Serum NCAM levels and cognitive deficits in first episode schizophrenia patients versus health controls

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Abstract

**Background:** Neural cell adhesion molecule (NCAM) is a glycoprotein and plays an important role in cell-cell adhesion, neural migration, neurite outgrowth, synaptic plasticity and brain development. We investigated the relationship between the serum NCAM concentration and cognitive deficit in first episode drug naïve schizophrenia (FES) patients.

**Methods:** Thirty FES patients and thirty healthy controls were recruited for this study. Psychiatric symptoms were assessed by the positive and negative syndrome scale (PANSS). Cognitive functions were assessed by measurement and treatment research to improve cognition in schizophrenia (MATRICS) and consensus cognitive battery (MCCB). Serum levels of NCAM were determined by ELISA.

**Results:** Schizophrenia patients had decreased serum NCAM concentrations than controls (~30%, p

**Conclusions:** There was a close relationship between the serum NCAM concentrations and cognitive deficits in FES patients. Since NCAM has an important role in neurodevelopmental processes, these results support the neurodevelopmental dysfunction hypothesis of schizophrenia and suggest that an altered NCAM may be one of the risk factors for schizophrenia including cognitive deficits.

Disciplines

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Serum NCAM levels and cognitive deficits in first episode schizophrenia patients versus health controls

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Neural cell adhesion molecule (NCAM), also called CD56, is a member of the immunoglobulin superfamily. It is expressed in both neurons and glial cells (Jorgensen and Bock, 1974). NCAM plays important roles in cell-cell adhesion, neural migration, neurite outgrowth, synaptic plasticity and brain development and is also involved in the processes of learning and memory formation (Kiryushko et al., 2004; Kiss and Muller, 2001; Ronn et al., 1998). Previous studies have suggested a close relationship between the dysregulation of NCAM system and schizophrenia (Poltorak et al., 1995; Zhang et al., 2014). Animal studies have found that mice lacking NCAM have impaired spatial learning and sensorimotor gating (Wood et al., 1998) and have disrupted long-term potentiation (Senkov et al., 2006). Furthermore, genetic association studies have identified NCAM as a candidate susceptibility gene for schizophrenia and its single nucleotide polymorphisms (SNPs) are associated with cognition deficits (Lewis et al., 2003; Sullivan et al., 2007). However, no study has investigated the relationship between the serum NCAM levels and cognitive deficits in first episode schizophrenia (FES) patients. Thus, the aim of this study was to investigate whether or not there are differences in serum NCAM levels between the FES patients and health controls, and the correlation between serum NCAM levels and cognitive function in FES patients.

The research was carried out after Beijing Huilongguan Hospital Institutional Review Board approval and written informed consent. Thirty FES patients were recruited and the diagnoses were made and confirmed based on the Structured Clinical Interview for DSM-IV (SCID). Thirty healthy control (HC) subjects were recruited through advertisements via the local community. Psychiatric symptoms were assessed by the positive and negative syndrome scale (PANSS). Cognitive function was assessed by measurement and treatment research to improve cognition in schizophrenia (MATRICS) and consensus cognitive battery (MCCB). Serum levels of NCAM were measured by ELISA kit following the manufacturer’s instruction (RayBiotech, Inc. Norcross). The sensitivity for NCAM measurement was 0.5pg/ml, with intra-assay coefficients from 3% to 6%. All the samples were assayed in triplicate.

There were no significant differences in age and gender distributions between FES and HC. HC had higher education than FES patients. There was a significantly
positive correlation between the education and serum NCAM levels (r=0.362, \( p=0.005 \)) considering all subjects.

Figure 1 shows that the serum NCAM levels were 30\% lower in FES patients compared with HC subjects (38.22±12.99 µg/ml vs 54.82±17.03 µg/ml, \( p<0.001 \)). Cognitive scores on MCCB were significantly lower in FES patients than healthy controls (87.00±10.58 vs 56.67±12.60, \( p<0.001 \)). The serum NCAM levels were positively correlated with the total scores of MCCB (r=0.438, \( p=0.003 \)). Multiple regression analysis confirmed that serum NCAM level was an independent contributor to MCCB total Scores.

The primary findings of this study were that NCAM levels were significantly lower in FES patients than healthy controls, and the decreased serum NCAM levels had a positive correlation with impaired cognitive function, which was an independent contributor to MCCB total Scores. However, several limitations of the study should be noted here. First, we measured NCAM in serum, but not in the cerebral spinal fluid or brain tissues. It was still uncertain whether peripheral NCAM levels can reflect similar changes in the central nervous system. The second was the relatively small sample size in each group. The correlation analyses were performed based on the combined group, future studies should verify these results in lager amount of sample. Third, the results showed that serum NCAM levels were significantly reduced in drug naïve first-episode patients. However, the effect of antipsychotic drug on NCAM expression still unknown. So, a longitudinal study may be required to examine the levels of NCAM of these FES patients following antipsychotic treatments.

In conclusion, our results demonstrated that FES patients had significantly lower levels of serum NCAM concentration, which were correlated with cognitive deficits. Since NCAM has an important role in neurodevelopmental processes, these results support the neurodevelopmental dysfunction hypothesis of schizophrenia and suggest that altered NCAM may be one of the biomarkers for schizophrenia, especially for cognitive impairment.
Figure 1. The neural cell adhesion molecule (NCAM) concentration in the FES patients was 30% lower than normal controls. ***: p < 0.001.