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Computerized Neurocognitive Test Performance in Schizophrenia: A Lifespan Analysis

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Abstract

Objective—Computerized neurocognitive batteries based on advanced behavioral neuroscience methods are increasingly used in large-scale clinical and genomic studies. Favorable construct validity in younger schizophrenia patients has been reported, but not in older patients. New variables afforded by computerized assessments were used to clarify age-associated cognitive impairment across the lifespan.

Methods—624 patients with schizophrenia and 624 healthy comparison (HC) subjects aged 16–75 completed a 1–2 hour computerized neurocognitive battery (CNB) that assessed abstraction and mental flexibility, attention, working memory, recognition memory (verbal, facial, spatial), language, visuospatial and emotion processing. Linear mixed effects models tested for group differences in accuracy, response time, and efficiency scores. Contrasts were stratified by age.

Results—91% of older (45+) and 94% of younger (<45) groups provided “good” data quality. After controlling for parental education and project, there were significant three-way interactions for diagnosis x domain x age group on all three outcome variables. Patients performed worse than HC across all neurocognitive domains, except in the oldest group of 60+ patients. Age-stratified analyses did not show differences between younger (16–45) and older patients (45–60, 60+), except for the attention domain. Older patients’ reduced working memory efficiency was due to worse speed, not accuracy. Older patients were quicker than younger patients in processing emotions.

Conclusions—Computerized assessments are feasible in large cohorts of schizophrenia patients. There is stable and generalized neurocognitive dysfunction across the lifespan in schizophrenia, albeit with fewer differences in some domains between older patients and HC after age 60. Speed-accuracy tradeoff strategies suggest deceleration of some frontal networks and improvements in speed of emotional processing.

Keywords

Schizophrenia; neuropsychology; aging

Objective

Cognitive deficits are reliable predictors of functional impairment in schizophrenia (1). Neurocognitive test performance on cross-sectional studies have shown medium to large effect size deficits across multiple neuropsychological domains for patients with

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schizophrenia compared to age-matched comparison subjects (2,3). Much of our understanding of cognitive deficits in schizophrenia is derived from traditional neuropsychological assessment methods, which use paper-and-pencil tests based on clinical experience with brain disorders. The advent of computerized neurocognitive batteries, which are based on functional neuroimaging experiments and cognitive neuroscience, has yielded further insights. Benefits of computerized neurocognitive methods include precise measurements of response times, a major index of performance unattainable in most traditional testing formats. Because the tests are narrowly defined to tap specific behavioral domains, they can yield more relevant measures linkable to circumscribed brain systems. They are also associated with increased accuracy of stimulus timing presentation, shorter assessment times, standardized administration, automatic scoring, convenient data storage and easy transport for bedside or home access (4–7). Concerns regarding computerized assessments revolve around the equivalence with paper and pencil methods and applicability to computer naïve populations (8). Technical issues have also been raised related to operating systems, displays, mouse/keyboard sampling rates and web-based assessments that can confound accuracy of timing and stimulus presentation, although there are ways described to protect against these confounds (7).

The National Institutes of Health (NIH) Toolbox initiative, part of the NIH Neuroscience Blueprint has recognized the value of computerized assessments and is developing a battery to measure cognitive, motor, sensory, and emotional functions (<http://www.nihtoolbox.org>). Upon completion, it is anticipated that the Toolbox will provide computerized cognitive measures available for use in a variety of studies for people aged 3–85. Furthermore, several commercial as well as research based computerized batteries have been made available. Some of these batteries have been applied to schizophrenia populations and include Cogtest (<http://www.cogtest.com>), CogLab (<http://coglab.wadsworth.com>), IntegNeuro (<http://www.rhisl.com/IntegNeuro.htm>), Cogstate (<http://www.cogstate.com>), Cambridge Neuropsychological Test Automated Battery (<http://www.cantab.com/camcog/default.asp>), MINDSTREAMS Cognitive Health Assessment (<http://www.neurotrax.com>), Cognitive Drug Research (<http://www.cognitivedrugresearch.com>), WebNeuro (<http://www.brainresource.com>) and Computerized Neuropsychological Test Battery (<http://jgp.sagepub.com/cgi/content/abstract/4/4/211>). A dual-display computerized testing system has also been recently described (Computerized Multiphasic Interactive Neurocognitive Dual Display System) that reportedly integrates the examiner by utilizing multi-media capabilities for automated presentation of digitally recorded human-voice instructions, point-of-contact electronic data acquisition, comprehensive interpretive report generation, integrated project/data management utilities, and interactive examiner training modules for certification-contingent access control (9).

