Project Research Paper

Microglial Single Cell Transcriptomics Reveal Drivers of Autism Severity

Abstract

Autism Spectrum Disorder (ASD) is a highly heterogeneous neurodevelopmental condition with substantial societal impact, characterized by impairments in communication, behavior, and lifelong adaptive functioning. Although ASD is strongly heritable, its molecular mechanisms—particularly those underlying differences in clinical severity—remain incompletely understood. Recent large-scale transcriptomic studies have identified reproducible molecular perturbations in ASD, including dysregulated immune and inflammatory signaling and altered neuronal and synaptic gene programs.

Here, we investigate severity-associated molecular heterogeneity in ASD using publicly available single-cell RNA sequencing data from postmortem human cortex (33 ASD donors, 30 matched controls), focusing on microglia to isolate severity-linked immune programs. Microglia are brain-resident immune cells increasingly implicated in neurodevelopment and ASD pathophysiology. ASD donors were stratified into low, intermediate, and high severity cohorts using clinically defined comorbidities (epilepsy and/or intellectual disability). Differential gene expression was performed using a donor-level pseudobulk approach with DESeq2 and Benjamini–Hochberg correction, followed by Gene Ontology (GO) Biological Process

enrichment.

Across severity contrasts, we identified 53 significant genes (low vs intermediate), 43 (intermediate vs high), and 135 (low vs high). Integrating differential expression and pathway enrichment across transitions, we classified candidate driver genes as early (12), late (30), or cumulative (90) contributors to ASD severity, suggesting a stepwise shift in microglial state with increasing severity. These findings provide mechanistic insight into microglial heterogeneity in ASD and nominate candidate pathways and genes for future functional validation.

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental condition marked by differences in social communication and behavior. [1] The term “spectrum” matters because people with ASD can vary widely in symptoms and support needs. [1] This clinical diversity creates a major challenge for biology: two individuals can share the same diagnosis while the molecular pathways underlying their symptoms differ. Many current approaches struggle to connect specific biological mechanisms to differences in severity in a clear, measurable way.

Over the past decade, transcriptomics has become a useful tool for studying ASD biology because it can capture patterns of gene expression across thousands of genes at once. Large postmortem brain studies have reported reproducible differences in ASD, often highlighting immune and inflammatory signaling and alterations in neuronal and synaptic gene programs. [4][5][6] However, many transcriptomic findings are reported as “ASD vs control” signatures. This can mask important heterogeneity across individuals, and the problem becomes even greater when severity is not incorporated into the analysis. If severity reflects meaningful biological

differences, then averaging across the entire ASD group may blur the signals that matter most.

Microglia are a relevant cell type for studying this problem. Microglia are the brain's resident immune cells, and they have active roles beyond inflammation. [4][5] They contribute to synaptic pruning, circuit refinement, and responses to environmental and developmental stressors. [4][5] Microglia can shift their gene expression programs depending on context, thereby reflecting changes tied to disease progression or increasing symptom burden. This makes microglia a strong candidate for testing whether ASD severity corresponds to stepwise shifts in transcriptional states in the brain.

Single-cell RNA sequencing (scRNA-seq) improves on earlier bulk transcriptomic approaches by measuring gene expression at the single-cell level and enabling analysis by cell type. [4][5] This is especially important in brain tissue because many cell types are mixed and can change in opposite directions. Focusing on microglia within a large public scRNA-seq dataset enables targeted questions: Which microglial genes change as severity increases? Are these changes consistent across severity transitions? Do the results suggest a single universal severity signature or multiple stage-specific programs?

These questions are addressed by stratifying ASD samples into severity cohorts using clinically defined comorbidities, including epilepsy and intellectual disability. Pairwise comparisons across severity levels are performed to identify transcriptional changes associated with progressive disease burden. Rather than only listing differentially expressed genes, results are also integrated across transitions. Candidate genes are then classified as early, late, or cumulative contributors based on when they appear during severity progression. The goal of this framework is to move

closer to a severity-aware molecular roadmap that prioritizes microglial pathways and candidate driver genes for future functional testing.

The main hypothesis guiding this work is that ASD severity is associated with distinct microglial transcriptional states that emerge in a stepwise pattern across severity transitions. This differs from a model in which all individuals share a single invariant microglial signature with more severe disease. The sections that follow describe the dataset and cohort definitions, as well as **the** analysis pipeline used to quantify severity-associated gene expression changes. They also present results from differential expression and pathway enrichment. Finally, they describe the driver classification framework used to identify stage-linked candidate genes for future validation.

Methods

I. Study design overview

A secondary analysis was performed on a publicly available single-cell RNA sequencing dataset generated from postmortem human prefrontal cortex. [5] The analysis focused on microglia and tested whether microglial gene expression changes follow stepwise patterns across transitions in ASD severity. A donor-level pseudobulk strategy was used to reduce cell-count imbalance and ensure that each donor contributed one profile to each comparison.

