

# Assessment of New-Onset Decline in SMI



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## Definitions of SCZ and Major NeuroCognitive Disorders

- SCZ
  - Six Month Duration of disability
  - Decline from Higher Functioning
  - Not caused by medical illness or mood disorder
- MND
  - Documented Cognitive impairments
  - Disability and decline from higher functioning
  - Not caused by delirium or mood disorder



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# Cognitive Functioning in Schizophrenia

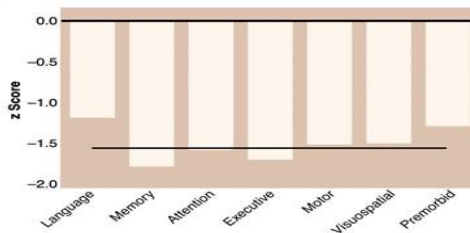
- Even in first episode patients there are multiple aspects of cognitive impairment
- Patients with schizophrenia perform poorly Across Ability Domains
  - Working and Episodic memory
  - Executive functioning
  - Attention and Processing Speed
- These impairments can be substantial at the time of the first episode
- Cognitive functioning is a major predictor of overall adaptive outcome



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## Level of Impairment at First Episode prior to treatment

**FIGURE 1. Deficits in Scores for Neuropsychological and Premorbid Abilities of 94 Patients With First-Episode Schizophrenia<sup>a</sup>**



Bilder RM et al. *Am J Psychiatry*. 2000;157(4):549-559.

<sup>a</sup> Relative to scores for healthy comparison subjects; by definition, the healthy comparison group had a mean score of zero on each scale. Premorbid ability score based on tests of general knowledge, vocabulary, and reading skill. The straight horizontal line indicates the average deficit for patients across scales (-1.53).



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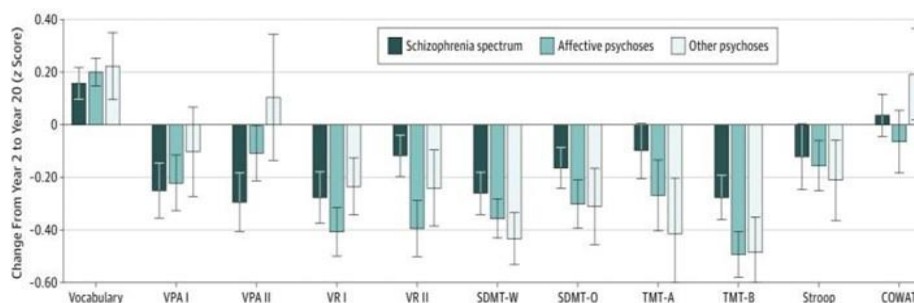
# Stability of Cognitive Impairment

- One of the hallmark features of cognitive functioning in schizophrenia is stability of impairment
- Even 20-year follow-ups find modest changes
- Normative performance is not worse when older



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## 20-Year Change in Cognitive Functioning



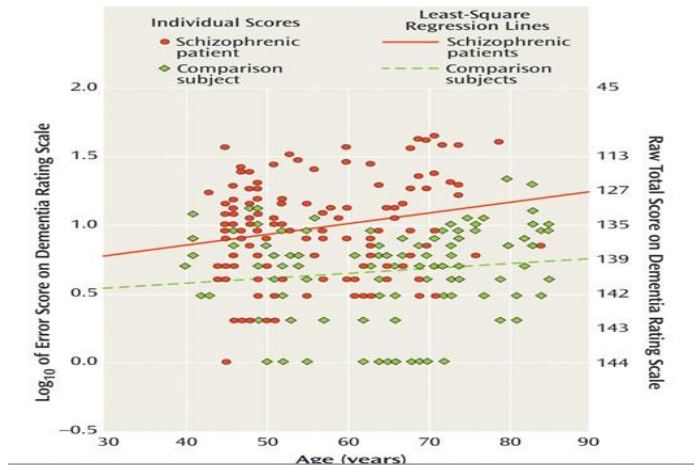
Fett AJ, et al. *JAMA Psychiatry*. 2020;77(4):387-396.  
Annualized global change:  $-0.01$  SD/Year for fluid;  $+0.01$  SD for crystallized



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## No Cross-Sectional Difference in Normative Performance Across the lifespan

FIGURE 1. Age-Related Variation in Cognitive Impairment<sup>a</sup> for 116 Older, Community-Dwelling Subjects With Schizophrenia and 122 Healthy Comparison Subjects



Eyler Zorrilla LT, et al.  
*Am J Psychiatry.*  
 2000;157(8):1324-1326.



