Schizophrenia Research xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Schizophrenia Research

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

A prospective analysis of the role of cognition in three models of aging and schizophrenia

Carl I. Cohen *, Tessa Murante

SUNY Downstate Medical Center, Brooklyn, NY, United States

ARTICLE INFO

Article history:
Received 6 April 2017
Received in revised form 12 June 2017
Accepted 14 June 2017
Available online xxxx

Keywords:
Schizophrenia
Cognitive functioning
Geriatrics
Elderly
Aging
Accelerated aging

ABSTRACT

Objectives: This study uses longitudinal data from a sample of older adults with schizophrenia spectrum disorder (OAS) to examine the role of cognition in 3 models of aging and schizophrenia–accelerated aging, paradoxical aging, and heterogeneity of course—and their clinical relevance.
Methods: The sample consisted of 103 community-dwelling persons aged 55 and over (mean = 61 years) with early-onset schizophrenia. Mean follow-up was 52.5 months (range: 12–116 months); 55% were men; 55% were white. We identified 21 potential predictor variables and used the Dementia Rating Scale (DRS) to assess cognition.
Results: There were no significant differences in the DRS at baseline (T1) and follow-up (T2). However, 20%, 22% and 58% of persons exhibited >0.5 effect size increase or decrease, or no change in their DRS scores, respectively; 19% were rapid decliners (>−2.11 pts/year) and 19% were rapid improvers (>+2.11 pts/year). In multivariable analysis, there were 3 predictors of higher DRS (T2): DRS (T1), decline in anxiety score, and race (white).
Conclusions: The heterogeneity model best characterized the trajectory of cognition in later life. The accelerated aging model did not represent typical cognitive trajectories since most individuals were stable or improved. The heterogeneous trajectories made it difficult to generalize about cognition's role in the paradoxical aging model. Despite the paucity of predictors, our findings suggested that it may be clinically productive to enlist remediation strategies that target anxiety and cognition, and direct more attention to non-white OAS.

1. Introduction

An understanding of cognition in older adults with schizophrenia (OAS) requires an appreciation of its role in three overlapping models of aging and schizophrenia. First, "accelerated aging" refers to the increased physical morbidity, mortality, and possible biomarkers of aging found in persons with schizophrenia (Jeste et al., 2011). Within this model, cognitive decline has been re-conceptualized from a neurodegenerative ("dementia praecox") to a neurodevelopmental trajectory in which most cognitive deficits occur early in the disorder followed by a slow downward slope more akin to that of non-mentally ill older adults (Ekerholm et al., 2012; Friedman et al., 2001; Harvey et al., 1995; Heaton et al., 2001; Irani et al., 2011; Jeste et al., 2011; Palmer et al., 2003; Rajji and Mulsant, 2008; Savla et al., 2006). However, some studies, especially of persons with long institutional histories, found more accelerated decline especially after age 65 as well as modestly higher rates of dementia in OAS (Friedman et al., 2001; Harvey, 2014; Harvey et al., 2010; Rajji and Mulsant, 2008), although the findings did not suggest patterns typical of Alzheimer's disease (Harvey et al., 2010).

Second, "paradoxical aging" refers to the concurrent decline in physical health and cognition with an improvement in subjective quality of life and psychosocial functioning (Jeste et al., 2011). This paradox is thought to be even more pronounced in OAS in which there are higher rates of mortality and physical disease in tandem with a trend towards fewer relapses, higher rates of clinical remission, and better self-management. It is not entirely clear as to what pattern cognition assumes in this model. For example, since diminished positive and negative symptoms have been found to be associated with better cognitive functioning (Friedman et al., 2001; Thompson et al., 2013), it is plausible that in some instances cognition might improve or remain stable if clinical symptoms attenuate in later life.

