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Physiology-based virtual reality training for social skills in schizophrenia

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PROTOCOL

We will implement the adaptive social VR game and determine the optimal dose. After we construct each subject's affective model with the machine-learning algorithm, we will test the effects of the adaptive VR games in 40 medicated outpatients with schizophrenia (SZ). Demographically matched control (CO) subjects (n=16) will only participate in the affective modeling and social and cognitive assessments but not in VR training (see Human Subjects section for details). To determine the optimal dose of VR training, it is necessary to conduct a valid assessment for social functioning pre- and post- treatment. Details of assessments are outlined below. Optimal dose of physiology-based, adaptive VR intervention is unknown but Tsang & Man[53] reported that just ten 30-minute sessions of conventional, non-adaptive VR training was sufficient to obtain an improvement in SZ. In our study, we will examine the effects of social VR training on social and cognitive measures, pre- and post-treatment. At baseline (t1), the PI's will use stratified randomization to assign SZ to two dose conditions: high vs. low. Stratified randomization is used to ensure that potential confounding factors (e.g. age, gender) are evenly distributed between groups. If possible, we will try to match the two groups on IQ, and the Social Functioning Scale[79], a broad measure of social functioning, but if it cannot be done, we will statistically adjust for them when we test for treatment effects. Everybody will train twice a week but the low dose group will train for 30 mins and the high dose group for 2 x 30 mins per visit. VR task performance will be recorded at each visit. At t1, social, cognitive and symptom assessments will be conducted. The research staff who administer assessments are blind to the group assignment and SZ are unaware which group they are in. The research assistants who supervise VR sessions will NOT conduct assessments because they will be aware of the dosing. After t1, subjects play the VR game for 2.5 weeks, at which point (t2), we repeat the social, cognitive and symptoms assessments plus a satisfaction survey. Then they train for another 2.5 weeks. At 5 weeks (t3), we repeat the assessments and the satisfaction survey. The behavioral measures have been used in intervention trials to be reliable across time with minimal practice effects, or offer alternate forms[85,100]. The satisfaction survey will solicit user feedback to improve our protocol in the future.

VR Training: SZ will play the "Day Out" game in the lab. Biosensors and eye tracking will be used. To boost adherence, we will call/text 2 hours before the visit. They will be paid after each visit and receive a bonus upon reaching the next level of difficulty in the game, and when they complete the training.

ASSESSMENTS.

VR Task Measures: The VR game has built-in performance measures, including but not limited to the total time spent on completing the specified task (e.g., find out avatar's birthday at the bus stop), number of errors following the sequential steps, number of successful social interactions with avatars and deviation from specified scenarios. The number of difficulty levels mastered by the participant will determine the overall performance. We will track the VR scores per session to determine the rate of learning.

Social Assessments:

(1) *Social Functioning Scale* *(SFS)*[79] has 79-items with 7 subscales: social engagement, interpersonal communication, daily living activities, recreation, social activities, independent living and employment. Raw scores of the subscales are converted to scaled score (m=100, SD=15). **(2) *Social Emotional Task from CogState***[82] (SET-CS) is a facial emotion recognition task within CogState (see below). ***(3) Bell Lysaker Emotion Recognition test** (BLERT)*[100]. Subjects view 10s vignettes of an actor talking about life. After each vignette, subjects select one emotion that was portrayed. There are 3 different stories portrayed in 7 emotions (21 total). Correct responses are summed. ***(4) Revised Eyes Test** (EYES*)[127] assesses the theory of mind[87]. It asks subjects to decide the mental state of a person from an image of his/her eyes. For each set of eyes, subjects select one word out of 4 choices that best describes what the person in the picture is thinking or feeling. There are 36 trials. These measures were selected for their validity, reliability, and coverage of important domains of social functioning[1,130]. Our VR game simulates and exercises social interactions, thus, targeting emotion recognition (BLERT, EYES, SET-CS), and theory-of-mind[87] (EYES, BLERT). Practicing these skills will likely lead to broad, beneficial consequences for social functioning (SFS).

Cognitive Assessments: (1) *Wechsler Abbreviated Scale of Intelligence* (WASI)[80] will estimate IQ at t1. It will not be repeated at t2 or t3. Baseline IQ may interact with the efficacy of social interventions[20,81]. **(2) *CogState***[82] is a computerized, standardized battery for assessing cognitive abilities (cogstate.com). It reliably detects cognitive changes over time, and shows minimal practice effects with repeated administrations[83,84]. It is widely used to measure cognition in treatment trials[84-86]. Results are automatically scored. It takes 30 minutes.

Clinical Symptoms: SAPS[74] and SANS[75] will be used to measure the severity of symptoms in SZ.

Satisfaction Survey: To obtain feedback about VR experience, we will give a 9-item survey that asks about difficulties, hurdles, enjoyment and motivational factors, and solicits suggestions.

