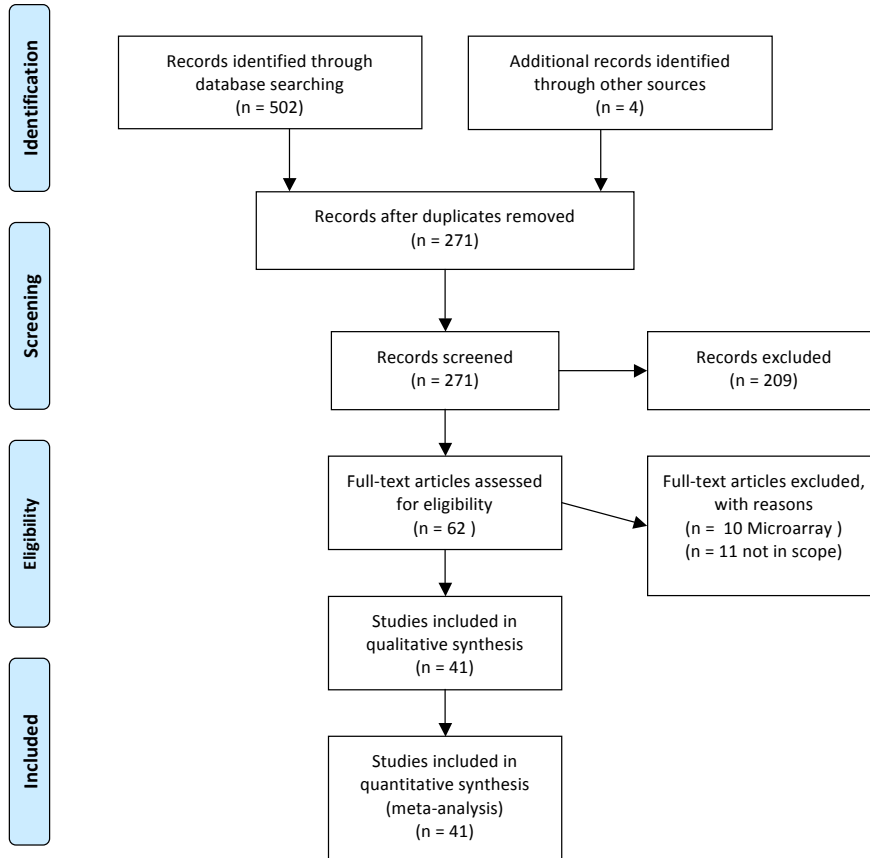


Supplementary Material



PRISMA 2009 Flow Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

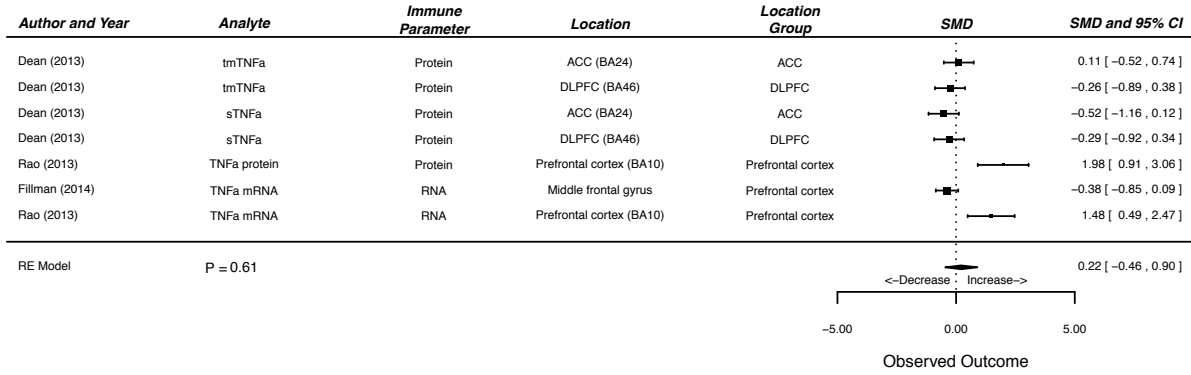
Figure 1: PRISMA Diagram

Supplementary Table 1: Classification of measured parameters in included studies: Categories and Subcategory as used as classifiers in the manuscript are indicated, along with the originally quantified variable.

