# **Supplementary Online Content**

Vossel KA, Beagle AJ, Rabinovici GD, et al. Seizures and epileptiform activity in the early stages of Alzheimer disease. *JAMA Neurol.* Published online July 8, 2013. doi:10.1001/jamaneurol.2013.136.

eTable. Clinical and demographic data for each case with epilepsy or subclinical epileptiform activity.

This supplementary material has been provided by the authors to give readers additional information about their work.

#### eTable: Clinical and demographic data for each case with epilepsy or subclinical epileptiform activity.

| Case | Dx   | PMH   | G | Н   | Age of onset of cog. decline (domain) | Age at dx of aMCI or AD | Age of 1 <sup>st</sup><br>seizure or<br>EEG<br>abnormality | MMSE<br>(0-30)<br>(age) | Seizure semiology and frequency  | MRI at age of dx of aMCI or AD   | EEG  | AED and dose<br>(mg)                                   | Efficacy/Tolerability  |
|------|------|---|---|-----|---------------------------------------|-------------------------|--|-------------------------|--|--|--|--|--|
| 1    | AD   | None  | М | R 5 | (memory)                              | 59                      | 61   | 26<br>(59)              | Global aphasia, once   | L>R hippocampal<br>and posterior<br>temporoparietal<br>atrophy                                   | (Sleep deprived) L<br>hemispheric<br>slowing, frequent L<br>anterior temporal<br>spikes (F7, T3) | LEV 500 bid  | Seizure-free but<br>discontinued after 1<br>month due to<br>irritability<br>Seizure-free |
| 2    | AD   | Prostate<br>cancer,<br>aortic valve<br>disease<br>HTN, PAF                  | М | R 8 | 2<br>(language)                       | 84                      | 84   | 22<br>(84)              | R arm shaking, as<br>frequent as 6<br>times a day  | R>L hippocampal<br>and L>R posterior<br>parietal atrophy   | Normal   | LEV 500 bid<br>LEV 1500 bid                            | Partial response<br>Seizure-free   |
| 3    | AD   | Migraines,<br>concussion<br>s/p ski<br>accident,<br>age 24                  | F | R   | 41<br>(memory)                        | 50                      | 44   | 28<br>(44)              | Jamais vu for 1<br>min, sometimes<br>followed by<br>exhaustion, up to<br>3-4 times a day;<br>déjà vu every two<br>months | L>R hippocampal<br>atrophy and bi-<br>parietal atrophy   | L temporal slowing<br>and L<br>frontotemporal (F7)<br>sharp waves                                | LTG 100 bid  Lorazepam as needed                       | Intolerable side<br>effect of blurred<br>vision<br>Rarely used                           |
| 4    | AD   | HTN, HL   | М | R 6 | 2<br>(memory)                         | 66                      | 51   | 24<br>(66)              | Déjà vu, up to 2-3<br>times a day  | Lateral parietal and<br>frontal atrophy,<br>hippocampal<br>atrophy, mesial<br>temporal sclerosis | Not performed  | CMZ<br>LTG 225-300 bid                                 | 7-month trial ineffective  Partial response  |
| 5    | AD   | HL  | F | R   | 65<br>(memory)                        | 68                      | 69   | 11<br>(69)              | Warm sensation in chest, disorientation, staring lasting 2-3 min, occurring up to 3 times a day                          | Not performed  | (Sleep deprived) Diffuse R hemispheric slowing with R temporal sharps and spikes                 | LTG 100 bid  | Seizure-free   |
| 6    | AD   | HL,<br>concussion<br>s/p fall at<br>age 63<br>(negative<br>head<br>imaging) | F | R   | 67<br>(memory)                        | 67                      | 67   | 23<br>(67)              | Speech arrest,<br>epilepsia partialis<br>continua  | Generalized cortical atrophy   | (LTM) Multiple<br>seizures centered<br>around frontal<br>vertex (Fz)                             | VPA 500 ER bid  LEV 1500 bid  LEV 1500 bid  TPM 25 bid | Neutral effects  Partial response  Seizure-free  |
| 7    | aMCI | HTN, HL,<br>vitamin D<br>deficiency   | М | R 7 | 1<br>(memory)                         | 73                      | 71   | 29<br>(73)              | Unresponsive,<br>humming/growling<br>lasting seconds to<br>minutes occurring<br>weekly                                   | Global atrophy,<br>scattered foci of<br>periventricular white<br>matter T2<br>hyperintensities   | L frontotemporal<br>spikes and sharp<br>waves  | LTG 100 bid  | Seizure-free; repeat<br>EEG on LTG<br>negative for<br>epileptiform activity              |

