Supplementary Table 1. Summary of statistical comparisons between young adult and aged animals. Table shows tissue class and arterial territory assignments, as well as abbreviations for each area surveyed. Post-hoc comparisons between young adult and aged animals in vessel density, vessel tortuosity, mean vessel diameter, and cortical thickness are shown for each region, tissue class or perfusion territory.

| Young-adult vs. Aged Comparisons | | | | Density | | | | Tortuosity | | | | Diameter | | | | Low Density Subsections | | | | (Cortical) Thickness | | | | |
|----------------------------------|-------------------------------------|-----------------|-----------|-----------------------------------|---------------|---------|-------|---------------------------------------|----------|-------|-------|--|----------|--------|-------|--|---------------|---------|-------|--|----------|-------|-------|---------------------------|
| Abbreviation | Full name | Tissue | Arterial | Territory Reference | Adjusted P | t | DE | % Change (Young adult- aged) | Adjusted | + | DE | % Change (Young adult- aged) | Adjusted | + | DE | % Change (Young adult- aged) | Adjusted P | t | DE | % Change (Young adult- aged) | Adjusted | + | DE | % Change (Young adult- |
| Abbreviation | Tui name | White | Territory | Images from | | | 51 | ageu) | | L. | DI | aged) | | | 51 | ageu) | | · | 51 | ageu) | | | DI | ageuy |
| C. Callosum | Corpus Callosum | matter | ACA | (Endepols et al., | <0.0001 | 7.194 | 48.8 | -26.83 | 0.4899 | 2.071 | 47.31 | -0.68552 | 0.9995 | 0.852 | 50.02 | 1.444328 | 0.0002 | 4.844 | 55.44 | 126.6047 | 0.5714 | 1.612 | 44.87 | 6.885645 |
| Fimbria | Fimbria | White matter | ACA | (Thomas et al., 2011) | 0.0826 | 2.874 | 55.59 | -11.63 | 0.8631 | 1.563 | 51.68 | -0.59473 | 0.0008 | 4.427 | 48.23 | 7.930941 | 0.9757 | 1.244 | 49.64 | 30.28617 | | | | |
| | Frontal Association | A 11 1 | | Images from (Endenois et al | 0.0750 | | | | | | | | | | | | | | | | | | | |
| FrA | Cortex | Cortical | ACA | Images from | 0.0759 | 2.907 | 54.82 | -7.824 | 0.0432 | 3.131 | 48.9 | 0.600343 | 0.6291 | 1.889 | 56.83 | 2.54152 | 0.9999 | 0.763 | 53.11 | -36.7971 | | | | |
| GI/DI | Insular Cortex | Cortical | MCA | (Rousselet et al., | 0.9087 | 1.47 | 53.4 | -3.289 | 0.2569 | 2.409 | 51.41 | 0.512821 | 0.0019 | 4.131 | 53.39 | 5.590513 | >0.9999 | 0.0999 | 53.96 | 3.795893 | 0.002 | 3.856 | 58.62 | -5.72391 |
| PRh/Ect | Perirhinal/Ectorhinal | Cortical | МСА | Images from (Rousselet et al., | <0.0001 | 5.976 | 52 11 | -16.04 | 0 7094 | 1 703 | 10 | 0.426621 | 0.0007 | 4 652 | 35.87 | 7 80759 | 0 591 | 1 944 | 47.09 | 53 73053 | 0.0014 | 3 078 | 58 5 | -6.07073 |