DATA ANALYSIS PLAN

Does the VR intervention elicit significant pre-post change on the targeted social attention, measures of social functioning (SFS, SET-CS, BLERT, EYES) and clinical symptoms (SAPS and SANS)? What are the specific treatment parameters that provide the optimal benefit when cost-benefit and other considerations are taken into account? To address training effects on the social assessments, we will use a linear mixed effects model (LMM) analytic approach because it allows for maximally flexible modeling of effects and parameters and for a principled treatment of missing data[128, 141].To address this question, we will conduct repeated measures LMM analyses. Specific contrasts will directly assess: **1)** The linearity of the slope of change within each group; **2)** Pairwise differences among time points within each group; and, **3**) Group differences in linearity and pairwise differences. Because our power calculations indicate that the most powerful tests of group differences will be provided by an ANCOVA framework (with pre-treatment values serving as the covariate)[112,134], we will also use this analytic approach to compare the two dose conditions. Although it is important to minimize Type 2 errors in an initial study, we will also generate multiplicity-corrected p values across the 5 primary measures using simulation-based approaches[142]. A similar approach will be used to analyze the clinical symptom and other measures (e.g., CogState) although a generalized linear mixed effects (GLMM) model may be needed to accommodate non-normal distributional properties of the measures[101]. With a particular emphasis on the set of social measures, we will also conduct analyses that assess effects on the set as a whole. Depending on the correlational structure of the measures, we will either: **1)** Form 1 or 2 linear composites using prior findings on the dimensional structure of the measures and our own analyses; or **2)** Conduct a multivariate analysis of variances using the flexible facilities of mixed-effects software to accommodate such models. We will assess clinically meaningful change by comparing the post-treatment SZ and normative distribution for each group[109,110]. To provide a more fine-grained assessment of the proximal effects of training we will assess change over days on the VR task measures (e.g., # of difficulty levels mastered) to assess the rate of learning across, within, and between the dose conditions. Generalized linear and generalized nonlinear mixed effects models will be used to carefully assess the functional form of change over time using several approaches: **a)** Polynomial growth models; **b)** Penalized spline analyses[108]; and, **c)** Non-linear mixed effects models[101,106] directly estimating parameters particularly relevant to learning[114]. It is important that analyses also address missing data and attrition because: (1) Minimization of drop-out is one of the goals of the VR intervention and will be an important determinant of the dose and duration to use in the R33 phase; and (2) To minimize biases, it is important to use a principled approach to the treatment of missing data on the other outcome measures. We will: (1) Conduct logistic regression and, if feasible, discrete survival analyses predicting drop-out based on weekly data; (2) Use pattern-mixture models and related approaches to estimate treatment effects in the presence of drop-out and assess how different patterns of attrition might moderate effects ; and, (3) Try to include in models auxiliary variables that predict drop-out [147,148]. Supplementary analyses will also test whether performance changes during the training phase mediate the effects of the intervention conditions on social functioning and symptom measures[131].

BIBLIOGRAPHY

1. Green MF, Penn DL, Bentall R, Carpenter WT, Gaebel W, Gur RC, Kring AM, Park S, Silverstein SM, Heinssen R. (2008) Social cognition in schizophrenia: an NIMH workshop on definitions, assessment, and research opportunities. *Schizophrenia Bull*, 34(6), 1211-1220.

2. Liberman RP, Kopelowicz A, Silverstein SM. (2005) Psychiatric rehabilitation. In: Sadock BJ, Sadock VA, (Eds) Comprehensive Textbook of Psychiatry. Baltimore, MD: Lippincott Williams & Wilkins. p. 3884-3930.

3. Huxley NA, Rendall M, Sederer L. (2000) Psychosocial treatments in schizophrenia: a review of the past 20 years. *Journal of nervous and mental disease*, 188(4), 187-201.

4. Kopelowicz A, Liberman RP, Zarate R. (2006). Recent advances in social skills training for schizophrenia. *Schizophrenia Bull,* 32, S12-S23.

5. Kurtz MM, Mueser KT (2008) A meta-analysis of controlled research on social skills training for schizophrenia. *Journal of consulting and clinical psychology*, 76(3), 491.

6. Kurtz MM, Richardson CL. (2012) Social Cognitive Training for Schizophrenia: A Meta-Analytic Investigation of Controlled Research. *Schizophr Bull,* 38(5): 1092-1104

7. Liu, C., Conn, K., Sarkar, N., Stone, W (2008) Physiology-based affect recognition for computer-assisted intervention of children with autism spectrum disorder. *Int J of Human-Computer Studies*, 66(9), 662-677.

8. Liu, C., Conn, K., Sarkar, N, Stone, W. (2008) Online Affect Detection and Robot Behavior Adaptation for Intervention of Children with Autism. *IEEE Transactions on Robotics*, 24, 4, 883-896.