| Case | Dx   | PMH  | G | Н | Age of onset of cog. decline (domain) | Age at dx of aMCI or AD | Age of 1 <sup>st</sup><br>seizure or<br>EEG<br>abnormality | MMSE<br>(0-30)<br>(age) | Seizure semiology and frequency   | MRI at age of dx of aMCI or AD                              | EEG  | AED and dose<br>(mg)   | Efficacy/Tolerability  |
|------|------|--|---|---|---------------------------------------|-------------------------|--|-------------------------|---|---|--|--|--|
| 8    | aMCI | Strep.<br>viridans<br>endo-<br>carditis s/p<br>CABG,                       | M | R | 65<br>(memory)                        | 68                      | 67   | 29<br>(68)              | Blank stare, then<br>unresponsiveness<br>for 5 min with or<br>without<br>convulsions,               | Global atrophy, mild<br>subcortical white<br>matter disease | 1 <sup>st</sup> : Normal<br>2 <sup>nd</sup> : Epileptiform<br>discharges over R<br>frontal region<br>3 <sup>nd</sup> (LTM): frequent | LEV XR 3000 qd   | Partial response;<br>returned to work and<br>felt "sharper"                          |
|      |      | aortic valve<br>replace-<br>ment;<br>pacemaker<br>for ictal<br>bradycardia |   |   |                                       |                         |  |                         | occurring up to twice a day   |   | R anterior temporal epileptiform discharges  | LEV XR 3000 qd<br>Pregabalin 75<br>bid   | Seizure-free   |
| 9    | aMCI | Type II<br>diabetes,<br>hypo-<br>thyroidism                                | F | R | 58<br>(memory)                        | 60                      | 58   | None                    | Aura of fear and epigastric rising sensation followed by loss of consciousness for 5 min, occurring | Mild senescent<br>changes                                   | L temporal<br>seizures and<br>interictal L anterior<br>temporal sharp<br>waves (F7,T3),<br>intermittent L                            | LEV 1500 bid<br>LEV 1500 bid<br>LTG 200 bid,<br>Pregabalin 225<br>bid<br>LTG 250 bid | Neutral effects  Partial response; side effect of fatigue  Seizure-free              |
|      |      |  |   |   |                                       |                         |  |                         | up to 5 times a<br>week   |   | temporal slowing   | Oxcarbazepine<br>450 bid   | COIZUIC IICC   |
| 10   | AD   | None   | M | R | 70<br>(memory)                        | 71                      | 70   | 16<br>(75)              | Staring spells<br>lasting 30 sec<br>occurring weekly;   | L hippocampal<br>atrophy and mild<br>periventricular white  | L temporal slowing   | LEV 1250 bid   | Partial response;<br>side effect of<br>irritability                                  |
|      |      |  |   |   |                                       |                         |  |                         | "slumps" lasting<br>minutes occurring<br>every few months   | matter<br>changes   |  | LEV 750 bid  | Partial response;<br>well tolerated  |
| 11   | AD   | None   | F | R | 49<br>(language)                      | 53                      | 53   | 23<br>(53)              | Subclinical<br>epileptiform<br>activity   | L>R parietal volume loss                                    | 1 <sup>st</sup> : intermittent left<br>frontotemporal<br>slowing<br>2 <sup>nd</sup> : (LTM) L frontal                                | LTG  | Intolerable side<br>effect of fatigue and<br>sensation of muscle<br>twitches in arms |
|      |      |  |   |   |                                       |                         |  |                         |   |   | epileptiform<br>discharges (Cz,<br>C3, F3) every few<br>minutes  | LEV 1000 bid   | Remained seizure-<br>free; repeat EEG on<br>LEV showed no<br>epileptiform activity   |

| Case | Dx   | PMH  | G | Н | Age of<br>onset of<br>cog. decline<br>(domain) | Age at dx of aMCI or AD | Age of 1 <sup>st</sup><br>seizure or<br>EEG<br>abnormality | MMSE<br>(0-30)<br>(age) | Seizure semiology and frequency  | MRI at age of dx of aMCI or AD  | EEG   | AED and dose<br>(mg) | Efficacy/Tolerability  |
|------|------|--|---|---|--|-------------------------|--|-------------------------|--|---|---|----------------------|--|
| 12   | aMCI | CAD s/p<br>angioplasty,<br>HTN   | M | R | 57<br>(memory)                                 | 67                      | 57   | 29<br>(67)              | Generalized tonic-<br>clonic, occurring<br>monthly to yearly                       | Atrophy of medial temporal lobes and amygdala                             | 2 routine and 1<br>multi-day EEG<br>negative for      | PHT                  | Partial response;<br>worsened cognitive<br>function  |
|      |      |  |   |   |  |                         |  |                         |  | 75  | epileptiform activity                                 | LTG                  | Discontinued because of rash   |
|      |      |  |   |   |  |                         |  |                         |  |   |   | Oxcarbazepine        | Partial response   |
|      |      |  |   |   |  |                         |  |                         |  |   |   | VPA                  | Partial response;<br>Side effects of<br>weight gain (>50<br>lbs), HTN, and<br>worsening of<br>cognitive function |
|      |      |  |   |   |  |                         |  |                         |  |   |   | LEV 1000 bid         | Seizure-free and improved cognitive function   |
| 13   | AD   | HL   | F | R | 84<br>(memory)                                 | 86                      | 86   | None                    | L arm rigidity,<br>postictal<br>confusion,<br>occurring weekly                     | General atrophy<br>and diffuse<br>periventricular white<br>matter disease | Not performed   | LTG 50 bid           | Seizure-free with improved cognitive and functional status   |
| 14   | aMCI | Remote   | F | R | 50   | 55                      | 41   | 30                      | Smelling foul odor   | Posterior cortical  | 1 <sup>st</sup> : L posterior                         | Carbamazepine        | Neutral effects  |
|      |      | history of<br>malaria,<br>concussion                                   |   |   | (memory)                                       |                         |  | (55)                    | followed by amnestic spells, occurring monthly                                     | atrophy   | temporal sharp<br>waves, L > R<br>temporal slowing in | Gabapentin           | Neutral effects  |
|      |      | s/p car<br>accident at   |   |   |  |                         |  |                         | to yearly; once  |   | temporal region  2 <sup>nd</sup> : left anterior      | TPM                  | Neutral effects  |
|      |      | age 48<br>(head CT   |   |   |  |                         |  |                         | shaking  |   | temporal sharp  | Zonisamide           | Partial response   |
|      |      | negative)  |   |   |  |                         |  |                         |  |   | Waves   | LTG 100 bid          | Partial response, improved cognition   |
| 15   | aMCI | HTN, hypo-<br>thyroidism,<br>renal cancer<br>s/p L<br>nephrec-<br>tomy | F | L | 54<br>(memory)                                 | 55                      | 54   | 27<br>(55)              | Amnestic spells with confusion followed by exhaustion, occurring weekly to monthly | Cortical atrophy,<br>few scattered white<br>matter T2<br>hyperintensities | (Sleep deprived)<br>mild diffuse slowing              | LEV 500 bid          | Partial response,<br>less amnestic spells,<br>stable cognition   |

