expression of ARs in the nasal tissue, trachea, and lungs. The nasal tissue exhibited the lowest baseline expression of ARs as compared to the lung and trachea which was further downregulated following adenosine treatment. Additionally, accumulation of endogenous adenosine in ADA-/- mice showed no signs of inflammation within the nasal tissue. Together, we demonstrated that topical adenosine effectively decreased inflammation and mucus production in a mouse model of viral ARS. DISCUSSION/SIGNIFICANCE: Previously, we found that topical adenosine dramatically enhances mucociliary clearance in the nose and sinuses. In this study, we found that nasal topical adenosine effectively decreased inflammation and mucus production in viral ARS. Our data suggest that nasal topical adenosine is an effective topical therapeutic option for viral ARS.

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Use of Implementation Science to Identify Implementation Determinants of Chronic Obstructive Pulmonary Disease Practice Guidelines

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OBJECTIVES/GOALS: COPD is a progressive airways disease that results in death or disability. There is poor uptake of clinical guidelines (CPG) to manage COPD and studies to bridge this implementation gap have shown inconsistent results. Using implementation science principles we aim to understand COPD-CPG implementation determinants from providers'perspective. METHODS/STUDY POPULATION: The study is being conducted in ten VA Primary Care Clinics. Guided by the Consolidated Framework for Implementation Research (CFIR), a conceptual framework developed to guide systematic assessment of multilevel implementation contexts, we are using semi-structured guides to conduct key informant qualitative interviews (physicians, physician extenders and nurses), to support a formative evaluation. CFIR domains relevant to the study were determined by a multidisciplinary team. Informants are identified through online outreach and voluntary participation. Sampling adequacy will be assessed by achievement of code saturation. A qualitative template analysis will be used to summarize the barriers and facilitators of each component of COPD-CPG organized by CFIR-domain. RESULTS/ANTICIPATED RESULTS: We anticipate a list of modifiable and non-modifiable contextual, recipient (provider and patient), and COPD CPG content (innovation) barriers to implementation. Many settings do not have critical elements of these CPG, such as a standardized inhaler education/assessment pathway, patient education material, or pulmonary rehabilitation referral pathway. Existing literature indicate reasons behind the insufficient uptake of COPD CPG include low familiarity with guidelines, perception of minimal value of guidelines by physicians, and time constraints; we will present contextual, recipient and innovation determinants specific to our setting. DISCUSSION/SIGNIFICANCE: This comprehensive assessment of barriers and facilitators to COPD-CPG will inform tool development and implementation strategies identification to improve COPD CPG uptake. COPD is the most common veteran lung disease. Improvement in COPD care has enormous potential for benefit for local veterans, as well as potential for wider dissemination.

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A Study of Cortical Thickness in Bilingual Children with Reading Disability (Dyslexia)*

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OBJECTIVES/GOALS: Dyslexia is a common Reading Disability (RD) affecting 7-12% of the population and is associated with less cortical thickness (CT) in bilateral brain regions. However, the interaction between RD and a bilingual experience on CT is unknown, even though bilingualism is also associated with altered CT. METHODS/STUDY POPULATION: We studied 48 Bilinguals assigned to the Typical Reader group based on Oral Reading Recognition Test (ORRT) scores above 90 (avg=107 ± 14), 47 Bilinguals assigned to the RD group based on ORRT scores below 85 (avg=77 ± 5), 45 English Monolingual Typical Readers with ORRT scores above 90 (avg=102 ± 13) and 47 Monolinguals with RD based on ORRT scores below 85 (avg=78 ± 5). Participants (all from the Adolescent Brain & Cognitive Development Study) were 11.9 ± 0.7 years of age and the 4 groups were matched for sex, self-ratings of English, nonverbal reasoning, and combined household income. Structural magnetic resonance images were analyzed using CAT12 and all four groups were entered into a factorial analysis. RESULTS/ANTICIPATED RESULTS: Surprisingly, the main effect of Reading Ability did not reveal any regions where RD manifested less CT than Controls (raising the possibility that the findings from the only two prior reports were due to small samples). The main effect of Language Background revealed less CT in bilinguals in bilateral perisylvian regions (inferior frontal gyri, superior temporal gyri, and left Heschl's gyrus) consistent with prior reports. There was no interaction of Reading Ability by Language Background. Taken together, we found no differences in CT in those with RD relative to Typical readers and no evidence that the dual language experience affected this result in any way. DISCUSSION/SIGNIFICANCE: The lack of interaction between Reading Ability and Language Background indicates that a dual-language experience does not affect CT differently in those with RD and reduces concerns that RD in those who are bilingual needs to be given separate consideration in studies of CT neuroanatomy.

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AMG487, A CXCR3 Antagonist, changes the Inflammatory Milieu in Familial Hemophagocytic Lymphohistiocytosis (FHL) Hepatitis

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OBJECTIVES/GOALS: Familial Hemophagocytic Lymphohistiocytosis (FHL) is a systemic inflammatory disease, causing acute liver failure (ALF). Elevated Interferon gamma (IFN-γ) results in increased hepatic transcription of the chemokines CXCL9 and

https://doi.org/10.1017/cts.2023.509 Published online by Cambridge University Press