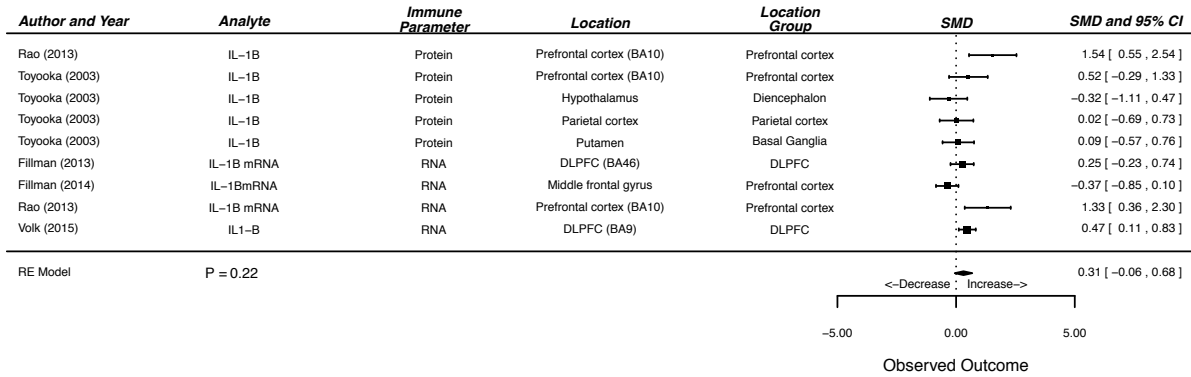
Category	Subcategory	Measurement	Frequency
Cell	Lymphocytes	CD20+ Cells	1
Cell	Lymphocytes	CD3+ Cells	1
Cell	Macroglia	Astrocytes	6
Cell	Macroglia	Astroglial Density	3
Cell	Macroglia	Ependymal discontinuities	1
Cell	Macroglia	GFAP+ Cells	25
Cell	Macroglia	GFAParea fraction	2
Cell	Macroglia	Glial cells	5
Cell	Macroglia	Gliosis	3
Cell	Macroglia	Nodular gliosis	1
Cell	Macroglia	Olig. Nuclear Area	1
Cell	Macroglia	Olig. Nuclear Diam.	1
Cell	Macroglia	Oligodendrocytes	6
Cell	Macroglia	S100B+ Glia	2
Cell	Macroglia	Subventricular rosettes	1
Cell	Microglia	CD68+ Microglia	9
Cell	Microglia	HLA-DP/DR/DQ	1
Cell	Microglia	HLADR+ Microglia	8
Cell	Microglia	IBA1+ Cells	1
Cell	Microglia	Microglia	6
Cell	Microglia	Microglia-activated	2
Cell	Microglia	Microglia-ramified	2
Cell	Microglia	Microglial Density	3
Cell	Microglia	QUIN+ Microglia	3
Molecular	Hormone	Cortisol	1
Molecular	Protein anti-inflamm	BDNF	1
Molecular	Protein anti-inflamm	IL-1R protein	1
Molecular	Protein anti-inflamm	IL-1RA	5
Molecular	Protein other	ALDH1L1	1
Molecular	Protein other	EAAT	1
Molecular	Protein other	GFAP protein	2
Molecular	Protein other	IgE	1
Molecular	Protein other	Vimentin	1
Molecular	Protein proinflamm	B-chain fibrinogen	1
Molecular	Protein proinflamm	CCR-4	1
Molecular	Protein proinflamm	CD11b protein	1
Molecular	Protein proinflamm	COX-2 protein	5
Molecular	Protein proinflamm	CRP	1
Molecular	Protein proinflamm	Calprotectin level	1
Molecular	Protein proinflamm	Glutathione-S-Transferase	1
Molecular	Protein proinflamm	IFNgamma	1
Molecular	Protein proinflamm	IL-1B	5
Molecular	Protein proinflamm	MIP-1B	1
Molecular	Protein proinflamm	MMP-1	1
Molecular	Protein proinflamm	NFkp50 protein	1
Molecular	Protein proinflamm	NFkp65 protein	1
Molecular	Protein proinflamm	Neurokinin1 Receptor	1
Molecular	Protein proinflamm	Resistin	1
Molecular	Protein proinflamm	SP1 TF	1
Molecular	Protein proinflamm	SP4 TF	1
Molecular	Protein proinflamm	TNFa protein	1