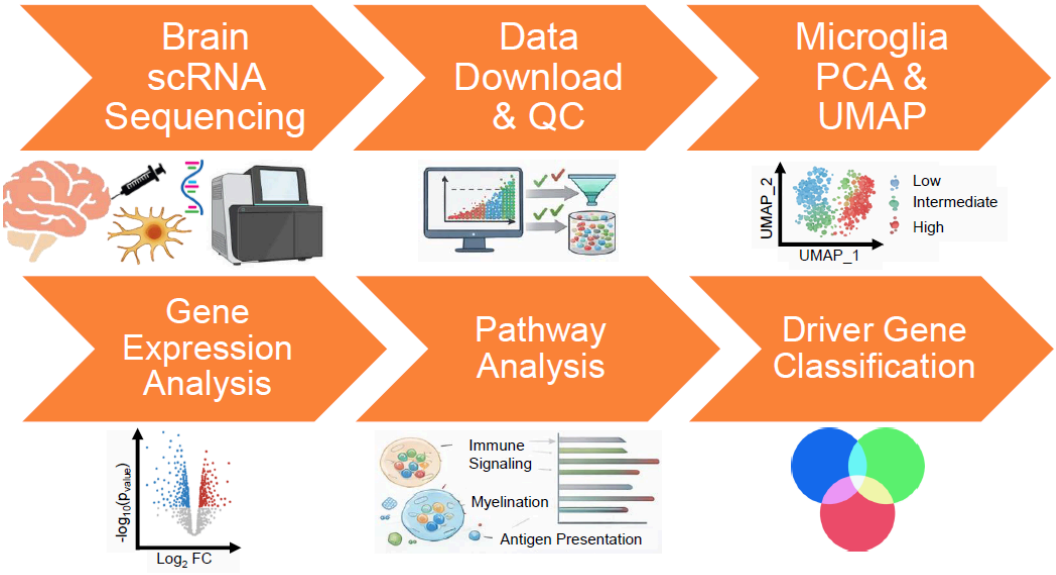

Figure 1. Methods Overview

II. Data source and cohort definition

- This study uses processed single-cell RNA sequencing data from postmortem human prefrontal cortex. The source dataset includes 33 ASD donors and 30 matched healthy controls. [5] The source study provides annotations across 35 brain cell types, and the analysis was restricted to microglia to isolate immune-related transcriptional programs linked to severity. [5] ASD donors were selected from the source dataset, and downstream analyses were restricted to microglia.
- Two exclusions were applied to reduce confounding and ensure severity could be assigned consistently. Donors with the 15q duplication genetic subtype were excluded because this subtype can introduce a strong molecular signal distinct from idiopathic ASD biology. [5] Donors with unreported clinical symptoms were also excluded because severity could not be assigned reliably. After these exclusions, 18 ASD donors remained

for severity-based comparisons.

- ASD severity was operationalized using clinically defined comorbidities; epilepsy and intellectual disability were used because they represent meaningful differences in impairment in the available clinical notes. Low severity was defined as no epilepsy and no intellectual disability (4 donors). Intermediate severity was defined as epilepsy without intellectual disability (7 donors). High severity was defined as both epilepsy and intellectual disability (7 donors).

De-Identified Patient ID	Age	Gender	Cause of Death		Clinical Symptoms	Disease Severity
KMC3	48	Male	Natural	Cancer, Gastric carcinoma	Hyperkinesis, Pica	Low
2NA6	16	Male	Accident	Blunt force trauma	Bipolar	
493	26	Male	Accident	Drowning	Blind	
FXMW	29	Male	Natural	Cardiac Arrest	ADHD	
5023	16	Male	Accident	Blunt force trauma	Epilepsy, Diabetes	Intermediate
9714	60	Male	Natural	Cancer, Pancreatic	Epilepsy	
19511	8	Male	Natural	Cancer (Sarcoma)	Epilepsy	
5302	16	Male	Natural	Diabetic Ketoacidosis	Epilepsy	
6041	19	Male	Natural	Seizure	Epilepsy	
8792	29	Male	Natural	Acute pancreatitis-Renal Failure	Epilepsy	
12457	29	Female	Natural	Seizure	Epilepsy	
2YK7	17	Female	Natural	NA	Intellectual Disability, Epilepsy	High
3HUF	23	Male	Natural	Pneumonia	Intellectual Disability, Epilepsy	
VPSP	20	Male	Natural	NA	Intellectual Disability, Epilepsy, ADHD	
8XCF	27	Male	Natural	Acute	Intellectual Disability,	

De-Identified Patient ID	Age	Gender	Cause of Death		Clinical Symptoms	Disease Severity
				pancreatitis-Renal Failure	Epilepsy	
M9H3	59	Female	Natural	Seizure, Cardiac Arrest	Intellectual Disability, Epilepsy	
5842	19	Male	Natural	Cardiac Arrest	Intellectual Disability, Epilepsy	
13161	24	Male	Natural	NA	Intellectual Disability, Epilepsy, ADHD	

Table 1. ASD donor metadata and severity cohort assignment used in this study.

