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Effect of Atypical Antipsychotics on Serum BDNF in an Egyptian First Samples of First Episode Schizophrenia Patients

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Abstract - Aim: The study is one of only few studies that was concerned with effect of atypical antipsychotics on serum Brain-Derived Neutorophic Factor (BDNF) level, as well as the relation between serum BDNF level and severity of symptoms. Methods: This was a prospective study conducted on 45 patients with first episode schizophrenia, patients were diagnosed by Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), severity of symptoms assessed by PANSS (Positive And Negative Syndrome) scale, serum level of BDNF was assessed in all patients before starting their medication and after 6 weeks of receiving atypical antipsychotic. Results: Serum BDNF levels were decreased after 6 weeks of treatment with atypical antipsychotic in patients with first episode schizophrenia, risperidone and quetiapine showed statistically significant decrease (p values 0.004, 0.041 respectively) in BDNF level after 6 weeks of therapy. PANSS score was decreased after 6 weeks of treatment with atypical antipsychotic in patients with first episode schizophrenia. Quetiapine showed the highest mean difference 65.4 **±** 13.5 and the amisulpride showed the least mean difference 43.7 **±** 4.9. There was no significant correlation between serum BDNF level and severity of the symptoms (p value 0.328), while we established a negative correlation between BDNF level and negative symptoms (r = -0.321). We did not establish significant differences (p value = 0.604) between subtypes of schizophrenia regarding BDNF level. Conclusions: Further cognitive, neuropsychological and psychopathological assessment could be useful to clarify the involvement of BDNF in the endophenotypic characteristics of schizophrenia.

Keywords: BDNF; first episode schizophrenia; atypical antipsychotic

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Introduction

Schizophrenia is a chronic brain disorder that affects 1% of the world population and is associated with disruption in social functioning, active symptoms include delusions, hallucinations, and disorganized speech [1]**.** The disease evolves in cycles of remissions and relapses, however, with treatment symptoms improve and likelihood of recurrence can be diminished.

The presence of cognitive deficits is obvious in patients with psychotic disorders. These affected cognitive domains include working memory, verbal memory, executive function, attention, speed of information processing and visuo-spatial abilities [2].

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Brain-derived neurotrophic factor (BDNF) plays a role in the development, regeneration, survival, and maintenance of neurons in the brain and in the differentiation of neural pathways including dopaminergic pathways as well as in the modulation of synaptic plasticity and dendritic growth in the adult brain [3]. It has also been shown to modulate neurotransmitter synthesis, metabolism and release [3].

BDNF interacts with other neurotransmitter systems implicated in schizophrenia, such as dopamine, glutamate, serotonin and GABA [4]**.** It has been found that there is a change in BDNF level in several brain regions and in serum of patients with schizophrenia [5].

As antipsychotics are known to be the most effective treatment for schizophrenia, their potential role in neuroprotection might be related to BDNF [6]. They are reported to influence BDNF levels to various degrees but the true influence of different antipsychotics on change in BDNF levels thus deserves further investigation [7].

First episode schizophrenia patients show a smaller amygdala, hippocampus, thalamus, and total cortical gray volume early in the disease course with minimal antipsychotic medication exposure. A smaller subcortical volume of the amygdala and the nucleus accumbens were significantly associated with poorer cognitive function in the reasoning/problem-solving domain. Being perceived as an emotion regulation center, our findings suggest that in the early stage of psychosis, the amygdala significantly contributes to the difficulty in problem solving in patients, which may have implications on identifying early intervention strategy to improve cognitive deficits in schizophrenia [8].

BDNF crosses the blood-brain barrier and serum concentrations strongly correlate with brain levels. It is assumed that low levels of BDNF have been associated with decreased hippocampal volume, an area that has been strongly related to schizophrenia. Identifying BDNF alterations in first episode psychosis (FEP) is a preliminary step to understand the role of BDNF in schizophrenia pathophysiology, as first episode patients are not affected by medication effects (in some cases), or other factors related with chronicity [9].

In this study we aimed to investigate the effects of antipsychotics on serum BDNF levels in patients with drug-naïve first-episode schizophrenia. Finally, we examined whether the changes in serum BDNF levels are associated with the severity of clinical symptoms.

