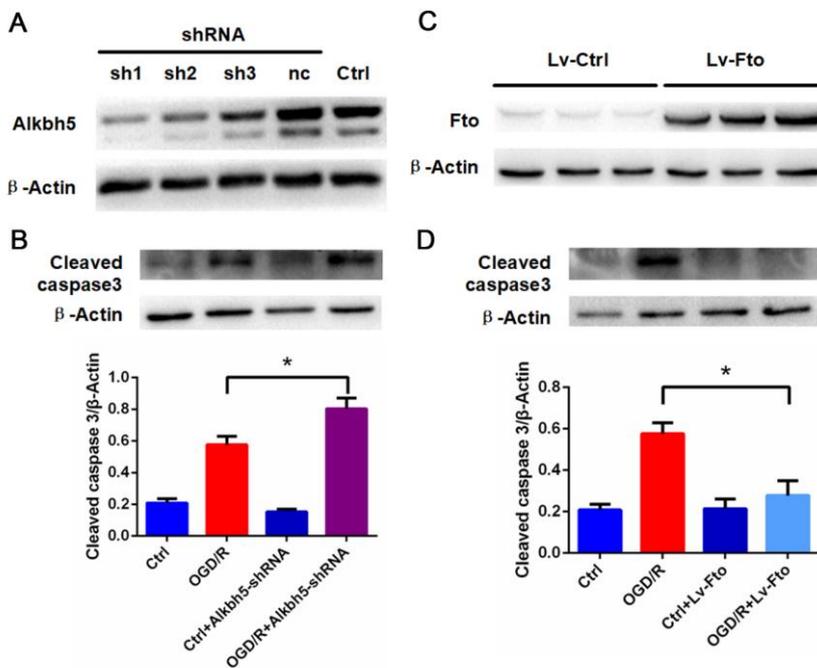


Supplementary Figure 1 The levels of other demethylases and methyltransferases in rat cerebral cortex after MCAO. (A) Representative images of Western blots of OGD/R treated primary neurons. Alkhh5 levels were determined by Western blot (mean \pm SEM; $n \geq 3$; *** $P < 0.001$ vs. Ctrl). (B) qRT-PCR images of MCAO treated rat cerebral cortex. Alkhh5 levels were analyzed by qRT-PCR (mean \pm SEM; $n = 3$; * $P < 0.05$ vs. sham). (C) qRT-PCR images of OGD/R treated primary neurons. Alkhh5 levels were analyzed by qRT-PCR (mean \pm SEM; $n \geq 3$; * $P < 0.05$ vs. Ctrl). (D) Immunohistochemical results of Mettl3 in rat cerebral cortex in two indicator groups: tawny staining for Mettl3 protein and light blue staining for hematoxylin. Scale bar = 100 μ m, and the small picture scale bar = 2000 μ m. Quantification of Mettl3 was shown (mean \pm SEM; $n = 3$; ns $P > 0.05$ vs. Sham).



Supplementary Figure 2. Alkhh5 knockdown enhanced OGD/R treated primary neuronal apoptosis and Fto overexpression attenuated OGD/R treated primary neuronal apoptosis. (A) Representative images of Western blots of primary neurons infected with Alkhh5-shRNA. Alkhh5 levels were determined by Western blot. Quantification of Alkhh5 protein levels showed a knockdown efficiency of over 70%. (B) Representative

images of Western blots of primary neuron infected with Alkbh5-shRNA. Cleaved-caspase3 levels were determined by Western blot (mean \pm SEM; n = 3; * P < 0.05 vs. OGD/R). (C) Representative images of Western blots of primary neurons infected with Lv-Fto. Fto levels were determined by Western blot. (D) Representative images of Western blots of primary neuron infected with Lv-Fto. Cleaved-caspase3 levels were determined by Western blot (mean \pm SEM; n = 3; * P < 0.05 vs. OGD/R).

Supplementary Table 1. The primers used in this study.

