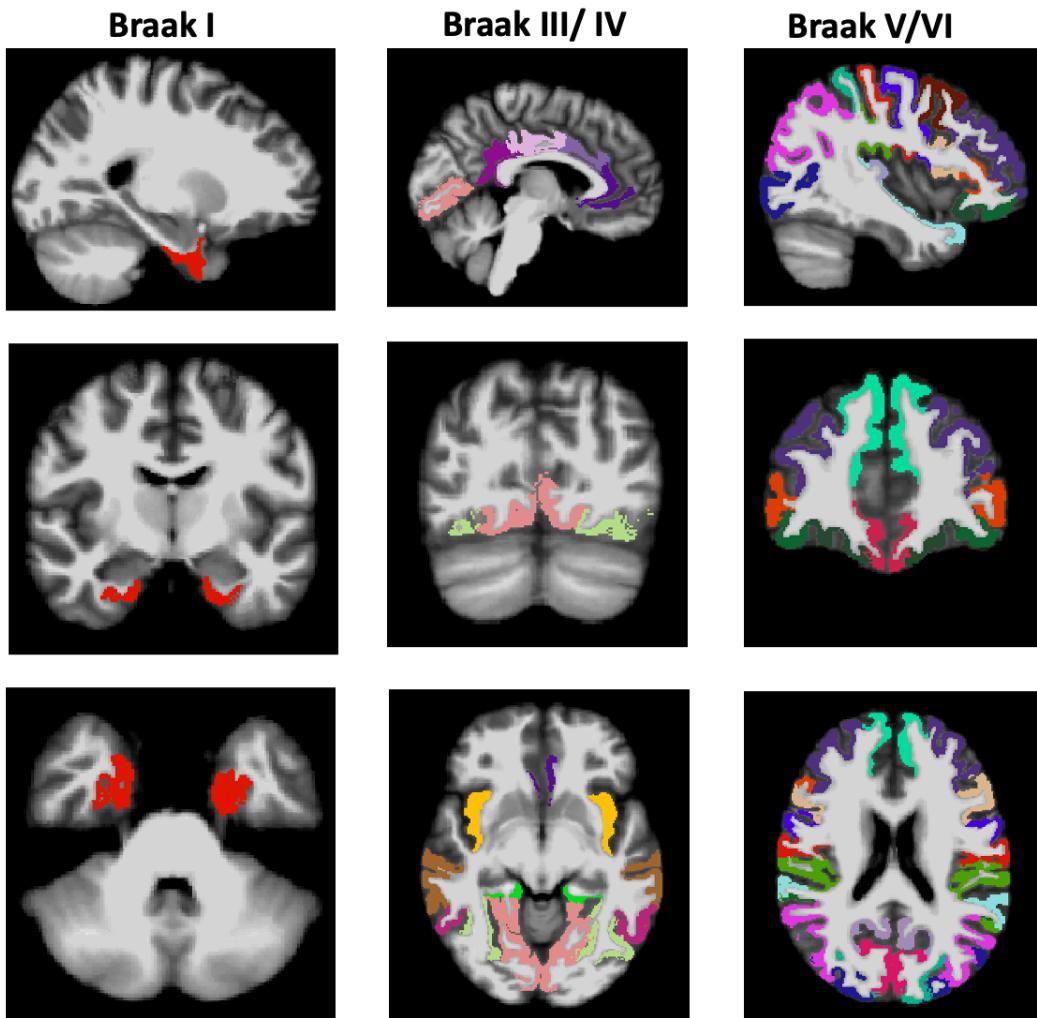


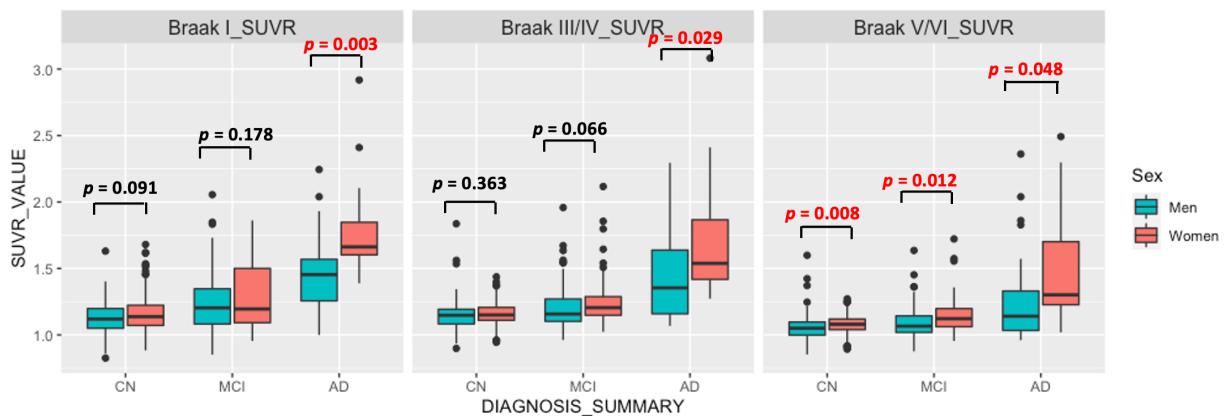
Supplementary materials

eFigure 1 Regions of Interests labeling



Composite regions of Braak stage shown in sagittal, coronal and axial plane. Braak I: entorhinal. Braak III/IV: parahippocampal, fusiform, lingual, amygdala, middletemporal, caudalanterior cingulate, rostralanteriorcingulate, posteriorcingulate, isthmuscingulate, insula, inferior-temporal, temporalpole. Braak V/VI: superiorfrontal, lateralorbitofrontal, medialorbitofrontal, frontalpole, caudalmiddlefrontal, rostralmiddlefrontal, parsopercularis, parsorbitalis, parstriangularis, lateraloccipital, parietalsupramarginal, parietalinferior, superiortemporal, parietalsuperior, precuneus, bankSuperiorTemporalSulcus, transversetemporal, pericalcarine, postcentral, cuneus, precentral, paracentral.

eFigure 2 Sex differences in tau PET by diagnosis



Boxplots showing sex comparisons of tau SUVR in Braak I, Braak III/IV and Braak V/VI regions in CN, MCI and AD. CN: cognitively normal, MCI: mild cognitive impairment, AD: Alzheimer's disease.

