Journal of Alzheimers Disease & Parkinsonism

Benson, J Alzheimers Dis Parkinsonism 2022, 12:5

Short Communication Open Access

# Oxygen Extraction Fraction (OEF) Metrics in Alzheimer's Disease and Parkinsonism

**Hannibal Benson***

*Department of Neuroradiology, University of Manchester, England, United kingdom*

***Corresponding author:** Dr Hannibal Benson, Department of Neuroradiology, University of Manchester, England, United kingdom, E-mail: Neurodegen@medicalres.org

**Received date:** 02-Sep-2022, Manuscript No. JADP-22-74254; **Editor assigned:** 05-Sep-2022, PreQC No. JADP-22-74254 (PQ); **Reviewed:** 19-Sep-2022, QC No. JADP-22-74254; **Revised:** 23-Sep-2022, Manuscript No. JADP-22-74254 (R); **Published:** 30-Sep-2022, DOI: 10.4172/2161-0460.22.12.553.

**Citation:** Benson H (2022) Oxygen Extraction Fraction (OEF) Metrics in Alzheimer's Disease and Parkinsonism. J Alzheimers Dis Parkinsonism 12:553.



## Description

The Oxygen Extraction Fraction (OEF) is calculated from the difference in cerebral arterial and venous oxygen content. Previous work has suggested that a healthy OEF value is approximately 40 [1]. Although OEF is preserved across multiple physiological states to maintain normal brain function, it is also known to be affected by certain cerebrovascular and neurodegenerative disorders. Historically, OEF metrics has been derived from PET/CT scans. These PET scans, while useful in a research context, have been cumbersome to use clinically. However, more contemporary MRI techniques have emerged, that have made measuring OEF metrics in a clinical setting more probable. To our knowledge, there have been no systematic reviews investigating OEF metrics in either Alzheimer's or Parkinson's (Parkinsonism) patients. Having a systemic review of OEF alterations in these diseases could enhance the diagnostic utility of measuring OEF in Alzheimer's/Parkinson's (Parkinsonism) patients. The goal of this systematic review is to investigate OEF metrics in these disease domains.

A PhD medical librarian with input of study investigators conducted the initial literature search. MEDLINE, PubMed, EMBASE, Web of Science, and Google Scholar were the databases utilized. Publications eligible for selection were stored in Rayyan. Screening, data extraction, statistical analysis, and reporting were performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A Newcastle-Ottawa scoring system was used for all publications. A two-physician reviewer system was utilized for deciding which articles to include/exclude. Our exclusion criteria were any of the following study types: review articles, conference abstracts in which the results and methodology is not clearly reported in the abstract, animal studies, or opinion letters. We also excluded studies that did not have a control arm. Due to technical advances in OEF imaging, we required studies to be published in 2002 or later.

## Dementia

7 studies met our inclusion criteria for Alzheimer's dementia. Researchers from John Hopkins University conducted a retrospective study on 143 cognitively healthy volunteers. They measured OEF metrics via TRUST MRI as well as APOE4 status. APOE4 carriers had a lower OEF compared with non-carriers (non-carriers, 41.1% ± 5.8; one E4 allele, 40.1% ± 4.9; two E4 alleles, 36.7% ± 4.5). Additionally, lower OEF was associated with lower executive function in the APOE4 carriers (b = 0.079 z score for each percent change in OEF; P=0.03), but there was no association between OEF and executive function for non-carriers. (P=0.05). Amyloid burden and OEF were independently associated with APOE4 but were not associated with one another [2]. However, there is at another study, which was co-sponsored by Mass General Hospital and Harvard, which does suggest an inverse association between OEF and increased amyloid burden [3]. A later cross-sectional study conducted by John Hopkins studied OEF metrics in Alzheimer's patients versus vascular cognitive impairment patients. They studied 65 subjects via TRUST MRI: 33 patients with Mild Cognitive Impairment (MCI), 7 with dementia, and 25 cognitively normal subjects. They found in Alzheimer's disease, OEF was reduced, due to decreased oxygen metabolism due to decreased neural activity. Conversely, in vascular diseases, OEF was normal or slightly elevated due to increased oxygen extraction, due to abnormally decreased blood flow [4]. Researchers from the Research Institute for Brain and Blood Vessels (Japan) found that patients with Alzheimer's tended to have a preserved vascular reactivity while vascular dementia patients tended to have reduced vascular reactivity [5].

There are other studies that do not necessarily reflect the findings above. A study from Aarhus University (Denmark) enrolled 18 patients with either clinical suspicion of Alzheimer's or a mild cognitive impairment. They found an elevated OEF in this patient group compared to healthy controls. However, it is unclear if all the subjects had Alzheimer's type dementia, opposed to other forms of dementia (vascular, etc.) [6]. A study from McGill studied 34 patients with Alzheimer's. They found a small, but non-statistically significant elevation in mean OEF in Alzheimer's from healthy controls [7]. A study from Kyoto University (Japan) studied the OEF values in Alzheimer's patients. Researchers found that OEF was slightly increased in these patients, but none of the differences were significant [8].

