Figure S1: GO term enrichment analysis (DAVID) for genes that were differentially expressed genes between NPCs and neurons in WT but not in *CHD8*$^{+/-}$ samples. (A) Genes expressed at higher levels in WT neurons than NPCs. (B) Genes expressed at lower levels in WT neurons than NPCs. P-value were corrected by Benjamini-Hotchberg method.

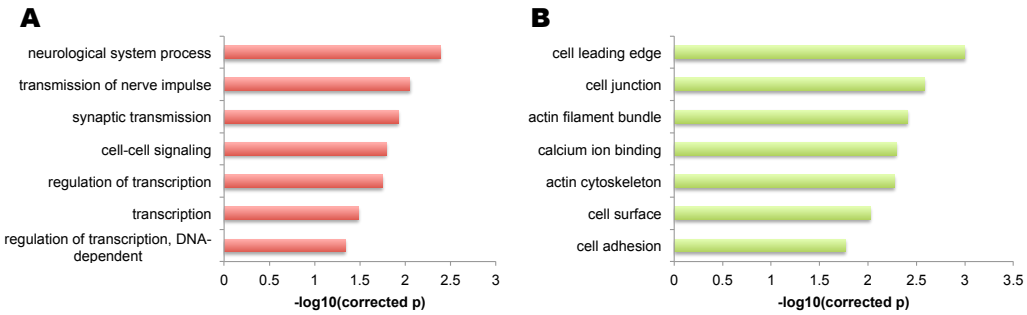

Figure S2: Expression of *CHD8* and brain volume associated DEGs in Brainspan. Expression values log2(FPKM+1) were scaled by row in heatmap. The numbers in parentheses below gene names represent Pearson's correlation coefficients (R) and p-values between *CHD8* and the corresponding gene. The order of genes was based on the correlation coefficients.

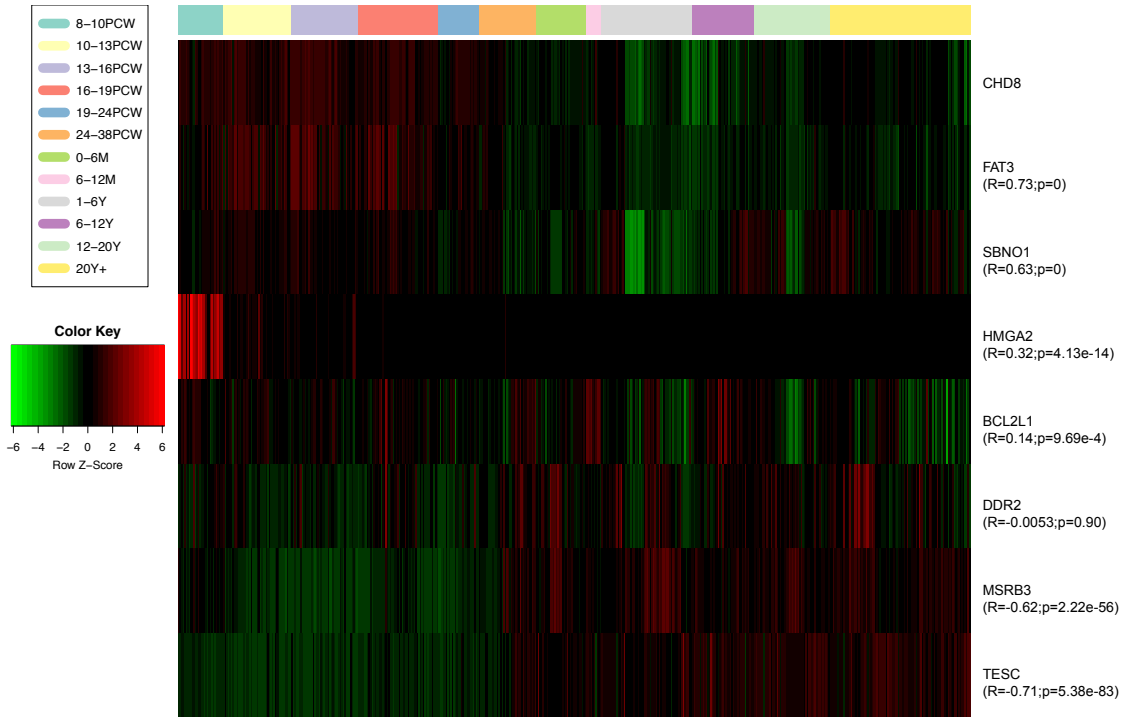

Figure S3: Comparison of the DEGs from current *CHD8*$^{+/-}$ analysis and previous *CHD8* knockdown studies. Genes were from NPC *CHD8*$^{+/-}$ (current data), NPC knockdown [1], NSC knockdown by two independent shRNAs (shC and shG) [2], SK-N-SH knockdown [3]. Also included DEGs from a previous transcriptomics profiling of organoids derived from ASD cases [4], with genes list from the TD11 and TD31 samples being combined. The red shading in each cell corresponds to the -$\log_{10}$P value for overrepresentation (Fisher's exact test, one-tailed), as shown in the color scale on the right (shown only if p<0.05). The first and the second number in each cell are the number of overlapping genes and the odd ratio of overlap to non-overlap, respectively. Numbers in the diagonal (grey cells) are the numbers of DEGs from previously studies that were also expressed in our samples.

