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Impaired emotion recognition accuracy after right-hemisphere stroke

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OBJECTIVES/SPECIFIC AIMS: Every year, approximately 800,000 Americans suffer a stroke. Supportive social environments are recognized as an important factor contributing to successful stroke recovery, yet, stroke lesions can affect brain areas important for socioemotional functioning, which could impair a patient's ability to maintain their social relationships. Specifically, emotion recognition, a fundamental socioemotional skill, is predominantly right-lateralized and may be impacted by right-hemisphere stroke. This research tests for emotion recognition impairments after right-hemisphere stroke and examines whether such deficits are associated with worse reported social support. METHODS/STUDY POPULATION: Twenty right-hemisphere stroke patients (9 female, 11 male) and 23 age-matched healthy control subjects (9 female, 14 male) completed laboratory testing including the Geneva Emotion Recognition Test Short. Subjects additionally completed a measure of self-reported social support using the Older Americans Resources and Services questionnaire. Emotion recognition accuracy was calculated using overall accuracy and valence accuracy (i.e. correctly rating a positive emotion as positive). RESULTS/ANTICIPATED RESULTS: Right-hemisphere stroke patients had lower overall emotion recognition accuracy than controls (patients; $M = 37.8\%$, $SD = 18.9\%$. controls; $M = 48.5\%$, $SD = 14.6\%$, $t(41)=2.11$, $p=.041$). Furthermore, patients had significantly lower valence accuracy (patients; $M = 84.5\%$, $SD = 10.7\%$. controls; $M = 90.0\%$, $SD = 5.2\%$, $t(41)=2.19$, $p = .035$), indicating that they more often mistook a positive emotion as a negative emotion, and vice-versa. Finally, within the right-hemisphere patient group, overall emotion recognition accuracy was trending to be positively correlated with self-reported social support ($rho = 0.397$, $p = .083$), suggesting that poor emotion recognition skills may be associated with worse social outcomes in the real-world. DISCUSSION/SIGNIFICANCE OF IMPACT: Our findings indicate that right-hemisphere stroke is associated with impaired emotion recognition. Future research could investigate whether an emotion recognition training may be beneficial for right-hemisphere stroke patient recovery.

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Juvenile Polyposis Syndrome Patients Without a Mutation in SMAD4 or BMPR1A: Clinical Presentation and Novel Drivers of Disease

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OBJECTIVES/SPECIFIC AIMS: Juvenile Polyposis Syndrome (JPS) is an inherited cancer predisposition syndrome sometimes attributed to a germline mutation in SMAD4 or BMPR1A. However, many patients meet clinical criteria for JPS without having a pathogenic alteration in either gene. Herein, we perform a cross-sectional analysis of JPS patients at a pediatric and adult tertiary referral center to understand potential differences in the clinical presentation and outcomes of patients with or without a known causative gene mutation. Additionally, we conduct whole exome sequencing (WES) on a subset of the pediatric patients to evaluate for novel genomic drivers of disease. METHODS/STUDY POPULATION: Data were abstracted from medical charts using IRB-approved protocols at the Children's Hospital of Philadelphia (CHOP) and the University of Pennsylvania (Penn). Records were reviewed for patients with a clinical diagnosis of JPS and genetic testing result and seen at either institution in the last 10 years (2008-2018). Patients recruited for sequencing were consented for blood draw through the CHOP IRB protocol, and had whole exome sequencing completed at 70X depth, with data analyzed through institutional pipeline. RESULTS/ANTICIPATED RESULTS: Records were reviewed for 41 patients at CHOP and 19 patients at Penn, for a total of 60 JPS patients. Mean age of CHOP cohort was 11 years: 58.5% male, mean length of follow up 3.9 years. Mean age Penn cohort was 33 years: 47.4% male, mean length of follow up 9.3 years. In the pediatric cohort, 7 patients (17%) had a mutation in BMPR1A (n=6) or SMAD4 (n=1); in the adult cohort, 15 patients (79%) had a mutation in BMPR1A (n=3) or SMAD4 (n=12). The average number of polyps in the pediatric cohort was not significantly higher in patients with a SMAD4 or BMPR1A mutation (9.3 polyps/year of surveillance with a SMAD4 or BMPR1A mutation, vs 5.7 polyps/year; p=0.19). In combined cohort review, all individuals that required gastrectomy and/or colectomy (n=8) as well as all those who developed gastrointestinal cancer (n=3) had a mutation in SMAD4 or BMPR1A. Of the patients who underwent whole exome sequencing (n=13), potential causative germline mutations were identified in four patients (30.8%); all potential drivers identified were within the TNF/BMP pathway. DISCUSSION/SIGNIFICANCE OF IMPACT: This data from a dual-institution review demonstrates that the rate of SMAD4/BMPR1A mutation in JPS is lower in a pediatric cohort compared to an adult cohort. Furthermore, although individuals with JPS may have similar clinical presentations in childhood regardless of whether or not a causative mutation is present, the presence of a mutation in SMAD4 or BMPR1A is associated with a more severe course of disease in adulthood. Further study and a larger cohort will be required to fully validate these findings. Approximately 30% of patients who underwent germline WES had a potential novel driver identified, with further validation underway.

