
	Baseline, at rest and breath holding	During neurocognitive testing				
Right MCA, cm/s						
Healthy control						
men (n=14)	37 (19.8) [34; 22-46]]	44 (11.9) [46; 36-56]	7 [12]	19% [35%]	0.026	0.06
women (n=28)	33(29.0) [29; 19-39]	54 (18.7) [57; 49-65]	21 [28]	64% [97%]		
First episode psychosis						
men (n=24)	43 (19.6) [43; 33-53]	43 (20.5) [38; 30-46]	0 [-5]	0 [-12%]		
women (n=21)	49 (19.5) [56; 46-67]	46 (21.0) [48; 39-57]	-3 [-8]	-6% [-14%]		
Left MCA, cm/s						
Healthy control						
men (n=14)	38 (21.7) [34; 22-46]	44 (15.2) [43; 34-53]	6 [9]	16% [26%]	0.020	0.07
women (n=28)	36 (28.9) [31; 21-40]	57 (16.1) [56; 49-64]	21 [25]	58% [81%]		
First episode psychosis						
men (n=24)	45 (19.4) [46; 36-56]	46 (19.0) [44; 36-52]	1 [-2]	-2% [-4%]		
women (n=21)	54 (16.3) [61; 50-72]	52 (17.3) [55; 47-63]	-2 [-6]	-4% [-10%]		

Data are presented as raw mean (standard deviation) and[mean adjusted for age and education; with adjusted 95% confidence intervals]

ABBREVIATIONS: Δ = absolute difference between BFV during neurocognitive testing and baseline at rest; Δ% = relative difference calculated as ((BFV during testing - baseline BFV) / baseline BFV); p = statistical significance of the study group and sex interaction effect on the change of BVF, calculated with mixed within-between subjects analysis of covariance; η² = partial Eta squared given as measure of the standardized effect size of the tested interaction

CONCLUSIONS:

MCA blood flow during the execution of several neurocognitive tests follows a sex specific fashion in patients with the first episode of psychosis compared to controls, possibly reflecting sex-based differences underlying psychotic processes.

Figure 1. Middle cerebral artery (MCA) blood flow velocity at rest and during the testing in healthy control and in first episode psychosis group; error bars represent 95% confidence intervals