| T MI/Let | Primary/Secondary | contical | WICA | Images from | 0.0001 | 5.570 | 52.11 | 10.04 | 0.7054 | 1.755 | 45 | 0.420021 | 0.0007 | 4.052 | 55.67 | 7.00735 | 0.551 | 1.544 | 47.05 | 55.75555 | 0.0014 | 3.570 | 56.5 | 0.07075 |
| M1/M2 | Motor Cortex | Cortical | ACA | (Endepols et al., | <0.0001 | 5.967 | 54.77 | -10.01 | 0.1429 | 2.669 | 49.99 | 0.599829 | 0.1572 | 2.638 | 45.92 | 3.51972 | 0.8716 | 1.55 | 46.39 | 80.94824 | 0.0078 | 3.429 | 58.4 | -5.62891 |
| S1FL | Somatosensory | Cortical | MCA | (Rousselet et al., | 0.0013 | 4.207 | 61.17 | -7.214 | 0.0889 | 2.854 | 52.17 | 0.515907 | 0.0207 | 3.395 | 47.56 | 4.828974 | 0.1792 | 2.569 | 52.68 | 95.3304 | 0.0024 | 3.802 | 59.82 | -6.17733 |
| | | | | Images from (Xiong | | | | | | | | | | | | | | | | | | | | |
| RS | Retrosplenial Cortex | Cortical | PCA | et al., 2017) | 0.0089 | 3.659 | 51.35 | -7.915 | 0.7957 | 1.674 | 49.98 | 0.429923 | 0.0003 | 4.781 | 42.62 | 8.438384 | >0.9999 | 0.5952 | 44.66 | -28.1231 | 0.0478 | 2.807 | 53.35 | -4.02641 |
| V1 | Cortex | Cortical | PCA | (Pula & Yuen, 2017) | 0.997 | 1.001 | 56.55 | -2.144 | 0.0224 | 3.414 | 38.82 | 0.598802 | >0.9999 | 0.3276 | 49.06 | -0.41708 | >0.9999 | 0.07711 | 46.38 | -2.32558 | 0.0005 | 4.336 | 52.19 | -5.51172 |
| HPC | Dorsal Hinnocampus | Subcortical | PCA | (Erdem et al. 1993) | 0.0007 | 4 4 2 1 | 56.5 | -9.855 | 0.0264 | 3 369 | 36 72 | 0 599315 | <0.0001 | 5 883 | 41 21 | 9 084084 | 0 9982 | 0 954 | 52.99 | 28 09917 | | | | |
| | Striatum | Subcorticut | . at | (Feekes & Cassell, | 0.0007 | | 50.5 | 5.055 | 0.0201 | 5.505 | 50.72 | 0.000010 | 1010001 | 5.005 | | 5.001001 | 0.5502 | 0.554 | 52.55 | 20.05517 | | | | |
| STR | (Caudate/Putamen) | Subcortical | MCA | 2006) | 0.0582 | 3.002 | 56.56 | -4.598 | 0.4014 | 2.19 | 45.83 | 0.427716 | <0.0001 | 5.347 | 49.38 | 7.820513 | 0.9928 | 1.095 | 38.72 | 92.99641 | | | | |
| Thalamus | Thalamus | Subcortical | PCA | (Schmahmann, 2003) | 0.2904 | 2.342 | 58.22 | -4.266 | 0.5514 | 1.999 | 42.29 | 0.344828 | <0.0001 | 6.603 | 46.72 | 10.07121 | >0.9999 | 0.5395 | 43.47 | 38.53484 | | | | |
| Uunathalamus | Uunotholomus | Cubeertical | DCA | (Danial 1066) | 0.0006 | 2 6 1 2 | 56.57 | 11.00 | 0.0505 | 2 100 | 40.70 | 0.694246 | 0.9606 | 1 552 | 40.67 | 2 725174 | >0.0000 | 0.520 | 40 77 | 17 74222 | | | | |
| пуроспанатиз | нурошаатыз | Subcortical | PCA | (Daniel, 1966) | 0.0096 | 5.015 | 50.57 | -11.09 | 0.0505 | 5.100 | 40.79 | 0.084540 | 0.8696 | 1.552 | 49.07 | 2.735174 | >0.9999 | 0.559 | 46.77 | 17.74222 | | | | |
| LA | Lateral Amygdala | Subcortical | MCA | (Merksz et al., 1978) | >0.9999 | 0.0201 | 41.76 | -0.07518 | 0.0064 | 3.764 | 51.33 | 0.861326 | 0.9982 | 0.9538 | 52.4 | 1.921132 | 0.9996 | 0.8469 | 35.81 | 46.00688 | | | | |
