thereafter ($p < 0.0001$). Etv6 expression decreases as B cells develop and is negatively correlated with Pax5 expression ($r^2 = 0.9993$; $p = 0.0167$). We next confirmed the expression patterns of ETV6 and PAX5 during B cell development in human samples. We found that ETV6 expression was higher in the early B cell fraction (CD10+, CD34+, CD19−, and CD20−) compared to the pre-B cell fraction (CD10+, CD34−, CD19+, CD20−). Conversely, we observed that PAX5 expression was higher in the preB cell fraction compared with the early B cell fraction. In Ba/F3 cells expressing ETV6 constructs, ETV6, but not ETV6 P214L overexpression significantly decreased Pax5 expression ($p \leq 0.05$). ETV6 is associated with the proximal GGAA site 72 base pairs upstream of the Pax5 TSS, but not GGAA sites further from the TSS. In addition, the transcriptional repressors SIN3A and HDAC3 were detected on the same regions of the Pax5 locus. We detected association of ETV6, SIN3A, and HDAC3 with the proximal GGAA site upon expression of WT ETV6, but not ETV6 P214L. DISCUSSION/SIGNIFICANCE OF IMPACT: Our results provide a mechanism of interaction for ETV6 and PAX5, 2 genes often disrupted in B-cell leukemia. These findings are significant because PAX5 misregulation results in a B cell development halt, lineage infidelity, and leukemogenesis. In continuing our studies, we have generated a transgenic mouse endogenously expressing the ETV6 P214L mutation by CRISPR/Cas9 editing, and these mice appear to have a thrombocytopenic phenotype similar to that observed in patients carrying the ETV6 P214L mutation. These animals will be the focus of our continued investigation of the mechanism by which ETV6 germline mutation results in a predisposition to leukemia. Our ultimate goal is a comprehensive understanding of how this process may be targeted more efficiently in patients with both heritable and sporadic forms of leukemia involving ETV6.

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Sleep, biological stress, and health in a community sample of toddlers living in socioeconomically disadvantaged homes

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OBJECTIVES/SPECIFIC AIMS: The purposes of this study are to examine the relationships among sleep characteristics (duration, efficiency), stress biomarkers, and child behavior problems among toddlers living in socioeconomically disadvantaged homes and how these characteristics change over time from age of 12 months to 24 months. Aim 1: examine changes in subjective and objective sleep characteristics from 12 to 24 months of age. Aim 2: examine changes in stress biomarkers from 12 to 24 months of age. Aim 3: examine the cross sectional and longitudinal relationships between sleep characteristics and stress response. Aim 4: examine the cross sectional and longitudinal relationships between sleep characteristics and toddlers' child behavior problems. METHODS/STUDY POPULATION: In this cross-sectional study we are recruiting parents with healthy toddlers from early head start programs and a community clinic to prospectively examine the relationships among sleep characteristics, stress biomarkers, and children's health. Data on sleep characteristics will include subjective and objective measures of sleep duration and efficiency and parental interactive bedtime behaviors to assist their toddlers' sleep initiation. Multi-systemic biomarkers of stress including cortisol, CRP, IL-6, and BMI, will be measured individually. The associations between sleep characteristics and the biomarkers, considered as a latent variable of the stress response, will be explored. Health measures will include secretory IgA and parent-reported behavioral problems. Generalized linear models will be used in the data analysis. RESULTS/ANTICIPATED RESULTS: To date we have obtained objective (9 days/nights of actigraphy) measures of 33 toddlers' sleep and subjective measures of parenting interactive behaviors. Using the Parental Interactive Bedtime Behavior (PIBB) Survey and subscales [active physical comforting, encourage autonomy, settle by movement, passive physical comforting (PPC), social comforting], we are currently reporting on the associations between PIBB and toddler's sleep characteristics. The sample included 33 toddlers (mean age = 1.33 years, SD = 0.54). The toddlers' sleep duration averaged 8.22 hours (SD = 0.86). There were statistically significant moderate associations between sleep duration and parents' PPC ($r = -0.41$, $p = 0.02$). Intra-individual variability in the amount of wake after sleep onset was also significantly associated with total PIBB and PPC ($r = 0.37$, $p = 0.05$; $r = 0.52$, $p = 0.002$, respectively). Intra-individual variability in the amount of sleep fragmentation within toddlers was significantly associated with total PIBB ($r = 0.36$, $p = 0.05$). DISCUSSION/SIGNIFICANCE OF IMPACT: Although active physical comforting (eg, rocking to sleep, patting or rubbing child's back) is most commonly associated with sleep patterns in infancy and toddlerhood among samples of higher socio-economic status, findings from this study suggest a stronger association between PPC (eg, presence of the parent in the room to fall asleep) and less sleep duration and more individual variability in night wakings. The biomarker data are currently being analyzed and results will be presented within the year. Taken together, these preliminary results and pending results will inform future intervention development that may address the role of parenting behavior in promoting health sleep early in life.

