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VAGUS NERVE ACTIVITY AND CYTOKINE RESPONSIVENESS IN PATIENTS WITH RHEUMATOID ARTHRITIS. R.S. Goldstein, A.N. Bruchfeld, M. Gallowitsch-Puerta, N. Patel, H. Yang, M. Rosas-Ballina, D.C. Lee, C.J. Czura, A.E. Sama, K.J. Tracey, The Feinstein Institute for Medical Research, North Shore-LIJ Health System, Manhasset, NY.

Recent literature has shown that the central nervous system can modulate the innate immune response through a rapid, local, and integrated mechanism. This pathway, termed the cholinergic anti-inflammatory pathway (CAP), acts via the vagus nerve through the neurotransmitter acetylcholine (Tracey, 2002). Activation of this pathway results in decreased proinflammatory cytokine production in in vitro experiments and in vivo models of inflammatory disease (Borovikova et al, 2000; Bernick et al, 2002). It has been observed that autonomic dysfunction develops in patients with diseases associated with cytokine excess, such as sepsis and rheumatoid arthritis (RA) (Hakala M and RK Niemela, 2000; Louthrenoo et al, 1999). However, the relationship between autonomic dysfunction and cytokine synthesis has not been explored. The purpose of this study is to explore the relationship between vagus nerve activity and cytokine synthesis in patients with RA compared to healthy subjects. A prospective observational study was performed at the North Shore-LIJ GCRC in subjects with RA and age- and sex-matched healthy volunteers (n = 12, 50 ± 10.9 years, n = 13, 42 ± 14.6, respectively). Vagus nerve activity was assessed by determining instantaneous heart rate variability (HRV) using parameters representing vagal nerve activity, including high-frequency power (HF), SDANN, and RMSSD. Blood was collected and stimulated with endotoxin and subsequently analyzed for the cytokines tumor necrosis factor (TNF) and high mobility box 1 protein (HMGB1). All measured components of HRV were attenuated in the RA subjects as compared to the healthy volunteers (HF power [msec^2] = 40 ± 8.8, 410 ± 122, $p < .01$, SDANN = 32 ± 4.5, 68 ± 12.9, $p < .05$, and RMSSD = 21 ± 0.41, 57 ± 11.1, $p < .01$, respectively). Cytokine analysis measuring serum TNF levels were attenuated in the RA group as compared to healthy volunteers (TNF [pg/mL] = 6,474 ± 2,028, 15,489 ± 1,514, $p < .01$, respectively). This supports our hypothesis that autonomic dysfunction, as reflected by lower vagal nerve output, may contribute to underlying dysfunctional cytokine activity during chronic inflammation. (Data presented as mean ± standard error and analyzed by two-tailed Student's t-test.)

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CARDIAC SYMPATHETIC DENERVATION PRECEDING PARKINSON DISEASE. D.S. Goldstein, Y. Sharabi, O. Bentho, G. Eisenhofer, Clinical Neurocardiology Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD.

All of more than 30 neuroimaging studies and at least 4 postmortem pathology studies have agreed that Parkinson disease entails a loss of myocardial noradrenergic innervation, implying that in addition to being a movement disorder from loss of nigrostriatal dopaminergic neurons, Parkinson disease is also a dysautonomia from loss of postganglionic noradrenergic neurons. Cardiac sympathetic denervation has been reported even in the earliest stages of the disease; however, whether the denervation can actually precede the movement disorder has been unknown. As part of an evaluation of hemodynamic instability suggesting pheochromocytoma, a 52-year-old man underwent 6-[18F]fluorodopamine scanning and other autonomic function tests. Four years later, over the course of 6–12 months, he developed slow movement, limb rigidity, masked face, and small handwriting and was diagnosed with mild Parkinson disease. Review of the earlier 6-[18F]fluorodopamine scan revealed that the patient had had markedly decreased 6-[18F]fluorodopamine-derived radioactivity throughout the left ventricular myocardium, confirmed by follow-up scanning. He also had had evidence of low baroreflex-cardiovagal gain and excessive adrenomedullary secretion, also confirmed at follow-up. In the interval, baroreflex-sympathoneural function declined, as indicated by development of abnormal beat-to-beat blood pressure responses to the Valsalva maneuver; however, the patient did not have orthostatic hypotension. The combination of denervation supersensitivity, baroreflex failure, and increased adrenomedullary secretion may have contributed to the patient's complaints related to neurocirculatory instability. The results lead to the proposition that cardiac sympathetic denervation may be a biomarker of presymptomatic Parkinson disease.

