2017

Hippocampal Sclerosis and Epilepsy in Elderly Population

Rauramaa Tuomas

OMICS Publishing Group

info:eu-repo/semantics/article
info:eu-repo/semantics/publishedVersion
© Authors
CC BY http://creativecommons.org/licenses/by/4.0/
http://dx.doi.org/10.4172/2161-0460.1000384

https://erepo.uef.fi/handle/123456789/5745
Downloaded from University of Eastern Finland's eRepository
Hippocampal Sclerosis and Epilepsy in Elderly Population

Tuomas Rauramaa1-3*, Alina Solomon4-5, Maria Pikkarainen12, Reetta Kälviäinen1-7 and Irina Alafuzoff3-5

1Department of Pathology, Kuopio University Hospital, Finland
2Institute of Clinical Medicine, Unit of Pathology, University of Eastern Finland, Finland
3Institute of Clinical Medicine, Unit of Neurology, University of Eastern Finland, Finland
4Institute of Clinical Medicine/Neurology, University of Eastern Finland
5Center for Alzheimer Research, Karolinska Institutet, Huddinge Sweden
6Department of Neurology, Kuopio University Hospital, Finland
7Department of Neurology, School of Medicine, University of Eastern Finland
8Department of Immunology, Genetics and Pathology, Rudbeck Laboratory, Uppsala University, Sweden
9Department of Pathology and Cytology, Uppsala University Hospital, Sweden

Abstract

Objective: In temporal lobe epilepsy, hippocampal sclerosis (HS) and Alzheimer’s disease (AD) pathological alterations in the hippocampus are frequently observed.

Methods: We assessed the clinicopathological characteristics of 30 aged subjects with HS originating from a large unselected autopsy cohort including 1,388 individuals.

Results: Overall, in 22 subjects AD related pathology and in 17 subjects TDP43 pathology, from mild, moderate to severe was seen. Five subjects out of 30 (17%) with HS had epilepsy.

Conclusion: A higher percentage compared to the reported prevalence of epilepsy in 0.6 percent of the adult population was observed, but more post mortem studies are urgently needed to investigate the pathological substrate for epilepsy in AD.

Keywords: Hippocampus; Postmortem; Hippocampal sclerosis; Epilepsy; Alzheimer

Introduction

In both epilepsy (EP) and in Alzheimer’s disease (AD), pathological alterations are seen within the neuroanatomical region of the hippocampus formation [1,2]. In AD, the hippocampal formation displays substantial pathology including AD related hallmark lesions such as neurofibrillary tangles and neuritic plaques [3]. Furthermore, many reports have indicated that a substantial number of AD subjects, in addition to the AD related lesions, also display TAR DNA binding protein 43 (TDP43) within the hippocampus [4-14]. TDP43 related pathology is primarily seen in subjects with frontotemporal lobar degeneration (FTLD) [15]. It has been reported that when TDP43 pathology is seen in the FTLD, severe loss of neurons is frequently observed within the Cornu Ammonis region 1 (CA1) of the hippocampal formation, a change reminiscent of hippocampal sclerosis (HS) [16]. In subjects with temporal lobe EP HS is the most common lesion [17,18].

In a recent study, assessing the hippocampal formation in a large unselected cohort including 1,388 aged subjects, we noted that a pathological alteration in the hippocampal region was present in 18% of the subjects. The alterations ranged from mild to severe and from vascular to degenerative. Interestingly, in 31 out of these 260 (12%) subjects with an alteration in the hippocampus, the lesion was reminiscent of HS with indisputable neuronal loss especially in the CA1 region and moderate to severe gliosis [19]. Thirty of the subjects with this particular type of HS lesion were adult to aged.

Thus, it became of interest to assess whether aged subjects with HS, alteration reminiscent of what is seen in young subjects with temporal lobe EP, display EP.

