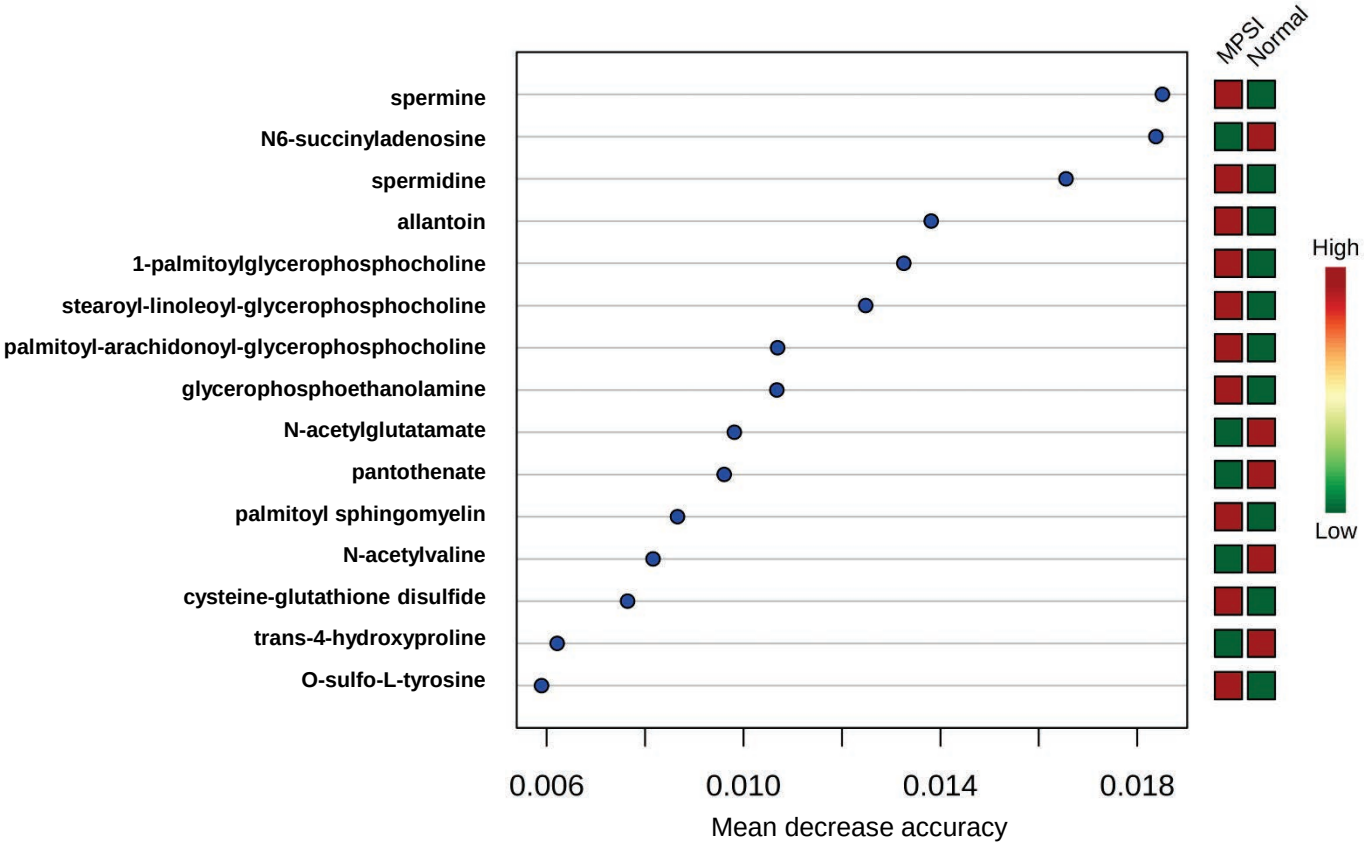
