Clinical Case Reports: Open Access

Yumed Text
OPEN ACCESS JOURNALS

Case Report | Vol 7 Iss 4
ISSN: 2582-5038
https://dx.doi.org/10.46527/2582-5038.317

The Role of Cerebral Amyloid Pet TAC in Diagnosis of Mild Cognitive Impairment

Mirko Avesani[1*], Francesca Giuffrida[2], Alfonso Ciccone[1] and Pierluigi Rossini[2]

[1]Asst Mantova, Civil Hospital "Carlo Poma", Department of Neurological Sciences, Division of Neurology - Centre Of Cognitive Impairment and Dementias, Italy

[2]Asst Mantova, Civil Hospital "Carlo Poma", Department of Services, Division Of Nuclear Medicine, Italy

[*]**Corresponding author:** Mirko Avesani, Asst Mantova, Civil Hospital "Carlo Poma", Department of Neurological Sciences, Division of Neurology - Centre Of Cognitive Impairment and Dementias, Italy; E-mail: mirko.avesani@gmail.com

Received: October 18, 2024; **Accepted:** November 06, 2024; **Published:** November 16, 2024

Abstract

Nowadays, nobody compared the intrinsic diagnostic power of FDG PET TC with Amy-PET when we have a patient affected by a minor form of mild cognitive impairment (MCI), in a prodromal stage of neuro cognitive impairment, when neuropsychological examination excludes not only impairment in activities of daily living (ADL) but also in instrumental activities of daily living (IADL). In this stage, more often, cerebral FDG PET TAC still demonstrates a normal metabolism of glucose in the cortical areas of the brain. We aimed to detect the role of cerebral Amy PET TC in determining the possible evolution from Neurocognitive and Mild Cognitive impairment, when cerebral FDG PET TAC doesn't still notice an alteration in glucose metabolism in the brain. This preliminary study let us to consider cerebral Amy PET TC very useful in a prodromic phase, named neurocognitive impairment, when the patient demonstrates, at neuropsychological test, a situation similar to "aging brain".

1. Introduction

Alzheimer's disease (AD) dementia and other neurodegenerative dementias are preceded by a prodromal phase, namely mild cognitive impairment (MCI), characterized by subtle clinical-neuropsychological changes [1], which are related to synaptic dysfunction and long-lasting pathological deposition of toxic proteins in the brain [2]. MCI is characterized by objective neuropsychological deficits in one or more cognitive domains without functional impairment in everyday life activities [1].

Citation: Avesani M, Giuffrida F, Ciccone A, et al. The Role of Cerebral Amyloid Pet TAC in Diagnosis of Mild Cognitive Impairment. Clin Case Rep Open Access. 2024;7(4):317.

Clinical longitudinal studies on MCI subjects provided evidence for different clinical outcomes, including conversion to AD or non-AD dementias, stabilization of cognitive profile, or even reversion to normal cognition [1,3].

In the prodromal phase, clinical-neuropsychological assessment has limited accuracy for the prediction of conversion to AD dementia [4,5].

To overcome this limit, diagnostic biomarkers such as neuroimaging (i.e., MRI, FDG-PET and amyloid-PET) and cerebrospinal fluid-CSF (i.e., Aβ42, total (t-Tau) and phosphorylated (p-Tau) Tau measures) have been included in the current research criteria for "MCI due to AD" [6].

So, the first study about diagnostic category about "MCI due to AD", was based on biomarker (Ab detected by PET and/or CSF), suggestive for neuronal injury, as below indicated by the TABLE 1.

TABLE 1. **Biomarker probability of AD etiology based on Ab detected by PET or by CSF examination, suggestive for neuronal injury.**

MCI criteria incorporating biomarkers

Diagnostic category	Biomarker probability of AD etiology	Aβ (PET or CSF)	Neuronal injury (tau, FDG, sMRI)
MCI-core clinical criteria	Uninformative	Conflicting/indeterminant/untested	Conflicting/indeterminant/untested
MCI due to AD—intermediate likelihood	Intermediate	Positive	Untested
		Untested	Positive
MCI due to AD—high likelihood	Highest	Positive	Positive
MCI—unlikely due to AD	Lowest	Negative	Negative

Abbreviations: AD, Alzheimer's disease; Aβ, amyloid beta peptide; PET, positron emission tomography; CSF, cerebrospinal fluid; FDG. fluorodeoxyglucose; sMRI, structural magnetic resonance imaging.

But it was necessary a decade to see as demonstrated an effective role of Amyloid PET TC (Amy-PET TC) in determining the diagnosis of "MCI due to AD", compared with other techniques (Ab in CSF or glucose metabolism in FDG PET TC).

