

Supplementary Information: Alzheimer's disease alters oligodendrocytic glycolytic and ketolytic gene expression

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Tables

Table S1. Cell-specific gene markers for neurons, astrocytes, oligodendrocytes, microglia

Cell Type	Cell Markers
Neuron	<i>STMN2</i>
	<i>SYN1</i>
	<i>SYT1</i>
	<i>GAD1</i>
	<i>CCK</i>
Astrocyte	<i>GFAP</i>
	<i>ALDH1L1</i>
	<i>AQP4</i>
	<i>GJA1</i>
	<i>SOX9</i>
Oligodendrocyte	<i>MOG</i>
	<i>MOBP</i>
	<i>SOX10</i>
	<i>GPR37</i>
Microglia	<i>TLR2</i>
	<i>CX3CR1</i>
	<i>IL1A</i>

Table S2. Clinical Dementia Rating (CDR) and Braak neurofibrillary tangle stage of AD cases and controls

AD cases were comprised of individuals with definitive diagnoses of AD. AD: Alzheimer's Disease (definite diagnosis according to the NINCDS-ADRDA criteria and had Braak NFT stage of IV or greater)

Control: Braak NFT stage of III or less, CERAD neuritic and cortical plaque densities of 0 (none) or 1 (sparse) AND lacked any of the following pathologic diagnoses: AD, Parkinson's disease (PD), DLB, VaD, PSP, motor neuron disease (MND), CBD, Pick's disease (PiD), Huntington's disease (HD), FTLN, hippocampal sclerosis (HipScl) or dementia lacking distinctive histology (DLNH)

	Knight-ADRC		Mayo Clinic Brain Bank		Mount Sinai Brain Bank	
	AD	Control	AD	Control	AD	Control
Sample Size	86	15	82	78	568	353
CDR = 0	3	9	--	--	4	118
CDR = 0.5	3	5	--	--	16	116
CDR = 1	6	1	--	--	41	44
CDR = 2	13	0	--	--	107	23
CDR = 3	61	0	--	--	167	23
CDR = 4	0	0	--	--	92	23
CDR = 5	0	0	--	--	141	6
Braak = 0	0	0	--	--	0	39
Braak = 1	1	5	--	--	5	80
Braak = 2	4	7	--	--	17	112
Braak = 3	2	1	--	--	30	97
Braak = 4	8	2	--	--	39	8
Braak = 5	35	0	--	--	106	3
Braak = 6	26	0	--	--	338	0
Braak = NA	10	0	--	--	33	14

Table S3. Number of genes removed by filters

Filters include insufficient expression levels, missing sex, or significant sex-related differences in expression (“Genes Removed”), and genes that were removed due to significant sex-related differences in expression alone (“Sex-Specific Genes”).

Dataset	Cell Type	Genes Removed	Sex-Specific Genes
Knight Parietal	Neuron	7862	96
	Astrocyte	1173	1052
	Oligodendrocyte	18	8
	Microglia	69	23
Mayo Cerebellum	Neuron	2776	2631
	Astrocyte	1381	334
	Oligodendrocyte	5946	3765
	Microglia	353	133
Mayo Temporal Cortex	Neuron	166	59
	Astrocyte	2233	2004
	Oligodendrocyte	210	109
	Microglia	901	519
MSBB Frontal Pole	Neuron	58	42
	Astrocyte	158	91
	Oligodendrocyte	67	40
	Microglia	9930	9526
MSBB Inferior Frontal Gyrus	Neuron	4141	10
	Astrocyte	371	110
	Oligodendrocyte	69	24
	Microglia	9929	9156
MSBB Parahippocampal Gyrus	Neuron	319	279
	Astrocyte	2101	2760
	Oligodendrocyte	433	347
	Microglia	506	229
MSBB Superior Temporal Gyrus	Neuron	472	407
	Astrocyte	2177	2150
	Oligodendrocyte	104	34
	Microglia	4027	4004

