We aim to examine the intrinsic activity of a functional pathway in patients with chronic orofacial pain. METHODS/STUDY POPULATION: This is the second phase of a parent study examining genetics, placebos, and the brain in temporomandibular disorders (TMD). We intend to recruit 120 of the original 398 TMD patients for this phase. Participants completed the Graded Chronic Pain Scale to assess TMD pain intensity and disability and the Pain Catastrophizing Scale. Behaviorally, pain catastrophizing scores and pain intensity and disability will be analyzed using structural equation modeling. Resting-state functional magnetic resonance imaging will be used to record intrinsic brain activity. The functional connectivity between the posterior cingulate, anterior insula, and periaqueductal grey will be assessed as a causal pathway relating pain catastrophizing to pain intensity and disability. Mediation analyses will be used to test causality. RESULTS/ANTICIPATED RESULTS: We anticipate that greater engagement in catastrophic thinking about pain increases the functional connectivity strength between the posterior cingulate, anterior insula, and periaqueductal grey, which ultimately leads to heightened perception of pain intensity and disability. Therefore, we expect to see increased functional connectivity in those with high pain catastrophizing levels as compared to those with low pain catastrophizing levels, and that this pathway will mediate the relationship between pain catastrophizing and pain intensity and disability. Further, we predict that helplessness will most strongly correlate with the change in functional connectivity as compared to rumination and magnification. Results will be presented in full at the conference. DISCUSSION/SIGNIFICANCE: Understanding how pain catastrophizing can influence chronic pain pathways will not only promote a more integrative approach to chronic pain management but will also help identify the mechanisms by which pain itself develops and persists in the particularly vulnerable pain population of TMD.

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Efficacy of the Insulin Infusion Calculator Protocol in the Optimization of Perioperative Blood Glucose Levels in the Cardiac Surgical Patients at UAB

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OBJECTIVES/GOALS: Insulin dosing is crucial for regulating blood glucose in cardiac surgery patients, yet it requires the use of cumbersome insulin dosing charts. To streamline this process, an electronic insulin calculator (IC) is trialed in the cardiac operating rooms and intensive care unit. This study compares glycemic control prior to and after institution of IC. METHODS/STUDY POPULATION: Using the EHR, a retrospective population of 3,164 cardiac surgery patient charts from 12/19/19 - 11/06/20 were obtained. Baseline, intra-operative, and ICU blood glucose values were obtained from each patients admission. Using this data, a baseline level of glycemic control throughout a cardiac surgery patients stay was established. A preliminary cohort of 244 patients were then chosen to be managed with the new IC. Baseline, intra-operative, and ICU blood glucose values were obtained in this group for comparison. Paired t tests were used to compare the IC group of patients to the retrospective group of patients. Additional subgroup analysis was performed to assess IC efficacy for on pump vs off pump cardiac surgeries. RESULTS/ANTICIPATED RESULTS: The 244 patients managed with the IC showed significantly reduced average blood glucose values during their time in the ICU compared to those previously not managed with the IC (185 mg% vs 153 mg%, p= 0.02). Additionally, a trend towards a reduction in last operating room blood glucose level was also noted. Lastly, average blood glucose levels were significantly reduced for patients undergoing on pump cardiac surgeries compared to off pump surgeries (157 mg% vs 149 mg%, p = 0.03). DISCUSSION/SIGNIFICANCE: Preliminary results suggest IIC to be associated with better intra and postoperative blood glucose control. More data is being collected to test its association with outcomes.

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Semaphorin7a expression in breast cancer promotes susceptibility to immune checkpoint blockade*

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OBJECTIVES/GOALS: The goal of this study is to decipher the mechanisms by which breast cancers evade the immune system to facilitate metastasis through the lymphatic vasculature. We believe this is caused, in part, by semaphorin 7A (SEMA7A) as its expression is associated with increased lymphatic vessels, tumor-associated macrophages, and metastasis in breast cancer. METHODS/STUDY POPULATION: We have observed that breast cancer cells, lymphatics, and macrophages exhibit SEMA7A-dependent expression of PD-L1 in vitro, which may make SEMA7A+ tumors more sensitive to anti-PD-1/PD-L1 immunotherapies. Therefore, we utilized multiple orthotopic, immunocompetent mouse models to determine if SEMA7A expression makes tumors more susceptible to immune checkpoint blockade. E0771 and 66cl4 mouse mammary carcinoma cells were injected orthotopically into the #4 mammary fat pads. Once tumors reached 50-100 mm^3 mice were injected intraperitoneally with 250ug of anti-PD-1, anti-PD-L1, or IgG control every third day. Tumors were measured with calipers every other day and harvested for flow cytometry to determine the effect of immune checkpoint blockade on the TME in SEMA7A+ tumors. RESULTS/ANTICIPATED RESULTS: We reveal that growth of SEMA7A overexpressing (OE) tumors, but not controls, was significantly slowed with both anti-PD-1 and anti-PD-L1 treatments. Flow cytometric analysis of cells from the TME revealed increased LECs, TAMs, and PoEMs in SEMA7A+ tumors, compared to controls – all populations had higher PD-L1 expression, which was decreased with both anti-PD-1 or anti-PD-L1. We also observed a decrease in PD-L1 expression on the tumor cells with treatment. Furthermore, LEC, TAM, and PoEM presence was decreased within the TME alongside increased presence of activated CD4 and CD8 T cells. Collectively, our results suggest that SEMA7A expression in breast cancers activates a major pathway associated with immune evasion and helps to establish a pro-tumor microenvironment. DISCUSSION/SIGNIFICANCE: SEMA7A expression establishes a pro-tumor microenvironment, which can be targeted with readily available FDA approved drugs such as immune checkpoint-based therapies. Since SEMA7A+ breast cancers have high rates of metastasis, more specific treatments for these patient populations should be explored.

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