We aim to determine the ECM ligands responsible for cell-ECM mediated mechanotransduction and the resulting phenotype in PCMs. METHODS/STUDY POPULATION: HiPSCs are differentiated to PCM and replated on substrate with 5 or 15 kPa PDMS that are coated with 5 or 25 ug/cm of either collagen I or fibronectin at sub-confluent density to restrict junction engagement to only costameres. Then, PCM are subjected to 10% cyclic mechanical strain at 1 Hz for 48 hours, with static culture as control. PCMs from all conditions are subsequently fixed and stained for cardiomyocyte-specific troponin T (TnT), pacemaking HCN4 channel, and pro-pacemaking transcription factors (Shox2, Isl1, Tbx3, Tbx18). Additionally, PCM cell size will also be assessed. RESULTS/ANTICIPATED RESULTS: Considering the amount of hypertrophy and myofilament in CMs correlates with mechanical strain, we expect a reduced degree of mechanotransduction in hiPSC-PCM on collagen I with a stiffness 15 kPa to induce smaller cell size with fewer myofilament and an upregulation of HCN4 and pro-pacemaking transcription factors than those on 5 kPa and those on fibronectin of either 5 or 15 kPa after cyclic strain. This is because COL1 is reported to have a lower signaling threshold but a limited sensitivity to force which contributes to the diminished mechanotransduction signaling. DISCUSSION/SIGNIFICANCE OF IMPACT: Effects of the microenvironment on hiPSC-PCMs via costamere mechanotransduction may provide insights for engineering biopacemakers with a suitable ECM, to potentially preserve automaticity in hiPSC-PCMs and sustain long-term pacemaking function, making biopacemakers a step closer to reality.

480

Shared mood and anxiety symptom variance as a prospective predictor of PTSD symptoms

Michelle Berry, Kavya Rajendran, Cristina Risco, Earta Norwood and Edward Bernat
The University of Maryland, College Park

OBJECTIVES/GOALS: Mood and anxiety disorders are a risk factor (Ozer et al., 2003) for posttraumatic stress disorder (PTSD) following trauma exposure. As such, a latent internalizing dimension may also be a risk factor. We examine how the shared variance between mood and anxiety symptoms (as in HiTOP; Kotov et al., 2021) impacts development of posttraumatic stress (PTS) symptoms, and symptom clusters. METHODS/STUDY POPULATION: Using data from a prior study of individuals who arrived at emergency rooms and were assessed at later time points (AURORA study; McLean et al., 2020), our sample included 1866 participants (1208 females, Mage = 38.49 years) with available data for the proposed analyses. A latent factor (INTtotal) was operationalized as the shared variance between mood and anxiety symptoms (PROMIS Anxiety and Depression; Cella et al., 2010) as well as PTS symptoms (PCL-5, Weathers et al., 2013). We computed a second internalizing factor excluding PTS symptoms (INTma) to isolate the contribution of baseline affect and anxiety from PTS at baseline. We examined how baseline PTS symptoms, INTtotal, and INTma compare as prospective predictors for PTS symptoms at later time points and how these variables predict individual PTS symptoms. RESULTS/ANTICIPATED RESULTS: Baseline INTma, INTtotal, and PTS symptoms were significant prospective predictors of PTS symptoms across all time points (all with $t > 10$, $p < .005$). When focusing on INTma relative to DSM-5 PTSD criterion (American Psychiatric Association, 2013), INTma significantly predicted later symptoms at six months posttrauma pertaining to Criterion D ($t = 18.88$, $p < .005$), negative alterations in cognition and mood, Criterion E ($t = 15.44$, $p < .005$) arousal and reactivity, and Criterion B, intrusion ($t = 15.44$, $p < .005$). INTma significantly predicted symptoms in Criterion C, avoidance, though to a lesser degree ($t = 12.87$, p DISCUSSION/SIGNIFICANCE OF IMPACT: These findings bolster the utility of examining PTSD risk factors through a transdiagnostic lens. INTma was predictive of later PTS symptoms, independent of baseline PTS. Our analyses reveal clinical implications for the assessment of PTSD, and the tailoring of treatment for patients high in internalizing following trauma exposure.

481

Endoscopic third ventriculostomy versus ventriculoperitoneal shunting for treatment of hydrocephalus in patients with myelomeningocele

Sasidhar Karuparti, Francisco Narro Garcia, Ashlynn Lizer and Jennifer M. Strahle
Washington University in St. Louis School of Medicine

OBJECTIVES/GOALS: Optimal hydrocephalus treatment with permanent cerebrospinal fluid (CSF) diversion in myelomeningocele (MMC) patients is not well understood, especially how treatment response varies with time of MMC repair. We evaluate two treatment methods in this population–endoscopic third ventriculostomy (ETV) and ventriculoperitoneal shunting (VPS). METHODS/STUDY POPULATION: We retrospectively identified patients from St. Louis Children's Hospital who were diagnosed with MMC prenatally and underwent either prenatal or postnatal repair and subsequently underwent permanent treatment for hydrocephalus (VPS or ETV +/- choroid plexus cauterization) between 2018 and 2024. The primary outcome was failure (defined as need for revision) of procedure and time to failure. All revisions were shunt insertions/revisions. Differences in preoperative and 6-month postoperative head circumference (HC) and WHO standard HC z-score were examined. Differences in preoperative and 6-month follow-up fronto-occipital horn ratios (FOHR), a validated age-independent measure of CSF within the brain, on CT and MRI were additionally examined. RESULTS/ANTICIPATED RESULTS: Eighty-three MMC patients were identified. 46 (55%) underwent CSF diversion: 37 (80.4%, 9 pre- and 28 postnatal) VPS and 9 (19.6%, 5 pre- and 4 postnatal) ETV +/- choroid plexus cauterization. Six (16%) VPS patients required revision vs. 3 (33%) ETV patients (Δ17%; 95% CI -9 – 50). Mean time to failure was longer after VPS vs. ETV (516, SD 470 vs. 34, SD 7 days) [Δ482; 95% CI 163 – 800]. The decrease between pre- and postoperative FOHR was greater after VPS vs. ETV (6 mo: -0.14, SD 0.10 vs. -0.03, SD 0.07) [Δ0.11; 95% CI 0.04 – 0.18]. Differences in pre- and postoperative HC were similar (VPS 5.67, SD 2.91 vs. ETV 4.04, SD 1.66 cm) [Δ1.63; 95% CI -0.71 – 3.98]. Greater, but not significant, z-score decreases were seen after VPS vs. ETV (-1.04, SD 2.22 vs. -0.13, SD 1.11) [Δ-0.91; 95% CI -2.68 – 0.86]. Similar trends were observed in pre- and postnatal MMC repair groups. DISCUSSION/SIGNIFICANCE OF IMPACT: Failure rates in MMC-associated hydrocephalus patients were greater in the ETV group, but no definitive conclusion can be made due to imprecision. Those treated with ETV have less time to failure and smaller FOHR decreases than those treated with VPS, indicating less CSF drainage. Due to the need for more subjects, future research should be multicenter.

https://doi.org/10.1017/cts.2024.1072