9. Welch, K. C., Lahiri, U., Liu, C., Weller, R., Sarkar, N., & Warren, Z. (2009). An affect-sensitive social interaction paradigm utilizing virtual reality environments for autism intervention. In: Human-Computer Interaction. Ambient, Ubiquitous and Intelligent Interaction. Springer Berlin Heidelberg. .pp.703-712

10. Bekele, E., Lahiri, U., Swanson, A., Crittendon, J., Warren, Z., & Sarkar, N. (2013). A Step Towards Developing Adaptive Robot-Mediated Intervention Architecture (ARIA) for Children With Autism.
IEEE Trans Neural Syst Rehabil Eng. 21(2): 10.1109/TNSRE.2012.2230188. PMC3860752

11. Bekele, E., Zheng, Z., Swanson, A., Crittendon, J., Warren, Z., & Sarkar, N. (2013). Understanding How Adolescents with Autism Respond to Facial Expressions in Virtual Reality Environments. Visualization and Computer Graphics, *IEEE Transactions* 19(4), 711-720.

12. Bellack AS, Green MF, Cook JA, Fenton W, Harvey PD, Heaton RK, Laughren T, Leon AC, Mayo DJ, Patrick DL, Patterson TL, Rose A, Stover E, Wykes T. (2007) Assessment of community functioning in people with schizophrenia and other severe mental illnesses: a white paper based on an NIMH-sponsored workshop. *Schizophr Bull*. 33(3): 805-22.

13. Couture, SM., Granholm, EL., Fish, SC. (2011). A path model investigation of neurocognition, theory of mind, social competence, negative symptoms and real-world functioning in schizophrenia. *Schizophrenia Res,* 125(2), 152-160.

14. Kupper Z, Ramseyer F, Hoffmann H, Kalbermatten S, Tschacher W (2010). Video-based quantification of body movement during social interaction indicates the severity of negative symptoms in patients with schizophrenia. *Schizophrenia Res*, 121, 90-100.

15. Pompili, M., Lester, D., Innamorati, M., Tatarelli, R., Girardi, P. (2008) Assessment and treatment of suicide risk in schizophrenia. *Expert review of Neurotherapeutics*, 8(1), 51-74.

16. Kreyenbuhl, J., Buchanan, RW, Dickerson, FB., Dixon, LB. (2010) The schizophrenia Patient Outcomes Research Team (PORT): Updated treatment recommendations 2009. *Schizophrenia Bull*, *36*, 94-103.

17. Pfammatter, M., Junghan, UM., Brenner, HD. (2006). Efficacy of psychological therapy in schizophrenia: conclusions from meta-analyses. *Schizophrenia Bull,* 32, S64–80.

18. Heinssen RK, Liberman RP, Kopelowicz A (2000) Psychosocial skills training for schizophrenia: lessons from the laboratory. *Schizophr Bull* 26:21–46

19. Bellack AS. (2004). *Social skills training for schizophrenia: A step-by-step guide*. The Guilford Press.

20. Granholm, E., McQuaid, JR., McClure, FS, Auslander, LA., Perivoliotis, D., Pedrelli, P, Jeste, DV. (2005). A randomized, controlled trial of cognitive behavioral social skills training for middle-aged and older outpatients with chronic schizophrenia. *American Journal of Psychiatry*, *162*(3), 520-529.

21. Lindenmayer, JP, McGurk, SR., Khan, A., Kaushik, S., Thanju, A., Hoffman, L., Herrmann, E. (2013). Improving social cognition in schizophrenia: a pilot intervention combining computerized social cognition training with cognitive remediation. *Schizophrenia Bull*. 39 (3): 507-517.

22. Penn DL, Roberts DL, Combs D, Sterne A. (2007) Best practices: the development of the social cognition and interaction training program for schizophrenia spectrum disorders. *Psychiatric Services*. 58:449–451

23. VISN 5 Mental Illness Research, Education, and Clinical Center (MIRECC) - VA Social Skills Training Program. http://mirecc.va.gov/visn5/training/social_skills.asp

24. Kreyenbuhl, J., Nossel, IR, & Dixon, LB. (2009). Disengagement From Mental Health Treatment Among Individuals With Schizophrenia and Strategies for Facilitating Connections to Care: A Review of the Literature. *Schizophrenia Bull, 35,* 696-703.

25. Kurtz, MM., Rose, J., Wexler, BE. (2011). Predictors of participation in community outpatient psychosocial rehabilitation in schizophrenia. *Community Mental Health Journal, 47,* 622-627.

26. Strickland, D. (1997) Virtual reality for the treatment of autism. Virtual reality in neuropsychophysiology. G. Riva, ed., IOS Press, Amsterdam, pp. 81-86.

27. Bellini, S., Peters, J. K., Benner, L., Hopf, A. (2007) A Meta-Analysis of school-based social skills intervention for children with Autism Spectrum Disorders*. J Remedial and Special Education*, 28(3), 153-162.

