Implementation of Acoustically Targeted Chemogenetics (ATAC) in Mice and Nonhuman Primates

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Neurological diseases affect a number of adults and have long-lasting impacts on everyday life. Existing and emerging techniques used to mitigate the effects of these diseases falter in a number of ways, including the lack of spatiotemporal control and the invasive nature of certain treatments. Acoustically Targeted Chemogenetics (ATAC) aims to rectify issues surrounding spatial, cell-type, and temporal specificity by utilizing a transient, non-invasive method, focused ultrasound blood brain barrier opening (FUS-BBBO), to transduce neurons with virally-encoded engineered chemogenetic receptors. These receptors then respond to systemically administered compounds, resulting in the activation or inhibition of neuronal activity. Developing ATAC for clinical usage involves a multilevel optimization operation to ensure scalability, efficacy, and safety. Optimization of this technique for application to the nonhuman primate (NHP) brain requires testing on mice to ensure that the lowest possible ultrasound pressure is being used without compromising efficacy. Analysis of histological data determined the optimal ultrasound pressure levels. Furthermore, a plan for implementation of ATAC in NHP was established for future studies.