The role and usefulness of cerebral Amy-PET TC compared to cerebral FDG PET TC has been recently confirmed as reported in a paper of 2020 [7].

This paper compares the role of Cerebrospinal fluid (CSF) amyloid marker with nuclear medicine techniques such as FDG PET TC vs Amy-PET TC.

The conclusion of the paper is interesting: cerebrospinal fluid (CSF) Aβ42/Aβ40 ratio (AβR) better agrees with Amyloid PET (Amy-PET) results compared to CSF Aβ42.

Not only. The use of FDG-PET and CSF-Tau markers in CSFAβR+/Amy-PET- discordant cases can support AD diagnosis. Disagreement between positive CSF AβR and negative Amy-PET in symptomatic aged AD patients could be due to the variability in plaques conformation and a negative Amy-PET scan cannot be always sufficient to rule out AD.

A previous study (Rubì et al, [8]) confirmed a moderate level of concordance between FDG-PET and CSF biomarkers, indicating their complementary value in diagnosing AD. So, the $Aß_{1-42}$ and pTau levels in CSF help to predict the patient FDG-PET cortical metabolic status. The results derived from a retrospective review carried out on 120 patients affected by MCI, evaluated by brain FDG-PET and a lumbar puncture for CSF biomarkers. In conclusion, this study confirmed that Cortical posterior hypometabolism on PET imaging with ^{18}F-FDG (FDG-PET), and altered levels of $Aß_{1-42}$ peptide, total Tau (tTau) and phosphorylated Tau (pTau) proteins in cerebrospinal fluid (CSF) were established diagnostic biomarkers in Alzheimer's disease (AD).

2. Object

But nowadays, nobody compares the intrinsic diagnostic power of FDG PET TC with Amy-PET when we have a patient affected by a minor form of mild cognitive impairment (MCI), in a stage of prodromal neuro cognitive impairment, when neuropsychological examination excludes not only impairment in activities of daily living (ADL) but also in instrumental activities of daily living (IADL). This is a stage when, more often, cerebral FDG PET TAC still demonstrates a normal metabolism in the cortical areas of the brain.

We aimed to detect the role of cerebral Amy PET TC in determining the possible evolution from Neurocognitive and Mild Cognitive impairment, when cerebral FDG PET TAC doesn’t notice an alteration in glucose metabolism.

3. Material And Methods

We studied four patients:
two affected by a prodromal neurocognitive impairment due to severe form of major depressive disorder, used as control, and two affected by an initial frontal-dysexecutive neurocognitive disorder al neuropsychological test, without depression, still autonomous, used as sample to study them in a phase characterized by cerebral FDG PET TAC negative, and MRI without significative atrophies.

We use two patients affected by similar cognitive impairment because we want to obtain a homogeneous result.

4. Results

In the first two patients, we did not detect, at neuropsychological evaluation, a significative impairment in cognitive functions. They demonstrated elevated values at depression scale [Hamilton Depressione Rating Scale (HDR-S] data were normal in both of them).

Cerebral FDG PET TC didn't detect areas of reduced glucose metabolism. Cerebral Amy-PET TC did not detect deposition of pathological amyloid plaques in the cerebral cortex.

These two patients, followed every six months, in the last two years did not change their cognitive functions, so they did not evolve in AD. They are considered as affected by "pseudo-dementia major depressive disorders".

It was interesting the preliminary study of the other two patients, without depressive symptoms.

They were not aware of the initial cognitive impairment faced by their relatives.

Their neuropsychological examination is in TABLE 2.

TABLE 2. **Neuropsychological Examination of the Last Two Patients**

MMSE (MINI MENTAL STATE EXAMINATION)	**CLOCK TEST**	**FRONTAL ASSESSMENT BATTERY (FAB)**
27/30	7/10	**7/18 (*)**
24/30	7/10	**8/18 (*)**

This table demonstrates a deficit in frontal lobe functions.

Only FAB test was alternated but, at clock test, although normal, in the sub items of it, both of them demonstrates theirselves unable to pose the minute hands, for a deficit in abstraction.

At MRI of the brain, there were no significative atrophies (linear indexes were normal).

At FDG PET TAC of the brain, glucose metabolism was still normal also in frontal lobe (FIG. 1a and 1b).

The interesting data derived from Amy PET (FIG. 2 & 3) of the brain, that identified pathological deposition of amyloid electively in pre-frontal cortex.