28. Moore, DJ, McGrath, P., Thorpe, J. (2000) Computer aided learning for people with autism - A framework for research and development. *Innovations in Education and Training International*, 37(3), 218-228.

29. Tartaro, A., Cassell, J. (2007) Using Virtual Peer Technology as an Intervention for Children with Autism. Towards Universal Usability: Designing Computer Interfaces for Diverse User Populations, J. Lazar, ed., John Wiley. Chichester, UK.

30. Standen, PJ, Brown, DJ. (2005) Virtual reality in the rehabilitation of people with intellectual disabilities: review. *Cyberpsychol Behav*, 8(3), 272-282

31. Chen, SH., Bernard-Opitz, V. (1993) Comparison of personal and computer-assisted instruction for children with autism. *Mental Retardation*, 31(6) 368-376.

32. Seymour, NE., Gallagher, AG, Roman, SA., O'Brien, MK., Bansal, VK., Andersen, DK., Satava, RM. (2002). Virtual reality training improves operating room performance: results of a randomized, double-blinded study. *Annals of Surgery*, 236(4), 458.

33. Chaer, RA., DeRubertis, BG., Lin, SC., Bush, HL., Karwowski, JK., Birk, D, Kent, KC. (2006). Simulation improves resident performance in catheter-based intervention: results of a randomized, controlled study. *Annals of Surgery*, 244(3), 34

34. Iacoboni M, Woods RP, Brass M, Bekkering H, Mazziotta JC, Rizzolatti G (1999) Cortical mechanisms of human imitation. *Science*, 286(5449):2526-8.

35. Iacoboni M (2005) Neural mechanisms of imitation. *Current opinion in neurobiology*. 15(6):632-7.

36. Schwartz BL, Mastropaolo J, Rosse RB, Mathis G, Deutsch SI (2006) Imitation of facial expressions in schizophrenia. *Psychiatry Res*, 145(2-3):87-94.

37. Salvatore, G., Dimaggio, G., & Lysaker, P. H. (2007). An intersubjective perspective on negative symptoms of schizophrenia: Implications of simulation theory. *Cognitive neuropsychiatry*, 12(2), 144-164.

38. Park S, Matthews NL, Gibson C (2008) Imitation, simulation and schizophrenia. *Schizophrenia Bull*, 34 (4) 698-707. PMC2632442

39. Matthews NL, Gold B, Sekuler R, Park S (2012) Gesture imitation in schizophrenia. *Schizophrenia Bull*. 39, 94-101. PMC3523902

40. Mazza, M., Lucci, G., Pacitti, F., Pino, M. C., Mariano, M., Casacchia, M., & Roncone, R. (2010). Could schizophrenic subjects improve their social cognition abilities only with observation and imitation of social situations? *Neuropsychological rehabilitation*, 20(5), 675-703.

41. Mitchell, P., Parsons, S., and Leonard, A. (2007) Using virtual environments for teaching social understanding to 6 adolescents with Autistic Spectrum Disorders. *J Autism Dev Disord*, 37(3), 589-600.

42. Cromby, JJ., Standen, PJ., & Brown, DJ. (1996) The potentials of virtual environments in the education and training of people with learning disabilities. *J Intellectual Disability Research*, 40, 489-501.

43. Bernard-Opitz, V., Sriram, N., & Nakhoda-Sapuan, S. (2001) Enhancing social problem solving in children with autism and normal children through computer-assisted instruction. *J Autism Dev Disord*, 31(4), 377-384.

44. Burge, J., Lane, T., Link, H., Qiu, S., Clark, V.P. (2009) Discrete dynamic Bayesian network analysis of fMRI data. *Hum. Brain Mapp*. 30, 122–137.

45. Yip, BC., & Man, DW. (2013). Virtual reality-based prospective memory training program for people with acquired brain injury. *NeuroRehabilitation,* 32(1), 103-115.

46. Rose, FD., Attree, BM., Brooks, BM., Johnson, DA. (1998) Virtual environment in brain damage rehabilitation: a rationale from basic neuroscience. In: Rive, G., Wiederhold, B.K., Molinari, E. (Eds.), Virtual Environments in Clinical Psychology and Neuroscience. IOS Press, The Netherlands.

47. McGeorge, P., Phillips, LH, Crawford, JR., Garden, SE., Sala, SD., Mine, AB., Callender, JS (2001) Using virtual environment in the assessment of executive dysfunction. *Presence* 10, 375–383

48. North, MM., North, SM., & Coble, JR. (1996). *Virtual reality therapy*. IPI Press.

49. Riva, G., Bacchetta, M., Baruffi, M., Rinaldi, S., Molinari, E. (1998) Experiential cognitive therapy: a VR based approach for the assessment and treatment of eating disorders. In: Riva, G., Wiederhold, B.K. (Eds.), Virtual Environments in Clinical Psychology and Neuroscience. IOS Press, The Netherlands.