The processed files include standard annotations and donor-level information from the source study, including cell type labels and donor/sample identifiers, as well as diagnosis, age, sex, and postmortem-related variables available in the source metadata, such as PMI and cause of death. The files also include genotype labels such as the 15q duplication flag. Clinical symptom reporting was incomplete for all ASD donors, and donors with insufficient symptom reporting were excluded from severity analyses because severity could not be consistently interpreted.

III. Microglia selection and quality control

Microglia were preannotated in the source dataset, and the microglia subset was exported for all downstream analyses. Cells were filtered to remove low-quality profiles using standard single-cell quality control criteria based on library size, detected gene counts, and mitochondrial gene expression. Cells with unusually low or high gene counts were removed to reduce the impact of empty droplets and multiplets. Cells with elevated mitochondrial transcript fractions were also removed to reduce the impact of stressed or dying cells. When doublet predictions

were available, predicted doublets were excluded from downstream analysis. The remaining microglia profiles were verified to show expected marker patterns consistent with microglial identity.

IV. Dimensionality reduction and visualization

Principal component analysis (PCA) was used to reduce the dimensionality of the microglial expression matrix and capture major sources of variation. UMAP was then applied to visualize microglial transcriptional states in 2D. These visualizations were used to assess whether severity groups separated along broad transcriptional axes and to confirm that microglia formed coherent clusters after filtering.

V. Pseudobulk aggregation at the donor level

To support donor-level statistical testing, pseudobulk count matrices were constructed by aggregating microglia raw counts within each donor. For each gene, counts were summed across all microglial cells from the same donor, producing a single gene-by-donor count matrix for microglia. Genes were filtered to remove features with very low information by retaining those with adequate counts across multiple donors; a typical filter required at least 10 total counts across at least 5 donors. The resulting count matrix was used as input to DESeq2, which performs normalization through size factors.

VI. Differential gene expression across severity comparisons

Differential expression analysis was performed using DESeq2 on donor-level pseudobulk counts. Severity group was treated as a categorical variable, and pairwise contrasts

across severity levels were tested. The primary contrasts were low versus intermediate, intermediate versus high, and low versus high. DESeq2 estimated size factors and dispersions from the count data and fit negative binomial generalized linear models to test for expression differences between cohorts. Multiple hypothesis testing was controlled using the Benjamini–Hochberg false discovery rate. Significant genes were defined as those with an adjusted p-value < 0.01 and an absolute log2 fold change > 2.5. Effect directions and effect sizes were reported for each comparison.

VII. Gene Ontology enrichment analysis

To interpret the biological functions represented by severity-associated gene sets, Gene Ontology (GO) Biological Process enrichment analysis was performed on significant genes from each contrast. clusterProfiler was used to test for over-representation of GO terms relative to an appropriate background gene universe. Enrichment p-values were corrected for multiple testing, and the most significant biological process themes were summarized for each severity transition.

VIII. Driver classification framework

Significant genes were classified into stage-linked driver categories by integrating results across severity transitions. Early drivers were defined as genes significant in low versus intermediate but not significant in intermediate versus high. Late drivers were defined as genes significant in intermediate versus high but not significant in low versus intermediate. Cumulative drivers were defined as genes significant in low versus high and consistent with a progressive change across severity levels, meaning the direction of effect matched the severity ordering. Global drivers

were defined as genes significant in all three severity contrasts. These categories were used to separate candidate genes that emerge early from those that appear later, and from those that accumulate across the full severity span.

IX. Software and reproducibility

Analysis was performed in R using Seurat for data handling and visualization, DESeq2 for pseudobulk differential expression, and clusterProfiler for enrichment analysis. The workflow was organized as a stepwise script that reads the microglia subset, performs filtering, constructs pseudobulk matrices, runs DESeq2 contrasts, performs GO enrichment, and outputs gene lists and figures. Generative AI tools were used only for code troubleshooting and validation of intermediate outputs. Key parameters and thresholds were documented in the code and supplementary methods so the analysis can be reproduced using the same input files.

X. Ethics and data access

This project used de-identified publicly available postmortem transcriptomic data. No new human-subjects data were collected, and no interventions were performed.