Subjects and Methods

This was a randomized prospective study. Patients were recruited from the inpatient and outpatient sectors of the Institute of Psychiatry, Ain Shams University. The institute is located in Eastern Cairo and serves a catchment area for about a third of Greater Cairo. It serves both urban and rural areas, including areas around Greater Cairo as well.

The sample consisted of forty five drug naïve Egyptian inpatient and outpatient patients with a diagnosis of first episode schizophrenia using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), their ages ranged between 18-60 years. We excluded patients who received multiple medications. Patients had other psychiatric or medical problems (brain lesions, dementia, delirium), mental retardation and mental sub normality, co- morbid substance use disorder or any other psychiatric disorders, patients with recurrent episodes, chronic patients and patients who received multiple medications.

After providing written informed consent to participate in the study**,** Semi-structured interview was performed to collect following data from patients as regards: age, marital status, education level occupation, residency and past medical and psychiatric history.

They were assessed by Structured Clinical Interview for DSM-IV, The Arabic version and PANSS scale [10-12]. In addition to assessing level of BDNF in serum in first visit and after 6 weeks of using atypical antipsychotic drug using ELISA kit [13]. Human Brain derived neurotrophic factor (BDNF) ELISA KIT (for RESEARCH USE ONLY. Not for clinical diagnosis use) CATALOG #:10186. The kits are used for the quantitative determination of human BDNF concentration in human species. It is an in vitro enzyme-linked immune sorbent assay for the quantitative measurement of Human BDNF in serum with detection range: (0.05 ng/mL - 10ng/mL) Laboratory investigations were done in the central Lab of Ain Shams University Hospital under standard sanitary conditions

All blood samples were collected by trained nurse under standardized condition, samples were transferred to the central lab of the university in the same day of sampling to be centrifuged and then serum was stored at -70 degree ˚C refrigerator until recruitment of required samples was done. Analysis of samples was done be trained technician has proper working experience with BDNF ELISA kits after finishing the required samples. The package contains 96 kits, 6 ones were used for standardization so the remaining 90 were used in the study for 45 patients (2 samples from each). We selected patients who are drug naïve and the first sample was withdrawn before taking any antipsychotic where its selection was part of management plan done by the institute clinicians and not the researcher to avoid any bias, the selection was according to previous response, family history, availability and affordability of the drug.

Statistical analysis

Data were entered into the SPSS for Windows 17th version (2009) and analyzed using descriptive and analytic analyses including frequencies, mean and standard deviations with percentage (for qualitative data), Paired t Test, Pearson Correlation Test (r), One Way ANOVA Test (F), Pearson Chi Square Test.

Results

Sociodemographic data and clinical profile

The participants of the study were 45 drug naïve patient with 1st episode schizophrenia estimated, majority of our cases were males (42, 93.3%), female (3,6 67%),with mean age 28.3 ± 9.7 years ranging from 18 to the eldest 59 years old. The marital status showed that most of them were single (35, 77.78%), cases showed almost equal distribution according to educational level where the highest percentage (12, 27%) finished preparatory school, the employment status showed that about (23, 51.1%) of them are manual workers. The cases came mainly from urban areas (22, 49%).

Most of cases were classified as having paranoid schizophrenia 73.3%, meanwhile the mean age of onset of the illness was 27 ± 9.5 years ranging from 17 to 58 years, and the mean duration of illness in months was 14.4 ± 6.5 ranging from 7 to 24 months.

After being diagnosed, antipsychotics were first prescribed to patients after first serum BDNF level was measured, risperidone was the most frequently prescribed atypical antipsychotic 22 (44.4%), 12 patients (26.6%) were on olanzapine, 5 (11%) on quetiapine, 4 (8.8%) on amisulpride, 2 (4.4%) on aripiprazole and 2 (4.4%) on asenapine.

Comparison between BDNF levels and PANSS score before and after 6 weeks of treatment with atypical antipsychotics

When comparing BDNF before and after six weeks of treatment with atypical antipsychotics, it has been shown that there was highly statistically significant difference using paired T test, the mean BDNF before treatment was 2.3 ± 1.06 and significantly lowered to 1.5 ± 0.7 (p Value <0.001).

