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Ten years of schizophrenia research cognition

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This year (2024) marks the 10th anniversary of *Schizophrenia Research*. *Cognition*, a journal focused on cognition in schizophrenia broadly defined. According to the mission statement this topic includes "clinical neuropsychology, neurocognition, social cognition, functional capacity, cognitive, affective, and social neuroscience, and aspects of everyday outcome as related to cognition". The goal of the editorial is not a full literature review, but a highlights list and a description of our plans.

In the 10 years of the journal, we have published 304 articles indexed in Pub Med, which have included several special issues:

A vision science perspective on schizophrenia.

Edited by Steven Silverstein, 2015

Schizophrenia, recovery and the self: A special issue on metacognition.

Edited by Paul Lysaker and Christopher Bowie, 2020

The evolution of cognitive impairment in schizophrenia.

Edited by Eva Velthorst, 2022

Cognitive impairments in an increasingly digital world.

Edited by Ann-Kathrin J Fett, 2022

Toward ecological validity in cognitive assessment.

Edited by Eve Lewandowsky, in process for 2024

Neurocognition, neuromodulation, and nutrition in schizophrenia.

Edited by Jijun Wang, in process for 2024

The international character of the journal is highlighted by the origin of special issues, with editors from Canada (Bowie), The Netherlands (Velthorst), the UK (Fett), and China (Wang). Our goal has always been to provide international coverage and our first volume, published in 2014, included articles from Italy, Norway, Israel, Canada, Japan, Germany, the UK, Australia, and Nigeria, as well as the United States.

We have established and maintained a diverse and international editorial board, which at this time includes representatives from 16 countries and a junior editorial board representing 4 countries. Women are well represented with 22 women members.

At the time the journal launched, Michael Green and I wrote an

introductory article/editorial entitled "Cognition in Schizophrenia: Past, Present, and Future" Green and Harvey (2014). This has been a popular article, being cited 355 times (Accessed via Google Scholar, August 1, 2024). As part of the paper, we reviewed the history of cognition in schizophrenia, the status, and took the risk of making some predictions about the future. Although there was little risk in reviewing the past, our estimations of what would be important in the immediate future and thereafter are open to review and self-criticism. In this editorial, I'll examine what happened in the field since 2014, how much of it showed up in *Schizophrenia Research. Cognition*, and how we did in terms of our longer term predictions.

In 2014, we argued that the important current scientific topics in cognition were Social Cognition, Social, Cognitive, and Affective Neuroscience, Treatment of Cognitive and Functional Deficits, Genomic influences on cognition, and the phase of illness. Predictions for the future included the examination of the influence of motivation on cognition, technology and cognition, and advances in animal models. As far as prognostication, we were right more than we were wrong and there are only a couple areas where we either failed to predict an important new development or expected more from the research area than was produced.

It is worth noting that much of the research that is related to our predictions was conducted by members of our editorial board. Many more publications than the 304 published in our journal were generated by this very strong group and many of the new developments reviewed below originated from one of more members of this board.

Research on a social cognition was clearly a correct prediction, in that several studies were subsequently conducted (Pinkham et al., 2018; Green et al., 2024). These studies examined existing social cognition measures across populations, made modifications, and spurred spin-off research which included research on environmental consequences of social cognitive deficits. One of the conclusions has been that current measures need improvement, but they can still be sensitive to targeted treatment. This is an ongoing and expanding research area and social,

cognitive, and affective neuroscience efforts are helping to shape new developments in the refinement of social cognitive research. About 100 of the 304 articles, we published addressed social cognition in some form, either as a sole or complementary focus of the paper. So, we can put a check next to our predictions regarding neuroscience as an important domain moving forward.

In the domains of treatment of cognition and functional deficits, we were clearly 3/4 correct, in that there has been a burst of research on computerized cognitive training, explications of the right way to deliver these interventions clinically, and expansion into treatment of social cognition. Multiple meta-analyses have shown that CCT is effective (Vita et al., 2021), improves functioning when paired with psychosocial interventions (Lejeune et al., 2021), is durable (Vita et al., 2024), and feasible when remotely delivered (Jagtap et al., 2022). Remote (Nahum et al., 2021) and in person (Kern et al., 2022) social cognitive training efforts have also been implemented. Efforts targeting the combination of psychosocial interventions and cognitive training have met with considerable success, particularly with highly specific treatment targets, like getting or keeping a job (Kern et al., 2018). About 10 % of our papers in the lifetime of the journal have addressed cognitive or social cognitive remediation. To increase this representation, we have a developing issue on factors related to treatment of cognition in schizophrenia, including nutrition and neuromodulation.