Materials and Methods

30 subjects with HS included derive from a large unselected cohort of 1388 subjects who underwent an autopsy with a systematic neuropathological evaluation between the years 1995-2005 in the Department of Pathology of the Kuopio University Hospital [19], both medical and autopsy findings were reviewed. The clinical medical records were reviewed by a clinical neurologist and the pathology reports by a neuropathologist. The original assessment included samples from at least 16 regions: frontal, temporal, parietal, precentral, occipital cortices, cingulate gyrus, striatum, basal forebrain including amygdala, thalamus, anterior and posterior hippocampus, midbrain including substantia nigra, pons including locus coeruleus, medulla, cerebellar vermis and cortex. All neuropathological diagnostic slides were re-assessed and the findings were re-evaluated according to the present generally accepted diagnostic standards and recommendations. HS lesion here was defined as substantial to complete neuronal loss in the hippocampal CA1 region with well-preserved neuropil and moderate to severe gliosis [19]. The demographics of the subjects fulfilling these criteria are summarized in Table 1.

Results

The clinicopathological findings are summarized in Table 1. The mean age at death was 80 ± 2 (standard error, S.E.) years and the majority of subjects were female (19 subjects). The most common cause of death was pneumonia (n=8), followed by infection/sepsis.

*Corresponding author: Tuomas Rauramaa, Kuopio University Hospital, Department of Clinical Pathology, P.O. Box 1777, FIN-70211, Kuopio, Finland, Tel: +358445346179; E-mail: tuomas.rauramaa@kuh.fi

Received September 15, 2017; Accepted October 06, 2017; Published October 13, 2017

Citation: Rauramaa T, Solomon A, Pikkarainen M, Kälviäinen R, Alafuzoff I, et al. (2017) Hippocampal Sclerosis and Epilepsy in Elderly Population. J Alzheimers Dis Parkinsonism 7: 384. doi: 10.4172/2161-0460.1000384

Copyright: © 2017 Rauramaa T, et al. 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.
(n=6), cardiac insufficiency (n=6), cardiac infarction (n=3), central nervous system infarction (n=4), neoplasia (n=2) and pulmonary embolism (n=1). Five out of 30 cases with HS (17%) had a history of EP. Seven subjects were cognitively unimpaired and displayed mild AD related pathology, i.e., primary age related tauopathy (PART) (20) or vascular alterations. None of these subjects displayed TDP43 pathology. Two out of these seven (21%) subjects with HS of hippocampal sclerosis and epilepsy.

