## INCLUSION OF WOMEN AND MINORITIES – PROJECT 3 – BIOMARKERS OF HUMAN EPILEPTOGENESIS AFTER TRAUMATIC BRAIN INJURY

This Project will include women and minorities. The recruitment of women and minorities for this Project will not follow any exact quota system but is anticipated to reflect the general distribution of ages as shown in large-scale epidemiologic studies of traumatic injury and hospitalization. While these reports differ in their estimates due to differences across countries and states as well as substantial methodological differences, we estimate that from 28 to 41% of the overall study enrollment will be of women and that minorities may constitute as much as 43% of the overall study enrollment. We know of no gender or minority selection biases in the Project's participating institutions, though we intend to closely track such issues over time.

There may be factors that affect blood samples between genders and between ethnicities. A long history of evidence supports such a statement. The topic continues to be assessed: to cite but one recent example, the Gutenberg Health Study of 15,010 individuals found a significant difference between genders with respect to mean platelet volumes (Panova-Noeva et al, 2016).

There may be differences between genders with respect to assessments of cEEG, though the literature is quite variable on this topic. For instance, a recent study in the mouse model of acquired epilepsy has shown marked sex-related differences in the latent period following brain injury (Twele et al 2016). A recent study of humans showed sex-based differences in likelihood of psychogenic nonepileptic seizures (Noe et al, 2012). However, a recent human study of epilepsy patients with focal cortical dysplasia found no gender differences (Tasi et al, 2012).

There may be factors in rsfMRI that point to differences between genders, though the literature is less substantial. A recent study did not detect any sex differences in default mode, salience, and frontal-parietal cognitive control network (Weissman-Fogel et al, 2014). However, other studies have identified sex differences in various sensory, motor, sub-cortical, or cognitive networks such as default mode, cognitive control, and language networks. For example, in men, increased functional network connectivity was found between several cognitive and sensory networks, but women showed increases between attention and right working-memory networks (Fillippi et al 2012). In a study of topological organization of human brain functional networks with 38 females and 48 males, a gender-hemisphere interaction was observed with males having a higher normalized clustering coefficient in the right hemispheric network but a lower clustering coefficient in the left hemispheric network (Tien et al 2012). A study of 16 healthy women and 15 healthy men has recently shown that women exhibited higher functional connectivity in general, including the prefrontal cortex, but menstrual cycle effects on resting states were not found (Hjelmervik et al, 2014). They concluded that sex differences in resting state fMRI may reflect sexual dimorphisms in the brain but not transitory activating effects of sex hormones on functional connectivity.

To our knowledge there are no studies on differences in cEEG or rsfMRI with respect to minorities or specific ethnicities.

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