We have previously described a publicly available research based computerized neurocognitive battery (CNB, <https://pennncnp.med.upenn.edu>) administered to patients with schizophrenia, relatives of these patients and healthy comparison subjects (5,10,11). This battery has demonstrated good test-retest reliability and sensitivity to diagnosis (11). It has been administered in large, multisite studies investigating the genetic architecture of candidate endophenotypic markers of schizophrenia such as the Multi-Generational Investigation of Schizophrenia [MGI, (12)], the Project Among African Americans to Explore Risks for Schizophrenia [PAARTNERS, (13)], and the Consortium on the Genetics of Schizophrenia [COGS, (14)]. The battery has been associated with favorable reliability and construct validity when compared to traditional paper-pencil batteries in healthy samples (5) and shown good correlations with paper-pencil measures in schizophrenia patients (10). It has also shown significant heritability of performance across neurocognitive domains in schizophrenia (12,15,16). The battery includes a comprehensive assessment of multiple cognitive domains relevant to schizophrenia research, including abstraction and

mental flexibility, attention, working memory, memory (verbal, facial, object), language, visuospatial and emotion processing. The CNB requires approximately 4 hours of online/lecture-based training for testers, as well as practice administrations which make it relatively easy to administer and score with inbuilt automated scoring procedures. Furthermore, its availability in the public domain and web-based administration has yielded large-scale normative and disease-specific data on thousands of individuals worldwide.

While the favorable reliability and construct validity of using computerized batteries has been reported in younger cohorts of adults with schizophrenia, the use of computerized measures with older patients with schizophrenia remains unexamined. Concern regarding administration of computer evaluations with older schizophrenia patients may involve assumptions about older individuals' unfamiliarity or discomfort with computers and potential poor tolerability of the method. Yet, computerized and pencil-and-paper tests have been both feasible and useful means of assessing cognitive function in community dwelling healthy adults over the age of 85 (6). Older patients with schizophrenia represent a vulnerable group additionally burdened by the substantial personal and economic costs of aging related cognitive and functional impairments. Indeed, geriatric schizophrenia has been the most expensive among all medical disorders based on per-capita Medicare and Medicaid expenses (17). As the numbers of elderly persons with schizophrenia rises rapidly over the next several decades, the healthcare and policy implications are hard to overstate (18). Yet, the nature and magnitude of cognitive impairments in this population have comparatively received less attention, notwithstanding debates about the neurodevelopmental or neurodegenerative course of the disorder with aging.

In younger cohorts, patients show moderate to large impairments across most neuropsychological domains with effect sizes ranging from -0.46 to -1.57 (2,3,19–23). Qualitative reviews of longitudinal studies in younger cohorts have indicated either stability in cognitive impairment over a year (24), no evidence of deterioration among community-dwelling adults (25) or mixed effects with deterioration in some aspects of cognition and sparing in others (26). A subgroup of approximately 30% of patients have previously demonstrated a chronic course of institutionalization associated with progressive cognitive and functional decline suggestive of a neurodegenerative course (27). In a recent quantitative meta-analysis focusing on older patients with schizophrenia, we found that over a 1–6 year follow-up period there was no greater decline on traditional paper-pencil based neuropsychological function in older cohorts of schizophrenia patients as compared to their age-matched peers, despite the presence of large deficits in both global ($d=-1.19$) and domain specific neuropsychological function ($d=-1.04$) (28). This supported the neurodevelopmental, relative to neurodegenerative hypotheses, although it has been suggested that traditional neuropsychological tests can be insensitive to progressive impairments in late-life schizophrenia due to floor effects (29). Tests that are more sensitive to complex information processing demands have been linked to age-associated impairments in late life even in outpatients with schizophrenia (30,31).

