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UPDATE ARTICLE

Functional capacity: a new framework for the assessment of everyday functioning in schizophrenia

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Historically, measures of everyday functioning have focused exclusively on real-world performance. Despite the unquestionable value of ''real-world functioning'', it has become clear that instruments for its assessment might not be as accurate as desirable. Functional capacity is a domain of everyday functioning that can be assessed through performance-based measures. In the last decade, functional capacity has become a cornerstone for the assessment of everyday functioning, since, alongside measures of real-world functioning, it provides a much more comprehensive picture of functional outcomes than any measurement alone. Functional capacity is more stable and less vulnerable to influence from environmental factors than other domains, and its correlation with cognitive functions has encouraged the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) project to suggest that a performance-based measure of functional capacity be included as a co-primary assessment of cognition in clinical trials. Functional capacity assessment instruments may be also useful in the evaluation of remission in schizophrenia. Validation of these instruments in different countries is desirable, and should always include cross-cultural adaptation; within large countries, adjustment for regional variations should be considered.

Keywords: Schizophrenia; disability; everyday functioning; functional capacity; real-world functioning

Introduction

Schizophrenia is one of the most disabling conditions affecting young people around the world.[1] It is currently defined by the presence of two or more of the following manifestations, lasting at least 1 month: delusions, hallucinations, disorganized thinking, grossly disorganized behavior, and negative symptoms.[2]

Subjects presenting with signs and symptoms of psychosis should be assessed along eight dimensions: the five aforementioned domains, cognition, depression, and mania.[3] Schizophrenia also involves impairment in one or more major areas of functioning, with attenuated signs or symptoms of the disturbance persisting for at least 6 months.[2] Despite the early descriptions of *dementia praecox* by Emil Kraepelin and of the fundamental symptoms of schizophrenia described by Eugen Bleuler[4] in the early 20th century, assessment of the cognitive and functional impact of this disorder only became possible after pharmacological treatments were made available, allowing patients to live in the community and face the challenges of this environment. Furthermore, the fact that remission of psychotic symptoms does not usually entail improvement in social and occupational functioning was only recognized – and led to a shift in the focus on outcomes in schizophrenia – in the past 20 years.[5]

Achievement of the typical milestones of adulthood, such as keeping a job, raising a family, or maintaining a home, is strongly dependent on performance in the activities of daily living.[6] The abilities to interact properly with others (social functioning), to deal with problems and issues at work (vocational functioning), and to perform activities such as paying bills or riding a bus (community functioning) constitute three of the main domains of what is known as everyday functioning. Patients with schizophrenia are less likely to achieve these functional goals than the general population.[7]

There are many reasons why someone may or may not succeed in the activities of everyday functioning. For instance, a lack of motivation to search for a job may be caused by several factors, including sociodemographic or environmental factors (such as high unemployment rates), slack financial resources, or even a reliance on disability benefits. Evidence also supports that high levels of negative[8] and depressive[9] symptoms in patients with schizophrenia have a negative impact on interpersonal skills. However, the best single predictor of functional outcome (everyday functioning or life milestones) seems to be cognition, which is especially impaired in schizophrenia.[10]

When studying the determinants of everyday functioning, it is very important to consider the difference between what a person is able to do (competence) and what they actually do (performance). The former is referred to as functional capacity, while the latter is known as real-world functioning.

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These constructs may be differently impacted by the determinants of everyday functioning outlined above. In recent years, a growing number of studies have focused on functional capacity,[8,11-15] as this variable appears to be less dependent on nonspecific environmental factors and, as such, be more sensitive to therapeutic interventions. Hence, functional recovery after treatment in schizophrenia is more likely to be readily observed through measures of functional capacity than through real-world functioning, since changes in the latter domain usually take longer to manifest. Additionally, functional capacity is evaluated by the direct observation of patient performance in simulated real-life situations, and, as such, is less dependent on patient or caregiver reports and more closely related to patient cognition itself.[16] The aim of this article is to review the topic of everyday functioning in schizophrenia, with an emphasis on the concept of functional capacity, its development, relevance, applicability to clinical trials, and utility in clinical practice.

