Towards remote digital phenotyping of cognition in schizophrenia

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Cognitive impairments are a core aspect of schizophrenia that persist during the course of the illness and drives disability as well as social and economic burden (Lepage et al., 2014; Kelly et al., *in press*). Yet, despite the impact of cognitive impairments on people with schizophrenia, quantifying and monitoring their cognitive capacities remain a challenge today (Keefe and Harvey, 2012; Keshavan et al., 2014). Encouraging new efforts, highlighted in this issue by Biagianti et al.' (2019) research on a new web-based battery to remotely assess cognition in individuals with schizophrenia and Morita et al.'s (2019) research on eye movement abnormalities and their association with cognitive impairments in schizophrenia, underscore how new digital technologies are enabling advances for the field. This commentary provides a perspective on the evolving potential of new mobile technologies such as smartphone applications and sensors to measure cognition in schizophrenia.

1. Traditional pen-and-paper cognitive batteries

Traditionally, cognition has been assessed in patients for research purposes using pen-and-paper validated cognitive tests. The Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative was developed to assess the cognitive domains specifically relevant to schizophrenia and related disorders (Marder and Fenton, 2004; http://www.brain.ucla.edu/matrics/). The MATRICS Consensus Cognitive Battery (MCCB) has been well validated in schizophrenia (e.g., Buchanan et al., 2010; Keefe et al., 2011; Kern et al., 2011) and is widely used. However, this battery requires an extensive training for assessors and a relatively long administration time (approximately 60 min). Alternative pen-and-paper, but shorter batteries (30-minute), have therefore emerged (e.g., the Brief Assessment of Cognition in Schizophrenia (BACS); Keefe et al., 2004).

Implementing these batteries in clinical settings remains challenging considering their administration time. Thus, very short cognitive instruments have also been developed for assisting clinician detection of cognitive deficits (e.g., Velligan et al., 2004; Purdon, 2005; Hurford et al., 2009; Nasreddine et al., 2005). These very brief assessments can be administered in about 15 min, require minimal additional equipment and have shown good psychometric properties (Cuesta et al., 2011; Jędrasik-Styła et al., 2014; Pino et al., 2008; Purdon, 2005; Rojo et al., 2010; Velligan et al., 2004; Wu et al., 2014). These instruments appear most useful when the goal is to identify patients who show more severe cognitive impairments. However, they do not provide broad coverage of the range of cognitive deficits in schizophrenia (Joyce and Roiser, 2007; Kremen et al., 2004).

2. Computer-based cognitive batteries

In recent years, we observed a rise of computer-based battery development to assess cognition in people with schizophrenia. Computerized cognitive batteries are particularly useful when research requires testing participants many times with alternate equivalent and precise stimuli presentation (Schatz and Browndyke, 2002). Furthermore, they can more easily be used in clinical setting for baseline cognitive assessments or program evaluation (Gualtieri, 2004). They offer more standardized, but also automated administration and scoring report which can lower the cost and time for each assessment (Collie et al., 2001; Collie et al., 2003).

From the many computerized cognitive batteries that have been developed, the Cogstate (https://www.cogstate.com) and the Cambridge Neuropsychological Test Automated Battery (CANTAB; http://www.cambridgecognition.com/cantab/) are the two most used and validated batteries in schizophrenia (Bakkour et al., 2014). More recently, the Cognitive Neuroscience Test Reliability and Clinical Applications for Schizophrenia (CNTRACS) consortium also developed a cognitive battery composed of a series of computer-based paradigms to assess specific cognitive and perceptual functions in schizophrenia (https://cntracs.ucdavis.edu/tasks; Gold, 2012; Sheffield et al., 2014). The CNTRACS battery can only be completed on computers, but Cogstate and CANTAB offer assessments on both computers and tablets. A novel version of the BACS battery on tablet (the BACS App) has also shown promise for assessing cognitive difficulties in schizophrenia (Atkins et al., 2017). Interestingly, in this issue Biagianti et al. (2019) have highlighted the potential of a novel web-based cognitive battery for schizophrenia that can be both administered and interpreted easily in real world clinical settings – where it is most needed.

