

and tocilizumab and, equally importantly, the lack of benefits of hydroxychloroquine, lopinavir-ritonavir and azithromycin in patients hospitalized with COVID-19. The speed and power of the results obtained from a trial of extreme simplicity, with a single-minded dedication to maximizing recruitment across a health system, are impressive.

By radical simplification of procedures to minimize patient and clinician burden, RECOVERY has provided an example of a sustainable rolling trial platform which allows the sequential evaluation of multiple agents. The simplicity and speed of RECOVERY did not come at the cost of sacrificing quality or the short-cutting of ethical or regulatory oversight. Instead, the RECOVERY investigators worked closely with both the ethics committees and the UK regulator in parallel with setting up the trial, achieving a hitherto unimagined speed of trial set-up.

I believe that we urgently need to apply the lessons learned from RECOVERY in mental health trials. We have previously identified the potential for large, streamlined trials in mental health⁶, although this approach remains unusual. One exception is the BALANCE trial comparing long-term treatments in bipolar disorder⁷. In this trial, we did radically simplify procedures and achieved a reasonably sized sample with a clear primary outcome. Building on the example of RECOVERY, we now need to scale up trials such as BALANCE by an order of magnitude to allow multiple arms and deliver strong evidence of modest (but worthwhile) treatment effects.

There is no shortage of important clinical questions that need answering via large-scale, streamlined, directly randomized studies. As with RECOVERY, we should initially focus on comparative efficacy of existing, licensed interventions, adding more innovative treatments once the platform is up-and-running. A prime illustrative example is the comparative efficacy of antidepressant drugs. A network meta-analysis reported that there are potentially clinically important differences between 21 available antidepressants, but that nearly all the comparative data are indirect and based on pre-regulatory approval trials⁸. This is a major gap in the evidence base and a substantial barrier to knowing which antidepressant might be most likely to be effective for any specific patient – the goal of precision psychiatry⁹.

Large-scale, streamlined trials should be designed in partnership with a broad range of stakeholders, including patients, regulators and industry, and recruiting a broad range of patients from routine clinical settings. Large-scale recruitment can be facilitated by using electronic health records. Progressing this idea using

the momentum and learning from RECOVERY seems to be an outstanding opportunity for mental health clinicians, researchers and patients, and needs to be supported by funders.

Finally, the COVID pandemic helps to clarify the relative strengths of randomized and observational studies. Early on, considerable publicity was given to small, uncontrolled reports of the potential benefits of hydroxychloroquine. A report of routinely collected observational data seemed to confirm this, only to be quickly retracted. RECOVERY found no benefit of hydroxychloroquine in severely ill patients, although there remains the possibility that it might be effective in very early or mild cases. This demonstrates the danger of retrospective analyses of data of uncertain provenance as well as the power of large simple randomized controlled trials.

On the other hand, observational data of infection rates following vaccinations were hugely reassuring, given the remaining uncertainties around vaccine efficacy in specific patient subgroups. Observational data can extend and confirm the results of randomized trials, which will always remain smaller and less representative. These data are increasingly available via electronic care records and, although susceptible to residual confounding even after multivariate propensity score matching, may be very valuable for post-marketing safety surveillance and confirmation of treatment effects in larger, more representative datasets.

In conclusion, despite the human tragedy and suffering, the COVID-19 pandemic has inspired some outstandingly creative responses from the international research community. We need to capture this and apply it to the major global challenge of mental illness, building on the developing international collaborative efforts. We should draw inspiration from just how much can be achieved so quickly with a clearly defined objective and common sense of purpose and urgency.

John R. Geddes

National Institute for Health Research (NIHR) Oxford Health Biomedical Research Centre, University of Oxford and Oxford Health NHS Foundation Trust, Oxford, UK

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DOI:10.1002/wps.20918

Metacognition in psychosis: a renewed path to understanding of core disturbances and recovery-oriented treatment

Consistent with early definitions of schizophrenia as marked by a fragmentation of thought, emotion and desire¹, psychosis is currently understood as involving deep disturbances in the sense that persons have of themselves and their connection with the world². Though endemic across psychosis³, it has remained un-

clear how to operationalize and measure the processes which underlie and sustain these alterations in self-experience.

One challenge for empirical research is that the sense anyone has of him/herself, given its intimacy, immediacy and elusiveness, is not easily measured. Validated assessments, for example,

of the oddness of thinking, thought disorder, reasoning biases, or the inaccuracy of judgments do not capture how people amidst psychosis experience their purposes, possibilities, and life trajectories differently⁴.