Assessment of everyday functioning

Real-world functioning

Historically, measurements of everyday functioning have focused on the endpoint of real-world performance, in an attempt to classify level of disability on the basis of daily activities carried out improperly or not at all. The inclusion of one such instrument, the Global Assessment of Functioning (GAF), in the DSM-III-R[17] illustrates the relevance of this topic in psychiatry at the end of the 20th century. Many instruments are currently available for the assessment of functioning.[18] Some of these were designed to improve existing scoring patterns, while others refined the concept of functioning by dividing it into several subdomains. The Personal and Social Functioning (PSP)[19] scale, for instance, measures four areas of functioning (socially useful activities; personal and social relationships; self-care; disturbing and aggressive behaviors) and, unlike the GAF, evaluates these domains independently from clinical symptoms. The Independent Living Skills Survey (ILSS)[20] is composed of nine subdomains which focus on and describe specific issues relevant to real-world functioning, such as care of possessions, leisure activities, and transportation and job skills. Given that each of these instruments has distinct aims and evaluation criteria, a recent study sought to identify the most effective method for measuring functioning in clinical trials. This investigation, known as the Validation of Everyday Real-world Outcomes (VALERO)[18] study, suggested that the six-domain Specific Level of Functioning (SLOF)[21] scale provides the best assessment of real-world functioning in terms of reliability and sensitivity to change.

Despite the unquestionable value of "real-world functioning" measurements, the process of their assessment may not be as accurate as desirable, leading to wrong and incomplete conclusions concerning everyday functioning. Direct observation of behavior is still the optimal means of assessing functioning[16,22]; however, the time and expense required to observe subjects in all possible life situations makes it unfeasible. Collecting data from informants is a very useful and much more cost-effective procedure, and some instruments have versions designed specifically for this purpose, such as the ILSS.[20] However, as many as one-third of patients do not have anyone who could serve as an informant,[23] and not all informants, even among those considered "high contact," seem equally informative.[24] Self-report is probably the simplest way of assessing everyday functioning. As expected, however, poor insight,[25] impaired cognitive functioning, and the presence of negative and depressive symptoms[14] all contribute to poor self-evaluation and inaccuracy of the information provided.

Functional capacity

Performance-based measures are an ingenious strategy for the assessment of everyday functioning, and have several methodological advantages over measures of real-world functioning. Performance-based instruments were first developed for use in populations with cognitive impairment, such as those with Alzheimer's disease.[22] These tools evaluate functional behavior through role-playing tasks in a controlled environment, and, as such, are independent of patient insight and do not require the presence of an informant.[16] As they are performed in controlled environments that may not correspond to the patient's actual life demands, performance-based instruments are considered measures of functional capacity. In addition to predicting real-world functioning, these instruments provide a much more comprehensive assessment of everyday functioning than any single measure alone. Moreover, although there is no "gold-standard" measure of functioning, performance-based instruments appear to be more accurate than self-report measures in predicting important milestones, such as living independently or staying employed.[26]

Several performance-based assessments of functional capacity are currently available. The first such measure designed specifically for patients with schizophrenia was the University of California, San Diego, Performance-based Skills Assessment (UPSA),[22] which encompasses five domains of community functioning: planning recreational activities, managing money, communicating, using public transportation, and household chores (preparing a shopping list). Subjects are asked to use props, such as real money or an unplugged telephone set, to demonstrate how they would perform each of these activities if they needed to in real life.

Since the UCSD was made available, many other instruments have been developed. The Social Skills Performance Assessment (SSPA)[27] and the Maryland Assessment of Social Competence (MASC)[28] rate social skills on the basis of performance in standardized role-plays – for instance, one requiring assertive communication with a landlord and another prompting the respondent to initiate a conversation with new co-workers. Competence to manage daily medication may be evaluated with the Medication Management Ability Assessment (MMAA).[29] In this instrument, patients are given instructions as to the appropriate use of each of their medications and, after an interval, are asked to demonstrate the proper dosage and administration of each medication in a role-play scenario. The adaptive functioning domain can also be evaluated by performance-based measures, such as the Test of Adaptive Behavior in

Schizophrenia (TABS).[30] This instrument was designed to assess the patient's ability to identify problems during the execution of a given task and change their strategy to achieve a proposed outcome. As in other similar instruments, this measure rates participant behavior during role-play situations. The Independent Living Scales (ILS) measure the cognitive skills required for independent living by assessing performance in five areas: memory/orientation, money management, managing home and transportation, health and safety, and social adjustment. In this instrument, subjects are asked to solve problems, demonstrate knowledge, or carry out specific tasks[31] (Table 1).