eTable 1 Top5 SNPs associated with tau PET in combined men and women group

| GENE | Chrom | Start_BP | End_BP | SNPs_N | Group | | Significant threshold |
|----------------|-------|-----------|-----------|--------|---------------------|-----------------------------------|-----------------------|
| | | | | | Top5_SNPs | Men + Women (N = 493) p values | |
| BIN1 | 2 | 127805599 | 127864730 | 63 | rs77059199_T | 0.00089522 | |
| | | | | | rs7567679_T | 0.00141111 | |
| | | | | | rs7559904_A | 0.00141111 | 0.00083333 |
| | | | | | rs147476865_T | 0.06317052 | |
| | | | | | rs3754619_A | 0.08335626 | |
| MS4A6A | 11 | 59939080 | 59952139 | 25 | rs7232_A | 0.02942496 | |
| | | | | | rs7935829_G | 0.04473068 | 0.002 |
| | | | | | rs2278867_T | 0.04473068 | |
| | | | | | rs72918674_T | 0.04473068 | |
| | | | | | rs12453_C | 0.04473068 | |
| DNAJA2 | 16 | 46989274 | 47007625 | 12 | rs79711283_G | 0.00017296 | |
| | | | | | rs12719758_G | 0.424859 | |
| | | | | | rs2034598_A | 0.46178753 | 0.00416667 |
| | | | | | rs12719759_T | 0.54998883 | |
| | | | | | rs8052160_A | 0.54998883 | |
| FERMT2 | 14 | 53323989 | 53417815 | 173 | rs113357081_A | 0.00279 | |
| | | | | | rs62003546_A | 0.04430138 | |
| | | | | | rs77026229_G | 0.08943171 | 0.00029762 |
| | | | | | rs75265722_T | 0.09727449 | |
| | | | | | rs62003545_G | 0.1207443 | |
| APOC1 | 19 | 45417577 | 45422606 | 11 | rs150966173_T | 0.19202594 | |
| | | | | | rs140480140_A | 0.19202594 | |
| | | | | | rs3925681_A | 0.36579121 | 0.00454545 |
| | | | | | rs12721056_T | 0.45813824 | |
| | | | | | rs12691088_A | 0.63612789 | |
| APOC1P1 | 2 | 45430060 | 45434643 | 7 | rs112871012_A | 0.23311746 | |
| | | | | | rs11271293_C | 0.23311746 | |
| | | | | | rs7259350_C | 0.23311746 | 0.00714286 |
| | | | | | rs7259004_C | 0.23311746 | |
| | | | | | rs113345881_G | 0.24766931 | |
| FAM193B | 11 | 176946790 | 176981548 | 49 | rs28425483_A | 0.08635007 | |
| | | | | | rs28626332_T | 0.11516826 | |
| | | | | | rs28473373_C | 0.1326902 | 0.00106383 |
| | | | | | rs2306761_A | 0.18199172 | |
| | | | | | rs60700381_T | 0.18199172 | |
| C2orf47 | 16 | 200820040 | 200828847 | 14 | rs17591211_A | 0.10249295 | |
| | | | | | rs7598665_C | 0.11869887 | |
| | | | | | rs281767_C | 0.20356514 | 0.00357143 |
| | | | | | rs6745617_A | 0.21275919 | |
| | | | | | rs16832105_G | 0.21275919 | |
| TYW5 | 14 | 200793634 | 200820459 | 47 | rs74614106_G | 0.02640354 | |
| | | | | | rs7573592_T | 0.09178929 | |
| | | | | | rs12693903_C | 0.09178929 | 0.00106383 |
| | | | | | rs12621809_G | 0.11869887 | |
| | | | | | rs7572840_A | 0.11869887 | |
| CR1 | 19 | 207669473 | 207815110 | 192 | rs78301018_C | 0.03298084 | |
| | | | | | rs113698814_G | 0.04328869 | |
| | | | | | rs12037841_T | 0.04506621 | 0.00026455 |
| | | | | | rs4562624_A | 0.04920513 | |
| | | | | | rs115096248_G | 0.06087642 | |

Note: Chrom: Chromosome; Start_BP: Start base position; End_BP: End base position.

SNPs_N: SNPs number within each gene.

Significance threshold after Bonferroni correction (0.05/SNP_N).

