# Supporting Information

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### SI Results

To evaluate the distribution of GABA current amplitudes of oocytes transplanted with membranes from single brains, temporal cortex membranes from a control brain (C3; Table S1) and from an Alzheimer's disease (AD) brain (AD13) were injected into 40 oocytes for each case, and GABA currents were measured in oocytes voltage-clamped to −80 mV (Fig. S1). The distribution of GABA current amplitudes from oocytes transplanted with the control was well described with both normal (Shapiro–Wilk $W$ test of normality) and log-normal functions with a small skewed tail ($\mu = 5.41$ and $\sigma = 0.32$; Kolmogorov $D$ test; Fig. S1); the distribution of responses from the oocytes with the transplanted AD membranes was well described only by a log-normal function ($\mu = 3.57$ and $\sigma = 0.58$) with a left tail limited by zero. The distribution of responses from a single experiment (i.e., an injection of a membrane preparation into oocytes from a single frog) was closely reproduced when pooled data from multiple injections were used. For example, the mean of the control C3 in a single experiment was 234 ± 10 nA and the median was 225 nA ($n = 40$ oocytes; Fig. S1*B*), whereas pooled data of the same control also had a normal distribution with a mean of 233 ± 32 nA and a median of 210 nA ($n = 18$ oocytes from seven experiments; Fig. S1*C*). In the case of the AD brain, shown in Fig. S1*B*, the mean was 41 ± 3 nA and the median was 38 nA ($n = 40$). Pooled data of the same case had also a log-normal distribution with a mean of 40 ± 6 nA and a median of 33 nA ($n = 13$ oocytes from three experiments; Fig. S1*C*). A similar pattern was observed in the rest of the cases studies. In general terms, samples with low responses tended to have slight log-normal distributions and samples with larger responses tended to have normal distributions. However, even in cases in which the distribution was log-normal, the median and the mean were very similar and linearly correlated ($n = 12$ AD cases and $n = 13$ control cases; Fig. S1*C*). The variability increased with samples that had larger GABA responses (Fig. S1*D*), as expected in a process of continuous fusion of human membranes into the oocyte membrane with the number of receptors per fused vesicle larger in such samples. Because of the presence of log-normal distributions in samples with low responses, and to avoid the effects of outliers on the mean, we chose the median as the "specific" amplitude of GABA currents of each subject's brain.

### SI Materials and Methods

Total RNA was isolated by using TRIzol (Invitrogen). mRNA was then isolated by using Oligotex (Qiagen). mRNA quantification was done by NanoDrop ND 1000 and quality assessment was assessed by running the samples in an Agilent Bioanalyzer 2100. The Bioanalyzer does not report an RNA integrity number for mRNA, but samples in which mRNAs were less than 1,000 bases were excluded from further experiments (two of 16 samples). mRNA was used as a quantitative PCR (qPCR) template to enhance detection of low-abundance transcripts (1). qPCR primers anneal on different exons, with the exception of Glu-2 and GABA α1, γ2, β2, and π.

1. Wang C, Kim T, Gao D, Vaglenov A, Kaltenboeck B (2007) Rapid high-yield mRNA extraction for reverse-transcription PCR. *J Biochem Biophys Methods* 70:507–509.

