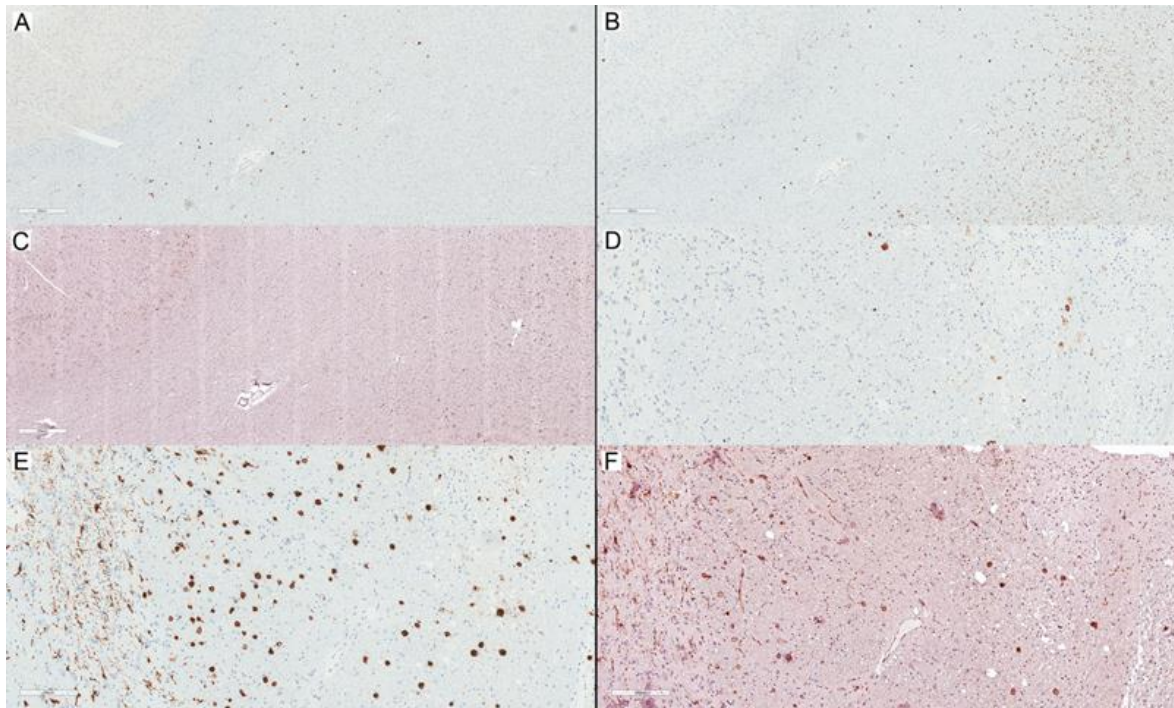


**Supplemental figure 1.** Definitions of semi-quantitative pathology. **(A)** Axonal spheroids score 1 (LFB-HE; scale bar: 50 µm). **(B)** Axonal spheroids score 1 (APP; scale bar: 50 µm). **(C)** Axonal spheroids score 2 (3–5/HPF) (APP; scale bar: 50 µm). **(D)** Axonal spheroids score 3 (6 or more/HPF) (APP; scale bar: 50 µm). **(E)** Microglia with ramified phenotype score 1 (1–9/HPF) (HLA-DR; scale bar: 50 µm). **(F)** Microglia with ramified phenotype score 2 (10–19/HPF) (IBA1; scale bar: 50 µm). **(G)** Microglia with ramified phenotype score 3 (20 or more/HPF) (IBA1; scale bar: 50 µm). **(H)** Microglia with amoeboid phenotype score 1 (1–9/HPF) (HLA-DR; scale bar: 50 µm). **(I)** Microglia with amoeboid phenotype score 2 (10–19/HPF) (HLA-DR; scale bar: 50 µm). **(J)** Microglia with amoeboid phenotype score 3 (20 or more/HPF) (HLA-DR; scale bar: 50 µm).



**Supplemental figure 2.** Comparison of HLA-DR and IBA1 immunostains. **(A)** Frequent axonal spheroids in the central region of the white matter (APP; scale bar: 500  $\mu$ m). **(B)** The area with frequent axonal spheroids is devoid of ramified microglia, but contains few microglia with amoeboid phenotypes (HLA-DR; scale bar: 500  $\mu$ m). **(C)** Similar area with IBA1 immunostain shows similar findings, but is more difficult to appreciate because of the non-specific background staining (IBA1; scale bar: 500  $\mu$ m). **(D)** Another area with higher magnification shows moderate to frequent axonal spheroids in the right side of the figure (APP; scale bar: 200  $\mu$ m). **(E)** The right side of the picture is devoid of ramified microglia, but contains frequent microglia with amoeboid phenotypes (HLA-DR; scale bar: 200  $\mu$ m). **(F)** Similar results with IBA1 immunostain for the ramified microglia, but much less sensitivity for microglia with amoeboid phenotypes (IBA1; scale bar: 200  $\mu$ m).