Thus, we hoped to further extend our understanding of the relationship between aging and cognitive performance in schizophrenia by assessing effects with new variables afforded by a computerized format. We examined the performance of a large age-stratified sample of schizophrenia patients and healthy comparison subjects on the CNB. We aimed to more closely examine the impact of aging across the lifespan in schizophrenia by comparing neurocognitive performance of “younger” and “older” patients with schizophrenia. The term “older” has been used variably in previous studies and reviews of schizophrenia, but for the current study we operationally defined it as schizophrenia in an individual over the age of 45. Given previous reports of age related decline in some elderly patients with schizophrenia, we more closely examined the performance of the “older” cohort by further

stratifying it into two groups aged 45–60 and over 60. We hypothesized that the use of a computerized battery sensitive to complex information processing demands would further clarify the presence and nature of age-associated cognitive impairments later in life in schizophrenia.

Methods

Participants

624 patients with schizophrenia and 624 healthy comparison (HC) subjects were randomly selected from the pool of individuals who had completed a CNB, and balanced for age, sex and race. Participants had completed the CNB while participating in collaborative studies with a consortium of research centers for MGI, PAARTNERS and COGS. Project specific inclusion/exclusion criteria and standardized recruitment and assessment methods have been detailed previously (12–14).

Computerized Neurocognitive Battery (CNB)

The CNB is administered by trained research staff in a fixed order using clickable menus. Administration time for individual batteries varies, but is approximately one hour and up to two when many tests are included. It is administered on a desktop or laptop computer, which includes a training module and an automated scoring program with direct data downloading. Following administration, data quality is coded by the test administrator to indicate if acquired data is “good”, “questionable” or “bad”. If data is considered “questionable” or “bad”, CNB administrators also input qualitative comments about the nature of the difficulties. Upon completion of the battery, test scores are standardized (z-scores; mean 0, standard deviation 1) based on an age-matched normative group of healthy participants in the CNB database, and grouped into summary measures by combining each subject’s z-scores on tests assessing the same functional domain (32,33). Three performance indices were calculated for the current analysis: 1) accuracy (Acc)—the number of correct responses, 2) speed (RT)—the median response time for correct responses and 3) efficiency z-scores (Eff) – calculated based on the average of the accuracy and response time z-scores $[(zAcc + zRT)/2]$. A variety of cognitive domains are assessed by the CNB (12) and are described below. For the current analysis we included data from all relevant research participants, but not all participants received all tests. Examples of stimuli are provided in Figure 1. The following domains and tests were included:

Abstraction and Mental Flexibility (ABF)—The Penn Conditional Exclusion Test or PCET (34,35) presents four objects at a time, and the participant selects the object that does not belong with the other three based on one of three sorting principles (Figure 2a). Sorting principles change and feedback guides identification. The Penn Abstraction, Inhibition and Working Memory Task or AIM is a measure of abstraction and concept-formation, with and without working memory (5,35). The participant first sees two pairs of stimuli on the top of the screen and one stimulus on the mid-bottom of the screen and needs to decide with which pair the stimulus on the bottom best belongs. Feedback is provided. In the second question type, the bottom stimulus flashes for less than a second and then the two pairs of stimuli appear on the top after a delay to isolate effects of working memory capacity. RAVEN is a computer adaptation of The Raven’s Progressive Matrices, which is a multiple choice task in which the participant must conceptualize spatial, design and numerical relations that range in difficulty from very easy to increasingly complex (5,36).

Attention (ATT)—The Penn Continuous Performance Test or PCPT (37) uses a continuous performance test paradigm where the participant responds to seven-segment displays

whenever they form a digit. Working memory demands are eliminated because the stimulus is always present when the subject provides the response.

Working Memory (WMEM)—AIM (memory trials only) and Letter-N-Back Test or LNB2 (1- and 2- back). The Letter N-Back is a measure of attention and working memory. Participants are asked to pay attention to flashing letters on the computer screen, one at a time, and to press the spacebar according to three different principles or rules: the 0-back, the 1-back and the 2-back. During the 0-back, the participant must press the spacebar whenever the letter X appears on the screen. During the 1-back, the participant must press the spacebar whenever the letter on the screen is the same as the previous letter (i.e. in the series “T”, “R”, “R”, the participant should press the spacebar upon appearance of the second “R”). During the 2-back, the participant must press the spacebar whenever the letter on the screen is the same as the letter before the previous letter (i.e. in the series “T”, “G”, “T”, the participant should press the spacebar upon appearance of the second “T”).

Spatial Memory (SMEM)—The Visual Object Learning Test or VOLT/SVOLT (32) presents 20 Euclidean shapes subsequently interspersed with foils immediately and at approximately 20 minutes (See Figure 2c).