| Case | Gender | Age at death | Cause of death | Brain weight (g) | Cognitive impairment | Seizures | Neuropathological findings, other than hippocampal sclerosis | TDP 43 in hippocampus | Significant general autopsy findings |
|------|--------|--------------|----------------|------------------|---------------------|----------|------------------------------------------------------------|-----------------------|--------------------------------------|
| 1    | f      | 70           | AD Braak III   | 1460             | No                  | No       | Acute brain hemorrhage and infarct                        | no                    | Renal transplant                      |
| 2    | m      | 62           | AD Braak IV    | 1440             | Yes                 | No       | No                                                          | no                    | Pneumonia                            |
| 3    | f      | 68           | Multiple old infarcts | 1320           | No                  | No       | Acute brain infarct                                        | no                    | Skull base chondroma                  |
| 4    | m      | 73           | Primary Age Related Tauopathy (PART) Braak II | 1425          | No                  | No       | Primary Age Related Tauopathy (PART) Braak II              | no                    | Pericarditis                          |
| 5    | m      | 79           | PART Braak I   | 1660             | No                  | No       | PART Braak I                                              | no                    | Gastrointestinal stromal tumor        |
| 6    | f      | 88           | PART Braak I   | 1255             | No                  | No       | PART Braak I                                              | no                    | Generalized tuberculosis              |
| 7    | m      | 94           | No            | 1300             | No                  | No       | Cerebral amyloid angiopathy (CAA)                         | no                    | Pneumonia                            |
| 8    | m      | 78           | AD related Braak II (bilateral HS) | 1270          | Yes                 | No       | AD related Braak II (bilateral HS)                        | no                    | Cardiac infarct                       |
| 9    | m      | 81           | AD related Braak I, CAA | 1375         | Yes                 | No       | AD related Braak I, CAA                                   | no                    | Generalized atherosclerosis           |
| 10   | m      | 88           | AD related Braak III | 1330         | Yes                 | No       | AD related Braak III                                      | yes                   | Diffuse large B-cell lymphoma         |
| 11   | m      | 61           | FrontoTemporal Lobar Degeneration (FTLD)-TDP43 | 900           | Yes                 | No       | FrontoTemporal Lobar Degeneration (FTLD)-TDP43            | yes                   | Pneumonia                            |
| 12   | f      | 68           | FTLD-TDP43     | 970              | Yes                 | No       | FTLD-TDP43                                                | yes                   | Generalized atherosclerosis           |
| 13   | f      | 70           | FTLD-TDP43     | 830              | Yes                 | No       | FTLD-TDP43                                                | yes                   | Generalized atherosclerosis           |
| 14   | f      | 83           | FTLD-TDP43, PART Braak I | 1340         | Yes                 | No       | FTLD-TDP43, PART Braak I                                  | yes                   | Generalized atherosclerosis           |
| 15   | f      | 93           | FTLD-TDP43     | 795              | Yes                 | No       | FTLD-TDP43                                                | yes                   | Cardiac granulomatous inflammation    |
| 16   | f      | 79           | Alzheimer’s disease (AD) Braak VI | 1190         | Yes                 | No       | Alzheimer’s disease (AD) Braak VI                        | no                    | Generalized atherosclerosis           |
| 17   | f      | 82           | AD Braak VI, cerebral amyloid angiopathy (CAA) | 740           | Yes                 | No       | AD Braak VI, cerebral amyloid angiopathy (CAA)            | yes                   | Generalized atherosclerosis           |
| 18   | f      | 85           | AD, Braak VI, Lewy body disease (LBD) Braak 5, CAA | 840           | Yes                 | No       | AD, Braak VI, Lewy body disease (LBD) Braak 5, CAA       | yes                   | Pulmonary tuberculosis                |
| 19   | f      | 85           | AD, Braak VI, LBD Braak 3, CAA | 1030          | Yes                 | No       | AD, Braak IV, multiple old infarcts                       | yes                   | Cardiac ischaemic scars               |
| 20   | f      | 86           | AD Braak IV, multiple old infarcts | 970           | Yes                 | No       | AD Braak IV, multiple old infarcts                       | no                    | Cardiac ischaemic scars               |
| 21   | f      | 88           | AD Braak VI, LBD Braak 3 | 1190         | Yes                 | No       | AD Braak VI, LBD Braak 3                                  | yes                   | Cardiac ischaemic scars               |
| 22   | f      | 90           | AD Braak VI   | 820              | Yes                 | No       | AD Braak VI                                              | yes                   | Pyelonephritis                        |
| 23   | f      | 97           | AD Braak V, Status post multiple old infarcts | 965           | Yes                 | No       | AD Braak V, Status post multiple old infarcts             | yes                   | Generalized atherosclerosis, cachexia |
| 24   | f      | 83           | Dementia with Lewy Bodies (DLB) Braak 4, PART Braak stage II | 1300         | Yes                 | No       | Dementia with Lewy Bodies (DLB) Braak 4, PART Braak stage II | no                    | Metastatic adeno carcinoma           |
| 25   | m      | 89           | DLBL Braak 4, AD Braak II, CAA | 1280          | Yes                 | No       | DLBL Braak 4, AD Braak II, CAA                            | yes                   | Acute myocardial infarct, lung small cell carcinoma |
| 26   | f      | 83           | Multiple old infarcts, AD related Braak III, CAA | 1200         | Yes                 | Yes      | Multiple old infarcts, AD related Braak III, CAA          | no                    | Chronic pyelonephritis                |
| 27   | f      | 84           | Multiple old infarcts, PART Braak I | 975           | Yes                 | Yes      | Multiple old infarcts, PART Braak I                      | yes                   | Cardiac ischaemic scars               |
| 28   | m      | 84           | Multiple old infarcts, AD related Braak II | 1345          | Yes                 | Yes      | Multiple old infarcts, AD related Braak II                | yes                   | Cardiac ischaemic scars               |
| 29   | f      | 86           | Multiple old infarcts, PART Braak I | 875           | Yes                 | Yes      | Multiple old infarcts, PART Braak I                      | no                    | Cholangitis, liver abscesses          |
| 30   | m      | 89           | Multiple old infarcts, AD Braak I | 1360         | Yes                 | No       | Multiple old infarcts, AD Braak I                        | yes                   | Generalized atherosclerosis           |

m: male; f: female; TDP43: TAR DNA-Binding Protein 43)

Citation: Rauramaa T, Solomon A, Pikkarainen M, Kälviäinen R, Alafuzoff I, et al. (2017) Hippocampal Sclerosis and Epilepsy in Elderly Population. J Alzheimers Dis Parkinsonism 7: 384. doi: 10.4172/2161-0460.1000384

