Schizophrenia Research xxx (xxxx) xxx

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Older versus middle-aged adults with schizophrenia: Executive functioning and community outcomes

Anjana Muralidharan [a, b, *], Anastasia Finch [a, 1], Christopher R. Bowie [c, d], Philip D. Harvey [e, f]

[a] VA Capitol Healthcare Network, Mental Illness Research Education and Clinical Center, 10 N. Greene Street, Baltimore, MD, 21201, USA
[b] Department of Psychiatry, University of Maryland School of Medicine, 655 W. Baltimore Street, Baltimore, MD, 21201, USA
[c] Department of Psychology, Department of Psychiatry, Queen's University, Kingston, ON, K7L3N6, Canada
[d] Center for Addiction and Mental Health, Toronto, ON, Canada
[e] Department of Psychiatry, Leonard M. Miller School of Medicine, 1120 NW 14th Street, Miami, FL, 33136, USA
[f] Research Service, Bruce W. Carter Miami VA Medical Center, 1201 NW 16th Street, Miami, FL, 33125, USA

ARTICLE INFO

Article history:
Received 10 October 2019
Received in revised form
31 October 2019
Accepted 3 November 2019
Available online xxx

Keywords:
Schizophrenia
Older adults
Executive function
Community functioning
Functional capacity

To the editors:

Older individuals with schizophrenia experience significant psychiatric, medical, and psychosocial challenges and are at elevated risk for early institutionalization (Cohen et al., 2015). Adults with schizophrenia exhibit cognitive impairment across the lifespan, and the age-associated burden of cognitive changes is substantially greater in this group compared to the general population (Loewenstein et al., 2012).

Impairment in executive function is thought to be a core component of schizophrenia (Wobrock et al., 2009); few studies have examined the impact of aging on this construct in this group. In one cross-sectional study, people with schizophrenia in their 40's and 50's exhibited greater impairment in executive functioning and overall cognitive function than those in their 20's and 30's (Mosiołek et al., 2016). Whether executive functioning is even worse among individuals with schizophrenia with increased ages, such as those in their 60's and 70's, is unknown.

The current study compared community-dwelling adults with schizophrenia above and below 60 on tests of executive functioning. A younger age cut-off is commonly used in this population due to a shortened life expectancy (Walker et al., 2015). We hypothesized that the above 60 group would exhibit worse performance. In exploratory analyses, controlling for global cognitive impairment, we examined whether executive function differentially impacts community functioning, as measured by performance-based assessments and clinician report, among older versus younger individuals.

The current study utilized baseline data from a longitudinal dataset of community-dwelling adults with schizophrenia (Bowie et al., 2006), recruited through outpatient programs within academic, state, and VA centers. Inclusion criteria were a diagnosis of schizophrenia or schizoaffective disorder, active symptomatology, and a Mini-Mental Status Exam above 18 (MMSE; Folstein et al., 1975). Participants were excluded for medical illness that could impact cognition. All participants 40 and above were included in the present analyses (N = 245); see Table 1.

The Positive and Negative Syndrome Scale (PANSS; Kay, 1991), a structured clinical interview, was used to assess positive and negative symptoms and general psychopathology (PANSS Total). Participants completed a comprehensive neurocognitive battery, including two assessments of executive functioning: the Wisconsin Card Sorting Test, categories completed (WCST-Cat; Heaton et al., 1993) and the Trail Making Test Part B, a measure of mental flexibility (TMT-B; Reitan, 1955). Functional outcomes were measured using (1) the UCSD Performance-Based Skills Assessment (UPSA Total; Patterson et al., 2001), which assesses performance across functional skill domains through role-plays (Bowie et al., 2006), and (2) the Specific Level of Function Scale (Harvey et al., 2011), a clinician-rated measure which assesses community functioning;

* Corresponding author. VA Capitol Healthcare Network, Mental Illness Research Education and Clinical Center, 10 N. Greene Street, Attn: MIRECC (Annex Bldg), Baltimore, MD 21201.
E-mail address: anjana.muralidharan2@va.gov (A. Muralidharan).
[1] Dr. Finch is presently at Triangle Neuropsychology Services, 3310 Croasdaile Drive, Suite 400, Durham, NC 27705.

https://doi.org/10.1016/j.schres.2019.11.001
0920-9964/Published by Elsevier B.V.

