therapeutic intervention for the prevention of impaired hypoglycemic counter-regulation in persons with diabetes.

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Low CD4 nadir linked to widespread cortical thinning in adults with HIV

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OBJECTIVES/GOALS: The history of immune suppression, especially CD4 nadir, has been shown to be a strong predictor of HIV-associated neurocognitive disorders (HAND). However, the potential mechanism of this association is not well understood. This study examined the relationship between CD4 nadir and brain atrophy. METHODS/STUDY POPULATION: Fifty-nine people with HIV participated in the cross-sectional study (mean age, 56.5±5.8; age range, 41-69; 15 females; 46 African-Americans). High resolution structural MRI images were obtained using a 3T Siemens scanner. From a comprehensive 7-domain neuropsychological test battery, a global deficit score (GDS) and HAND diagnoses were determined for each participant. The correlation between CD4 nadir (the lowest ever lymphocyte CD4 count) and cortical thickness was investigated using a vertex-wise non-parametric approach with a conservative statistical threshold of $p<0.05$ (FWE-corrected). RESULTS/ANTICIPATED RESULTS: Out of the 59 participants, 12 met standard Frascati criteria for asymptomatic neurocognitive impairment (ANI) and two met the criteria for mild neurocognitive disorder (MND). Across all participants, low CD4 nadir was associated with widespread cortical thinning, especially in the frontal and temporal regions. Higher GDS (indicating worse global neurocognitive function) was associated with bilateral frontal cortical thinning, and the association largely persisted in the subset of participants who did not meet HAND criteria. DISCUSSION/SIGNIFICANCE OF IMPACT: These results suggest that the low CD4 nadir may be associated with widespread neural injury in the brain, especially in the frontal and temporal regions. This spatial profile might contribute to the prevalence/phenotypes of HAND in the cART era, such as the frequently observed deficits in the executive domain.

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Magneto-electric nanoparticles (MENs) cobalt ferrite-barrium titanate (CoFe2O4–BaTiO3) for non-invasive neuromodulation†

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OBJECTIVES/GOALS: Our goal is to develop a non-invasive stimulation technique using magneto-electric nanoparticles (MENs) for inducing and enhancing neuronal activity with high spatial and temporal resolutions and minimal toxicity, which can potentially be used as a more effective approach to brain stimulation. METHODS/STUDY POPULATION: MENs compose of core-shell structures that are attracted to strong external magnetic field (~5000 Gauss) but produces electric currents with weaker magnetic field (~450 Gauss). MENs were IV treated into mice and drawn to the brain cortex with a strong magnetic field. We then stimulate MENs with a weaker magnetic field via electro magnet. With two photon calcium imaging, we investigated both the temporal and spatial effects of MENs on neuronal activity both *in vivo* and in vitro. We performed mesoscopic whole brain calcium imaging on awake animal to assess the MENs effects. Furthermore, we investigated the temporal profile of MENs in the vasculatures post-treatment and its toxicities to CNS. RESULTS/ANTICIPATED RESULTS: MENs were successfully localized to target cortical regions within 30 minutes of magnetic application. After wirelessly applying ~450 G magnetic field between 10-20 Hz, we observed a dramatic increase of calcium signals (i.e. neuronal excitability) both *in vitro* cultured neurons and *in vivo* treated animals. Whole brain imaging of awake mice showed a focal increase in calcium signals at the area where MENs localized and the signals spread to regions further away. We also found MENs stimulatory effects lasted up to 24 hours post treatment. MEN stimulation increases c-Fos expression but resulted in no inflammatory changes, up to one week, by assessing microglial or astrocytes activations. DISCUSSION/SIGNIFICANCE OF IMPACT: Our study shows, through controlling the applied magnetic field, MENs can be focally delivered to specific cortical regions with high efficacy and wirelessly activated neurons with high spatial and temporal resolution. This method shows promising potential to be a new non-invasive brain modulation approach disease studies and treatments.

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Mechanisms of Prophage-Mediated Virulence Driving Community-Acquired MRSA Contagion

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OBJECTIVES/GOALS: We recently identified a CA-MRSA strain in Brooklyn, New York (USA300-BKV) causing an outbreak of severe skin infections in predominantly healthy children. The evolution of USA300-BKV included acquisition of a novel prophage, and our objective is to identify the prophage-encoded gene(s) and mechanism responsible for increased bacterial virulence. METHODS/STUDY POPULATION: We deleted candidate genes from a novel mosaic block of phage-encoded genes in USA300-BKV that have been shown to enhance virulence in a murine skin infection model. Deletion mutants and complemented clones will be evaluated *in vivo* to identify culprit genes and determine the effect of lineage-specific genetic variation on the phenotype. Complementary studies include a comprehensive characterization of phage and bacterial genes expressed during lysogeny *in vitro* using RNA sequencing (RNA-Seq), and *in vivo* using a targeted approach focusing on known bacterial virulence and phage lytic pathways as well as candidate genes identified by *in vitro* studies. RESULTS/ANTICIPATED RESULTS: Comparison of otherwise isogenic lab strains showed that the mosaic block of phage genes present in USA300-BKV enhance skin abscess size in mice, confirming previous results. As this region of the phage, named mΦ11, does not contain known toxin genes, we hypothesize that mΦ11 modulates expression of bacterial host genes to enhance virulence. Thus, transcriptional profiles of CA-MRSA containing mΦ11 and selected deletion mutants are expected to reveal changes in known or novel virulence factors compared to controls. Candidate regulators specific to the mosaic block include an adenine methyltransferase linked to changes in global gene expression of other bacterial species. DISCUSSION/SIGNIFICANCE OF IMPACT: Our

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