XI. Robustness and sensitivity checks

Several robustness checks were performed to assess whether findings were stable and not driven by a single modeling choice. Differential expression was rerun with alternative significance thresholds to confirm that effect directions and the highest-ranked genes were consistent across reasonable cutoffs. The stability of driver categories was tested by evaluating whether early, late, and cumulative labels remained similar across varying thresholds. Potential influence from any

single donor was evaluated using a leave-one-donor-out approach, recomputing key gene lists after removing each donor in turn. Donor-level differences in microglial cell counts were assessed as a potential source of bias, and pseudobulk analysis was repeated after applying minimum cell-count requirements per donor and, where feasible, downsampling microglia to a common cell count. Finally, top GO enrichment themes were compared across sensitivity runs to confirm that the same biological processes remained enriched even when individual genes moved in or out of the significant set.

Results

I. Microglia transcriptional landscape across ASD severity

Microglia were first evaluated for broad shifts in transcriptional state across severity groups. The UMAP projection indicated that microglia from low-, intermediate-, and high-severity cohorts occupied both shared and distinct transcriptional regions. The overall pattern suggested a gradual shift in global microglial state across severity groups rather than complete separation into three non-overlapping clusters. This supports a model in which severity differences reflect progressive changes along a continuum of microglial states.

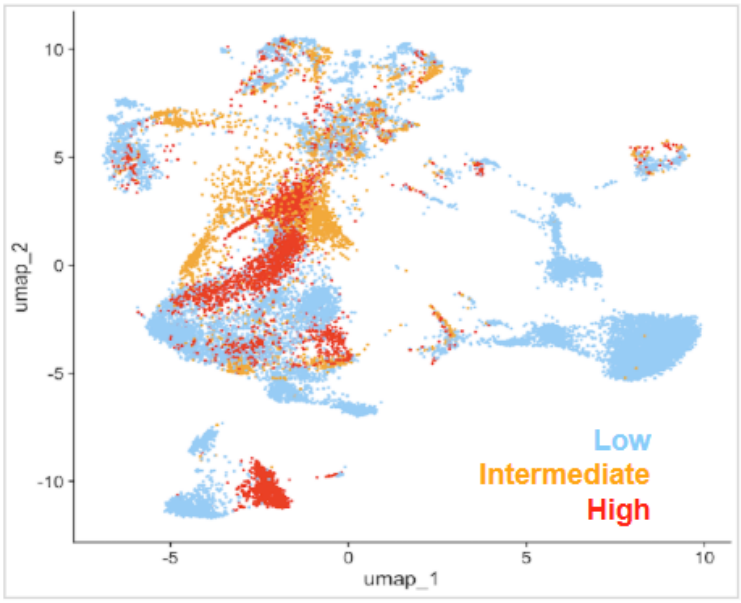

Figure 2. UMAP projection of microglia transcriptional profiles across ASD severity cohorts. Each dot represents a unique cell. Cells from each cohort occupy shared and distinct transcriptional clusters, suggesting a progressive alteration in global cell states.

II. Differential expression across severity transitions

Severity-associated differences in gene expression were assessed using pairwise comparisons across severity levels. Low versus intermediate severity yielded 53 significant genes (45 upregulated, 8 downregulated). Intermediate versus high severity yielded 43 significant genes (32 upregulated, 11 downregulated). Low versus high severity yielded 135 significant genes (129 upregulated, 6 downregulated). The larger gene count in the low versus high comparison was expected because it spans the greatest severity difference. The consistent skew toward upregulated genes across comparisons suggests that increasing severity is associated with increased activation of specific microglial programs.

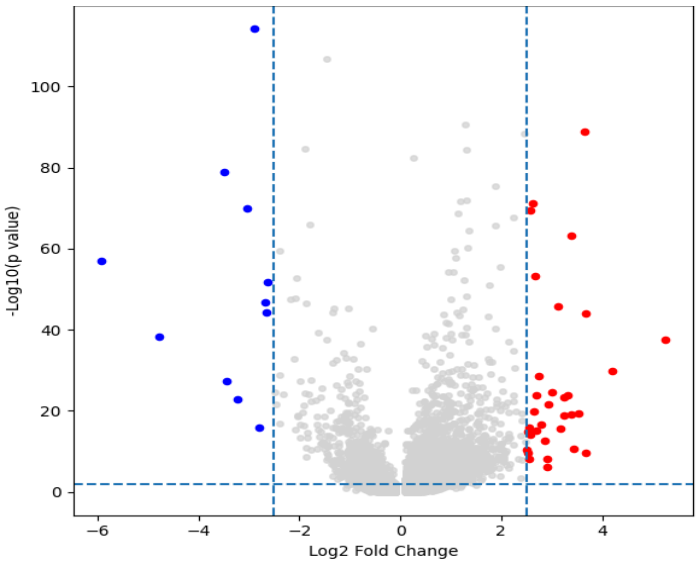

Figure 3. Volcano plot of significantly upregulated (red) or downregulated (blue) genes (individual dots) between intermediate and high severity ASD microglia.