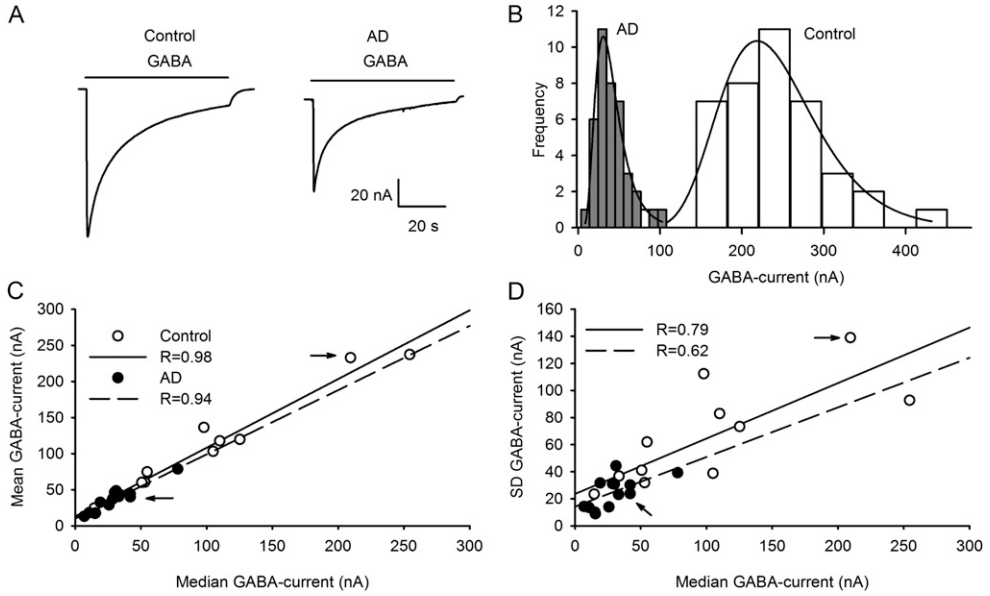


**Fig. S1.** Distribution of amplitudes of GABA currents elicited by microtransplanted receptors. (*A*) Sample currents elicited by 1 mM GABA in oocytes injected with membranes from an AD brain (AD13) or a control brain (C3). (*B*) Distribution of peak GABA current amplitudes elicited in oocytes injected with membranes from a control brain (C3; mean ± SEM, 234 ± 10 nA; median, 225 nA; *n* = 40 oocytes) or an AD brain (AD13; 41 ± 3 nA; median, 38 nA; *n* = 40 oocytes) injected into oocytes from the same frog. Continuous black lines are the fittings of a log-normal function (*Left*) and a normal function (*Right*) to the GABA current amplitude histograms. (*C*) Plot of the mean vs. the median of 13 control (non-AD) brains and 12 AD brains. Each point corresponds to a single brain (pooled data from an average of 17 oocytes per point from *n* = 3–7 different experiments). Note that there is a linear correlation between mean and median in the AD and control groups. Arrows in *C* and *D* indicate the same control and AD brains shown in *A*. The mean and median of pooled data for the control brain (233 ± 32 nA; median, 210 nA; *n* = 18 oocytes from *n* = 7 experiments) and the AD brain (40 ± 6 nA; median, 33 nA; *n* = 13 oocytes from n = 3 experiments) were similar to those obtained from a single injection. (*D*) Plot of the SD of the mean vs. the median of the same brains shown in *C*. The continuous line is the linear fit to the control group and the discontinuous line is the linear fit to the AD group.

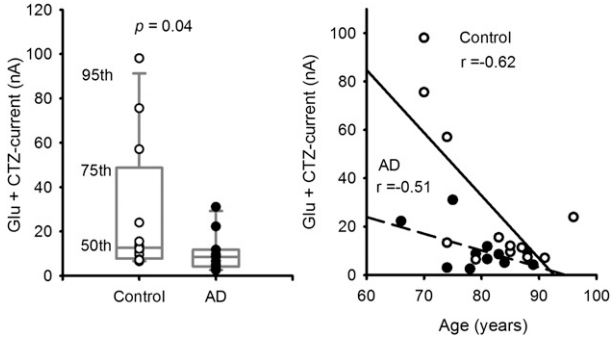


**Fig. S2.** Glutamate currents in AD. *Left*: Box plot of specific glutamate plus CTZ current per case grouped by diagnosis of AD or lack thereof (control). Each point is the specific current of a single case. The AD group (*n* = 11 cases, 99 oocytes) gave smaller responses than the control group (*n* = 12 cases, 119 oocytes) with a mean ± SD of 10 ± 9 nA and 28 ± 31 nA, respectively. The medians for AD and control groups were 8.5 nA and 12.5 nA. Whiskers above and below the boxes indicate the 95th and fifth percentiles. *Right*: Plot of specific glutamate plus CTZ currents vs. age. Solid line is the linear regression fit to data from the control group and the broken line is for the AD group.