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EVALUATION OF NEUROPEPTIDE CONCENTRATIONS IN SERUM SAMPLES ANALYZED BY ENZYME-LINKED IMMUNOSORBENT ASSAY. L.O. Goodwin,[1] X.P. Wang,[1] C. Goodwin,[1] D. Guzowski,[1] C. Gawel,[1] A. Chandrasekaran,[1] K. Mann-Finnerty,[2] C. Correll,[3] [1]Molecular Genetics/Core Facility, [2]General Clinical Research Center, [3] Hillside Psychiatric Facility, The Feinstein Institute for Medical Research, Manhasset, NY.

Background: Clinical investigators are interested in elucidating the role of neuropeptides in diverse physiological processes. Neuropeptides act as integrative chemical messengers, from one discrete neuronal population to another. These molecules are also involved in coupling transductive events from neurons to immune cells regulating many biological functions, metabolism, and disease. Neuropeptide degradation is controlled by proteolytic enzymes and affected by disease states such as pain and analgesia, appetite control, inflammation, sepsis, mood, and affective behavior. Clarifying levels and pathways of circulating neuropeptides could drive the design of effective drugs to modulate the metabolic processes. **Methods:** We measured serum concentrations of nine different neuropeptides including NPY, AGRP, aMSH, MCH, CCK, CART, peptide YY(3–36), GLP, and Galanin by commercially available enzyme-linked immunosorbent assay (ELISA) kits (Pheonix Pharmaceuticals, Austin, TX). The peptide extraction method was essentially as recommended by the ELISA manufacturer. Micro BCA assay was used to measure total protein concentration. **Results:** The analysis of 9 neuropeptides from frozen serum samples (current GCRC study) by competitive ELISA were within the low range of the standard curve for each of the ELISAs (0.01–10 ng/mL). Considerable CV (coefficient of variability) in some duplicate samples was seen due to sensitivity of the ELISA or interference of abundant proteins within the serum samples. Thus, we analyzed the effect of peptide extraction of the serum samples. Different amounts (0–50 ng/mL) of peptideYY(3–36) was spiked into normal human serum to assess assay sensitivity. Spiked normal and four clinical sera samples were subjected to peptide extraction, and total protein and peptide YY(3–36) concentrations found for all paired extracted and nonextracted samples. There were no significant protein losses in the extracted samples as analyzed with BCA assay. However, there are significant reductions (≈50%) in peptide YY(3–36) concentrations in the four clinical serum samples that underwent peptide extraction. Peptide YY(3–36) neuropeptide may complex with bulky abundant proteins such as albumin. Removal of proteins from these serum samples did not yield higher sensitivity or improve CV, in the absence of concentrating the sera, which would reduce the sample volume and number.

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A CLINICAL STUDY OF THE EFFICACY OF THE THERAPEUTIC APPLICATION OF PLATELET-RICH PLASMA GEL ON THE SAPHENOUS VEIN HARVEST SITE IN CORONARY ARTERY BYPASS GRAFTING. L.E. Greiten, J. Copeland III, R. Bose, G. Sethi, Department of Cardiothoracic Surgery, University of Arizona College of Medicine, Tucson, AZ.

The application of platelet-rich plasma gel (PRP) to surgical wounds has been advocated during the past 11 years; however, very few studies of the efficacy of PRP gel have been performed within the cardiovascular surgery arena. Patients undergoing coronary artery bypass grafting (CABG), in which the saphenous vein is harvested, have a 10–20% risk of wound complications to the leg. Application of PRP provides hyperphysiologic levels of growth factors to the wound, with perceived benefits including less patient discomfort, shorter hospital stays, and a decreased incidence of postoperative surgical site infection. Publication of the data has the potential to impact the use of PRP gel in the cardiothoracic setting and beyond. The study's protocol dictates that the patient is used as their own control, with PRP being applied to specified incision sites during the time of surgery. To date, 14 patients (7 diabetics) have been enrolled, 31 sites used as control, and PRP application to 38 sites. Evaluations are made beginning 24 hours postoperatively addressing issues of pain, numbness, erythema, infection, swelling, and general healing. Both qualitative and quantitative evidence offer diminutive substantiation to warrant PRP application. However, the goal of the study is to evaluate patients for a minimum of 6 weeks postoperatively in order to comprehensively determine any benefits. There have been no incidences of infection in either control or application site, and only one incidence of delayed/accelerated healing has been observed in a patient with pitting peripheral edema beginning 3 days postoperatively. Ultimately, a patient population of 30–40 individuals is to be followed from which more conclusive results can be obtained.