Third, "heterogeneity of course" refers to the various trajectories and outcomes found in schizophrenia (Shmukler et al., 2015). Recent longitudinal studies of OAS have found not only diverse outcomes but fluctuations in clinical course and life quality measures in later life among an appreciable proportion of people (Cohen and Iqbal, 2014; Cohen et al., 2015). This is in contradistinction to earlier observations that schizophrenia attains a "quiescent "or "stable" end-stage (Belitsky and McGlashan, 1993; Ciompi, 1980). Further clarification is needed with respect to cognition since several preliminary studies found varying

* Corresponding author at: Division of Geriatric Psychiatry, SUNY Downstate Medical Center, MSC1203, 450 Clarkson Avenue, Brooklyn, NY 11203-2098, United States.
E-mail address: carl.cohen@downstate.edu (C.I. Cohen).

http://dx.doi.org/10.1016/j.schres.2017.06.022
0920-9964/

patterns of cognitive functioning in middle-aged and older persons with schizophrenia, with one group observing that as many participants cognitively improved as declined (about one-sixth in each category) over a 15-month period (Savla et al., 2006).

Jeste et al. (2011) urged that systematic longitudinal investigations be undertaken to disentangle the interactions between physical, cognitive, and psychosocial aging in persons with schizophrenia. A mean age criterion of 55 or greater—a demarcation typically used for "older adults" (He et al., 2015)—has been achieved by only 13 longitudinal studies (Bowie et al., 2005; Friedman et al., 2001; Friedman et al., 2002; Girard et al., 2011; Harvey et al., 1996; Harvey et al., 1999a; Harvey et al., 2010; Harvey et al., 1999b; Harvey et al., 1995; McGurk et al., 2000; Palmer et al., 2003; Putnam and Harvey, 2000; Ribe et al., 2015). For many of these studies, the time interval between follow-up observations was short with the exception of Ribe and colleagues' Danish population study; e.g., interval range for all studies: 1 year to 18 years; median 16.5 months; mode 1 year. Moreover, 11 of the 13 longitudinal studies have been with chronically institutionalized patients or mixed-setting patients, although 85% of OAS now reside in community settings (Cohen et al., 2015).

Therefore, the aim of this study is to clarify the role of cognitive functioning within the three models and their clinical relevance using prospective data (mean: 52.5 months) drawn from a community-dwelling, multi-racial sample of OAS. We will empirically approach this aim by addressing the specific items listed below:

- To determine the trajectories of cognitive functioning over the study period and to examine whether there is a more rapid cognitive decline among the oldest persons.
- To identify those factors that predict change in cognition on follow-up assessment.

2. Method

2.1. Sample

The schizophrenia sample, which was recruited from outpatient programs, day programs, and supportive residences, consisted of a stratified convenience sample of 250 persons with schizophrenia spectrum disorder aged 55 and over living in New York City who developed the disorder prior to age 45. Persons with early-onset disorder comprise about four-fifths of OAS. A description and rationale for the sample is provided in detail elsewhere (Diwan et al., 2007; Cohen and Iqbal, 2014). Participants were required to have a chart diagnosis of schizophrenia or schizoaffective disorder based on the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition-TR* criteria (American Psychiatric Association, 2000and meet a lifetime illness review adapted from Jeste and coauthors (Jeste et al., 1997). Because of the multiple instruments requiring recall of current and past activities, persons with moderate to severe cognitive impairment were excluded from the study at both the baseline and follow-up interviews; this was defined as scores of <5 on the Mental Status Questionnaire (Kahn et al., 1960). The study was approved by the institutional review board at SUNY Downstate Medical Center and each participant gave written informed consent. The initial rejection rate was 7%.

