Reviewer's report

Title: The longitudinal interplay between negative and positive symptom trajectories in patients under antipsychotic treatment: a post hoc analysis of data from a 1-year study

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Reviewer: Massimiliano Buoli

Reviewer's report:

The study investigates the relation between positive and negative symptoms in schizophrenia and the effects of antipsychotic treatment on these domains. The paper is well presented, the methods are clear and the topic is of interest. However a number of points have to be clarified and revised.

Major Revisions

1) Clinical dimensions of schizophrenic illness are not limited to positive and negative ones. Cognitive symptoms, disorganization and severity should have been considered. As disorganization and cognitive symptoms are related to negative dimension, perhaps the observed improvement in negative symptoms is the result of the change in other dimensions.

2) It is established that atypical antipsychotics can improve negative symptoms, but, after treatment with atypical agents, a number of patients present residual negative symptoms as well as cognitive impairment that have a strong impact on social functioning and quality of life.

3) The presented neurotransmitter model of schizophrenia is partial. Glutamatergic system is thought to be involved both in negative and positive symptoms of schizophrenia.

4) Two variables can be correlated but independent. Of note none of the reported Pearson coefficients indicate a strong correlation between negative and positive symptoms (>0.7)

5) The sample is not homogenous. The patients probably have different duration of illness (schizophreniform patients in comparison with schizophrenic ones) with clearly implication in term of treatment response. In addition schizoaffective patients have a different treatment response and outcome respect to schizophrenics and they had not to be included in the sample.

Minor Revisions

1) Most of patients were previously treated with first generation antipsychotics that can have modified clinical presentation

2) PANSS baseline total scores indicate a moderate severity of illness. The rate of severity is predictive of treatment response so that in case of more severe patients the results could have been different.
3) Comorbid psychiatric diagnoses were cross-sectional or life-time? If cross sectional, what type of mood disorder was comorbid in 21.6% of patients? Was psychotic bipolar disorder accurately excluded?

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

Roche consultant