There has been an explosion of research on the genomics of cognition in the general population, with studies using aggregated datasets being published with more than 3 million cases (Okbay et al., 2022). One of the truly interesting aspects of this research is the overlap of polygenic scores in the general population with those in serious mental illness, including schizophrenia (Bigdeli et al., 2022). Multiple analyses have suggested that genomic correlates of cognition are associated with risk for schizophrenia (Zheutlin et al., 2019) and that polygenic scores for cognition in schizophrenia and bipolar samples are overlapping with similar polygenic scores for educational attainment in general population samples as well as bipolar disorder (Smeland et al., 2020). Polygenic scores for cognition, educational attainment, and intelligence in the general population are correlated with polygenic scores for cognitive performance in samples of participants with schizophrenia and bipolar disorder (Harvey et al., 2020) These data could inform treatment pharmacological development in that if the genomics and factor structure of cognition seem similar across conditions and in HC, why should drug development focus on neurobiological factors specifically correlated with schizophrenia? We have published somewhat fewer articles with this focus, but around 20 of our papers addressed this topic directly or indirectly.

Since 2014, there have been many papers on cognition across the phases of illness, attempting to consider the entire lifetime course (Fett et al., 2022). Hundreds of studies have evaluated the prominence of cognitive deficits in prodromal populations (e.g., Carrión et al., 2015). These studies have also shown state dependence for both cognition and related disability, in that fully remitting prodromal cases appear to have improvement in both cognition and concurrent everyday disability (Harvey and Jones, 2019; Lam et al., 2018). Importantly, studies on this population have clearly highlighted the need for earlier detection of the prodrome, because there is no apparent progression of cognitive impairment in cases who convert to psychosis and the most cognitively impaired cases at the time of their detection are the ones at highest risk for conversion (Carrión et al., 2018).

At the other end of the spectrum, data on the lifetime course of cognition in schizophrenia have suggested that changes in performance can be detected, albeit with small effect sizes (Fett et al., 2022). One of our special issues addressed this challenge and published several papers addressing course-related changes in a variety of different subpopulations, including analyses of large samples of individuals sampled over the lifespan and characterized for both cognitive performance and functional outcomes (Romanowska et al., 2022). Overall, close to half of our articles reference the course of illness, whether it is the

characteristics of the prodrome, early psychosis, first episode psychosis, or late life features. Clearly this will remain an important topic of research.

As far as motivation and cognition, there has been a very large-scale movement to examine sensitivity to rewards in people with schizophrenia and this motivational feature has turned out to be quite important. Domains investigated included estimation of the value of various rewards, willingness to expend effort for greater or smaller rewards, and the potential influence of reward sensitivity to sustained performance of cognitively relevant everyday functional acts (Green et al., 2015).

This research area has been robust and highly informative. Going beyond a Skinnerian concept of operant behaviors mapping onto reinforcers that are equivalent to each other, with differences in the correlation between behavior and reward being determined by schedules, this data has provided insights into why cost-benefit assessments underlying motivated behaviors seem very different in schizophrenia compared to the general population. Again, motivation and cognition, whether it is motivation in general, for productive activities, or for treatment engagement has been the topic of more than 25 of our papers.

Technology and cognition was also a good guess on our part. The relentless advances of technology and the challenges in access on the part of disadvantaged populations such as people with schizophrenia have interacted to create a digital divide that compromises the ability to function without the acquisition of cognitively demanding and often behaviorally challenging skills. Again, a special issue addressed this topic, focusing both on the challenges that technology provides to SCZ participants (Czaja et al., 2017) as well as the potentially ground-breaking opportunities that technology provides to normalize functioning (Bell et al., 2022).

