http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v14i08.09

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Nanotechnology - Based Drug Delivery in Psychiatry

A Framework for Targeted Neuropsychiatric Interventions in Brain Disorders

Authors

Gamarelanbia Idris Amara[1], Ahmed Amara Gabrelsid[2], Wifag Saber Ali[3], Rana Khodr Saleh[4], Ibrahim Abdelrahim Ibrahim Humaida[5], Rodina Nasreldeen Ahmed Idris[6]

[1]Sudan Medical Specialization Board, Khartoum, Sudan
[2]Department of Computer Science, The American University of Cairo, Cairo, Egypt
[3]Faculty of Arts, Department of Psychology, Al-Neelain University, Muscat, Oman
[4]Faculty of Social Sciences, Imam Al-Ouzai University, Doha, Qatar
[5]Psychology Dept. Faculty of Arts/Omdurman Islamic Psychology
[6]Faculty of Medicine, University of Khartoum, Khartoum, Sudan.

Abstract

NPSDs are among the principal sources of disability worldwide, yet there is still a lack of sufficient efficacy and target engagement of existing medications. The limitation is mainly associated with poor targeting capacity of pharmacotherapy and delays and incomplete responses in treatment. It is due to a considerable incongruity between systemic delivery methods and brain architecture characterized by specific features of its neurobiological organization.

This study considers the problem of drug delivery in the context of modern approaches to treatment of neuropsychiatric conditions. We discuss the use of nanotechnologies for targeted drug delivery in neuropsychiatry as both a scientific concept and a method. Preclinical and translational data regarding mechanisms of enhancement of drug bioavailability, regional targeting, and lowering systemic exposure are considered. Among limitations are potential neurotoxicity and uneven biodistribution. A shortage of randomized controlled trials also limits the possibilities for further research. The key idea is that nanotechnologies can provide an innovative approach to spatiotemporal drug delivery in the brain.

Keywords: *Nanotechnology; Psychiatry; Blood–Brain Barrier; Drug Delivery Systems; Neuropsychiatric Disorders; Precision Psychiatry; Nanomedicine; Neuroinflammation; Conceptual Framework*

© 2026 The Author(s). This article is licensed under the Creative Commons Attribution 4.0 International (CC BY 4.0) License: https://creativecommons.org/licenses/by/4.0/

1. Introduction: Reframing the Problem in Psychiatry

Contemporary neuropsychiatry faces no scarcity of drugs; rather, it lacks precision regarding the methods with which such drugs act on targeted circuits within the brain. The bulk of psychoactive medications are prescribed with a systemic mode of administration despite their actual effect taking place

through a precise and localized neuronal circuit. This leads to three common deficiencies inherent in psychiatric treatment: the inability to target certain circuits, limited and irregular permeation through the BBB, and large individual variability of drug efficacy even when applied to the same condition.

The BBB prevents all macromolecules and over 98% of low molecular weight compounds from penetrating into the brain.[1] Thus, most drugs considered suitable for neuropsychiatric applications cannot reach the target due to inefficient delivery or, even when they can, do so through a non-selective process that results in off-target effects that manifest as adverse side effects.

Herein lies the core problem with the current approach, as it represents a systemic application of pharmaceuticals to treat conditions arising from faulty functioning of a particular network. One potential solution would be the introduction of nanotechnology in the field.

2. Nanotechnology as a Conceptual Shift

The application of nanotechnology within psychiatry does not mean simply having an advanced drug carrier but a radical rethinking of how drugs interact with the brain. This transition is characterized by three critical components:

- Spatial control: ability to deliver therapeutic drugs to specified parts of the brain or particular cells
- Temporal control: capacity to adjust the kinetics of drug delivery based on the biological processes involved in it
- Biological adaptability: ability of nanocarriers to respond to the local microenvironmental conditions in the brain

Nanoparticles are engineered systems with diameters ranging from 1 to 100 nm, capable of delivering drugs in a targeted manner and working as an integrative complex during transportation and release.[2] With the development of different types of nanocarriers, such as polymeric, liposomal, solid lipid nanoparticles, and dendrimers, it became possible to package psychoactive substances, prevent their degradation by enzymes, and direct their action toward the necessary targets within the central nervous system.