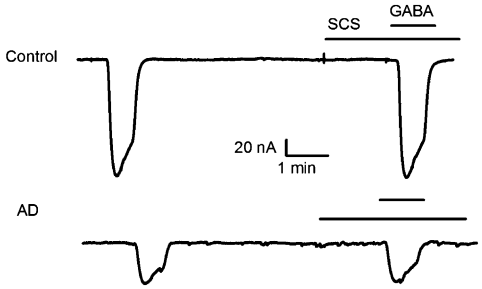


**Fig. S3.** No effects of salicylidene salicylhydrazide on GABA currents. High doses of SCS (10 μM) did not change the GABA (10 μM) current response of oocytes injected with control or AD membranes.

**Table S1. Tissue information**

| Case | Age, y | Sex | Braak plaque | Braak tangle | PMI, h | ST, mo |
|---|---|---|---|---|---|---|
| | | | Control | | | |
| *C1**,† | 67 | M | ND | ND | 2.7 | 132 |
| *C2*† | 70 | M | ND | ND | 4.6 | 139 |
| *C3**,‡,§ | 70 | M | ND | 0 | 5.2 | 112 |
| *C4**,†,‡,§ | 74 | F | B | II | 2.8 | 82 |
| *C5*†,‡ | 74 | F | ND | II | 2.8 | 114 |
| *C6*†,‡ | 79 | F | ND | I | 4.3 | 141 |
| *C7**,†,‡ | 83 | M | 0 | II | 1.8 | 79 |
| *C8**,†,§ | 85 | M | A | III | 3.2 | 81 |
| *C9**,†,‡ | 85 | F | A | III | 4.3 | 65 |
| *C10**,†,‡,§ | 87 | F | 0 | I | 4.5 | 102 |
| *C11*† | 88 | F | A | II | 5.2 | 68 |
| *C12**,†,‡ | 91 | F | A | II | 3.8 | 45 |
| *C13*†,‡ | 96 | M | 0 | II | 3.6 | 73 |
| | | | AD | | | |
| *A1** | 61 | F | C | VI | 2.8 | 87 |
| *A2**,† | 62 | M | ND | ND | 2.5 | 152 |
| *A3*†,‡ | 66 | M | ND | ND | 3.0 | 170 |
| *A4**,†,‡ | 74 | F | C | IV | 4.5 | 83 |
| *A5*† | 75 | M | ND | V | 2.7 | 130 |
| *A6**,†,‡,§ | 78 | M | C | VI | 5.1 | 92 |
| *A7**,†,‡,§ | 79 | M | C | V | 3.7 | 65 |
| *A8**,†,‡,§ | 81 | M | B | V | 1.9 | 52 |
| *A9*†,‡ | 81 | M | C | VI | 2.5 | 90 |
| *A10**,‡ | 83 | M | B | VI | 3.6 | 49 |
| *A11*†,‡ | 83 | F | C | VI | 2.4 | 96 |
| *A12**,†,‡,§ | 84 | F | C | VI | 1.8 | 99 |
| *A13**,†,‡ | 88 | M | C | VI | 3.0 | 78 |
| *A14**,†,§ | 89 | F | ND | VI | 5.0 | 117 |

Braak plaque staging A, B, and C indicates the progression of amyloid deposition; 0, no plaques were observed. Braak tangle staging shows the spatiotemporal progression of neurofibrillary tangles as described by Braak and Braak (1). ND, not determined; PMI, postmortem interval; ST, storage time duration.

*Cases used for PCR.

§Cases used for Western blots.

†Cases used for amplitude of GABA currents.

‡Cases used for concentration–response curves.