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Longitudinal Recovery of Speech Motor Function Following Facial Transplantation

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OBJECTIVES/SPECIFIC AIMS: Using a novel biomechanical-based motor speech assessment alongside commonly used clinically-based motor speech assessments, the goal of this study was to describe longitudinal recovery in speech movements and functional speech in a cohort of 5 patients following facial transplantation. METHODS/STUDY POPULATION: Five participants who had received either full or partial face transplantation were included in this study. Each participant received a unique facial graft from their donor, which included varied amounts of soft tissue, facial musculature, nerve, and bone. Two participants were early in the recovery period and were assessed from zero to 24 months post-transplantation. Three participants were late in the recovery period and were assessed from 36 to 60 months post-transplantation. Each participant completed two data collection sessions and the average time between sessions was 20.4 months. At each session, orofacial movements were recorded using a 3D motion capture system. A 4-sensor head marker

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was used to subtract head movement (translation and rotation) from the facial markers. The analyses in this study were restricted to two markers: midline lower lip and a virtually calculated midline jaw marker. A marker at the top of the nose bridge was used as the origin point. The following kinematic variables were obtained from each lip-jaw movement time-series: peak movement speed (mm/s), and displacement (mm). Each patient was instructed to perform 10 repetitions of the phrase "buy bobby a puppy" at his or her typical speaking rate and volume. Sentence-level intelligibility was obtained using the Sentence Intelligibility Test (SIT) and word-level intelligibility was obtained using the Word Intelligibility Test, using standard procedures. Intelligibility, measured in percentage of words correctly transcribed, and speaking rate, measured in words per minute (wpm), was derived from the SIT sentences for each patient. Intelligibility, measured in percentage of words correctly chosen via multiple choice was derived from the Word Intelligibility Test. RESULTS/ANTICIPATED RESULTS: Effect sizes (Cohen's d) across the 10 trials of "buy bobby a puppy" were computed to assess the effects of recovery time on range of motion and speed of the lower lip alone, the jaw alone, and the lower lip and jaw together for both range of motion and for speed. The largest effect sizes were observed for increased range of motion and increased speed of the articulators for participants within 24 months of surgery. Smaller effect sizes were observed for these parameters for the participants in the later stages of recovery, with some participants showing declines in range of motion and speed of some but not all articulators. Descriptive statistics indicate that both speech and word intelligibility improvements are most notable in the first two years following transplantation and appear to plateau during the later stages of recovery. Only two out of five of our participants achieved "normal" speech intelligibility (i.e., >97%) at five years post-transplantation. DISCUSSION/SIGNIFICANCE OF IMPACT: Biomechanical assessment revealed that kinematic recovery of articulator range of motion and speed appears most significant in the first two years following surgery, but that improvement continues to some degree as far as five-years post-transplant. Clinically-based assessments suggest that gains in intelligibility appear to plateau by 3-years post-surgery.