Category	Subcategory	Measurement	Frequency
Molecular	Protein proinflamm	cPLA2 IVA protein	1
Molecular	Protein proinflamm	iNOS protein	1
Molecular	Protein proinflamm	iPLA2 IVA protein	1
Molecular	Protein proinflamm	pSer294 FADD	2
Molecular	Protein proinflamm	sPLA2 IVA protein	1
Molecular	Protein proinflamm	sTNFa	2
Molecular	Protein proinflamm	tmTNFa	2
Molecular	Protein proinflamm	total FADD	1
Molecular	RNA anti-inflamm	BDNF mRNA	1
Molecular	RNA anti-inflamm	IL1-R mRNA	1
Molecular	RNA other	GFAP mRNA	3
Molecular	RNA other	MHC1 mRNA	2
Molecular	RNA proinflamm	C3 mRNA	2
Molecular	RNA proinflamm	CD11b mRNA	1
Molecular	RNA proinflamm	COX-2 mRNA	3
Molecular	RNA proinflamm	IL-1 RL1 mRNA	1
Molecular	RNA proinflamm	IL-18 mRNA	1
Molecular	RNA proinflamm	IL-1B mRNA	2
Molecular	RNA proinflamm	IL-1BmRNA	1
Molecular	RNA proinflamm	IL-6 mRNA	2
Molecular	RNA proinflamm	IL-6st mRNA	1
Molecular	RNA proinflamm	IL-8 mRNA	2
Molecular	RNA proinflamm	NFKB	1
Molecular	RNA proinflamm	NFkp50 mRNA	1
Molecular	RNA proinflamm	NFkp65 mRNA	1
Molecular	RNA proinflamm	SERPINA3 mRNA	2
Molecular	RNA proinflamm	SP1 TF	1
Molecular	RNA proinflamm	SP4 TF	1
Molecular	RNA proinflamm	TNFR1	2
Molecular	RNA proinflamm	TNFR2	2
Molecular	RNA proinflamm	TNFa mRNA	2
Molecular	RNA proinflamm	cPLA2 IVA mRNA	1
Molecular	RNA proinflamm	iNOS mRNA	1
Molecular	RNA proinflamm	iPLA2 IVA mRNA	1
Molecular	RNA proinflamm	sPLA2 IVA mRNA	1

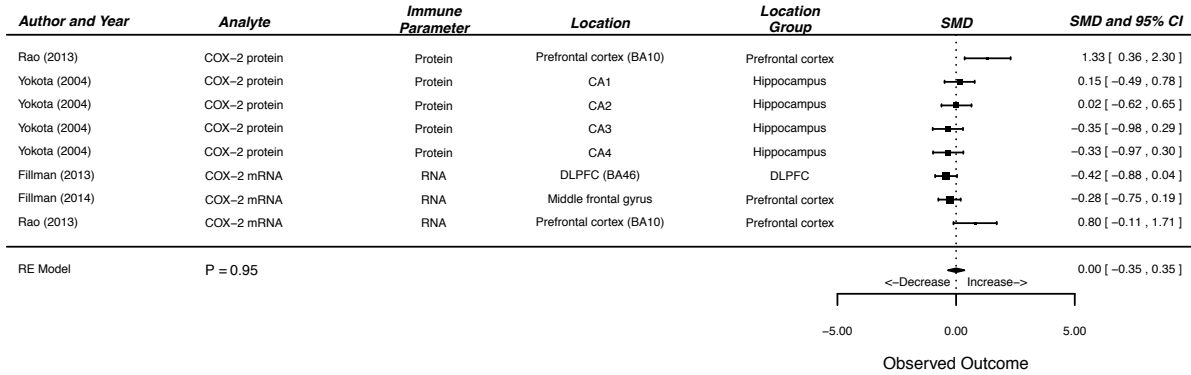
Studies Measuring TNFa



Studies Measuring IL1-B



Studies Investigating Cox-2



Studies Investigating GFAP

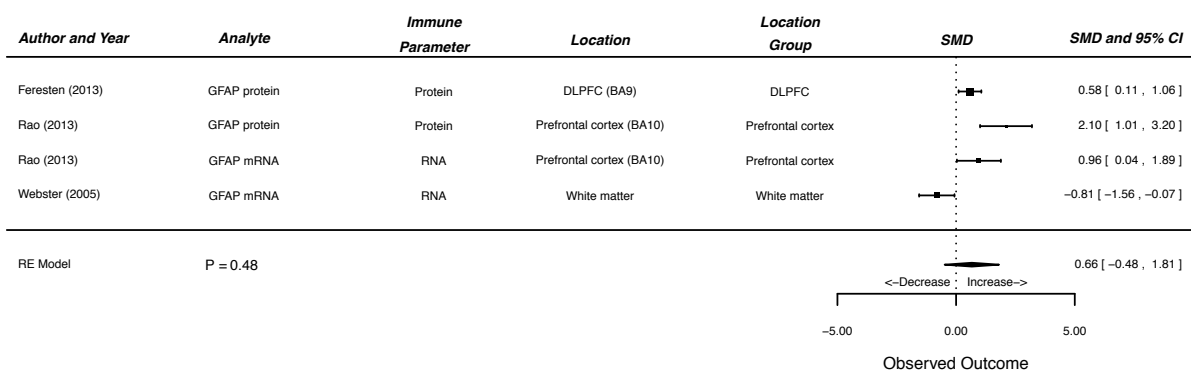


Figure 2: Subgroup Analysis on Molecular Parameters: Forest plots depicting substudies on frequently assessed molecular markers