| Case | Dx | PMH   | G | Н | Age of onset of cog. decline (domain) | Age at<br>dx of<br>aMCI<br>or AD | Age of 1 <sup>st</sup><br>seizure or<br>EEG<br>abnormality | MMSE<br>(0-30)<br>(age) | Seizure semiology and frequency  | MRI at age of dx of aMCI or AD  | EEG   | AED and dose<br>(mg)                                  | Efficacy/Tolerability   |
|------|----|---|---|---|---------------------------------------|----------------------------------|--|-------------------------|--|---|---|---|---|
| 16   | AD | HTN, HL,<br>psoriasis,<br>OSA,<br>concussion<br>at age 10<br>s/p fall off<br>swing, "bell<br>rung" as<br>high school<br>football<br>player          | M | R | 61<br>(memory)                        | 66                               | 61   | 27<br>(64)              | Metallic taste followed by abdominal discomfort and nausea lasting 5 min, followed by fatigue and confusion, occurring daily to weekly | Mild subcortical ischemia   | No abnormal activity  | LTG 100 qam<br>and 200 qhs                            | Partial response  |
| 17   | AD | non-<br>Hodgkin's<br>lymphoma in<br>remission,<br>HTN, hypo-<br>thyroidism,<br>myoclonus,<br>concussion<br>s/p fall off<br>sofa at age<br>1.5 years | F | R | 66<br>(language)                      | 70                               | 74   | 9 (71)                  | Focal motor<br>seizure with<br>altered<br>consciousness<br>evolving into<br>generalized<br>convulsions,<br>occurring once              | L sided<br>hippocampal<br>atrophy   | 1st: L hemispheric<br>slowing<br>2nd: R epileptiform<br>discharges (C4,<br>P4) maximal over<br>R midtemporal<br>region and<br>background<br>slowing                         | LTG 50 bid  | Seizure-free, neutral effects on myoclonus  |
| 18   | AD | Diet-<br>controlled<br>diabetes<br>type 2, HL,<br>facial<br>myoclonus<br>and aphasia<br>exacerbated<br>by   | F | R | 55<br>(language)                      | 59                               | 59   | 24<br>(59)              | Generalized tonic-<br>clonic seizure<br>once; jerking<br>during sleep  | Posterior parietal atrophy  | (LTM done prior to<br>1 <sup>st</sup> seizure)<br>Epileptiform<br>discharges over L<br>posterior temporal<br>region (T3, T5)  | PHT 15 mg/kg<br>oral load<br>Levetiracetam<br>250 bid | Worse facial myoclonus  Seizure-free; facial myoclonus abated; nighttime jerking      |
| 19   | AD | buproprion  Ulcerative colitis, HL, tongue cancer removed, concussion s/p car accident at age 70  | F | R | 69<br>(memory)                        | 77                               | 74   | 29<br>(75)              | Disorientation and<br>hallucinations<br>evolving into<br>convulsive<br>seizure, occurring<br>once                                      | Diffuse cortical<br>atrophy, mild<br>periventricular<br>white matter<br>disease | L anterior and mid-<br>temporal sharp-<br>wave discharges<br>(~1 sec each)<br>occurring up to<br>twice a min; unable<br>to repeat phrases<br>during epileptic<br>discharges | LEV 125 bid   | lessened Seizure-free; 36- hour LTM while weaning LEV showed no epileptiform activity |

| Case | Dx   | РМН   | G | Н | Age of onset of cog. decline (domain) | Age at<br>dx of<br>aMCI<br>or AD | Age of 1 <sup>st</sup><br>seizure or<br>EEG<br>abnormality | MMSE<br>(0-30)<br>(age) | Seizure semiology and frequency  | MRI at age of dx of aMCI or AD   | EEG  | AED and dose<br>(mg) | Efficacy/Tolerability   |
|------|------|---|---|---|---------------------------------------|----------------------------------|--|-------------------------|--|--|--|----------------------|---|
| 20   | AD   | Prostate cancer s/p prostatec- tomy, concussion s/p bus accident age 10, myoclonus exacerbated by exposure to bright lights | M | R | 63<br>(language)                      | 63                               | 69   | 7<br>(68)               | Collapse/tonic spells x 2 min occurring monthly to yearly  | Moderate cortical atrophy  | L frontal spike and generalized photoparoxysmal response of 2 Hz polyspike and wave time-locked with flashing lights occurring maximally in a bifrontal distribution | PHT 200 bid          | Neutral effects on myoclonus and seizures; developed more cognitive fluctuations, agitation, inanition, apathy, clumsiness, imbalance with falls, incoherent speech; also developed gingival hyperplasia Seizure-free with reduced myoclonus; improved cognitive and motor function |
| 21   | AD   | None  | F | R | 66<br>(memory)                        | 67                               | 67   | 18<br>(67)              | Subclinical<br>epileptiform<br>activity  | Moderate cortical atrophy R>L  | R>L<br>frontotemporal<br>sharp discharges  | LEV 1500 qd          | Anxiety, confusion, diarrhea  |
| 22   | aMCI | Pacemaker<br>for asystole<br>following<br>seizure   | F | R | 68<br>(memory)                        | 70                               | 68   | 28 (70)                 | Metallic taste and smell, electrical sensation in head, nausea, fatigue, and loss of awareness, sometimes evolving into generalized convulsions, occurring weekly to monthly | Normal   | Generalized slowing  | LTG 100-250 bid      | Partial response<br>(breakthrough<br>complex partial<br>seizures without<br>secondary<br>generalization); LTG<br>250 bid caused<br>imbalance and<br>tremor; LTG dosage<br>optimized at 225 mg<br>bid; improved short-<br>term memory  |
| 23   | aMCI | Rheumatoid<br>arthritis,<br>anemia of<br>chronic<br>disease   | M | R | 64<br>(memory)                        | 66                               | 64   | 28<br>(66)              | Déjà vu occurring<br>daily then<br>lessened in<br>frequency  | Diffuse cerebral<br>atrophy most<br>significantly in<br>temporoparietal<br>distribution, with<br>bilateral<br>hippocampal<br>atrophy | Not performed  | None                 | Not applicable  |