Thus, meaning that nanotechnology will replace the existing concept of systemic pharmacology with a new approach, where drug delivery is engineered as a necessary part of therapy.

3. The Blood–Brain Barrier: From Obstacle to Design Parameter

The BBB is an extremely specialized multicellular complex that provides exceptional protection in maintaining brain homeostasis and controlling the transport of ions and molecules between the brain and blood cells.[3] Its existence is critical for proper neurological activity; on the contrary, its dysfunction has been linked to various neurological problems like neuroinflammation, neurodegeneration, and pathologies associated with stroke or Alzheimer's disease.

The field of nanotechnology has found ways to overcome the BBB by designing new ways through it. In particular, three main approaches can be distinguished in this regard:

- Receptor-mediated transport (RMT): use of nanoparticles modified with receptors of natural BBB receptors like insulin or transferrin receptors to exploit natural pathways
- Lipidic vesicles: liposomes and solid lipid nanoparticles to take advantage of lipophilicity of the BBB endothelium
- Targeting of surface ligands: addition of apolipoprotein E, polysorbate 80, or other ligands to bind to the endogenous transporters

Use of receptor-mediated transport involving peptidomimetic monoclonal antibodies targeted against the endogenous BBB receptors, like the insulin or transferrin receptor, helps redesign biologics to form a neuropharmaceutical that passes through the BBB.[4] Yet the true conceptual progress here goes beyond just crossing the BBB, which is the more serious challenge of ensuring that the therapeutic agent reaches the correct neural targets in sufficient concentrations while maintaining its biological activity and minimizing off-target effects.

4. Rethinking Side Effects as a Systems-Level Phenomenon

Side effects due to psychotropic medications are normally seen through the lens of toxicity, unwanted actions of the substance on unintended body areas. The emergence of nanotechnology brings another viewpoint; the majority of side effects might actually stem from the non-specific distribution of drugs in the bloodstream. The use of nanostructures can decrease systemic exposure and enhance the selectivity for CNS, thus enabling the reduction of doses without diminishing or even increasing therapeutic effects.

Nasal administration of nano-sized particles has already been proven capable of delivering drugs into the brain at an accelerated pace, increasing bioavailability and thus ensuring faster onset of pharmacological effect, and decreasing systemic exposure as well.[5] Such approach, applied to clinical psychopharmacology, will change the view on side effects as an inevitable part of the process into an engineering challenge.

On the other hand, the very introduction of nanoparticles introduces a number of factors yet unknown. Tissue deposition, immunogenicity, and neurovasculature interaction represent new issues that need thorough research before clinical application.

5. Neuropsychiatric Applications: Preclinical and Translational Mapping

5.1 epression

The use of nanotechnology to treat depression involves developing treatments that target brain circuits involved in the regulation of moods. Recent research has demonstrated improved drug distribution and efficacy, in addition to increased uptake into the brain and controlled release via the intranasal administration of nanoparticulate formulations.[5] The nanoencapsulation of selective serotonin reuptake inhibitors and new drugs such as ketamine has been studied in attempts to facilitate faster onset of treatment and increase specificity in prefrontal cortex and hippocampal regions.

5.2 Schizophrenia

The current understanding of schizophrenia emphasizes dysfunction of neural connectivity rather than localized pathology, a hypothesis which details well with the concept of spatially-targeted delivery via nanotechnology.[6] The use of nanocarriers for the delivery of antipsychotics could lead to reduced drug doses while still achieving adequate receptor occupancy in the brain's striatum, thus helping prevent the occurrence of side effects such as extrapyramidal symptoms and metabolic complications. Studies using polymers containing risperidone and haloperidol have been successful.

5.3 Anxiety and PTSD

PTSD and anxiety disorders are characterized by disruptions to the fear network involving amygdala-hippocampal structures. Direct delivery to these brain regions through nanocarriers carrying anxiolytic drugs allows one to manipulate fear memory extinction and reconsolidation processes with much higher selectivity compared to oral and intravenous drug delivery currently employed.