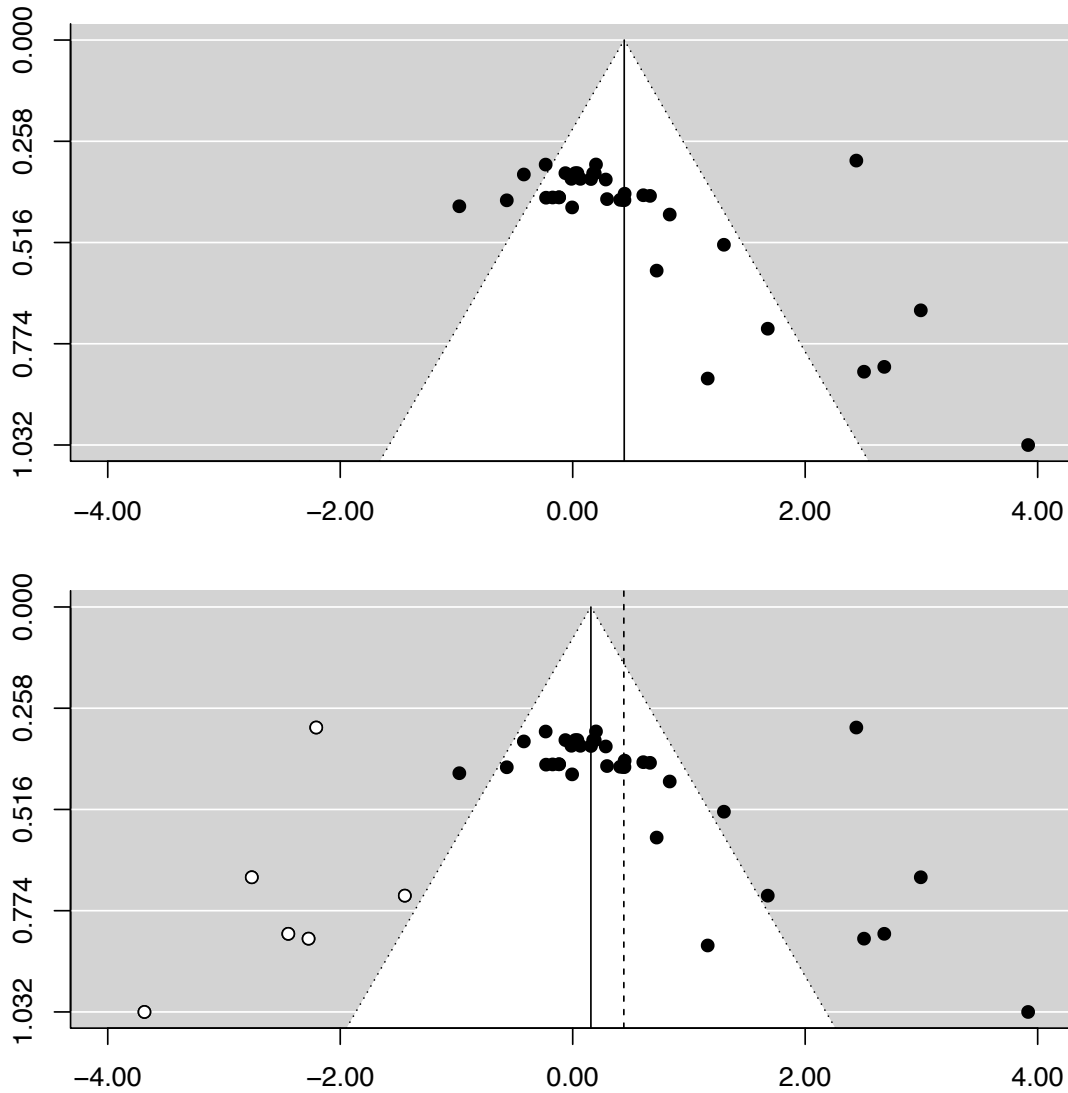


Figure 3: **Funnelplot of Studies Investigating Microglia.** This graphic shows the Standard Error of study cohorts on the y-axis and the cohorts' point estimates on the x-axis, individual studies are depicted as closed circles (top). It is expected that individual study estimates are symmetrically distributed around the pooled mean, with more precise studies (smaller SE, higher on the y-axis) being closer to the pooled mean (as indicated by the white triangle). The present graph shows an increased number of studies right of the pooled mean, indicating potential irregularities in inter-study consistency. A stabilized estimate by the 'trim and fill' method by Duval and Tweedie, in which 'missing' studies are imputed, shows that the increase in microglial number is highly dependent on the few outlying studies ($p = 0.008$). The bottom graph shows the imputed studies (open circles) and the shift of the summary estimate (dotted line without imputed studies, solid line with imputed studies).

