

Update on Cognition



WHEN DOES COGNITIVE DECLINE OCCUR in the Period Prior to the First Episode of Schizophrenia?

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ABSTRACT

Cognitive impairment is common in people with schizophrenia. These impairments are detectable prior to any signs of illness in people who are destined to develop the disease and they are as severe at the time of the first psychotic

episode as they are after many years of illness. It was formerly believed that the major decline from the minor impairments seen in childhood to those seen at the time of the first episode occurred during the prodrome. Recent data suggests that there is little cognitive decline during the prodrome and

that at the detection of the prodrome, decline has already occurred. Thus, the period of cognitive decline must be very early in the prodrome to psychosis.

KEY WORDS

schizophrenia, cognition, prodrome

One of the more robust findings seen in the study of schizophrenia is that patients at the time of their first identified episode have cognitive impairments that are similar in profile and nearly identical in severity to those seen in people with a more chronic course of the illness.¹ Similarly robust is the finding that cognitive impairments are also seen prior to the onset of illness in individuals who are destined to develop schizophrenia at some later time.² There are some very interesting inconsistencies in these findings, some of which may be related to the conceptualization of when the first episode of schizophrenia actually begins.

Large-scale studies and meta-analyses have found that individuals who are assessed in childhood or adolescence prior to the onset of detectable symptoms of schizophrenia perform about 0.5 standard deviation (SD) worse than the normative population on mean of measures of cognitive and intellectual functioning.² Meta-analyses of the level of impairment seen at the time of the first episode of schizophrenia find more impairment, somewhere in the range of 1.0 SD worse, than population standards.¹ Thus, there is a difference of 0.5 SD in functioning that must have occurred at some time between the premorbid period and the time of the first episode. These findings are consistent across a number of different countries, cultures, and

systems of care, suggesting that these are quite robust findings.

Conceptualizations of the changes in cognitive functioning seen between the premorbid and first episode periods have suggested that these changes must be occurring during the prodrome for the illness, the period of time when subtle (or greater) changes in functioning and symptomatology occur. One of the interesting developments of the past 10 years has been an increase in interest in detection of prodromal states and

The negative symptoms also represent “diluted” versions of the classical symptoms of schizophrenia and other symptoms more similar to those seen in decreased ideational richness. Studies of cognitive functioning during the prodromal period have yielded some very interesting findings. It has been shown, for instance, that in individuals showing high-risk, positive symptoms, certain cognitive impairments at the time of the detection of the prodrome predict increased risk of development of a

The most consistent predictor of the development of psychosis that is measured at the detection of the prodromal state has been verbal episodic memory.⁴ Verbal episodic memory refers to the ability to learn verbal information, in either list or story form, and then to recall and recognize this information after a period of delay.

their potential treatment in order to avert the onset of a psychotic condition.³ Over the course of this research, tools have been developed that have notably increased the sensitivity of assessments of subpsychotic symptoms during this period. These instruments, in the right hands, are able to identify both positive (psychotic) and negative (deficit) symptoms that are more subtle than those examined with structured psychiatric rating scales, and these subclinical symptoms do not meet the criteria for a diagnosis of a psychotic disorder.

The psychotic symptoms identified by these scales are either subclinical variants of classical psychotic symptoms, such as hallucinations or unusual thought content. They also include some symptoms more akin to those seen in schizotypal personality disorder (SPD), including perceptual aberrations and magical thinking.

diagnosable clinical syndrome. The most consistent predictor of the development of psychosis that is measured at the detection of the prodromal state has been verbal episodic memory.⁴ Verbal episodic memory refers to the ability to learn verbal information, in either list or story form, and then to recall and recognize this information after a period of delay.

What is challenging, however, is that there has been very little data showing that verbal episodic memory, or any other cognitive domain, shows decline during the prodromal period in individuals who develop psychosis. In fact, the evidence has been consistently negative. In the very few studies completed to date, there has been no evidence of deterioration during the prodrome.⁵ Some have found that individuals who have the greatest impairment at the time of the detection of their prodrome are

more likely to develop psychosis, but have detected no additional worsening in their performance during the prodromal period.⁶ Thus, these studies have not clarified when the decline from premorbid levels to first episode levels occurs.

One possibility to consider is that by the time the prodrome is detected, the decline has already occurred. Since the symptoms that are detected by these very sensitive prodromal measures are qualitatively similar to those in psychosis, it may be possible that the state that is detected by these instruments is not a prodrome, but rather the first stages of a psychotic condition. It is quite possible that individuals with high scores on measures of positive prodromal symptoms and with substantial cognitive changes are not in the development stages of psychosis, but that the condition has already developed. As a result, by the time certain prodromal states are detected, the illness has already occurred.

This possibility is supported by the fact that many of the subclinical symptoms identified in the prodromal assessments are similar to those seen in SPD. Individuals with SPD have cognitive impairments, but they are much more similar in severity to those seen in individuals who eventually develop schizophrenia when assessed in the premorbid stage⁷ rather than after the development of the illness. One of the main differences between SPD and schizophrenia is the level of severity of psychotic symptoms, but a second consistent difference is reduced levels of cognitive impairment.⁸ Thus, individuals with SPD do not progress to psychosis, and neither do their cognitive impairments progress to the level seen in schizophrenia.

It is quite reasonable to argue

that the increase in sophistication in the assessment of subclinical psychotic symptoms makes it easier to identify people who are in the earliest stages of psychosis, with some overlap with the clinical symptoms of SPD. Those prodromal cases who also show substantial cognitive changes at the time of detection of their prodrome may constitute the group who is in the early stages of psychosis and the others may be at risk to show more stable personality and behavioral changes consistent with a personality disorder such as SPD.

TAKE HOME POINTS

We still have not identified the time when cognitive change occurs in individuals who are destined to develop schizophrenia, because at the time their prodrome is detected, the cognitive changes appear to have already developed. The timing of the additional worsening, from premorbid to first episode, is still not known.

Although still tentative, the evidence suggests that individuals who appear to have a “prodromal” state who do not show evidence of cognitive changes may be at lower risk for the eventual development of psychosis. These individuals may show other adjustment problems such as SPD.

Additional predictors, other than clinically assessed prodromal states, will be required to identify individuals whose cognitive functioning is about to decline prior to the development of schizophrenia and related conditions.

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THE TAKE HOME POINTS

- The timing of the additional worsening, from premorbid to first episode, is still not known.
- Evidence suggests individuals with a “prodromal” state may be at lower risk for development of psychosis.
- Additional predictors will be required to identify individuals whose cognitive functioning is about to decline.

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