Face Memory (FMEM)—The Computerized Penn Face Memory Test (CPF) presents 20 digitized faces followed by an immediate recognition trial with targets interspersed with 20 foils equated for age, gender, and ethnicity. Participants indicate whether or not they recognize each face immediately and at approximately 20 minutes.

Verbal Memory (VMEM)—The Penn Word Memory Test (CPW) presents 20 target words followed by an immediate recognition trial with targets interspersed with 20 distracters equated for frequency, length, concreteness, and low imageability using Paivio’s norms (Figure 2b). Delayed recognition is measured at 20 minutes. The Penn List Learning Test or PLLT (5) is a measure of verbal learning and verbal memory modeled after the California Verbal Learning Test (38). The test is composed of immediate recall, short delay recall, short delay cued recall, long delay recall and long delay cued recall sessions for a series of 16 words.

Language (LAN)—Penn’s Verbal Reasoning Test (PVRT) is a brief test of verbal intellectual ability (39). It is a multiple-choice task in which the participant responds to verbal analogy problems.

Spatial Processing (SPA)—The Computerized Judgment of Line Orientation (CJOLO) is a computer adaptation of Benton’s test. Participants see two lines at an angle and indicate the corresponding lines on a simultaneously presented array.

Emotion Processing (EMO)—Identification of facial affect was tested with a 40-item Emotion Intensity Discrimination Test or EDF40 (40). Each stimulus presents two faces of the same individual showing the same emotion (happy or sad) with different intensities. The participant selects the more intense expression. Sets are balanced for gender, age, and ethnicity (See Figure 2d). The Penn Emotion Recognition Task or ER40 is a measure of emotion recognition (41). Participants are shown a series of 40 faces, one at a time, and asked to determine what emotion the face is showing for each trial (happy, sad, anger, fear and no emotion).

Statistical Analysis

Differences between groups for demographic variables were tested using 2-sample t-tests or chi-square tests. Linear mixed effects models were used to test for differences in accuracy, response time, and efficiency scores. The mixed model approach was preferred over a repeated measures analysis of variance (ANOVA) model because each subject with any missing test score is deleted in an ANOVA procedure, or imputed values are used, with each of these alternatives presenting unique problems. Each model included fixed effects for diagnosis (schizophrenia, HC group), functional domain (9 cognitive domains), age group (age<45, age 45+) and the interaction terms. Parental education and project from which data were collected were also included in the models. In addition, a random effect for subject was included which accounts for the repeated measurements from each of the domain scores from each subject. When the three way diagnosis x domain x group interaction was statistically significant, we performed pair wise comparisons of schizophrenia patients vs. HC subjects, stratified by domain, for each of the age groups ("younger" <45 and "older" 45+). We further examined differences between the younger and older patients by running difference contrasts for schizophrenia - comparison groups, stratified by domain. Bonferroni adjustments were made to the p-values for the contrasts to account for multiple comparisons ($p<0.005$). Standardized beta estimates were derived for the demographic variables. We repeated the above procedures by further age-stratifying the 45+ age group into two groups (age 45–60, 60+). Some large negative z-scores were present in the database, so our primary analysis included all available data points, but truncated any z-scores with values lower than -5 and set them equal to -5. We performed sensitivity analyses to see how the outliers impacted the results. First, we excluded any z-scores with values lower than -5, and next we included all data points with the negative outliers as calculated (i.e. without truncation). All analyses were performed using SAS version 9.1 (SAS Institute, Cary, NC).

Results

Examination of CNB administrator status codes indicated that of the valid data we collected, "good complete data" was obtained from 82% of the younger group and 76% of the older group. "Incomplete but good data" was further obtained from less than 9% of the younger group and 12% of the older group. "Questionable" or "bad" data was obtained from 6% of the younger group and 9% of the older group, which were subsequently dropped from the analyses. Qualitative reviews of the administrator comments suggest that difficulties were due to incomplete practice trials of some tests, concentration difficulties or low effort, mouse or keyboard handling difficulties, frustration or refusal to complete and motor/visual difficulties.

Table 1 shows that the older (aged 45–75) and younger (aged 16–44) groups were equally matched across demographic variables, except for parental education where HC subjects had higher levels of parental education than patients. For the sensitivity analysis, there were no significant changes to the main findings if all z-scores were included or if z-scores <5 were excluded.