| Case | Dx   | РМН  | G | Н | Age of<br>onset of<br>cog. decline<br>(domain) | Age at<br>dx of<br>aMCI<br>or AD | Age of 1 <sup>st</sup><br>seizure or<br>EEG<br>abnormality | MMSE<br>(0-30)<br>(age) | Seizure semiology and frequency   | MRI at age of dx of aMCI or AD                        | EEG   | AED and dose<br>(mg)    | Efficacy/Tolerability   |
|------|------|--|---|---|--|----------------------------------|--|-------------------------|---|---|---|-------------------------|---|
| 24   | AD   | HL, hypo-<br>thyroidism                              | F | R | 55<br>(memory)                                 | 60                               | 64   | 6 (63)                  | Generalized tonic-<br>clonic, occurring<br>monthly  | Parietal atrophy<br>(L>R) and mild<br>frontal atrophy | Not performed   | LEV 125- 250<br>bid     | Seizure-free; LEV<br>250 bid caused<br>irritability, which<br>improved slightly<br>with reduction to 125<br>bid |
| 25   | AD   | Remote<br>uterine<br>cancer, s/p                     | F | R | 64<br>(memory)                                 | 66                               | 66   | 19<br>(66)              | Disorientation and speech arrest often progressing  | R>L hippocampal atrophy and scattered                 | Normal  | PHT 400 qd              | Breakthrough<br>generalized tonic-<br>clonic seizures   |
|      |      | abdominal<br>hysterectom<br>y-bilateral<br>salpingo- |   |   |  |                                  |  |                         | to generalized<br>tonic-clonic<br>seizures with<br>week-long  | subcortical T2<br>hyperintensities                    |   | LEV 500 bid             | Partial response;<br>used for only a few<br>days before<br>switching to LTG                                     |
|      |      | oophorec-<br>tomy                                    |   |   |  |                                  |  |                         | postictal confusion, occurring monthly  |   |   | LTG 100 bid             | Partial response. No generalized tonic-clonic seizures  |
| 26   | AD   | Sjögren's<br>syndrome,<br>remote<br>history of       | F | R | 56<br>(executive)                              | 59                               | 56   | 25<br>(59)              | L hand shaking<br>and clawing and<br>brief lapses of<br>consciousness   | Normal  | R temporal slowing and sharp waves  | PHT 100-200 qd          | Neutral effects; tried<br>for a few weeks but<br>developed<br>intolerable nausea                                |
|      |      | meningitis<br>and<br>transverse                      |   |   |  |                                  |  |                         |   |   |   | CMZ 200 qd              | Neutral effects;<br>developed confusion<br>and somnolence   |
|      |      | myelitis,<br>thyroid                                 |   |   |  |                                  |  |                         |   |   |   | VPA                     | Immediately did not tolerate  |
|      |      | cancer s/p<br>resection                              |   |   |  |                                  |  |                         |   |   |   | LEV 250 qd              | Intolerable dizziness,<br>poor concentration,<br>headaches and<br>nausea  |
|      |      |  |   |   |  |                                  |  |                         |   |   |   | LTG 25 bid              | Seizure-free; LTM on<br>LTG showed no<br>epileptiform activity  |
| 27   | aMCI | Sjögren's<br>syndrome                                | F | R | 74<br>(memory)                                 | 78                               | 74   | 27<br>(78)              | Staring spells and expressive aphasia, occurring every 3-4 months. Once developed L leg shaking and altered consciousness | Global cortical and hippocampal atrophy               | 1 <sup>st</sup> : R frontal<br>epileptiform activity<br>2 <sup>nd</sup> : Rare bursts of<br>R frontal slowing | LEV 500 qam,<br>750 qhs | Seizure-free; did not<br>tolerate higher doses<br>(1500 mg/day) due<br>to poor<br>concentration                 |