| Primer name | | Sequence |
|-------------|-----------|----------------------------|
| Alkbh5 | Alkbh5 F | CGGAAGTACCAGGAGGACTCAGAC |
| | Alkbh5 R | GGATGCCGCTCTTCACCTTGC |
| Fto | Fto F | GACCGTCCTGCGATGATGAAGTG |
| | Fto R | CCTGTCCACCAAGTTCTCGTCATG |
| Mettl3 | Mettl3 F | CACGCTGCCTCAGATGTTGACC |
| | Mettl3 R | CTGACCTTCTTGCTCTGCTGTTCC |
| Mettl14 | Mettl14 F | TGAGAGGCTTAGACCGAAGTCACC |
| | Mettl14 R | GACCACGGCCAGCAGATGTTC |
| Bcl2 | Bcl2 F | CACGGTGGTGGAGGAAGTCT |
| | Bcl2 R | TCCACAGAGCGATGTTGTCC |
| WTAP | WTAP F | AGAACATCCTTGTCATGCGGCTAG |
| | WTAP R | TCGGCTGCTGAACTTGCTTGAG |
| VIRMA | VIRMA F | GGTGCTAAGAGGCTGGTACAAGTCTG |
| | VIRMA R | TGGAGGAGGAGGTGGAGGAGAG |
| RBM15 | RBM15 F | AGGTTCTGGCAGCGGGGATG |
| | RBM15 R | CGGCTCACATACACGGCTTCTATC |

Supplementary Table 2. The reagents used in this study.

| Reagents | Company | Catalogue Number |
|--------------------------------------|--------------------------|------------------|
| Neurobasal medium | Thermo fisher scientific | 21103-049 |
| B-27 Supplement (50X), serum free | Thermo fisher scientific | 17504-044 |
| L-Glutamine | Thermo fisher scientific | 25030-081 |
| Hanks' Balanced Salt Solution (HBSS) | Thermo fisher scientific | 14170-112 |
| Trypsin-EDTA (0.25%) | Thermo fisher scientific | 25200-072 |
| DMEM, no Glucose | Thermo fisher scientific | 11966-025 |
| Fetal bovine serum (FBS) | Thermo fisher scientific | 10099-141 |
| 0.25% Trypsin | Thermo fisher scientific | 15050-057 |
| PBS | Thermo fisher scientific | C20012500BT |
| DMEM, High Glucose | Thermo fisher scientific | C11995500BT |
| Penicillin-Streptomycin | Thermo fisher scientific | 15140-122 |
| BCA Protein Assay Kit | Thermo fisher scientific | 23227 |
| West Femto | Thermo fisher scientific | 34094 |
| Gold Antifade Mountant with DAPI | Thermo fisher scientific | P-36931 |
| Polyethylenimine | Polysciences | 23966-1 |
| TEMED | Sigma-Aldrich | T9281 |

| | | |
|-----------------------------------|------------------------|-------------|
| 1-Bromo-3-chloropropane | Sigma-Aldrich | B9673 |
| Glycerol | Solarbio life sciences | G8190 |
| Tween-20 | Solarbio life sciences | T8220 |
| DMSO | Solarbio life sciences | D8370 |
| RIPA buffer | Solarbio life sciences | R0010 |
| Hoechst 33342/PI Double Stain Kit | Solarbio life sciences | CA1120 |
| Protein Phosphatase Inhibitor | Solarbio life sciences | P1260 |
| 0.01M PBS | Solarbio life sciences | P1010 |
| Sodium dodecylsulfate (SDS) | Solarbio life sciences | S8010 |
| 1.5M Tris-HCl | Solarbio life sciences | T1010 |
| 1M Tris-HCl | Solarbio life sciences | T1020 |
| Acrylamide | Solarbio life sciences | A1010 |
| Poly-L-lysine Solution | Solarbio life sciences | P2100 |
| Sodium acetate | Solarbio life sciences | A1070 |
| Ammonium persulfate substitute | Beyotime Biotechnology | ST005 |
| SDS-PAGE Sample Loading Buffer | Beyotime Biotechnology | P0015 |
| Stripping buffer | Beyotime Biotechnology | P0025 |
| Skim milk | BD | 232100 |
| Albumin bovine | Generay Biotechnology | 0332 |
| Paraformaldehyde | Macklin | P804536 |
| Isoflurane | RWD life science | R510-22 |
| Chloral hydrate | Meilunbio | MB4202 |
| WesternBright ECL | Advansta | K-12045-D10 |
| Cell Counting Kit-8 assay kit | Dojindo | CK04-500 |
| <i>EcoR</i> I | Takara | 1611 |
| <i>Xba</i> I | Takara | 1634 |
| T4 DNA Ligase | Takara | 2011A |
| <i>E. coli</i> DH5 α | Takara | 9057 |
| Ampicillin | Solarbio life sciences | A8180 |
| Plasmid Mini Kit | Qiagen | 12123 |
| EndoFree Plasmid Maxi Kit | Qiagen | 12362 |
| Agarose | Meilunbio | MB2555 |
| Tryptone | Oxoid | LP0042 |
| Yeast extract | Oxoid | LP0021 |
| actinomycin D | MedChemExpress | HY-17559 |