The UPSA is the most widely used measure of functional capacity in the U.S., likely because it has good psychometric properties,[12,32] is comprehensive, and requires no special training for administration or interpretation. The UPSA has already been adapted and validated for use in many countries around the world.[33-38] A brief version of this instrument (UPSA-B), including two of the five original domains, has also been developed and demonstrated adequate psychometric properties.[39]

Over the last 10 years, the role of functional capacity in the complex process that leads to functional outcomes has been increasingly investigated. The significant association of functional capacity with cognitive function and its ability to predict real-world functional outcomes were taken into consideration by members of the NIMH-MATRICS project panel, who suggested that a performance-based measure of functional capacity and an interview-based measure of cognition be included as co-primary measures in their clinical trials.[40] This proposal was clearly in agreement with Food and Drug Administration (FDA) requirements for the approval of any potential "cognitive-enhancing" drug, which were initially applied to studies of drugs seeking an indication for Alzheimer's disease, but are now also mandatory for schizophrenia.

According to the FDA, changes in cognitive measures, as assessed by neuropsychological tests, must be accompanied by improvements which are relevant to both clinicians and consumers, thus demonstrating "face validity". Real-world functioning measures were not taken into account, despite their high potential face validity, because changes in functioning may take too long to be detected in clinical trials. Additionally, demographic variables (e.g., disability benefits) may prevent any change at all in functional outcome, even when cognitive improvement is evident.[41] In a study conducted to identify candidate instruments for this co-primary assessment, both the UPSA and MASC demonstrated good psychometric properties and were considered acceptable for this purpose, along with two interview-based scales.[42] Ultimately, the MATRICS Co-Primary and Translation (MATRICS-CT) consortium launched the Validation of Intermediate Measures (VIM) Study, which selected the UPSA as the leading co-primary measure of functional capacity for use in clinical trials.[43]

Performance-based instruments are also being used in the validation process of many new interview-based cognition scales. The UPSA, for instance, was used in construct validation of the Schizophrenia Cognition Rating Scale (SCoRS)[44] and, more recently, in the validation process of the Cognitive Assessment Interview (CAI), alongside the TABS.[45] The VALERO study,[18] conducted to evaluate functional rating scales, also included a measure of functional capacity (UPSA-B) in an attempt to identify the scale or scales most robustly related to performance-based measures of cognition and everyday living skills.

Relationship between functional capacity, everyday functioning, and related variables

Functional capacity has become a vitally important subdomain of everyday functioning, because of the growing body of evidence supporting its relationship with cognitive performance and real-world functioning, which it probably mediates to some extent.

Data on functional capacity support its strong correlation with cognitive function.[46] More specifically, studies have found processing speed, episodic memory, and executive functions to be associated with community activities (as measured by UPSA), while working memory, episodic memory, and verbal fluency have been found to be more strongly associated with social competence (SSPA).[47] Overall, it seems that working memory is the strongest single predictor of functional capacity, as measured by UPSA-B.[15]

Demographic factors such as age, gender, education, and ethnicity are significantly associated with performance-based measures of everyday functioning. Age and education, in particular, have been found to be strongly related to social competence, as evaluated by the SSPA.[48] Subdomains of social cognition, such as theory of mind[49] and the perception of negative emotions,[50] also appear to mediate the relationship between cognitive functions and functional capacity, especially social skills (MASC).

Some evidence suggests that negative symptoms contribute directly to functional capacity,[51] with negative impacts on the community (UPSA), social (SSPA), and medication management (MMAA) domains. The influence of negative

Table 1 Performance-based measures of functional capacity

Instrument	Domain	Props	Administration time (minutes)
University of California, San Diego, Performance-based Skills Assessment (UPSA)	Community activities	Yes, many	30
Test of Adaptive Behavior in Schizophrenia (TABS)	Adaptive behavior in community activities	Yes, many	30
Independent Living Scales (ILS)	Instrumental activities of daily living	Yes, many	45
Social Skills Performance Assessment (SSPA)	Social skills	Yes, few	10
Maryland Assessment of Social Competence (MASC)	Social skills	Yes, few	30
Medication Management Ability Assessment (MMAA)	Medication management	Yes, some	15

symptoms on functional capacity has been found to be partially mediated by processing speed.[52] Better abstract reasoning capacity is associated with higher scores in measures of functional capacity.[53] This may be attributable to methodological factors, since performance-based instruments are essentially role-playing exercises.