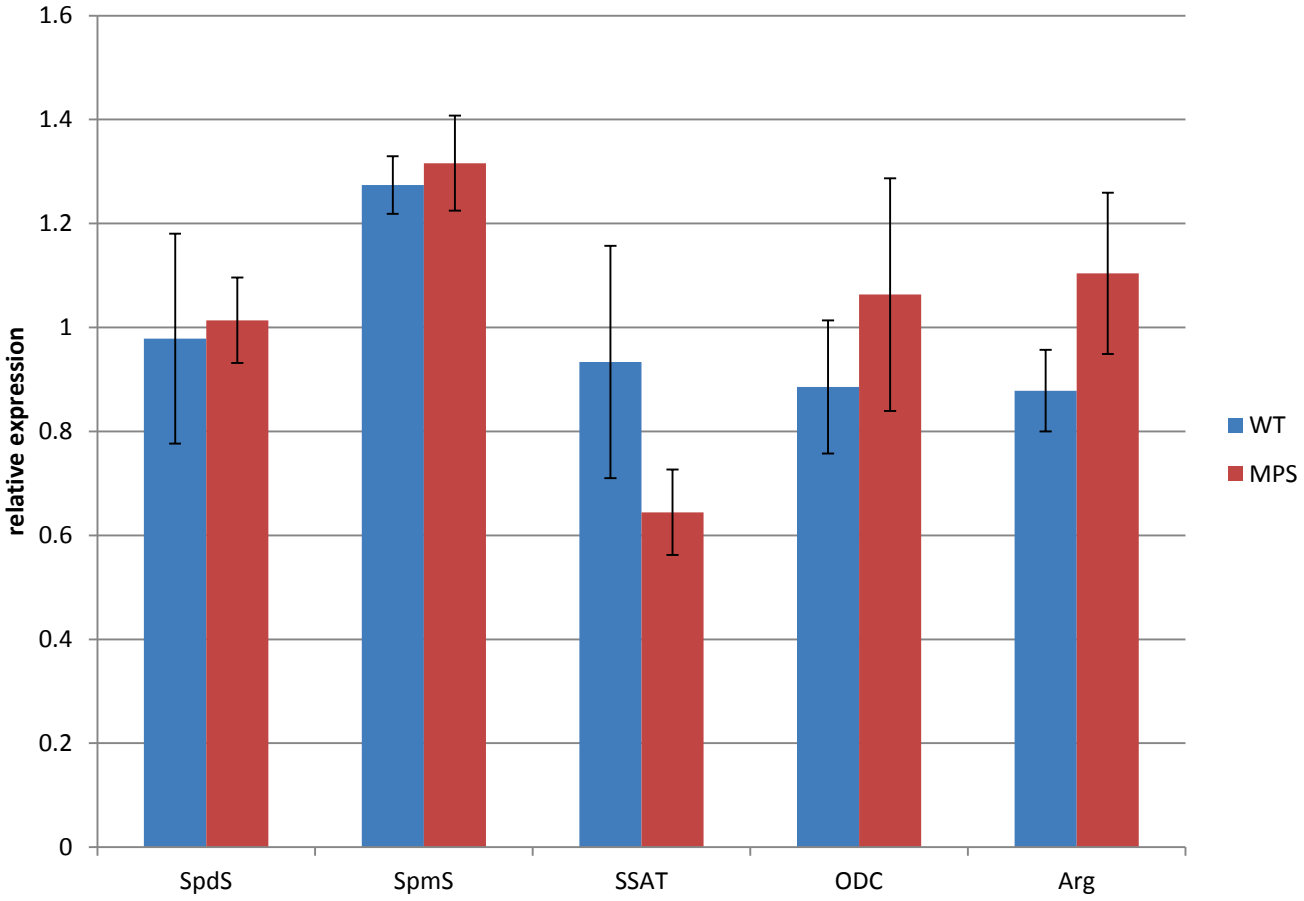