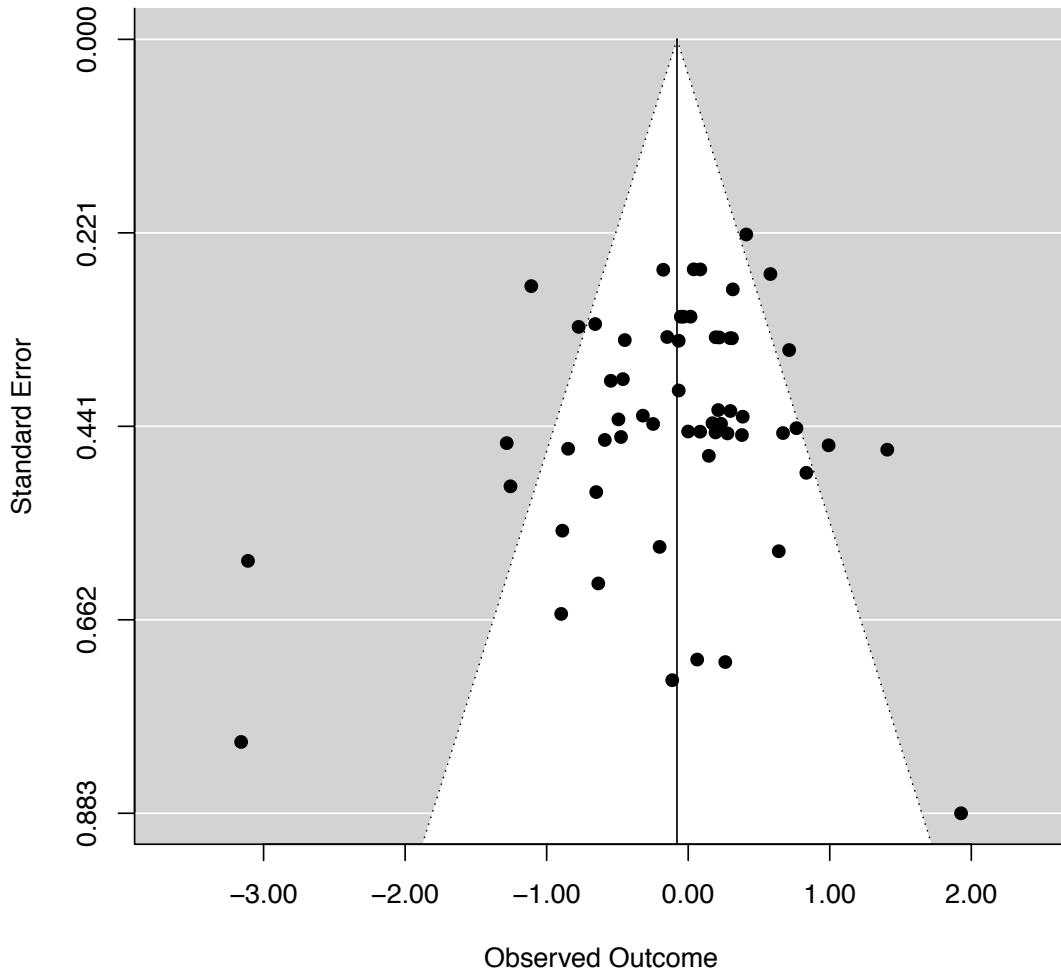


Figure 4: **Funnelplot of Studies Investigating Macroglia.** The present graph shows no asymmetry (Egger's regression test, $p = 0.19$)

