416

MRI Findings in Preterm Infants Associated with Strabismus*

Jacob I. Strelnikov[1], Rachel Lean[2], Christopher D. Smyser[2,3,4], Cynthia Rogers[2,3], Mae Gordon[1], John R. PruettJr.[2], Susan Culican[3], Savannah Seupaul[1], Alisha Dhallan[1] and Margaret Reynolds[1]
[1]Department of Ophthalmology & Visual Sciences, Washington University School of Medicine, USA; [2]Department of Psychiatry, Washington University School of Medicine, USA; [3]Department of Pediatrics, Washington University School of Medicine, USA; [4]Department of Radiology, Washington University School of Medicine, USA and [5]Department of Ophthalmology and Visual Neurosciences, University of Minnesota Medical School, USA

OBJECTIVES/GOALS: Prematurity and perinatal brain injury are known risk factors for strabismus. In this study, we sought to understand the link between neonatal neuroimaging measures in very preterm infants and the emergence of strabismus later in life. Study findings may inform if neonatal brain MRI could serve as a prognostic tool for this visual disorder. METHODS/STUDY POPULATION: This study draws from a longitudinal cohort of very preterm infants (VPT, < 30 weeks gestation, range 23 – 29 weeks) who underwent an MRI scan at 36 to 43 weeks postmenstrual age (PMA). Anatomic and diffusion MRI data were collected for each child . A subset of thirty-three patients in this cohort had records of an eye exam, which were reviewed for a history of strabismus. Patients with MRI scans demonstrating cystic periventricular leukomalacia or grade III/IV intraventricular hemorrhage were classified as having brain injury. Clinical variables with a known association to strabismus or diffusion metrics were included in a multivariable logistic regression model. Diffusion tractography metrics were screened for association with strabismus on univariable analysis prior to inclusion in the regression model. RESULTS/ANTICIPATED RESULTS: A total of 17/33 (51.5%) patients developed strabismus. A logistic regression model including gestational age, PMA at MRI, retinopathy of prematurity (ROP) stage, brain injury, and fractional anisotropy of the right optic radiation was significant at the .001 level according to the chi-square statistic. The model predicted 88% of responses correctly. Each decrease of 0.01 in the fractional anisotropy of the right optic radiation increased the odds of strabismus by a factor of 1.5 (95% CI 1.03 – 2.06; p = .03). Patients with brain injury had 15.8 times higher odds of strabismus (95% CI 1.1 – 216.5; p = .04). Gestational age (OR 1.7; 95% CI 0.9 – 3.3; p = .1) and stage of ROP (OR 0.6; 95% CI 0.2 – 2.0; p = .4) were not significant predictors of strabismus in the multivariable model. DISCUSSION/SIGNIFICANCE: Our findings suggest that strabismus in VPT patients may be related to specific changes in brain structure in the neonatal period. The identified association between neonatal optic radiation microstructure and strabismus supports the possibility of using brain MRI in very preterm infants to prognosticate visual and ocular morbidity.

417

Identifying Biomarkers of Social Threat Sensitivity Associated with Social Anxiety and Depressive Symptoms in Adolescents*

Madison Politte-Corn[1] and Kristin A. Buss[2]
[1]Penn State Clinical and Translational Science Institute and [2]The Pennsylvania State University

