

In Review

# Cognition, Function, and Disability in Patients With Schizophrenia: A Review of Longitudinal Studies

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This paper aims to review longitudinal studies assessing the impact of cognition on function in patients with schizophrenia. PubMed and Scholars Portal were searched using search terms related to schizophrenia, cognition, function, and longitudinal studies. Some functional abilities have been studied more than others. Some studies suggest that the impact of cognition on function depends on the severity of baseline cognitive deficits. Other studies suggest that the impact of cognition on function depend on what phase of the illness the patient is in or what stage in that particular function the patient is involved in. Finally, few studies assessed interactions between cognition and other aspects of schizophrenia in predicting function, such as functional capacity, insight, motivation, and negative symptoms. More longitudinal and comprehensive studies are needed. A focus on community living is of high public significance as patients with schizophrenia continue to grow old. Future studies should also focus on the longitudinal interactions between cognition and other dimensions of schizophrenia as well as on the biological factors that underlie these interactions.



## Cognition, fonction et incapacité chez des patients souffrant de schizophrénie : une revue des études longitudinales

Cet article vise à examiner les études longitudinales évaluant l'effet de la cognition sur la fonction des patients souffrant de schizophrénie. Des recherches ont été effectuées dans PubMed et Scholars Portal à l'aide de mots clés liés à la schizophrénie, la cognition, la fonction, et les études longitudinales. Certaines capacités fonctionnelles ont été étudiées plus que d'autres. Des études suggèrent que l'effet de la cognition sur la fonction dépend de la gravité des déficits cognitifs au départ. D'autres études font valoir que l'effet de la cognition sur la fonction dépend de la phase de la maladie ou du stade de cette fonction où se situe le patient. Enfin, peu d'études ont évalué les interactions entre cognition et autres aspects de la schizophrénie pour prédire la fonction, comme la capacité fonctionnelle, l'intuition, la motivation, et les symptômes négatifs. Il faut plus d'études longitudinales et exhaustives. Mettre l'accent sur la vie dans la communauté est d'une grande importance publique car les patients souffrant de schizophrénie continuent de vieillir. Les futures études devraient aussi se pencher sur les interactions longitudinales entre la cognition et d'autres dimensions de la schizophrénie, ainsi que sur les facteurs biologiques qui sous-tendent ces interactions.

Schizophrenia affects more than 24 million adults, worldwide, and about a quarter of a million in Canada.<sup>1,2</sup> It is associated with a tremendous personal, social, and economic burden.<sup>3</sup> Most of its burden is due to the functional disabilities from which patients with schizophrenia suffer. Patients with schizophrenia have difficulty succeeding at school, obtaining or maintaining a job, having social relationships, living independently, and, even for some, taking care of their basic daily needs.

Cognitive deficits are considered core features in schizophrenia<sup>4,5</sup> and have been found to be strongly associated with patients' functional disabilities.<sup>6</sup> These strong associations are mostly based on cross-sectional studies. However,

numerous longitudinal studies have also shed light on the predictive power of cognition on functional outcomes. In addition, other dimensions of the illness are thought to moderate or mediate the relations between cognitive abilities and functional outcomes. These dimensions include motivation<sup>7</sup> and social cognition.<sup>8</sup> Functional outcomes are also the product of interactions between environmental factors—for example, having an opportunity for schooling or a safe environment to form social relationships—and the abilities to perform functional tasks.<sup>9</sup> Thus functional capacity, as assessed by performance-based functional measures, has also been proposed as a distinct dimension in schizophrenia.

Here, we summarize the current understanding of cognitive deficits in schizophrenia and how they relate to the various phases of the illness. Then we review the literature on the relation between cognition and function in patients with schizophrenia as assessed in longitudinal studies.