As demonstrated in table 1, the paired T test found that only the risperidone and quetiapine showed statistically significant decrease in BDNF level after 6 weeks of therapy when comparing between the effects of each atypical antipsychotic used on BDNF serum level, Paired T test showed that there was statistical highly significant correlation where all scores were lowered.

On comparing PANSS scores pre- and post treatment using paired T test showed that there was statistical highly significant correlation where all scores lowered p value < 0.001. The total PANSS score had a mean of 139 ± 13.9 pretreatment and significantly decreased to 84.4 ± 12.7 after 6 weeks of therapy.

The effect of each atypical antipsychotics used on PANSS score before and after six weeks of treatment has been shown in figure 1.

Relation between serum BDNF level and clinical and sociodemographic variables

The sociodemographic factors were correlated to BDNF serum level before treatment and showed no statistically significant difference except for the social class evaluation where the middle class showed statistically significant higher mean 3 ± 1.3 compared to high

Table 1. Serum BDNF (Brain-derived Neurotrophic factor) level pre-& post treatment across different antipsychotics

Atypical Antipsychotic prescribed	BDNF level						Differences		Paired Test	
	Before treatment			After 6 Weeks of treatment						
	Mean	±	SD	Mean	±	SD	Mean	SD	t	P-value
Olanzapine (n=12)	2.058	±	0.809	1.538	±	0.781	0.521	1.228	1.469	0.170
Risperidone (n=20)	2.718	±	1.369	1.500	±	0.825	1.218	1.667	3.266	0.004
Aripiprazole (n=2)	2.025	±	1.096	1.675	±	1.308	0.350	2.404	0.206	0.871
Quetiapine (n=5)	2.140	±	0.303	1.500	±	0.224	0.640	0.481	2.973	0.041
Amisulpride (n=4)	2.400	±	0.583	2.000	±	0.657	0.400	1.175	0.681	0.545
Asenapine (n=2)	2.125	±	0.177	1.350	±	0.354	0.775	0.177	6.200	0.102
ANOVA F	0.719			0.334						
ANOVA P-value	0.613			0.889						

class mean 1.8 ± 0.8 and low social class 2.2 ± 0.8. (p value 0.035) as shown in table 2, also ANOVA test was used to study the difference among different type of schizophrenia in the sample and their BDNF level before receiving treatment and found no statistical difference. The undifferentiated BDNF mean was 2.6 ± 1.6, followed by paranoid cases' BDNF level mean 2.3 ± 0.8, catatonic cases 'mean BDNF was 1.7 ± 1.06 and the lowest BDNF mean was among Hebephrenic cases 1.6 ± 0.

Moreover, there is no significant correlation between BDNF serum level and total positive and general PANSS score but we found negative correlation between BDNF level and negative symptoms (r= -0.321, p value 0.031).

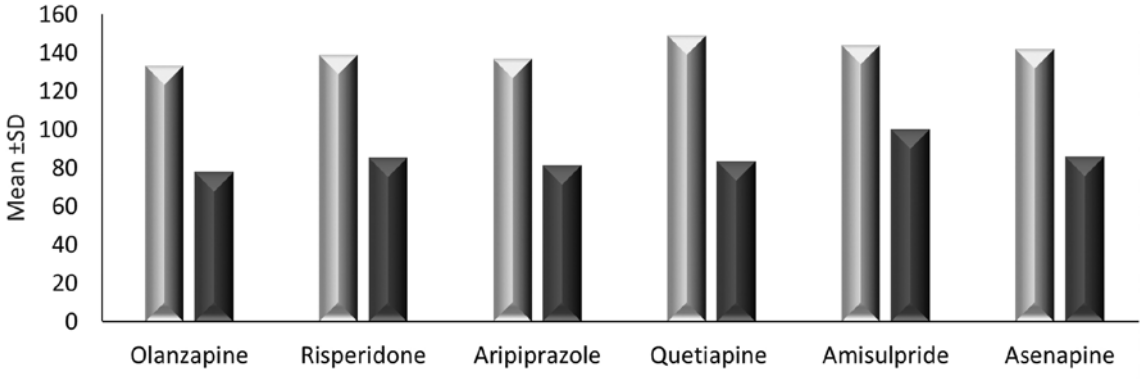

Figure 1. Bar chart demonstrates mean total PANSS (Positive and Negative Syndrome Scale) score before and after treatment with different atypical antipsychotics