| Case | Dx   | PMH  | G | Н | Age of<br>onset of<br>cog. decline<br>(domain) | Age at dx of aMCI or AD | Age of 1 <sup>st</sup><br>seizure or<br>EEG<br>abnormality | MMSE<br>(0-30)<br>(age) | Seizure semiology and frequency  | MRI at age of dx of aMCI or AD   | EEG  | AED and dose<br>(mg)       | Efficacy/Tolerability  |
|------|------|--|---|---|--|-------------------------|--|-------------------------|--|--|--|----------------------------|--|
| 28   | AD   | OSA s/p<br>uvuloplasty,<br>HL, 2<br>concussions<br>s/p falls at<br>age ~54                       | M | R | 58<br>(memory)                                 | 60                      | 58   | 29/30<br>(59)           | Burning smell<br>followed by sense<br>of fear and<br>nausea then<br>unconsciousness<br>for 2 min,<br>occurring monthly           | Global atrophy,<br>predominantly<br>posterior cortical                                     | Normal   | LTG 150 bid                | Partial response;<br>LTG 100 bid was<br>less effective   |
| 29   | aMCI | Pacemaker<br>for ictal<br>bradycardia,<br>HL   | M | R | 73<br>(memory)                                 | 76                      | 74   | 26<br>(76)              | Lightheadedness,<br>then blank stare<br>for 30 sec,<br>occurring weekly<br>to monthly  | Not performed (CT<br>brain showed mild<br>volume loss and<br>mild white matter<br>disease) | (Sleep deprived)<br>normal   | Lacosamide 50<br>bid       | Seizure-free; lower<br>doses were partially<br>effective   |
| 30   | aMCI | Bladder<br>cancer s/p<br>chemo-<br>therapy, mild   | M | R | 74<br>(memory)                                 | 77                      | 75   | 26<br>(77)              | Sudden<br>behavioral arrest<br>with eyes closed,<br>lasting seconds to   | Mild global atrophy<br>and scattered T2<br>hyperintensities                                | 1st: normal<br>2nd: L temporal<br>small-sharp spikes<br>during sleep   | LTG 25 bid                 | Urticarial rash after 3 weeks (seizure-free during this time)  |
|      |      | aortic regurgitation   |   |   |  |                         |  |                         | minutes, followed<br>by disorientation,<br>occurring 6-10<br>times a month   |  | (normal variant) 3rd (LTM): focal epileptiform discharges over L anterior temporal region                                | VPA 250 qhs                | Partial response   |
| 31   | aMCI | HTN, HL,<br>type II<br>diabetes,<br>CAD, Hypo-<br>thyroidism,<br>mild<br>concussion<br>at age 18 | M | R | 64<br>(memory)                                 | 67                      | 66   | 29<br>(67)              | Global prickling<br>feeling, jaimais vu,<br>profound panic<br>and fear, lasting<br>few min, occurring<br>daily                   | Normal   | None   | None                       | n/a  |
| 32   | AD   | Hypo<br>thyroidism,<br>CAD, sleep<br>apnea on<br>CPAP  | M | R | 65<br>(memory)                                 | 71                      | 63   | 28<br>(71)              | Blank stare,<br>followed by<br>generalized tonic-<br>clonic seizure,<br>lasting 2-3 min,<br>occurring every                      | Generalized<br>atrophy, mild<br>periventricular white<br>matter disease                    | 1 <sup>st</sup> : R temporal<br>slowing<br>2nd: bilateral<br>anterior slowing<br>3rd: epileptiform<br>discharges arising | PHT 300 bid  LTG 200 bid   | Partial response;<br>Side effects of<br>dizziness, lethargy,<br>ataxia, cognitive<br>worsening<br>Partial response |
|      |      |  |   |   |  |                         |  |                         | few months   |  | independently from both temporal lobes   | LTG 200 bid<br>LEV 500 qhs | Seizure-free   |
| 33   | AD   | Myoclonus  | F | R | 60<br>(language)                               | 63                      | 64   | 27<br>(64)              | Rigid and pale for<br>10 sec, followed<br>by being upset<br>and confused for<br>several hours,<br>occurring monthly<br>to yearly | Mild white matter disease  | None   | VPA 375 tid                | Partial response   |

Abbreviations: AD=Alzheimer's disease, AED=antiepileptic drug, aMCI=amnestic mild cognitive impairment, bid=twice a day, CABG=coronary artery bypass graft, CAD=coronary artery disease, CMZ=carbamazepine, cog.=cognitive, CPAP= continuous positive airway pressure, dx=diagnosis, G=gender, H=handedness, HTN=hypertension, HL=hyperlipidemia, L=left, LEV=levetiracetam,

LTG=lamotrigine, LTM=long-term video-EEG monitoring, MMSE=Mini-Mental State Exam, OSA=obstructive sleep apnea, PAF=paroxysmal atrial fibrillation, PHT=phenytoin, PMH=past medical history, s/p=status post, qam=every morning, qd=every day, qhs=every bedtime, qpm=every evening, R=right, SD=standard deviation, tid=three times a day, TPM=topiramate, VPA=valproic acid.