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## Reports of Dementia in SMI

- 74,170 individuals with a diagnosis of schizophrenia
- At 66 years of age, the prevalence of diagnosed dementia was 27.9% among individuals with schizophrenia compared with 1.3% in the group without SMI. By 80 years of age, the prevalence of dementia diagnoses was 70.2% in the group with schizophrenia and 11.3% in the group without SMI.
- Stroup TS, et al. *JAMA Psychiatry.* 2021;78(6):632-641



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## It may be dementia, but it is not AD

- Purohit DP, et al. Alzheimer disease and related neurodegenerative diseases in elderly patients with schizophrenia: a postmortem neuropathologic study of 100 cases. *Arch Gen Psychiatry*. 1998;55(3):205-211.
- Although 72% of the patients with schizophrenia showed cognitive impairment, AD was diagnosed in only 9% of the patients and other dementing diseases were diagnosed in only 4% of the patients.
- In the 87 cases lacking a neuropathologic diagnosis of AD or other dementing disorders, the mean (+/-SD) Clinical Dementia Rating Scale score was 2.21 (+/-1.14), with 43 of the cases scoring 3 or higher



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## Cross Sectional Comparison: AD, SCZ, HC

- AD and Schizophrenic patients (n=66) were matched on MMSE scores, age, and relative education
- Healthy controls (n=66) were matched to AD and schizophrenic patients on relative education and age
- Davidson M et al., *Am J Psychiatry*. 1996;153(10):1274-1279.



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## Comparison of the Severity of Cognitive Deficits in AD and Schizophrenia

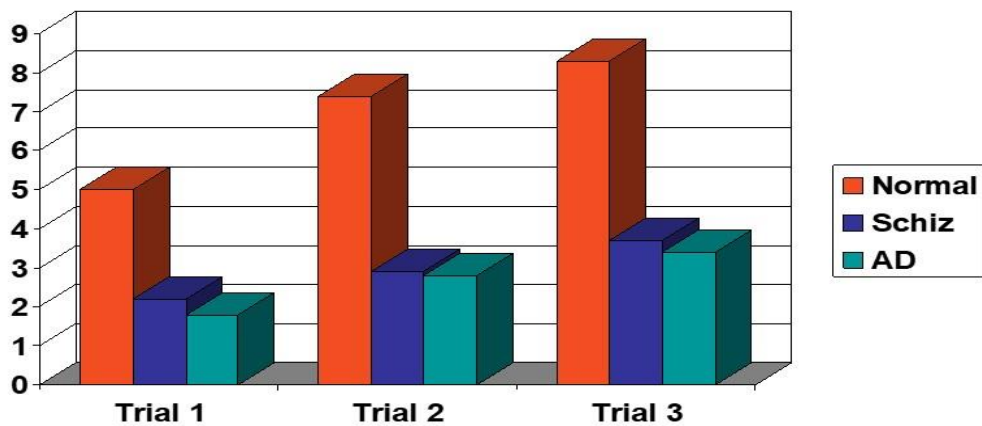
- Delayed recall Schiz > AD
- Delayed recognition Schiz > AD
- Learning rate Schiz = AD
- Verbal Skills Schiz < AD
- Executive Functions Schiz < AD
- Praxic Skills Schiz < AD

Davidson et al., 1996



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## Verbal Learning: Schizophrenia vs. AD vs. Normal

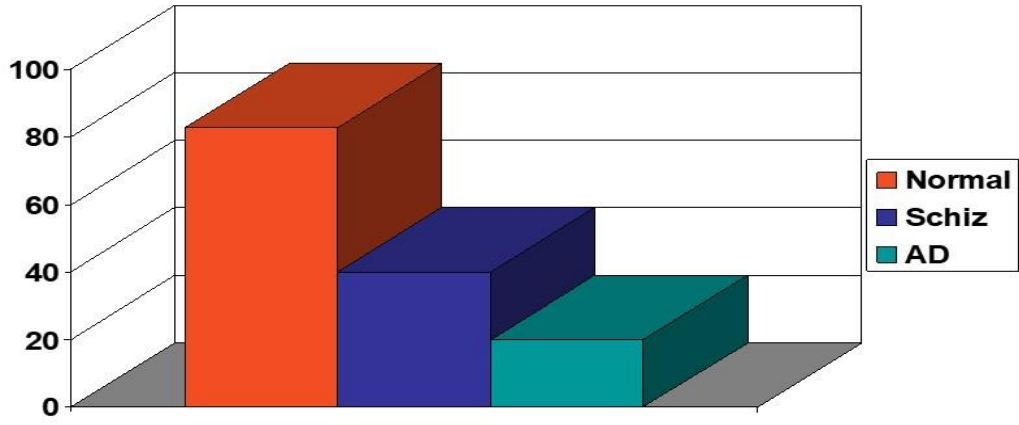


Norm > Schiz = AD;  $p < .05$



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## Delayed recall Savings: Schiz vs. AD vs. Normal