Table 2. Sociodemographic and clinical characteristics & BDNF (Brain-Derived Neurotrophic factor) serum level

		BDNF level before treatment					
		N	Mean	±	SD	T or F	P-value
Gender	Male	42	2.380	±	1.007	-0.292	0.772
	Female	3	2.567	±	1.994		
Marital status	Single	35	2.269	±	0.699	2.075	0.102
	Engaged	1	3.700	±	0.000		
	Married	7	2.607	±	2.020		
	Divorced	1	1.600	±	0.000		
	Widow	1	4.700	±	0.000		
Residence	Rural	9	1.917	±	0.739	2.147	0.129
	Urban	22	2.320	±	0.906		
	Slums	14	2.811	±	1.341		
Educational level	Illiterate/read & write	4	2.375	±	0.250	1.255	0.303
	Primary	5	3.160	±	1.320		
	Preparatory	12	1.950	±	0.674		
	Secondary	7	2.186	±	0.384		
	Technical institute	9	2.767	±	1.710		
	University	8	2.344	±	0.947		
FH of psychiatric illness	Negative	36	2.461	±	1.157	0.368	0.694
	1st degree relative	4	2.113	±	0.379		
	2nd degree relative	5	2.120	±	0.610		
Social Class	High	5	1.860	±	0.884	3.645	0.035
	Middle	12	3.038	±	1.384		
	Low	28	2.211	±	0.818		
Type of Schizophrenia	Paranoid	33	2.379	±	0.855	0.624	0.604
	Hebephrenic	1	1.600	±	0.000		
	Catatonic	2	1.750	±	1.061		
	Undifferentiated	9	2.672	±	1.693		

Discussion

The current study is a cohort (follow up) study and to the best of the authors knowledge, it is one of few studies in Egypt which was interested to explore the effect of atypical antipsychotics use on serum BDNF levels in drug naive first episode patients so we avoided the effect of previous medications or very long duration of illness which could affect the results.

Sociodemographic and clinical data of the sample study

Regarding mean age was 28.3 ± 9.7 years ranging from 18 to 59 years old which is similar to the mean age of patients assessed in many other similar studies conducted on patients

Table 3. Serum BDNF (Brain-Derived Neurotrophic factor) level and PANSS (Positive and Negative Syndrome Scale) subscale scores

Correlations		
	BDNF level Before Treatment	
	r	P-value
Total PANSS Before	-0.149	0.328
	BDNF level Before Treatment	
	r	P-value
Total Positive PANSS Before	0.130	0.394
Total Negative PANSS Before	-0.321	0.031
Total General PANSS Before	-0.156	0.306

with first episode schizophrenia, they found that the mean age would be 29.71 ± 10.21 years [14,15], majority of cases were males (94%) of sample while the females (6%) this was in agreement with the distribution found in the study by Ajami and associates, where 40 of cases were males (76%) and 12 cases were females (24%), this may be attributed by earlier age of onset of schizophrenia in men than women [16].

Most of cases were classified as having paranoid schizophrenia 73.3%, followed by undifferentiated 20%, 4% were catatonic and only 2% were of the hebephrenic type which is similar to the distribution found in the study of Rizos and associates where 71.4% of cases were of the paranoid type and 29.6% of cases were of the hebephrenic type [14]**.** Also, Lee and Kim found that 86.2% of cases were of the paranoid type and 13.8% were of undifferentiated type which comes in agreement with the studied fact that paranoid schizophrenia is the most common type of schizophrenia and its prevalence rate ~0.5% of the general population [17-19].

Cases were prescribed atypical antipsychotic as follows: 44.4% were on risperidone, 26.6% were on olanzapine, 11% were on quetiapine, 8.8% were on amisulpride, 4.4% on aripiprazole and 4.4% on asenapine which is similar to who treated 54% of the patients with risperidone, 30% with olanzapine and 15% with aripiprazole due to availability and low cost of risperidone if compared to other atypical antipsychotics [20].