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CLINICAL SCIENCE RESEARCH PROGRAM: THE MISSING MENTOR? D.A. Hall, M. Efird, J. Sheeder, D. Smith, C. Wells, T. Box, A.L. Shroyer, University of Colorado Health Science Center, Denver, CO.

Purpose: To fulfill a requirement of the clinical science (CLSC) course "Clinical Outcomes Assessment" at the University of Colorado, participating students in the program designed a survey to evaluate student perceptions related to the Clinical Research Training Program (CRTP) and to identify opportunities for improvement. **Methods:** The students designed a 99-question series in an on-line Web-based survey using a 5-point Likert scale to evaluate the structures, processes, and outcomes that might be anticipated from any successful NIH K-30 funded program. The survey covered the following domains: (1) self- assessments related to accreditation for GME research-related competencies; (2) course scheduling; (3) support required for manuscript/grant writing; (4) faculty mentorship; and (5) career development goals and planning. Respondents were asked about both the courses taken and their manuscript/grant writing productivity. **Summary of Results:** Sixty-five (56%) students responded. Results for the five domains included (1) statistically significant improvement in student perceptions related to their self-assessment for competencies from the start of the program to the time of survey; (2) student responses increased from "unsure"/"disagree" toward "agree" for the following constructs: (a) devise/rigorously test experimental hypotheses; (b) relate clinical research to the development of new modalities; (c) comply with ethical standards; (d) successfully conduct a clinical research project; and (e) select/apply the appropriate research method/statistical approach to a given research question. The most striking result, however, was that the CRTP was not successful in coordinating faculty mentor support for student research projects. When a mentorship was documented to exist outside of the program, almost all students were satisfied that their faculty mentoring relationship had successfully met their expectations. Approximately 78% of the student survey respondents noted a lack of satisfaction with the CLSC Program's support to find a primary faculty mentor who met their research project needs and long-term career goals. **Conclusions:** Overall, the CRTP students indicated the curriculum was successfully meeting their needs. Given that the program currently has over 78 dedicated graduate school faculty, representing a wide diversity of clinical and analytical disciplines, the survey finding that many students were missing a faculty mentorship relationship was unanticipated. Although other NIH funding options for "Mentoring a Mentor" programs exist, the program students recommended that NIH support K-30 programs incorporating this type of mentoring outreach as well as providing fiscal incentives to mentors in the future.

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CHARACTERIZATION OF DEPRESSIVE SYMPTOMS AND CD4 IN A COHORT OF HIV-POSITIVE HISPANIC WOMEN IN PUERTO RICO. R. Hechavarría, D. Blass, T. Ginebra, E. Maldonado, R. Mayo, L. Melendez, B. Santiago, V. Wojna, University of Puerto Rico, Medical Science Campus, San Juan, Puerto Rico.

Hispanic women represent one of the fastest growing groups with HIV infection in the United S. In Puerto Rico 27.4% of the reported cases of HIV/AIDS are women (1996–2004). Research focusing specially on women living with HIV is now gaining scientific attention since it has been clearly established that there are important biological, psychological, emotional, and social differences between men and women. Mood disorders, life events, stress, quality of life, and other psychosocial factors have been related to the immune function; the most common is depression. Depression is a psychological condition common in individuals with medical illnesses; estimated prevalence rates vary from 20 to 50%. An association between clinical depression and altered immune state has been suggested but has not been consistently demonstrated. The purpose of this pilot study is to correlate depressive symptoms with patients' immune state in a cohort of Hispanic HIV-positive women. A total of 47 HIV-positive women from the longitudinal cohort of NeuroAIDS program at the Medical Science Campus of the University of Puerto Rico signed informed consent. Inclusion criteria included HIV-positive women aged 18–50 years with a nadir CD4 cell count < 500 cell/mm^3 during the last year. Evaluation included participant's history, neurological and neuropsychological evaluations, and the psychosocial domain of the Menopause-Specific Quality of Life Questionnaire (MENQOL). Analysis was performed using Spearman's correlation. The mean values included age 37 (7.3), nadir CD4 cell count 218 cells/mm^3 (130). The mean

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