Table S4. Number of AD cases and controls with genes that passed filtering criteria for each brain region

AD Cases and Controls		
Brain Region	AD	Control
Knigh Parietal	62	13
Mayo Cerebellum	65	64
Mayo Temporal Cortex	80	76
MSBB Frontal Pole	108	44
MSBB Inferior Frontal Gyrus	101	38
MSBB Parahippocampal Gyrus	100	38
MSBB Superior Temporal Gyrus	110	37

Table S5. Bonferroni corrected α -values by brain region and cell type for glycolytic genes

Brain Region	Neuron	Astrocyte	Oligodendrocyte	Microglia
Knight Parietal	0.01	0.002778	0.002632	0.002632
Mayo Cerebellum	0.002778	0.0025	0.005	0.0025
Mayo Temporal Cortex	0.0025	0.0025	0.0025	0.0025
MSBB Frontal Pole	0.0025	0.0025	0.0025	0.003571
MSBB Inferior Frontal Gyrus	0.0025	0.0025	0.0025	0.002632
MSBB Parahippocampal Gyrus	0.0025	0.0025	0.0025	0.0025
MSBB Superior Temporal Gyrus	0.01667	0.002632	0.002632	0.004545

Table S6. Bonferroni corrected α -values by brain region and cell type for ketolytic genes

Brain Region	Neuron	Astrocyte	Oligodendrocyte	Microglia
Knight Parietal	0.0125	0.0125	0.008333	0.008333
Mayo Cerebellum	0.0125	0.0025	0.01667	0.008333
Mayo Temporal Cortex	0.01	0.0025	0.01	0.01
MSBB Frontal Pole	0.008333	0.01	0.008333	0.025
MSBB Inferior Frontal Gyrus	0.008333	0.008333	0.008333	0.01
MSBB Parahippocampal Gyrus	0.008333	0.01	0.01	0.008333
MSBB Superior Temporal Gyrus	0.0125	0.008333	0.008333	0.0125

Table S7. Empirical p-values by brain region and cell type.

Brain Region	Neuron	Astrocyte	Oligodendrocyte	Microglia
Knigh Parietal	0.001138	0.05065	0.02488	0.2112
Mayo Cerebellum	0.0002759	2.618×10^{-14}	2.358×10^{-7}	0.002181
Mayo Temporal Cortex	5.622×10^{-5}	8.338×10^{-13}	7.343×10^{-9}	0.003816
MSBB Frontal Pole	1.616×10^{-5}	0.02522	0.003687	0.02903
MSBB Inferior Frontal Gyrus	0.0001757	0.02208	0.0003743	0.01374
MSBB Parahippocampal Gyrus	5.051×10^{-12}	6.677×10^{-5}	4.462×10^{-9}	0.005368
MSBB Superior Temporal Gyrus	3.975×10^{-5}	0.01814	0.0005621	0.06082

Table S8. Glycolytic genes in neurons included from each dataset

Dataset	Genes
Knigh t Parietal	<i>SLC2A3, GAPDH, HK2, PGAM1, PGK1</i>
Mayo Cerebellum	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, GAPDH, GPI, HK1, HK2, PDHA1, PFKM, PFKP, PGAM1, PGK1, PKM, TPI</i>
Mayo Temporal Cortex	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Frontal Pole	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Inferior Frontal Gyrus	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Parahippocampal Gyrus	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Superior Temporal Gyrus	<i>SLC2A4, HK2, PFKL</i>

Table S9. Glycolytic genes in astrocytes included from each dataset

Dataset	Genes
Knight Parietal	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
Mayo Cerebellum	<i>IRS1, SLC2A1, SLC2A4, ALDOA, GAPDH, HK2, PFKP, PGAM1, PKM, TPI1</i>
Mayo Temporal Cortex	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Frontal Pole	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Inferior Frontal Gyrus	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Parahippocampal Gyrus	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Superior Temporal Gyrus	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>