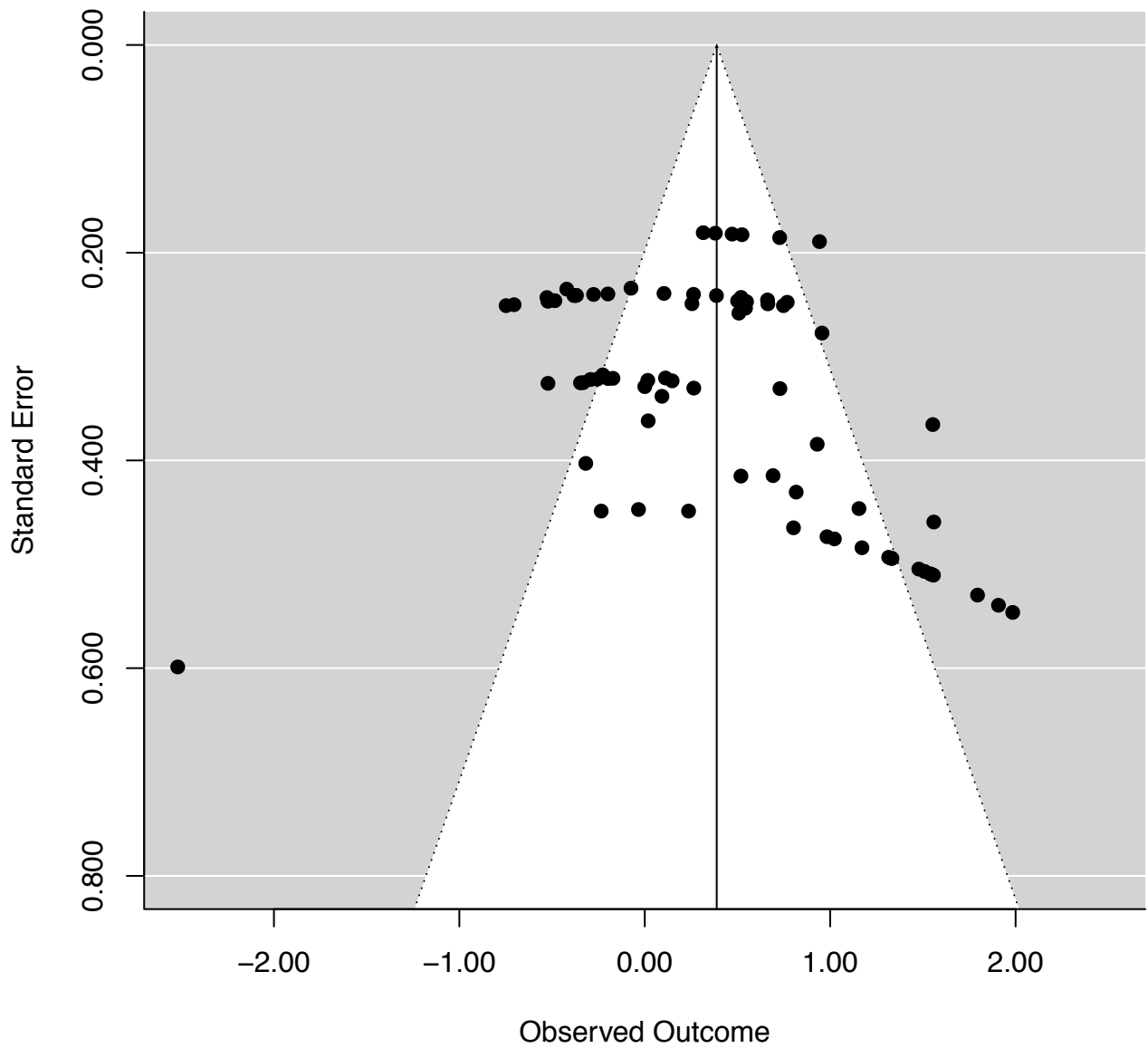


Figure 5: **Funnelplot of Studies Investigating Pro-Inflammatory Molecules.** The present graph shows no asymmetry (Egger's regression test, $p = 0.50$)

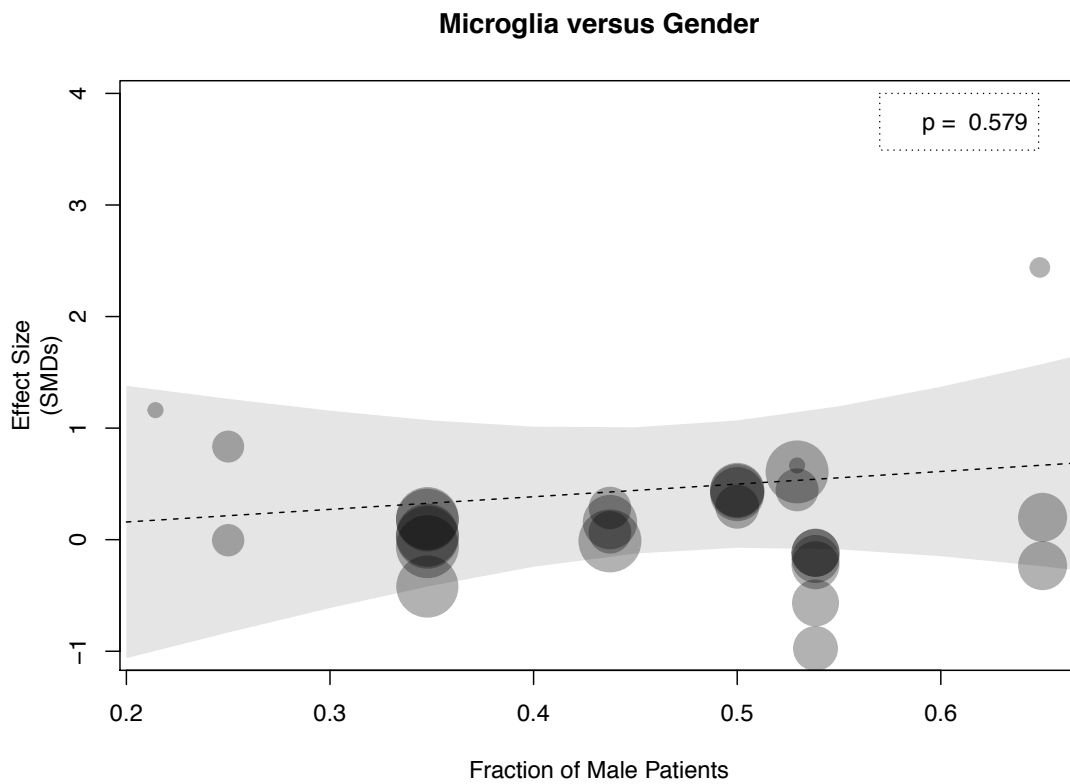


Figure 6: **Effect of Gender on Microglial Cell Increase:** Meta-analytic scatterplot showing the relationship between the fraction of male subjects in a given study cohort and the increase in microglia in patients versus controls. The size of each dot is proportional to the weight of each study cohort in the nested model. There was no significant relationship between proportion of male patients and increase in microglia ($p=0.58$)