After adjusting for participant's parental education and project and truncating any outliers with z-scores of < -5, the results of the mixed model analysis showed that for accuracy there was a significant three way interaction for diagnosis x domain x age group [$F(8, 8190)=3.13, p=0.0015$]. After using a Bonferroni correction ($p<0.005$), younger and older schizophrenia patients were significantly less accurate than HC subjects in all domains. The differences between domain scores for the older and younger patient groups were non-significant, except for the ATT domain where the difference between older patients and HC subjects was significantly larger than in the younger group [$t(8190)=3.53, p=0.0004$]. When further examining age-stratified effects in the older patient group, the differences

between domain scores for the 45–60 group did not differ from that of the 60+ age group. However, when compared to their respective HC group, the patients aged 45–60 had significantly reduced accuracy in all domains; yet in the oldest age group of 60+ individuals patients were significantly less accurate than HC only for ATT [$t(2601) = 3.17, p = 0.0015$] and EMO [$t(2601) = 2.89, p = 0.0039$]. Parental education was positively associated with accuracy [$F(1, 8190) = 50.52, p < 0.0001$; standardized beta = 0.14] while type of project that the data was derived from [$F(4, 8190) = 2.06, p = 0.083$] was not a significant contributor.

For response time, there was again a significant three way interaction for diagnosis x domain x age group [$F(8, 8123) = 8.88, p < 0.0001$]. Schizophrenia patients were significantly slower than HC subjects in all domains, for older and younger groups. The difference between older patients and controls was significantly greater compared to the younger group for ATT [$t(8123) = 5.08, p < 0.0001$] and WMEM [$t(8123) = 3.46, p = 0.0005$], but for EMO domain younger patients were comparatively slower than their age matched comparison group than were the older patients [$t(8123) = 2.92, p = 0.0035$]. When further examining age-stratified effects in the older patient group, the differences between domain scores for the 45–60 age group did not differ from the 60+ age group. When compared to their respective HC group, both groups of older patients performed significantly worse than their age-matched HC group on all domains. Higher parental education [$F(1, 8123) = 9.08, p = 0.0026$; standardized beta = 0.065] was associated with better performance while project [$F(4, 8123) = 2.29, p = 0.057$] was not.

For efficiency, there was again a significant three way interaction for diagnosis x domain x age group [$F(8, 8191) = 6.67, p < 0.0001$]. Younger and older schizophrenia patients had significantly reduced efficiency than their age-matched HC groups in all domains. The differences from HC between the older and younger patient groups were non-significant in all domains, except for ATT [$t(8191) = 5.35, p < 0.0001$] and WMEM [$t(8191) = 2.84, p = 0.0045$] where the differences were greater in the older patients than the younger patients. When further examining age-stratified effects in the older patient group, the differences between domain scores for the 45–60 group did not differ from that of the 60+ age group in any domain. However, when compared to their respective HC group, the patients aged 45–60 performed significantly worse on all domains; yet in the oldest age group of 60+ individuals, patients were significantly less efficient than HC only for ATT [$t(2602) = 3.87, p = 0.0001$], SMEM [$t(2602) = 3.50, p = 0.0005$] and WMEM [$t(2602) = 3.23, p = 0.0012$]. Higher parental education was positively associated with efficiency scores [$F(1, 8191) = 38.62, p < 0.0001$; standardized beta = 0.13] while project [$F(4, 8191) = 2.74, p = 0.027$] was not. Figure 2 shows CNB performance of participants stratified by age.

Conclusions

The introduction of computerized neurocognitive batteries offers more precise response time measurements, more narrowly defined behavioral domain measures, increased accuracy of stimulus timing presentation, shorter assessment times, standardized administration, automatic scoring, convenient data storage and easy transport for bedside or home access. While there are some technical and theoretical concerns raised about computerized assessments (7,8), previous work has reported favorable reliability and construct validity of using computerized measures in younger cohorts of adults with schizophrenia. Yet, the performance of older patients with schizophrenia on computerized measures has not been unexamined. Using one of the largest samples of older schizophrenia patients examined to date, we found that 94% of the younger participants and 91% of the older participants provided “good” data quality when completing a 1–2 hour long research based computerized neurocognitive battery. Qualitatively, the main difficulties in older and younger groups revolved around incomplete practice trials of some tests due to concentration difficulties or

low effort and mouse or keyboard handling difficulties. But these difficulties were only found in 9% of the older cohort and 6% of the younger cohort. Overall, this supports the feasibility of using computerized measures to assess cognition across the lifespan in schizophrenia. It may also allay concerns about older patients' unfamiliarity or discomfort with computers and potential poor tolerability of computerized assessments.