Table S10. Glycolytic genes in oligodendrocytes included from each dataset

Dataset	Genes
Knight Parietal	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PGAM1, PGK1, PKM, TPI1</i>
Mayo Cerebellum	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
Mayo Temporal Cortex	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Frontal Pole	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Inferior Frontal Gyrus	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Parahippocampal Gyrus	<i>IRS1, IRS2, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Superior Temporal Gyrus	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>

Table S11. Glycolytic genes in microglia included from each dataset

Dataset	Genes
Knight Parietal	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
Mayo Cerebellum	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
Mayo Temporal Cortex	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Frontal Pole	<i>INSR, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PGAM1, PGK1, PKM, TPI1</i>
MSBB Inferior Frontal Gyrus	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Parahippocampal Gyrus	<i>INSR, IRS1, IRS2, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, GAPDH, GPI, HK1, HK2, PDHA1, PFKL, PFKM, PFKP, PGAM1, PGK1, PKM, TPI1</i>
MSBB Superior Temporal Gyrus	<i>INSR, IRS1, SLC2A1, SLC2A3, SLC2A4, ALDOA, ENO2, HK1, PGK1, PKM, TPI1</i>

Table S12. Ketolytic genes in neurons included from each dataset

Dataset	Genes
Knight Parietal	<i>SLC16A1, SLC16A3, ACAT1, OXCT1</i>
Mayo Cerebellum	<i>SLC16A1, ACAT1, OXCT1</i>
Mayo Temporal Cortex	<i>SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Frontal Pole	<i>SLC16A1, SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Inferior Frontal Gyrus	<i>SLC16A1, SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Parahippocampal Gyrus	<i>SLC16A1, SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Superior Temporal Gyrus	<i>SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>

Table S13. Ketolytic genes in astrocytes included from each dataset

Dataset	Genes
Knight Parietal	<i>SLC16A1, SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
Mayo Cerebellum	<i>SLC16A1, ACAT1, OXCT1</i>
Mayo Temporal Cortex	<i>SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Frontal Pole	<i>SLC16A1, SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Inferior Frontal Gyrus	<i>SLC16A1, SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Parahippocampal Gyrus	<i>SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Superior Temporal Gyrus	<i>SLC16A1, SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>

Table S14. Ketolytic genes in oligodendrocytes included from each dataset

Dataset	Genes
Knight Parietal	<i>SLC16A1, SLC16A3, ACAT1, OXCT1</i>
Mayo Cerebellum	<i>SLC16A1, ACAT1, OXCT1</i>
Mayo Temporal Cortex	<i>SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Frontal Pole	<i>SLC16A1, SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Inferior Frontal Gyrus	<i>SLC16A1, SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Parahippocampal Gyrus	<i>SLC16A1, SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Superior Temporal Gyrus	<i>SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>

Table S15. Ketolytic genes in microglia included from each dataset

Dataset	Genes
Knight Parietal	<i>SLC16A1, SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
Mayo Cerebellum	<i>SLC16A1, SLC16A3, ACAT1, BDH1, OXCT1</i>
Mayo Temporal Cortex	<i>SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Frontal Pole	<i>SLC16A3, OXCT1</i>
MSBB Inferior Frontal Gyrus	<i>SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Parahippocampal Gyrus	<i>SLC16A1, SLC16A3, SLC16A7, ACAT1, BDH1, OXCT1</i>
MSBB Superior Temporal Gyrus	<i>SLC16A1, SLC16A3, SLC16A7, OXCT1</i>