| Case | Dx | PMH                                   | G | Н | Age of onset of cog. decline (domain) | Age at dx of aMCI or AD | Age of 1 <sup>st</sup><br>seizure or<br>EEG<br>abnormality | MMSE<br>(0-30)<br>(age) | Seizure semiology and frequency  | MRI at age of dx of aMCI or AD                         | EEG  | AED and dose<br>(mg)  | Efficacy/Tolerability  |
|------|----|---------------------------------------|---|---|---------------------------------------|-------------------------|--|-------------------------|--|--|--|---|--|
| 34   | AD | HL, anti-<br>phospholipid<br>antibody | М | R | 74<br>(memory)                        | 77                      | 76   | 30<br>(76)              | Acute spells of profound confusion and   | Bilateral cortical<br>and hippocampal<br>atrophy; age- | L temporal sharp<br>and slow wave<br>complexes                                       | LEV 250 bid   | Partial response;<br>repeat EEG on LEV<br>was normal                     |
|      |    | and<br>elevated                       |   |   |                                       |                         |  |                         | amnesia, occurring weekly  | appropriate periventricular white                      | •  | LTG   | Not tolerated; more confusion  |
|      |    | factor VIII<br>on<br>coumadin         |   |   |                                       |                         |  |                         | to monthly   | matter disease   |  | Zonisamide 100<br>qhs                                       | Seizure-free   |
| 35   | AD | Chronic<br>myelo-<br>genous           | F | R | 79<br>(apathy)                        | 86                      | 85   | 13<br>(86)              | Decreased vocalization, then R-sided tonic-  | Not performed (CT brain showed diffuse atrophy and     | Diffuse slowing  | PHT 400 qd  | Neutral effects;<br>developed sedation<br>and ataxia                     |
|      |    | leukemia                              |   |   |                                       |                         |  |                         | clonic activity sometimes with generalization followed by a post-ictal state, occurring in clusters yearly | periventiricular<br>white matter<br>disease)           |  | LEV 1000 qam,<br>750 qpm                                    | Partial response   |
| 36   | AD | sleep apnea<br>on CPAP,               | М | R | 58<br>(memory)                        | 64                      | 62   | 27<br>(62)              | Generalized tonic-<br>clonic for 1 min   | Bilateral<br>hippocampal<br>volume loss and            | Semi-rhythmic 5-6<br>Hz slowing in<br>bilateral                                      | PHT 500 qd  | Seizure-free   |
|      |    | HL,B12<br>deficiency,<br>depression   |   |   |                                       |                         |  |                         | followed by postictal state, occurring 4 times total   | minimal cortical<br>atrophy                            | frontotemporal regions   | LTG 150 bid   | Seizure-free   |
| 37   | AD | Depression, sleep                     | F | R | 67<br>(memory)                        | 75                      | 72   | 29<br>(72)              | Gastric upset, heavy chest,  | Diffuse cortical and hippocampal                       | 1 <sup>st</sup> : frontal intermittent   | LEV 1000 bid  | Partial response   |
|      |    | apnea,<br>HTN, HL                     |   |   |                                       |                         |  |                         | increased respiratory rate,  | atrophy (L>R),<br>periventricular/                     | rhythmic delta<br>activity   | Zonisamide<br>1000 bid                                      | Partial response   |
|      |    |                                       |   |   |                                       |                         |  |                         | physical agitation,<br>traveling<br>numbness,<br>burping, and  | subcortical white matter disease                       | 2 <sup>nd</sup> (sleep<br>deprived):<br>epileptiform spike<br>discharges in L        | LEV 500 qd<br>LTG 25 qd                                     | Briefly used but had several breakthrough seizures                       |
|      |    |                                       |   |   |                                       |                         |  |                         | urgent need to<br>urinate, followed<br>by sleepiness and<br>atony; episodes<br>lasting minutes             |  | frontotemporal<br>region (F7),<br>paroxysmal bursts<br>of semirhythmic,<br>frontally | Carbamazepine<br>extended<br>release 200 bid<br>VPA 750 bid | Used for 2 months<br>and had one<br>possible seizure<br>Partial response |
|      |    |                                       |   |   |                                       |                         |  |                         | and occurring 2-<br>10 times a day   |  | predominant<br>diffuse delta   | VPA 1000 bid  | Delirious and sedated  |
|      |    |                                       |   |   |                                       |                         |  |                         |  |  | activity<br>3 <sup>rd</sup> (LTM 6 days<br>while zonisamide                          | VPA 250 bid<br>LTG 12.5 qd                                  | Partial response   |
|      |    |                                       |   |   |                                       |                         |  |                         |  |  | weaned off): sharp<br>waves in L<br>frontotemporal<br>lobe (F7)                      | VPA 250 bid<br>Lacosamide 50<br>qd                          | Partial response   |