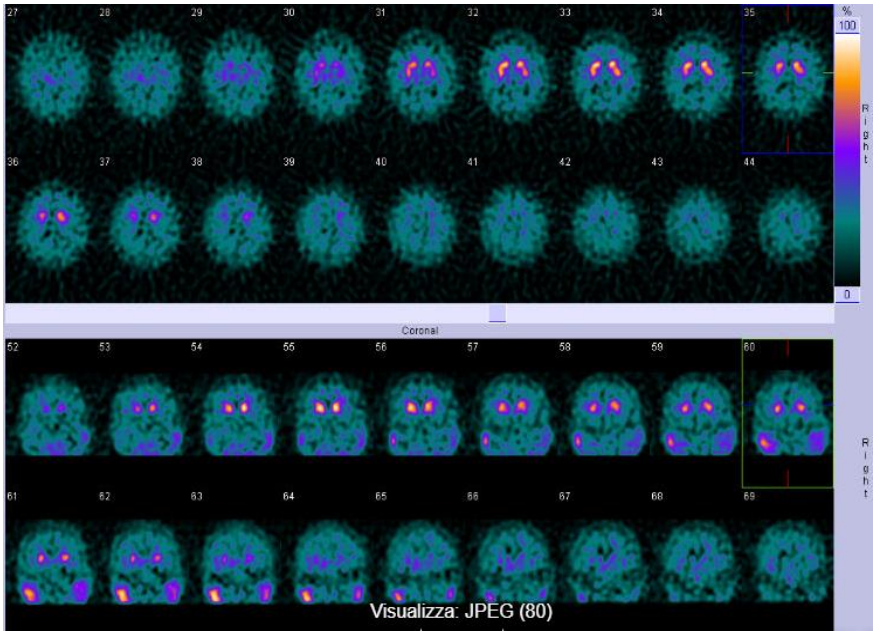

FIG. 1a. **SPECT DAT SCAN negative in first patient.**

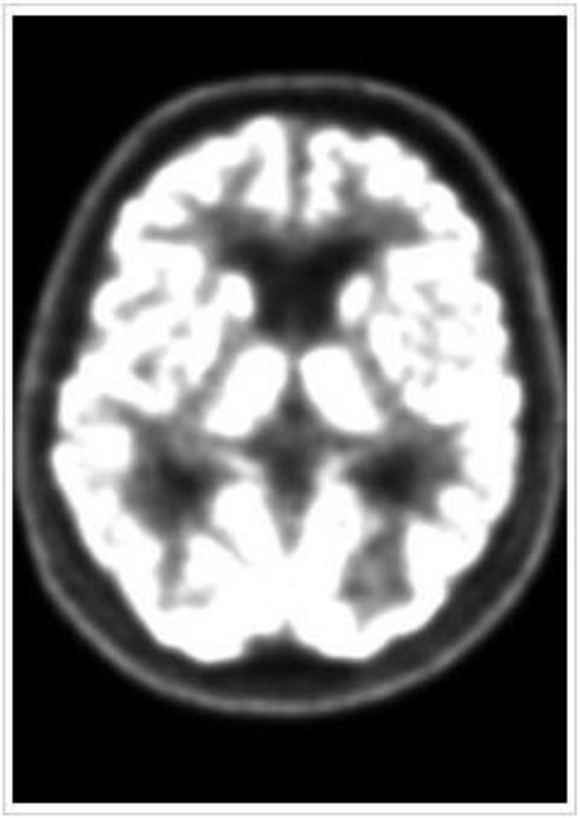

FIG. 1 b. **FDG PET TAC negative in first patient.**

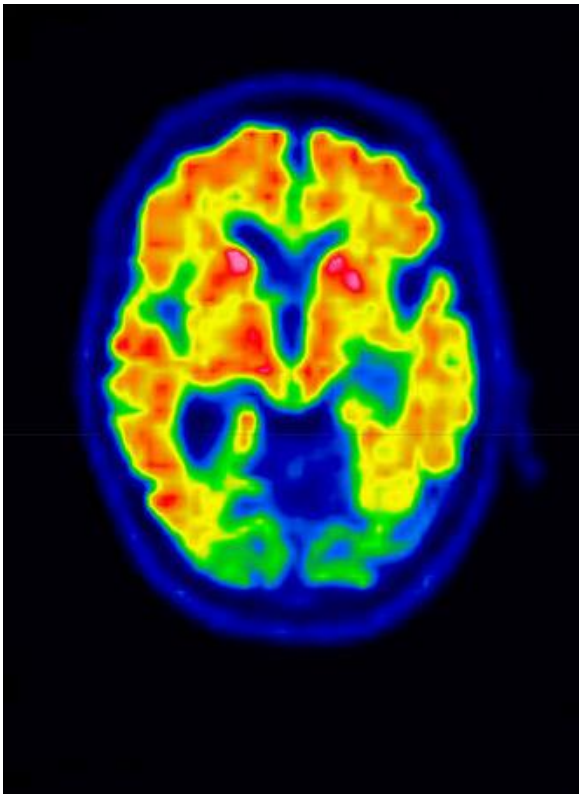

FIG. 2. **First patient: PET TAC with Vizamyl, positive both in cortical and in subcortical areas.**