| SNR | Substantia Nigra Pars Reticulata | Subcortical | MCA | (Sonne & Beato, 2019) | 0.081 | 2.88 | 56.27 | -7.34 | 0.0809 | 2.904 | 46.81 | 0.85034 | 0.9887 | 1.142 | 57.69 | 1.869631 | 0.001 | 4.535 | 34.42 | 169.4276 | | | | |
| | Anterior Cerebral | | | | | | | | | | | | | | | | | | | | | | | |
| ACA | Artery Middle Cerebral | | | | <0.0001 | 5.911 | 56.73 | -12.8327 | | | | | | | | | 0.0228 | 2.769 | 54.9 | 56.45514 | | | | |
| MCA | Artery | | | | 0.0005 | 4.335 | 44.91 | -7.73626 | | | | | | | | | 0.1087 | 2.134 | 51.46 | 43.79865 | | | | |
| PCA | Posterior Cerebral | | | | 0.0007 | 4 125 | 59.73 | -6 6942 | | | | | | | | | 0 1097 | 2 128 | 53 63 | 41 56311 | | | | |
| | /usely | | | | 0.0007 | 4.125 | 55.75 | 0.0342 | | | | | | | | | 0.1057 | 2.120 | 55.05 | 41.50511 | | | | |
| WM | White Matter | | | | <0.0001 | 6.614 | 50.76 | -22.4813 | | | | | | | | | 0.0007 | 3.962 | 51.86 | 84.23272 | | | | |
| CGM | Cortical Gray Matter | | | | <0.0001 | 5.33 | 54.07 | -8.65645 | | | | | | | | | 0.998 | 0.1599 | 45.06 | -4.41696 | | | | |
| | Subcortical Gray | | | | | | | | | | | | | | | | | | | | | | | |
| SGM | Matter | | | | 0.0008 | 4.125 | 54.6 | -5.83602 | | | | | | | | | 0.0401 | 2.56 | 50.02 | 52.99632 | | | | |

Supplementary Table 2. Summary of previous research estimating vessel loss with aging. Review of existing literature on microvascular loss, excluding studies that focused on arterioles or larger vessels. Includes information on subject species, brain region, method of vascular labeling, age, measurement metric, and time-adjusted magnitude of change in vessel density. Negative values indicate vessel loss. Some values are approximations based on interpretations of figures.

| | | | | | | | | % change |
|--|----------------|---|--|--|------------|------------------|------------------|-------------|
| | | | | | | | | / 12 |
| Author | Animal | Area | Method | Age | months | metric | % change | months |
| (Hunziker et al., 1979) (Hunziker et al., 1979) | Human Human | Precentral gyrus Precentral gyrus | Alkaline phosphatase | 19-94 y/o (group means approx 32-90) 19-94 y/o (group means approx 32-90) | 696 696 | length | -2 | 0 |
| (Meier-Ruge et al., 1980) | Human | Putamen | Alkaline phosphatase | 19-94 y/o (group means approx 32-90) | 696 | length | 60 | 1 |
| (Meier-Ruge et al., 1980) | Human | Putamen | Alkaline phosphatase | 19-94 y/o (group means approx 32-90) | 696 | volume | 84 | 1.5 |
| (Meier-Ruge et al., 1980) (Meier-Ruge et al., 1980) | Human Human | Cortex | Alkaline phosphatase | 19-94 y/o (group means approx 32-90) 19-94 y/o (group means approx 32-90) | 696 | volume | -4 | -0.1 |