Summary across comparisons

Comparison	Significant Genes	Up-regulated	Down-regulated
1) Low vs Intermediate	53	45	8
2) Intermediate vs High	43	32	11
3) Low vs High	135	129	6

Table 2. Differential Microglial Gene Expression with ASD Severity

III. Functional themes from pathway enrichment

Gene Ontology (GO) Biological Process enrichment was performed for significant genes from each severity comparison to interpret associated functional changes. Enriched processes clustered into themes including immune signaling and antigen presentation, with a

myelination-related theme also appearing in the enrichment summary. Together, these findings support a model in which microglia exhibit increasing immune activation across severity transitions and suggest later-stage changes that may relate to broader glial or tissue remodeling programs.

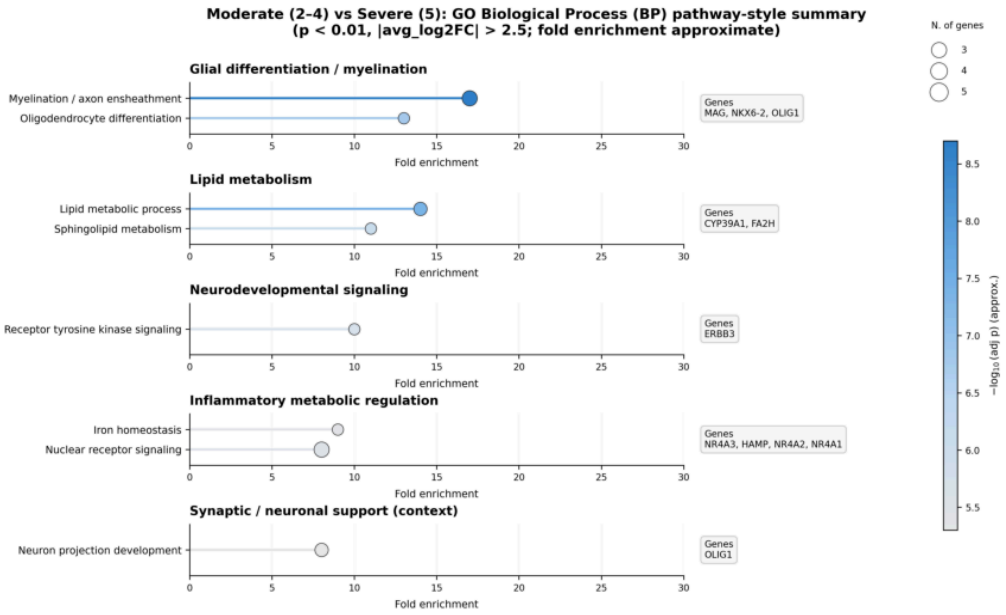

Figure 4. Moderate Vs Severe GO Biological Process pathway-style summary

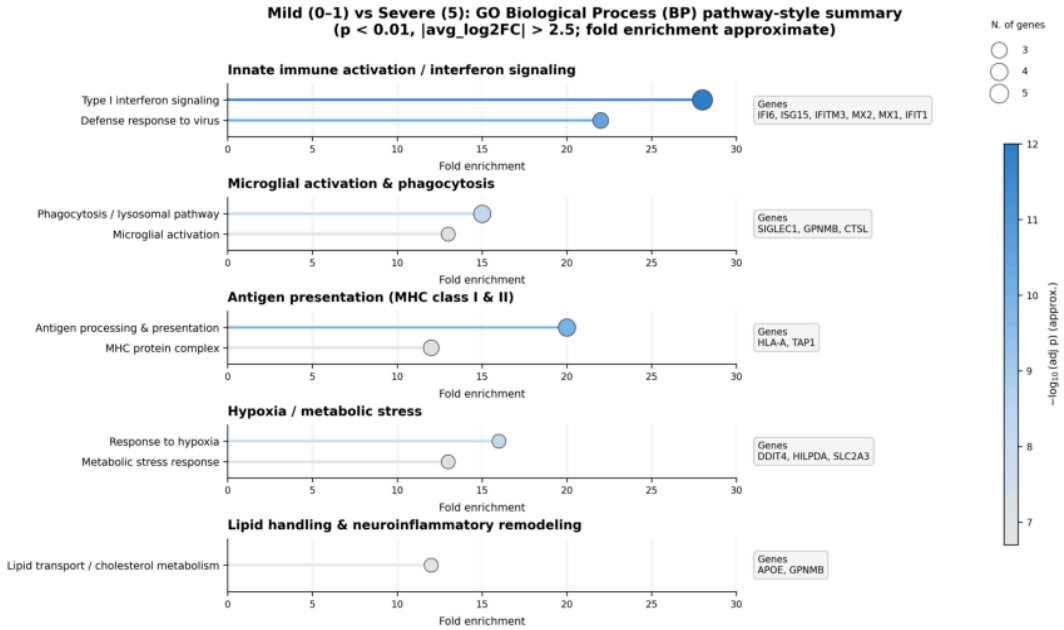

Figure 5. Mild Vs Severe GO Biological Process pathway-style summary

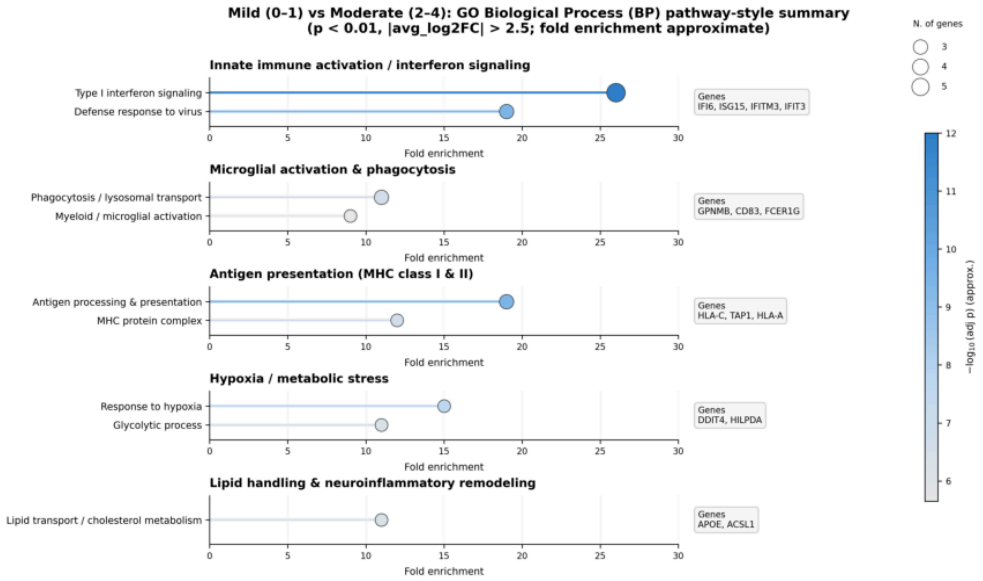

Figure 6. Mild Vs Moderate GO Biological Process pathway-style summary

IV. Driver gene classification across severity progression

Differential expression results were integrated across severity transitions to classify genes into

early, late, cumulative, and global driver categories based on their timing across progression. This framework produced 12 early drivers, 30 late drivers, and 90 cumulative drivers; no genes met criteria for global drivers. The absence of global drivers suggests that severity is not explained by a single universal microglial signature, and instead supports stage-linked programs that emerge at different points along severity progression.