Table 1: Demographics of hippocampal sclerosis and epilepsy.
Discussion

Seventeen percent of the adult/aged subjects with HS, as defined here, displayed EP during life. Two of these subjects were cognitively unimpaired. Out of the remaining three cognitively impaired subjects, AD related changes were observed in one and vascular alterations in two. Thus, one out of eight AD patients with HS (13%) had suffered from EP during life. It has been reported that the incidence of EP in the elderly (65+ years) eastern Finnish population was 145.4/100000 in 2008 [21]. Furthermore, the incidence has been shown to increase with age in the Nordic population [21-23]. The reported prevalence of EP in dementia and AD varied from 5% to 64% [24-34]. When all cognitively unimpaired subjects with HS were lumped together here, three out of 23 (11%) had displayed EP during life, thus indicating a high frequency, when compared to the general population.

However, our results are not directly comparable with previously published reports. Here we assessed only those subjects that displayed HS independent of the final diagnosis. This selection was chosen due to the strong association found between EP and HS. Post-mortem studies on elderly patients with EP are sparse or include only a small number of subjects [24,29,35-37].

In 2013, it was reported that while assessing the post-mortem brains of 122 EP patients, HS was seen in up to 45% of the adult subjects [37], thus, indicating that HS is fairly common in adults with EP. In this study neurodegeneration was also common in the elderly subjects but was not considered causative for EP.

Noteworthy, TDP43-pathology has been reported to be relatively common in AD [4-14] and in line with this, TDP43-pathology was observed in as many as 88% of our cases with severe AD related pathology (Braak stages V-VI). It should be noted that clinical studies reporting that EP is common in AD include all subjects with AD diagnosis. Whether EP is associated with AD related pathology within the hippocampal formation was not assessed here.

In three of our subjects with EP, the primary brain alteration was vascular in origin. EP in these cases is most likely related to the tissue damage and might be regarded as symptomatic EP [38] and not related to neurodegeneration or HS. Noteworthy, five of our 23 demented subjects had a final diagnosis of FTLD-TDP, and none of these subjects had displayed EP during life. Thus, our observations are in line with previous reports indicating that TDP43 pathology, even if being associated with HS, does not increase the risk for seizures [39,40].

Conclusion

In summary, our findings indicate that 17% of the subjects with HS displayed EP, and that one out of eight AD patients with HS (13%) suffered from EP, but that none out of the five FTLD patients with TDP43 pathology and HS had EP. Additional clinopathological studies are certainly merited to investigate the pathological substrate for EP in AD.

Acknowledgement

The authors thank the medical laboratory technologists Tarja Kauppinen, Mrs. Merja Fali, Mr. Heikki Luukkonen and Mr. Hannu Tiiainen for their skilful technical assistance and Meena Strömqvist for her critical reading of the manuscript. This study has been Authorized by the Ethics Committee of Kuopio University Hospital and the Finnish National Authority for Medicolegal Affairs. This study has been supported by the UCB Pharma Nordic Epilepsy Grant 2008, EVO funds from Kuopio University Hospital, Finnish Epilepsy Research Foundation, and the Finnish Cultural Foundation. Reetta Kälviäinen has received speaker’s honoraria from Eisai, UCB, and Orion; honoraria for membership of advisory boards from Eisai, Fennomedical, GW Pharmaceuticals, Pfizer, Sage Therapeutics and UCB; and research support for her institute from the Academy of Finland, UCB, and Eisai. Other authors report no conflicts of interest.

