

## Radiobiology in Nowadays: Review in the News Trends in Radiopharmacy and in Psychiatric Diagnosis

Sebastião David Santos-Filho\* and Roberto Levi Jales

\*Clínica Serviço de Imagem Médica, Petrópolis, Natal, RN, Brazil.

Received August 03, 2021; Revised October 11, 2021; Accepted October 14, 2021

### ABSTRACT

**Introduction:** In Nuclear medicine radiopharmaceuticals or radiobiocomplex are used to obtain images of the human body to recognize alterations in the physiology and to identify metabolic problems. The psychiatric diagnosis of different mental disturbs is nowadays a good resource and a data bank of the obtained images is made to attend the clinic use. Using a mathematical language, the nuclear medicine inform that the obtained image belongs to a psychiatric group of diseases.

**Objective:** The authors pretend to review the news publications done with radiopharmaceuticals, nuclear medicine and psychiatry to elucidate the applications in these areas.

**Methods:** It was searched in June 30th 2021, the PubMed database articles published in the last 5 years with the following keywords: nuclear medicine and radiopharmaceuticals and psychiatry as a review and systematic review works.

**Results:** Then it was founded 38 works in the PubMed database. Only 17 were as a free full text article. It was selected 7 articles that have a mention about medical image diagnostic for psychiatric disorders and the use of radiopharmaceuticals. These were described using the methods, results and conclusions about the research they were proposed.

**Conclusions:** By the way, the psychiatrics pass by to have information about of mental disease, their classification, prognostic and diagnose suggestions by data bank.

**Keywords:** Radiobiology, Radiobiocomplex, Nuclear medicine, Radiopharmacy, Psychiatry, Medical image diagnosis, Data bank

### INTRODUCTION

In Nuclear medicine radiopharmaceuticals or radiobiocomplex [1] are used to obtain images of the human body to recognize alterations in the physiology and to identify metabolic problems [2-4]. The use of radiopharmaceuticals in medicine was recommended along the years to diagnostic diseases of the human system [5].

Radiopharmaceuticals as well as HMPAO [6], SESTAMIBI [7], ECD [8], and others that use  $^{99m}\text{Tc}$  as a probe to identify the target organs metabolic physiology, and in psychiatric diagnosis they are still used too [9-15]. Other works using FDG could also identify cerebral altered activity [16-18], because FDG with the probe of glucose labelling with  $^{18}\text{F}$  as a marker of the metabolic activity of the brain using glucose or the lack of its activity because the neurons are damaged.

The psychiatric diagnosis of different mental disturbs is nowadays a good resource and a data bank of the obtained images is made to attend the clinic use [12]. This data with

nuclear medicine imagens has a differential of figures obtained from patients' brains that could be useful in our days [9-12].

The psychiatry is one of the more needy medical specialties, in terms of complementary examinations, and the cerebral SPECT done with HMPAO could be used to help the clinician in doubt cases. In some cases when we have the association of cerebral SPECT with computed tomography and/or magnetic resonance could precede the mental diseases diagnostic. Using a mathematical

**Corresponding author:** Sebastião David Santos-Filho, Clínica Serviço de Imagem Médica, Petrópolis, Natal, RN, Brazil, E-mail: sdavidsfilho@gmail.com

**Citation:** Santos-Filho SD & Jales RL. (2022) Radiobiology in Nowadays: Review in the News Trends in Radiopharmacy and in Psychiatric Diagnosis. *Int J Med Clin Imaging*, 8(1): 400-406.

**Copyright:** ©2022 Santos-Filho SD & Jales RL. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

language, the nuclear medicine inform that the obtained image belongs to a psychiatric group of diseases (for example, bipolarity, schizophrenia, and others) [11].

In this work authors pretend to review the news publications done with radiopharmaceuticals, nuclear medicine and psychiatry to elucidate the applications in these areas.