BNNF levels and PANSS score before and after treatment with antipsychotics

The current study investigated the levels of serum BDNF in patients with first episode schizophrenia before starting any medications where its mean was found to be 2.3 ± 1.06 and lowered to 1.5 ± 0.7 after 6 weeks of receiving treatment with atypical antipsychotics, on comparing between the effect of each atypical antipsychotic used on BDNF serum level it was found that the level of BDNF before and after treatment showed no statistically significant difference among different atypical antipsychotics and only the risperidone and quetiapine showed statistically significant decrease in BDNF level after 6 weeks of therapy. The reason explained in one previous study reported that hippocampal tissue loss in first-episode schizophrenia shown on MRI was associated with a functional polymorphism of BDNF [21]. A showed a significantly positive association between low serum BDNF levels and reduction in hippocampal volumetric at the onset of schizophrenia [14]. Taken together, our finding of lower serum levels of BDNF in the first episode patients with schizophrenia

suggests that deficit in this neurotrophic factor may contribute to the structural and functional alterations of brain in the initial phase of schizophrenia, supporting the hypothesis that neurodevelopmental disturbances may be involved in the pathogenesis of schizophrenia. [4,22].

Contrary to the current study what was reported by Li and associates who investigated serum brain-derived neurotrophic factor levels following electroconvulsive therapy and antipsychotic treatment in patients with schizophrenia founded increased BDNF level after ECT and medication which might be due to the effect of ECT and different patient population on which the study was conducted. The reason for this inconsistency may be related to different sample sources, length of the disease, length of untreated psychosis, length of current illness or episode, anti-psychotic drug dose or illness severity between studies [19].

In Yoshimura and associates 2010 study which evaluated the comparative effect of risperidone, olanzapine, and aripiprazole on plasma levels of catecholamine metabolites and BDNF in first-episode unmedicated schizophrenic patients, authors reported that none of these three atypical antipsychotic drugs alter BDNF levels within 8 weeks of treatment [20]. The main reason for the discrepant finding could be due to the fact that they measured plasma level of BDNF while ours measured the serum levels which are two different compartments.

Furthermore, Chen and Huang 2011 measured serum BDNF levels in 53 patients with paranoid schizophrenia during a relapse and again 4 weeks following the administration of antipsychotic treatment (with risperidone in 32 cases, and clozapine in 21 cases), however, serum BDNF was significantly increased in the subgroup receiving risperidone compared to that receiving clozapine [23]. These inconsistent findings with the present study may be because they studied the effect of atypical antipsychotics on patients in relapse not those with first episode schizophrenia.

Moreover, Chiou and Huang in 2017 established a study in Taiwan to determine whether there is a difference in serum BDNF levels between patients with drug-naïve first-episode schizophrenia and healthy subjects and to investigate the effects of antipsychotics on serum BDNF levels in patients with drug-naïve first-episode schizophrenia after 4 weeks of antipsychotic treatment founded that the serum BDNF levels were not significantly elevated whereas the serum BDNF levels were significantly elevated in the 16 patients treated with risperidone. Those incongruent findings with our results could be attributed to the different patient populations, lower sample size than that of the current study and shorter duration before and after drug administration [24].

With regards to PANSS score the inter group difference was studied before and after treatment showing that there was no statistically significant difference between antipsychotics regarding the total PANSS score. and when comparing between the effect of each type of atypical antipsychotic on total (positive, negative and general) PANSS score, we found also that quetiapine showed the highest mean difference and the amisulpride showed the least mean difference in decreasing each of (positive, negative and general) total scores separate.

This is similar to a study showed a significant decrease in PANSS scores after 6 weeks of treatment with both antipsychotics (risperidone and olanzapine) [15]. Also, at Li and associates 2016 [19]. Gonzalez-Pinto and associates 2010 who found that the total PANSS score significantly decreased after therapy with atypical antipsychotics, which illustrate the effectiveness of different atypical antipsychotics in improvement of symptoms of schizophrenia [25].