References

1. Noebels JA (2011) A perfect storm: Converging paths of epilepsy and Alzheimer’s dementia intersect in the hippocampal formation. Epilepsia 52: 39-46.
2. Höller Y, Trinka E (2014) What do temporal lobe epilepsy and progressive mild cognitive impairment have in common? Front Syst Neurosci 8: 58.
3. Duyckaerts C, Delatour B, Potier MC (2009) Classification and basic pathology of Alzheimer disease. ActaNeuropathol 118: 5-36.
4. Josephs KA, Whitwell JL, Knopman DS, Hu WT, Stroh DA, et al. (2008) Abnormal TDP-43 immunoreactivity in AD modifies clinicopathologic and radiologic phenotype. Neurology 70: 1850-1857.
5. Josephs KA, Murray ME, Whitwell JL, Parisi JE, Petrucelli L, et al. (2014) Staging TDP-43 pathology in Alzheimer’s disease. ActaNeuropathol 127: 441-450.
6. Josephs KA, Whitwell JL, Weigand SD, Murray ME, Tosakulwong N, et al. (2014) TDP-43 is a key player in the clinical features associated with Alzheimer’s disease. ActaNeuropathol 127: 611-624.
7. Amador-Ortiz C, Lin WL, Ahmed Z, Personnett D, Davies, et al. (2007) Hippocampal sclerosis dementia differs from hippocampal sclerosis in frontal lobe degeneration. ActaNeuropathol 113: 245-252.
8. Araki T, Mackenzie IJ, Hasegawa M, Nonoka T, Nizato K, et al. (2009) Phosphorylated TDP-43 in Alzheimer’s disease and dementia with Lewy bodies. ActaNeuropathol 117: 125-136.
9. Davidson YS, Raby S, Foulds PG, Robinson A, Thompson JC, et al. (2011) TDP-43 pathological changes in early onset familial and sporadic Alzheimer’s disease, late onset Alzheimer’s disease and Down’s syndrome: Association with age, hippocampal sclerosis and clinical phenotype. ActaNeuropathol 122: 703-713.
10. Higashi S, Iseki E, Yamamoto R, Minegishi M, Hino H, et al. (2007) Concordance of TDP-43, tau and alpha-synuclein pathology in brains of Alzheimer’s disease and dementia with Lewy bodies. Brain Res 1184: 284-294.
11. Hu WT, Josephs KA, Knopman DS, Boeve BF, Dickson DW, et al. (2008) Temporal lobar predominance of TDP-43 neuronal cytoplasmic inclusions in Alzheimer disease. ActaNeuropathol 116: 215-220.
12. King A, Sweeney F, Bodl I, Troakes C, Maekawa S, et al. (2010) Abnormal TDP-43 expression is identified in the neocortex in cases of dementia pugilistica, but is mainly confined to the limbic system when identified in high and moderate stages of Alzheimer’s disease. Neuropathology 30: 408-419.
13. Uryu K, Nakashima-Yasuda H, Forman MS, Kwong LK, Clark CM, et al. (2008) Concomitant TAR-DNA-binding protein 43 pathology is present in Alzheimer disease and corticobasal degeneration but not in other tauopathies. J Neuropathol Exp Neurol 67: 555-564.
14. Nag S, Yu L, Capuano AW, Wilson RS, Leurgans SE, et al. (2015) Hippocampal sclerosis and TDP-43 pathology in aging and Alzheimer disease. AnnNeurol 77: 942-952.
15. Neumann M, Sampathru DM, Kwong LK, Truax AC, Micsenyi MC, et al. (2006) Ubiquitin-positive TDP-43 in frontotemporal lobar degeneration and amyotrophic lateral sclerosis. Science 314: 130-133.
16. Hatanpaa KJ, Raisanen JM, Herndon E, Burns DK, Foong C, et al. (2014) Hippocampal sclerosis in dementia, epilepsy and ischemic injury: differential vulnerability of hippocampal subfields. J Neuropathol Exp Neurol 73: 136-142.
17. Thom M (2014) Review: Hippocampal sclerosis in epilepsy: A neuropathology review. Neuropathol Appl Neurolobiol 40: 520-543.
18. Blümcke I, Spreafico R (2012) Cause matters: a neuropathological challenge to human epilepsies. Brain Pathol 22: 347-349.
19. Rauramaa T, Pikkarainen M, Englund E, Ince PG, Jellinger K, et al. (2013) Consensus recommendations on pathologic changes in the hippocampus: A postmortem multicenter inter-rater study. J Neuropathol Exp Neurol 72: 452-461.
20. Crary JF, Trojanowski JQ, Schneider JA, Abisambra JF, Abner EL, et al. (2014) Primary age-related tauopathy (PART): A common pathology associated with human aging. ActaNeuropathol 128: 755-766.
21. Sillanpää M, Lastunen S, Helenius H, Schmidt D (2011) Regional differences and secular trends in the incidence of epilepsy in Finland: A nationwide 23 year registry study. Epilepsia 52: 1857-1867.