Community skills, as measured by the UPSA, have been found to be associated with and predict with good accuracy the ability of patients with schizophrenia to live independently in the community.[12] More specifically, UPSA score appears to be a good predictor of community responsibility, which includes activities such as household duties or paid employment, in community-dwelling patients.[13,54]

Functional capacity, as assessed by the UPSA, correlates moderately with real-world functioning,[44] but there is good evidence to suggest that it may actually be a mediator between real-world functioning and neuropsychological factors.[8,11] However, while everyday living skills appear to be the most important predictor of home functioning,[12] blunted affect and passive-apathetic social withdrawal accounted for all variance in real-world social outcomes in a recent study,[55] suggesting that these domains may be differently impacted by external factors.

Finally, an important corollary of these observations is that competence does not always translate into performance, even when cognition and skills are preserved. As expected, negative symptoms contribute to the gap between competence and performance,[56] especially through subtle traits such as defeatist beliefs and lack of motivation.[57] It appears that the dysfunctional attitudes[56] described in cognitive theory, as well as low self-efficacy[58] and depressive symptoms,[7] also contribute negatively to the conversion of capacity into functioning.

The use of functional capacity measures in clinical trials

A PubMed search conducted by our research group in July 2014 using the keywords "functional capacity," "functional competence" OR "functional ability" AND "schizophrenia" retrieved 164 articles, of which 10 reported on clinical trials of cognitive or functional enhancement using functional capacity scores as an outcome.[59-68] While the first report meeting these criteria was published in 2006, most of the remaining articles were published in the last 3 years, probably after the aforementioned recommendations were implemented by the FDA. Five of these trials were designed to evaluate the effects of drug therapy with atypical antipsychotics (risperidone, quetiapine, lurasidone), a neuropeptide (davunetide), or other potential cognition-enhancing drugs. The remaining studies evaluated cognitive and functional remediation programs involving exercises for planning, problem-solving, and functioning skills, as well as cognitive training itself. The design and results of these clinical trials are summarized in Table 2.

Future perspectives

Researchers and psychiatrists must make a serious effort to go beyond the relief of delusions and hallucinations in the treatment of schizophrenia, since this is a relevant, but insufficient outcome. True remission, in the current approach, should also include functional and cognitive outcomes.[69] However, despite the availability and continued development of modern antipsychotics, psychosocial interventions, and cognitive training programs, there remains an enormous difference between the actual outcomes of "remitted" patients and what they could achieve based on their premorbid potential. Currently, real-world functioning may be problematic as a marker of recovery in schizophrenia, as many environmental factors may have a negative influence on and delay remission. Nevertheless, functional capacity instruments could address this issue and provide a safer, more readily assessed measure of clinical remission that takes everyday functioning into account.

The likely emergence of new drugs with effects on specific cognitive domains and their associated functional outcomes will require additional instruments validated for assessment of these domains. As it is unlikely that any single instrument will be able to cover all aspects of functioning impacted by clinical trials, researchers must choose the instrument that best matches their aims and hypothesis. Clinical trials of specific interventions for cognitive and functional remediation will also require functional assessment tools which are sensitive to change. As noted above, both existing and new versions of performance-based measures of functional capacity will certainly play a key role in this process.

All performance-based instruments available to date were developed in major cities of high-income, developed countries, i.e, the United States. The demands of everyday life in this setting and the skills required to meet them may differ from those experienced in smaller cities or rural areas, even within the United States itself. The UPSA, for instance, evaluates communication and transportation skills through proper use of a telephone set and interpretation of bus routes on a map. People living in small towns are unlikely to be familiar with bus maps, simply because this mode of transport is not a part of their everyday lives. Additionally, differences in cultural and educational background between subjects from developed and developing countries may also hinder translation during the validation process. Therefore, cultural adaptation is an essential part of the cross-cultural validation of functional capacity instruments, and should even be considered in the case of large countries with regional cultural variations.[70,71] To our knowledge, the only developing country that has published data on the validation of a performance-based measure of functional capacity (UPSA) has been China. The strong influence of variations in educational levels across the sample led to a careful interpretation of scores on complex functional skills, such as banking and telephone usage, even among healthy participants.[36]

A recent review[72] maintained that functional impairment is a candidate endophenotype for severe mental illness. The authors argued that measures of functional capacity are strongly related to neuropsychological performance and real-world outcomes, minimally affected by confounders such as symptoms and environmental features, and show similar scores across diverse

Table 2 Summary of the experimental design and results of clinical trials having functional capacity as outcome