Nevertheless, it is possible to evaluate processes that underlie the subjective disturbances that characterize psychosis. The sense anyone has of him/herself is enabled by the integration of experience. A sense of oneself in the world is made possible by the active synthesis of discrete experiences into a larger sense in which the relationship of those discrete experiences lends meaning to one another².

One line of research has proposed that metacognition is a process whose disruption could result in alterations of self-experience in psychosis². Metacognition, across disciplines, refers to the awareness of one's own thoughts and behaviors, and the ability to therefore monitor and alter behavior⁵. Applied to subjective experience in psychosis, an integrative model has conceptualized metacognition as a spectrum of activities that range from awareness of discrete cognitive, emotional and embodied experiences to the synthesis of those experiences into a broader awareness of the self, others and one's place in the community⁴.

Metacognition, in this integrated model, extends beyond isolated judgments, and involves processes that enable awareness of and reflection upon experience in socially situated and intersubjective contexts⁶. It allows for persons to have available, in a given moment, the kind of sense of self, others, and emergent challenges necessary to adaptation and cooperation with others².

Applied to psychosis, this model has offered several significant advances. First, it has been accompanied by the development of a tool for measuring metacognitive capacity as a continuous variable: the Metacognitive Assessment Scale Abbreviated (MAS-A)⁴. The MAS-A differentiates metacognitive capacity according to its focus on the self, others, one's community, and the use of metacognitive knowledge. It provides subscales corresponding to these four dimensions. Higher scores on each subscale reflect a sense which involves greater levels of the integration of information, while lower scores quantify more fragmented experiences⁴.

With adequate psychometric properties, the MAS-A has allowed for quantitative studies of subjective experience in psychosis internationally^{2,4,6}. Relatively greater metacognitive deficits have been detected in adults diagnosed with multiple phases of psychosis compared to healthy controls, people with non-psychiatric medical adversity, and others with less severe psychopathology.

Illuminated in these studies are qualities of how individuals experience themselves as they seek to make sense of what has happened to them and what they need. Results of these studies indicate, for example, that many individuals with psychosis are able to identify discrete embodied, cognitive and emotional states, but struggle to form a coherent sense of self in which these experiences are cohesively related to one another. Thus, we are afforded a chance to dimensionally measure the experience of fragmentation which may compromise chances of the experience of oneself as an active agent in the world with coherent possibilities and purposes.

The link of these alterations to disturbances in daily life are confirmed empirically by findings that graver metacognitive deficits within psychosis are linked to concurrent and prospective decrements in psychosocial functioning, including social behaviors, negative symptoms, and relatedly intrinsic motivation. Research has also found that changes in metacognition accompany changes in other aspects of function².

This work may offer an even more substantial advance as it goes beyond the recognition of a new variable affecting psychosocial functioning in psychosis. Contemporary research has affirmed that complex arrays of social and biological factors create and sustain psychosis⁷. Metacognition not only allows for the study of psychosis as multidetermined, but it offers a view of an underlying process that links social, biological and psychological phenomena in a fluidly interacting network which culminates in any number of possible outcomes.

As supported in a recent network analysis⁸, metacognitive capacity may act as a central node in a complex array of heterogeneous neurocognitive domains and symptoms in psychosis. In such a network, metacognitive capacity may deeply influence outcome, not only directly, but also via its influence as a node connecting and affecting the relationships among different biopsychosocial elements. Metacognition thus allows for a larger nuanced picture of the forces which shape psychosis, moving from genetics and basic brain function to socio-political issues, to phenomenology of the unique suffering, history and possibilities of a person diagnosed with psychosis.

Finally, maybe most plainly, if deficits in metacognition leave persons unable to make sense of and manage experiences that accompany psychosis, then treatment which ameliorates these deficits may open unique paths to recovery. Here, there are implications for both the general principles of recovery-oriented management as well as the development of unique treatment approaches.

Concerning the common elements of recovery-oriented management, metacognitive research suggests that, in order to promote a personal awareness and approach to managing psychosis, treatment has to be intersubjective in nature and emphasize joint meaning making rather than primarily offering clinician-directed approaches to symptom reduction and skill acquisition².

One intervention specifically developed on the basis of this work, metacognitive reflection and insight therapy (MERIT)⁹, is an integrative treatment which is responsive to patients' level of metacognitive capacity and explicitly seeks to promote the growth of this capacity over time⁶. With promising initial empirical support⁹, this operationalized treatment stands as an example of an innovation that may uniquely address the loss of persons' sense of themselves and promote self-directed recovery.