**METHODOLOGY**

It was searched on June 30th 2021, the PubMed database articles published in the last 5 years with the following key-words: nuclear medicine and radiopharmaceuticals and

psychiatry as a review and systematic review works. Then it was founded 38 works that only 17 were as a free full text article. It was selected 7 articles that have a mention about medical image diagnostic for psychiatric disorders and the use of radiopharmaceuticals. These were described using the methods, results and conclusions about the research they were proposed. These findings were presented through tables bellow.

**RESULTS**

In **Table 1** it is analyzed the methods and results presents in 7 articles chosen from the research in PubMed.

**Table 1.** Presentation of principal methods and results founded.

Article	Methods	Results
Chandra [13]	This review provides an overview of the current status and applications of in vivo molecular imaging of AD pathology, specifically amyloid, tau, and microglial activation.	PET imaging studies were included and evaluated as potential biomarkers and for monitoring disease progression. Although the majority of radiotracers showed the ability to discriminate AD and MCI patients from healthy controls, they had various limitations that prevent the recommendation of a single technique or tracer as an optimal biomarker.
Ducharme [14]	A systematic literature search with a narrative review was performed to determine all bvFTD-related diagnostic evidence for the following topics: bvFTD history taking, psychiatric assessment, clinical scales, physical and neurological examination, bedside cognitive tests, neuropsychological assessment, social cognition, structural neuroimaging, functional neuroimaging, CSF and genetic testing. For each topic, responsible team members proposed a set of minimal requirements, optimal clinical recommendations, and tools requiring further research or those that should be developed. Recommendations were listed if they reached a 585% expert consensus based on an online survey among all consortium participants.	New recommendations include performing at least one formal social cognition test in the standard neuropsychological battery for bvFTD. We emphasize the importance of 3D-T1 brain MRI with a standardized review protocol including validated visual atrophy rating scales, and to consider volumetric analyses if available. We clarify the role of 18F-fluorodeoxyglucose PET for the exclusion of bvFTD when normal, whereas non-specific regional metabolism abnormalities should not be over-interpreted in the case of a psychiatric differential diagnosis. We highlight the potential role of serum or CSF neurofilament light chain to differentiate bvFTD from primary psychiatric disorders.
Fuller [15]	Unifying the knowledge gained from the past three decades of research in the world’s largest single-mutation autosomal dominant Alzheimer’s	As this specific mutation is virtually 100% penetrant for the development of the disease by midlife, we use a previously defined median age

	<p>disease kindred - a family in Antioquia, Colombia with the E280A mutation in the Presenilin1 gene - will provide new directions for Alzheimer's research and a framework for generalizing the findings from this cohort to the more common sporadic form of Alzheimer's disease.</p>	<p>of onset for mild cognitive impairment for this cohort to examine the trajectory of the biological and cognitive markers of the disease as a function of the carriers' estimated years to clinical onset. Studies from this cohort suggest that structural and functional brain abnormalities - such as cortical thinning and hyperactivation in memory networks - as well as differences in biofluid and in vivo measurements of Alzheimer's related pathological proteins distinguish Presenilin1 E280A mutation carriers from non-carriers as early as childhood, or approximately three decades before the median age of onset of clinical symptoms</p>
<p>Meyer [16]</p>	<p>On the basis of a preliminary meta-analysis of currently available studies with inclusion of multiple disease groups, we estimated that the diagnostic sensitivity and specificity for visual PET readings supported by voxel-based statistical analyses for diagnosis of atypical parkinsonian syndromes are 91.4% and 90.6%, respectively. The diagnostic specificity of 18F-FDGPET for diagnosing multiple-system atrophy, progressive supranuclear palsy, and corticobasal degeneration was consistently shown to be high (.90%), whereas sensitivity was more variable (.75%).</p>	<p>Taken together, the current literature underscores the utility of 18F-FDG PET for diagnostic evaluation of parkinsonism and the promising role of 18F-FDG PET for assessment and risk stratification of cognitive impairment in PD.</p>
<p>Niccolini [17]</p>	<p>MEDLINE, ISI Web of Science, Cochrane Library, and Scopus electronic databases were searched for articles published until 29th March 2016 and included brain PET studies in progressive supranuclear palsy (PSP), multiple system atrophy (MSA), and corticobasal syndrome (CBS). Only articles published in English and in peer-reviewed journals were included in this review. Case-reports, reviews, and non-human studies were excluded.</p>	<p>Seventy-seven PET studies investigating the dopaminergic system, glucose metabolism, microglial activation, hyperphosphorylated tau, opioid receptors, the cholinergic system, and GABAA receptors in PSP, MSA, and CBS patients were included in this review. Disease-specific patterns of reduced glucose metabolism have shown higher accuracy than dopaminergic imaging techniques to distinguish between parkinsonian syndromes. Microglial activation has been found in all forms of atypical</p>

