

SERUM TESTOSTERONE, EMOTION AND COGNITIVE FUNCTIONING DEFICITS IN PATIENTS WITH ANOREXIA NERVOSA: A TASK SWITCHING STUDY

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ABSTRACT

Objective: To examine relationship between testosterone, emotional intelligence (EI), affective control and cognitive functioning in patients with anorexia nervosa (AN).

Methodology: Fifty women diagnosed with restrictive subtype of AN from Bahawal Victoria Hospital Bahawalpur, Civil Hospital Bahawalpur and Nishtar Hospital Multan from April 2016 to February 2017 and fifty healthy demographically matched women took part in the study. Serum testosterone levels were obtained from medical reports not older than two weeks of the day when testing session was conducted. Participants completed measures of EI, affective control and task switching.

Results: Anorexics women showed reduced testosterone level (mean 22.44 ± 0.73 ng/dl) as compared to healthy individuals (mean 31.80 ± 2.02 ng/dl). Women with AN demonstrated under developed emotional capacity (mean 84.28 ± 2.74 vs. 123.30 ± 4.79), affective control deficits (mean 4.92 ± 1.04 vs. 2.64 ± 0.69) and impaired task switching (mean 110.76 ± 5.77 vs. 47.66 ± 4.62 seconds) in contrast to healthy individuals. Serum testosterone, EI and duration of amenorrhea were found as significant predictors of task switching performance in patients with AN ($p < 0.001$, $R^2 = .78$).

Conclusion: Serum testosterone, duration of amenorrhea and emotional intelligence can serve as a marker of impaired cognitive functioning in patients with anorexia nervosa.

Key Words: Testosterone, Emotional intelligence, Anorexia nervosa, Cognition

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INTRODUCTION

Anorexia Nervosa (AN) is a serious life threatening medical and mental condition characterized by restricted energy intake, intense fear of gaining weight and disturbance in self-perceived weight and body shape. AN is associated with various endocrine disturbances, particularly reduced serum testosterone levels¹. Other examples include deregulation of leptin, cortisol, glucose, thyroid and reproductive function². Lower testosterone levels are associated with cognitive decline³. Mechanism involves either testosterone being metabolized to dihydrotestosterone and binds to androgen receptor or converted to estradiol through aromatase enzyme⁴. Testosterone has neuroprotective effects by: (i) increasing concentration of nerve growth factor in hippocampus and forebrain (ii) inhibiting production of β -amyloid peptide and Tau phosphorylation known to accelerate cognitive impairment^{5,6}. AN is also associated with cognitive and emotion functioning deficits^{7,8}.

These cognitive dysfunctions correlate with abnormal activity in ventrolateral prefrontal cortex⁹, temporal-orbito-frontal lobes, fronto-striatothalamic circuits, amygdala and insula¹⁰.

Recently, emotional intelligence (EI) has gained attention of researchers due to its association with health problems¹¹. EI is defined as social competencies, abilities and skills to deal effectively with challenges and demands of daily life. Impaired EI refers to cognitive-affective disturbance of emotion management¹². Patients with AN show lower EI and emotion processing deficits^{13,14}. Cognitive and affective control are intertwined because these mental processes share neural projections from anterior cingulate cortex in order to integrate these separate domains for optimal behavioral response¹⁵. There is a gap in the literature to understand whether emotion and cognitive functioning are intertwined in AN. In the current study, emotion processing was examined as EI and affective control whereas cog-

nitive functioning was assessed as task switching ability. In more recent years, affective control has captured attention of researchers¹⁶. It is defined as the ability to regulate emotions and mood fluctuations. Impaired affective control characterizes many neuropsychological disorders¹⁷.

Task switching is a higher order cognitive function which requires flexibility and cognitive control for set-shifting when the task changes. Efficient performance involves manipulation of cognitive resources specifically attention and memory. Neural basis of task switching involves prefrontal cortex mainly because decision to several dimensions of stimuli are required¹⁸.