50. Riva, G. (2002) Virtual reality for health care: the status of research. *Cyberpsychol. Behav*. 5, 219–225.

51. Zhang, L., Abreu, BC., Seale, GS., Masel, B., Christiansen, CH., Ottenbacher, KJ (2003) A virtual reality environment for evaluation of a daily living skill in brain injury rehabilitation: reliability and validity. *Arch. Phys. Med. Rehabil*. 84, 1118–1124.

52. Lam, YS., Tam, SF., Man, DWK.,Weiss, PL. (2004) Evaluation of a computer -assisted 2D interactive virtual reality system in training street survival skills of people with stroke. Proc. 5th Intl Conf. Disability, Virtual Reality and Assoc.Tech., UK: Oxford.

53. Tsang, MM., Man, DW. (2013) A virtual reality-based vocational training system (VRVTS) for people with schizophrenia in vocational rehabilitation. *Schizophrenia Res*.

54. Kurtz, MM, Baker, E, Pearlson GD, Astur RS (2007) A Virtual Reality Apartment as a Measure of Medication Management Skills in Patients With Schizophrenia: A Pilot Study. *Schizophr Bull*. 33(5): 1162-1170

55. Parsons, S., Mitchell, P., & Leonard, A. (2004) The use and understanding of virtual environments by adolescents with autistic spectrum disorders. *J Autism Dev Disord*, 34(4), 449-466.

56. Strickland, D., Marcus, LM., Mesibov, GB., Hogan, K (1996) Brief report: two case studies using virtual reality as a learning tool for autistic children. *J Autism Dev Disord*, 26(6), 651-659.

57. Yang, W, Johnson, GL, Gomez, SM. (2008) Data-driven modeling of cellular stimulation, signaling and output response in RAW 264.7 cells, *Journal of Molecular Signaling*, 3,11.

58. Solomatine, DP. (2002) Data-driven modeling : paradigm, methods, experiences. *Proc. 5th Int. Conference on Hydroinformatics*, 757-763.

59. Conn, K., Warren, Z., Liu, C., Sarkar, N., & Stone, W. (2009) Adaptive Robotic Techniques in Children with Autism: Strategies for Utilizing Physiological Data to Optimize Engagement during Computer-Based Interactions. *In Proc. of International Meeting for Autism Research (IMFAR*), (Poster presentation).

60. Rani, P., Liu, C. C., Sarkar, N., & Vanman, E. (2006) An empirical study of machine learning techniques for affect recognition in human-robot interaction. *Pattern Analysis and Applications*, 9(1), 58-69.

61. Liu, C., Conn, K., Sarkar, N., & Stone, W. (2007). Online affect detection and adaptation in robot assisted rehabilitation for children with autism. In: Robot and Human interactive Communication, RO-MAN. *The 16th IEEE International Symposium.* 588-593.

62. Conn, K., Liu, C., Sarkar, N., Stone, W.L., & Warren, Z. (2008) Towards affect-sensitive assistive intervention technologies for children with autism. In: Jimmy Or (Ed.), Affective Computing: Focus on emotion expression, synthesis and recognition. 365-390.

63. Conn, K., Liu, C., Sarkar, N., Stone, W., Warren, Z. (2008) Affect-sensitive assistive intervention technologies for children with autism: An individual-specific approach. Robot and Human Interactive Communication, RO-MAN. 442–447.

64. Conn, K. (2009) Psychophysiological Analysis of Affective States in Human-Computer Interaction for Children with Autism Spectrum Disorders. Ph.D. Dissertation. Vanderbilt University, TN.

65. Agrawal P, Liu C., Sarkar, N. (2008) Interaction between human and robot: An affect-inspired approach. *Interact. Stud*. 9(2) 230-257.

66. Lacey JI, Lacey BC. (1958) Verification and extension of the principle of autonomic response-stereotypy. *American Journal of Psychology*, 71(1), 50-73.

67. Lang PJ, Bradley MM, Cuthbert BN. (2008). International affective picture System (IAPS): Affective ratings of pictures and instruction manual. Technical Report A-8. University of Florida, Gainesville, FL.

68. Cobb SVG, Nichols S, Ramsey A., Wilson JR. (1999) Virtual reality-induced symptoms and effects. *Presence,* 8, 169-186.

69. Bancroft, WJ. (1995) Research in Nonverbal Communication and Its Relationship to Pedagogy and Suggestopedia. ERIC.

70. Groden J, Diller A, Bausman M, Velicer W, Norman G, Cautela J. (2001) The development of a stress survey schedule for persons with autism and other developmental disabilities. *J Autism and Dev Disord*, 31, 207–217.

71. Spence, S. (2003) Social Skills training with children and young people: theory, evidence and practice. *Child and Adolescent Mental Health*, 8, 84-96.