| (Bell and Ball, 1981) | Human | Hippocampus | Alkaline phosphatase | 38-74 y/o | 432 | length | -16 | -0.4 |
| (Mann et al., 1986) | Human | Frontal cortex | Alkaline phosphatase | 26-96 y/o | 840 | length | -46 | -0.7 |
| (Mann et al., 1986) (Mann et al., 1986) | Human | Frontal cortex | Alkaline phosphatase | 26-96 y/o | 840 840 | area | -35 No change | -0.5 |
| (Mann et al., 1986) | Human | Temporal cortex | Alkaline phosphatase | 26-96 y/o | 840 | area | No change | 0 |
| (Bell and Ball, 1990) | Human | Visual cortex | Alkaline phosphatase | 31-79 y/o | 576 | length | -16 | -0.3 |
| (Abernethy et al., 1993) | Human | PVN hypothalamus | Alkaline phosphatase | 30-85 y/o 30-85 y/o | 660 660 | length | -49 No change | -0.9 |
| (Buée et al., 1993) | Human | Cortex | Vascular HSPG | 49-79 y/o | 360 | area | -28 | -0.9 |
| (Farkas et al., 2006) | Human | White matter | Hematoxylin-eosin staining | 40-90y/o | 600 | length | No change | 0 |
| (Brown et al., 2007b) | Human | White matter | Alkaline phosphatase | 57-90 y/o | 396 | area | -64 | -1.9 |
| (Burns et al., 1981) | Macaque | Frontal cortex | Microfil | 10-20y/o | 120 | area | -22.2 | -2.2 |
| (Burns et al., 1981) | Macaque | Frontal cortex | Microfil | 4-20y/o | 192 | area | -27.8 | -1.7 |
| (Sturrock, 1977) | Mouse | Indusium griseum | CD21 | 7.22 m/a | 10 | longth | No change | 14.5 |
| (Murugesan et al., 2012) (Murugesan et al., 2012) | Mouse | White matter | CD31 | 7-23 m/o | 16 | length | -19.5 | -14.5 |
| (Murugesan et al., 2012) | Mouse | Hippocampus | CD31 | 7-23 m/o | 16 | length | -26.4 | -19.8 |
| (Moeini et al., 2018) | Mouse | S1 barrel cortex | Fluroescent plasma label | 7.5-26 m/o | 18.5 | volume | -17 | -11 |
| (Keeson et al., 2018) (Klein and Michel. 1977) | Rat | S1 cortex Frontal and Occipital cortex | Evans Blue plasma label Windel's thionin | 3.5-16.5 m/o 6-25 m/o | 13 | number | -8 -21 | -7.4 |
| (Bär, 1978) | Rat | Occipital cortex | | 6-30 m/o | 24 | | 19 | 9.5 |
| (Knox and Oliveira, 1980) | Rat | Cortex | Toluidine blue | 4-23 m/o | 19 | number | -7.9 | -5 |
| (Burns et al., 1981) (Wilkinson et al., 1981) | Rat | Cortex | Microfii Latex and luconvl blue perfusion | 35-800 d/o 13-120 w/o | 25.5 | area number | 39 10 | 18.4 |
| (Hinds and McNelly, 1982) | Rat | Olfactory bulb | Toluidine blue | 3-36 m/o | 33 | length | -15 | -5.5 |
| (Casey and Feldman, 1985) | Rat | Brainstem | Toluidine blue | 3-33 m/o | 30 | volume | -27.4 | -11 |
| (Buchweitz-Milton and Weiss, 1987) (Hughes and Lantos, 1987) | Rat | Cortex | Alkaline phosphatase, FITC dextran | 9-30.5 m/o 3-22 5 m/o | 21.5 | length | -29.5 | -16.5 |
| (Meier-Ruge and Schulz-Dazzi, 1987) | Rat | Parietal cortex | Alkaline phosphatase | 12-36 m/o | 24 | volume | 10 | 0.5 |
