Independent Replication of Reliability, Convergent Validity, and Treatment Sensitivity of an Abbreviated PANSS in an Adolescent Schizophrenia Double-Blind RCT

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ABSTRACT

Background: Global regulatory initiatives have increased the number of pediatric psychopharmacology trials. Challenges in ensuring valid and reliable data in such trials include developmental limitations in symptom description, the need to combine and calibrate information from varied sources, including patients and parents/caregivers, and a dearth of pediatric-specific scales [1,2]. Pediatric schizophrenia trials, with few exceptions, have used for primary efficacy assessment the (adult) Positive and Negative Syndrome Scale (PANSS) [3], a complex and lengthy 30 item measure that has been extensively studied and shown to pose ratings challenges even in the adult populations for whom it was designed. For this reason, using data from an NIMH pediatric psychosis trial [4], we previously conducted a retrospective study using confirmatory factor analysis and graded response item response theory to develop and explore the validity of a short form of the PANSS optimized for use with youths [5]. Results suggested that a 10 item version could still produce reliable information about five different symptom dimensions and a good overall total score estimate highly correlated with the 30 item version. Replication in an independent sample, however, is crucial before recommending wider adoption. Therefore, the present study performed secondary analyses on a separate large, double-blind, placebo-controlled trial to investigate and confirm the psychometric properties in a second sample. As with the initial work, the hypotheses were that the reliability would be acceptable and that sensitivity to treatment effects would not differ significantly from the 30 item version. **Method**. The 6-week, double-blind, parallel group, acute phase data from the Johnson & Johnson sponsored completed, positive, paliperidone study [6] were accessed from the YODA secure data environment. The trial included 201 12-17 year olds randomly allocated to placebo or one of three fixed doses of paliperidone. Analyses were performed using the mirt, lavaan, sjstat and psych packages in R, using the same syntax and methods as the prior analyses [4], with mixed regressions using random intercepts and partial eta-squared as the effect size estimate for time, treatment, and time x treatment interaction effects. **Results**. The 10 item vs. 30 item versions had similar average interitem correlations (.25 and .25), as well as similar partial eta-squared values for time – .37 [.32 to .41] versus .41 [.36 to .45], treatment (all .00) and time x treatment (.007 versus .003 for the full length). IRT models indicated similar reliability as in the development sample, with good precision across a similar range of severity. **Conclusion**. The 10 item version of the PANSS replicated well in an independent, larger sample using double-blind RCT data. The similar sensitivity to treatment effects is particularly promising given the substantial reduction in scale length and corresponding decreases in required rater training, interview length, and respondent burden.

BACKGROUND

- Global regulatory initiatives have increased the number of pediatric psychopharmacology trials.
- Challenges in ensuring valid and reliable data in such trials include developmental limitations in symptom description, the need to combine and calibrate information from varied sources, including patients and parents/caregivers, and a dearth of pediatric-specific scales [1,2].
- Pediatric schizophrenia trials, with few exceptions, have used for primary efficacy assessment the (adult) Positive and Negative Syndrome Scale (PANSS) [3], a complex and lengthy 30 item measure that has been extensively studied and shown to pose ratings challenges even in the adult populations for whom it was designed.
- For this reason, using data from an NIMH pediatric psychosis trial [4], we previously conducted a retrospective study using confirmatory factor analysis and graded response item response theory to develop and explore the validity of a short form of the PANSS optimized for use with youths [5].
- Results suggested that a 10 item version could still produce reliable information about five different symptom dimensions and a good overall total score estimate highly correlated with the 30 item version.
- Replication in an independent sample, however, is crucial before recommending wider adoption.
- Therefore, the present study performed secondary analyses on a separate large, double-blind, placebo-controlled trial to investigate and confirm the psychometric properties in a second sample.
- As with the initial work, the hypotheses were that the reliability would be acceptable and that sensitivity to treatment effects would not differ significantly from the 30 item version.

METHOD

- The 6-week, double-blind, parallel group, acute phase data from the Johnson & Johnson sponsored completed, positive, paliperidone study [6] were accessed from the YODA secure data environment.
- The trial included 201 12-17 year olds randomly allocated to placebo or one of three fixed doses of paliperidone.
- Analyses were performed using the mirt, lavaan, sjstat and psych packages in R, using the same syntax and methods as the prior analyses [4], with mixed regressions using random intercepts and partial eta-squared as the effect size estimate for time, treatment, and time x treatment interaction effects.

RESULTS

- The 10 item vs. 30 item versions had similar average interitem correlations (.25 and .25), as well as similar partial eta-squared values for time – .37 [.32 to .41] versus .41 [.36 to .45], treatment (all .00) and time x treatment (.007 versus .003 for the full length)
- IRT models indicated similar reliability as in the development sample, with good precision across a similar range of severity

CONCLUSION

- The 10 item version of the PANSS replicated well in an independent, larger sample using double-blind RCT data.
- The similar sensitivity to treatment effects is particularly promising given the substantial reduction in scale length and corresponding decreases in required rater training, interview

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