		<p>parkinsonism and reflects the known distribution of neuropathologic changes in these disorders. Opioid receptors are decreased in the striatum of PSP and MSA patients. Subcortical cholinergic dysfunction was more severe in MSA and PSP than Parkinson's disease patients although no significant changes in cortical cholinergic receptors were seen in PSP with cognitive impairment. GABAA receptors were decreased in metabolically affected cortical and subcortical regions in PSP patients.</p>
Walker [18]	<p>We therefore performed three literature searches and evaluated the selected studies for quality of design, risk of bias, inconsistency, imprecision, indirectness and effect size. Critical outcomes were the sensitivity, specificity, accuracy, positive/negative predictive value, area under the receiving operating characteristic curve, and positive/negative likelihood ratio of FDGPET in detecting the target condition. Using the Delphi method, a panel of seven experts voted for or against the use of FDG PET based on published evidence and expert opinion.</p>	<p>Of 91 studies selected from the three literature searches, only four included an adequate quantitative assessment of the performance of FDG PET. The majority of studies lacked robust methodology due to lack of critical outcomes, inadequate gold standard and no head-to-head comparison with an appropriate reference standard. The panel recommended the use of FDG PET for all three clinical scenarios based on nonquantitative evidence of clinical utility.</p>
Zhang [19]	<p>In this review, we will overview the recent development of TSPO PET tracers, focusing on the radioligand design, radioisotope labeling, pharmacokinetics, and PET imaging evaluation. Additionally, we will consider current limitations, as well as translational potential for future application of TSPO radiopharmaceuticals</p>	<p>This review aims to not only present the challenges in current TSPO PET imaging, but to also provide a new perspective on TSPO targeted PET tracer discovery efforts. Addressing these challenges will facilitate the translation of TSPO in clinical studies of neuroinflammation associated with central nervous system diseases.</p>

In **Table 2** it is compared the conclusions obtained in those 7 articles founded.

**DISCUSSION**

In nuclear medicine the use of radiopharmaceuticals to diagnostic brain disturbs is well known [1,2,5]. In psychiatry the use of radiobiocomplex to obtain diagnose about behavior findings in disturbed people is still a new

approach although there are some data-bank that are used to do the diagnostic [9-12].

All the selected authors in their works used radiopharmaceuticals and nuclear medicine procedures to try to diagnostic and following mental disturbs, it is a beginning of a new way to look the brains commitments that could alter the human health life, and the use of radiopharmaceuticals as a tool to diagnose and follow this disturbs.