3. Potential for smartphone-based cognitive assessment

The rapid rise of mobile technologies has opened new possibilities for cognitive assessment in schizophrenia. Like the rest of the global

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population, people with severe mental illnesses increasingly own and use smartphones (Torous et al., 2018a). The potential for smartphone-based cognitive assessments derives not only from the fact that computerized assessments, as discussed above, could be offered in a more accessible and scalable format, but also from the new functional, environmental, and longitudinal data afforded by today's smartphones.

Smartphones offer both a broader assessment of cognition and related phenotypes (i.e. physiologic measures such as heart rate and skin conductance) as well as a dynamic assessment in relation to changes in symptoms, exercise, sleep, stress, and environment. There is an increasing interest in using mobile technologies to measure cognition in diverse clinical populations, like Alzheimer's and other dementia related disorders (Chinner et al., 2018). However, the research on smartphone-based assessments of cognition remains nascent. A recent comprehensive review identified only 12 articles, none of which investigated the use of smartphone cognitive assessment in schizophrenia or other mental illnesses (Moore et al., 2017). Table 1 presents the pros and cons of smartphones-based and other types of cognitive assessments in schizophrenia.

4. Active, passive and metadata

The potential of using digital smartphone devices to assess cognition can be best conceptualized through classifying assessments into three categories: active data, passive data, and metadata.

Active data involve engagement by individuals on the smartphone, such as a survey of their cognition or a modified version of a well-known pen-and-paper cognitive test (e.g., the Trail Making A and B tests; Reitan, 1958). Few studies have reported on cognitive testing via surveys or other active data tasks on smartphones (e.g., Polokoff, 2014; Allard et al., 2014), and none that we are aware of for schizophrenia. Without directly capturing cognition on a smartphone, one study did show a correlation between smartphone active data and reinforcement learning in schizophrenia (Moran et al., 2017). Cognition mediated the relationship between self-reported real time assessment of symptoms and clinically assessed symptoms, underscoring the practical implications of cognition in clinical care and the feasibility of using active data from smartphones assessments in schizophrenia.

Passive data requires no active engagement and includes automatically collected data by the smartphone such as location (GPS), mobility (accelerometer), touch screen (sensors), voice (microphone), socialness (anonymized phone call, text messages logs etc.). The many smartphone sensors and automatic data logging may in some cases be a proxy for human behavior and thus a potential digital marker for some aspects of cognition. One pilot study examined digital markers of cognitive functioning using touch screen data in healthy adults; with 7 days of touch screen data, their smartphone application strongly predicted standardized cognitive test scores (Dagum, 2018). The lack of any research using these passive data methods associated with cognition in schizophrenia also highlights the need for such studies. Interestingly, recent research by Morita et al. (2019), quantifying cognitive

impairments in schizophrenia with eye movement abnormalities, suggests the next frontier for cognitive assessment could be sensors like smart glasses that may passively monitor cognition without even the need for a smartphone application.

Finally, metadata refers to the additional information collected when people complete an active task or use an application (e.g., time between targets on a specific task, frequency of the application's use or of survey's completion). Metadata might offer novel insights about patient's cognition that is not available using sensors or traditional metrics. Metadata collected on a smartphone have been associated with clinical self-reported active data, suggesting clinical relevance (Torous et al., 2018b). Nonetheless, this type of information remains largely unexplored and future studies investigating metadata in relation to cognition in schizophrenia or other mental health disorders are needed.