Correlation between BDNF and sociodemographic, clinical variables

On studying the correlation between serum BDNF level of the cases and their total score of PANSS before starting treatment was non-significant which means that no significant cor-

relation between serum BDNF level and severity of the symptoms and this goes in agreement with Suzan and associates 2017 [15]**.** Chiou and Huang 2017 who showed the same results as all these studies were conducted on cases with first episode schizophrenia [24].

The relation between the PANSS score and serum BDNF levels was investigated in another study and although a positive correlation was discovered between PANSS positive subscale scores and serum BDNF levels, no significant relation was found between PANSS negative subscale scores and serum BDNF levels [26]. Likewise, a study detected a negative correlation between serum BDNF levels and both positive and negative subscale scores [27]. In addition to two studies that reported no significant relation between serum BDNF levels and PANSS positive subscales although detecting a positive correlation between PANSS negative subscale scores and serum BDNF levels [28,29]. The difference in results may be attributed to clinical conditions of the patients, duration of the illness or the ethnic variation of allele frequency depending on BDNF gene polymorphism.

With regards to relation of BDNF and sociodemographic variables a study found statistically significant difference regarding to gender whereas serum BDNF was significantly increased in the 15 male subjects and not in the 17 females. This discrepancy may be due to different gender distribution recruited originally in the study [23].

When studying the difference among each type of schizophrenia in the sample and their BDNF level pre-therapeutically found no statistical difference which is close to Lee and Kim 2009 who found no differences between paranoid and undifferentiated subtype in correlation with BDNF serum level, it might be due to the small sample size which couldn't represent all subtypes of schizophrenia [17]. The correlation between BDNF serum level pre-treatment and clinical aspect of the illness among cases (age of onset in years and duration of illness in months) showed no statistically significant correlation [17].

In conclusion, Serum BDNF levels decreased after 6 weeks of treatment with atypical antipsychotic in patients with first episode schizophrenia. Risperidone and quetiapine showed statistically significant decrease in BDNF level after 6 weeks of therapy. There is no significant correlation between serum BDNF level and total score of PANSS before starting treatment which means that no significant correlation between serum BDNF level and severity of the symptoms.

There is a negative correlation between BDNF level and negative symptoms. There was no significant difference between subtypes of schizophrenia regarding BDNF level.

The present study has several limitations; small sample size, it did not distinguish the effects of the different antipsychotics on serum BDNF levels due to the small sample size of the patient group (only) 45 patients is a limitation, results should be carefully interpreted, especially findings for antipsychotics that were given to only a handful of participants. Therefore, these findings may be considered preliminary until a research on a bigger sample with enough statistical power to consider multiple antipsychotics (this is explained by number of kits used (96 kits used for 45 patients before and after use of Antipsychotics) 6 ones were used for standardization, this was done for financial causes. And as for the treatment response and whether there was change in treatment option after 6 weeks, most probably some patients didn't show the full response and needed maximization, Augmentation or shift but this was not further tracked, as it was not our point of research.

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Conflict of interest

None to declare.