Of the original sample, we determined the status of 162 persons (65%), of whom 40 were deceased, 4 were in nursing homes, and too disabled to be interviewed, 14 refused to be interviewed, and 88 persons could not be located; 104 participated in the follow-up interview, but one person was excluded because of incomplete cognitive data. A comparison of those with complete data who participated in the follow-up study (n = 103) with those who were not included for any reason (n = 147) indicated that that were no differences at baseline between groups in terms of gender, race, median income, residential status, positive or negative symptoms, quality of life indices, anxiety scores, rates of clinical or subclinical depression, number of physical disorders, or the Dementia Rating Scale (DRS; Coblentz et al., 1973) scores; the latter being the focus of this study. There were statistically significant differences between the two groups in age (Drop-outs: 62.0 ± 5.7; follow-up group: 60.6 ± 5.2; Mann-Whitney U = 6429, df = 248, p = 0.04), although the absolute differences were small. Of the 103 persons who participated in the follow-up interviews, the mean follow-up period was 52.5 months (range: 12 to 116 months); 54% were male with 55% Caucasian, 37% African American, 8% Latino, and 1% "other." A matched community comparison group for age, race, gender, income consisting of 113 persons aged 55 years and older was identified using randomly selected block groups, without replacement, as the primary sampling unit, and is described in detail elsewhere (Diwan et al., 2007).

2.2. Instruments

Potential variables for analysis were derived from literature reviews of cross-sectional and longitudinal studies of OAS (Friedman et al., 2001; Harvey et al., 1999a; Harvey et al., 1999b; Irani et al., 2011; Kalache et al., 2015; Thompson et al., 2013) and from variables identified in the general literature on cognition and aging (Albert et al., 1995; Bolton et al., 2008; Gerretsen et al., 2014; Gulpers et al., 2016; Jedrziewski et al., 2007; Kim et al., 2012; Krueger et al., 2009; Pan et al., 2015; Pfistermeister et al., 2017; Saraçlı et al., 2015; Thomas and O'Brien, 2008). Based on these studies we identified 21 predictor variables along with 5 covariates (4 demographics – gender, age, race, education – baseline DRS scores and time interval between baseline and follow-up) (see Table 1) that were derived from the following instruments: The Positive and Negative Syndrome Scale (Kay et al., 1992), which was used to generate the positive symptom score (Items P1–P7), negative symptom score (Items N1-7), an anxiety score (Item G2), and a lack of judgment and insight score (Item G12); Center for Epidemiological Studies-Depression Scale (CES-D; Radloff, 1977); the Quality of Life Index (Ferrans and Powers, 1985); the CAGE questionnaire (Ewing, 1984), with any positive response indicating possible alcohol misuse; Cognitive Coping Strategy Scale (Cohen et al., 2011), a 7-item scale that contains items concerning reframing one's thinking about various stressors and/or trying to remain positive; the Multilevel Assessment Inventory and the Physical Self-Maintenance Scale (Lawton et al., 1982) were used to elicit a "Physical Illness Score" that represented the sum of 11 illness categories and the 8-item Instrumental Activities of Daily Living Scale (higher scores indicate better functioning); the Network Analysis Profile (Sokolovsky and Cohen, 1981) was used to generate the number of confidantes; the Financial Strain Scale (Pearlin et al., 1981), with higher scores indicating less strain. Medication Side Effects Scale that was derived from 22 questions related to neurological and autonomic side effects of medications. Items on the general questionnaire were used to determine various sociodemographic characteristics, the number of psychotropic medications being used, the age of illness onset, duration of illness, and the mean frequency of psychiatric services (scoring: daily = 7; weekly = 1; monthly = 0.25; and so forth).

To assess cognitive functioning, we used the DRS (Coblentz et al., 1973). The DRS is a widely used instrument that had excellent psychometric properties in studies of middle-aged and older adults with schizophrenia. Its 5 subscales assess the following cognitive domains: attention, initiation and perseveration, construction, conceptualization, and memory. The internal reliabilities (Cronbach's alpha) of the total DRS scores for the community comparison and schizophrenia groups were 0.76 and 0.85, respectively.

The internal reliability scores for the other scales ranged from 0.67 to 0.97. The project staff trained interviewers with the assistance of audiotapes and videotapes. Interviewers were periodically monitored using audiotapes of their interviews. The intra class correlations (ICC) ranged from 0.79 to 0.99 on these scales.

Please cite this article as: Cohen, C.I., Murante, T., A prospective analysis of the role of cognition in three models of aging and schizophrenia, Schizophr. Res. (2017), http://dx.doi.org/10.1016/j.schres.2017.06.022