Figures

Figure S1: Glycolysis in Astrocytes

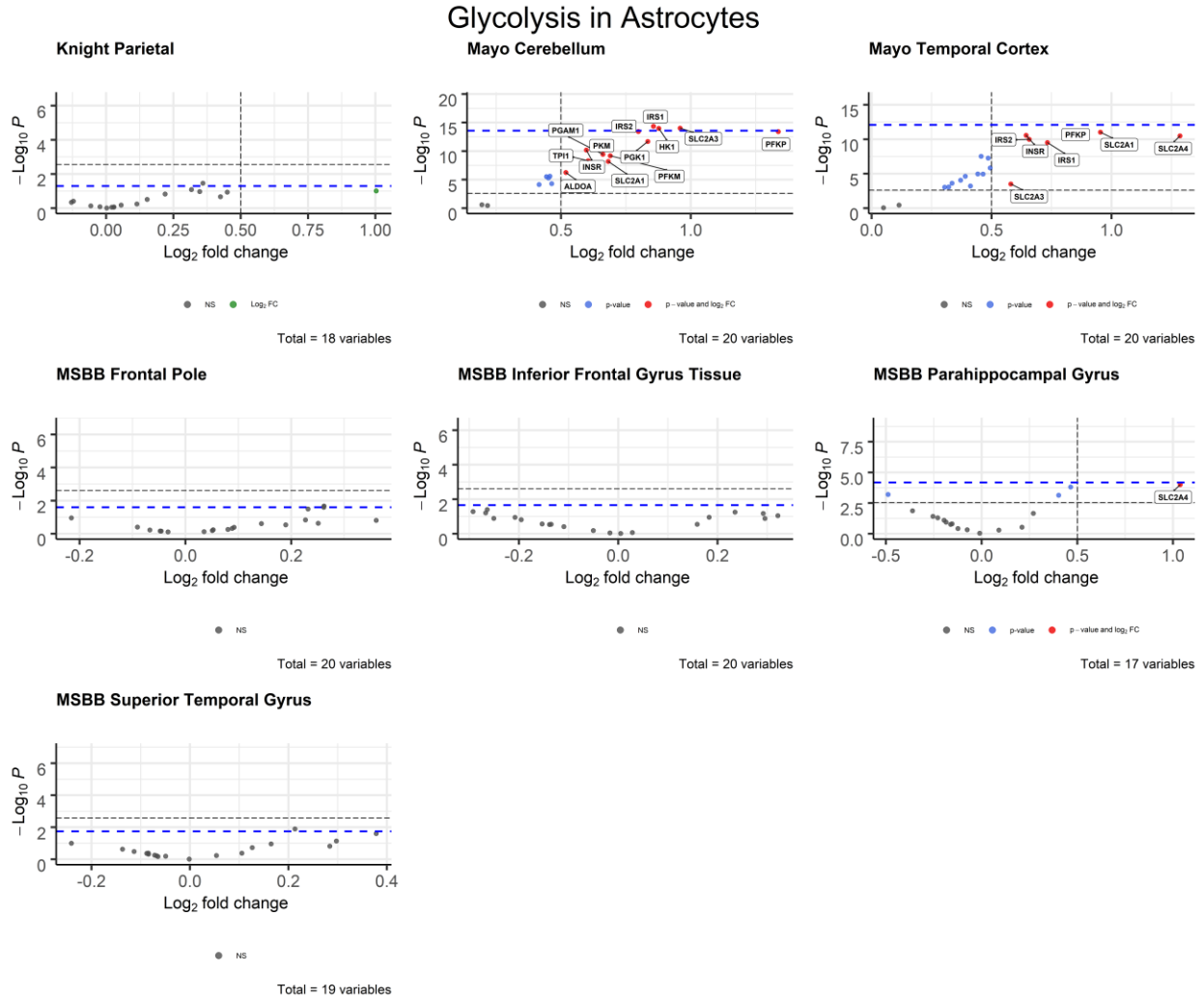


