

**P063** Primed microglia in the brain: an accident waiting to happen  
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Neurodegenerative diseases such as prion disease and Alzheimer's disease are associated with chronic microglial activation. This microglial activation is atypical in the ME7 model of prion disease in that it shows minimal pro-inflammatory cytokine expression. However, the brains of these animals are primed to produce greater inflammatory responses to subsequent intracerebral (i.c.) or intraperitoneal (i.p.) challenges with bacterial endotoxin. There is evidence that systemic infections and central insults can exacerbate neurodegeneration. Here we demonstrate that i.c challenge with LPS results in considerable neutrophil accumulation and cell death in the brain parenchyma of prion-diseased animals compared to similar LPS challenges in normal animals. These challenges also produce marked microglial and neutrophil IL-1 $\beta$  and iNOS expression. We have also used quantitative PCR to assess levels of transcripts for the cytokines IL-1 $\beta$ , IL-6, TNF $\alpha$  and TGF $\beta$ 1 after i.p. challenge with LPS. LPS produced greater increases in the transcription of pro-inflammatory cytokines in ME7-diseased mice than in NBH mice, but did not induce TGF $\beta$ 1. Peripheral challenge with LPS caused cell death in the hippocampus, thalamus and cortex of these animals, as assessed by TUNEL and activated caspase-3 staining. This cell death did not occur in normal animals treated with LPS. These results show that both peripheral and central infections exacerbate brain inflammation and can contribute to cell death during neurodegeneration.