5. From pen-and-paper to remote digital phenotyping of cognition

While most assessments of cognition in schizophrenia are not validated for mobile devices or for repeated uses outside of a controlled laboratory setting – such new uses could offer the potential of novel discoveries (Fig. 1). Furthermore, brief and valid cognitive tests on smartphone could advance the way clinicians consider assessing cognition in their practice. Even though mobile cognitive assessments may never have the same degree of reliability as standard assessments, mobile assessments have the advantage of automatically capturing the context and the local environment. This ability to capture multimodal data and thus perhaps more dynamic snapshots of the patients as they interact with their environment introduce a new window in understanding the lived experiences and needs of those with schizophrenia. Together, the advances in Biagianti et al.' (2019) web-based and Morita et al.'s (2019) eye movement-based cognitive assessment demonstrate how such multimodal data may soon be used not only in research but also in clinical care settings. The availability of remote and less expensive digital assessments of cognition could also help scaling up cognitive assessments in resource-poor countries world-wide. Such implementation will require monitoring as there can be multifactorial variables mediating the process, including cultural factors.

The transition from pen-and-paper to mobile technology is not simple and should not be rushed – but with more work, mobile technology may become an option of choice for assessing cognition in the future. Factors such as training aspects and data interpretation will require careful consideration and may vary depending on the nature and purpose of cognitive assessments, whether it is for diagnostics, periodic evaluation or for intervention. Mobile data must also be anonymized, encrypted, well protected and not used in an invasive or cohesive manner. Finally, identifying cognitive deficits in schizophrenia is also only half of the challenge and must be matched with accessible services for cognitive remediation treatments.

To date, data on mobile technology for cognitive assessments in schizophrenia is sparse, but the field is ready to conduct systematic ecological momentary evaluations of cognition. The reliability and validity

Table 1
Pros and cons of various types of cognitive assessments in schizophrenia.

|	Traditional pen-and-paper cognitive batteries	Short pen-and-paper cognitive instruments	Computer-based cognitive batteries	Smartphone-based cognitive assessments
PROS	• Many cognitive domains assessed • More comprehensive • Well validated in schizophrenia	• Short duration • Can identify individuals who have cognitive deficits • Well validated in schizophrenia	• Easy to administer • Automatic scoring • More standardized administration • Some have been validated in schizophrenia	• Easy to administer • Automatic scoring • Accessibility • Broader assessment of cognition and related phenotypes • Can provide dynamic profile of cognition
CONS	• Need extensive training to administer • Long duration for administration • Manual scoring	• Do not provide a comprehensive profile of cognitive deficits • Manual scoring	• Require specific software and access to a computer • Costs associated with license and/or scoring	• Require a smartphone • Need for validation, careful monitoring and further testing • Potential confounds to consider when assessed outside of the clinic/lab
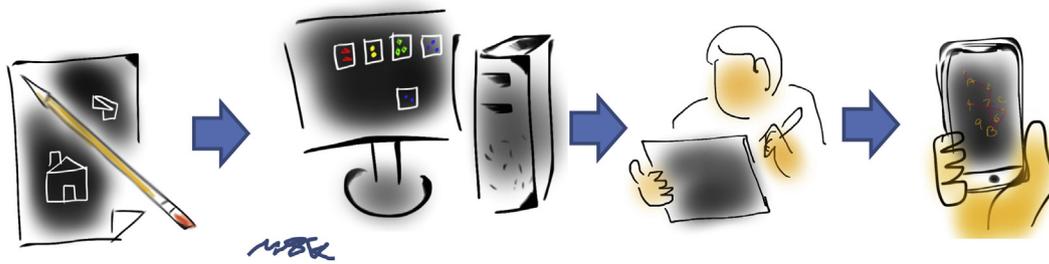
Fig. 1. The journey from pen-and-paper to smartphones via desktops and tablets enabling remote cognitive testing.

of a smartphone-based approach for assessing cognition also need to be further investigated but preliminary supporting reports exist (Sliwinski et al., 2016). Creating such evidence in an ethical manner will help ensure progress towards this goal and realization of the potential of digital health to advance progress in schizophrenia.

Conflict of interest

The authors do not have any conflict of interest to declare.

Contributors

SG and JT wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

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