# Nanopsychiatry: the future is here

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**Abstract**

**Introduction, Problem Statement, and aim:** Psychiatry is a relatively newer medical specialty which studies the human mind. Nanotechnology has recently taken the world by storm. This includes the study of psychiatric disorders. Depression has established itself as a leading cause of morbidity and mortality worldwide with frightening statistics. In this paper, we aim to explore the contributions of nanotechnology in the evolvement of the study and treatment of depression. We also aim to see to it that awareness of the existence of such technologies is raised so that all researchers and scientists, irrespective of background, are guaranteed access to this ever-evolving knowledge, despite it being at its infancy.
**Research Methodology:** The authors searched all accessible databases (Scopus, PubMed, Google Scholar, etc.) and downloaded all available papers on the topic. This resulted in the exclusion of some closed-access publications, duplications, and non-peer reviewed articles. Following this, we assessed whether or not the papers were addressing the topic in the manner that aligned with our aim for this paper.
Having selected all papers available that aligned with our aims, the papers were divided equally between the aforementioned authors. Each of whom looked into the papers assigned to them and summarized the data existent within the paper. Following this, the authors gathered all the data they have collected through the aforementioned process and edited the work so as to create a readable review. **Applications of Nanopsychiatry in depression:** In this paper, we looked into the possible applications of Nanopsychiatry in combating depression. We illustrate the possible implications of nanotechnology in the delivery of antidepressants to patients in a timely and effective manner.

*Keywords*: Naonotechnology; Nanomedicine; Nanopsychiatry; Depression; Haloperidol; Psychiatry

"The future of psychiatric treatments depends on Nanotechnology"(1)

## Introduction:

In 1808, the term 'psychiatry' was first coined (2) by JC Reil (1759-1813) (2–4). Depression is a mental health disorder that causes significant morbidity and mortality. In fact, approximately speaking, around 5% of adults suffer from the illness (5). Whenever the functionality of the brain is discussed, the works of Wundt and James are discussed, these being a) structuralism and b) functionalism, respectively (1,6).
As is well known in the field of mental health, a number of causes can be attributed to mental disorders. These include, but are not limited to, the following: i) environmental factors, ii) genetic factors, iii) social stigma, iv) social issues, v) stress, etc.
Data indicates that neuropsychiatric disorders (of which, depression is one) carry a heavier burden in higher-income countries as opposed to their lower-income counterparts (7). It also clearly states that unipolar depression is highly likely to lead the world charts of burden of disease (7).

## Aim:

The aim of this paper is to illustrate the manners in which nanotechnology can be applied in the treatment of depression. This is a look into the future of the treatment of depression.

## Problem Statement/Justification:

Rates of depression are at an all-time-high. With that being said, it is of the upmost importance that we, as providers of healthcare, namely, mental healthcare, work, in an aggressive manner, towards seeing to it that all sensible options of treatment are explored 'no stone left unturned' so as to see to it that we not only improve outcomes (decreased morbidity and mortality rates), but also increase our power to predict and prevent depression.
With evidence suggesting that long-term levels of treatment-resistant-depression (TRD) manifesting themselves at approximately 40% (8), it is of crucial importance that the topic is explored.
In this paper, we aim to address the former point by exploring the latest nanotechnological options for addressing depression.

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Limitations to this include the inaccessibility of a number of papers (due to paid walls, nation-wide restrictions, etc.…).

**Depression:**

'Far more than any other type of illness, mental disorders are subject to negative judgments and stigmatization.'(9)

The DSM-V (10) divides depression into:

i) Disruptive mood dysregulation
ii) Major Depressive Disorder (including major depressive episode)
iii) Persistent Depressive Disorder (dysthymia)
iv) Premenstrual dysphoric disorder
v) Substance/medication-induced depressive disorder
vi) Depressive disorder due to another medical condition
vii) Other specified depressive disorder
viii) Unspecified depressive disorder

Data indicates that the lifetime prevalence rate of Major Depressive Disorder (MDD) ranges between 4 and 14% (11). This further 'hammers down' our aforementioned statement discussing the seriousness of depressive disorders and the threat they bring to the well-being of the world.