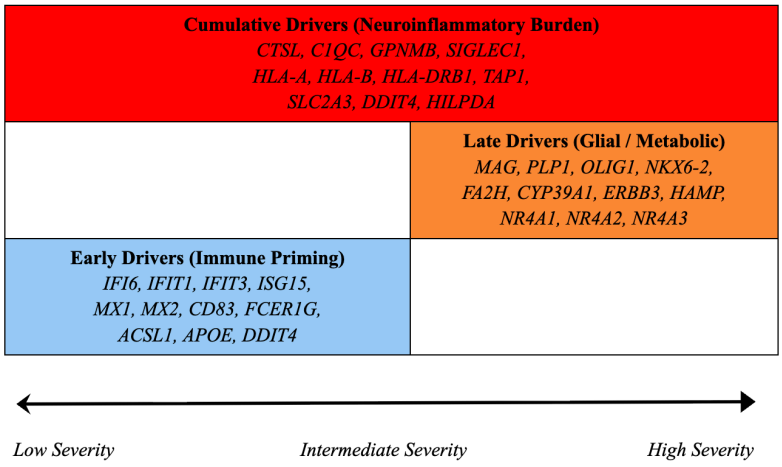

Figure 7. Candidate Microglia ASD Severity Driver Genes

The table summarizes the classification of significant, non-overlapping genes across each stage of ASD severity. Disease severity is associated with distinct drivers on a shared continuum.

Type	Significant genes
Early Driver	12
Late Driver	30
Cumulative Driver	90
Global Driver	0

Table 3. Classification of significant, non-overlapping genes across each stage

V. Representative candidate genes in each driver class

Early drivers were dominated by immune priming signals, including interferon-associated and innate immune genes such as *IFI6, IFIT1, IFIT3, ISG15, MX1, and MX2,* along with *CD83, FCER1G, ACSL1, APOE, and DDIT4.* Late drivers included genes linked to glial and metabolic remodeling and stress-response programs, including *MAG, PLP1, OLIG1, NKX6-2, FA2H, CYP39A1, ERBB3, HAMP, and the NR4A1/NR4A2/NR4A3* family. Cumulative drivers were enriched for neuroinflammatory burden and antigen presentation signals, including *CTSL, C1QC, GPNMB, SIGLEC1, HLA-A, HLA-B, HLA-DRB1, TAP1, SLC2A3, DDIT4, and HILPDA.* Collectively, these representative genes align with the pathway themes and support a stepwise model that begins with immune priming, shifts toward later remodeling signals, and accumulates into a broader inflammatory and antigen presentation burden at higher severity.