## Methods

MEDLINE was searched on June 20, 2012. The search aimed to update a previous review<sup>10</sup> and thus the cited references in that review were retrieved first. The search was also limited to 1999 and onward following the rationale in that review.<sup>10</sup> The search terms that were used included “schizophrenia OR schizoaffective” AND “cognition OR neuropsychology” AND “function AND longitudinal.”

This search identified 163 publications. All of the titles or abstracts were read by 2 authors, and relevant papers were selected and reviewed. In turn, cited and citing articles not identified in our search but that appeared relevant were also retrieved and reviewed. We retained reports on studies of cognition and function in adults with schizophrenia or related disorders if they were longitudinal. We classified the results based on functional outcome. We also highlighted the studies that focus on the interactions between cognition and other aspects of schizophrenia in determining functional abilities

## Results

### *Cognitive Deficits in Schizophrenia Across the Lifespan*

Cognitive deficits are observed across all phases of schizophrenia. Generalized cognitive dysfunction has been commonly reported among people at high risk for developing psychosis.<sup>11,12</sup> In contrast, the literature is mixed about specific cognitive domains, with deficits in verbal memory commonly observed.<sup>13,14</sup>

As patients develop their FEP, their cognitive deficits are more established and pervasive. Patients with an FEP are also impaired in general cognition and across most all specific domains. The severity of impairment varies among the various domains. The most pronounced deficits are observed in information processing speed and verbal and visual memory, while the smallest deficits (though still moderate in magnitude) are observed in attention and motor processing speed.<sup>5</sup>

In the chronic phase of the illness, cognitive deficits seem to be stable in magnitude relative to age-matched healthy control subjects.<sup>15</sup> As they experience normal age-related changes in cognition, patients continue to be impaired, compared with control subjects. However, they do not seem to experience

### Abbreviations

ADL	activities of daily living
FEP	first-episode psychosis
MMSE	Mini-Mental State Examination
QoL	quality of life

### Clinical Implications

- Cognitive deficits associated with schizophrenia predict trajectories in almost all functional domains.
- Numerous schizophrenia dimensions, for example, functional capacity, insight, and motivation, are likely to moderate or be synergistic on the impact of cognition on function.

### Limitations

- Future studies are needed to address gaps in the literature, especially about community living.
- Future studies are needed to investigate the associations between the above-mentioned dimensions and cognition, and their impact on function.

an interaction between aging and schizophrenia manifesting itself in an accelerated cognitive decline.<sup>16</sup>

Late in life, patients with schizophrenia continue to experience age-related declines in various cognitive domains. However, they may also experience accelerated cognitive decline in verbal memory and processing speed when they reach their 70s.<sup>17</sup> Such acceleration in cognitive decline has also been reported among a subgroup of older patients with schizophrenia who were chronically institutionalized. It was estimated that these patients—who represent a minority among older patients with schizophrenia—decline cognitively after the age of 65 by 1 point/year on the MMSE,<sup>18</sup> compared with 3 points/year for patients with Alzheimer disease.<sup>19</sup>

In summary, cognitive deficits are present and they are core features in schizophrenia throughout all phases of the illness. Next we present the results of our review on how these deficits impact patients' functional abilities.

### Community Living

Patients with schizophrenia usually require an assisted living environment to maintain living in the community. Only a couple of studies assessed the longitudinal relation between cognition and ability to live in the community. Verbal memory predicted level of functional dependence and ability to live in the community among hospitalized patients.<sup>20</sup> Attention and verbal and working memory have also been found to predict community living among adolescents with early onset schizophrenia.<sup>21</sup>

### Self-Care

The ability to perform self-care tasks is critical to maintain living in the community. Overall cognitive function, comprising language, verbal memory, and visuospatial ability, strongly predicted change in ADLs among institutionalized older patients with schizophrenia.<sup>22</sup> Patients typically have severe cognitive impairments and poor outcomes precluding them from living in the community. In contrast, cognition did not predict changes in ADLs among patients with FEP,<sup>23</sup> who are relatively less impaired and better functioning than institutionalized patients, or among community-dwelling patients.<sup>24</sup> In these populations, other

factors, such as physical health, are probably more likely to play a role in determining self-care abilities.