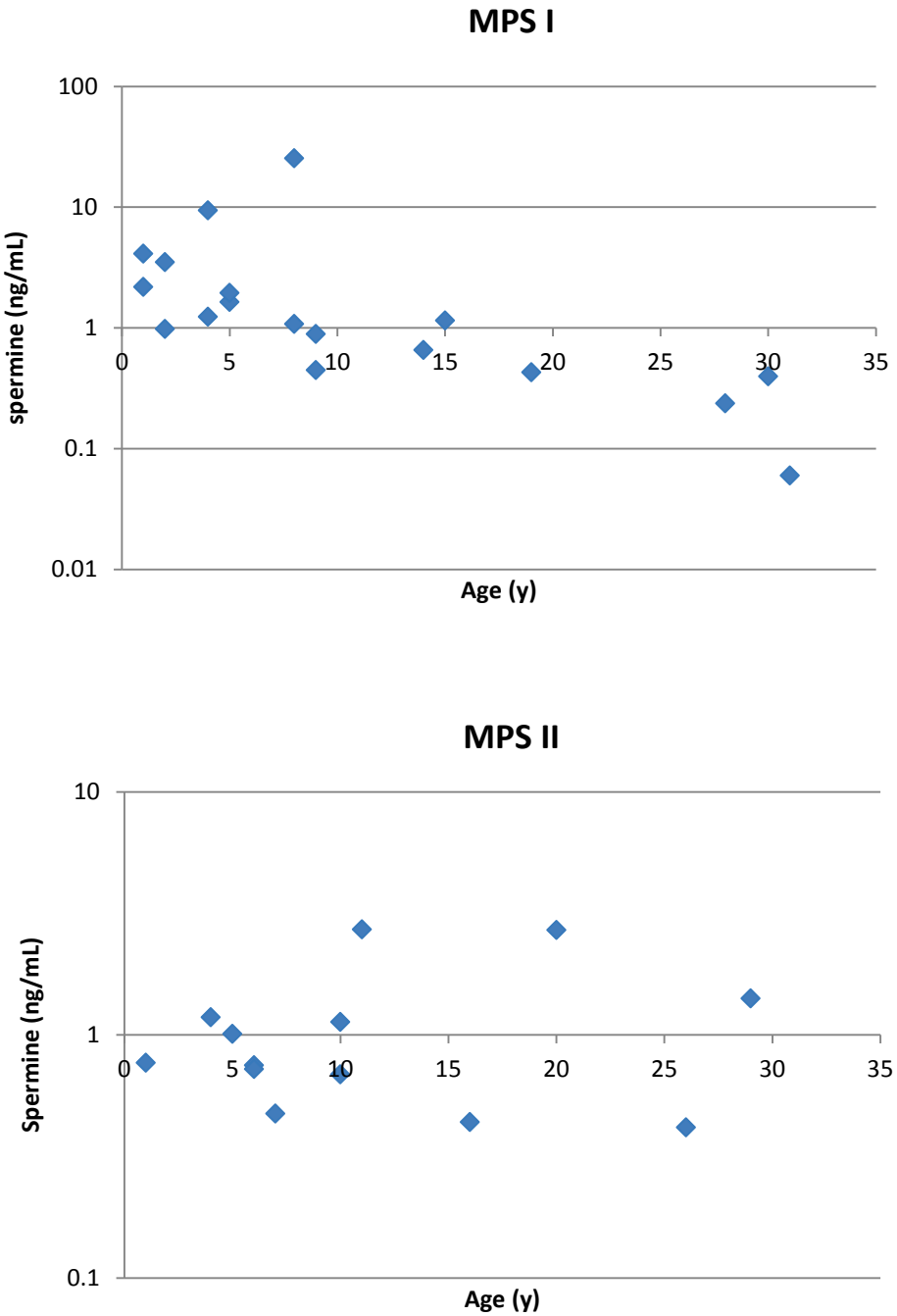
Supplemental Figure 1. Mean decrease accuracy for metabolites identified by random forest analysis.