72. Gresham, FM., MacMillan, DL. (1997) Social competence and affective characteristics of students with mild disabilities. *Review of Educational Research*, 67(4), 377-415.

73. Dowd T, Tierney J. (2005) Teaching Social Skills to youth. Boys Town Press.

74. Andreasen NC. (1983) The Scale for the Assessment of Positive Symptoms (SAPS). Iowa City, IA: The University of Iowa.

75. Andreasen NC. (1983) The Scale for the Assessment of Negative Symptoms (SANS). Iowa City, IA: The University of Iowa.

76. Mausbach BT, Harvey PD, Goldman SR, Jeste DV, Patterson TL (2007) Development of a brief scale of everyday functioning in persons with serious mental illness. *Schizophr Bull*. 33:1364-1372.

77. Mausbach BT, Depp CA, Cardenas V, Jeste DV, Patterson TL (2008) Relationship between functional capacity and community responsibility in patients with schizophrenia: differences between independent and assisted living settings. *Community Ment Health* J. 44:385-391

78. Bellack AS, Brown CH, Thomas-Lorhman S. (2006) Psychometric characteristics of role play assessments of social skill in schizophrenia. *Behav Ther*. 37:(4):339-352.

79. Birchwood M, Smith J, Cochrane R, Wetton S, Copestake S. (1990) The Social Functioning Scale. The development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. *Br J Psychiatry*, 157:853-9.

80. Wechsler D. (1999) Wechsler Abbreviated Scale of Intelligence™ (WASI™). Pearson.

81. Granholm E, McQuaid JR, Link PC, Fish S, Patterson T, Jeste, DV (2008). Neuropsychological predictors of functional outcome in Cognitive Behavioral Social Skills Training for older people with schizophrenia. *Schizophrenia Res*, 100(1-3), 133.

82. Betts J, Mckay J, Maruff P, Anderson V (2006). The development of sustained attention in children: The effect of age and task load. *Child Neuropsychology*, 12(3), 205-221.

83. Hammers D, Spurgeon E, Ryan K, Persad C, Heidebrink J, Barbas N, Giordani, B. (2011) Reliability of repeated cognitive assessment of dementia using a brief computerized battery. *A J Alzheimer's disease and other dementias*, 26(4), 326-333.

84. Murthy NV, Mahncke H, Wexler BE, Maruff P, Inamdar A, Zucchetto M, Alexander R (2012) Computerized cognitive remediation training for schizophrenia: An open label, multi-site, multinational methodology study. *Schizophrenia Res*, 139(1), 87-91.

85. Pietrzak RH, Olver J, Norman T, Piskulic D, Maruff P, Snyder PJ. (2009). A comparison of the CogState Schizophrenia Battery and the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Battery in assessing cognitive impairment in chronic schizophrenia. *J Clinical and Experimental Neuropsychology*, 31(7), 848-859.

86. Maruff P, Thomas E, Cysique L, Brew B, Collie A, Snyder P, Pietrzak RH. (2009). Validity of the CogState brief battery: relationship to standardized tests and sensitivity to cognitive impairment in mild traumatic brain injury, schizophrenia, and AIDS dementia complex. *Archives of Clinical Neuropsych*, 24(2), 165-178.

87. Carruthers P, Smith PK. (1996) Theories of Theory of Mind: Cambridge University Press.

88. Chartrand TL, Bargh JA (1999) The chameleon effect: the perception-behavior link and social interaction. *JPSP*, 76(6):893-910.

89. Grossman ED, Blake R (2002) Brain Areas Active during Visual Perception of Biological Motion. *Neuron*, 35(6):1167-75

90. Kim J, Park S, Blake RB (2011) Perception of biological motion in schizophrenia and healthy individuals: a behavioral and fMRI study. *PLOS One*, 6(5): e19971.PMC3098848

91. Talairach J, Tournoux P (1988). Co-planar stereotaxic atlas of the human brain. Thieme, New York

92. Cunningham JB, McCrum-Gardner E. (2007) Power, effect and sample size using G Power: practical issues for researchers and members of research ethics committees. *Evidence Based Midwifery*, *5*, 132-136.

93. Yerkes RM, Dodson JD. (1908). The Relation of Strength of Stimulus to Rapidity of Habit-Formation. *J Comparative Neurology and Psychology*, 18, 459-482.

94. Russell S, Norvig P (2003) Artificial Intelligence. A modern Approach. In S. Russell and P. Norvig (Eds.), Prentice Hall Series, New Jersey.

95. Conati C, Chabbal R, Maclaren H. (2003) A Study on using biometric sensors for monitoring user emotions in educational games. Workshop on Assessing and Adapting to User Attitudes and Affect: Why, When and How? in conjunction with User Modeling (UM-03), Johnstown, USA.

