The New York Assessment of Adverse Cognitive Effects of Neuropsychiatric Treatment (NY-AACENT)

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Methodological Question

Is the NY-AACENT a valid measure for evaluation of cognitive side effects in adolescents with schizophrenia?

Introduction (Aims)

- Adverse cognitive side effects of medication may impact the treatment and functional capacity of patients with schizophrenia[1].
- While there are well-established instruments to assess cognitive performance in schizophrenia, there is a lack of scales that focus on medication side-effects on cognition, particularly in adolescents.
- The *New York Assessment for Adverse Cognitive Effects of Neuropsychiatric Treatment* (**NY-AACENT**) was developed in response to regulatory concerns on drug-induced cognitive impairment in adolescents participating in clinical trials.
- We examined the validity of the **NY-AACENT**, an instrument designed to assess the severity of cognitive side effects of antipsychotic drugs on adolescents.

Methods

- The study participants consisted of 146 randomized adolescent outpatients ages 13 to 17 years old, with a current diagnosis of schizophrenia participating in a multicenter, double-blinded, placebo controlled, randomized withdrawal design trial of aripiprazole (treatment=98, placebo=48)[2].
- The **NY-AACENT** was used to identify changes in cognition associated with medication side effects.
- The **NY-AACENT** consists of seven items, each is derived from the domains identified by the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS)[3] (see Figure 1).
- The **NY-AACENT** has three components: a patient form, caregiver form, and clinician form. The first two components are completed by a clinician on the basis of separate evaluations with a patient and caregiver. The last component is completed by the interviewer on the basis of interview information, clinical judgement, and collateral sources (Table 1).
- The **NY-AACENT** summary scores from the clinician form was analyzed for this study.
- Construct validity of the **NY-AACENT** was assessed by examining convergent and discriminant validity. Convergent validity was tested using Pearson's correlation coefficients (r) between selected **NY-AACENT** items and conceptually-related items of the UKU side effect rating scale[4,5]. Discriminant validity was assessed using the Positive and Negative Syndrome Scale (PANSS)[6].
- In addition, we investigated the correlations between cognitive side-effects and quality of life as measured with the PQ-LES-Q[7]. As the PQ-LES-Q has opposite score rankings versus other scales in this analysis, PQ-LES-Q scores were reversed for comparison.

Results

- The two-way ANCOVA indicated a significant main effect for treatment ($p < .001$) and interaction between treatment and visit ($p = 0.002$), and an insignificant main effect for visit ($p = 0.643$) (Figure 2). The covariate (item) significantly influenced the severity scores ($p < .001$). These results indicate that the placebo group had lower severity scores than the treatment group. Although the difference of the severity scores between the two groups fluctuate across visits, the **NY-AACENT** tracks valid cognitive side effects.
- Convergent and discriminant validity were assessed by calculating the correlation coefficients between the instruments at baseline visit of the double-blind maintenance phase (Table 2).
- Fair to good convergent validity was demonstrated by significant correlations between the **NY-AACENT** and the UKU cognition items at baseline visit: Working Memory ($r = 0.71$), Verbal Memory ($r = 0.73$), and Visual Memory ($r = 0.64$) were correlated with Failing Memory (item 1.4 from the UKU). Attention ($r = 0.70$) was correlated with Concentration Difficulties (item 1.1 from the UKU).
- Discriminant validity versus the PANSS showed moderate-low or no correlations, indicating that **NY-AACENT** items differentially characterize cognitive side-effects, rather than other symptoms of schizophrenia.
- The correlation coefficients of the **NY-AACENT** and the PQ-LES-Q were low to moderate, except for two **NY-AACENT** items (i.e., speed of processing and social cognition).

Conclusions

- The results of preliminary statistical analyses suggest that the **NY-AACENT** has the potential to be a valid and useful psychiatric instrument to evaluate the presence and severity of cognitive side effects in adolescents being treated with antipsychotic agents.
- The **NY-AACENT** demonstrated strong correlations against a validated side effect scale and weak correlations with the disease severity scale, suggesting the scale measures what it claims to measure.
- Moreover, compared to measures evaluating QoL, some item correlations were negative with non-significant p-values, indicating side effects may not affect QoL in some domains.
- Further factor analysis and Principal Component Analysis are needed to group items that measure a common construct and remove non-efficient items. Ongoing studies will address the reliability of the **NY-AACENT**.