Random forest classification was performed for metabolite data from MPS I and normal samples, and predicted the genotype group with 90% accuracy. The mean decrease in predictive accuracy was calculated with the omission of each metabolite individually from the random forest analysis as a measure of the importance of each metabolite for defining between-group differences in the CSF metabolome.

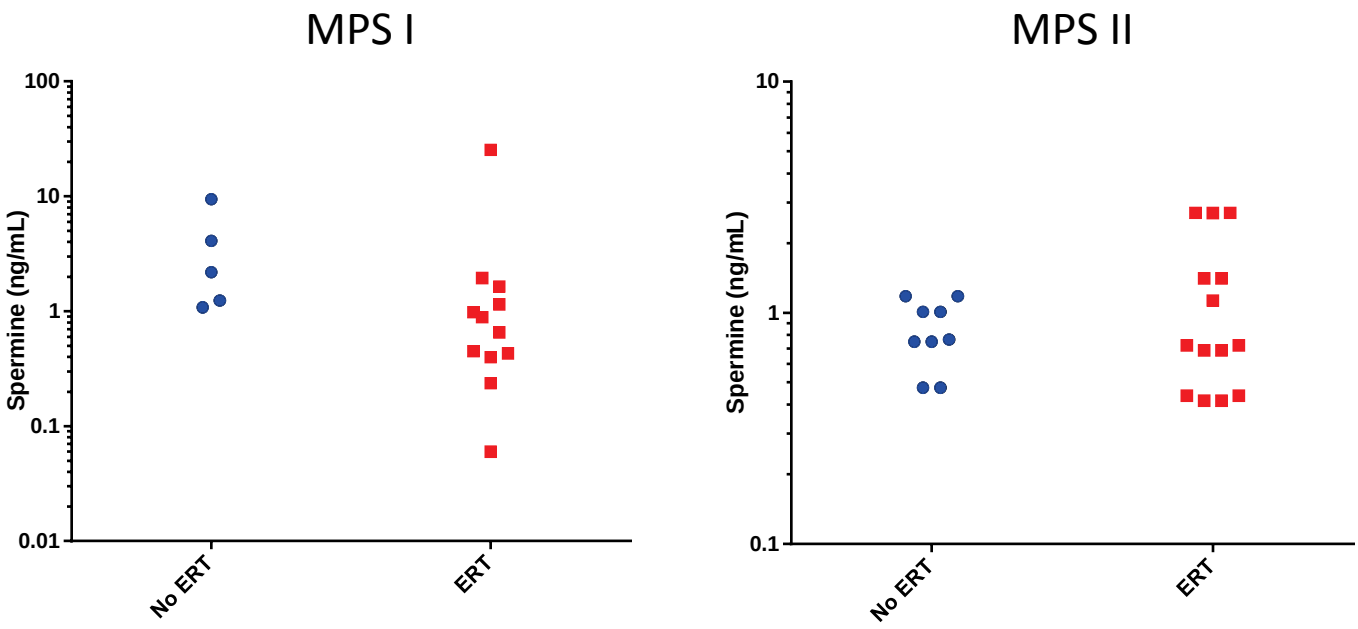


Supplemental Figure 2. Expression of enzymes in the polyamine synthetic pathway in MPS I dog brain samples.

Total RNA was extracted from frontal cortex samples of 3 normal dogs and 5 MPS dogs. Transcripts for arginase (Arg), ornithine decarboxylase (ODC), spermine synthase (SpmS), spermidine synthase (SpdS), spermine-spermidine acetyltransferase (SSAT), and glyceraldehyde phosphate dehydrogenase (GAPDH) were measured by quantitative PCR. Values are expressed relative to the GAPDH control. Error bars = SEM.