**Table 2.** Comparison of the conclusions of the articles founded.

Article	Conclusion
Chandra [13]	This review has demonstrated promising results regarding the role of PET molecular imaging in the diagnosis of AD and MCI and their underlying pathological processes, supporting its use as research tool and an adjunct in clinical practice. Also highlighted are a number of areas of uncertainty and various tracers' limitations. The interplay between amyloid, tau, and neuroinflammation is an exciting new area of investigation that has only recently become possible through the development of an expanded repertoire of PET tracers. Given the proposal that the role of neuroinflammation in AD pathogenesis changes over the disease course, future multitracer longitudinal studies are required.
Ducharme [14]	We hope that the dissemination of these recommendations will make the assessment of late-onset behavioral changes more systematic to improve detection of bvFTD and minimize false diagnoses. This is of key importance to ensure that patients suffering with PPD are offered evidence-based psychiatric treatments for their conditions.
Fuller [15]	Significant abnormalities in plasma, CSF, and brain-based AD pathology, as well as differences in brain structure and function (despite preserved cognition) are evident in carriers of the PSEN1 E280A mutation as early as three-and-a-half decades before the median age of onset of AD-related cognitive decline. Findings from the Colombian kindred have laid the groundwork for better understanding the prognostic value of fluid and <i>in vivo</i> imaging markers of ADAD.
Meyer [16]	18F-FDG PET allows for accurate differentiation between PD and APSs, which is of paramount therapeutic and prognostic importance. Furthermore, 18F-FDG PET provides a highly specific differential diagnosis between the APS subtypes MSA, PSP, and CBD. However, given the limited accuracy of the clinical diagnosis as the reference standard, future studies with post-mortem verification are needed to validate the diagnostic imaging patterns particularly in tauopathies
Niccolini [17]	PET molecular imaging has provided valuable insight for understanding the mechanisms underlying atypical parkinsonism. Changes at a molecular level occur early in the course of these neurodegenerative diseases and PET imaging provides the means to aid differential diagnosis, monitor disease progression, identify of novel targets for pharmacotherapy, and monitor response to new treatments.
Walker [18]	Despite widespread use of FDG PET in clinical practice and extensive research, there is still very limited good quality evidence for the use of FDG PET. However, in the opinion of the majority of the panelists, FDG PET is a clinically useful imaging biomarker for idiopathic PD and atypical parkinsonism associated with dementia.
Zhang [19]	This review aims to not only present the challenges in current TSPO PET imaging, but to also provide a new perspective on TSPO targeted PET tracer discovery efforts. Addressing these challenges will facilitate the translation of TSPO in clinical studies of neuroinflammation associated with central nervous system diseases.

Chandra and his collaborators showed the new promising use of PET molecular imaging in the diagnosis of some

neurological process [13]. Pet molecular image of the brain involves increase or decrease glucose metabolism.

Other authors emphasized the use of PET associated with some radiopharmaceuticals as FDG that it is useful for central nervous system diseases [16-19]. Those are metabolic reasons for the brain function and the use of glucose labelling with <sup>18</sup>F is the tool to discover it.

Others discussed the use of radiopharmaceuticals for diagnostic in psychiatry cases like dementia [14,15]. The diagnostic in psychiatry has an advance in the use of this radiopharmaceuticals that could improve images of the brain function discovering the disturbs origin of those diseases.

Although, the methodologies utilized in their works, all are convinced that the nuclear medicine is the way to diagnostic and following the patients with some brain disturbs [13-19], what is not well-determined by the psychiatrist today.

### CONCLUSION

The mental disease tends to be understood as a cerebral disease, to see how the brain works pass by to be a priority, and the perfusion scintigraphy, the way to sustain it.

The use of FDG as a tool to determine metabolic brain function could help the psychiatry about some lesions into the brain that could be caused by metabolic disturbs.

The use of HMPAO radiopharmaceutical that through the haemato-encephalic barrier immediately before the endogenous injection, could be an option more useful for the PET scan studies in mental disturbs that today no causes are described.

By the way, the psychiatrics pass by to have information about of mental disease, their classification, prognostic and diagnose suggestions by data bank.

More research would be done to cover all aspects of diagnostic medicine that could help the psychiatry in the discover of brain function and to treat brain disfunctions.

### ACKNOWLEDGMENTS

We thanks to Clínica Serviço de Imagem Médica, that supporting this work.