Neuroimaging studies have demonstrated that distinct neural networks are activated during cognitive (prefrontal cortex, anterior cingulate cortex) and affective control (medial prefrontal cortex, amygdala). Balanced interaction between cognitive and affective control is necessary for self-regulation and decision making¹⁹. In contrast, disturbed interaction between cognition and emotion processing has been observed in several neuropsychological disorders²⁰⁻²². Somatic marker hypothesis suggests that impaired emotion signaling leads to cognitive deficits such as patients with lesions of the ventromedial prefrontal cortex, amygdala and insular cortices demonstrate low EI and decision making deficits²². Neural circuits subserving emotional states and higher order cognitions overlap^{23,24}. Therefore, changes in human behavior, actions, and attitudes result from dysfunctions of this cortical network²⁵. Biopsychosocial approach suggest that mental processes are inseparably connected and psychological disorders are characterized by dynamic neural systems composed of interconnected brain structures. Emotional processes interact with cognitive functions and influence top down control and self-regulation. This integration is disrupted and apparent in psychiatric and neurodegenerative disorders disconnecting major feedback pathways to neuraxis²⁶.

The current study was designed with following objectives: (i) to compare serum testosterone levels between anorexics and healthy individuals (ii) to compare anorexic patients with healthy controls on measures of EI, affective control and task switching (ii) to examine relationship between serum testosterone levels, EI, affective control and task switching in AN.

Given that neurocognitive changes were associated with AN and serum testosterone levels, it was hypothesized that patients with AN would show reduced serum testosterone levels and deficits in task switching, affective control and EI in contrast with healthy controls. Further, serum testosterone levels, EI and affective control would be significant predictors of task switching performance.

METHODOLOGY

The study was approved by board of studies of The Islamia University of Bahawalpur and was conducted following the principles outlined in Helsinki Declaration. Fifty women diagnosed with restrictive subtype of AN according to Diagnostic and Statistical Manual for Mental Disorders (version 5)²⁷ at Bahawal Victoria Hospital, Civil Hospital Bahawalpur and Nishtar Hospital Multan participated in the study from April 2016 to February 2017. Inclusion criterion for patients were (i) age range between 15 to 25 years (ii) female gender (iii) diagnosed with restrictive subtype of AN (vi) body mass index below 17.5 kg/m² (v) medical report having testosterone examined. Exclusion criterion for patients were as follows: (i) present or previous symptomology of substance use, psychiatric/neurological condition except AN as screened through Mini International Neuropsychiatric Interview²⁸ (ii) using oral contraceptives (iii) receiving hormone therapy (e.g., androgen or DHEA). Fifty healthy women were contacted from local community with the inclusion criterion same as followed for patients except body mass index between normal range (18.50 -24.99 kg/m²) according to World Health Organization guidelines. Exclusion criterion were same as for patients. Serum testosterone levels (assessed in early follicular phase i.e., 1-7 day of menstrual cycle) were obtained from their medical record not older than two weeks of the date of the testing session.

BarOn Emotional Quotient Inventory (BarOn EQ-i) was used as a measure of EI²⁹. It is a 133 statement scale assessing EI on a five-point response set: 1= not true of me to 5= true of me. Total EI score is interpreted as: atypically well-developed emotional capacity= 130 & above; extremely well-developed emotional capacity= 120-129; well-developed emotional capacity= 110-119; adequate emotional capacity= 90-109; underdeveloped emotional capacity= 80-89; extremely underdeveloped emotional capacity= 70-79 and atypically underdeveloped emotional capacity= below 70. The alpha reliability of BarOn EQ-i is between 0.60-0.70. Affective Control Scale (ACS) was administered to assess affective control³⁰. ACS consists of 42 items assessing control on anger, depressed mood, anxiety and positive affect. Two-week test-retest reliability is 0.78. High score reflects deficient affective control. Trail Making Test-part B (TMT-B) was used to assess task switching ability³¹. The test requires the subject to alternate between series of numbers and letters, for instance 1,A, 2,B, 3,C, 4,D..... The performance is interpreted as deficient if the time taken to perform the test exceeds 91 seconds. Larger switch costs (i.e., time taken to perform TMT-B) shows task switching impairment. Participants gave written informed consent. Following they were administered BarOn EQ-i, affective control scale and TMT-part B in a single testing session.