The comprehensive neurocognitive assessment also allowed further clarification of the relationship between aging and cognitive performance in schizophrenia. Our data indicated that there was significantly reduced accuracy, speed and efficiency for both younger and older schizophrenia patients when compared to their age-matched healthy comparison groups across the neurocognitive domains of the CNB. This replicates robust observations of large and generalized deficits in younger schizophrenia patients' performance on computerized neurocognitive tasks (10,11) and extends these findings to later in the lifespan. This finding is consistent with the traditional paper-pencil based literature that has also shown large global and domain specific neuropsychological dysfunction in older individuals with schizophrenia (28,42).

Further examination of age-stratified effects did not reveal significant differences in accuracy, response time or efficiency scores in the older group, aged 45–60 and those over 60 years of age. However, it is worth noting that while younger patients and those aged 45–59 performed significantly worse than their respective healthy comparison groups on all domains, in the oldest group of 60+ individuals, patients were less accurate than comparison subjects only for attention and emotion processing and less efficient in attention, working memory and spatial memory. In the remaining domains, the gap between patients and comparison groups was small and statistically non-significant. This indicates that with the noted exceptions, in the very old group there is either a normative decline in abstraction, facial memory, verbal memory, language and spatial processing or a relative improvement in patients' performance on these domains. Overall however, there appears to be stability of neurocognitive impairment across the lifetime in schizophrenia, without support for a hypothesis of widespread cognitive degeneration emerging later in life in patients with schizophrenia.

In addition to being one of the few domains that showed persistent impairment in accuracy and efficiency in patients relative to their HC group, even in the 60+ age group, the domain for attention was further notable since it showed greater reductions in both accuracy and response time, hence efficiency, for older patients relative to younger ones. Deficits in attention are often considered to be central features of the clinical presentation of schizophrenia and have garnered support as candidate endophenotypes (11). In our battery attention is assessed using the Penn Continuous Performance Test, a measure of visual sustained attention. CPT impairments have been shown in first episode patients with schizophrenia followed longitudinally even in clinically remitted states (43). Much of the prior work with older cohorts has focused on measures of brief attention like the digit span (44–46). Consistent with our findings, one prior study with older patients used auditory CPT errors as an index for sustained attention and found similar age-related decline in patients and comparison subjects (47). The apparent age related decline in this domain might reflect inefficiency of frontal networks for sustained attention. Some have suggested that the mechanism that causes cognitive aging is a general reduction in attentional resources (48) and future investigation is needed to examine whether schizophrenia is associated with greater decomposition of networks recruited in sustained attention compared to other brain systems.

The use of a computerized battery further permitted the evaluation of individual differences in strategy that are relevant for speed–accuracy tradeoffs (49). Efficiency of performance,

which reflected the degree to which participants effectively slowed their response time in order to maintain accuracy levels, provided uniquely valuable information about testing strategies. For instance, we found that compared to younger patients, older patients' lower efficiency in the working memory domain reflected reduced speed, but not accuracy. On the whole, older patients' performed at similar accuracy levels as younger patients across the neurocognitive domains of the CNB. Consistent with this finding, working memory accuracy has been stable in non-institutionalized outpatients with schizophrenia across the life span (50). A functional magnetic resonance imaging investigation of middle-aged and older patients with schizophrenia showed that even though accuracy was near normal on a spatial working memory task when the processing demands of the task were within their performance capacity, patients demonstrated an aberrant pattern of brain response (51). Thus, our observation of longer response times to complete working memory tasks by older cohorts may reflect inadequacy in the neural networks subserving working memory functions in this older group. This inefficiency appears to extend late into life, as evident in persistent impairment demonstrated by the 60+ patients.