Interestingly, attention, verbal memory, and working memory predicted personal living skills among adolescents with early onset schizophrenia.<sup>21</sup> Considering the more pronounced and generalized cognitive impairment that these adolescents experience, compared with adults at their FEP,<sup>5</sup> it is not surprising that, as among older and institutionalized patients, associations between cognition and ADLs are observed among adolescents with early onset schizophrenia.

### **Social Function**

Numerous studies assessed the relations between cognition and social function. Attention, fluency, memory, and working memory have been found to predict social function in a 1-year follow-up study of patients with FEP.<sup>23</sup> Short-term memory and working memory also predicted social function among chronic patients following an acute exacerbation.<sup>25</sup> Verbal memory also predicted social function among adolescents with early onset schizophrenia during a period of about 1 year.<sup>21</sup> These young patients are typically close to their age at onset.

In contrast, executive function predicted social function among chronic and stable patients participating in a rehabilitation program.<sup>26</sup> Similarly, in an epidemiologic study among patients with FEP, executive and visuospatial function predicted social competence during 10 years of follow-up.<sup>27</sup> Executive function, processing speed, and working memory also predicted social function among a small group of patients with early onset schizophrenia after a 13-year follow-up period.<sup>28</sup>

Finally, some studies did not find noticeable predictions between cognition and social function among chronic and stable patients<sup>24,29,30</sup> or among chronic patients following acute hospitalization.<sup>31</sup>

### **Quality of Life**

During an average of 15 years of retrospective assessment, numerous cognitive measures have been shown to predict satisfaction among various functional domains. Memory predicted satisfaction with income, ADLs, and general health. Motor skills predicted satisfaction with family contact. Working memory predicted satisfaction with social contacts.<sup>32</sup> In contrast to the above relations between specific cognitive functions and specific aspects of QoL among community-dwelling patients, global cognitive impairment, as assessed by the MMSE,<sup>18</sup> predicted health-related QoL among inpatients with schizophrenia.<sup>33</sup>

### **Work**

Most patients with schizophrenia do not work. In one clinical trial that randomly assigned patients to a vocational rehabilitation program, patients who achieved employment did not differ cognitively from those who did not.<sup>34</sup> Patients' general intellectual ability, attention, visual memory, vigilance, executive function, and motor function predicted the number of hours they remained employed.<sup>34</sup> General

cognitive function was also found to predict occupational adjustment following an acute hospitalization.<sup>31</sup> In addition to obtaining a job, cognitive functions predicted improvements in work performance, including performance in work habits, cooperativeness, and work quality.<sup>35</sup> In particular, attention strongly predicted improvement in the initial learning phase of employment, while verbal memory was the strongest predictor of continuous improvement in the later phase of employment.<sup>36</sup> Attention was also found to predict maintaining employment during a 2-year follow-up period,<sup>37</sup> while verbal memory predicted employment among chronic patients<sup>1-3</sup> 5 years following an acute hospitalization.<sup>38</sup> These findings are consistent with an epidemiologic study demonstrating that executive and visuospatial function predicted work performance during 10 years of follow up among patients with FEP.<sup>27</sup>

Performance on working memory, attention, and early perceptual processing, and verbal memory and processing speed, was also found to predict return to work among patients following stabilization of their FEP.<sup>39</sup>

### **Composite Measures of Function**

Among patients with FEP, global cognition has been shown to predict performance on a composite measure of ADLs, employment, performance as a homemaker, schooling, and social interactions outside of family.<sup>40</sup> Similarly, attention,<sup>40-42</sup> executive function,<sup>40</sup> memory,<sup>41</sup> and verbal comprehension<sup>43</sup> have been shown to predict function using composite measures of hospitalization, occupational functioning, social functioning, and symptomatology<sup>41</sup>; ADLs, employment, performance as a homemaker, schooling, and social interactions outside of family<sup>40</sup>; self-care, social function, and work<sup>43</sup>; and occupational and social function.<sup>42</sup>