Discussion

This study aimed to test whether ASD severity is associated with stepwise changes in microglial gene expression, and the results support that model. Microglia showed gradual shifts in transcriptional state across severity groups, and differential expression increased as severity differences widened. The low versus high comparison yielded the largest number of significant genes, and most of these were upregulated with increasing severity. This pattern suggests that higher severity is associated with stronger activation of specific microglial programs rather than

random changes across the transcriptome.

A key finding is that severity-associated genes did not form a universal signature that appeared in every severity transition. The driver framework produced early, late, and cumulative drivers, but no global drivers. This supports the idea that ASD severity may reflect stage-linked biological programs. Early drivers included interferon and innate immune-related genes, which may reflect early immune priming in microglia. Late drivers included genes linked to glial and metabolic remodeling and stress response programs, which may reflect shifts in tissue state or microglial functional roles at higher severity. Cumulative drivers included signals for antigen presentation and inflammatory burden, suggesting that microglia may progressively intensify immune-related activity as severity progresses.

These findings connect to prior transcriptomic work that has reported immune and inflammatory dysregulation in ASD. [4][5][6] This project adds a severity-aware perspective by not treating ASD as a single group. Instead, severity transitions are tested and genes are organized by when they appear during progression. This structure can help prioritize candidates for follow-up because early drivers may relate to initial pathway activation, while cumulative drivers may relate to longer-term burden. This framework can also be extended to other cell types from the same dataset and applied to additional ASD datasets to test whether the same stage-linked patterns generalize.

There are important limitations that should guide interpretation. Severity was operationalized using comorbidities, and epilepsy and intellectual disability may not capture all dimensions of ASD severity. The severity groups were small after exclusions, limiting statistical power and

generalizability. Postmortem brain samples reflect end-stage biology and do not directly establish causality or the timing of pathway activation during development. Additional confounders may exist because postmortem variables and medication history can influence gene expression, and not all covariates may be available or controlled in the processed dataset used here.

Despite these limitations, this work provides a structured molecular view of microglial ASD severity. The results suggest a stepwise pattern that includes immune priming, later remodeling-related programs, and cumulative antigen presentation and inflammatory burden at higher severity. Future work should validate these driver classes in independent cohorts and test their functional roles using experimental systems that model microglial activation states. This can include replication in other single-cell datasets, integration with spatial transcriptomics, and functional perturbation studies that test whether early drivers influence downstream cumulative programs.

Limitations

This study uses postmortem single-cell transcriptomic data, which limits what the results can prove. Postmortem gene expression reflects biology at the time of death and can be influenced by factors unrelated to ASD severity. These factors can include agonal state, postmortem interval, cause of death, and tissue handling. Some of these variables may be available in metadata, but they may not be fully controlled in the processed dataset used here. This means the results should be interpreted as associations rather than causal mechanisms.

Severity definition is another major limitation. **Severity was operationalized** using epilepsy and intellectual disability because these were available as clinically defined comorbidities in the records. This approach is imperfect because ASD severity is multidimensional and includes language ability, adaptive functioning, and behavioral features that are not fully captured by these two comorbidities. Epilepsy and intellectual disability can also have biological effects of their own, so some signals that appear as severity-linked may partially reflect these comorbidities rather than ASD progression alone. This underscores the importance of independent validation using more detailed clinical severity measures.

The sample size is limited after applying exclusion criteria and stratifying donors by severity. Only 18 ASD donors remained for severity-based comparisons, and the low severity group included 4 donors. Small groups reduce statistical power and increase the likelihood that individual donors influence results. Small group size also limits the ability to include covariates in differential expression models. This can leave residual confounding from age, sex, PMI, medication exposure, or other clinical factors if they differ across severity bins.

Cell-type and region-specificity also limit generalization. This work focuses only on microglia from the prefrontal cortex, and ASD-related biology may differ across brain regions and cell types. Microglial states can also be influenced by local neuronal activity and tissue context, so results from the cortex may not generalize to other regions. Even within microglia, there can be substate heterogeneity, and severity-associated signals may reflect shifts in subpopulation proportions rather than within-state changes.

There are also analytic limitations tied to pseudobulk and threshold choices. Pseudobulk reduces cell-level noise and avoids treating cells from the same donor as independent, but it can mask microglial subcluster-specific effects if opposing changes cancel out during aggregation. Differential expression results can also vary depending on filtering criteria and significance thresholds, and driver classification depends on which genes cross significance in each contrast. This is why sensitivity analyses are important, and they help show whether the main conclusions remain stable under reasonable parameter changes.