Data was analyzed through SPSS (version 20). Demographic and clinical characteristics were assessed using descriptive statistics. Group differences on serum testosterone, BarOn EQ-i, ACS, and TMT-part B were examined through multivariate analysis of variance (MANOVA) with Group as a fixed factor. Bivariate correlations were computed to assess relationship between serum testosterone levels, EI, affective control and task switching ability in patients with AN.

Regression analysis was conducted to find out predictor of task switching performance in anorexic patients with demographic/clinical characteristics, affective control, EI as independent variables and task switching as dependent variable.

RESULTS

Results of MANOVA showed significant differences between patient and control group on serum testosterone $F(1, 98) = 948.40, p < 0.001, \eta^2 = .90$; EQ-i $F(1,$

$98) = 2515.45, p < 0.001, \eta^2 = .96$; ACS $F(1, 98) = 164.97, p < 0.001, \eta^2 = .62$; and TMT $F(1, 98) = 3639.44, p < 0.001, \eta^2 = .97$. Patients showed under developed emotional capacity, deficient affective control and task switching deficits in contrast with controls (Table 2).

Bivariate correlations analysis showed significant association of total testosterone with scores on BarOn EQ-i ($r = .77, p < 0.001$), Affective control scale ($r = -.51, p < 0.001$) and TMT-B ($r = -.87, p < 0.001$), as shown in Table 3.

Regression analysis showed testosterone as significant predictor of task switching performance $F(7, 49) = 22.19, p < 0.001, R^2 = .78$; testosterone $\beta = -.75, t = -6.41, p < 0.001$; BarOn EQ-i $\beta = -.25, t = -1.93, p = .059$; duration of amenorrhea $\beta = -.09, t = -1.26, p = .21$; age at disease onset $\beta = -.01, t = -1.44, p = .88$; duration of illness $\beta = .03, t = .41, p = .68$; BMI $\beta = -.01, t = -.16, p = .87$; and ACS $\beta = -.11, t = -1.25, p = .21$ failed to reach the level of significance with AN.

Table 1: Characteristics of patients with anorexia and control group

Characteristics	AN Group, n=50 M (SD)	Control group, n=50, M (SD)	t (df), p
Age (range 15-25 years)	19.03 (2.74)	20.22 (2.74)	t (49)=1.96, p=.05
Education (range 9-14 years)	11.55 (1.74)	11.36 (1.80)	t (59)=0.64, p=.519
Height (cm)	161.36 (2.36)	161.00 (2.17)	t (49)=.99, p=.32
Weight (kg)	39.78 (1.94)	52.18 (1.36)	t (49)=43.18, p<0.001
BMI (kg/m ²)	14.90 (0.78)	20.88 (0.79)	t (49)=36.16, p<0.001

Table 2: Multivariate analysis of variance for group differences between patients with anorexia nervosa and healthy controls on total testosterone, BarOn EQ-i, ACS and TMT-B

Variables	Patients (n=50)			Controls (n=50)		
	M (SD)	95% CI LB	95% CI UB	M (SD)	95% CI LB	95% CI UB
EQ-i	84.28 (2.74)	83.27	85.28	123.30 (4.79)	122.26	124.27
ACS	4.92 (1.04)	4.52	5.01	2.64 (0.69)	2.47	2.96
TMT-B	110.76 (5.77)	109.07	118.82	47.66 (4.62)	46.47	49.22
Testosterone (ng/dl)	22.44 (0.73)	22.05	22.81	31.80 (2.02)	31.45	32.21

EQ-i= Emotional quotient- inventory; ACS= Affective control scale; TMT-B= Trail Making Test-B.