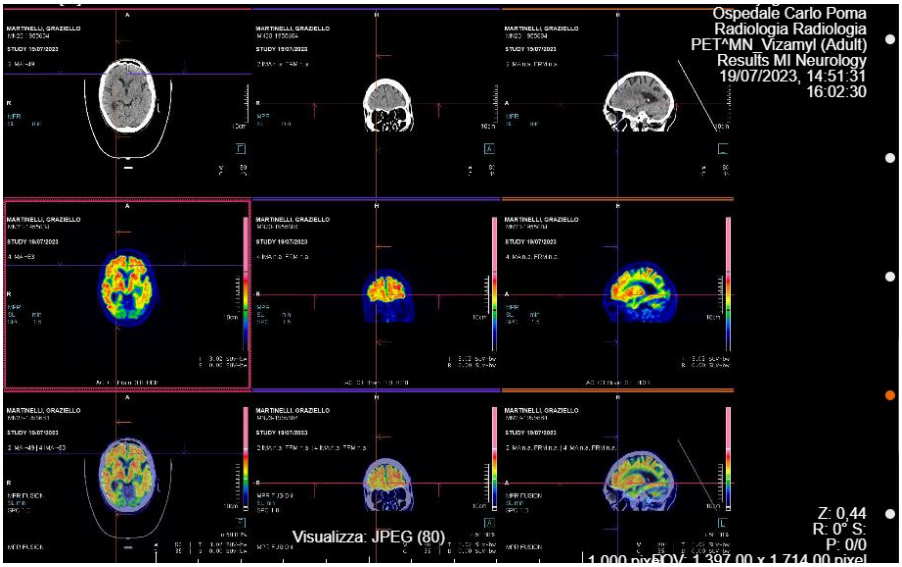

FIG. 3. **First patient: PET TAC with Vizamyl, positive both in cortical and in subcortical areas.**

5. Discussion

This preliminary study let us to consider cerebral Amy PET TC very useful in a prodromic phase, named neurocognitive impairment, when the patient demonstrates, at neuropsychological test, a situation similar to “aging brain”.

NEUROCOGNITIVE CHANGES IN AGING. Aging brain is charaterized by cognitive change as a normal process of aging. Some cognitive abilities, such as vocabulary, are resilient to brain aging and may even improve with age. Other abilities, such as conceptual reasoning, memory, and processing speed, decline gradually over time. There is significant heterogeneity among older adults in the rate of decline in some abilities, such as measures of perceptual reasoning and processing speed [9]. It's characterized by a frontal lobe dysfunction, with impairments in abstraction, organization, problem solving, learning, attention in a patient still autonomous in ADL and IADL. Several of these patients still drive their car. Also, neuroimaging of Aging Brain is normal [10], even if, in aging brain evolving in Neurocognitive ad Mildo Cognitive impairment, it's possibile to detect a particular atrophy in prefrontal cortex [11].

In the FIG. 4, we see the possible atropic areas.

We know, from literature, that almost half of them evolve in Neurocognitive impairment, and the major of these, in Mild Cognitive Impairment (MCI), in its different variants (a-MCI if amnesic; m-MCI if multi-domain; f-MCI if behavioural impairment is prevalent). Among MCI patients, almost half of them evolves in neurodegenerative dementias (not only AD) in a time frame of two years [12].

So, it's very important to identify, with these new techniques, the Neurocognitive and Mild Cognitive impairments with evolutionary character, to start a therapy aiming to slow down the evolution at the final stage of dementia, when patients are obliged to bed and in the throes of Neuropsychiatric Disorder (NPS).

