

19 The Effect of Asthma on Activation of Brain Neurocircuits



Melissa A. Rosenkranz, Ph.D.¹, Michael D. Evans, M.S.¹, Jeanette A. Mumford, Ph.D.¹, Stephane Esnault, Ph.D.², Richard J. Davidson, Ph.D.¹, and William W. Busse²; ¹University of Wisconsin-Madison, Madison, WI, ²University of Wisconsin School of Medicine and Public Health, Madison, WI.

RATIONALE: Depression and anxiety are frequent co-morbidities in asthma, though neither the underlying mechanisms nor pathways between the lung and brain are established. We have previously shown an inhaled allergen provocation of asthma activates brain neurocircuits associated with emotion. As a consequence, we hypothesized that emotion neurocircuitry activation occurs in asthma in relationship to underlying disease severity and may have effects on cognitive function.

METHODS: Functional magnetic resonance imaging was used to measure brain responses to emotional stimuli in 107 participants with mild-to-severe asthma. Principal component analysis (PCA) was used to create composite scores that represent disease severity (e.g. lung functions, medication use and disease control) and T2-inflammation. Finally, to evaluate the cognitive consequences of long-term asthma, cognitive testing was performed on a subset with severe asthma.

RESULTS: Significant relationships were found between measures of disease severity and activation of the insula – a key component of a brain network that acts to determine the importance of internal sensory information from the body. Other areas of brain activation were found in relationship to FeNO values and lifetime burden of disease (severity X asthma duration). We also found that a greater lifetime burden of asthma was inversely related to measures of cognitive function; with greater severity for a longer time, cognitive function was lower.

CONCLUSIONS: Brain networks associated with emotion are activated in relationship to measures of asthma severity. Furthermore, our data suggest that a consequence of greater asthma severity for a longer duration may be a reduction in cognitive function.

20 Role of Periostin in Brazilian Patients with Aspirin Exacerbated Respiratory Disease



Julianne Alves Machado¹, Daniel L. Cordeiro, MD², Thais Nociti Mendonca, MD², Marcelo Leite³, Ricardo Demarco², Ricardo Lessa², Adriana Murashima³, Leilane Nogueira², Marina Dias³, Adriana S. Moreno, PhD⁴, Wilma Lima², and Luisa Karla P. Arruda, MD PhD FAAAAI⁵; ¹Medical School of Ribeirao Preto, Ribeirão Preto, Brazil, ²Medical School of Ribeirao Preto, Ribeirao Preto, Brazil, ³medical School of Ribeirao Preto, Ribeirao Preto, Brazil, ⁴Ribeirão Preto Medical School - University of São Paulo, Ribeirão Preto, Brazil, ⁵University of São paulo, Ribeirão Preto Medical School, Ribeirão Preto, Brazil.

RATIONALE: Aspirin exacerbated respiratory disease (AERD) is characterized by chronic rhinosinusitis with nasal polyps, asthma and hypersensitivity to Aspirin/NSAIDs. Increased levels of periostin have been described in patients with AERD. We evaluated serum periostin in Brazilian patients with AERD, and compared to patients with Perennial Allergic Rhinitis (PAR) and healthy individuals.

METHODS: Twenty-nine patients (20F/9M) with AERD underwent polyp biopsy through nasofibrosocopy. Control groups of 12 patients with PAR (9F/3M) and 19 healthy subjects (11F/8M) had samples collected during rhinoplasty. Eosinophils were quantitated in blood, and in polyp tissue or nasal mucosa. Total IgE was determined by ImmunoCAP, and serum periostin by ELISA. Eosinophils in high power field (HPF), eosinophils/mm³ in blood, total IgE and serum periostin levels in patients with AERD were compared with those with PAR and healthy subjects.

RESULTS: Patients with AERD were older than patients with PAR patients and healthy controls (median 54, 30 and 29 years, respectively, p=0.0001). Peripheral blood eosinophils were higher in AERD as compared to PAR and healthy individuals (median 640/mm³, 200/mm³ and 100/mm³). Median tissue eosinophils were 113.3, 2.5 and 0.7cells/

HPF in AERD, RAP and healthy individuals, respectively (p<0.05). Mean serum periostin levels were 109.9ng/ml(range 59.4-236.6); 102.4ng/mL(range 57.9-147.8); and 83.6ng/mL(range 40.1-139.5), in AERD, RAP and healthy individuals, respectively (AERD vs. healthy subjects, p=0.01).

CONCLUSIONS: In a subset of Brazilian patients with AERD, we observed higher blood and tissue eosinophils, as compared to patients with PAR and healthy individuals, and elevated serum periostin, indicating a strong type 2 response in AERD patients in our area.

21 The effect of gastroesophageal reflux and proton pump inhibitors on respiratory tract infections in patients with asthma



Monica Tang, MD¹, Robert J. Henderson, MS², Janet T. Holbrook, MPH, PhD², and Jason E. Lang, MD, MPH¹; ¹Duke University, Durham, NC, ²Johns Hopkins University, Baltimore, MD.

RATIONALE: Co-morbid gastroesophageal reflux disease (GERD) is a significant factor associated with poor asthma control. Treatment with proton pump inhibitors (PPIs) have not consistently improved asthma control and there is evidence that PPIs may increase the risk of respiratory tract infections (RTIs). We aimed to study how GERD diagnosis and PPI treatment affect the risk of RTIs and related sequelae among children and adults with asthma.

METHODS: RTIs and RTI-related morbidity from four large asthma trials were analyzed for associations with self-reported GERD and PPI use. The primary outcome was rate of visits with an RTI, documented using standardized clinic visit interviews. Secondary outcomes included asthma exacerbations requiring systemic steroids. Multivariable negative binomial regression was used. Models controlled for age, gender, ethnicity, race, BMI classification, atopy, use of H2 antagonists or antacids, GERD symptom frequency, and study.

RESULTS: There were 1181 total subjects: 643 children (58 with GERD, 162 on a PPI) and 538 adults (138 with GERD, 78 with a PPI). In children, GERD did not increase the rate of RTI or RTI-related asthma exacerbations. PPI use was associated with increased rates of RTIs (rate ratio 1.2, 95% CI 1.0-1.4, p=0.04) and RTI-related asthma exacerbations (rate ratio=1.8, 95% CI 1.1-3.0, p=0.02). In adults, GERD and PPI use did not affect the rates of RTIs or RTI-related asthma exacerbations.

CONCLUSIONS: Independent of GERD, PPI use is associated with increased rates of RTI and associated asthma exacerbations in children but not adults with asthma.