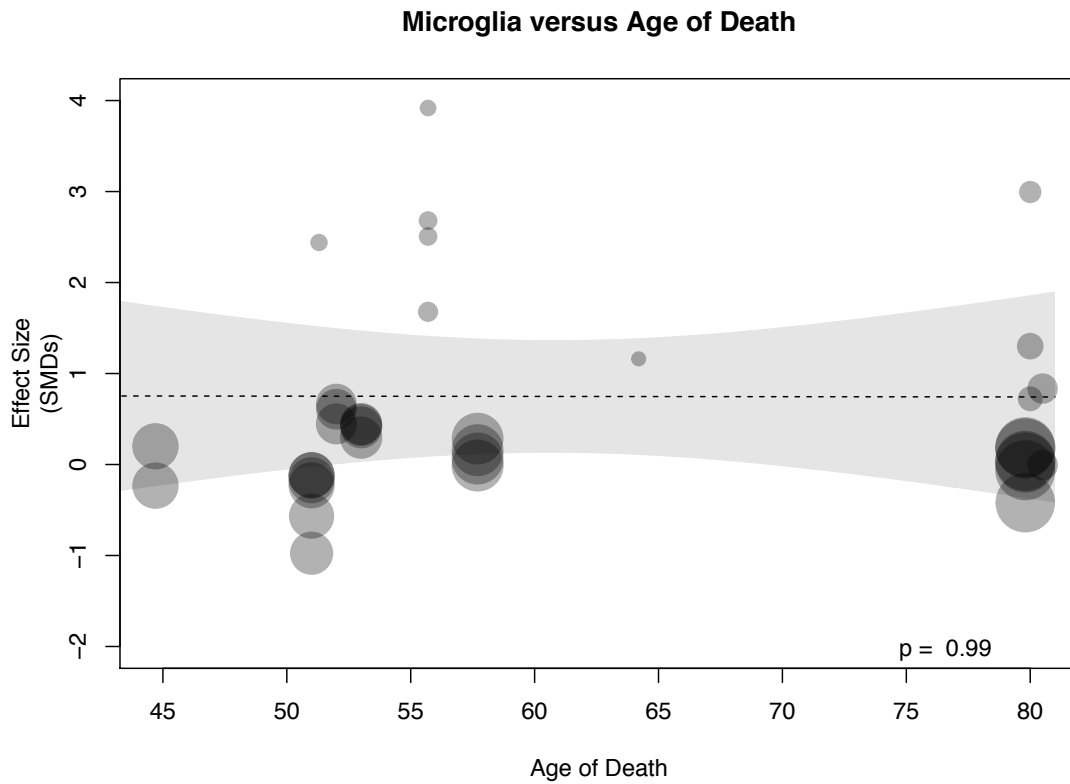


Figure 7: **Effect of Age of Death on Microglial Cell Increase:** Meta-analytic scatterplot showing the relationship between the average age of death in a given study cohort and the increase in microglia in patients versus controls. The size of each dot is proportional to the weight of each study cohort in the nested model. There was no significant relationship between average age of death and increase in microglia ($p=0.99$)