Table 1
Demographics and Descriptive Statistics by Age Group (N = 245).

Variable	Below 60 Years (n = 181)	60 and Above (n = 64)
	N (%)	N (%)
Gender		
Male	136 (75.1%)	42 (65.6%)
Female	42 (23.2%)	22 (34.4%)
Race		
White	84 (46.4%)	44 (68.8%)
African-American	59 (32.6%)	12 (18.8%)
American Indian/Alaskan Native	2 (1.1%)	1 (1.6%)
Multiracial	12 (6.6%)	1 (1.6%)
Marital Status		
Never married	90 (49.7%)	34 (53.1%)
	M (SD)	**M (SD)**
Age (Years)	51.83 (5.16)	67.82 (7.15)
Education (Years)	12.69 (2.34)	12.59 (3.14)
[a]PANSS Total	40.85 (10.22)	38.35 (12.34)
[b]Non-EF Cognitive Composite**	.12 (0.84)	-.55 (1.20)
[c]TMT-B**	152.41 (60.36)	176.11 (58.96)
[d]WCST-Cat	1.17 (1.36)	0.81 (1.01)
[e]UPSA Total	74.82 (15.79)	70.53 (19.80)
[f]SLOF-Fx*	105.30 (13.36)	98.61 (18.48)

Notes. PANSS = Positive and Negative Syndrome Scale; Non-EF Cognitive Composite = Non-Executive Function Cognitive Composite; TMT-B = Trail Making Test Part B; WCST-Cat = Wisconsin Card Sorting Test, Categories Completed; UPSA = University of California San Diego Performance-Based Skills Assessment; SLOF = Specific Levels of Functioning scale.
* Significant difference between age groups on Mann-Whitney U Tests at $p < .05$.
** Significant difference between age groups on Mann_Whitney U Tests at $p < .001$.
[a] PANSS total score with higher scores reflecting more severe psychopathology.
[b] Factor score reflecting a composite of the following neuropsychological tests: Letter-Number Sequencing, Digit Span, Verbal Fluency, Rey Auditory Verbal Learning Test, Animal Naming, Boston Naming Test, Trail Making Test Part A, and Digit Symbol.
[c] Scores can range from 0 to 240 s, with higher scores reflecting more impaired performance.
[d] Scores can range from 0 to 6, with lower scores reflecting more impaired performance.
[e] Scores can range from 0 to 100, with higher scores reflecting higher functional capacity.
[f] Scores can range from 24 to 120 with lower scores indicating more assistance is needed to perform functional skills.

for the present study, a composite of interpersonal relationships, work skills, and daily activities domains (SLOF-Fx) was utilized.

To calculate a measure of global cognitive impairment, excluding executive function, unrotated principal components analysis was utilized to create a factor score (Non-EF Cognitive Composite) from the following neuropsychological measures: animal naming, phonemic fluency (F-A-S), digit span, digit symbol, letter-number sequencing, the Boston Naming test, Trail Making Test Part A, and total learning from trials 1–5 of the Rey Auditory Verbal Learning Test. Mann-Whitney U tests were conducted to compare participants above and below 60 years on PANSS Total, Non-EF Cognitive Composite, WCST-Cat, TMT-B, UPSA Total, and SLOF-Fx. Next, a regression-based bootstrapped approach to linear moderation (Hayes, 2013) was used to examine age (above/below 60) as a moderator of the relationships between executive function (WCST-Cat, TMT-B) and functional outcomes (UPSA Total, SLOF-Fx), controlling for psychiatric symptoms (PANSS Total) and global cognitive impairment (Non-EF Cognitive Composite). Analyses were conducted using IBM SPSS Version 24.0.

Descriptive statistics are in Table 1. See Table 2 and 3 in supplementary materials for bivariate correlations separated by group. There was a significant difference between individuals older and younger than 60 on Non-EF Cognitive Composite ($U = 2{,}980$, $p = .002$), TMT-B ($U = 6526.00$, $p = .009$), and SLOF-Fx ($U = 2944.00$, $p = .031$). There were no other significant differences between age groups.

