Abstracts must contain the background, hypothesis, methods, results to date (if ongoing) and discussion/conclusions. **Not to Exceed 350 Words.** Typed font must be Times New Roman and no smaller than 11 Pt. Do not use continuation pages, tables, or illustrations.

**Objectives:** To evaluate the relationship between glial activation assessed by $^{[1]}$C-PBR28 PET, and neuronal integrity and gliosis/neuroinflammation measured by $^1$H-MRS spectroscopy in people with amyotrophic lateral sclerosis (ALS).

**Background:** Prior MRS studies show alterations in brain metabolites in the motor cortices and brain stem in people with ALS and our group provided in vivo evidence of increased glial activation in ALS using the radiotracer $^{[1]}$C-PBR28 PET. Combining multiple neuroimaging modalities is of importance to unraveling ALS disease mechanisms. To our knowledge, this is the first study to evaluate the relationship between glial activation, measured by $^{[1]}$C-PBR28 PET, and brain metabolites assessed by $^1$H-MRS.

**Methods:** A total of 28 participants (16 ALS-Limb, 7 ALS-Bulbar; 5 PLS) were included in this study. The participants underwent brain imaging using MR/PET with the radiotracer $^{[1]}$C-PBR28 and simultaneous $^1$H-MRS. The data acquired from multiple single-voxels (20 X 20 X 20 mm$^3$) located in five positions in the brain, left motor cortex (21 subjects), right motor cortex (19 subjects), brain stem (8 subjects), frontal cortex (8 subjects), and parietal cortex (13 subjects). LCmodel was used to analyze $^1$H-MRS data and to measure brain metabolite ratios pertaining to neuronal viability (N-acetylaspartate/creatine, NAA/Cr) and glial activation/inflammation (myo-Inositol, mI/Cr). Freesurfer’s tools used to create 3D volumes that mimic the MRS Voxels. These volumes were moved and co-registered to the anatomical images, then $^{[1]}$C-PBR28 uptake was calculated for every brain parcellate within these volumes. Pearson correlations were conducted to study the relationship between $^{[1]}$C-PBR28 uptake and brain metabolite ratios within each voxel.

**Results:** Pearson correlation coefficient revealed an inverse relationship between glial activation, represented by $^{[1]}$C-PBR28 uptake and NAA/Cr in the left motor cortex (r = -0.51; p = 0.01) but not in other brain regions. In addition, a positive relationship was found between $^{[1]}$C-PBR28 uptake and ml/Cr, both markers of gliosis/inflammation, in the right motor cortex (r = 0.56; p = 0.01) and brain stem (r = 0.78; p=0.02). No correlations were detected in the frontal or parietal cortices.

**Conclusion:** Glial activation (↑PBR28 uptake) correlates with neuronal damage (↓NAA) and gliosis/neuroinflammation (↑mI) in brain regions affected in ALS.