**Treatment of depression:**
For the time being, anti-depressants manifest themselves as the first-line treatments immediately following diagnosis (1,11). Antidepressants are divided into: a) SSRIs, b) cyclic drugs, and c) MAOIs with SSRIs being the go-to treatment for all depressed patients (12). These medications, despite being first-line, have a, at best, moderate (40-60%) effect on major depressive episodes, with even lower remission rates (30-45%) (11,13–15).
Furthermore, it is urged that individuals diagnosed with depression undergo psychotherapy (16), namely:

i) CT

ii) CBT
iii) IPT
iv) CBASP
v) PST
vi) PI

CT and CBT were developed by Beck and colleagues'(17,18), IPT was developed by Klerman and Weissman (19,20), McCullough developed CBASP (21,22), PST was developed by Gath, Catalan, Mynors-Wallis, and colleagues (23), and PI was developed by Hobson; after which it was further developed by Guthrie and Shapiro (16,24–26).
Back in 2020, Radaic and colleagues clearly illustrated the available routes for utilization when it comes to drug delivery (27)
Of the commonly used drugs in psychiatry in general is haloperidol (28); ergo, it is important that we look into nanotechnological applications of the drug. In 2007, Budhian and colleagues PLGA and PLA filled with haloperidol were created using Sonication and homogenization methods (29). Following this train of thought, it is logical to assume that the same methodology may be applicable towards other medications; ergo, allowing for the use of this technology in the delivery of antipsychotic drugs (30).

**What is Nanotechnology?:**
Nanotechnology is art of studying matter of miniscule size (1-100 nm) and manifesting innovation in that field.
The notion can be traced back to when Zsigmondy (the 1925 Nobel Prize Laureate in Chemistry) first introduced the idea of a 'nanometer' (31).
However, the pivot point of nanotechnology can be traced back to the legendary Richard Feynman, who was the 1965 Nobel Prize Laureate in Physics and the deliverer of the famous 1959 "There's Plenty of Room at the Bottom" where he clearly illustrated his idea of manipulating matter at a smaller (atomic) level than was then believed possible (31). Of course, it is of importance that we understand that particle size is of the importance as it should approximately be 100 nm (32).
Despite this, it was only in the 1970s that the term 'nanotechnology' was coined; this can be attributed to the Japanese scientist Norio Taniguchi (31).
By the 1980s, nanotechnology had gained traction on a number of fronts and this era can be termed the 'golden era of nanotechnology' (31). Using the available data at the time, Eric Drexler of Massachusetts Institute of Technology (MIT) wrote ''Engines of Creation: The Coming Era of Nanotechnology'' in 1986 (33).
Another pivotal point in the evolution of nanotechnology was with the magnificent work of Iijima of Japan, who developed carbon nanotubes in the early 1990s (34).
Of the historically significant moments regarding the evolution of nanotechnology was when President William (Bill) Clinton of the United States promoted the support of research in the rapidly evolving science that is nanotechnology when addressing Caltech back in January of 2001 (31).
Another point in time where the United States (US) government played a significant role in seeing to it that nanotechnology receives the attention it deserves was when President GW Bush signed the '21st Century Nanotechnology Research and Development Act', which resulted in creation of the 'National Nanotechnology Initiative' (NNI) (31). Nowadays, this is part of a hierarchy with the President's Cabinet-level National Science and Technology Council (NSTC) residing at its pinnacle (35).
Another critical implication of nanotechnology is in the delivery of topically-administered drugs which are infamous for possessing a low bioavailability (36).

**What is Nanopsychiatry:**

Nanopsychiatry is a newly, yet rapidly emerging science which looks into the usage of nanoparticles in the designing of drugs, tools for diagnosis, and treatments for a number of psychiatric/neurologic illnesses (1). It is a branch of nanomedicine which is the science that looks into the application of nanotechnology into advancement of the well-being of humans (37). For the purpose of assessing and tracking some of the physiological mechanisms of a typical brain, nanomaterials have become a crucial component of experimental neurophysiology (38). Of the leading reviews in this field is the one done by Sanchez and colleagues who clearly illustrated what Nanopsychiatry is and all the possible applications (39).

One of the many reasons why this science has manifested itself as innovative and a source of interest is the fact that nanoparticles possess the capability to pass a number of biological barriers (e.g. the Blood-Brain-Barrier (BBB)), marking them as potential drug delivery systems (40). With a significant number of psychiatric diseases being treated via antipsychotic/ anti-depressive drugs (41), it is of the upmost importance that we see to it that we utilize these as much as possible.