Figure S2: Glycolysis in Microglia

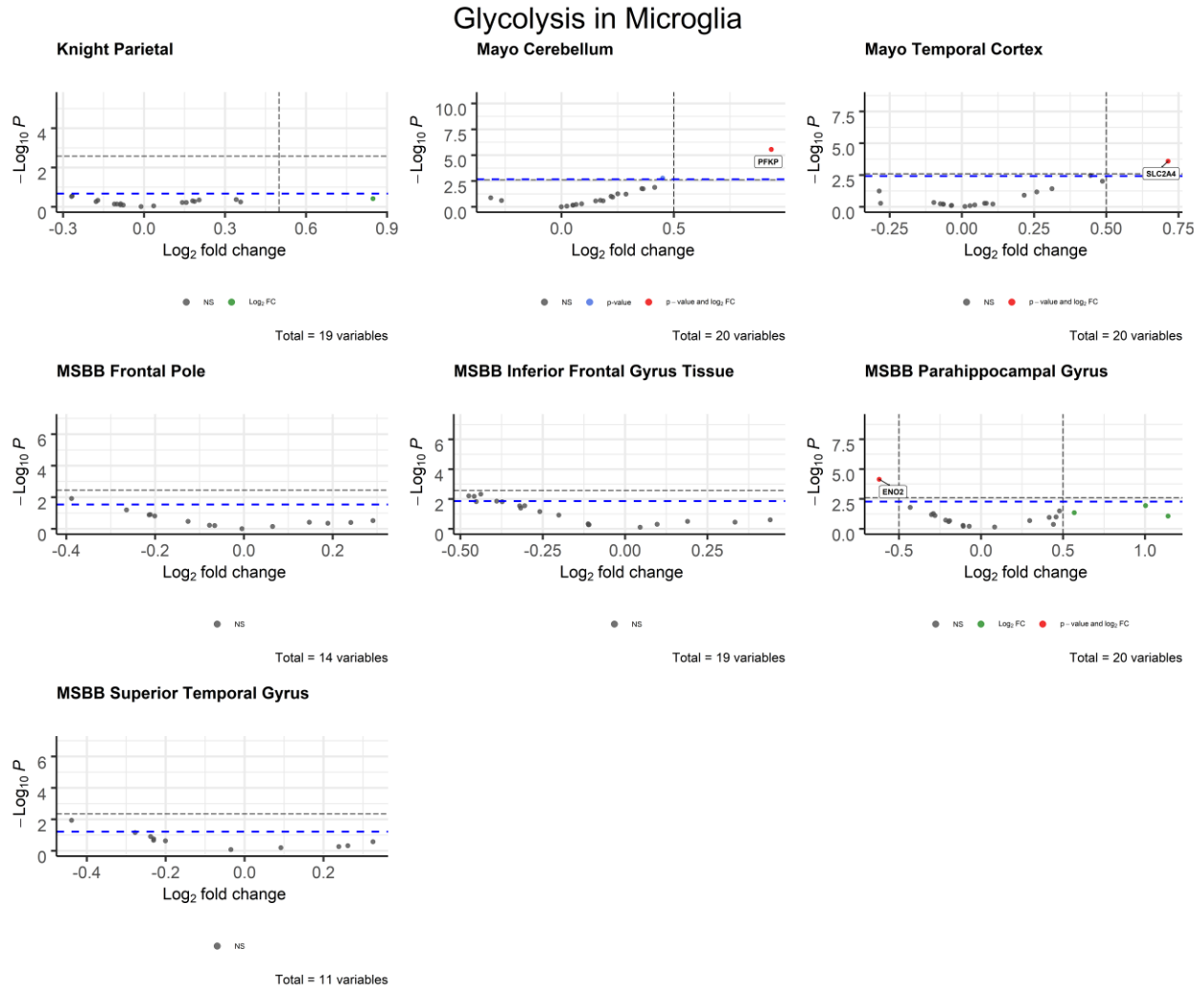


Figure S3: Ketolysis