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Perspective

Disruptive innovation in psychiatry

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Disruptive innovation is a cornerstone of various disciplines, particularly in the business world, where paradigm-altering approaches are often lauded. As a construct, *disruptive psychiatry* can be considered to embody such an approach by the pursuit of innovations within the field which test boundaries and shake up the status quo. Given the importance of addressing the current mental health pandemic, and the deficit of highly effective pharmacological treatments for various conditions, innovative disruptive thinking is required. Significant promise exists via the provision of potentially more effective innovative therapeutic options, including digital interventions, psychedelic medicines, microbiome-altering treatments, brain stimulation technology, and nanotechnology-based delivery systems. These approaches may be further advanced by individualization of the treatments using computational technology (including quantum computing, machine learning, and artificial intelligence) and genomics.

Keywords: disruptive innovation; quantum computing; psychedelics; microbiome; computational psychiatry; nanotechnology

Disrupting the current paradigm with innovation

Disruptive innovation is a cornerstone of various disciplines, particularly in the business world, where paradigm-altering approaches are often lauded.[1] *Disruptive psychiatry*, as a construct, can be considered to embody such an approach by the pursuit of innovations within the field which test boundaries and shake up the status quo. Given the importance of addressing the current mental health pandemic, and the deficit of highly effective pharmacological treatments for various conditions, innovative disruptive thinking is required to provide more effective treatment options.

Innovative interventions

Promising disruptive treatment approaches include the use of (1) psychedelic-based medicines, including the development of psychedelic drug analogues (with further research into standardized psychoactive plant-based medicines, such as cannabinoid therapies), (2) microbiome-altering therapies, (3) improved drug delivery systems (including nanotechnology), (4) digital therapies, and (5) brain-stimulation technology advances.

First, classical psychedelics, which were studied over decades prior to prohibition in the late 1960s, have been the subject of a recent reinvigoration of research, with a growing number of randomized controlled trials (RCTs). These agents have a strong affinity with the 5-HT_{2A} receptor, and may increase global brain connectivity while reducing default mode network activity (effects on neuroplasticity have also been revealed).[2] RCT and meta-analytic level data are available for classical serotonergic psychedelic agents (in particular psilocybin) in treating depression,[3,4] with preliminary evidence for other psychedelics, such as lysergic acid diethylamide (LSD) and Ayahuasca (a plant medicine combination of dimethyltryptamine and monoamine oxidase inhibitors (MAOIs) [harmala alkaloids]); while

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3,4-methylenedioxymethamphetamine (MDMA) for the treatment of post-traumatic stress disorder (PTSD) has positive phase 3 data.[5] Psychedelic interventions should be applied within a psychotherapeutic framework to lessen safety issues, and to improve clinical response via enhanced psychosocial integration of the experience.[6] An additional integrated approach involving the application of psychedelics with virtual reality (in particular via graded therapy application) included in the psychotherapeutic treatment model (for conditions, such as PTSD, social anxiety/phobias/obsessive-compulsive disorder (OCD), and addictive behaviors) may provide additional therapeutic gains. The use of haptic suits may also be a vehicle to provide data for both phenotyping and personalized treatment adjustment. In any event, while current data regarding psychedelics are encouraging (safety considerations notwithstanding),[7] it is noted that studies with larger sample sizes are required, and that these interventions suffer from challenges around maintaining adequate blinding.

Second, data are increasingly confirming that the microbiome (involving microbes from over 60 genera of bacterial species) affects neurobiological function.[8,9] The microbiome has a role in the synthesis of neurotransmitters, vagal nerve communication, and immune and inflammation modulation, with preclinical data suggesting that altering the bacterial species in the intestinal system may be a potential treatment (via the gut–brain axis).[8,10] An example of this approach is via the prescription of a high-prebiotic diet and/or probiotic interventions (although the data at present are recognized as mixed), and via fecal microbiota transplantation (reducing, e.g., *Faecalibacterium*, which has been linked to depression).[8] As detailed above, the employment of high-powered computational approaches will be able to inform the relationship between healthy or unhealthy microfloral composition and neurobiological pathology/mental disorders. Further, the future tailored application of microbiome-modulating treatment according to a person's microbial composition. It is, however, currently recognized that there are no firm data on the optimal microbial species composition and the appropriate prescription, and personalized microbiome cocktails are a fair way off at present.