22. Forsgren L, Bucht G, Eriksson S, Bergmark L (1996) Incidence and clinical characterization of unprovoked seizures in adults: A prospective population-based study. Epilepsia 37: 224-229.

23. Olafsson E, Hauser WA, Ludvigsson P, Gudmundsson G (1996) Incidence of epilepsy in rural Iceland: A population-based study. Epilepsia 37: 951-955.

24. Hauser WA, Morris ML, Heston LL, Anderson VE (1986) Seizures and myoclonus in patients with Alzheimer’s disease. Neurology 36: 1226-1230.

25. Romanelli MF, Morris JC, Ashkin K, Cohen LA (1990) Advanced Alzheimer’s disease is a risk factor for late-onset seizures. Arch Neurol 47: 847-850.

26. Amatniek JC, Hauser WA, DeiCastillo-Castaneda C, Jacobs DM, Marder K, et al. (2006) Incidence and predictors of seizures in patients with Alzheimer’s disease. Epilepsia 47: 867-872.

27. Sulkava R (1982) Alzheimer’s disease and senile dementia of Alzheimer type. A comparative study. Acta Neurol Scand 65: 636-650.

28. Volicer L, Smith S, Volicer BJ (1995) Effect of seizures on progression of dementia of the Alzheimer type. Dementia 6: 258-263.

29. Mendez MF, Catanzaro P, Doss RC, Arguello R, Frey WH 2nd (1994) Seizures in Alzheimer’s disease: Clinicopathologic study. J Geriatr Psychiatry Neurol 7: 230-233.

30. Risse SC, Lampe TH, Bird TD, Nochlin D, Sumi SM, et al. (1990) Myoclonus, seizures, and paratonia in Alzheimer disease. Alzheimer Dis Assoc Disord 4: 217-225.

31. Irizarry MC, Jin S, He F, Emond JA, Raman R, et al. (2012) Incidence of new-onset seizures in mild to moderate Alzheimer disease. Arch Neurol 69: 368-372.

32. Amatniek JC, Hauser WA, DeiCastillo-Castaneda C, Jacobs DM, Marder K, et al. (2006) Incidence and predictors of seizures in patients with Alzheimer’s disease. Epilepsia 47: 867-872.

33. Imfeld P, Bodmer M, Schuerch M, Jick SS, Meier CR (2013) Seizures in patients with Alzheimer’s disease or vascular dementia: a population-based nested case-control analysis. Epilepsia 54: 700-707.

34. Vossel KA, Beagle AJ, Rabinovici GD, Shu L, Lee SE, et al. (2013) Seizures and epileptiform activity in the early stages of Alzheimer disease. JAMA Neurol 70: 1158-1166.

35. Margerison JH, Corsellis JA (1966) Epilepsy and the temporal lobes. A clinical, electroencephalographic and neuropathological study of the brain in epilepsy, with particular reference to the temporal lobes. Brain 89: 499-530.

36. Meencke HJ, Janz D (1984) Neuropathological findings in primary generalized epilepsy: A study of eight cases. Epilepsia 25: 8-21.

37. Novy J, Belluzzo M, Cabocio LO, Catarino CB, Yogarajah M, et al. (2013) The lifelong course of chronic epilepsy: The Chalfont experience: Brain 136: 3187-3199.

38. Schorvon S (2014) The concept of symptomatic epilepsy and the complexities of assigning cause in epilepsy. Epilepsy Behav 32: 1-8.

39. Thom M, Liu JY, Thompson P, Phadke R, Narkiewicz M, et al. (2011) Neurofibrillary tangle pathology and Braak staging in chronic epilepsy in relation to traumatic brain injury and hippocampal sclerosis: A post-mortem study. Brain 134: 2969-2981.

40. Lee EB, Lee VM, Trojanowski JQ, Neumann M (2008) TDP-43 immunoreactivity in anoxic, ischemic and neoplastic lesions of the central nervous system. Acta Neuropathol 115: 305-311.

Citation: Rauramaa T, Solomon A, Pikkarainen M, Kälviäinen R, Alafuzoff I, et al. (2017) Hippocampal Sclerosis and Epilepsy in Elderly Population. J Alzheimers Dis Parkinsonism 7: 384. doi: 10.4172/2161-0460.1000384