Microglia versus Duration of Illness

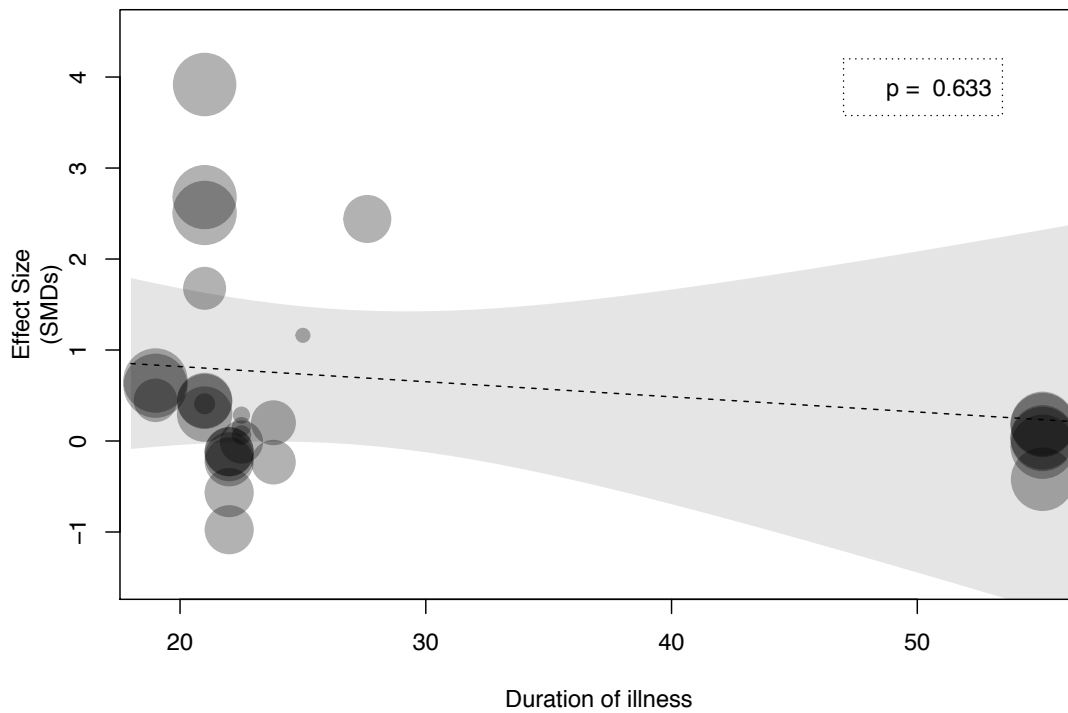


Figure 8: **Duration of Illness and Microglial Cell Increase:** Meta-analytic scatterplot showing the relationship between the average duration of illness in schizophrenic patients in a given study cohort and the increase in microglia in patients versus controls. The size of each dot is proportional to the weight of each study cohort in the nested model. There was no significant relationship between duration of illness and increase in microglia ($p=0.63$)

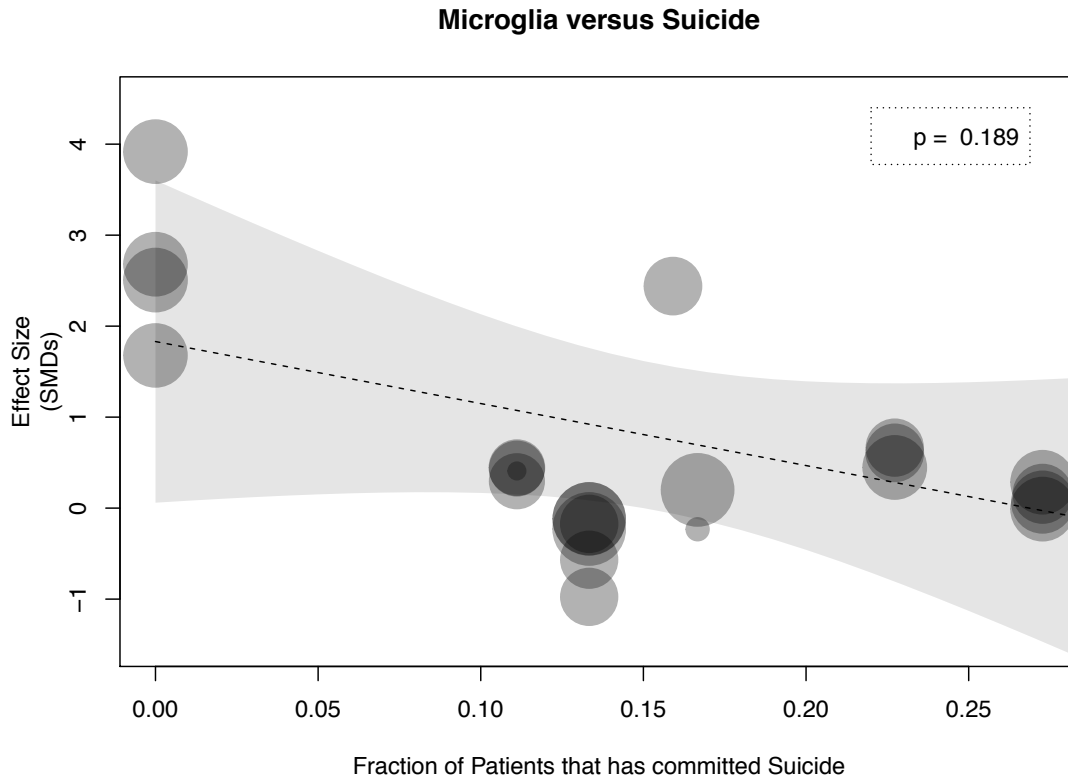


Figure 9: **Fraction of Patients that Commits Suicide and Microglial Cell Increase:** Meta-analytic scatterplot showing the relationship between proportion of death due to suicide in schizophrenic patients in a given study cohort and the increase in microglia in patients versus controls. The size of each dot is proportional to the weight of each study cohort in the nested model, a single study can be represented by multiple dots if multiple microglia measurements have been performed. There was no significant relationship between proportion of suicides and increase in microglia ($p=0.19$).