The increased utilization of digital technologies, in particular via smartphones, will advance the future application of digital phenotyping, which can facilitate tailored treatment.[11] This approach can be provided at a relatively low-cost, which can also be applied as remote interventions (delivered via mental health focused Apps). The use of digital technology (collecting real-time data via smartphone and wearable technology) underpinned by artificial intelligence algorithms may provide interactive individualized application of psychological techniques, while health-promoting lifestyle elements (including adequate nutrition, physical activity, sleep hygiene, and reduced substance/alcohol use), can be delivered (potentially via interactive chatbots).[12,13]

The use of nanotechnology offers the potential to increase the bioavailability of medicines via unique delivery methods (e.g., in nanoparticle or liposomal forms) to have greater central nervous system (CNS) biological activity.[14] Typically, polymeric micelles are typically created with amphiphilic polymers to form micelles to entrap the drug, while liposomes are vesicles formed by trapping fluid by phospholipid molecules (a benefit for nonpolar agents). Such compounds are usually under 100 nanomoles and offer a greater chance of crossing the blood–brain barrier. There are, however, noted concerns over toxicity (especially regarding immune reactions), in particular in brain imaging application used in the form of quantum dots. The use of organic chemical compounds may address this concern, with more research being needed to develop safe nanotherapies.

While not an innovative disruptive technology per se (owing to general medical acceptance), further technological developments of brain stimulation technology (noninvasive [e.g., transcranial magnetic stimulation] or invasive [e.g., deep-brain] stimulation) offer a potential to provide enhanced neurocircuitry modulation.[15] There is also the potential for such technologies to be provided for patients to take home with teleguided instruction, thus reducing logistical and financial imposts. The development of superconducting quantum well interferometry device (SQUID) technology[16] also provides the potential to measure subtle magnetic fields, which may contribute to the assessment of neurophysiological pathology, and even manipulating these fields for therapeutic benefit. While evidence is nascent for SQUID's potential application as a treatment option for psychiatric disorders, it is worthy of further attention. Finally, it can be noted that the aforementioned technologies may be combined with a range of biological and psychological interventions to augment the treatment effect.

Advancing a personalized-medicine approach

To enhance the beneficial potential of innovative interventions, advances in an individualized precision-medicine approach are of utmost significance.[17] Currently, the continuing adoption advocated in the DSM-5 of a reductive model with the fixed (primarily binary) categorical diagnostic perspective[18] is emblematic of the current metaphorical straight jacket the field is presently bound by. The emerging field of computational psychiatry promises to enhance our understanding of the multilevel nexus between biological data (involving neurocircuitry, cells, and underpinning genetics) and the presentation of psychophysiological symptoms.[17,19] Such an approach is feasible given recent advances in quantum computing, machine learning, and artificial intelligence. It is likely that 100+ qubit quantum computers will be available, and this will allow the processing power to enable the analysis of complex "big data" to progress a diagnostic approach, which is more tethered to neuroscience. For instance, the use of computational psychiatry employing quantum computing can assess complex genetics information (e.g., via the genome-wide association studies) and advanced neural network algorithms.[20] This can be facilitated via deep-learning from artificial intelligence to assist in diagnosis and predictive response to pharmacological treatments. Such an application may involve the integration of real-time MRI and epigenetic data. Additionally, supercomputing can utilize block chain-based technology for healthcare data collection and storage, to provide an integration of clinical and biomarker data to assist in better patient management. Advances in quantitative electroencephalography (qEEG; and other future devices) may also provide the ability to phenotype patients to characterize likely response to interventions.

Use of point-of-care devices, including finger-prick blood collection and the application of microarrays, will enhance the assessment of an abundance of biomarker data (including chromosomal, epigenetic, single-nucleotide polymorphism (SNP), inflammatory cytokine, and nutrient information).[21] It is, however, recognized that we still cannot yet canvass clearly what is occurring behind the blood–brain barrier in the brain itself, and that peripheral biomarkers may not truly reflect this. Further advances in brain-training software also tentatively hold promise,[22] while developments in quantum technology may assist in the creation of a new generation of wearable magnetoencephalograph devices.[23] Although devices are currently external and/or wireless, for example, smartphones and wearable devices, there remains the futuristic potential of surgically implanting brain–computer interfaces directly into the CNS to modulate neuronal activity. Telepsychiatry has vastly expanded in recent years (in part rapidly advanced due to COVID-19), and has shown to be effective, especially when embedded within an integrated care model.[24] Insurance and regulatory challenges are, however, noted to still exist in some jurisdictions. Regardless, it is highly unlikely the genie will be put back in the bottle, and telepsychiatry will no doubt be proven over time to be a significant public health benefit.

The aforementioned technological advances will enable the delivery of mental healthcare moving through the phases of diagnosis, prescription/therapy, and follow-up/maintenance of patients. It is, however, recognized that data privacy considerations are critical, and significant research is still required for these to be considered mainstream.

Final comment

To successfully innovate in the field of psychiatry for sustained patient benefit, the above approaches are advised to occur within an integrative biopsychosocial treatment model, which still emphasizes human and biophilic connection.[24] This is critical to address the interface between interrelated biological systems, and address complex psychosocial elements.[1] If we act boldly now with an open-minded pursuit of disruptive innovation, the field of psychiatry can foundationally transform over the next decade.

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