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References

1. Ross CA, Margolis RL, Reading SAJ, Pletnikov M, Coyle JT. Neurobiology of schizophrenia. Neuron. 2006;52:139-53.
2. Hauser M, Zhang JP, Sheridan EM, Burdick KE, Mogil R, Kane JM, et al. Neuropsychological test performance to enhance identification of subjects at clinical high risk for psychosis and to be most promising for predictive algorithms for conversion to psychosis: a meta-analysis. J Clin Psychiatry. 2017;78:e28-40.
3. Nurjono M, Lee J, Chong SA. A review of brain-derived neurotrophic factor as a candidate biomarker in schizophrenia. Clin Psychopharmacol Neurosci. 2012;10:61-70.
4. Shoval G, Weizman A. The possible role of neurotrophins in the pathogenesis and therapy of schizophrenia. Eur Neuropsychopharmacol. 2005;15:319-29.
5. Ikeda Y, Yahata N, Ito I, Nagano M, Toyota T, Yoshikawa T, et al. Low serum levels of brain-derived neurotrophic factor and epidermal growth factor in patients with chronic schizophrenia. Schizophr Res. 2008;101:58-66.
6. Asevedo E, Gadelha A, Noto C, Mansur RB, Zugman A, Belangero SI, et al. Impact of peripheral levels of chemokines, BDNF and oxidative markers on cognition in individuals with schizophrenia. J Psychiatr Res. 2013;47:1376-82.
7. Rizos EN, Papadopoulou A, Laskos E, Michalopoulou PG, Kastania A, Vasilopoulos D, et al. Reduced serum BDNF levels in patients with chronic schizophrenic disorder in relapse, who were treated with typical or atypical antipsychotics. World J Biol Psychiatry. 2010;11:251-5.
8. Fan F, Xiang H, Tan S, Yang F, Fan H, Guo H, et al. Subcortical structures and cognitive dysfunction in first episode schizophrenia. Psychiatry Res Neuroimaging. 2019;286:69-75.
9. Toll A, Mané A .Brain-derived neurotrophic factor levels in first episode of psychosis: A systematic review. World J Psychiatry. 2015;22:154-9.
10. First A, Michael B, Spitzer C. Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version (SCID-1). Washington, D.C.: American Psychiatric Press; 1997.
11. El Missiry A, Sorour A, Sadek A, Fahy T, Mawgoud MA, Asaad T. Homicide and Psychiatric Illness, An Egyptian Study. Cairo: Faculty of Medicine, Ain Shams University; 2003.
12. Hermes EDA, Sokoloff DM, Stroup TS, Rosenheck RA. Minimum clinically important difference in the Positive and Negative Syndrome Scale using data from the CATIE Schizophrenia Trial. J Clin Psychiatry. 2012;73:526.
13. Lee BC, Choi IG, Kim YK, Ham BJ, Yang BH, Roh S, et al. Relation between plasma brain-derived neurotrophic factor and nerve growth factor in the male patients with alcohol dependence. Alcohol. 2009;43:265-9.
14. Rizos E, Papathanasiou MA, Michalopoulou PG, Laskos E, Mazioti A, Kastania A, et al. A Longitudinal Study of Alterations of Hippocampal Volumes and Serum BDNF Levels in Association to Atypical Antipsychotics in a Sample of First-Episode Patients with Schizophrenia. PLoS One. 2014;09:e87997.
15. Suzan KM, Mihaljevic-Peles A, Sagud M, Bajs Janovic M, Ganoci L, Grubisin J, et al. Brain-derived neurotrophic factor serum and plasma levels in the treatment of acute schizophrenia with olanzapine or risperidone: 6-week prospective study. Nord J Psychiatry. 2017;71:513-20.
16. Ajami A, Hosseini SH, Taghipour M, Khalilian A. Changes in Serum Levels of Brain Derived Neurotrophic Factor and Nerve Growth Factor-Beta in Schizophrenic Patients Before and After Treatment. Scan J Immunol. 2014;80:36-42.
17. Lee BH, Kim YK .Increased plasma brain-derived neurotropic factor, not nerve growth factor-Beta, in schizophrenia patients with better response to risperidone treatment. Neuropsychobiology. 2009;59:51-8.
18. Skokou M, Gourzis P. Demographic features and premorbid personality disorder traits in relation to age of onset and sex in paranoid schizophrenia. Psychiatry Res. 2014;215:554-9.
19. Li J, Ye F, Xiao W, Tang X, Sha W, Zhang X, et al. Increased serum brain-derived neurotrophic factor levels following electroconvulsive therapy or antipsychotic treatment in patients with schizophrenia. Eur Psychiatry. 2016;36:23-8.
20. Yoshimura R, Ueda N, Hori H, Ikenouchi-Sugita A, Umene-Nakano W, Nakamura J. Different patterns of longitudinal changes in plasma levels of catecholamine metabolites and brain-derived neurotrophic factor after administration of atypical antipsychotics in first episode untreated schizophrenic patients. World J Biol Psychiatry. 2010;11:256-61.
21. Szeszko PR, Lipsky R, Mentschel C, Robinson D, Gunduz-Bruce H, Sevy S, et al. Brain-derived neurotrophic factor val-66met polymorphism and volume of the hippocampal formation. Mol Psychiatry. 2005;10:631-6.
22. Durany N, Thome J. Neurotrophic factors and the pathophysiology of schizophrenic psychoses. Eur Psychiatry. 2004;19:326-37.
23. Chen CC, Huang TL. Effects of antipsychotics on the serum BDNF levels in schizophrenia. Psychiatry Res. 2011;189:327-30.
24. Chiou YJ, Huang TL. Serum brain-derived neurotrophic factors in Taiwanese patients with drug-naive first-episode schizophrenia: Effects of antipsychotics. World J Biol Psychiatry. 2017;18:382-91.
25. González-Pinto A, Mosquera F, Palomino A, Alberich S, Gutiérrez A, Haidar K, et al. Increase in brain-derived neurotrophic factor in first episode psychotic patients after treatment with atypical antipsychotics. Int Clin Psychopharmacol. 2010;25:241-5.
26. Chen DC, Wang J, Wang B, Yang SC, Zhang CX, Zheng YL, et al. Decreased levels of serum brain derived neurotrophic factor in drug-naïve first-episode schizophrenia: relationship to clinical phenotypes. Psychopharmacology. 2009;207:375-80.
27. Rizos EN, Rontos I, Laskos E, Arsenis G, Michalopoulou PG, Vasilopoulos D, et al. Investigation of serum BDNF levels in drug-naive patients with schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry. 2008;32:1308-11.
28. Reis HJ, Nicolato R, Barbosa IG, Teixeira do Prado PH, Romano-Silva MA, Teixeira AL. Increased serum levels of brain-derived neurotrophic factor in chronic institutionalized patients with schizophrenia. Neurosci Lett. 2008;439:157-9.
29. Huang TL, Lee CT. Associations between serum brain-derived neurotrophic factor levels and clinical phenotypes in schizophrenia patients. J Psychiat Res. 2006;40:664-8.