5.4 Neuroinflammation as a Target Across Several Psychiatric Disorders

Neuroinflammation is increasingly recognized as a common denominator between several psychiatric conditions, including depression, schizophrenia, and PTSD. Nanotechnology provides the possibility to deliver anti-inflammatory agents selectively to particular regions of the brain, something that is not possible to achieve through general systemic administration.[3] The transport of anti-inflammatory drugs with the help of nanoparticles functionalized on the surface to pass through the BBB and microglia-rich brain regions appears to be one of the most promising near-term applications of nanomedicine.

It should be emphasized that all the data mentioned above are primarily obtained preclinically or experimentally. Significant physiological differences exist between humans and rodents that must not be overlooked when considering translatability issues.

6. Safety, Toxicity, and Translational Uncertainty

Safety issues related to nanoparticles used in the CNS are currently being explored. There are multiple mechanisms which can cause adverse effects on neuronal function:

- Oxidative stress and mitochondrial dysfunctions due to the formation of reactive oxygen species caused by interaction between nanoparticles and cells, which might cause lipid, nucleic acid, protein oxidation, and which affect the brain in particular because of its high metabolic activity and relatively low antioxidant capacity
- Nerve inflammation due to the stimulation of microglia, as was shown in vitro and in vivo experiments
- Biodistribution of nanoparticles during prolonged exposure in brain tissue, which includes possible accumulation in certain types of neurons
- The effect of nanomaterials on the processes of immunology and neurovasculature

Oxidative stress and inflammation caused by reactive oxygen species induced by nanoparticles can lead to the damage of proteins, membranes, and DNA; it represents one of the major factors leading to neurotoxicity.[7] However, these safety issues are not obstacles for further investigations and development. At present, the majority of scientific evidence available comes from animal studies and in vitro experiments. It is important that extrapolations be done with utmost care when trying to apply the results obtained in humans.

7. Ethical and Neurophilosophical Considerations

The potential to introduce psychoactive substances with unprecedented precision is accompanied by a host of ethical challenges that transcend traditional pharmacology-based risk/benefit considerations. In particular, the following four concerns call for further investigation:

- Cognitive/affective manipulation: targeting specific circuits related to memory, emotions or motivation brings into question issues of distinction between treatment and enhancement, as well as defining true therapeutic effect
- Neuronal privacy and autonomy: ability to target specific neuronal circuits raises concerns regarding mental privacy and the integrity of subjective experience
- Issues of informed consent: patients undergoing neuropsychiatric nanotherapy will require information not only about traditional pharmacological risk factors, but also about the consequences of precise modulation of certain circuits, thus calling for an entirely new approach to scientifically informed consent
- Non-targeted behavioral modification: the very high level of precision associated with nanopsychiatry means that any non-targeted influence will affect nearby neural circuits very specifically and possibly unpredictably

This list of ethical problems firmly places the discipline within the sphere of neuroethics and philosophy of mind.

8. Conceptual Model

This suggested transformation may be illustrated by the shift between two paradigms:

Traditional paradigm: Systemic administration of drugs → distribution into the bloodstream → incomplete and nonselective distribution into the brain → systemic side effects and CNS side effects due to broad distribution

Nanotechnology paradigm: Nanocarrier design → targeted delivery into the CNS by receptor-mediated and surface-engineering approaches → release into selected neural circuits → localized effect with minimal systemic distribution

Rather than being the end of pharmacological unpredictability, this transformation illustrates the relocation of such unpredictability from one scale to another. Rather than dealing with issues of poor CNS penetration and unwanted side effects due to the distribution, new issues of biodistribution, immunogenicity, and long-term deposition arise.

9. Scoping Synthesis

This paradigm synthesizes evidence and theory related to the following three categories: the physiological barriers posed by the blood-brain barrier and systemic toxicity; the nano-engineering techniques used to address these challenges; and the translational applications to psychiatry in progress.