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GABA-A receptor binding is abnormal in sensory-motor integration brain regions in Cervical Dystonia

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OBJECTIVES/SPECIFIC AIMS: Determine whether GABA-A receptor binding is abnormal and linked to dystonia symptoms in cervical dystonia (CD). METHODS/STUDY POPULATION: There is increasing evidence that a key pathophysiological mechanism in adult-onset focal dystonia is a reduction in inhibitory control over the sensorimotor network. Results from a recent 11C-flumazenil PET imaging study suggest that abnormal inhibitory signaling in genetic and sporadic forms of dystonia may be due to reduced GABA-A binding. It remains unknown whether CD, the most common form of adult-onset focal dystonia, is associated with abnormal GABA-A binding. The goal of this research is to determine if GABA-A receptor binding is abnormal and linked to dystonia symptoms in CD. RESULTS/ANTICIPATED RESULTS: We investigated whole brain GABA-A binding in 15 CD patients (11F; 64 ± 8 y) and 15 healthy controls (10F; 64 ± 9 y) using 60-minute dynamic 11C-flumazenil PET scans. GABA-A receptor binding potential (BP) was estimated using a simplified reference tissue model. A 2-sample *t*-test was used to identify voxel-wise GABA-A BP differences between groups, and a regression analysis used to test for correlations between GABA-A BP and disease severity as measured with the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS). A conventional region of interest analysis was also conducted to quantify BP changes within the sensorimotor network using the automated anatomical labeling atlas. DISCUSSION/SIGNIFICANCE OF IMPACT: CD patients have reduced GABA-A receptor binding compared with healthy controls, with the greatest reduction seen within the sensorimotor region of the thalamus. Furthermore, reductions in GABA-A binding in brain regions associated with coupling sensory and motor information predict motor severity. These findings support that reduced GABAergic signaling within sensorimotor integration regions is a key mechanism underlying dystonic symptoms in CD and could help inform the development of better, more targeted treatment options.

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Development of a clinically relevant rabbit surgical model for investigation of the host response to polypropylene mesh for pelvic organ prolapse

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OBJECTIVES/SPECIFIC AIMS: Mesh properties, such as stiffness, porosity, and weight have been shown to correlate with the degree of mesh integration with vaginal tissue. Previous research in rhesus macaques implanted with polypropylene mesh differing in stiffness, porosity, and weight showed differences in vaginal deterioration following mesh implantation. These differences were correlated with a foreign body response, consisting primarily of activated, proinflammatory M1 macrophages. Previous studies have determined that the early macrophage polarization profile following biomaterial implantation is a strong indicator of overall tissue integration downstream. However, these early responses have not been previously observed in the appropriate surgical models. Prior work from our laboratory in developing a cytokine delivery system has shown that shifting the macrophage response at the host-implant interface from a pro-inflammatory M1 phenotype to an anti-inflammatory M2 phenotype in the first 14 days postimplantation resulted in enhanced integration of the mesh with the surrounding tissues. The present study develops an in vivo model clinically relevant surgical model to investigate the modulation of the host response to mesh. Utilizing a moderately-sized animal, we can feasibly implant mesh using the "gold standard" abdominal sacrocolpopexy procedure and evaluate the changes in the host immunologic response at early (14 d) and tissue remodeling outcomes at late stages (90 and 180 d) of implantation. METHODS/STUDY POPULATION: Commercially available heavyweight and lightweight mesh was used to investigate the modulation of the immune response. A custom MTI SILAR Automated Dip Coating machine is used to uniformly coat the mesh in a reproducible manner. An adapted radio frequency glow discharge method is used to create a stable negative charge on the surface of the mesh, followed by the sequential deposition of polycationic and polyanionic polymers to provide a stable, conformal, nanoscale coating. Chitosan served as the polycation, chosen because of its known antimicrobial and biocompatibility properties. Dermatan sulfate served as the polyanion, chosen for its important role in regulating extracellular matrix

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