**Electronic Supplementary File-3**

Schizophrenia phenomenology revisited: positive and negative symptoms are strongly related reflective manifestations of an underlying single trait indicating overall severity of schizophrenia.

Abbas F. Almulla a, Hussein Kadhem Al-Hakeim b, Michael Maes\* c, d, e

a Medical Laboratory Technology Department, College of Medical Technology, The Islamic University, Najaf, Iraq. E-mail: [abbass.chem.almulla1991@gmail.com](mailto:abbass.chem.almulla1991@gmail.com).

b Department of Chemistry, College of Science, University of Kufa, Iraq. E-mail: [headm2010@yahoo.com](mailto:headm2010@yahoo.com).

c\* Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand;

d Department of Psychiatry, Medical University of Plovdiv, Plovdiv, Bulgaria;

e IMPACT Strategic Research Centre, Deakin University, PO Box 281, Geelong, VIC, 3220, Australia.

**Results of PLS and SIMCA**

*SmartPLS*

First we tested the reflective – reflective HCM described in the statistics section. This PLS analysis was performed in subjects with MNP with age and MMSE (single indicators) predicting the main higher order construct (HOC) named “overall severity of schizophrenia” (OSOS) LV (extracted from the 8 domains). The HCM model also includes two lower order constructs (LOC) with more concrete traits, namely a first LOC extracted from PHEM symptoms and a second LOC extracted from negative symptoms. Inspection of cross-loadings showed that FTD is part of the PHEM LOC and PMR is part of the negative LOC. Finally, we also examined the association between the OSOS HOC and a general psychopathology LV extracted from ShBPRS, ShPANSSg, shHAM-D, and total HAMA-A scores. The model showed a good fit with SRMR = 0.071, and all constructs showed excellent Cronbach alpha (all > 0.858), rho\_A (all > 0.871), composite reliability (all > 0.862) and AVE (> 0.621) values while all loadings in the outer models were significant at p<0.001 and > 0.671. Nevertheless, the model lacks discriminant validity as indicated by the Fornell-Larcker ctiterion and HTMT ratio. The latter showed that discriminant validity was not established for many pairs including the PMEM and Negative (0.966), PHEM and General (0.992) and Negative and General (0.978) LOCs. There was a strong relationship between the OSOS LV and General LV scores (r=0.860, p<0.0001, n=120). We also tested other symptom combinations including psychotic symptoms (hallucinations, delusions, suspiciousness) or positive symptoms (hallucinations, delusions, excitation, hostility, and disorganized thinking) versus negative symptoms and found no discriminatory validity, yielding inadequate models.

**Table 6** shows the results of a second complete consistent PLS analysis with age and MMSE as indicators and the OSOS LV as output variable and using the factor weighting scheme on 5000 bootstrap samples. All factor scores obtained by PLS factor analysis of the symptom domains loaded highly (all > 0.707). Moreover, composite reliability and Cronbach alpha and rho\_A values were all very high (all > 0.9) while AVE was 0.682 (indicating good internal consistency reliability and convergent validity). The results of CTA support a reflective model which is in agreement with our hypothesis. Blindfolding shows a construct cross-validated communality of Q2=0.614, indicating good predictive relevance. Consequently, we have performed the same analyses in all subjects combined. Table 6 shows that all symptom domains loaded highly on the LV and that this LV has excellent internal consistency reliability and convergent validity. In the total study group, CTA supports a reflective model, while blindfolding shows a construct cross-validated communality of Q2=0.774, indicating a very good predictive relevance.

SIMCA

Using the 8 symptom domains as input variables to build PCA models we did not find any indication of outliers in the control and MNP PCA models and therefore no subjects were omitted from the models. MNP was modeled using 6 PCs, while controls were modeled using 3 PCs. All input variables showed significant modeling power in both classes (all > 0.7404) while also the discriminant power was significant, in decreasing order of power: hostility (352.2469), PMR (83.8985), excitation (48.3529), mannerism (35.7912), SANS (23.9502), FTD (17.2292), PANSSnegative (13.21411) and psychosis (11.6959). We found that the model-to-model distance was 565.73 indicating a huge separation of both classes. **ESF-2,** **Figure 5** shows the Si/S0 vs Hi plot and the distances of all subjects allocated to the test set to the critical limits of the control class, as well as their leverage to the same class. All MNP and control subjects were correctly authenticated as belonging to their target class while no aliens could be detected (e.g. MNP subjects intruding the critical limits of the control class). In addition, no outsiders were detected and also the classification table showed that all cases were correctly classified yielding an accuracy of 100%. We performed a second SIMCA whereby the MNP class (training set) was modeled with hostility, PMR, excitation, mannerism, and psychosis and projected the test set into this SIMCA model. We found that 57 MNP patients were correctly authenticated as belonging to the MNP class while 3 cases fell outside the critical limits, one with an increased distance to the model and 2 who showed increased leverage. Since no outsiders were detected and no aliens (controls intruding the MNP class) the sensitivity of these symptom domains for MNP was 95% and specificity 100%. We performed a third SIMCA analysis whereby the SANS negative symptom subdomains (flattening, alogia, apathy, anhedonia, and attention) were used to model MNP. Projecting the subjects of the test set into the target class showed that 51 MNP cases were authenticated as belonging to the target class while 8 cases showed an increased distance to the MNP model and one an increased leverage. Since there were no aliens (controls intruding the MNP class), the sensitivity is 85% with a specificity of 100%.