## Parkinson's Disease

No studies met our inclusion criteria that reported OEF in primary Parkinson's. There was a study that did report OEF values in patients with vascular dementia with Parkinson's features. Although we have an Alzheimer's section in this paper, given the Parkinsonism features in the patients is a principal study arm of this study, we decided to include this study in our Parkinson's section. The study was sponsored by the Neurological Department of Ghent University Hospital (Belgium). No whole brain OEF value was given, but all brain regions had an OEF greater than 50. However, in most brain regions, this study failed to demonstrate a statistically significant difference between vascular dementia patients with and without Parkinson's symptoms [9]. There is limited evidence that OEF metrics can help better understand the pathophysiology of Parkinson's treatments. In a study conducted by Aarhus University Hospital in Denmark, changes

in OEF (in combination with changes in CMRO2) pointed to the potential neuroprotective effects of NMDAR antagonists. However, this study failed to demonstrate statistically significance [10,11].

## Conclusion

Our work suggests that there is a distinct OEF pattern in Alzheimer's patients. This pattern is a reduced absolute OEF from baseline with preserved vascular reactivity. This has the potential to change how Alzheimer's is diagnosed. By quantitively differentiating Alzheimer's from other types of dementia that can lead to more tailored treatments. Also, perhaps imaging with OEF metrics can lead to an earlier diagnosis. As dementia, Alzheimer's or otherwise, is non-reversible, earlier intervention could lead to a more gradual cognitive decline. This could lead to increased quality adjusted life years for these patients.

A limitation of our study was that the encompassing studies, due to heterogeneity, could not be combined to do a meta-analysis. Also, some of the results from our included studies had conflicting results. However, while there are studies that contradict the reported patten of reduced OEF, these studies either fail to solely analyze Alzheimer's patients or fail to demonstrate statistical significance.

There is a need for higher caliber investigations into how OEF metrics change in Parkinson's disease patients. Perhaps such research could help lead to earlier detection and/or better monitoring of Parkinson's disease (Parkinsonism). For example, OEF metrics could be monitored for response to treatment. OEF metrics could also shed more light on progression of Parkinson's. By studying changes in OEF metrics, in combination with other biomarkers, over time in Parkinson's patients, we could learn whether dopaminergic neuronal decay happens steadily or has a pattern of a steady state/flair pattern.

## References

1. Leenders KL, Perani D, Lammertsma AA, Heather JD, Buckingham P, et al. (1990) Cerebral blood flow, blood volume and oxygen utilization. Normal values and effect of age. Brain 113: 27-47.
2. Lin Z, Sur S, Soldan A, Pettigrew C, Miller M, et al. (2019) Brain Oxygen Extraction by Using MRI in Older Individuals: Relationship to Apolipoprotein E Genotype and Amyloid Burden. Radiology 292(1): 140-148.
3. Bryant AG, Manhard MK, Salat DH, Rosen BR, Hyman BT, et al. (2021) Heterogeneity of Tau Deposition and Microvascular Involvement in MCI and AD. Curr Alzheimer Res 18(9):711-720.
4. Jiang D, Lin Z, Liu P, Sur S, Xu C, et al. (2020) Brain Oxygen Extraction Is Differentially Altered by Alzheimer's and Vascular Diseases. J Magn Reson Imaging 52(6):1829-1837.
5. Nagata K, Sato M, Satoh Y, Watahiki Y, Kondoh Y, et al. (2002) Hemodynamic aspects of Alzheimer's disease. Ann N Y Acad Sci 977:391-402.
6. Eskildsen SF, Gyldensted L, Nagenthiraja K, Nielsen RB, Hansen MB, et al. (2017) Increased cortical capillary transit time heterogeneity in Alzheimer's disease: a DSC-MRI perfusion study. Neurobiol Aging, 50:107-118.
7. Lajoie I, Nugent S, Debacker C, Dyson K, Tancredi FB et al. (2017) Application of calibrated fMRI in Alzheimer's disease. Neuroimage Clin 15:348-358.
8. Fukuyama H, Ogawa M, Yamauchi H, Yamaguchi S, Kimura J et al. (1994) Altered cerebral energy metabolism in Alzheimer's disease: a PET study. J Nucl Med 35(1):1-6.
9. De Reuck J, Siau B, Decoo D, Santens P, Crevits L et al. (2001) Parkinsonism in patients with vascular dementia: clinical, computed- and positron emission-tomographic findings. Cerebrovasc Dis 11(1):51-58.
10. Borghammer VM, Ostergaard K, Rodell A, Bailey C, Cumming P (2008) Effect of memantine on CBF and CMRO2 in patients with early Parkinsons disease. Acta Neurol Scand 117(5):317–323.
11. Irwin DJ, Hurtig HI (2018) The Contribution of Tau, Amyloid-Beta and Alpha-Synuclein Pathology to Dementia in Lewy Body Disorders. J Alzheimers Dis Parkinsonism 8(4):444.