Temporal Lobe Epilepsy (TLE) is frequently associated with changes in protein composition and post-translational modifications (PTM) that exacerbate the disorder. O-linked-β-N-acetyl glucosamine (O-GlcNAc) is a PTM occurring at serine/threonine residues that is derived from and closely associated with metabolic substrates. The enzymes O-GlcNActransferase (OGT) and O-GlcNAcase (OGA) mediate the addition and removal, respectively, of the O-GlcNAc modification. The goal of a study was to characterize OGT/OGA and protein O-GlcNAcylation in the epileptic hippocampus and to determine and whether direct manipulation of these proteins and PTM's alter epileptiform activity.

They observed reduced global and protein specific O-GlcNAcylation and OGT expression in the kainate rat model of TLE and in human TLE hippocampal tissue. Inhibiting OGA with Thiamet-G elevated protein O-GlcNAcylation, and decreased both seizure duration and epileptic spike events, suggesting that OGA may be a therapeutic target for seizure control. These findings suggest that loss of O-GlcNAc homeostasis in the kainate model and in human TLE can be reversed via targeting of O-GlcNAc related pathways [1)].

1)
Sanchez RG, Ryley Parrish R, Rich M, Webb WM, Lockhart RM, Nakao K, Ianov L, Buckingham SC, Broadwater DR, Jenkins A, de Lanerolle NC, Cunningham M, Eid T, Riley K, Lubin FD. Human and rodent temporal lobe epilepsy is characterized by changes in O-GlcNAc homeostasis that can be reversed to dampen epileptiform activity. Neurobiol Dis. 2019 Jan 6. pii: S0969-9961(18)30370-X. doi: 10.1016/j.nbd.2019.01.001. [Epub ahead of print] PubMed PMID: 30625365.