Technology has also been deployed for remote assessment of cognition (Russell et al., 2021) and social cognition (Parrish et al., 2022) with performance-based tests as well as momentary assessment of everyday functioning (Jones et al., 2021). As noted below, there has been a burst of interest in accuracy of self-assessment of cognition and functioning and most of the research advances have been focused on using technology, including performance based assessments and momentary assessments of everyday activities. Technology approaches have refined assessment of everyday functioning, related alterations in social cognition to alterations in suicidal ideation and allowed for examination of the convergences of momentary psychotic experiences with cognitive performance and self-assessment of performance. Our special issue on ecologically valid cognitive assessment is also going to have strong representation of technology as a central strategy for ecological validity of assessment of cognition.

We missed in two areas, one a false positive (animal models) and one a false negative (self-assessment and awareness of cognitive and functional deficits. Animal models have made less progress and cognitively relevant self-assessment much more progress than we estimated.

The most compelling work on animal models of cognition during the past decade has come from attempts to translate assessments of human cognitive deficits relevant to schizophrenia to valid animal assessment (Young and Geyer, 2015). Successful efforts to develop sustained attention (Roberts and Young, 2022), reward sensitivity and risk based decision making tests have been reported (Cavanagh et al., 2022). Successful efforts to examine touchscreen response entry have also been accomplished (Olguin et al., 2023). At the same time, neurobiological models of the origin of cognitive deficits are not markedly advanced since 2014. One compound with substantial potential for cognitive enhancement, the muscarinic M1/M4 agonist Kar XT (xanomeline plus trospium) was developed with a substantial reliance on animal models, but that research was done in the 1990s.

One of the most rapidly developing cognition and functioning research topics has been in the domain of self-assessment and momentary evaluation of performance on cognitive, social cognitive, and functional capacity indices. Global and specific competence assessments

have been collected with retrospective reports, informant impressions, and momentary technology-related data capture. As noted above, we had a special issue on this topic and multiple other papers have addressed various forms of challenges in self-assessment.

Mis-estimation of momentary cognitive and functional capacity performance has been related to a few state and trait related factors, including momentary mood states (Jones et al., 2021), failure to adjust confidence estimates to momentary performance feedback (Badal et al., 2023), poorer global performance (Jones et al., 2019), and location and social context data collected contemporaneously to the self-assessment data

Introspective accuracy is the new and commonly used term for self-assessment and there are elements of both accuracy of self-assessment and directional biases when errors are made. Global cognitive performance predicts accuracy of self-assessment, but directional biases do not seem to be related to cognitive performance (Gorora et al., 2024). As impairments in everyday functioning are correlated with both errors in self-assessment and response biases, this is likely to be a topic of future research. Several models of cognitive challenges in schizophrenia, including the hyperfocusing hypothesis (Luck et al., 2019), seem related to challenges in these domains. It seems likely that a generalized focus on self-generated information, in contrast to information originating from the environment, combined with reduced capacity limiting multitasking, may be potential causal factor in at least some self-assessment errors. This will be an area of considerable research in the future.

Going Forward.

We are making a couple of minor changes. To accommodate longer pages, we are increasing our official word limits, although they were never enforced previously. Review papers, as is common with most journals, are the most highly cited papers. We are also planning on doing annual special issues, with guest editors from inside and outside the current editorial board. We it is now explicit that papers on cognition that focus largely on other conditions are also acceptable to submit, as long as their results information research on schizophrenia.

Finally, we have two special issues to be published after our two open issues close.

The first will be on the language processes that inform cognition and social cognition, to be edited by two editorial board members: Amelie Achim from Canada and Marta Bosia from Italy. The announcement is forthcoming. The second is a 10-year anniversary issue to be edited by me. The topics are open, but we are interested in review and empirical papers that expand the topics covered in the first 10 years of the journal. That announcement is also forthcoming.

Thanks to the editorial board for their support, to the authors for their submissions, and the publisher, Susie Sun, from Elsevier, who provides guidance, assistance, and perspective. Keep us in mind going forward and help us meet our goal of expanding our number of articles published per year to more than 50.

CRediT authorship contribution statement

Philip D. Harvey: Conceptualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

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He receives royalties from the Brief Assessment of Cognition in Schizophrenia (Owned by WCG Endpoint Solutions, Inc. and contained in the MCCB).

He is chief scientific officer of i-Function, Inc. and Scientific Consultant to EMA Wellness, Inc.

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 $^{^{1}\,}$ # indicates editorial board member as an author.

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