Učinak atipičnih antipsihotika na serumski BDNF u egipatskih pacijenata s prvom epizodom shizofrenije

Sažetak - Cilj: Istraživanje je jedno od rijetkih koje se bavilo učinkom atipičnih antipsihotika na razinu moždanog neurotrofnog čimbenika (*engl.* Brain-derived neurotrofic factor- BDNF) u serumu, kao i povezanost razine BDNF-a u serumu s težinom simptoma. Metode: Provedeno je prospektivno istraživanje na 45 bolesnika s prvom epizodom shizofrenije. Pacijentima je dijagnoza utvrđena pomoću strukturiranog kliničkog intervjua za DSM-IV poremećaje (SCID-I), težina simptoma procijenjena je putem pozitivne i negativne sindromske skale (engl. Positive And Negative Syndrome scale - PANSS), a razina BDNF-a u serumu je izmjerena u svih bolesnika prije početka uzimanja lijekova i šest tjedana nakon liječenja atipičnim antipsihoticima. Rezultati: Utvrđena je snižena razina serumskog BDNF-a nakon šest tjedana liječenja atipičnim antipsihoticima u bolesnika s prvom epizodom shizofrenije. Risperidon i kvetiapin pokazali su statistički značajno sniženje (p vrijednosti 0,004,-0,041) razine BDNF nakon šest tjedana liječenja. Ukupni rezultat na PANSS ljestvici je snižen nakon šest tjedana liječenja atipičnim antipsihoticima u bolesnika s prvom epizodom shizofrenije. Kvetiapin je pokazao najveću srednju razliku 65,4 ± 13,5, a amisulprid najmanju srednju razliku 43,7 ± 4,9. Nije bilo značajne korelacije između razine BDNF-a u serumu i težine simptoma (p vrijednost = 0,328), dok smo utvrdili negativnu korelaciju između razine BDNF-a i negativnih simptoma (r =-0,321). Nismo utvrdili značajne razlike (p vrijednost = 0,604) između podtipova shizofrenije s obzirom na razinu BDNF-a. Zaključak: Daljnja kognitivna, neuropsihološka i psihopatološka procjena mogla bi biti od koristi u pojašnjavanju povezanosti BDNF-a s endofenotipskim karakteristikama shizofrenije.

Ključne riječi: BDNF; prva epizoda shizofrenije; atipični antipsihotik