96. Mayer JS, Park S. (2012) Working memory encoding and false memory in schizophrenia and bipolar disorder in a spatial delayed response task. *J of Abnormal Psychology,* 121(3):784-794

97. Thakkar KN, Park S (2012) Impaired passive maintenance and spared manipulation of internal representations in patients with schizophrenia. *Schizophrenia Bull.* 38, 787-795 (PMID 21205676)

98. Thakkar KN, Nichols HS, McIntosh LG, Park S (2011) Disturbances in body ownership in patients with schizophrenia: evidence from the rubber hand illusion and case study of a spontaneous out-of-body experience. *PLoS One* 6(10): e27089 (PMID 22073126)

99. Peterman JS, Christensen A, Giese M, Park S (2014) Extraction of social information from gait in schizophrenia. *Psychological Medicine* 28: 1-10

100. Bell M, Bryson G, Lysaker, P. (1997). Positive and negative affect recognition in schizophrenia: a comparison with substance abuse and normal control subjects. *Psychiatry Research*, 73(1) 73-82.

101. Stroup, WW (2013). Generalized linear mixed models: Modern concepts, methods, and applications. Boca Raton, FL: CRC Press.

102. Maxwell SE, Delaney HD. (2013) Designing experiments and analyzing data: A model comparison perspective. Routledge.

103. Allison PD (2002). Missing Data. Thousand Oaks, CA: Sage.

104. Westfall PH, Young SS. (1993). Resampling-based multiple testing: Examples and methods for p-value adjustment. New York: John Wiley & Sons.

105. Fitzmaurice GM, Laird NN, Ware JH. (2004). *Applied Longitudinal analysis.* Hoboken, NJ: Wiley Interscience

106. Vonesh EF (2012). *Generalized linear and nonlinear models for correlated data: Theory and applications using SAS®*. Cary, NC: SAS Institute.

107. Mulder J, Klugkist I, van de Schoot R, Meeus WHJ, Selfhout M, Hoijtink H (2009). Bayesian model selection of informative hypotheses for repeated measurements. *J Mathematical Psychology, 53,* 530-546.

108. Durbán M, Harezlak J, Wand MP, Carroll RJ (2005) Simple fitting of subject-specific curves for longitudinal data. *Statistics in Medicine, 24,* 1153-1167.

109. Jacobson NS, Truax P (1991) Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. *J Consulting and Clinical Psychology, 59*, 12-19.

110. Evans C, Margison F, Barhkam M (1998). The contribution of reliable and clinically significant change methods to evidence-based mental health. *Evid. Based Menthal Health*, 1, 70-72.

111. Kraemer HC, Thiemann S. (1989) A strategy to use soft data effectively in randomized controlled clinical trials. *J Consulting Clinical Psychology, 57,* 148-154.

112. Maxwell, SE. (1998). Longitudinal designs in randomized group comparisons: When will intermediate observations increase statistical power? *Psychological Methods, 3,* 275-290.

113. Steiger, J.H. (2004). Beyond the F-Test: Effect Size Confidence Intervals and Tests of Close Fit in the Analysis of Variance and Contrast Analysis. Psychological Methods, 9, 164–182.

114. Cudeck R. Harring JR. (2007). Analysis of nonlinear patterns of change with random coefficient models. *Annual Review of Psychology*, 58, 615-637.

115. Gentili R, Han CE, Schweighofer N, Papaxanthis C (2010) Motor Learning Without Doing: Trial-by-Trial Improvement in Motor Performance During Mental Training. *J Neurophysiology*, 104(2), 774–783.

116. Fadiga L, Buccino G, Craighero L, Fogassi L, Gallese V, Pavesi G (1998) Corticospinal excitability is specifically modulated by motor imagery: a magnetic stimulation study. *Neuropsychologia*, 37(2), 147–158.

117. Thakkar KN, Peterman JS, Park S (2014) Altered brain activation during action imitation and observation in schizophrenia: a translational approach for studying social dysfunction. *A J Psychiatry,* 171:539-548. PMID24626638

118. Corrigan PW, Davies-Farmer RM, Stolley MR (1990) Social cue recognition in schizophrenia under variable levels of arousal. *Cognitive Therapy and Research*, 14(3), 353-361.

119. Nakamura J, Csikszentmihalyi M. (2002) The Concept of Flow. In: Handbook of Positive Psychology, SJ Lopez and CR Snyder (Eds). Oxford University Press: London.

120. Jackson SA., et al., (1998) Psychological correlates of flow in sport. *J Sport and Exercise Psychology*, 20: p. 358-378.

121. Ghani JA., Deshpande SP. (1994) Task characteristics and the experience of optimal flow in human-computer interaction. *Journal of Psychology*, 128: p. 381-391.

122. O'Neil, S. (1999) Flow theory and the development of musical performance skills. *Bulletin of the Council for Research in Music Education,* 141: p. 129-134.

123. Liu C, Rani P, Sarkar N, Chen S (2009) Dynamic Difficulty Adjustment in Computer Games Through Real-Time Anxiety-Based Affective Feedback. *Int J Human-Computer Interaction*, 25(6): p. 506-529.