| (Meier-Ruge and Schulz-Dazzi, 1987) | Rat | Parietal cortex | Alkaline phosphatase | 12-36 m/o | 24 | length | -7.5 | -3.8 |
| (Black et al., 1989) (Jucker and Meier-Ruge, 1989; Jucker et al., 1990) | Rat | Visual cortex Hippocampus | Toluidine blue | 12-22 m/o 18-27 5 m/o | 9.5 | number | No change -21 | -26.5 |
| (Jucker and Meier-Ruge, 1989; Jucker et al., 1990) | Rat | Parietal cortex | Alkaline phosphatase | 18-27.5 m/o | 9.5 | number | -26 | -32.8 |
| (Amenta et al., 1995a) | Rat | Frontal cortex | Alkaline phosphatase | 12-24 m/o | 12 | number | -41.8 | -41.8 |
| (Amenta et al., 1995a) | Rat | Frontal cortex | Alkaline phosphatase | 12-24 m/o | 12 | length | -30.1 | -30.1 |
| (Amenta et al., 1995a) | Rat | Occipital cortex | Alkaline phosphatase | 12-24 m/o | 12 | length | -5.6 | -5.6 |
| (Amenta et al., 1995a) | Rat | Hippocampus | Alkaline phosphatase | 12-24 m/o | 12 | number | -48.7 | -48.7 |
| (Amenta et al., 1995a) | Rat | Hippocampus | Alkaline phosphatase | 12-24 m/o | 12 | length | -25 | -25 |
| (Amenta et al., 1995b) (Amenta et al., 1995b) | Rat | Frontal cortex Frontal cortex | Alkaline phosphatase | 12-27 m/o 12-27 m/o | 15 | length | -28.2 | -22.6 |
| (Amenta et al., 1995b) | Rat | Occipital cortex | Alkaline phosphatase | 12-27 m/o | 15 | number | -17.8 | -14.2 |
| (Amenta et al., 1995b) | Rat | Occipital cortex | Alkaline phosphatase | 12-27 m/o | 15 | length | -12.2 | -9.7 |
| (Amenta et al., 1995b) (Amenta et al., 1995b) | Rat | Ammons horn Ammons horn | Alkaline phosphatase | 12-27 m/o | 15 | length | -26.5 | -21.2 |
| (Amenta et al., 1995b) | Rat | Dentate | Alkaline phosphatase | 12-27 m/o | 15 | number | -19.4 | -15.5 |
| (Amenta et al., 1995b) | Rat | Dentate | Alkaline phosphatase | 12-27 m/o | 15 | length | 20.4 | 16.3 |
| (Villena et al., 2003) (Villena et al., 2003) | Rat | LGN | Toluidine blue | 3-28 m/o 3-28 m/o | 25 | number | 69.3 19.4 | 9.3 |
| (Villena et al., 2003) | Rat | LGN | Toluidine blue | 3-28 m/o | 25 | volume | 36.4 | 17.5 |
| (Villena et al., 2003) | Rat | LGN | Toluidine blue | 3-28 m/o | 25 | area | 29 | 13.9 |
| (villena et al., 2003) (Villena et al., 2003) | Rat Rat | LGN LGN | Toluidine blue | 18-28 m/o 18-28 m/o | 10 | number | -3.1 -3.2 | -3.7 |
| (Villena et al., 2003) | Rat | LGN | Toluidine blue | 18-28 m/o | 10 | volume | -6.3 | -7.6 |
| (Villena et al., 2003) | Rat | LGN | Toluidine blue | 18-28 m/o | 10 | area | -4.7 | -5.6 |
| (Villar-cheda et al., 2009) (Villar-cheda et al., 2009) | Rat | Substantia Nigra | RECA1 | 4-14 m/o 4-24 m/o | 10 | number | -14 -21 | -16.8 |
| (Ndubuizu et al., 2000) | Rat | Cortex | GLUT-1 | 3-24 m/o | 21 | number | -10.3 | -5.9 |
