

14th International Conference on Generic Drugs and Biosimilars & 9th Global Experts Meeting on Neuropharmacology

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Detection of novel serum biomarkers that predict selective serotonin reuptake inhibitor treatment outcome in south Indian population with major depressive disorder

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Statement of the Problem: Depression is the fifth leading cause of disability worldwide and is a major contributor to the global burden of diseases. Selective Serotonin Reuptake Inhibitors (SSRIs) are amongst the most commonly prescribed antidepressants. Antidepressant effects are generally not seen until 2- 4 weeks of treatment, when the rates of suicides are also high. Response to treatment with SSRIs varies considerably between patients. The aim of this study was to identify biomarkers which predict response to antidepressants and those that change during antidepressant treatment.

Methodology: 50 patients were recruited from Dept. of Psychiatry, Sri Ramachandra Medical College Hospital, a tertiary care hospital, Chennai, India, after IEC approval. Patients with unipolar depression (DSM- V criteria) with a minimum baseline score of 15 on the 21- HAM-D scale, being started on SSRIs, were recruited. After 8 weeks of treatment, responders were defined as those with at least 50% decrease in HAM-D score or a total score of ≤ 7 . hsCRP (high sensitivity C-reactive protein), BDNF (Brain derived neurotrophic factor) and NRG1 β 1 (Neuregulin 1 beta 1) were analysed using commercially available ELISA kits.

Findings: Mean age was 41.4 years. Response rate was 58%. The HAM-D score decreased after treatment from 20.04 to 10.26 (p value: < .001). The responder and non-responder groups were compared and analysed. There was no significant correlation between baseline NRG1 β 1 levels and response.

Conclusion & Significance: Low levels of serum hsCRP and high levels of BDNF prior to treatment predicted better response to SSRIs in patients with MDD and also changed longitudinally during treatment with SSRIs. Pre-treatment serum levels of NRG1 β 1 did not predict outcome to treatment but did decrease during treatment with SSRIs. Hence, these can be candidate markers in predicting response prior to starting treatment with SSRIs.

Comparison of baseline biomarker levels between responders and non-responders:

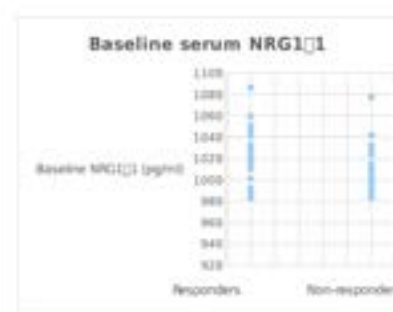
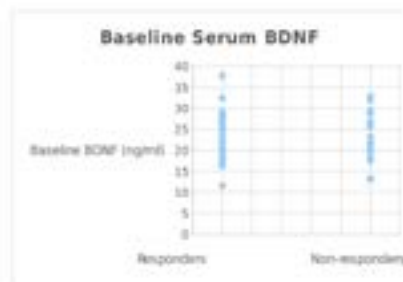
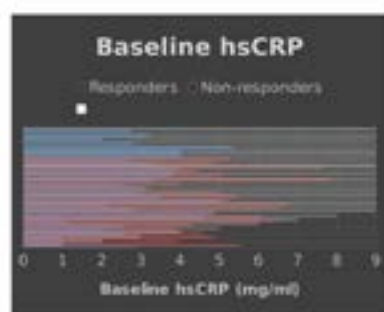
	RESPONDERS (n=29)		NON-RESPONDERS (n=21)	
	Baseline	Post-treatment	Baseline	Post-treatment
Mean hsCRP	3.13	2.17* (p<0.001)	5.25	4.11* (p<0.001)
Mean BDNF	26.11	30.81* (p<0.001)	18.6	21.98* (p=0.001)
Mean NRG1 β 1	1017.58	983.93* (p=0.00)	1010.6	1009.53
*Statistically significant				

CORRELATIONS

	Change in HAM-D (Correlation coefficient)
Baseline hsCRP	-0.375*
Baseline BDNF	0.413*

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Recent Publications:

1. Brydon L, Harrison NA, Walker C, Steptoe A, Critchley HD. Peripheral inflammation is associated with altered substantia nigra activity and psychomotor slowing in humans. *Biol Psychiatry*. 2008;63:1022–1029.
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3. Hamer M, Batty GD, Marmot MG, Singh-Manoux A, Kivimäki M. Antidepressant medication use and C-reactive protein: results from two population-based studies. *Brain, behavior, and immunity*. 2011 Jan 31;25(1):168-73.
4. Hashimoto K (2010) Brain-derived neurotrophic factor as a biomarker for mood disorders: an historical overview and future directions. *Psychiatry Clin Neurosci* 64(4):341–357. doi:10.1111/j.1440-1819.2010.02113.x
5. Fernandes CC, Pinto-Duarte A, Ribeiro JA, Sebastião AM (May 2008). "Postsynaptic action of brain-derived neurotrophic factor attenuates alpha7 nicotinic acetylcholine receptor-mediated responses in hippocampal interneurons". *The Journal of Neuroscience*. 28 (21): 5611–8. PMID 18495895. doi:10.1523/JNEUROSCI.5378-07.2008.
6. Huang TL, Lee CT, Liu YL. Serum brain-derived neurotrophic factor levels in patients with major depression: effects of antidepressants. *J Psychiatr Res* 2008;42:521–5.
7. Santarelli L, Saxe M, Gross C, Surget A, Battaglia F, et al. (2003) Requirement of hippocampal neurogenesis for the behavioral effects of antidepressants. *Science* 301: 805–809.
8. Surget A, Tanti A, Leonardo ED, Laugeray A, Rainer Q, et al. (2011) Antidepressants recruit new neurons to improve stress response regulation. *Mol Psychiatry*.
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Biography

Varsha Ramesh has completed her MD Pharmacology and is currently pursuing her PhD under Indian Council of Medical Research. She is working on detecting novel serum biomarkers and genetic polymorphisms related to outcomes to treatment with Selective Serotonin Reuptake Inhibitors in patients with moderate to severe depression.

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