The role of gut microbiota in the susceptibility of Parkinson disease development

Dimitri Koutouzis, Jose Antonio Pino, Sharona S. Harris, Marisol Quiroz, Mansour Mohamadzadeh and Gonzalo Enrique Torres

OBJECTIVES/SPECIFIC AIMS: Several clinical studies have established a correlation between changes in relative bacterial populations in the gut and Parkinson disease. However, few published experiments have been able to parse out whether these associations are causative or correlative. Our aim is to determine how bacteria in the gut may impact the health and resilience of dopaminergic signaling. Our experiment was designed to test whether a gut microbiome that is controlled by the gut microbiome is altered in mice with Parkinson disease. METHODS/STUDY POPULATION: Aged (3, 6, and 9) with 100 µg of bacteria exclusively used in this experiment. Mice were orally gavaged every 3 days (D0, D3, and D9) with 100 µg of bacteria. Mice were treated with PBS (control) or the gavage of bacteria suspension. Tissue preparation—brains were quickly extracted and the striatum was isolated and homogenized in either RIPA buffer with protease inhibitors (for Western blot analysis) or in 0.1 N HClO4 (for HPLC processing). The homogenates were processed through fractional centrifugation to remove cellular debris. Lysate samples were frozen at –80°C until ready for analysis. Protein expression quantification—expression of proteins were measured using intensity of bands from Western blots. Lysates were denatured prior to loading with 10% β-mercaptoethanol and 30-minute incubation at 37°C. All immunoblotting were normalized to immunoreactivity to α-tubulin. Immunoblot intensity was determined using the ImageJ software. Dopamine/dopamine metabolite quantification HPLC analysis was used to detect dopamine and dopamine metabolite concentration. Aliquots of the lysate were injected onto a C18 column using a mobile phase consisting of 50 mM H2NaO4P (pH 3.0). The mobile phase was pumped through the system at 0.3 mL/minute. RESULTS/ANTICIPATED RESULTS: Measured total dopamine concentration through HPLC analysis in the striatum showed no significant differences in the brain between mice. The metabolites DOPAC and HVA had an elevated measured concentration in the bacteria-treated group relative to the control group. Western blot analysis showed decreased immunoreactivity for DAT and TH in the bacteria-treated group compared with the control group. There was no significant difference in the immunoreactivity for VMAT2. DISCUSSION/SIGNIFICANCE OF IMPACT: This study demonstrates that dopamine signaling dynamics in the midbrain can be altered by changes in the gut flora in mice. These results further substantiate the impact of the gut-brain axis and may even point to a potential avenue of bolstering the resilience of dopaminergic neurons in preventing the onset of PD. Further experiments must be performed to understand the mechanism of the observed changes and to determine if these changes have any salutary effect.

Impacts of a long-term community-university partnership on investigator-initiated research at an Urban Research University

Emily Zimmerman, Chanel Bea, Alicia Aroche and Alex Krist

OBJECTIVES/SPECIFIC AIMS: Engaging Richmond is a community-university partnership, made up of local residents and university faculty and staff that was established in 2011 with an NIH supplement to a Clinical and Translational Science Research Award at Virginia Commonwealth University (VCU). The primary aims of the supplement were to (1) to conduct community-based participatory research (CBPR) on the leading causes of health disparities perceived by the Richmond community and (2) to thereby highlight community needs and assets and build capacity for future community-engaged research (CEnR). The goal was to prepare a community-focused, community-prioritized, health equity report while building capacity, strengthening relationships, and discovering local barriers to CEnR, and then to stimulate, facilitate, and inform future CEnR at VCU. METHODS/STUDY POPULATION: This is a case study exploring the impact of 1 community-university partnership on investigator-initiated research using historical and qualitative data. RESULTS/ANTICIPATED RESULTS: Although Engaging Richmond received only 12 months of support from the NIH supplement that provided its initial funding, the community-university partnership has worked continuously since its formation in 2011. This work has not only helped to build connections with the community and key stakeholders, it has also contributed substantially to the resources available to university faculty pursuing CEnR. Specifically, we find that Engaging Richmond has contributed to investigator initiated research in the following ways, either working as co-investigators or in a consultative capacity: consultation on proposal development (5 projects); assisted with instrument development (4 projects); participant recruitment (7 projects); data collection and analysis (6 projects); dissemination (5 projects). In addition to collaboration on projects, Engaging Richmond has increased institutional capacity for CEnR through its contributions to the Annual Community Engaged Institute at the university and the Center of Clinical and Translational Science’s Community Review Board (CRB). The CRB helps researchers work successfully in a community setting, enhance the research design, help to improve study implementation and assist with translation and dissemination of findings.

Effects of cortical stimulation of the noninfarcted Versus peri-infarcted motor cortex

Seraña-Kaye Kinley-Cooper and DeAnna Adkins

OBJECTIVES/SPECIFIC AIMS: The objectives of this study are to determine whether high-frequency ipsi-lesion or low-frequency contra-lesion ECS improves forelimb function following experimental stroke in aged animals with focal and large strokes. We also want to investigate whether ECS-induced improvements in motor function are related to an enhancement of neural structural plasticity (dendrites and synapses) and changes in growth promoting (BDNF) and growth inhibiting (Nogo-A) expression in the infarcted motor cortex in young and aged animals. METHODS/STUDY POPULATION: We will...