Finally, driver classification provides a structured way to prioritize candidates, but it does not confirm functional causality. Genes labeled as early, late, or cumulative are candidates based on statistical patterns and may include downstream responders rather than upstream drivers. Functional experiments are needed to test whether manipulating these genes changes microglial behavior or downstream neural outcomes. Because of these limitations, the conclusions of this study should be viewed as a severity-aware prioritization framework that generates testable hypotheses rather than a final mechanistic explanation of ASD progression.

Conclusion and future directions

This work provides a severity-aware framework for interpreting transcriptomic heterogeneity in microglia and can help move beyond a single ASD-versus-control signature.

The main contribution is a structured approach to mapping gene expression changes across severity transitions and prioritizing candidate genes as early, late, or cumulative. This type of staging view can be useful because it supports hypothesis generation aligned with progression. It

can also help researchers focus functional studies on a smaller set of candidates tied to specific stages, rather than treating all differentially expressed genes as equally informative.

A scalable aspect of this approach is that it can be applied to many existing public datasets without requiring new sample collection. [7] The same pipeline can be rerun on other single-cell ASD resources and on other brain regions from the same study. It can also be extended beyond microglia by applying the same severity transition analysis to neurons, astrocytes, oligodendrocytes, and endothelial cells. This would allow comparisons of whether severity-linked patterns are cell-type specific or shared across multiple cell populations. The approach can also be adapted to other neurodevelopmental and neuropsychiatric disorders in which severity varies across individuals and can support cross-disorder comparisons of immune and remodeling programs.

This framework can also support translational directions, but those uses require careful validation. In the long term, a severity-aware gene set could inform biomarker discovery and guide the development of objective molecular staging tools. These tools could help stratify research cohorts and evaluate whether interventions shift molecular states toward less severe profiles. However, this work is not a diagnostic tool, and postmortem findings cannot be directly transferred to clinical decision-making without additional evidence.

Several validation steps are needed before broader applications are appropriate. First, driver categories should be replicated in independent ASD single-cell datasets and in additional cohorts with larger sample sizes. Second, severity definitions should be tested using more detailed clinical measures when available, and the framework should be evaluated to determine whether

it holds when controlling for additional covariates. Third, spatial transcriptomics can test whether the same microglial programs are localized to specific cortical layers or tissue microenvironments. Fourth, functional validation is needed to test causality, and this can include perturbation experiments in human iPSC-derived microglia, microglia-neuron co-culture systems, or organoid models. These steps would help distinguish upstream regulatory drivers from downstream response genes.

Overall, this work provides a scalable, extensible way to organize transcriptomic results by severity progression. It can guide future studies toward stage-linked mechanisms and help prioritize microglial pathways that may contribute to differences in impairment. The most important next steps are replication and functional validation, which are necessary to translate these findings into clinically meaningful tools or interventions.

Work Cited

[1] American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). American Psychiatric Publishing.

[2] Autism and Developmental Disabilities Monitoring Network Surveillance Year 2008 Principal Investigators, & Centers for Disease Control and Prevention. (2012). Prevalence of autism spectrum disorders—Autism and Developmental Disabilities Monitoring Network. MMWR Surveillance Summaries, 61(3), 1–19.

[3] Shattuck, P. T., Durkin, M. S., Maenner, M., Newschaffer, C., Mandell, D. S., Wiggins, L., Bakian, A. V., & Baio, J. (2009). Timing of identification among children with an autism spectrum disorder: Findings from a population-based surveillance study. Journal of the American Academy of Child & Adolescent Psychiatry, 48(5), 474–483. https://doi.org/10.1097/CHI.0b013e31819b3841

[4] Velmeshev, D., Schirmer, L., Jung, D., Haeussler, M., Perez, Y., Mayer, S., Bhaduri, A., Goyal, N., Rowitch, D. H., & Kriegstein, A. R. (2019). Single-cell genomics identifies cell type specific molecular changes in autism. Science, 364(6441), 685–689. https://doi.org/10.1126/science.aav8130

[5] Wamsley, B., Jagadish, N., Varma, V., & Geschwind, D. H. (2024). Molecular cascades and cell type-specific signatures in ASD revealed by single-cell genomics. Science, 384(6698), eadh2602. https://doi.org/10.1126/science.ad

[6] Kong, S. W., Collins, C. D., Shimizu-Motohashi, Y., Holm, I. A., Campbell, M. G., Lee, I. H., Kohane, I. S., & Kunkel, L. M. (2012). Characteristics and predictive value of blood transcriptome signature in males with autism spectrum disorders. PLoS ONE, 7(12), e49475. https://doi.org/10.1371/journal.pone.0049475

[7] Emani, P. S., Liu, J. J., Ruppin, E., & Gerstein, M. B. (2024). Single-cell genomics and regulatory networks for 388 human brains. Science, 384(6698), eadi5199. https://doi.org/10.1126/science.adi5199