Table 3: Bivariate correlations between total testosterone and scores of patients with anorexia nervosa (n=50) on BarOn EQ-i, ACS, TMT-B

Variables	BarOn EQ-i	ACS	TMT	Testosterone
BarOn EQ-i	1	r = -.63*, p<.001	r = -.74*, p<.001	r = .77*, p<.001
ACS	r = -.63*, p<.001	1	r = .42*, p<.01	r = -.51*, p<.001
TMT	r = -.74*, p<.001	r = .42*, p<.01	1	r = -.87*, p<.001
Testosterone	r = .77*, p<.001	r = -.51*, p<.001	r = -.87*, p<.001	1

EQ-i= Emotional quotient- inventory; ACS= Affective control scale; TMT-B= Trail Making Test-B.

DISCUSSION

There were several important results: (i) patients with AN showed reduced serum testosterone levels as compared with healthy controls (ii) patients with AN showed under developed EI, deficient affective control and impaired task switching abilities in contrast with controls (ii) serum testosterone, duration of amenorrhea and EI were found as significant predictors of task switching ability in patients with AN. Reduced levels of serum testosterone has been associated with cognitive decline because testosterone has neuroprotective function against deposits of β -amyloid peptide and Tau phosphorylation^{3,6}. Neurotoxic effects are well known to accelerate cognitive deficits such as dementia. Further, testosterone regulate nerve growth in hippocampus and forebrain. These brain areas are involved in cognitive functions, for example memory, recall, attention and information processing⁵. Patients with AN suffer from hormonal abnormalities such as reduced serum testosterone¹, but relationship between testosterone, cognition and EI have never been examined. Therefore, the current study was a first attempt to fill in this gap in literature.

Results of the present study are consistent with previous findings of lower testosterone in anorexics as compared with healthy individuals¹. Most importantly, inverse correlation of testosterone with reaction times taken to perform TMT-B indicates deficits in working memory, recall and information processing in patients with AN. Positive association of testosterone with EI indicates that testosterone is involved in social cognition as well. Previous studies suggest that testosterone plays role in human social cognition^{32,33}. Previous research has suggested deficient affect regulation and cognitive impairment in patients with AN^{7,8}. These abnormalities have been associated with brain structural changes in temporal-orbito-frontal lobes, fronto-striathalamic circuits, amygdala and insula. Neurocognitive deficits that involve cognitive inflexibility and social cognition are due to weak integration of cortical (insula, fron-

to-parietal network) and subcortical structures (thalamus, hippocampus, amygdala) of the brain in patients with AN⁹. Task switching in the current study involved cognitive flexibility. Switching requires efficient manipulation of cognitive resources such as working memory, recall, attention, etc. Larger switch costs in the present study suggest working memory difficulties and cognitive rigidity in patients with AN. Previous research also suggest visuo-spatial working memory deficits and cognitive rigidity during verbal and non-verbal decision making in patients with AN whereas these deficits were not present in healthy controls³⁴. Impaired decision making to cognitive stimuli reduces processing speed which can be indexed as larger switch costs. Task switching involves set-shifting pertaining to each task when the task gets alternated. Deficient switching ability shows lack of attention, impaired inhibitory control and inability to adapt task/environment related demands. Decreased thalamus activation in patients with AN reduces the capacity to ignore task irrelevant information, thus increases switch costs¹⁵. As neural basis of impaired EI and cognitive performance rely on prefrontal cortex¹⁷, deficits in EI and affective control in patients were also observed in the current study. This might be the reason that EI was found as a significant predictor of task switching performance.

LIMITATIONS

There are few limitations of the current study. Cross sectional examination would have been informative if other types of AN might be included in the sample. A comparison of cognitive performance with bulimics would provide detailed insight in to the biological mechanism.

CONCLUSION

Testosterone, duration of amenorrhea and EI can serve as significant marker of task switching deficits in patients with AN. A comprehensive cognitive rehabilitation might be helpful in treatment and prevention of socio-cognitive deficits patients with AN.

FUTURE DIRECTIONS

Future directions are to assess whether (i) testosterone levels must be examined after weight gain in AN (ii) emotion and cognitive deficits appear after weight gain in anorexics (iii) EI and task switching deficits can be improved with some training.

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CONTRIBUTORS

AG conceived the idea, planned the study and drafted the manuscript. SJ helped acquisition of data, did statistical analysis and critically revised the manuscript. All authors contributed significantly to the submitted manuscript.