The most critical omission noted here is the utter lack of clinical trials in humans for any nano psychiatry intervention. While preclinical studies have yielded encouraging results, this does not replace clinical trials, which will eventually be necessary. The current state of research is still at the very beginning of a translational stage at which there are many unanswered questions.

10. Future Directions

New uses of artificial intelligence and machine learning in the context of nanocarrier design provide the possibility for predictive models to be created for key delivery factors such as particle size, loading efficacy, and biodistribution of drugs, making the development of CNS-directed therapeutics a predictable process rather than an experimental one.[8] The combination with the concept of responsive drug release systems that can alter their operation depending on certain changes in local neurochemistry or neurophysiology is the aim for the future.

Nanomedicine combined with neuroimaging markers, circuit-directed diagnosis of mental illnesses, and Research Domain Criteria (RDoC), which describe psychopathologies from a neurobiological perspective, may lead to a truly personalized approach to psychiatry where treatment options would be chosen based not only on diagnosis but also on the patient's particular brain dysfunction.

11. Conclusion

For starters, the use of nanotechnology in psychiatry must go beyond the realm of merely being a technological advancement in pharmacology; the paradigm must evolve from an era of systemic pharmacology where drug delivery is imprecise, to one of engineering and precision where neurocircuits can be targeted specifically.

The discipline has yet to mature into a full-fledged area of scientific research. Its transition from concept to clinical practice would need extensive human trials as well as stringent standards regarding safety, multidisciplinary research involving neuroscience, engineering, and philosophy, along with the drafting of new ethical and regulatory guidelines that take into account the capabilities provided by these technologies. However, the way forward may not necessarily be smooth-sailing since there will likely be challenges along the way. Nonetheless, the idea itself is sound and worth exploring.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The author declares no competing interests.

Funding

Not applicable.

Acknowledgements

Not applicable.

Authors information

Not applicable.

References

1. Alberto M, Paiva-Santos AC, Veiga F, Pires PC. Lipid and polymeric nanoparticles: successful strategies for nose-to-brain drug delivery in the treatment of depression and anxiety disorders. *Pharmaceutics.* 2022;14(12):2742. doi:10.3390/pharmaceutics14122742
2. Insel TR. Rethinking schizophrenia. *Nature.* 2010;468(7321):187–193. doi:10.1038/nature09552
3. Kreuter J. Drug delivery to the central nervous system by polymeric nanoparticles: what do we know? *Advanced Drug Delivery Reviews.* 2014;71:2–14. doi:10.1016/j.addr.2013.08.008

4. Pardridge WM. Drug delivery to the brain: the vascular route. *Drug Discovery Today.* 2007;12(1–2):54–61. doi:10.1016/j.drudis.2006.10.013
5. Pardridge WM. Targeted delivery of protein and gene medicines through the blood–brain barrier. *Clinical Pharmacology & Therapeutics.* 2015;97(4):347–361. doi:10.1002/cpt.18
6. Pardridge WM. Advanced blood–brain barrier drug delivery. *Pharmaceutics.* 2023;15(1):93. doi:10.3390/pharmaceutics15010093
7. Saraiva C, Praça C, Ferreira R, Santos T, Ferreira L, Bernardino L. Nanoparticle-mediated brain drug delivery: overcoming blood–brain barrier to treat neurodegenerative diseases. *Journal of Controlled Release.* 2016;235:34–47. doi:10.1016/j.jconrel.2016.05.044
8. Win-Shwe TT, Fujimaki H. Nanoparticles and neurotoxicity. *International Journal of Molecular Sciences.* 2011;12(9):6267–6280. doi:10.3390/ijms12096267
9. Wohlfart S, Gelperina S, Kreuter J. Transport of drugs across the blood–brain barrier by nanoparticles. *Journal of Controlled Release.* 2012;161(2):264–273. doi:10.1016/j.jconrel.2011.08.010
10. Yousfan A, Al Rahwanji MJ, Hanano A, Al-Obaidi H. A comprehensive study on nanoparticle drug delivery to the brain: application of machine learning techniques. *Molecular Pharmaceutics.* 2023;21(1):333–345. doi:10.1021/acs.molpharmaceut.3c00880