| Case | Dx | PMH   | G | Н | Age of onset of cog. decline (domain) | Age at<br>dx of<br>aMCI<br>or AD | Age of 1 <sup>st</sup><br>seizure or<br>EEG<br>abnormality | MMSE<br>(0-30)<br>(age) | Seizure semiology and frequency  | MRI at age of dx of aMCI or AD  | EEG  | AED and dose<br>(mg)   | Efficacy/Tolerability   |
|------|----|---|---|---|---------------------------------------|----------------------------------|--|-------------------------|--|---|--|--|---|
| 38   | AD | Pacemaker<br>for ictal<br>bradycardia<br>(captured on<br>LTM)           | M | R | 58<br>(apathy)                        | 59                               | 59   | 24 (59)                 | Sinking<br>sensations of hot<br>and cold down<br>center of body and<br>diaphoresis,<br>lasting several<br>min, occurring in<br>clusters every 15-<br>60 min all day,<br>every 2 weeks  | Not performed (CT<br>brain showed R>L<br>dorsolateral<br>atrophy)   | 1st (3 -day LTM) bi-<br>hemispheric<br>slowing during<br>sinking spells,<br>occasional L<br>temporal slowing<br>2nd (2-day LTM):<br>mild slowing, no<br>events captured  | Oxcarbazepine<br>750 bid<br>LTG 150 bid                                    | Neutral effects  Neutral effects  |
| 39   | AD | Essential<br>tremor, HTN  | F | R | 71<br>(memory)                        | 74                               | 77   | 16<br>(74)              | Arm myoclonus<br>with occasional<br>loss of postural<br>tone and<br>confusion, every<br>5-10 min for 1 hr,<br>every 2-3 days   | Temporal > parietal atrophy bilaterally   | 1 <sup>st</sup> : focal L hemispheric slowing and rare L central epileptiform discharges 2 <sup>nd</sup> (2 hour): L- sided diffuse slowing and occasional sharpened elements over L central region                | VPA 125 qam,<br>250 qpm<br>VPA 125 qam,<br>250 qpm<br>Clonazepam 0.5<br>qd | Partial response  Not tolerated due to imbalance  |
| 40   | AD | Type II<br>diabetes,<br>HTN, HL,<br>hypo-<br>thyroidism,<br>sleep apnea | F | R | 80<br>(memory)                        | 81                               | 80   | 25<br>(81)              | Sudden fear,<br>lightheadedness,<br>rhinorrhea,<br>trembling in chest,<br>and fatigue,<br>lasting 60 sec,<br>occurring monthly;<br>once generalized<br>with postictal R<br>gaze deviation, L-<br>sided weakness<br>and neglect | Mild cortical and<br>hippocampal<br>atrophy, scattered<br>T2 hyperintensities<br>in periventricular<br>and subcortical<br>regions and<br>cerebellum | Focal R<br>hemisphere<br>polymorphic delta<br>slowing  | LEV 125 qam,<br>250 qpm  | Allergy during dose escalation  Not tolerated due to behavioral worsening   |
| 41   | AD | HTN,<br>coccidio-<br>mycosis<br>treated                                 | M | R | 73<br>(memory)                        | 74                               | 72   | 24 (74)                 | Head turning to R with R hemibody jerking for minutes, followed by mutism for over an hour, then aphasia with paraphasic errors, occurring every few months  | Generalized<br>atrophy with mild<br>periventricular white<br>matter disease   | 1 <sup>st</sup> : semi-rhythmic<br>slowing over L<br>frontal region with<br>superimposed<br>epileptiform<br>discharges<br>2 <sup>nd</sup> (4-day LTM):<br>rare L temporal<br>slowing and L mid-<br>temporal sharps | Oxcarbazepine 600 bid Oxcarbazepine 600 bid LEV 500 bid                    | Not tolerated due to<br>encephalopathy,<br>decreased appetite,<br>and generalized<br>weakness<br>Partial response<br>Seizure-free |

| Case | Dx | PMH   | G | Н | Age of onset of cog. decline (domain) | Age at dx of aMCI or AD | Age of 1 <sup>st</sup><br>seizure or<br>EEG<br>abnormality | MMSE<br>(0-30)<br>(age) | Seizure semiology and frequency  | MRI at age of dx of aMCI or AD   | EEG  | AED and dose<br>(mg)     | Efficacy/Tolerability                        |
|------|----|---|---|---|---------------------------------------|-------------------------|--|-------------------------|--|--|--|--------------------------|--|
| 42   | AD | Type II<br>diabetes,<br>sleep apnea<br>on CPAP,<br>h/o possible | M | R | 69<br>(memory)                        | 76                      | 73   | 19<br>(78)              | Myoclonic jerks in<br>single or multiple<br>limbs every 1-3<br>sec, with<br>occasional   | Generalized cortical atrophy, mild vascular disease  | 1 <sup>st</sup> (on VPA):<br>central midline<br>spikes<br>2 <sup>nd</sup> (on LEV 500<br>mg/day): polyspike  | VPA 750/day  LEV 250 bid | Neutral effects  Partial response            |
|      |    | concussion<br>s/p fall<br>during<br>college                     |   |   |                                       |                         |  |                         | perseverations<br>and agitation,<br>lasting 20-30 min,<br>occurring hourly to<br>daily   |  | discharges (Cz-<br>Fz), time-locked to<br>clinical myoclonus<br>3 <sup>rd</sup> (2 hours while<br>on LEV 500<br>mg/day): normal                    | Clonazepam 1.5<br>bid    | Partial response                             |
| 43   | AD | Type II<br>diabetes,<br>HTN, HL                                 | M | R | 79<br>(memory)                        | 80                      | 79   | 23/24<br>(80)           | Staring spells,<br>unresponsive and<br>afterwards<br>confused, lasting<br>15 min, occurring<br>twice separated<br>by weeks   | Bilateral<br>hippocampal<br>atrophy  | 1 <sup>st</sup> : normal,<br>2 <sup>nd</sup> (1-day LTM):<br>normal  | None                     | n/a  |
| 44   | AD | Migraines,<br>depression,<br>myoclonus                          | F | R | 57<br>(language)                      | 59                      | 58   | 1 (59)                  | Subclinical<br>epileptiform<br>activity  | Bilateral insular and temporal lobe atrophy (L>R), and bilateral hippocampal and parietal atrophy  | 1st: occasional spike and wave activity in L temporal region 2nd: bursts of bicentrally predominant diffuse slowing 3rd: L>R bihemispheric slowing | LEV750 bid               | Initially improvement in language            |
| 45   | AD | HTN, HL,<br>CAD s/p<br>stent                                    | M | L | 76<br>(language)                      | 79                      | 78   | 29<br>(77)              | Woozy, disoriented, blank expression, repeating self, shuffled walking, occasionally followed by generalized atony with loss of consciousness, lasting minutes to hours, occurring monthly | Hippocampal<br>atrophy, (R>L),<br>bilateral insular and<br>orbitofrontal<br>atrophy, subcortical<br>and periventricular<br>white matter<br>changes | None   | LTG 50 qam, 25<br>qpm    | Seizure-free (partial<br>response on 25 bid) |