eTable 2 Top5 SNPs associated with tau PET in women and men separately

| GENE | Chrom | Start_BP | End_BP | SNPs_N | Group | | | | Significance threshold |
|----------------|-------|-----------|-----------|--------|----------------------|-------------------|----------------------|-------------------|------------------------|
| | | | | | women (N = 246) | | men (N = 247) | | |
| | | | | | Top5_SNPs | p values | Top5_SNPs | p values | |
| BIN1 | 2 | 127805599 | 127864730 | 63 | rs147476865_T | 0.01577858 | rs35920137_A | 0.0011585 | 0.00083333 |
| | | | | | rs142568045_C | 0.05490897 | rs77059199_T | 0.00345319 | |
| | | | | | rs143767206_G | 0.05490897 | rs7567679_T | 0.00566339 | |
| | | | | | rs2276574_A | 0.07719561 | rs7559904_A | 0.00566339 | |
| | | | | | rs115255114_T | 0.10307578 | rs1060743_G | 0.11472545 | |
| MS4A6A | 11 | 59939080 | 59952139 | 25 | rs7232_A | 0.05710199 | rs7232_A | 0.12098079 | 0.002 |
| | | | | | rs610932_T | 0.09764167 | rs7935829_G | 0.2612379 | |
| | | | | | rs634475_G | 0.09764167 | rs2278867_T | 0.2612379 | |
| | | | | | rs662196_C | 0.09764167 | rs72918674_T | 0.2612379 | |
| | | | | | rs631853_T | 0.09764167 | rs7946992_C | 0.2612379 | |
| DNAJA2 | 16 | 46989274 | 47007625 | 12 | rs79711283_G | 0.00111533 | rs79711283_G | 0.16202567 | 0.00416667 |
| | | | | | rs12719758_G | 0.15414969 | rs12925077_A | 0.05758995 | |
| | | | | | rs12719759_T | 0.23223133 | rs12719758_G | 0.53993138 | |
| | | | | | rs8052160_A | 0.23223133 | rs2034598_A | 0.58927407 | |
| | | | | | rs1362406_T | 0.23223133 | rs8054039_T | 0.86371401 | |
| FERMT2 | 14 | 53323989 | 53417815 | 173 | rs113357081_A | 0.00027548 | rs62003546_A | 0.13123348 | 0.00029762 |
| | | | | | rs7157639_T | 0.06018762 | rs62003545_G | 0.17038086 | |
| | | | | | rs71428504_A | 0.07198405 | rs35485994_T | 0.18769877 | |
| | | | | | rs12888114_T | 0.0721469 | rs117646236_G | 0.25304284 | |
| | | | | | rs77026229_G | 0.09616229 | rs75892454_C | 0.26959518 | |
| APOC1 | 19 | 45417577 | 45422606 | 11 | rs12721056_T | 0.00750681 | rs12691088_A | 0.07508622 | 0.00454545 |
| | | | | | rs3925681_A | 0.01207624 | rs12721046_A | 0.0963631 | |
| | | | | | rs12691088_A | 0.04591775 | rs150966173_T | 0.13331381 | |
| | | | | | rs150966173_T | 0.0954043 | rs140480140_A | 0.13331381 | |
| | | | | | rs140480140_A | 0.0954043 | rs12721051_G | 0.22021443 | |
| APOC1P1 | 2 | 45430060 | 45434643 | 7 | rs73033507_T | 0.01826804 | rs114448690_A | 0.4572346 | 0.00714286 |
| | | | | | rs112871012_A | 0.43939819 | rs113345881_G | 0.45861798 | |
| | | | | | rs111271293_C | 0.43939819 | rs12871012_A | 0.45861798 | |
| | | | | | rs7259350_C | 0.43939819 | rs111271293_C | 0.45861798 | |
| | | | | | rs7259004_C | 0.43939819 | rs7259350_C | 0.45861798 | |
| FAM193B | 11 | 176946790 | 176981548 | 49 | rs2306761_A | 0.02474836 | rs28626332_T | 0.01483779 | 0.00106383 |
| | | | | | rs60700381_T | 0.02474836 | rs2246566_G | 0.02229868 | |
| | | | | | rs185798693_T | 0.12501759 | rs2544815_A | 0.02229868 | |
| | | | | | rs77823252_T | 0.13353651 | rs2545803_C | 0.02229868 | |
| | | | | | rs335459_G | 0.21944761 | rs2544816_C | 0.02229868 | |
| C2orf47 | 16 | 200820040 | 200828847 | 14 | rs281767_C | 0.07662676 | rs6745617_A | 0.15103314 | 0.00357143 |
| | | | | | rs34998043_G | 0.14334724 | rs16832105_G | 0.15103314 | |
| | | | | | rs17591211_A | 0.17600808 | rs76225625_T | 0.15103314 | |
| | | | | | rs281766_T | 0.17986186 | rs16832106_G | 0.15103314 | |
| | | | | | rs166845_T | 0.17986186 | rs281766_T | 0.37054131 | |
| TYW5 | 14 | 200793634 | 200820459 | 47 | rs74614106_G | 5.04E-06 | rs16832051_C | 0.03693479 | 0.00106383 |
| | | | | | rs115171681_G | 0.03202494 | rs16832081_G | 0.13922373 | |
| | | | | | rs1704191_C | 0.07662676 | rs16832086_A | 0.13922373 | |
| | | | | | rs281764_G | 0.07662676 | rs7556976_C | 0.15103314 | |
| | | | | | rs3114090_A | 0.11490738 | rs62180489_A | 0.15103314 | |
| CR1 | 19 | 207669473 | 207815110 | 192 | rs115528293_A | 0.01751096 | rs113698814_G | 0.00019929 | 0.00026455 |
| | | | | | rs78301018_C | 0.01915838 | rs115096248_G | 0.00024124 | |
| | | | | | rs4844600_A | 0.02856484 | rs78150633_A | 0.00024124 | |
| | | | | | rs12037841_T | 0.0306193 | rs144047769_C | 0.00049349 | |
| | | | | | rs4562624_A | 0.0306193 | rs41274770_G | 0.00049349 | |