Moderation analyses controlled for PANSS Total and Non-EF Cognitive Composite. There was a significant effect of age on the relationship between TMT-B and UPSA Total ($b = -0.24$; 95% CI [-0.4652, −0.0281]; bootstrap $p = .027$), with TMT-B significantly predicting UPSA Total among older ($B_1 = -0.35$, $p = .002$) but not younger ($B_2 = -0.10$, $p = .126$) participants. There was a significant effect of age on the relationship between TMT-B and SLOF-Fx ($b = -0.43$; 95% CI [-0.7678, −0.1014]; bootstrap $p = .011$), with TMT-B significantly predicting SLOF-Fx among younger ($B_0 = 0.27$, $p = .004$) but not older ($B_1 = -0.16$, $p = .347$) participants. There was a significant effect of age on the relationship between WCST-Cat and UPSA Total ($b = 0.3426$; 95% CI [0.0722, 0.6130]; bootstrap $p = .013$), with WCST-Cat predicting UPSA Total among older ($B_1 = 0.32$, $p = .016$) but not younger ($B_0 = -0.03$, $p = .640$) participants. There was a trend for an effect of age on the relationship between WCST-Cat and SLOF-Fx ($b = 0.3966$; 95% CI [-0.0491, 0.8423]; bootstrap $p = .081$), with a trend for a stronger relationship among older ($B_1 = 0.35$, $p = .102$) versus younger ($B_0 = -0.04$, $p = .634$) participants.

The present study found that older individuals with schizophrenia showed greater impairment in community functioning and mental flexibility, compared to middle-aged individuals with schizophrenia. This extends findings from Mosiolek and colleagues (2016) and suggests worsening deficits in executive function among geriatric adults with schizophrenia when compared to middle-aged groups.

Results from moderation analyses suggest executive functioning plays a larger role in functioning as individuals with schizophrenia age. Executive dysfunction was generally more strongly associated with poorer functional outcomes among older versus younger participants, controlling for global cognitive function. Younger individuals may have been better able to overcome executive function deficits by drawing on additional resources, such as social support.

Limitations of this study must be noted, including the cross-sectional design and the fact that executive function assessment consisted of only two measures.

In summary, older adults with schizophrenia and executive dysfunction may be in particular need of targeted intervention. Cognitive skills training has been shown to improve cognitive flexibility and problem-solving skills among older adults (Nguyen et al., 2019) and adults with schizophrenia (Wykes et al., 2011);

Please cite this article as: Muralidharan, A et al., Older versus middle-aged adults with schizophrenia: Executive functioning and community outcomes, Schizophrenia Research, https://doi.org/10.1016/j.schres.2019.11.001

these approaches could be tailored and leveraged to improve outcomes among older adults with schizophrenia.

Contributors

Dr. Harvey obtained the research funding and designed the overall study with Dr. Bowie. Dr. Bowie supervised data collection. Drs. Muralidharan and Finch conceptualized the research question and conducted data analyses. Dr. Muralidharan oversaw the writing of the manuscript. All four authors contributed to the writing of this manuscript. All authors contributed to and have approved the final manuscript.

Role of the funding source

This research was funded by NIMH grant MH 63116 to Dr. Harvey and the U.S. Department of Veterans Affairs VISN 3 MIRECC. Dr. Muralidharan is supported by VA Rehabilitation Research and Development Career Development Award IK2RX002339. The funding sources had no role in the study design, in the collection, analysis and interpretation of data, in the writing of the report, or in the decision to submit the article for publication.

Declaration of competing interest

Dr. Muralidharan and Dr. Finch have no conflicts of interest to report with regard to this work. Dr. Harvey has received consulting fees or travel reimbursements from Alkermes, Boehringer Ingelheim, Intra-Cellular Therapies, Minerva Pharma, Otsuka America, Regeneron Pharma, Roche Pharma, Sunovion Pharma, Takeda Pharma, and Teva during the past year. He receives royalties from the Brief Assessment of Cognition in Schizophrenia. He is chief scientific officer of i-Function, Inc. He has a research grant from Takeda and from the Stanley Medical Research Foundation. Dr. Bowie has received consulting fees from Boehringer Ingelheim, Lundbeck Pharma, Otsuka Digital Health, and Takeda Pharma. He has received grant support from Lundbeck, Pfizer, and Takeda.