OBJECTIVES/GOALS: Increases in anxiety and depression during adolescence may be related to increased biological reactivity to negative social feedback (i.e., social threat sensitivity). Our goal was to identify biomarkers of social threat sensitivity, which may provide unique etiological insight to inform early detection and intervention efforts. METHODS/STUDY POPULATION: Adolescents aged 12-14 (N=84; 55% female; 80% White; 69% annual family income <$70,000) were recruited. Youth viewed a series of happy, neutral, and angry faces while eye-tracking and electroencephalogram (EEG) data were recorded to capture cognitive and neural markers of sensitivity to social threat (i.e., an angry face). Fixation time and time to disengage from angry faces were derived from eye-tracking and event-related potentials were derived from EEG, which index rapid attention capture (P1), attention selection and discrimination (N170), and cognitive control (N2). Adolescents also completed a social stress task and provided salivary cortisol samples to assess endocrine reactivity. Social anxiety and depressive symptoms were self-reported concurrently and one year later. RESULTS/ANTICIPATED RESULTS: Latency to disengage from threatening faces was associated with lower N2 amplitudes (indexing poor cognitive control; r= -.24, p = .03) and higher concurrent social anxiety (r = .28, p = .01). Higher N170 amplitudes, reflecting attentional selection and discrimination in favor of threatening faces, predicted increases in depressive symptoms one year later (b= .88, p = .02). No other neurophysiological measures were associated with each other or with concurrent or prospective symptomatology. DISCUSSION/SIGNIFICANCE: Eye-tracking and EEG measures indexing difficulty disengaging from social threat and poor cognitive control may be biomarkers of social anxiety, which could be utilized as novel intervention targets. High N170 amplitudes to social threat, derived from EEG, may have clinical utility as a susceptibility/risk biomarker for depressive symptoms.

418

The antiplatelet effects of EPA, an omega-3 fatty acid, are mediated by its 12-lipoxygenase metabolite, 12-HEPE

Krista Goerger[1], Taekyu Lee[1], Devin Gilmore[1], Michelle Tran[2], Theodore R. Holman[2] and Michael Holinstat[1]
[1]University of Michigan and [2]University of California Santa Cruz

OBJECTIVES/GOALS: To determine whether cardioprotective effects observed in individuals taking dietary supplementation with eicosapentaenoic acid (EPA), an ω-3 polyunsaturated fatty acid, are realized by altering platelet function, and if these effects are mediated through the 12-lipoxygenase derived metabolite, 12-hydroxyeicosapentaenoic acid (12-HEPE). METHODS/STUDY

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POPULATION: Washed platelets or platelet rich plasma from healthy human donors were treated with EPA and 12-HEPE to assess their ability to inhibit platelet activation. Platelets were stimulated with agonists targeting different steps of the hemostatic response to vascular injury. Platelet aggregation, dense granule secretion, surface expression of integrin αIIbβ3 and P-selectin, and clot retraction were analyzed. To assess signaling through Gαs-GPCRs and protein kinase A activity, phosphorylation of vasodilator-stimulated phosphoprotein (VASP) was examined via western blot following treatment with EPA or 12-HEPE. RESULTS/ANTICIPATED RESULTS: EPA and 12-HEPE dose-dependently inhibit both collagen and thrombin-induced platelet aggregation. Furthermore, 12-HEPE more potently attenuates dense granule secretion and surface expression of platelet activation markers, integrin αIIbβ3 and P-selectin, in comparison to EPA. Plasma treated with EPA delayed thrombin-induced clot retraction, while 12-HEPE had no effect. Additionally, treatment with 12-HEPE increases phosphorylation of VASP, suggesting it could signal through the activation of the eicosanoid Gαs-GPCRs. DISCUSSION/SIGNIFICANCE: Here, we show for the first time that EPA directly inhibits platelet activation through its 12-LOX metabolite, 12-HEPE. These findings provide further insight into the mechanisms underlying the cardioprotective effects of EPA. A better understanding of current PUFA supplementations can inform treatment and prevention of cardiovascular diseases.

419

Intramuscular immunization with rVCG-MECA vaccine elicits stronger chlamydial specific immune response than intranasal immunization

Medhavi FNU, Tanner Tayhlor, Richardson Shakyra, Jones Leandra, Bell Counrtnee, Josesph U. Igietseme, Omosun Yusuf and Eko Francis
Morehouse School of Medicine