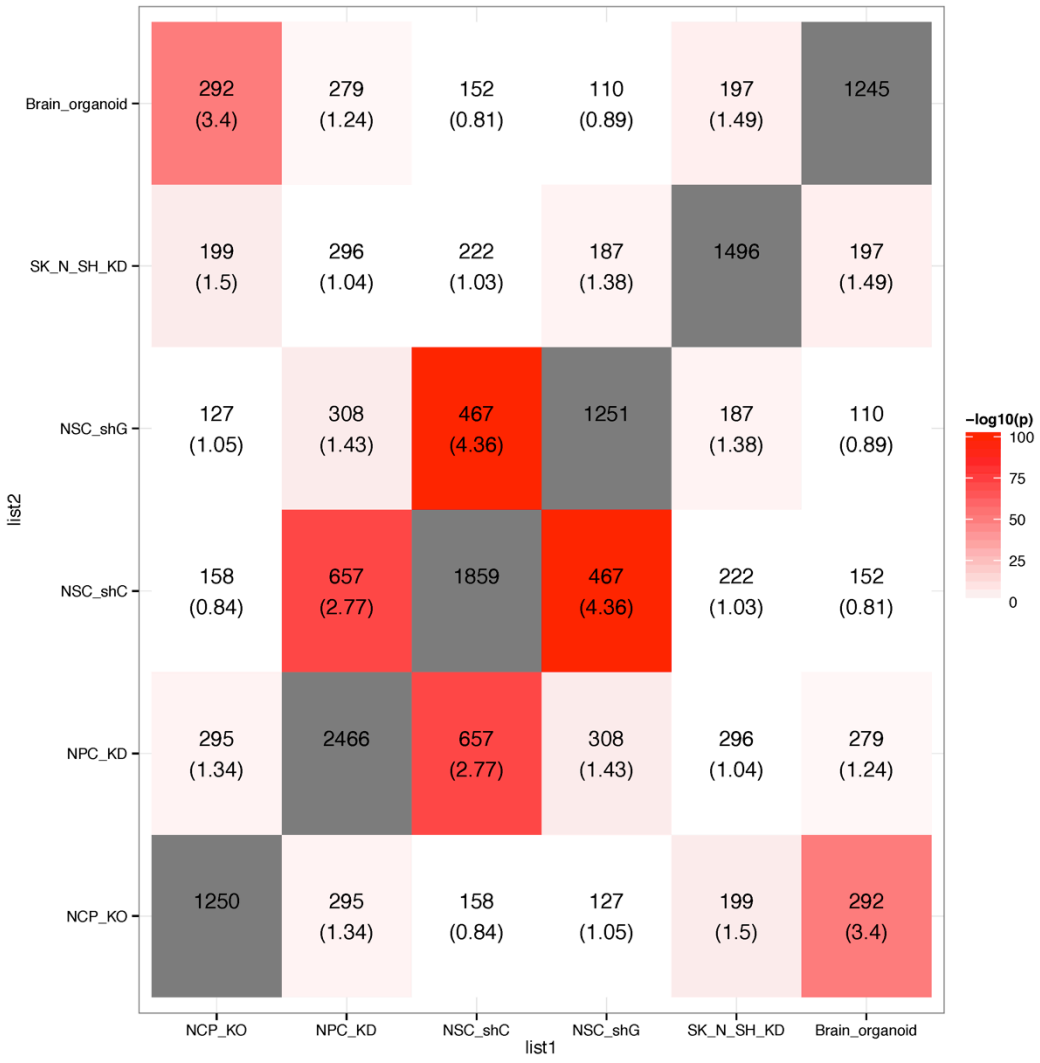

Table S1: Summary of RNA-seq quality.

Sample Name	Number of Pairs	Number of Mapped Pairs	exonic rate	intronic rate	intergenic rate	Median FPKM (genes)	Mean FPKM (genes)	Num of Genes (FPKM > 1)
control1_NPC	27,240,051	23,463,095	0.6088	0.34	0.0512	1.4672	67.8968	12,878
control2_NPC	24,248,402	21,275,566	0.7087	0.2567	0.0346	1.6287	110.7046	13,096
KO1_NPC	29,955,073	26,832,796	0.6494	0.3091	0.0415	1.8454	83.6047	13,294
KO2_NPC	24,531,882	21,941,336	0.6512	0.3092	0.0396	1.7143	95.6639	13,136
control1 _neuron	30,352,377	26,864,628	0.6307	0.3197	0.0496	1.6354	101.8777	13,158
control2_neuron	26,833,384	23,538,348	0.7356	0.221	0.0434	2.1256	107.5034	13,589
KO1_neuron	32,077,864	28,112,380	0.6372	0.3216	0.0412	2.6096	123.6631	14,062
KO2_neuron	28,613,352	24,164,270	0.7064	0.256	0.0376	2.5386	113.1035	14,030

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