Another domain where older patients showed a differential style of responding compared to younger patients was in emotional processing. Since emotion processing is typically not assessed in traditional neuropsychological evaluations, this is a domain that has been neglected in studies of elderly schizophrenia patients. Yet since social cognitive processes such as emotional processing act as key mediators between core (nonsocial) cognition and functional outcome (52,53), it is an area requiring further attention. In our study, surprisingly older patients were relatively quicker than younger patients when identifying and discriminating facial emotions. Previous work in younger cohorts has shown that impaired emotional functioning is a prominent feature of schizophrenia and is highly heritable (12,15). The socio-emotional selectivity theory posits that aging is associated with directed attention towards emotionally meaningful situations and goals due to perceived limitations on time (54). This could account for why older patients were more likely to provide rapid responses when making decisions about the emotions on faces. Yet, structural and functional impairments in the neural circuitry underlying emotion processing have been robustly noted in patients (55,56) and likely account for the observed stable impairments in accuracy and overall inefficiency of facial emotion recognition.

While our data do not support the hypothesis that there is a global neurodegenerative course associated with patients with lower levels of functional deficits at baseline (57), long-stay institutionalized patients were not the focus of our investigation. The current study was also limited by the presence of some outliers in our data who may have been representative of more impaired individuals. We attempted to account for these outliers by conducting a sensitivity analysis, and found no remarkable differences when outliers were excluded, truncated or included. Another limitation of our study lies in the variability for the number of subjects who completed various CNB tasks within a cognitive domain. Since this analysis was conducted with data from different projects, the tasks included in a battery varied slightly across projects. This introduces some inconsistency in the composition of the cognitive domains being assessed, yet the cognitive constructs (e.g. "verbal memory") remained consistent in our analysis. Also because the ensuing length of the batteries across projects varied slightly (from 1–2 hours) we cannot account for differential rates of fatigue and task order effects. We did however examine the impact of project in our analyses and found that it was not a significant contributor in the models. Finally, the groups in our sample were unequally matched for parental education. While parental education contributed to the overall variance in the models, effect sizes were small and cannot account for the findings.

These limitations notwithstanding, our findings indicated that older patients with schizophrenia were able to tolerate a computerized neurocognitive battery. Their performance was also consistent with a large body of prior research indicating stability of generalized neurocognitive dysfunction in patients diagnosed with schizophrenia across the lifespan. We replicated and further extended this line of work in a very large sample to show that sensitive computerized measures can provide additional information about speed-accuracy trade-off strategies used by older patients when challenged with cognitive tasks. For instance, speed of emotional processing abilities improved with age in schizophrenia, although accuracy with which emotions were identified and discriminated remained impaired throughout the lifespan. Conversely, inefficiency in working memory functions in older patients was driven by longer response times and not reduced accuracy. On a sustained attention task, older patients were less accurate and slower than younger patients. This may reflect more rapid deterioration with aging in schizophrenia of some frontal system networks involving attention and working memory, but more work is needed to further delineate the putative brain regions involved. Overall, there is stable and generalized neurocognitive dysfunction across the lifespan in schizophrenia, albeit with improvement in some domains after age 60.

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Click on the object that does not belong.

REACTION

DEFINITELY YES

PROBABLY YES

PROBABLY NO

DEFINITELY NO

YES

I have seen the shape.

NO

I have not seen the shape.

Figure 1.

Figure 2.

Table 1

Sample Demographic Characteristics

Variable	Older		Significance Test	Younger		Significance Test
	HC (n=197)	Scz (n=197)		HC (n=427)	Scz (n=427)	
Age (M + SD)	53.24±6.24	52.18 ±5.77	t(392)=1.75, p=0.08	31.13 ±7.59	31.39 +8.07	t(852)= - 0.48, p=0.63
Parental Ed (M ± SD)	12.13 ±3.38	11.35 ±3.91	t(392)=2.12, p=0.03	14.32 ±3.16	13.81 ±3.47	t(852)=2.23, p=0.02
Sex (%Ma:%Fe)	42:58	42:58	$\chi^2_1=0$	55:45	55:45	$\chi^2_1=0$
Race (%C:%AA)	42:58	42:58	$\chi^2_1=0$	43: 57	43: 57	$\chi^2_1=0$
Handedness (%R:%L:%Mi)	91:8:1	91:7:2	$\chi^2_2=0.33$, p=0.84	89:8:3	86:13:1	$\chi^2_2=5.76$, p=0.06

HC – Healthy comparison subjects; Scz – Patients with schizophrenia; M – Mean; SD – Standard deviation; Ed – Education; Ma – Male; Fe – Female; C – Caucasian; AA – African American; R – Right; L – Left; Mi – Mixed