OBJECTIVES/GOALS: We prioritize Chlamydia's public health impact, aim to develop rVCG-MECA for practical use, study robust immunity for effective strategies, and assess animal models for human vaccination adaptation. Our work highlights rVCG-MECA's translational significance in public health. METHODS/STUDY POPULATION: Female Mice C57BL/6J mice (N=8) were immunized intramuscularly(IM) and intranasally(IN) and boosted twice, two weeks apart, with rVCG-MECA, once with live Chlamydia (C. trachomatis serovar D elementary bodies) and PBS. Specific mucosal and systemic immune responses were characterized. Vaccine efficacy was determined from chlamydia shedding following the transcervical challenge. Additionally, Chlamydia-specific cytokine (IFN-γ and IL-4) production by splenic and ILN T cells was assessed after 16 weeks RESULTS/ANTICIPATED RESULTS: Immunization with rVCG-MECA via intramuscular and intranasal routes triggered notable humoral responses in systemic and mucosal tissues. Intramuscular vaccination produced higher IgG2c levels in both tissues, while intranasal vaccination led to elevated IgA levels in mucosal tissues. rVCG-MECA-immunized mice exhibited significantly higher IFN-γ (Th1) secretion compared to IL-4 (Th2), with intramuscular immunization showing the highest IFN-γ levels. These findings anticipate robust immune responses, promising protection against Chlamydia, particularly through the intra muscular route. Overall, our results support rVCG-MECA as a promising Chlamydia vaccine, aligned with public health goals. DISCUSSION/SIGNIFICANCE: This study suggests that IM and IN immunization with rVCG-MECA induces immune effectors such as IFN-gamma and IgG2c that mediate chlamydial clearance in the genetical tract.

420

Computable Phenotyping with "Big Data" as a Foundation for Artificial Intelligence Algorithm Construction: Puberty as a Transdisciplinary Case Example

David (DJ) SchnabelJr. and Lorah D. Dorn
The Pennsylvania State University

OBJECTIVES/GOALS: Artificial intelligence (AI) depends on quality machine learning (ML) algorithms constructed with high-quality training data. This TL1 trainee project develops a disease-agnostic computable phenotype framework for ML algorithm construction, modeling male puberty as a case example. METHODS/STUDY POPULATION: A computable phenotype of male puberty was constructed to answer the question: "Does early pubertal timing increase the risk of developing type II diabetes (T2D) in males?" A computable phenotype of males < 18 years old was created in the TriNetX© Diamond Network utilizing Boolean operator data queries. TriNetX© contains patient electronic health record information (ICD-10 diagnoses, anthropometric measures). An exploratory analysis of patient counts reflecting various computable phenotypes allowed for outcome (T2D) comparison of males diagnosed with precocious puberty (E30.1, ICD code for early pubertal timing) to those without, controlling for body mass index (BMI). RESULTS/ANTICIPATED RESULTS: Subjects (n=12,996,132) displayed the following computable phenotype: Male, < 18 years old, without ever having a BMI documented >85th percentile. Males diagnosed with precocious puberty (E30.1) were 6.89 times more likely to develop T2D when aged 14-18 years old than those without (OR 6.89, 95% CI: 5.17-9.19, p<0.0001). Next steps involve training a ML model on each computable phenotype groupings' health data, with anticipated results identifying underlying salient pathophysiologic variables. A generalized computable phenotype approach is further developed to: 1) explore clinical questions in large databases like TriNetX©, and 2) model disease development with AI/ML algorithm construction. DISCUSSION/SIGNIFICANCE: Computed phenotypes reveal males with precocious puberty may have increased T2D risk. Next steps utilize subject data to train an AI/ML algorithm, model development to identify salient pathophysiologic variables, and synthesize a generalized AI/ML developmental research framework for dissemination.

423

Innovation in MS Patient Care: Linking Cognitive Health and Myelin Integrity

Ashley Pike, GA James, ML Calvert, CD Kilts, RL Archer and T Wolfe
University of Arkansas for Medical Sciences (UAMS)

OBJECTIVES/GOALS: Our objective is to develop a patient-friendly application addressing the progression of cognitive impairments in multiple sclerosis (MS) patients. This initiative aims to augment individualized care and precision management of a major MS comorbidity by generating a cognitive health brain map for each patient. METHODS/STUDY POPULATION: Using the UAMS COMS

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