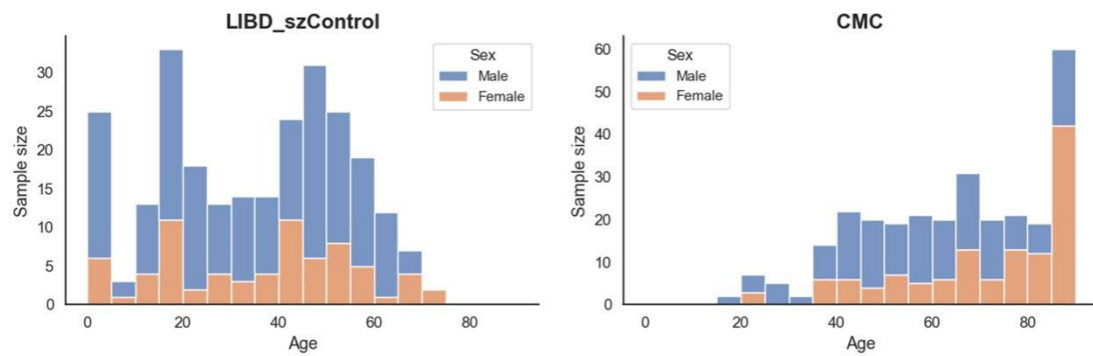
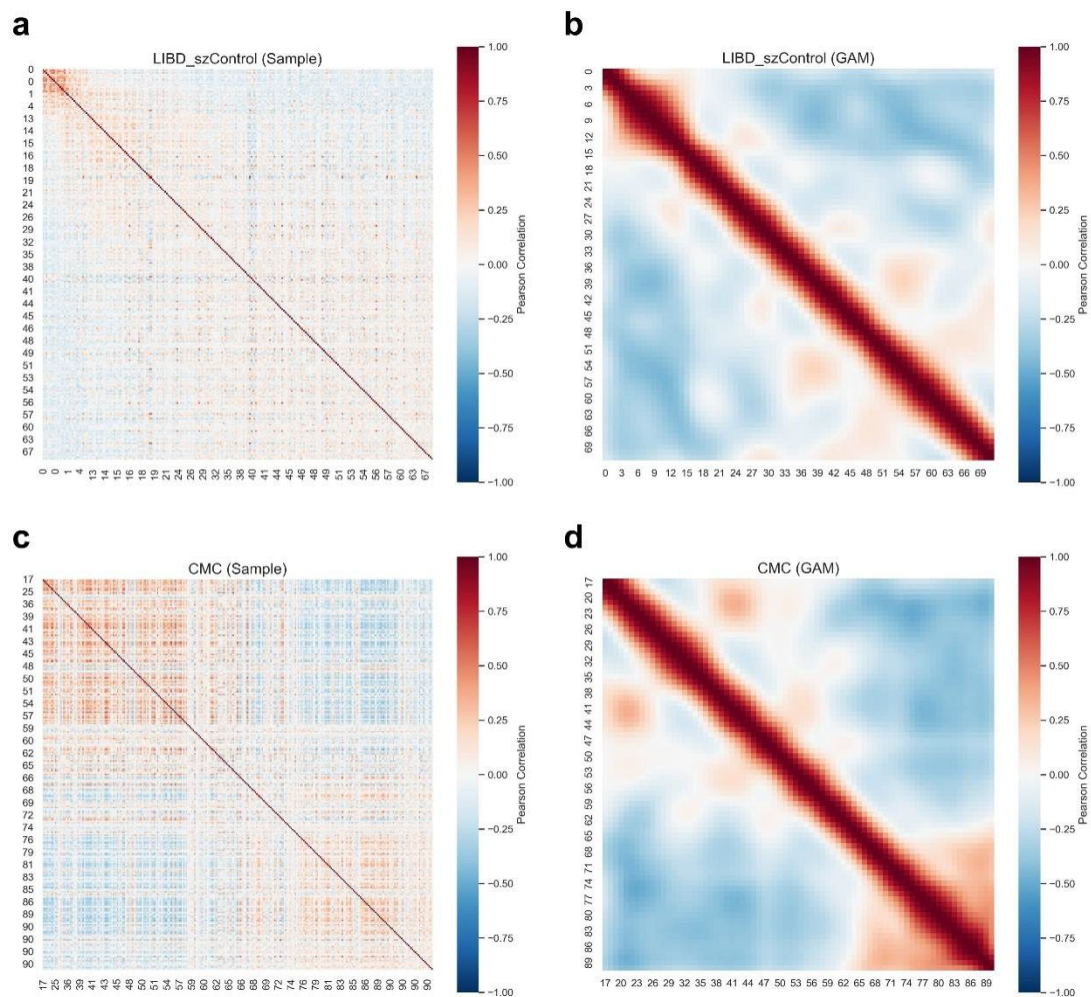


Supplementary Figures



Supplementary Figure 1. Sex and age distribution of samples in the developmental dynamic expression dataset. Age is shown on the x-axis, starting from 0 years and grouped into 5-year intervals, while the y-axis indicates the number of samples. Colors represent sex.



Supplementary Figure 2. Heatmaps of Pearson correlation coefficients based on either age- or sex-based clustering.

stratified samples or GAM-predicted expression. (a, c) Correlation matrices calculated from the original expression profiles of the samples, with samples ordered by increasing age. (b, d) Correlation matrices calculated from GAM-predicted expression profiles, with samples similarly ordered by age.

a

Schizophrenia-associated genes in the PDE4 family						
Gene name	Chromosome	Start position	End position	Variant number	Gene-based P	Conditional P
PDE4B	1	65791733	66375497	200	1.25E-08	1.25E-08
PDE4D	5	58968164	60485875	722	1.48E-07	1.48E-07

b

Age-specific score (calculated by REZ) of PDE4 family genes			
Gene name	8-18 (years)	20-40 (years)	70-100 (years)
PDE4B	1.2919426	0.022201404	0.30839053
PDE4D	-0.423499345	0.33552614	-0.949399

c

Log2 fold changes of PDE4 family genes under antipsychotic drug perturbations			
Gene name	trifluoperazine	pimozide	rolipram
PDE4B	0.16	0.25	-0.34
PDE4D	-2.02	-1.69	-1.13

Supplementary Figure 3. Integrated analysis of PDE4 family genes in schizophrenia across genetic association, age specificity, and pharmacological perturbation. (a) Association of PDE4 family genes with schizophrenia, showing gene-level evidence from genetic analyses. (b) Age-specific score (calculated by REZ) of PDE4 family genes, highlighting temporal dynamics across developmental stages. (c) Log2 fold changes (treatment versus control) of PDE4 family gene expression under antipsychotic drug perturbations, indicating transcriptional responses to pharmacological intervention.

Supplementary Tables

Supplementary Table 1. GWAS summary statistics of nine complex diseases and traits.

Phenotype	Abbrevi ation	Source	Reference (PMID/URL)	Ancestry	N(sample)
Alzheimer disease	AD	PGC	30617256	European	455,258
Attention Deficit Hyperactivity Disorder	ADHD	PGC	36702997	European	225,534
Bipolar disorder	BIP	PGC	34002096	European	413,466
Major depression	MDD	PGC	30718901	European	807,553

Schizophrenia	SCZ	PGC	35396580	European	320,404
Intelligence	IQ	GWAS Catalog	29942086	European	269,867
Neuroticism	NEU	GWAS Catalog	30643256	European	523,783
Sleep duration	SD	GWAS Catalog	30846698	European	446,118
Smoking	SMK	GWAS Catalog	30643258	European	518,633