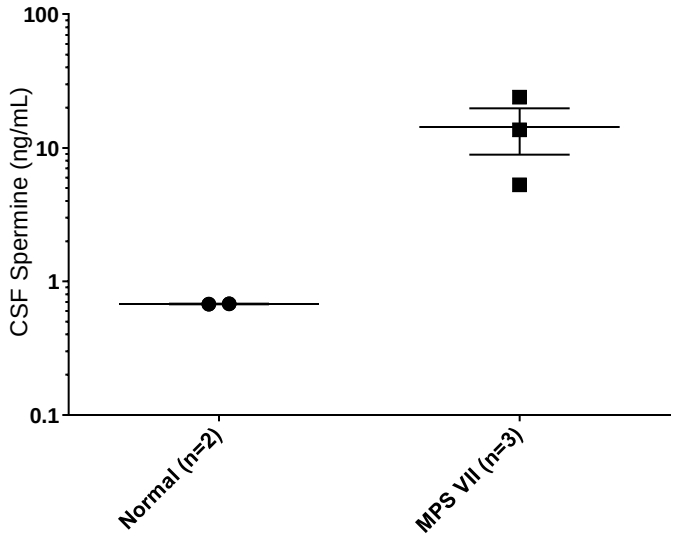


Supplemental Figure 3. CSF spermine vs age in MPS I and MPS II patients. CSF spermine was measured by LC-MS/MS assay. Each data point represents a different patient. MPS I patients treated with HSCT are excluded.

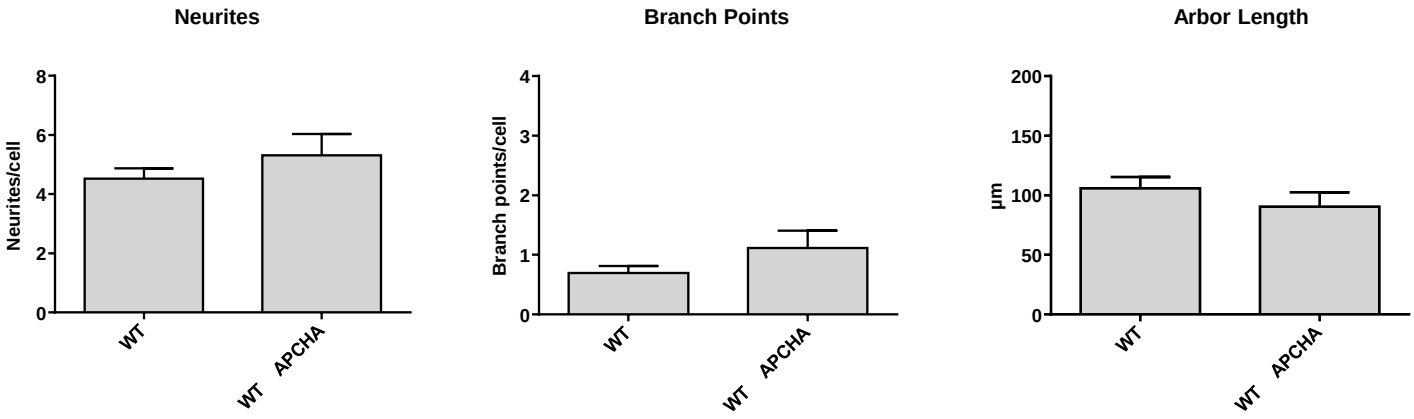


Supplemental Figure 4. CSF spermine in MPS I and II patients undergoing treatment with enzyme replacement therapy.

CSF spermine was measured by LC-MS/MS assay. Each data point represents a different patient. MPS I patients treated with HSCT are excluded. There were no significant differences between ERT treated and untreated patient CSF samples (T-test with Welch's correction).



Supplemental Figure 5. Spermine concentration in MPS VII dog CSF.
Spermine concentration was measured by a quantitative isotope dilution LC-MS/MS assay in CSF samples from 3 MPS VII dogs and 2 normal dogs.



Supplemental Figure 6. No impact of APCHA treatment on WT neuron growth. Cortical neurons harvested from E18 wild-type mouse embryos were treated with the spermine synthase inhibitor, APCHA, 24 hours after plating. Phase contrast images were acquired 96 hours after plating, and neurite number, length, and branching were quantified for randomly selected neurons from duplicate cultures per treatment condition by a blinded reviewer. There were no significant differences between the treatment groups (two-tailed T test).