Replication of a Statistical Method to Reduce Pseudospecificity and Enhance Understanding of Score Changes Among PANSS Factors

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The Methodological Question Being Addressed: Factor analyses of the Positive and Negative Syndrome Scale (PANSS) conducted so far have revealed varying degrees of intercorrelation. Consequently, improvement in a clinical domain of interest (e.g., negative symptoms) could be associated with and hence may be attributable to another correlated domain (e.g., positive symptoms) and is often considered "pseudospecific." This study addresses the methodological question whether other statistical approaches can be utilized to reduce this pseudospecificity.

Introduction (Aims): At the February 2017 meeting of ISCTM, Loebel et al presented a method to transform PANSS factor scores to reduce the correlations that exist among the Marder factors.[1] In this study, the goal of the transformations is to reduce the correlations that exist within the 5-factor model (Marder factors).

Methods: This study is a post hoc application of the method utilized by Loebel et al to data generated from a Phase 2, randomized, double-blind, placebo-controlled study of TAK-063 (a potent, selective phosphodiesterase 10A inhibitor) vs. placebo in patients with acutely exacerbated symptoms of schizophrenia. The ratings of 30 items in PANSS were transformed to factor scores using a score matrix identified by factor analysis conducted on all change from baseline PANSS data as provided by Loebel et al. The score matrix consisted of coefficients multiplying the numerical ratings of each PANSS item differentially for each of the factor scores.

Results: Primary results of study TAK-063_2002 have been reported elsewhere (the least squares mean difference in change from baseline between TAK-063 and placebo was 5.46 points on the total PANSS score with a standard error of 3.44, p=0.115 and effect size 0.308).[2] The transformed results in Study 2002 for TAK-063 are remarkably similar to those of Loebel et al. The correlations among the Marder scores (change from baseline to endpoint) were generally above 0.40. With the transformation, the correlations between Marder and transformed PANSS factor scores (change from baseline to endpoint) were increased with most correlations being greater than 0.7 and ranging from 0.6 to 0.96. The correlations among the transformed PANSS factor scores (change from baseline to endpoint) were considerably smaller than the correlations within the Marder scores.

Conclusions:

Utilizing the transformation method to PANSS factors from the TAK-063_2002 study yielded results similar to those reported by Loebel et al for a drug with a different mechanism of action.

The correlations among the transformed PANSS factors are considerably smaller than those seen on the Marder factors.

Reducing the correlations between factor scores may be a more accurate representation of antipsychotic effects.

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References:

1. Loebel T, Hopkins S. A new PANSS factor analysis intended to reduce pseudospecificity among domains and enhance understanding of symptom change in antipsychotic-treated patients with schizophrenia. Poster presented at: 13th Annual Scientific Meeting of the International Society for CNS Clinical Trials and Methodology (ISCTM); February 21-23, 2017; Washington, DC.
2. Macek T, McCue M, Ogrinc F, et al, A phase 2, randomized, double-blind, placebo-controlled, parallel-group, 6-week study to evaluate the efficacy and safety of TAK-063 in subjects with an acute exacerbation of schizophrenia. Poster presented at: 16th International Congress on Schizophrenia Research; March 24-28, 2017; San Diego, CA. Abstract M20.