J Alzheimers Dis Parkinsonism 2018, Volume 8
DOI: 10.4172/2161-0460-C1-037

Corneal confocal microscopy: An imaging surrogate end point for mild cognitive impairment and dementia

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Background: The risk of dementia in people over 60 is 1 in 10. Imaging biomarkers of neurodegeneration could facilitate early diagnosis of dementia. Corneal confocal microscopy (CCM), a non-invasive ophthalmic technique may act as an imaging end point for neurodegeneration in patients with mild cognitive impairment (MCI) and dementia.

Aim: Aim of the study is to evaluate the diagnostic ability of CCM for MCI and dementia and determine the association between corneal nerve fiber loss and cognitive and physical impairment.

Methods: 79 patients with MCI (n=32), dementia (n=26) and age matched cognitively healthy controls (n=21) underwent clinical examination, neuropsychological testing, neuroimaging and CCM. Corneal nerve pathology was quantified by measuring corneal nerve fiber density (CNFD), branch density (CNBD) and length (CNFL).

Results: Comparing cognitively healthy controls to patients with MCI and dementia, there was a significant reduction in CNFD, CNBD and CNFL (P<0.01 and P<0.0001, respectively). CNFL was significantly different between controls vs. MCI vs. dementia (25.67 [SD 5.85] mm/mm2 vs. 19.61 [SD 5.85] mm/mm2, P<0.01 vs. 15.65 [SD 7.19] mm/mm2, P=0.04, respectively). The AUC/sensitivity and specificity of CNFL for identifying patients with MCI were 0.75, 95% CI 0.66-0.90/72%/71% and for dementia 0.85, 95% CI 0.70-0.95/81%/81%, with a cut-off point of <21 mm/mm2 for optimal diagnostic accuracy for dementia. Adjusted for confounders, corneal nerve fiber loss was associated with declining cognitive function (P<0.01-<0.001) and increased physical disability (P=0.03- <0.01).

Conclusion: This original research advocates CCM as a surrogate end point for neurodegeneration in patients with MCI and dementia, as the diagnostic accuracy of CCM for the detection of dementia is comparable to established Alzheimer's disease biomarkers. Furthermore, we show a strong association between corneal nerve fiber loss with cognitive decline and physical disability.