Note: Chrom: Chromosome; Start_BP: Start base position; End_BP: End base position.

SNPs_N: SNPs number within each gene.

Significance threshold after Bonferroni correction (0.05/SNP_N).

eTable 3 Sex-specific significant SNPs associated with partial volume corrected tau PET

| Women (N = 246) | | | | | Men (N = 247) | | | | |
|-----------------|-------|------------------------|-------------|-----------------------|---------------|-------|------------------------|-------------|-----------------------|
| GENE | SNP_N | Significance threshold | SNPs | p value | GENE | SNP_N | Significance threshold | SNPs | p value |
| DNAJA2 | 16 | 0.004 | rs79711283 | 0.003 | CR1 | 192 | 2.65×10^{-4} | rs113698814 | 1.81×10^{-4} |
| FERMT2 | 173 | 2.98×10^{-4} | rs113357081 | 9.70×10^{-5} | CR1 | 192 | 2.65×10^{-4} | rs115096248 | 7.19×10^{-6} |
| TYW5 | 47 | 0.001 | rs74614106 | 2.60×10^{-7} | CR1 | 192 | 2.65×10^{-4} | rs78150633 | 7.19×10^{-6} |

Note: 1. SNP_N: number of SNPs with each gene from the genetic data.

2. Significance threshold after Bonferroni correction (0.05/SNP_N)

eTable 4 Number of Participants with genotypes of SNPs in secondary analysis

| SNPs | Women-specific SNPs | | | | | | Men-specific SNPs | | | | | | | | | | | |
|-----------|---------------------------------|----|----|----------------------------------|----|----|-------------------------------|----|----|-------------------------------|----|----|-------------------------------|----|----|------------------------------|----|----|
| | DNAJA2 rs79711283 (MAF=7.3%) | | | FERMT2 rs113357081 (MAF=1.4%) | | | TYW5 rs74614106 (MAF=1.1%) | | | CR1 rs113698814 (MAF=2.1%) | | | CR1 rs115096248 (MAF=1.3%) | | | CR1 rs78150633 (MAF=1.3%) | | |
| Genotype | AA | AG | GG | TT | TA | AA | AA | AG | GG | AA | AG | GG | CC | CG | GG | GG | GA | AA |
| Women (N) | 211 | 35 | 0 | 239 | 7 | 0 | 241 | 5 | 0 | 239 | 6 | 1 | 239 | 7 | 0 | 239 | 7 | 0 |
| Men (N) | 213 | 31 | 3 | 240 | 7 | 0 | 241 | 6 | 0 | 233 | 13 | 0 | 241 | 6 | 0 | 241 | 6 | 0 |