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General Information

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Are external grants or funds being used to support this research?: No external grants or funds are being used to support this research.
How did you learn about the YODA Project?: Internet Search

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yoda_project_coi_form_for_data_requestors_2016_-_li-signed.pdf
yoda_project_coi_form_for_data_requestors_2016_-_alex.pdf

Certification

Certification: All information is complete; I (PI) am responsible for the research; data will not be used to support litigious/commercial aims.
Data Use Agreement Training: As the Principal Investigator of this study, I certify that I have completed the YODA Project Data Use Agreement Training

Associated Trial(s): NCT00866996 - A Multi-center Randomized Parallel Group Study Evaluating Treatment Outcomes of Concerta (Extended Release Methylphenidate) and Strattera (Atomoxetine) in Children With Attention-deficit/Hyperactivity Disorder

What type of data are you looking for?: Individual Participant-Level Data, which includes Full CSR and all supporting documentation

Research Proposal

Project Title

Applications of Item Response Theory to Clinical ADHD Research: Increased Precision of Treatment Effect Estimation

Narrative Summary:
Rating scales serve as a necessary tool for clinicians who wish to determine presence and severity of ADHD symptoms. Therefore, accurate measurement of symptomatology is essential. Item response theory (IRT), a latent variable model, presents an opportunity to improve the way we measure baseline clinical symptoms of ADHD and estimate change over the course of treatment. This study aims to model change in ADHD symptoms as a function of treatment within the IRT framework in order to examine treatment sensitivity as measured by latent traits across several pharmacotherapies.

Scientific Abstract:
Background: Item response theory (IRT), a latent variable model, presents an opportunity to improve the way we measure treatment response.
Objective: This study aims to model change in ADHD symptoms as a function of treatment within the IRT framework using a multidimensional model of ADHD symptoms.
Study Design: The proposed study will use longitudinal ADHD-RS-IV from the requested trial to compare latent dimension treatment sensitivity through modeling of latent change in the ADHD trait within a multi-level IRT framework.
Participants: Participants include all children ages 6 to 17 who were rated using the ADHD-RS-IV by a trained clinician.
Main Outcome: Latent dimension means and variances to evaluate change from baseline to endpoint.
Measure(s): ADHD-RS-IV, age, gender, and comorbid diagnoses.
Statistical Analysis: A multiple group multilevel longitudinal item bifactor model will be used to estimate latent change scores in the ADHD construct over treatment.

Brief Project Background and Statement of Project Significance:
Attention-deficit/hyperactivity disorder (ADHD) is an externalizing behavioral disorder that affects between 5 and 10 percent of youth (Polanczyk, Silva de Lima, Biederman, & Rohde, 2007). A number of rating scales exist for the purpose of measuring symptoms of ADHD for children and adolescence including the CPRS (Conners, Sitarenios, Parker, & Epstein, 1998), SNAP-IV (Swanson, 1992), and the ADHDRS-IV (DuPaul, Anastopoulos, Power, Reid, Ikeda, & McGoey, 1998). Rating scales serve as a necessary tool for clinicians who wish to determine presence and severity of ADHD symptoms, in addition to monitoring response to treatment (Conners, 1997). Because the best method for detecting the effectiveness of a treatment is through perceived changes in symptoms, accurate measurement of symptomatology is essential. However, as advances in quantitative methodology have improved measurement in domains such as physical functioning, emotional distress, and pain, clinical research in ADHD has lagged behind.
Item response theory (IRT), a latent variable model, presents an opportunity to improve the way we measure baseline clinical symptoms of ADHD and treatment response. Successful IRT modeling of rating scales has enabled the Patient-Reported Outcomes Measurement Information System (PROMIS) Cooperative Group and NIH to create more precise, flexible, and reliable forms. Traditionally, change in ADHD symptoms over the course of treatment are estimated using summed scores. However, using this approach it appears that all pharmacotherapies produce relatively uniform reductions across inattention and hyperactivity/impulsivity with varying effect sizes depending on the specific treatment. Unlike summed scores, latent variable models produce orthogonal dimensions. It is possible that when independent sources of variability are identified, we may find that different treatments in fact produce differential reduction across latent dimensions. To maximize the potential of IRT application in ADHD measurement, we must also capitalize on the increasing availability of data previously collected by investigators and companies that have a stake in the advancement of research and treatment.
This proposal aims to model change in ADHD symptoms as a function of treatment within the IRT framework in order to examine item-level treatment sensitivity across several pharmacotherapies used to treat ADHD.

The results of this IRT analysis are predicted to identify a more concise and presumably more sensitive change index which could have research and clinical value both in diagnosis and in treatment assessment. Results will be submitted for publication in psychological methods journals.

Specific Aims of the Project:
This study aims to use the best fitting model of ADHD-RS-IV items to model change in latent dimensions of ADHD over the course of treatment. We hypothesize that different pharmacotherapeutic approaches will produce differential reduction in orthogonal latent dimensions of ADHD symptoms.

What is the purpose of the analysis being proposed? Please select all that apply. Research that confirms or validates previously conducted research on treatment effectiveness
Participant-level data meta-analysis
Participant-level data meta-analysis will pool data from YODA Project with other additional data sources

Research Methods

Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:
Baseline and treatment endpoint ADHD-RS-IV scores will be used for all participants 6 to 17 who completed NCT00866996, titled “A Multi-center Randomized Parallel Group Study Evaluating Treatment Outcomes of Concerta (Extended Release Methylphenidate) and Strattera (Atomoxetine) in Children with Attention-deficit/Hyperactivity Disorder” to estimate differences in latent change in symptoms of ADHD over the course of treatment.