CXCL10. Inhibition of their receptor CXCR3 may reduce leukocyte recruitment and ameliorate hepatitis. METHODS/STUDY POPULATION: To determine the functional role of the IFN-γ-induced ligands, CXCL9 and CXCL10, in hepatic leukocyte recruitment via CXCR3 we used a prf-/- mouse infected with Lymphocytic Choriomeningitis Virus (LCMV) in our well-established model mimicking human FHL. We used AMG487, a small molecule CXCR3 antagonist, while maintaining intact IFN-γ signaling. Mice were sacrificed 10 days after infection when mice developed features of FHL: cytopenias, organomegaly, elevated serum ferritin and sCD25, and hepatic inflammation. Hepatic inflammation was characterized using flow cytometry, liver histology and noninvasive markers of hepatitis (ALT, liver size). RESULTS/ANTICIPATED RESULTS: AMG487 did not ameliorate the overall disease phenotype with mice developing similar FHL characteristics compared to control, including weight loss, elevation of ALT and sIL-2r as well as degree of thrombocytopenia and anemia. There was significant reduction of recruitment of CXCR3+CD4+ T cells and B cells in mice treated with AMG487. This indicates the importance of CXCR3 receptor in humoral response in FHL hepatitis. In addition, treatment with AMG487 resulted in reduction of CXCR3 expression in hepatic inflammatory monocyte (iMonos) measured by mean fluorescence intensity (MFI). DISCUSSION/SIGNIFICANCE: This is the first pre-clinical experience using AMG487, a small molecule CXCR3 antagonist, to treat FHL hepatitis. AMG487 changed the hepatic inflammatory milieu, reducing CD4 T-cell and B-cell recruitment, as well as CXCR3 expression on iMonos. However, it did not ameliorate FHL hepatitis and other therapeutic approaches should be pursued.

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Eliminating System xc- Signaling Between Astrocytes and Neurons Selectively Impairs Complex Cognition

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OBJECTIVES/GOALS: We aim to discover safer and more effective therapeutics for CNS disorders. Current therapeutic development is hindered by dosing out drugs for safe consumption. By identifying proteins with narrow functional roles in the brain (i.e., behavioral control), we can develop drugs targeting these proteins for improved treatment safety and efficacy. METHODS/STUDY POPULATION: We focused on an evolutionarily new, non-neuronal, non-synaptic glutamate signaling mechanism, system xc- (Sxc). Sxc activity was eliminated by mutating the gene Slc7a11 through pronuclear injection of zinc-finger nucleases into Sprague Dawley rat embryos to create a line of rats lacking Sxc (MSxc). To confirm Sxc mutation, we verified that tissue from MSxc rats had a complete lack of xCT, which is the regulatory subunit of Sxc that is encoded by Slc7a11. We also verified that astrocyte cultures generated from MSxc tissue lacked cystine-evoked glutamate release. Next, we measured development (body weight), CNS regulation of metabolism, and other indicators of generalized, non-specific brain function as well as behaviors that are reliant on behavioral control, such as impulse control and response inhibition. RESULTS/ANTICIPATED RESULTS: Eliminating Sxc was not lethal and did not impair development or produce widespread changes in brain function as is commonly observed when deleting other glutamate mechanisms. MSxc rats did not differ from wildtype in growth rate, central regulation of metabolism as reflected by absolute or diurnal changes in core body temperature, locomotor activity in a familiar or novel environment, or simple forms of cognition such as novel object recognition, or operant responding (food and cocaine-reinforced). In contrast, behaviors that rely on behavioral control were impaired. MSxc rats displayed deficits in impulse control and behavioral flexibility. We hypothesize that MSxc rats will also show deficits in response inhibition using the stop signal reaction time task, a common metric used in clinical populations. DISCUSSION/SIGNIFICANCE: Eliminating Sxc activity in rats produced deficits in behaviors reliant on impulse control, without impacting development or simple brain function. These results show the potential of targeting Sxc to restore behavioral control without generating therapeutically limiting adverse effects resulting from non-specific changes in brain function.

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Odorant exposure decreases mortality in a Dravet Syndrome mouse model

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OBJECTIVES/GOALS: Our goal was to explore the actions of odorants on mortality and seizures in a DS mouse model (scn1a+/-), which have spontaneous seizures and high rate of SUDEP. We hypothesize that odorants that have actions on olfactory->extended amygdala pathways will decrease SUDEP, potentially through attenuation of neuronal activation in the extended amygdala. METHODS/STUDY POPULATION: Dravet syndrome mice (heterozygous scn1a+/-) were exposed for at least eight hours a day to either 2-phenylethanol (2PE, rose odor), lemon extract, or vehicle odorant in group housed cages. This was repeated daily for 15 days starting at postnatal day 20/21. Mortality in each group was recorded. A subset of 2PE-exposed animals had an extended washout period following odorant exposure to continue to determine the long-term effect of odorant exposure on mortality. RESULTS/ANTICIPATED RESULTS: Our preliminary results show a strong trend for decreased mortality in the 2PE-exposed group (16.1% mortality (n=31) vs 38.5% mortality in vehicle control (n=26), p=0.06, Barnard's test). Survival analyses show similar results (p=0.056 Kaplan-Meier curve, p=0.046 when removing those animals that died before completing day one of exposure). The lemon scent-exposed animals had a non-significant increase in mortality compared to controls from our preliminary experiments (50% mortality, n=8). Overall, these results suggest that mortality effect is dependent on specific odorants and that this effect is transient. DISCUSSION/SIGNIFICANCE: Our preliminary data support that odorant exposure can decrease mortality in a Dravet Syndrome mouse model, suggesting that more work to determine the mechanism of action and circuitry involved may illuminate new targets and therapies for preventing SUDEP in epilepsy patients.

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Understanding Structural and Dynamic Effects of the EWS-FLI1 interactome on the EWS Low Complexity Domain Function

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OBJECTIVES/GOALS: The EWSR1-FLI1 gene fusion is implicated as a source of oncogenic activity in the majority of Ewing sarcoma

https://doi.org/10.1017/cts.2023.509 Published online by Cambridge University Press