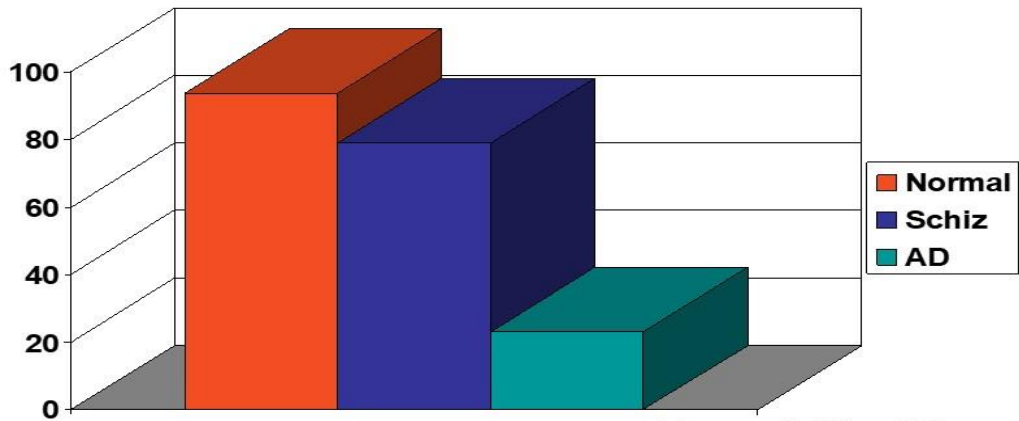


Norm>Schiz>AD;  $p<.05$



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## Delayed Recognition Discrimination



Norm=Schiz>AD;  $p<.05$



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# Longitudinal 6-year study

- Friedman JI, et al. Six-year follow-up study of cognitive and functional status across the lifespan in schizophrenia: a comparison with Alzheimer's disease and normal aging. *Am J Psychiatry*. 2001;158(9):1441-1448.
- Patients with schizophrenia (N=107) were followed over 6 years and assessed with the Clinical Dementia Rating and the Mini-Mental State Examination. The schizophrenic subjects were compared to 136 healthy comparison subjects and 118 Alzheimer's disease patients age 50 and older who were assessed over a similar follow-up period.



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# Course of CDR and MMSE

FIGURE 1. Proportional Risk for Cognitive and Functional Decline<sup>a</sup> Over a 6-Year Follow-Up Period Among Patients With Schizophrenia (N=107)

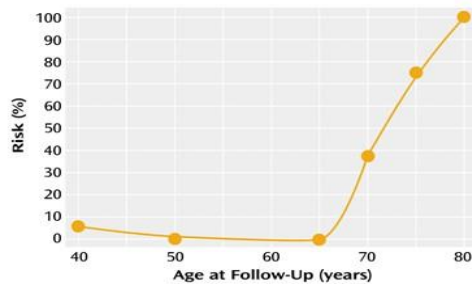
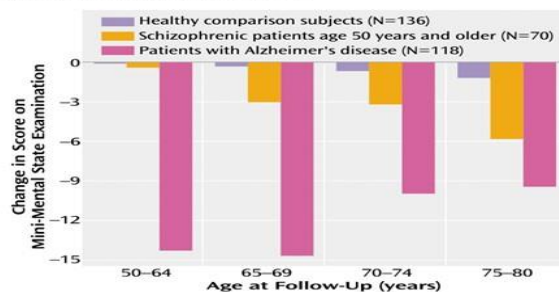


FIGURE 3. Change in Score on the Mini-Mental State Examination Over a 6-Year Follow-Up Period Among Healthy Comparison Subjects, Patients With Schizophrenia, and Patients With Alzheimer's Disease



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## What does this mean?

- Cognitive impairment is present over the lifespan in SMI and is “discovered” at assessments in later life, leading to high prevalence that is not consistent with postmortem or cognitive data
- Often clinicians making the discovery are not familiar with how severe cognitive impairments are in SMI
- Longitudinal rapid cognitive decline is limited to a small subset and they are generally very old



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## How do you assess for new onset impairment?

- Focus on longitudinal information that suggests either stability or significant decline in a short term (e.g., annual) basis.
- Neuropsychological assessment if delivered should focus on delayed recall, particularly development of impairment in delayed recognition memory which is a hallmark of cortical dementia
- Informants who know the patients well are required. Although cognitive and functional performance manifests considerable day to day stability in older schizophrenia patients, people with SMI can have a bad day
- View older people with schizophrenia and bipolar disorder similarly, in that cognitive impairments differ in their severity but have very similar profiles across the conditions. Further, long-term follow studies of bipolar illness find not remitting and non-exacerbating deficits over time.
- Ensure that exacerbating cognitive deficits are not due to anticholinergic burden, to which people with SMI become more sensitive as they age.



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