in Astrocytes

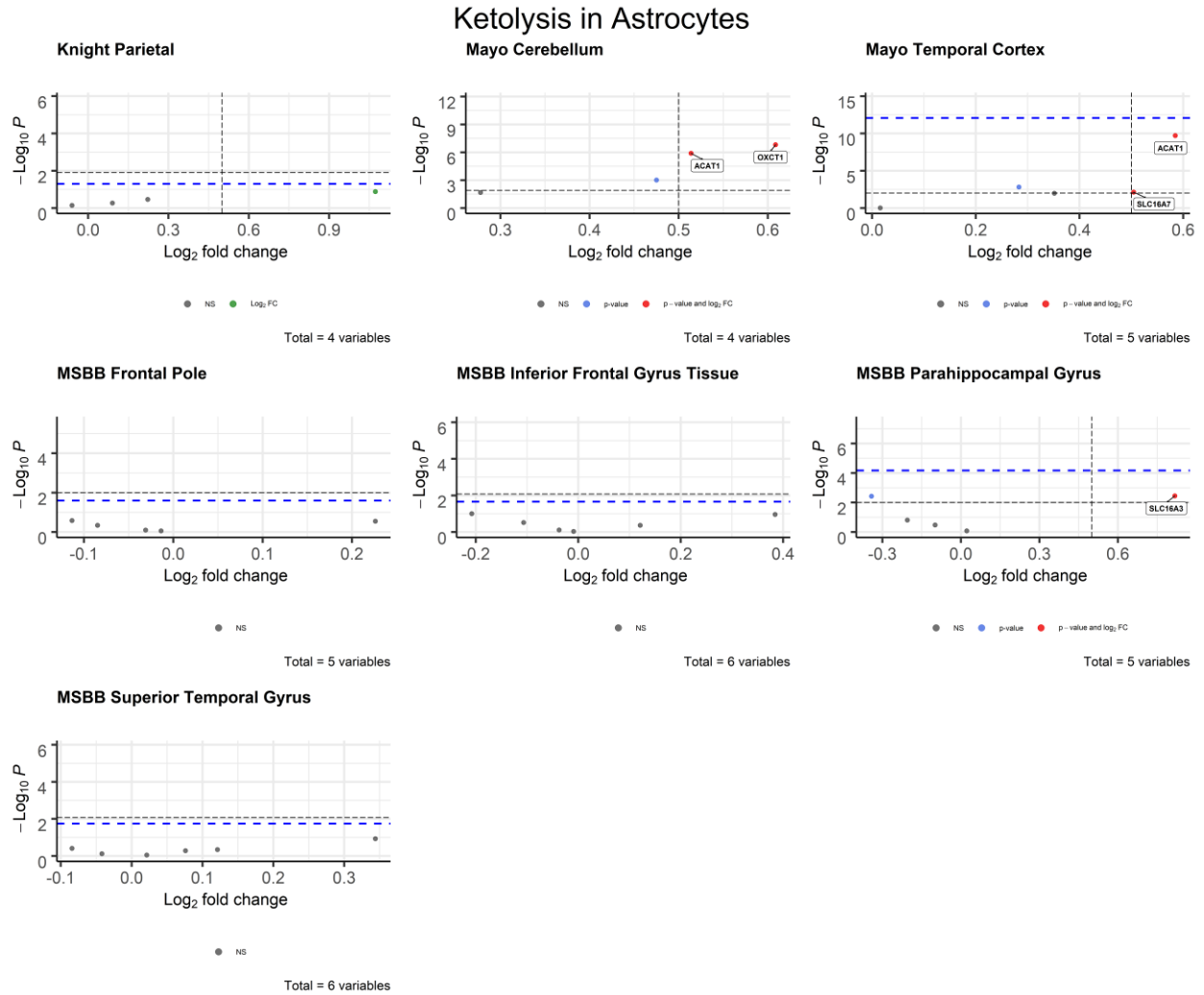


Figure S4: Ketolysis in Microglia