Such relations have also been found among chronic patients<sup>44,45</sup> and among people with ultra-high risk for psychosis during 2 to 13 years of follow-up and irrespective of their conversion to psychosis.<sup>46</sup>

### **Relations Between Cognition and Other Variables in Predicting Functional Outcome**

One study<sup>47</sup> assessed the relation between cognition, functional capacity, and real-world functional outcomes. Among 127 patients with schizophrenia or schizoaffective disorder, cognition predicted performance on a composite, real-world functional outcome measure at residence, schooling, and work during a 10-month follow-up period. Interestingly, performance on a functional capacity measure did not add to the validity of predicting real-world function, suggesting that such functional capacity measures could be redundant when combined with cognitive measures.<sup>47</sup>

In a study<sup>48</sup> of 130 patients with schizophrenia or schizoaffective disorder assessing the relation between cognition, motivation, and psychosocial function, cognition and not motivation was found to cause change in psychosocial function during a 1-year period. In contrast, psychosocial change caused change in motivation that, in turn, predicted change in cognition. These findings suggest that motivation

moderates the impact of cognition on functional outcome and that enhancing motivation could enhance this impact.<sup>48</sup> Another longitudinal study<sup>49</sup> assessed cognition and motivation and their impact on function among 21 patients with schizophrenia. In this study, motivation but not cognition was found to predict function at 6-month follow-up.<sup>49</sup> However, the measure that was used in this study to assess function (Quality of Life Scale)<sup>50</sup> is heavily weighted toward negative and deficit symptoms of schizophrenia, including amotivation, which could explain that finding.

In addition to functional capacity and motivation, numerous other variables could affect functional outcomes in patients with schizophrenia and are likely to interact with cognition. Premorbid adjustment has been shown to affect functional outcomes in patients with schizophrenia.<sup>51</sup> It has also been associated with severity of cognitive deficits in these patients.<sup>52</sup> Duration of untreated psychosis is another feature that is strongly associated with clinical outcome.<sup>53,54</sup> Whether it is also related to long-term functional outcomes through an interaction with cognition is yet to be determined. Finally, clinical insight has been associated with short-term outcomes of patients with schizophrenia, especially regarding medication adherence. However, its relation to long-term functional outcomes remains unclear.<sup>55</sup>

## Conclusions

Numerous longitudinal studies assessed the relation between cognition and function in patients with schizophrenia. Some functional abilities have been studied more than others. In particular, the impact of cognition on the ability to live in the community is scarcely studied. This is a major gap in the literature, given that more than 80% of patients with schizophrenia, including older patients, live in the community.<sup>56</sup>

Although it may be too speculative to draw some generalizations based on the available literature, few observations are worth mentioning. The literature on self-care suggests that predictive power of cognitive deficits in determining the trajectory of functional abilities, and in relation to other variables, depends on the level of baseline cognitive deficits. The literature on social function and occupational abilities suggest that the nature of the cognitive deficits that predict a certain function depend on the phase of the illness that the patient is in or the stage in that particular function the patient is involved in.

Finally, few longitudinal studies assessed the nature and course of interactions between cognition and other aspects of schizophrenia in predicting function. A promising model suggests a moderating effect of negative symptoms on the impact of cognition on function, with a positive feedback resulting in enhanced motivation as function improves. Future studies could focus on whether such positive feedback is mediated by change in functional capacity, including social cognition, or whether it necessitates changes in real-world function. Future models could also study the relation between positive symptoms or insight, considering that they are potentially modifiable dimensions

of the illness. Characterizing the functional impact of various dimensions of schizophrenia and their underlying genetics and brain structural and functional changes will eventually lead to the identification of novel interventions to restore patients' functional abilities.

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