| (Ndubuizu et al., 2010) | Rat | Corpus Callosum | GLUT-1 | 3-24 m/o | 21 | number | -2.6 | -1.5 |
| (Ndubuizu et al., 2010) (Ndubuizu et al., 2010) | Rat Rat | Striatum Hippocampus | GLUT-1 GLUT-1 | 3-24 m/o 3-24 m/o | 21 | number number | -10.3 | -5.9 |
| (Shao et al., 2010) | Rat | White matter | Collagen 4 | 7-27 m/o | 20 | length | -18.6 | -11.2 |
| (Shao et al., 2010) | Rat | White matter | Collagen 4 | 7-27 m/o | 20 | volume | -23.5 | -14.1 |
| (Zhang et al., 2012) (Desiardins et al., 2014) | Rat | Hippocampus S1 cortex | RECA1 Eluroescent plasma label | 5-34 m/o 3-24 m/o | 29 | length | -40 | -16.6 |
| (Desjardins et al., 2014) | Rat | S1 cortex | Fluroescent plasma label | 3-24 m/o | 21 | volume | -20.6 | -11.8 |
| (Tang et al., 2016) | Rat | Cortex & Striatum | Lectin | 3-24 m/o | 21 | number | -3.5 | -2 |
| (Tang et al., 2016) (Schager & CE Brown, current) | Rat | Cortex & Striatum | GLUT-1 FITC Devtran Plasma Label | 3-24 m/o | 21 | number length | -10.6 | -6.1 |
| (Schager & CE Brown, current) | Mouse | Fimbria | FITC Dextran Plasma Label | 3.5-19.5 m/o | 16 | length | -11.6 | -8.7 |
| (Schager & CE Brown, current) | Mouse | FrA | FITC Dextran Plasma Label | 3.5-19.5 m/o | 16 | length | -7.8 | -5.9 |
| (Schager & CE Brown, current) | Mouse | GI/DI PRh/Ect | FITC Dextran Plasma Label | 3.5-19.5 m/o | 16 | length | -3.3 | -2.5 |
| (Schager & CE Brown, current) | Mouse | M1/M2 | FITC Dextran Plasma Label | 3.5-19.5 m/o | 16 | length | -10 | -12 |
| (Schager & CE Brown, current) | Mouse | \$1FL | FITC Dextran Plasma Label | 3.5-19.5 m/o | 16 | length | -7.2 | -5.4 |
| (Schager & CE Brown, current) | Mouse | RS | FITC Dextran Plasma Label | 3.5-19.5 m/o | 16 | length | -7.9 | -5.9 |
| (Schager & CE Brown, current) | Mouse | HPC | FITC Dextran Plasma Label | 3.5-19.5 m/o | 16 | length | -2.1 | -1.0 |
| (Schager & CE Brown, current) | Mouse | STR | FITC Dextran Plasma Label | 3.5-19.5 m/o | 16 | length | -4.6 | -3.4 |
| (Schager & CE Brown, current) | Mouse | Thalamus | FITC Dextran Plasma Label | 3.5-19.5 m/o | 16 | length | -4.3 | -3.2 |
| (Schager & CE Brown, current) | Mouse | LA | FITC Dextran Plasma Label | 3.5-19.5 m/o 3.5-19.5 m/o | 16 | length | -11.1 | -8.3 |
| (Schager & CE Brown, current) | Mouse | SNR | FITC Dextran Plasma Label | 3.5-19.5 m/o | 16 | length | -7.3 | -5.5 |

Supplementary Figure 1. Visual guide of sampling areas. Figure describes stereotaxic levels and bounds of sampling locations for each brain area. These bounds guided ROI locations for each area in microsphere analysis and determined bounds and possible stereotaxic levels for confocal microscopy of vascular density.



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