References

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Patient Form / Parent Form

1. Do you have trouble remembering things that people (parents, teachers, friends) have said to you, immediately after you hear them?	Patient has trouble remembering things that people (parents, teachers, friends) have just said immediately after hearing them?
☐ Not Present	☐ Not Present
☐ A little bit bothersome / a **mild** problem	☐ A little bit bothersome / a **mild** problem
☐ Somewhat bothersome / a **moderate** problem	☐ Somewhat bothersome / a **moderate** problem
☐ Quite bothersome / a **severe** problem	☐ Quite bothersome / a **severe** problem
☐ Very bothersome / an **extreme** problem	☐ Very bothersome / an **extreme** problem

Clinician Form

1. **Working Memory:** Trouble remembering things that people (parents, teachers, friends) have just said?				
☐ Present During Past Week	☐ Evident During Visit	☐ Not Drug Related	☐ Mild	☐ Functional/ Role Impairment
☐ Not Present in Past Week	☐ Not Evident During Visit	☐ Due to Study Drug	☐ Moderate	☐ No Functional/ Role Impairment
		☐ Other Drug	☐ Severe	☐ Not Applicable
		☐ Drug/Drug Interaction	☐ Extreme	
		☐ Not Applicable	☐ Not Applicable	

Table 1. Example of NY-AACENT item: Item 1 Working Memory

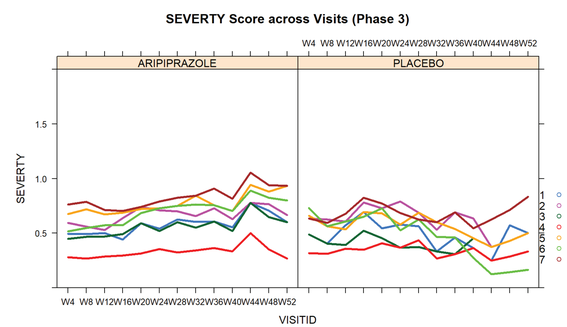

Figure 1. Severity Item Score across Phase 3 Visits
*Note: 1=Working Memory; 2=Attention/Vigilance, 3=Verbal Learning/Memory, 4=Visual Learning/Memory, 5=Reasoning & Problem Solving, 6=Speed of Processing, and 7=Social Cognition.

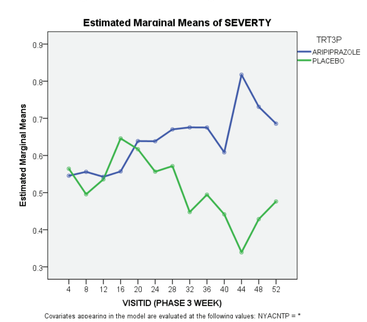

Figure 2. Estimated Marginal Means of Severity Scores overtime across Treatment Groups

Convergent and Discriminant Validity at Baseline Visit

Items	Correlation Coefficient
Item 1, Working Memory	
UKU 1.4, Failing Memory	0.709
Item 2, Attention/Vigilance	
UKU 1.1, Concentration Difficulties	0.695
PQLESQ 12, Paying Attention	0.310
PANSS G11, Poor Attention	0.457
Item 3, Verbal Learning/Memory	
UKU 1.4, Failing Memory	0.729
PQLESQ 3, School or Learning	0.173
PANSS N6, Lack Of Spontaneity And Flow Of Conversation	0.003
PANSS N7, Stereotyped Thinking	-0.188
Item 4, Visual Learning/Memory	
UKU 1.4, Failing Memory	0.642
PQLESQ 3, School or Learning	0.155
PANSS N6, Lack Of Spontaneity And Flow Of Conversation	0.033
Item 5, Reasoning/Problem Solving	
PQLESQ 8, Getting Things Done	0.196
PANSS N5, Difficulty In Abstract Thinking	0.110
PANSS P2, Conceptual Disorganization	0.047
Item 6, Speed of Processing	
PQLESQ 13, Your Energy Level	0.016
UKU 1.2, Asthenia/Lassitude/Increased Fatiguability	0.278
PANSS G7, Motor Retardation	0.044
Item 7, Social Cognition	
PQLESQ 5, Getting Along With Friends	-0.037
PQLESQ 6, Getting Along With Your Family	0.088
PANSS G16, Active Social Avoidance	0.378
PANSS N2, Emotional Withdrawal	0.300
PANSS N3, Poor Rapport	-0.114
PANSS N7, Stereotyped Thinking	0.005

Table 2.