Study	Intervention	Target variable of interest	Design	n	Duration	Patient diagnosis	Measure of FC	Conclusions
Bowie[59]	CR	Functional competence	Early vs. long-term course	39	12 weeks	Schizophrenia	SSPA, UPSA, and MMAA	Treatment feasibility: both groups Clinical meaningful: early > long-term
Harvey[60]	DT	Neurocognitive performance and functional capacity	Lurasidone vs. quetiapine vs. placebo (DB)	267	6 weeks, 3 months, and 6 months	Schizophrenia	UPSA-B	6 weeks: no differences 3 months/6 months: lurasidone > quetiapine = placebo
Twamley[61]	CT	Domains of cognition	PhT alone vs. PhT + CT (RC)	69	12 weeks	DSM-IV primary psychotic disorders	UPSA	Effects on attention, verbal memory and functional capacity: PhT + CT > PhT alone
Bowie[62]	CR	Functional competence and real-world functioning	CR vs. FAST vs. CR + FAST (RC)	107	12 weeks	Schizophrenia	SSPA and UPSA	CR strongly enhanced neurocognition Improvements in functional competence: CR + FAST > CR or FAST alone
Javitt[63]	DT	Cognition and functional capacity	Davunetide vs. placebo (MC, DB, RC)	63	12 weeks	Schizophrenia	UPSA	Effects on cognition: davunetide = placebo Effect on UPSA: davunetide > placebo
Velligan[64]	DT (AZD3490)	Cognition	AZD3490 vs. placebo (RC)	440	12 weeks	Schizophrenia	UPSA	Effect on cognition and functional capacity: AZD3490 = placebo
Rodewald[65]	PPST or TBC	Functional capacity	PPST (computer-assisted) vs. TBC	89	10 sessions	Schizophrenia	O-AFP*	Effect on functional capacity: PPST = TBC
Vesterager[66]	CT	Cognitive and everyday functional capacity	TaU vs. TaU + CT (MC, DB, RC)	Enrollment ongoing	Ongoing	First-episode psychosis within F2 spectrum in ICD-10	UPSA-B	Description of the development of a study protocol: results not yet published
Buchanan[67]	DT	Cognitive impairment	MK-0777 vs. placebo (MC, DB, RC)	60	4 weeks	DSM-IV Schizophrenia	UPSA	Effects on cognitive impairment: MK-0777 > placebo (small effect)
Harvey[68]	DT	Social competence and neuropsychological performance	Quetiapine vs. risperidone (MC, DB, RC)	673	8 weeks	Schizophrenia	SSPA	Improvements in social competence: quetiapine = risperidone Social competence correlates with neuropsychological measures

CR = cognitive remediation; CT = cognitive training; DB = double-blind; DT = drug trial; FAST = Functional Adaptation Skills Training; FC = functional capacity; MC = multicenter; MMAA = Medication Management Ability Assessment; O-AFP = Osnabrücker Arbeitsfähigkeiten Profil; PhT = pharmacotherapy; PPST = Planning and Problem-solving Training; RC = randomized controlled; SSPA = Social Skills Performance Assessment; TaU = treatment as usual; TBC = Training addressing Basic Cognitive functions; UPSA = University of California San Diego Performance-based Skills Assessment; UPSA-B = University of California San Diego Performance-based Skills Assessment, brief version.
*This instrument is only available in German and was therefore not mentioned in this review.

populations and even different countries, such as the U.S. and Sweden.[34] However, research into functional capacity and its genetic correlates in the prodromal stage of schizophrenia is still incipient, and no studies have investigated the familial nature of functional impairment.

In summary, over the past decade, functional capacity has become an essential domain for assessment of everyday functioning. Alongside actual real-world functioning, it provides a comprehensive picture not only of ''what'' patients can and cannot do, but also of ''how'' and ''why''. The emergence of new treatment strategies targeting cognitive remediation will have a clear impact on functional capacity. The inclusion of a performance-based measure of functional capacity as a co-primary measure of cognition in the MATRICS batteries is a result of this conceptual change, and should encourage continuous improvement of the psychometric properties of existing instruments as well as the development of new and more specific measures and their validation for use in different settings and cultures. Lastly, the current approach of remission in schizophrenia demands the assessment of everyday functioning during the course of clinical follow-up, and functional capacity measures seem to be appropriate tools for this purpose.

Disclosure

The authors report no conflicts of interest.

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