Paul H. Lysaker¹, Ilanit Hasson-Ohayon²

¹Richard L. Roudebush VA Medical Center, Indiana University School of Medicine, Indianapolis, IN, USA; ²Bar-Ilan University, Ramat Gan, Israel

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DOI:10.1002/wps.20914

The evolving nosology of personality disorder and its clinical utility

There has been increasing consensus that the classification of personality disorder in the DSM-IV and ICD-10 was no longer fit for purpose. There was no good evidence that there are nine to eleven discrete personality disorder categories, the system was too complex, and most categories were not used. The evidence pointed toward the dimensional nature of personality disturbance, with severity being the strongest determinant of disability and prognosis¹.

It was therefore not surprising that the American Psychiatric Association in the DSM-5 and the World Health Organization in the ICD-11 moved toward dimensional models of personality disorder classification. The DSM-5 Work Group proposed a model that included an evaluation of severity (Criterion A) and a description of 25 traits (Criterion B) which were organized into five domains, as well as six individual personality disorders based on DSM-IV categories. The proposal was rejected, but published in the DSM-5 Section III and labelled the Alternative Model of Personality Disorders. Despite not being part of the official classification, the model has acquired an acronym – AMPD – and has received multiple studies evaluating its utility and validity.

The ICD-11 model also involves a dimensional measure of severity (mild, moderate and severe personality disorder) and a subsyndromal condition called “personality difficulty”. Once severity has been determined, the personality dysfunction can be further delineated using one or more of the five trait domains labelled negative affectivity, detachment, disinhibition, dissociation and anankastia. The model does not retain traditional personality types, with the exception of a borderline specifier².

Research on the AMPD model progressed rapidly once a self-report instrument, the Personality Inventory for DSM-5 (PID-5), was developed. This instrument demonstrated adequate psychometric properties, including a replicable factor structure, convergence with existing personality instruments, and expected associations with clinical constructs³. Contradicting the beliefs of the DSM-5 Committee that the AMPD model lacked clinical utility, clinicians reported that the model demonstrated stronger relationships to ten of eleven clinical judgments than the DSM-5 categories⁴.

Due to its more recent development, the ICD-11 model has received less clinical scrutiny. However, studies generally report good construct validity and test/retest reliability⁵. Five domains also appear to be the best fitting model for traditional personality disorder symptoms, although the anankastia, detached and dissociation domains may be more clearly delineated than the negative affective and disinhibition domains⁶.

It has been documented that the AMPD traits (measured us-

ing the PID-5) can describe the ICD-11 trait domains⁷. Despite being derived independently, the AMPD and ICD-11 share four of the five domains; the exceptions are anankastia in the ICD-11 and psychoticism in the AMPD. Both models show relative continuity with traditional personality disorder categories and capture most of their information. The ICD-11 model is superior in capturing obsessive-compulsive personality disorder, whereas the DSM-5 model is superior in capturing schizotypal personality disorder⁸.

In addition, both models show some continuity with dimensions of personality in the general population, measured using the Five Factor Model. Negative affectivity is linked with neuroticism, detachment with low extraversion, disinhibition with low conscientiousness, and dissociation with low agreeableness. The ICD-11 anankastia is linked with high conscientiousness, while AMPD psychoticism does not particularly align with any of the five factors⁸.

On the face of it, both new models seem more “true” to the existing evidence about personality pathology than the DSM-5 official classification. Yet, the most important rationale for making such a paradigm shift – the development and evaluation of treatments – has not yet been subjected to significant study. It should be noted that there is little justification for retaining the old model of personality disorder classification regardless of how the new model performs. Only borderline personality disorder has an evidence base, and this essentially tells us that a host of treatments are similarly effective and none have shown specific efficacy for this disorder as opposed to general psychological distress and dysfunction⁹.

Nevertheless, treatment studies using the new classification are urgently needed. A number of frameworks have been put forward which, on the basis of a careful assessment of severity and trait domains, lead to a coherent and holistic formulation which is usually shared with the patient and results in the adoption of a consensual approach to treatment⁹.

A potential problem is the retention of traditional personality disorder categories in both models. In the AMPD model, six individual personality disorders are retained. Since non-personality disorder specialist clinicians generally only use three diagnoses (borderline personality disorder, antisocial personality disorder, and personality disorder not otherwise specified), a danger is that they will simply continue with their current practice. The ICD-11 model only retains one personality disorder – the borderline personality disorder specifier – but its inclusion may also compromise the change to more evidence-based practice. While the old categories have no scientific underpinnings, their familiarity may