

Increased Serum BDNF Levels in Schizophrenia Subjects After Intensive Neuroplasticity-Based Cognitive Training

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Introduction

•Animal studies indicate that increases in brain-derived neurotrophic factor (BDNF) signaling are related to the beneficial effects of cognitive stimulation on brain health. For example, rodents provided access to a running wheel or housed in cognitively stimulating environments exhibit increased levels of BDNF in several regions of their brains (Russo-Neustadt 1999, Young 1999).

•In this study, we investigated the relationship between serum BDNF levels and the response to neuroplasticity-based cognitive training in subjects with schizophrenia.

Methods

Twenty-eight subjects, stratified by IQ and symptom severity, were randomly assigned to either targeted cognitive training (TCT) or a control condition of graphically interesting computer games (CG).

Both groups participated in the intervention for 1 hour per day, 5 days per week, and both believed they were receiving an "active" treatment.

We measured serum BDNF levels at baseline and after 2, 12, and 26 weeks of TCT intervention in 16 schizophrenia subjects and in 12 age and IQ-matched schizophrenia subjects undergoing CG condition.

See POSTER #257 (Vinogradov et al.) for details of the cognitive remediation intervention.

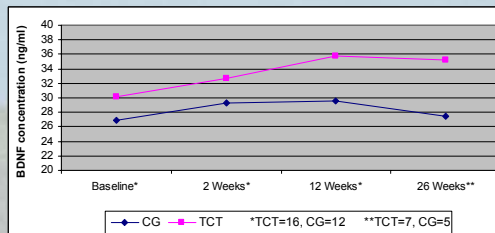
Table 1: Subject Demographics of TCT and CG groups

	CG	TCT
Number of Subjects	12	16
Gender	3 Female	5 Female
Mean Age	48.5	43.9
Mean IQ	97.4	105.8
Mean PANSS-E Score (2=mild Symptoms)	2.25	2.11
Baseline BDNF concentration	26.9	28.0

Results

- Baseline serum BDNF levels were negatively correlated with baseline neurocognitive function (Neurocognitive Composite Index Score††) in the total sample of 28 subjects ($r = -0.4$, $p < 0.05$).
- In the TCT group, but not in the CG group, serum BDNF levels increased by ~20% after 12 weeks of training (~60 hours) and remained increased in a subgroup of patients who completed 26 weeks (~130 hours) of training (group differences ns).

Graph 1: Serum BDNF Levels in Schizophrenia Patients Receiving Targeted Cognitive Training (TCT) or Computer Games Control Condition (CG)



- After 12 weeks of training, increased serum BDNF levels were positively correlated with improved processing speed z-scores ($r = 0.4$, $p < 0.05$) and improved overall neurocognitive general composite index ($r = 0.4$, $p < 0.07$) in the TCT group, but not in the CG group.

Table 2: Correlations Between Neurocognitive Change and Change in Serum BDNF Levels After 12 Weeks of Training

	BDNF Change (12 Weeks – Baseline)	
	CG (N=12)	TCT (N=16)
Processing Speed Z-Score Change†	$r = -0.03$ $p < 0.5$	$r = 0.4$ $p < 0.05$
Neurocognitive Composite Index Z-Score Change††	$r = -0.10$ $p < 0.4$	$r = 0.4$ $p < 0.07$

Conclusions

These findings indicate that:

- 1) Lower serum BDNF levels in subjects with schizophrenia show a significant association with poorer neurocognitive functioning.
- 2) Intensive neuroplasticity-based cognitive training appears to result in a sustained increase of about 20% in serum BDNF levels in schizophrenia subjects over a 12-week period (and possibly longer). This effect is not seen in subjects undergoing a computer-games control condition.
- 3) Increased serum BDNF levels are significantly associated with improved processing speed and improved overall neurocognitive functioning in subjects who underwent 12 weeks of the neuroplasticity-based cognitive training, but not the control condition subjects.
- 4) We suggest that increased serum BDNF levels may reflect a trophic response in hippocampal and cortical neurons as a result of neuroplastic changes induced by the targeted cognitive training.

†Composite consists of Digit Symbol Coding, Trails A, Trails B, Category Fluency

††Composite consists of Digit Symbol Coding, Trails A, Trails B, Category Fluency, Zero-Back Hits, Letter Number Sequencing, Spatial Span, HVLIT immediate recall, HVLIT delayed recall, BVMT immediate recall, BVMT delayed recall, NAB Mazes, Tower of London

References

Russo-Neustadt A, Beard RC, Cotman CW (1999). Exercise, antidepressant medications, and enhanced brain derived neurotrophic factor expression. *Neuropsychopharmacology*. 21(5):679-82.

Young D, Lawlor PA, Leone P, Dragunow M, During MJ (1999). Environmental enrichment inhibits spontaneous apoptosis, prevents seizures and is neuroprotective. *Nat Med*. 5(4):448-53.