1. Braak H, Braak E (1995) Staging of Alzheimer's disease-related neurofibrillary changes. *Neurobiol Aging* 16:271–278.

**Table S2. Multivariate analysis of mRNA expression**

| Variable 1 | Variable 2 | *r* | *P* value* |
|---|---|---|---|
| | Control | | |
| *GABRG2*† | *GABRA1* | 0.9918 | <0.0001 |
| *Gephyrin* | *GABRB1* | 0.9886 | 0.0002 |
| *GABRB1* | *GABRA1* | 0.9854 | 0.0003 |
| *GABRG2* | *GABRB1* | 0.984 | 0.0004 |
| *Gephyrin* | *GABRG2* | 0.9736 | 0.001 |
| *Gephyrin* | *GABRA1* | 0.9707 | 0.0013 |
| *GABRG2*† | *GABRA2* | 0.9614 | 0.0005 |
| *Gephyrin* | *GABRB3* | 0.9432 | 0.0047 |
| *GABRA2* | *GABRA1* | 0.9272 | 0.0026 |
| *GABRB3* | *GABRB1* | 0.9117 | 0.0113 |
| *GABRA5* | *GABRA2* | 0.9099 | 0.0045 |
| *GABRA5*† | *GABRG2* | 0.9006 | 0.0057 |
| *GABRA5* | *GABRA1* | 0.874 | 0.0101 |
| *GABRB3*† | *GABRA1* | 0.7924 | 0.0336 |
| *GABRA5*† | *GABRB3* | 0.7743 | 0.041 |
| | AD | | |
| *GABRG2*† | *GABRA1* | 0.9644 | <0.0001 |
| ***GABRG2*** | ***GABRB3*** | **0.9418** | **0.0001** |
| *GABRB3*† | *GABRA1* | 0.8954 | 0.0011 |
| ***GABRG1*** | ***GABRB1*** | **0.8394** | **0.0092** |
| ***GABRG1*** | ***GABRB2*** | **0.7881** | **0.0202** |
| *GABRA5*† | *GABRB3* | 0.7769 | 0.0138 |
| ***GABRB2*** | ***GABRB1*** | **0.7233** | **0.0426** |
| *GABRG2*† | *GABRA2* | 0.6916 | 0.039 |
| *GABRA5*† | *GABRG2* | 0.6779 | 0.0448 |

Bold letters are correlations not found in the control.
*Pearson product–moment method.
†Correlations common to control and AD.

**Table S3. Primers used for qPCR**

| Primer name | Sequence |
|---|---|
| GAPDHF | TCGACAGTCAGCCGCATCTTCTTT |
| GAPDHR | ACCAAATCCGTTGACTCCGACCTT |
| GluR2F | AACACTGCAAGCTGTGCTGGATTC |
| GluR2R | AGTCCAGAATTACACGCCGTTCCT |
| GluR3F | GCGAAAGTCCAAGGGAAAGTTCG |
| GluR3R | CAGTTTTAATACTGCCAGGTTAACAGC |
| GabaA1F | ATAGCCTTCCCGCTGCTATTTGGA |
| GabaA1R | TTCCCAGTGCAGAGGACTGAACAA |
| GabaA2F | TGTGCCTGCAAGAACTGTGTTTGG |
| GabaA2R | TGGCAGTTGCATAAGCCACTTTGG |
| GabaA5F | AGTCCATCGCTCACAACATGACCA |
| GabaA5R | AGCTGCCAAATTTCAGAGGGCAAG |
| GabaG1F | GACCCTGCATTTGGGAAACTGTGT |
| GabaG1R | TCAATTACTGTGGGCCTCACTCCT |
| GabaG2F | CGCCCAAGATCAGCAACCATTCAA |
| GabaG2R | TGTCTCCAAGCTCCTGTTCGACAA |
| GabaB1F | TTGTGTTTGTGTTCCTGGCTCTGC |
| GabaB1R | TTTCCAGGGTGCTGAGGAGAATGT |
| GabaB2F | TCCCGCATATTCTTCCCAGTGGTT |
| GabaB2R | TCCAGTGGGAGGCCATGTTtTAGTT |
| GabaB3F | ACCGTTCAAAGAGCGAAAGCAACC |
| GabaB3R | TTCTCGAGGCATGCTCTGTTTCCT |
| GabaR1F | ATTTCAGCATGAGGCCTGGCTTTG |
| GabaR1R | GCTGAGGTTGTTGGTGCTTGGAAA |
| GabaPiF | GGCTGGTGTTTGAAGGCAACAAGA |
| GabaPiR | ATACAGGACCGTGCCATTGGAGAA |
| GabaDeltaF | AGCGATGAATGACATCGGCGACTA |
| GabaDeltaR | ACTCCATGTTGGCCTCTGAGATGT |
| GepherynF | TGGTGAACAGCCAACTCAGACAGT |
| GepherynR | GAGCTTGCACCAGAATTCGCACTT |