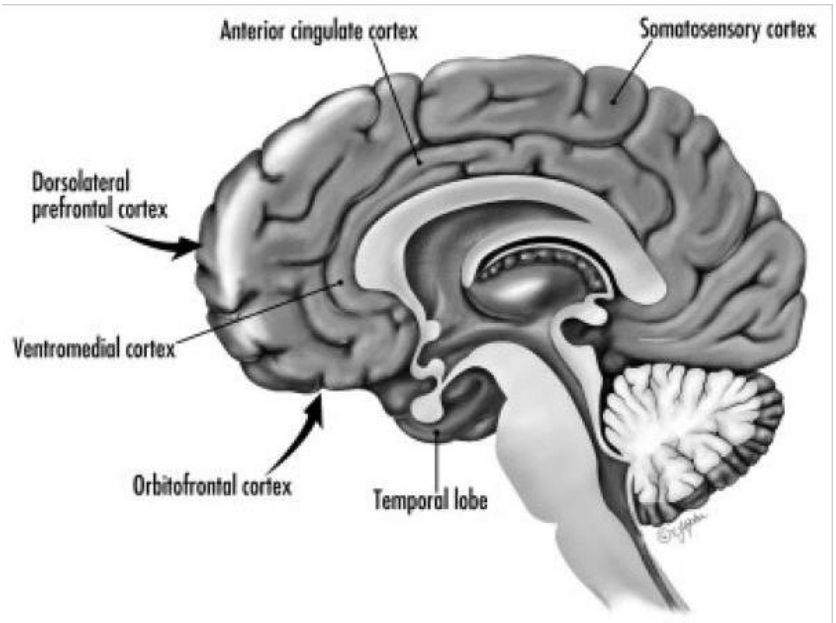

FIG. 4. **Prefrontal cortex (orbitofrontal, dorsolateral frontal, and frontopolar regions) : atrophy is associated with deficits in executive function, working memory and increase perseveration [11]. Keep the arrows and the lables Dorsolateral prefrontal cortex and Orbitofrontal cortex. On top of the arrows on the left hand side include term: prefrontal corte. Modified from Dickson et al, [13].**

6. Conclusions

Cerebral Amy PET let us identify, in a prodromic phase, when FDG PET TC was still normal, the aging brain evolved in Neurocognitive and Mild Cognitive Impairment. This anticipation let us treat the patients almost two years before the evolution in dementia, and this let the patients live a better residual life, with a better quality of life, more preserved autonomies (both in ADL and IADL) and with a better control of Neuropsychiatric Syndromes (NPS).

These results also let us understand the pathogenetic role of b-amyloid in evolution from MCI to dementia and so, in the next future, when monoclonal antibodies against beta amyloid will be approved by FDA, to treat these patients with them, in order to stop the evolution of these neurodegenerative pathologies.

REFERENCES

1. Petersen RC, Roberts RO, Knopman DS, et al. Mild cognitive impairment: ten years later. Arch Neurol. 2009;66(12):1447-55.
2. Pievani M, Filippini N, van den Heuvel MP, et al. Brain connectivity in neurodegenerative diseases--from phenotype to proteinopathy. Nat Rev Neurol. 2014;10(11):620-33.
3. Mitchell AJ, Shiri-Feshki M. Rate of progression of mild cognitive impairment to dementia--meta-analysis of 41 robust inception cohort studies. Acta Psychiatr Scand. 2009;119(4):252-65
4. Löppönen M, Räihä I, Isoaho R, et al. Diagnosing cognitive impairment and dementia in primary health care -- a more active approach is needed. Age Ageing. 2003;32(6):606-12.
5. Storandt M, Morris JC. Ascertainment bias in the clinical diagnosis of Alzheimer disease. Arch Neurol. 2010;67(11):1364-9.
6. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 2011;7(3):270-9.
7. Lombardi G, Pupi A, Bessi V, et al. Challenges in Alzheimer's Disease Diagnostic Work-Up: Amyloid Biomarker Incongruences. J Alzheimers Dis. 2020;77(1):203-17.
8. Rubí S, Noguera A, Tarongí S, et al. Concordance between brain 18F-FDG PET and cerebrospinal fluid biomarkers in diagnosing Alzheimer's disease. Rev Esp Med Nucl Imagen Mol (Engl Ed). 2018;37(1):3-8.
9. Wisdom NM, Mignogna J, Collins RL. Variability in Wechsler Adult Intelligence Scale-IV subtest performance across age. Arch Clin Neuropsychol. 2012;27(4):389-97.
10. Ota Y, Shah G. Imaging of Normal Brain Aging. Neuroimaging Clin N Am. 2022;32(3):683-98.
11. Raz N, Gunning-Dixon FM, Head D, et al. Neuroanatomical correlates of cognitive aging: evidence from structural magnetic resonance imaging. Neuropsychology. 1998;12(1):95-114.
12. Petersen RC. Mild Cognitive Impairment. Continuum (Minneap Minn). 2016;22(2 Dementia):404-18.
13. Dickson VV, Tkacs N, Riegel B. Cognitive influences on self-care decision making in persons with heart failure. Am Heart J. 2007;154(3):424-31.