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Mechanisms of sebaceous skin microbial community remodeling through microenvironment modulation.

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OBJECTIVES/SPECIFIC AIMS: To understand the mechanisms of how a non-antimicrobial can reshape a commensal microbe community to cure a ubiquitous human disease. METHODS/STUDY POPULATION: Whole genome sequencing of bacterial isolates, metabolomic investigations of previously collected skin microbe isolates from patients, and structural investigations of a protein from these skin microbes. RESULTS/ANTICIPATED RESULTS: Metabolic pathways associated with adaptation to a changing skin microenvironment, novel antimicrobial characterization, and a structural understanding of a novel nutrient acquisition protein. DISCUSSION/SIGNIFICANCE OF IMPACT: Multiple angles of this investigation are poised to improve current non-antimicrobial dermatologic treatments and they have the potential to impact microbe-related diseases in other human microenvironments.

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Mesenchymal Stem Cell Extracellular Vesicle Delivery in a Shear-Thinning Hydrogel For Therapy in an Acute Myocardial Infarction Model: A Comparative Analysis

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OBJECTIVES/SPECIFIC AIMS: The primary aim is to assess differences in therapeutic effect between MSC and EPC EVs on acute ischemic rat hearts through delivery in a biocompatible and shear-thinning hydrogel. Primary outcomes for therapeutic assessment include an in-vitro angiogenesis assay and in-vivo hemodynamic analysis, mainly identifying differences in ejection fraction and contractility. Secondary hemodynamic outcomes include cardiac output, stroke volume, and end-diastolic pressure volume relationship (EDPVR). Secondary structural outcomes include post-mortem scar analysis and immunohistochemistry (IHC) staining for angiomyogenesis. METHODS/STUDY POPULATION: MSCs and EPCs will be cultured according to previously published protocols. EVs will be isolated from cultured cell lines through precipitation methods with polyethylene glycol. EVs will be qualitatively analyzed with nanoparticle tracking analysis (NTA) and flow cytometry. The shear thinning hydrogel (STG) will be constructed using a hyaluronic backbone conjugated to adamantane or beta-cyclodextrin, ultimately facilitating guest-host interactions with shear thinning properties. Controls and treatment groups mixed with the hydrogel will be injected into the border zone of infarcted Wistar rat hearts immediately following a left anterior descending artery ligation. Hemodynamic assessment will be performed at four weeks through left ventricular catheter based pressure-volume recordings. Ex-vivo analysis will include scar thickness assessment using Masson collagen staining and IHC stain for vessel (anti-vonWillebrand factor; anti-Isolectin) and myocyte formation (anti-cardiac Troponin I). RESULTS/ANTICIPATED RESULTS: We hypothesize that, in-vitro, MSC-EVs will demonstrate non-inferior angiogenic potential as compared to EPC-EVs. We posit that MSC-EVs will demonstrate superior therapeutic effect to EPC-EVs in-vivo as measured by functional hemodynamics and structural assessment. We have successfully isolated MSC and EPC EVs and have validated uniformity across EV populations (Figure 1). Preliminary data from the angiogenesis assay (n=3) demonstrated that MSC-EV and EPC-EV produce non-significantly different angiogenic potential as measured by number of vascular meshing extremes (p=0.144) and length of master vascular segment (p=0.193), with significant differences compared to either positive or negative controls. DISCUSSION/SIGNIFICANCE OF IMPACT: Novel regenerative therapies are needed for patients with a history of AMI given current limitations to therapy and sequelae of ischemic heart disease. Delivery of extracellular vesicles through a shear-thinning gel is a novel "off-the-shelf" translational approach to address the current clinical need.

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Metabolomic Markers of Methotrexate Response in Juvenile Idiopathic Arthritis

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OBJECTIVES/SPECIFIC AIMS: In this study, a semi-targeted metabolomics approach is used to identify metabolic markers of

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