With a focus on crossing the BBB, a number of drugs are currently available with nanofromulations. A number of drugs currently being investigated have reached the clinical trial stage (42).

**Recommendations:**

i) The immediate conduction of research projects pretraining to the application of nanotechnology in psychiatric practice

ii) The immediate allocation of financial and logistical resources towards the conduction of the aforementioned researches

**Authors' Note:**

All authors contributed equally to the formulation of this work.

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**References:**

1. Harini K, Girigoswami K, Girigoswami A. Nanopsychiatry : Engineering of nanoassisted drug delivery systems to formulate antidepressants. Int J Nano Dimens. 2022;13(3):256–66.
2. Marneros A. Psychiatry's 200th birthday. British Journal of Psychiatry. 2008;193(1):1–3.
3. Christian J, Ostfriesland R. NDB-Artikel. 1937;
4. Binder DK, Schaller K, Clusmann H. The seminal contributions of Johann-Christian Reil to anatomy, physiology, and psychiatry. Neurosurgery. 2007;61(5):1091–6.
5. Osman HI, Salaheldeen S. A look into the correlation between Major Depressive Disorder (MDD) and physical activity. International Journal of Research Publications. 2022;97(1):228–34.
6. Littlewood R. Psychiatry's culture. Int J Soc Psychiatry. 1996;42:245–68.
7. Saraceno B, Dua T. Global mental health: The role of psychiatry. European Archives of Psychiatry and Clinical Neuroscience. 2009;259(SUPPL. 2):109–17.
8. Forte A, Baldessarini R, Tondo L, Al. E. Long-term morbidity in bipolar-I, bipolar-II, and unipolar major depressive disorders. J Affect Disord. 2015;178:71–78.
9. Rossler W. A millennia-long history of social exclusion and prejudices. The European Molecular Biology Organization [Internet]. 2016;17(9):1250–3. Available from: https://www.embopress.org/doi/epdf/10.15252/embr.201643041
10. AMERICAN PSYCHIATRIC ASSOCIATION. DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS. FIFTH. Washington, DC. London, England: American Psychiatric Publishing; 2013.