Main Outcome Measure and how it will be categorized/defined for your study:
Latent change in ADHDRS-IV inattention and hyperactivity/impulsivity subscales will be evaluated from baseline to last available treatment end-point to examine treatment differences.

Main Predictor/Independent Variable and how it will be categorized/defined for your study:
In the latent change treatment model, baseline and treatment endpoint ADHD-RS-IV scores will be used.

Statistical Analysis Plan:
A longitudinal, multidimensional IRT model will be used to estimate change from baseline to treatment endpoint to compare pharmacotherapies used in the requested trial. Item parameters will be fixed at values determined in study 1.

Models will likely be estimated in flexMIRT (Cai, 2013) using maximum marginal likelihood via the Bock-Aitkin EM algorithm (Bock & Aitkin, 1981), which will also handle missing data. The use of flexMIRT is necessary due to the complexity of the IRT model (e.g. multiple group, multilevel). Several indices of model fit will be reported and used to assess the fit of the model. Due the possibility of many response patterns (4^9) and a sparse contingency table, the M2 statistic will be reported (Cai & Hansen, 2013). Root mean square error of approximation (RMSEA; Steiger & Lind, 1980) will also be reported in addition to marginal fit (chi-square) and LD (chi-square) statistics for further evaluation and discussion of model fit.

Project Timeline:
The project will start as soon as data, or decisions regarding data, have been received. Analyses will be completed within three months following receipt of data. The manuscript will be drafted by the end of the 2016 calendar year and immediately submitted for publication.

Dissemination Plan:
The purpose of these analyses is to supplement dissertation research. Publication of results will occur by June 2017, and will be submitted to journals such as Psychological Medicine, Journal of Attention Disorders, and Psychological Assessment.

Bibliography:
Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. Journal of the Royal Statistical Society. Series B (Methodological), 57(1), 289–300.

Bock, R. D., & Aitkin, M. (1981). Marginal maximum likelihood estimation of item parameters: Application of an EM algorithm. Psychometrika, 46, 443–459.

Bussing, R., Fernandez, M., Harwood, M., Hou, W., Garvan, C. W., Eyberg, S. M., & Swanson, J. M. (2008). Parent and teacher SNAP-IV ratings of attention deficit hyperactivity disorder symptoms psychometric properties and normative ratings from a school district sample. Assessment, 15(3), 317-328.

Cai, L. (2013). flexMIRT R version 2: Flexible multilevel multidimensional item analysis and test scoring [Computer software]. Chapel Hill, NC: Vector Psychometric Group.

Cai, L., & Hansen, M. (2013). Limited information goodness of fit testing of hierarchical item factor models. British Journal of Mathematical and Statistical Psychology, 66(2), 245-276.

Cai, L., Thissen, D., & du Toit, S. H. C. (2011). IRTPRO: Flexible, multidimensional, multiple categorical IRT modeling [Computer software]. Lincolnwood, IL: Scientific Software International.

Cella, D., Riley, W., Stone, A., Rothrock, N., Reeve, B., Yount, S., ... & Group, P. C. (2010). The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. Journal of clinical epidemiology, 63(11), 1179-1194.

Centers for Disease Control and Prevention. (2015). Attention-deficit/hyperactivity disorder (ADHD). Retrieved from http://www.cdc.gov/ncbddd/adhd/data.html.

Conners, C. K. (1997). Rating scales in attention-deficit/hyperactivity disorder: use in assessment and treatment monitoring. The Journal of clinical psychiatry, 59(Suppl 7), 24-30.
Conners, C. K., Sitarenious, G., Parker, J. D., & Epstein, J. N. (1998). The revised Conners' Parent Rating Scale (CPRS-R): factor structure, reliability, and criterion validity. Journal of Abnormal Child Psychology, 26(4), 257-268.

DuPaul, G. J., Anastopoulos, A. D., Power, T. J., Reid, R., Ikeda, M. J., & McGoey, K. E. (1998). Parent ratings of Attention-Deficit/Hyperactivity Disorder symptoms: Factor structure and normative data. Journal of Psychopathology and Behavioral Assessment, 20(1), 83-102.

Embretson, S. E., & Reise, S. P. (2000). Item response theory for psychologists. Lawrence Erlbaum Associates Inc.; Mahwah, NJ.

Lahey, B. B., Pelham, W. E., Loney, J., Lee, S. S., & Willcutt, E. (2005). Instability of the DSM-IV subtypes of ADHD from preschool through elementary school. Archives of General Psychiatry, 62(8), 896-902.

Langer, M. (2008). A reexamination of Lord's Wald test for differential item functioning using item response theory and modern error estimation (Unpublished doctoral dissertation).

Polanczyk, G., Silva de Lima, M., Horta B. L., Biederman, J., & Rohde, L. A. (2007). The worldwide prevalence of ADHD: a systemic review and metaregression analysis. American Journal of Psychiatry, 164(4), 942-948.

Samejima, F. (1969). Estimation of latent ability using a response pattern of graded scores. Psychometric Monograph, No. 17.

Steiger, J. H. & Lind, J. C. (1980). Statistically Based Tests for the Number of Common Factors. Paper presented at the annual meeting of the Psychometric Society, May, Iowa City, IA.

Woods, C. M., Cai, L., & Wang, M. (2013). The Langer-Improved Wald test for DIF testing with multiple groups: evaluation and comparison to two-group IRT. Educational and Psychological Measurement, 73(3), 532-547.