124. Rani P, Liu C, Sarkar N (2008) Interaction between Human and Robot - an Affect-inspired Approach. *Interaction Studies*, 9(2): p. 230-257.

125. Lahiri U, Bekele E, Dohrmann E, Warren Z, Sarkar N (2013) Design of a Virtual Reality Based Adaptive Response Technology for Children With Autism. *IEEE Trans Neural Syst Rehabil Eng.* 21(1): 10.1109/TNSRE.2012.2218618. PMC3867261

126. Kuriakose S, Sarkar N, Lahiri U (2014) A step towards an intelligent Human Computer Interaction: Physiology-based affect-recognizer. *IHCI* 1-6

127. Baron-Cohen, S. Wheelwright, S. and Hill, J. (2001). The 'Reading the mind in the eyes' test revised version: A study with normal adults, and adults with Asperger Syndrome or High-Functioning autism. Journal of Child Psychology and Psychiatry 42:241-252

128. Verbeke, G. & Molenberghs, G. (2000) Linear mixed models for longitudinal data. New York: Springer.

129. Bekele E, Bian D, Peterman JS, Park S, Sarkar N. (in press) Comparison of Facial Emotional Expression Processing in Virtual Reality and Static IAPS pictures for adults with Schizophrenia. *Human Computer Interactions Proceedings.*

130. Pinkham, AE, Penn, DL, Green, MF, Buck, B, Healey, K, & Harvey, PD. (in press). The social cognition psychometric evaluation study: results of the expert survey and RAND panel. Schizophrenia Bulletin.

131. Bauer, D.J., Preacher, K.J., & Gil, K.M. (2006). Conceptualizing and testing random indirect effecs and moderated mediation in multilevel models. New procedures and recommendations. *Psychological Methods,* 11, 142-163.

132. Helms, R.W. (1992). Intentionally incomplete longitudinal designs: I. Methodology and comparison of some full span designs. *Statistics in Medicine,* 11*,* 1889-1913.

133. Kelly, K. (2005). The effects of nonnormal distributions on confidence intervals around the standardized mean difference: Bootstrap and parametric confidence intervals. Educational and Psychological Measurement*, 65,* 51-69

134. Maxwell, S.E., Cole, D.A., Arvey, R.D., & Salas, E. (1991). A comparison of methods for increasing power in randomized between-subjects designs. *Psychological Bulletin, 110*, 328-337.

135. Olatunji, B. O., Etzel, E., Tomarken, A., Ciesielski, B., & Deacon, B. (2011). The effects of safety behaviors on health anxiety: An experimental investigation. *Behaviour Research and Therapy, 49*, 719-728.

136. Olejnik, S., & Algina. J. (2000). Measures of effect size for comparative studies: Applications, interpretations, and limitations. *Contemporary Educational Psychology, 25,* 241-286.

137. Rosenthal, R., Rosnow, R.L., & Rubin, D.B. (2000). *Contrasts and effect sizes in behavioral research*. Cambridge UK: Cambridge University Press.

138. Selya, A.S., Rose, J.S., Dierker, L.C., Hedeker, D., & Mermelstein, R.J. (2012). A practical guide to calculating Cohen's f^2, a measure of local effect size, from PROC MIXED. *Frontiers in Psychology, 3,* article 111.

139. Snidjers, R., & Boskers, R. (1999). *Multilevel Analysis: An Introduction to Basic and Advanced Multilevel Modeling*. London: Sage.

140. Stroup, W.W. (2002). Power analysis based on spatial effects mixed models: A tool for comparing design and analysis strategies in the presence of spatial variability. *Journal of Agricultural, Biological, and Environmental Statistics, 7,* 491-511.

141. Weiss, R. E. (2005). Modeling Longitudinal Data. Springer. NY.

142. Westfall, P.H., Tobia, R.D., & Wolfinger, R.D. (2011). *Multiple Comparisons and Multiple Tests Using SAS* (2nd Ed.). Cary, NC: SAS institute, Inc.

143. van Erp, T. G., Preda, A., Nguyen, D., Faziola, L., Turner, J., Bustillo, J., et al. (2014). Converting positive and negative symptom scores between PANSS and SAPS/SANS. *Schizophrenia research*, 152(1), 289-294.

144. Harding, B., Torres-Harding, S., Bond, G. R., Salyers, M. P., Rollins, A. L., & Hardin, T. (2008). Factors associated with early attrition from psychosocial rehabilitation programs. *Community mental health journal*, 44(4), 283-288.

145. Kurtz, M. M., Rose, J., & Wexler, B. E. (2011). Predictors of participation in community outpatient psychosocial rehabilitation in Schizophrenia. *Community mental health journal*, *47*(6), 622-627.

146. Ambady, N., & Skowronski, J. (2008). First Impressions. Guilford.