Acknowledgements

This research was funded by NIMH grant MH 63116 to Dr. Harvey and the U.S. Department of Veterans Affairs VISN 3 MIRECC. Dr. Muralidharan is supported by VA Rehabilitation Research and Development Career Development Award IK2RX002339. This manuscript is result of work supported with resources and the use of facilities at the U.S. Department of Veterans Affairs VISN 5 MIRECC. All authors who contributed to this paper are listed as authors. No professional medical writer was involved in any portion of the preparation of the manuscript. This work reflects the authors' personal views and in no way represents the official view of the Department of Veterans Affairs or the U.S. Government.

Appendix ASupplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2019.10.058.

References

Bowie, C.R., Reichenberg, A., Patterson, T.L., Heaton, R.K., Harvey, P.D., 2006. Determinants of real-world functional performance in schizophrenia subjects: correlations with cognition, functional capacity, and symptoms. Am. J. Psychiatry 163 (3), 418–425.

Cohen, C.I., Meesters, P.D., Zhao, J., 2015. New perspectives on schizophrenia in later life: implications for treatment, policy, and research. Lancet Psychiatr. 2 (4), 340–350.

Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J. Psychiatr. Res. 12 (3), 189–198.

Harvey, P.D., Raykov, T., Twamley, E.W., Vella, L., Heaton, R.K., Patterson, T.L., 2011. Validating the measurement of real-world functional outcomes: phase I results of the VALERO study. Am. J. Psychiatry 168 (11), 1195–1201. https://doi.org/10.1176/appi.ajp.2011.10121723.

Hayes, A.F., 2013. Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach. Guilford Press, New York.

Heaton, R.K., Chelune, G.J., Talley, J.L., Kay, G.G., Curtiss, G., 1993. Wisconsin Card Sort Test Manual: Revised and Expanded. Psychological Assessment Resources, Odessa, FL.

Kay, S.R., 1991. Positive and Negative Syndromes in Schizophrenia Assessment and Research. Brunner/Mazel Inc., New York.

Loewenstein, D.A., Czaja, S.J., Bowie, C.R., Harvey, P.D., 2012. Age associated differences in cognitive performance in older patients with schizophrenia: a comparison with healthy older adults. Am. J. Geriatr. Psychiatry 20, 29–40.

Mosiołek, A., Gierus, J., Koweszko, T., Szulc, A., 2016. Cognitive impairment in schizophrenia across age groups: a case–control study. BMC Psychiatry 16 (1), 37.

Nguyen, L., Murphy, K., Andrews, G., 2019. Cognitive and neural plasticity in old age: a systematic review of evidence from executive functions cognitive training. Ageing Res. Rev. 53, 1009–1012. https://doi.org/10.1016/j.arr.2019.100912.

Patterson, T.L., Goldman, S., McKibbin, C.L., Hughs, T., Jeste, D.V., 2001. UCSD performance-based skills assessment: Development of a new measure of everyday functioning for severely mentally ill adults. Schizophr. Bull. 27 (2), 235–245.

Reitan, R.M., 1955. The relation of the Trail Making Test to organic brain damage. J. Consult. Clin. Psychol. 19 (5), 393–394. https://doi.org/10.1037/h0044509.

Walker, E.R., McGee, R.E., Druss, B.G., 2015. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. JAMA psychiatry 72 (4), 334–341.

Wobrock, T., Ecker, U.K., Scherk, H., Schneider-Axmann, T., Falkai, P., Gruber, O., 2009. Cognitive impairment of executive function as a core symptom of schizophrenia. World J. Biol. Psychiatry 10 (4–2), 442–451.

Wykes, T., Huddy, V., Cellard, C., McGurk, S.R., Czobor, P., 2011. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. Am. J. Psychiatry 168 (5), 472–485.