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Brief report

No changes in serum epidermal growth factor levels in patients with schizophrenia

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Abstract

A recent report demonstrated that serum levels of epidermal growth factor (EGF) were significantly decreased in patients with schizophrenia, suggesting that impaired EGF signaling might be associated with the pathophysiology of schizophrenia. Our goal in the present study was to determine whether serum levels of EGF are altered in patients with schizophrenia. We found that serum levels of EGF in drug-naive ($n=15$) or medicated patients ($n=25$) with schizophrenia did not differ from those of age- and sex-matched normal controls ($n=40$). However, we found a significant correlation between serum EGF levels and BPRS scores in the combined groups of patients. Therefore, our results do not support the claim that EGF plays a role in the pathogenesis of schizophrenia, but they suggest that EGF may serve as a state marker, that is, as an index of symptom-linked deficits.

Keywords: Schizophrenia; Epidermal growth factor (EGF); Growth factor; Cytokine; Neurotrophic factor; Neurodevelopmental

1. Introduction

Schizophrenia is a devastating disorder affecting approximately 1% of the general population worldwide. The hypothesis that schizophrenia has a neurodevelopmental origin has gained much attention in the research community (Murray et al., 1992; Lewis and Lieberman, 2000). Several lines of evidence suggest that cytokines, growth factors, and neurotrophic factors may play an important role in the pathophysiology of schizophrenia (Kronfol and Remick, 2000; Buka et al., 2001; Torrey and Yolken, 2001).

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In this context, of interest is a recent report showing that epidermal growth factor (EGF) protein levels are significantly decreased in the postmortem brains of patients with schizophrenia, and that serum EGF levels in both medicated and drug-free patients with the disorder are also markedly reduced as compared with normal controls (Futamura et al., 2002). In the central nervous system, EGF has been shown to serve as a neurotrophic factor to enhance cell proliferation and neuronal differentiation (Xian and Zhou, 1999), and these findings have been interpreted by the authors to be evidence that impaired EGF signaling might be associated with the pathophysiology of schizophrenia (Futamura et al., 2002). However, in the study of Futamura et al. (2002), drug-naive patients ($n=4$) and chronic patients ($n=45$; mean age: 47.0 years old) were included in the analysis of serum EGF levels. Thus, the results could be accounted for by the effect of antipsychotic medication. Furthermore, Futamura et al. (2002) did not examine the relationship between serum EGF levels and clinical variables such as the severity of symptoms in patients with schizophrenia (Futamura et al., 2002). If there was a strong relationship between serum EGF levels and the severity of patient symptoms, the pathogenetic role of EGF might be even more significant. Therefore, we measured serum EGF levels in drug-naive and medicated patients with schizophrenia and age- and sex-matched normal controls, and we also examined the possible relationship between serum EGF levels and clinical symptoms.

2. Methods

Forty patients with schizophrenia (mean: 35.5 years; 20 men and 20 women) and 40 age- and sex-matched healthy subjects (mean: 36.5 years; 20 men and 20 women) participated in this study. All of the subjects provided written informed consent for participation in the study after the procedure had been fully explained. The ethics committee of Chiba University Graduate School of Medicine approved the present study. All patients were diagnosed according to DSM-IV, and symptomatology was evaluated by a senior psychiatrist using the Brief Psychiatric Rating Scale (BPRS). Of the study patients, 15 (37.5%) were drug-naive (Table 1). Antipsychotic drugs administered to the remaining medicated patients ($n=25$) were chlorpromazine (62.5–200 mg/day; $n=3$), levomepromazine (25–100 mg/day; $n=2$), propericyazine (15 mg/day; $n=1$), fluphenazine (1.79 mg/day; $n=1$), clocapramine (150 mg/day; $n=1$), thioridazine (75 mg/day; $n=1$), haloperidol (1.5–9 mg/day; $n=5$), bromoperidol (6 mg/day, $n=1$), risperidone (3–16 mg/day; $n=16$), zotepine (25–225 mg/day; $n=3$), quetiapine (300–750 mg/day; $n=5$), or olanzapine (10–20 mg/day; $n=3$). Of the medicated patients, 12 patients were *currently* receiving multiple antipsychotic drugs for treatment. The normal controls had no history of psychiatric or neurological disorders and showed no abnormalities in routine laboratory examinations.

To minimize any time-related variations in the levels of serum EGF, serum samples were collected

Table 1
Characteristics of normal controls, drug-naive and medicated patients

	Normal controls	Drug-naive patients	Medicated patients	*P* value
Sex (M/F)	20/20	7/8	13/12	0.95[a]
Age, years (range)	36.5 ± 14.6 (20–70)	34.7 ± 16.0 (19–61)	36.0 ± 13.2 (20–65)	0.92[b]
Onset, years (range)	–	33.8 ± 15.3 (18–57)	21.2 ± 4.95 (13–35)	0.0005[c]
Illness duration, years (range)	–	1.09 ± 1.36 (0–5)	14.1 ± 9.87 (0.25–41)	<0.0001[c]
BPRS score (range)	–	26.9 ± 15.4 (6–58)	19.2 ± 12.4 (2–56)	0.09[c]
Chlorpromazine equivalents (mg)	–	–	727 ± 412 (113–1900)	
EGF (pg/ml)	411 ± 217	331 ± 226	481 ± 241	0.13[b]

Age, onset, illness duration, and BPRS score were shown in the mean ± SD (range).
The value of EGF was shown in the mean ± SD.
[a] The comparison among three groups was performed by chi-square test.
[b] The comparison among three groups was performed by ANOVA.
[c] The comparison between two groups was performed by *t*-test.