| Case | Dx | PMH   | G | Н | Age of<br>onset of<br>cog. decline<br>(domain) | Age at<br>dx of<br>aMCI<br>or AD | Age of 1 <sup>st</sup><br>seizure or<br>EEG<br>abnormality | MMSE<br>(0-30)<br>(age) | Seizure semiology and frequency  | MRI at age of dx of aMCI or AD  | EEG   | AED and dose<br>(mg)  | Efficacy/Tolerability   |
|------|----|---|---|---|--|----------------------------------|--|-------------------------|--|---|---|---|---|
| 46   | AD | HTN, HL   | M | R | 59<br>(memory)                                 | 64                               | 66   | 25<br>(68)              | Sudden feeling of<br>dread/intense fear<br>and diaphoresis,<br>lasting minutes,<br>occurring in<br>clusters over 2-3<br>days once a<br>month           | L hippocampal<br>atrophy and<br>possible L mesial<br>temporal sclerosis;<br>mild global atrophy<br>and patchy white<br>matter changes | Normal (done at<br>age 64 prior to<br>seizures)   | None  | n/a   |
| 47   | AD | HTN, HL,<br>endometrial<br>cancer s/p<br>hyster-<br>ectomy,<br>meningitis<br>age 2<br>without<br>sequelae | F | R | 55<br>(executive)                              | 57                               | 56   | 23<br>(57)              | Subclinical<br>epileptiform<br>activity  | Mild cortical atrophy   | 3-4 R anterior<br>temporal<br>epileptiform<br>discharges  | None  | n/a   |
| 48   | AD | Migraines,<br>depression  | F | R | 50<br>(memory)                                 | 58                               | 54   | 26<br>(55)              | Overwhelming rancid smell followed by nausea/vomiting, lasting 1 min, occurring monthly  | Mild hippocampal<br>and cortical atrophy  | 1 <sup>st</sup> : normal<br>2 <sup>nd</sup> : R<br>frontotemporal<br>spikes and sharp<br>waves                | VPA 1500 ER qd<br>VPA 1500 ER<br>qd,<br>Carbamazepine<br>LTG 50 bid | Partial response  Carbamazepine not tolerated (ataxia)  Seizure-free  |
| 49   | AD | Type II<br>diabetes,<br>HL, HTN,<br>depression,<br>uterine<br>fibroids s/p<br>hysterec-<br>tomy           | F | R | 56<br>(memory)                                 | 69                               | 69   | 17<br>(69)              | Generalized tonic-<br>clonic occurring 4<br>times over a few<br>days   | Moderate global<br>cortical atrophy and<br>subcortical<br>ischemic vascular<br>disease  | None  | VPA 1000 ER qd  | Seizure-free  |
| 50   | AD | Uveitis in<br>childhood,<br>depression/<br>anxiety,<br>prostate<br>cancer                                 | M | R | 60<br>(memory)                                 | 63                               | 69   | 4 (70)                  | Generalized tonic-<br>clonic and<br>myoclonic<br>seizures lasting 1-<br>2 min followed by<br>postictal<br>confusion,<br>occurring weekly<br>to monthly | Generalized cortical atrophy  | (1.5-day LTM) Diffuse slowing and generalized spike-wave discharges accompanying intermittent myoclonic jerks | Gabapentin 300 bid  VPA 375 ER bid                                  | Not tolerated due to aggressiveness  Emergence of myoclonic jerks and breakthrough generalized tonic-clonic seizures  No efficacy |

| Case | Dx | PMH   | G | Н | Age of onset of cog. decline (domain) | Age at<br>dx of<br>aMCI<br>or AD | Age of 1 <sup>st</sup><br>seizure or<br>EEG<br>abnormality | MMSE<br>(0-30)<br>(age) | Seizure semiology and frequency  | MRI at age of dx of aMCI or AD  | EEG  | AED and dose<br>(mg) | Efficacy/Tolerability     |
|------|----|---|---|---|---------------------------------------|----------------------------------|--|-------------------------|--|---|--|----------------------|---------------------------|
| 51   | AD | Pacemaker<br>for ictal<br>bradycardia,<br>HTN,<br>anxiety | F | R | 57<br>(memory)                        | 61                               | 61   | 24<br>(61)              | Generalized<br>atonic seizures<br>lasting 30 sec,<br>occurring twice in<br>a month | Mild hippocampal<br>atrophy R>L   | 1 <sup>st</sup> : occasional<br>frontal intermittent<br>delta activity<br>2 <sup>nd</sup> : 3-5 sec<br>episodes of 2-3<br>hertz bifrontal<br>sharp and slow<br>wave activity | LTG 25 bid           | Seizure-free              |
| 52   | AD | HTN   | F | R | 74<br>(memory)                        | 77                               | 82   | none                    | Subclinical<br>epileptiform<br>activity  | Generalized cortical atrophy  | Multifocal but predominantly L frontotemporal sharps   | None                 | n/a                       |
| 53   | AD | HTN, HL,<br>kidney<br>stones                              | М | R | 65<br>(memory)                        | 70                               | 70   | 24<br>(70)              | Subclinical<br>epileptiform<br>activity  | Diffuse atrophy,<br>particularly in<br>parietal regions,<br>and subtly<br>increased T2 signal<br>in the hippocampi<br>L>R | Intermittent bursts<br>of bitemporal<br>slowing (R>L) with<br>R temporal sharp<br>waves  | None                 | n/a                       |
| 54   | AD | HTN, HL   | М | R | 45<br>(memory)                        | 55                               | 55   | 27<br>(55)              | Subclinical<br>epileptiform<br>activity  | Normal  | Fragments of<br>generalized<br>epileptiform<br>discharges  | LTG 200 bid          | Remained seizure-<br>free |