### REFERENCES

- Bernardo-Filho M, Santos-Filho SD, Moura EG, Maiworm AI, Orlando MM, et al. (2005) Drug interaction with radiopharmaceuticals: A review. *Braz Arch Bio Technol* 48: 13-27.
- Manabe O, Kikuchi T, Sholte AJ, Mahdiui EI, Nishii R, et al. (2018) Radiopharmaceutical tracers for cardiac imaging. *J Nucl Cardiol* 25: 1204-1236.
- Gialleonardo YD, Wilson DM, Keshari KR (2016) The potential of metabolic imaging. *Semin Nucl Med* 46: 28-39.
- Vallanhajosula S, Killeen R, Osborne JR (2010) Altered biodistribution of radiopharmaceuticals: Role of radiochemical/pharmaceutical purity, physiological, and pharmacologic factors. *Semin Nucl Med* 40: 220-241.
- Drozdovitch V, Brill A, Callahan R, Clanton J, DePietro A, et al. (2015) Use of radiopharmaceutical in diagnostic nuclear medicine in the United States: 1960-2010. *Health Phys* 108: 520-537.
- Kaya GC, Bekis R, Kirimca F, Ertay A, Gure A, et al. (2001) Use of technetium-99m HMPAO scintigraphy for the detection of amiodarone lung toxicity in a rabbit model. *Eur J Nucl Med* 28: 346-350.
- Kim CK, Kim S, Krynycky BR, Machac J, Inabnet WB (2002) The efficacy of sestamibi parathyroid scintigraphy for directing surgical approaches based on modified interpretation criteria. *Clin Nucl Med* 27: 246-248.
- Kabasakal L (2000) Technetium-99, ethylene dicysteine: A new renal tubular function agent. *Eur J Nucl Med* 27: 351-357.
- Jales RLC, Santos-Filho SD (2020) Discussion of review on protocols treatments of Arachnoid Cysts explored by nuclear medicine. *EC Clin Med Case Rep* 3(6): 147-152.
- Jales RLC, Santos-Filho SD (2020) Approaches of nuclear medicine in psychiatry: perfusion against function, the psychiatric question. *EC Clin Med Case Rep* 3(3): 1-5.
- Jales RLC, Santos-Filho SD (2021) Psychiatric diagnostic confirmed by cerebral simple proton emission computed tomography (SPECT). *Jap J Clin Med Res* 1: 1-3.
- Amen D, Trujillo M, Newberg A, Willeumier K, Tarzwell R, et al. (2011) Brain SPECT imaging in complex psychiatric cases: an evidence-based, underutilized tool. *Open Neuroimag J* 5: 40-48.
- Chandra A, Valkimadi PE, Pagano G, Cousins O, Dervenoulas G, et al. (2019) Applications of amyloid, tau, and neuroinflammation PET imaging to Alzheimer's disease and mild cognitive impairment. *Hum Brain Mapp* 40: 5424-5442.
- Ducharme S, Dols A, Laforce R, Devenney E, Kumfor F, et al. (2020) Recommendations to distinguish behavioral variant frontotemporal dementia form psychiatric disorders. *Brain* 143: 1632-1650.
- Fuller JT, Cronin-Golomb A, Gatchel JR, Norton DJ, Guzmán-Vélez E, et al. (2019) Biological and Cognitive markers of presenilin1 E280A autosomal dominant Alzheimer's disease: A comprehensive

review of the Colombian kindred. *J Prev Alzheimers Dis* 6: 112-120.

16. Meyer PT, Frings L, Rücker G, Hellwig S (2017) <sup>18</sup>F-FDG PET in Parkinsonism: Differential diagnosis and evaluation of cognitive impairment. *J Nucl Med* 58: 1888-1898.
17. Niccolini F, Politis M (2016) A systematic review of lessons learned from PET molecular imaging research in atypical parkinsonism. *Eur J Nucl Med Mol Imaging* 48: 2244-2254.
18. Walker Z, Gandolfo F, Orínis S, Garibotto V, Agosta F, et al. (2018) Clinical utility of FDG PET in Parkinson's disease and atypical parkinsonism associated with dementia. *Eur J Nucl Med Mol Imaging* 45: 1534-1545.
19. Zhang L, Hu K, Shao T, Hou L, Zhang S, et al. (2021) Recent developments on PET radiotracers for TSPO and their applications in neuroimaging. *Acta Pharm Sin B* 11: 373-393.