11. Vázquez GH, Bahji A, Undurraga J, Tondo L, Baldessarini RJ. Efficacy and Tolerability of Combination Treatments for Major Depression: Antidepressants plus Second-Generation Antipsychotics vs. Esketamine vs. Lithium. Journal of Psychopharmacology. 2021;35(8):890–900.
12. Naber D, Bullinger M. Should antidepressants be used in minor depression? Dialogues Clin Neurosci. 2018;20:223–8.
13. Baldessarini R. Chemotherapy in Psychiatry: Pharmacologic Basis of Treatments for Major Mental Illness. 3rd ed. New York, NY: Springer-Verlag.; 2013.
14. Rush A, Kraemer H, Sackeim H, Al. E. Report by ACNP Task Force on response and remission in major depressive disorder. Neuropsychopharmacology. 2006;31:1841–53.
15. Yuan Z, Chen Z, Xue M, Al. Et. Application of antidepressants in depression: Systematic review and meta-analysis. J Clin Neurosci. 2020;80:169–181.
16. Frank E, Novick D, Kupfer DJ. Antidepressants and psychotherapy: A clinical research review. Dialogues in Clinical Neuroscience. 2005;7(3):263–72.
17. Beck A. Cognitive therapy: past, present, and future. In: Mahoney MJ, eds. Cognitive and Constructive Psychotherapies: Theory, Research, and Practice. New York, NY: Springer Publishing Co; 1995. 29–40 p.
18. Beck A, Rush A, Shaw B, Emery G. Cognitive Therapy of Depression. New York, NY: Guilford Press; 1979.
19. Weissman M, Markowitz J, Klerman GA. Comprehensive Guide to Interpersonal Psychotherapy. New York, NY: Basic Books; 2000.
20. Klerman G, Weissman M, Rounsaville B, Chevron E. Interpersonal Psychotherapy of Depression. New York, NY: Basic Books; 1984.
21. Keller M, McCullough J, Klein D, et. al. A comparison of nefazodone, the cognitive behavioral-analysis system of psycho-therapy, and their combination for the treatment of chronic depression. N Engl J Med. 2000;342:1462–70.
22. McCullough J. Treatment for Chronic Depression: Cognitive Behavioral Analysis System of Psychotherapy (CBASP). New York, NY: Guilford Press; 2000.
23. Mynors-Wallis L, Davies I, Gray A, Barbour F, Gath D. A randomised controlled trial and cost analysis of problem-solving treatment for emotional disorders given by community nurses in primary care. Br J Psychiatry. 1997;170:113–9.
24. Hobson R. Forms of Feeling: The Heart of Psychotherapy. New York, NY: Basic Books; 1985.
25. Guthrie E, Moorey J, Margison F, et. al. Cost-effectiveness of brief psychodynamic-interpersonal therapy in high utilizers of psychiatric services. Arch Gen Psychiatry. 1999;56:519–26.
26. Guthrie E, Moorey J, Barker H, Margison F, McGrath G. Psychodynamic-interpersonal psychotherapy in patients with treatment resistant psychiatric symptoms. Br J Psychother. 1998;15:155–66.
27. Radaic A, Martins-de-Souza D. The state of the art of nanopsychiatry for schizophrenia diagnostics and treatment. Nanomed Nanotechnol Biol Med. 2020;28:102222–8.
28. Fan X, Yang J, Loh XJ, Li Z. Polymeric janus nanoparticles: Recent advances in synthetic strategies, materials properties, and applications. Macromol Rapid Commun. 2019;40:1800203.
29. Budhian A, Siegel SJ, Winey KI. Haloperidol loaded PLGA nanoparticles: Systematic study of particle size and drug content. Int J Pharm. 2007;336:367–75.
30. Puri R, A Berhe S, O Akala E. pH-sensitive polymeric nanoparticles fabricated by dispersion polymerization for the delivery of bioactive agents. Pharmac Nanotechnol. 2017;5:44–66.
31. Hulla JE, Sahu SC, Hayes AW. Nanotechnology: History and future. Human and Experimental Toxicology. 2015;34(12):1318–21.
32. Fond G, Macgregor A, Miot S. Nanopsychiatry— the potential role of nanotechnologies in the future of psychiatry: A systematic review. Eur Neuropsychopharmacol. 2013;23:1067–71.
33. Drexler KE. Engines of Creation: The Coming Era of Nanotechnology. New York, NY: Anchor Books; 1986.
34. Iijima S. Helical microtubules of graphitic carbon. Nature. 1991;354:56–8.
35. NSCT, CoT, NSET. The National Nanotechnology Initiative Supplemen. National Science and Technology

Council. 2015;88.
36. Raghu PK, Bansal KK, Thakor P, Bhavana V, Madan J, Rosenholm JM, et al. Evolution of nanotechnology in delivering drugs to eyes, skin and wounds via topical route. Pharmaceuticals. 2020;13(8):1–30.
37. Ghosh S, Girigoswami K, Girigoswami A. Membrane-encapsulated camouflaged nanomedicines in drug delivery. Nanomedicine. 2019;14:2067–82.
38. Zhang M, Bishop BP, Thompson NL, Hildahl K, Dang B, Mironchuk O, et al. Quantum dot cellular uptake and toxicity in the developing brain: Implications for use as imaging probes. Nanoscale Adv. 2019;1:3424–42.
39. Sobarzo-Sánchez E, Mohammad Nabavi, S. Uriarte E, Santana L. Nanoparticles in the treatment of mental disorders: A new tool in the psychiatric medication. Curr Top Med Chem. 2015;15:282–6.
40. Heidarzadeh M, Gürsoy-Özdemir Y, Kaya M, Abriz AE, Zarebkohan, A., Rahbarghazi R, Sokullu E. Exosomal delivery of therapeutic modulators through the blood–brain barrier; promise and pitfalls. Cell & Biosc. 2021;11:1–28.
41. Koliatsos VE, editor. Neuropsychiatry, An Issue of Psychiatric Clinics of North America. 1st ed. Elsevier; 2020.
42. Li X, Tsibouklis J, Weng T, Zhang B, Yin G, Feng G, et al. Nano carriers for drug transport across the blood–brain-barrier. J Drug Target. 2017;25:17–28.