Objective. The goals of this review are to provide background information on the definitions and applications of the general term “biomarker” and to highlight the specific roles of breast imaging biomarkers in research and clinical breast cancer care. A search was conducted of the main electronic biomedical databases (PubMed, Cochrane, Embase, MEDLINE [Ovid], Scopus, and Web of Science). The search was focused on review literature in general radiology and biomedical sciences and on reviews and primary research articles on biomarkers in breast imaging over the 15 years ending in June 2017. The keywords included “biomarker,” “trial endpoints,” “breast imaging,” “breast cancer,” “radiomics,” and “precision medicine” in the titles and abstracts of the papers.

Conclusion. Clinical breast care and breast cancer–related research rely on imaging biomarkers for decision support. In the era of precision medicine and big data, the practice of radiology is likely to change. A closer integration of breast imaging with related biomedical fields and the creation of large integrated and shareable databases of clinical, molecular, and imaging biomarkers should allow the field to continue guiding breast cancer care and research.

Database
American Roentgen Ray Society
Title: Alcohol Biomarkers Associated with Obstructive Sleep Apnea

Author: R. Gregory Lande, Cynthia T. Gragnani, Miriam Pourzand & Despina Hangemanole

Journal: Substance Use & Misuse

Volume: Published online: 21 Nov 2017

Doi: 10.1080/10826084.2017.1385080

Abstract

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Database

Taylor & Francis Online Journals
Adolescent environmental enrichment prevents behavioral and physiological sequelae of adolescent chronic stress in female (but not male) rats

Brittany L. Smith, Rachel L. Morano, Yvonne M. Ulrich-Lai, Brent Myers, Matia B. Solomon & James P. Herman

Stress

Published online: 22 Nov 2017

10.1080/10253890.2017.1402883

Abstract

The late adolescent period is characterized by marked neurodevelopmental and endocrine fluctuations in the transition to early adulthood. Adolescents are highly responsive to the external environment, which enhances their ability to adapt and recover from challenges when given nurturing influences, but also makes them vulnerable to aberrant development when exposed to prolonged adverse situations. Female rats are particularly sensitive to the effects of chronic stress in adolescence, which manifests as passive coping strategies and blunted hypothalamic-pituitary-adrenocortical (HPA) stress responses in adulthood. We sought to intervene by exposing adolescent rats to environmental enrichment (EE) immediately prior to and during chronic stress, hypothesizing that EE would minimize or prevent the long-term effects of stress that emerge in adult females. To test this, we exposed male and female rats to EE on postnatal days (PND) 33–60 and implemented chronic variable stress (CVS) on PND 40–60. CVS consisted of twice-daily unpredictable stressors. Experimental groups included: CVS/unenriched, unstressed/EE, CVS/EE and unstressed/unenriched (n = 10 of each sex/group). In adulthood, we measured behavior in the open field test and forced swim test (FST) and collected blood samples following the FST. We found that environmental enrichment given during the adolescent period prevented the chronic stress-induced transition to passive coping in the FST and reversed decreases in peak adrenocortical responsiveness observed in adult females. Adolescent enrichment had little to no effect on males or unstressed females tested in adulthood, indicating that beneficial effects are specific to females that were exposed to chronic stress.

Database

Taylor & Francis Online Journals
Understanding posttraumatic growth of paratriathletes with acquired disability

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Disability and Rehabilitation

Published online: 15 Nov 2017

10.1080/09638288.2017.1402961

Abstract

Purpose: To examine the relevance of key components of Organismic Valuing Theory of Growth through Adversity in understanding posttraumatic growth amongst paratriathletes with acquired disability.

Methods: Semi-structured interviews informed by organismic valuing theory of growth through adversity were conducted with 14 elite paratriathletes (eight male, six female). To increase the likelihood that participants had experienced posttraumatic growth, a short form of the Posttraumatic Growth Inventory was completed prior to interview participation. Interview data were analyzed using directed content analysis.

Results: Although the initial response to disability was largely negative, paratriathlon experiences were reported to be a mechanism through which growth was facilitated. In particular, participants suggested that social, competence, empowerment, and identity development processes were instrumental in facilitating posttraumatic growth.

Conclusions: Analysis identified themes largely consistent with the main tenets of organismic valuing theory of growth through adversity, supporting its utility in understanding response to a traumatic event and subsequent growth. These findings also suggest that para sport may be an efficacious means for promoting posttraumatic growth, especially for individuals with severe initial reactions to their disability. Lastly, findings suggest that fostering perceptions of competence, autonomy, and social connection may promote posttraumatic growth.

Database

Taylor & Francis Online Journals
Purpose: To evaluate serum levels of visfatin, resistin and adiponectin in patients with erosive (E) and non-erosive (NE) osteoarthritis (OA) of the hand (HOA) compared to normal controls (NC).

Methods: 94 outpatients with E HOA and NE HOA and 21 NC were enrolled. The radiological assessment of both hands was performed according to the Kellgren–Lawrence and Kallman score. Patients were divided into two subsets (lone HOA or generalized OA) based on clinically OA involvement of knee and hip. Serum visfatin, resistin and adiponectin levels were determined by ELISA assay.

Results: Visfatin was significantly higher in E HOA patients in comparison to NC and NE HOA group. Resistin showed a significant increase in both E HOA and NE HOA groups versus NC, in particular in generalized OA. No significant differences among groups were found in adiponectin. The Kallman score was more severe in the two subsets of E HOA patients compared to NE HOA.

Conclusions: This study showed increased levels of resistin in erosive and non-erosive HOA, and higher visfatin levels in E HOA in comparison to NE HOA. These data suggest the adipokines possible role in the pathogenesis of HOA and their potential usefulness as biomarkers of the disease.
Both youth and long-term vitamin D status is associated with risk of type 2 diabetes mellitus in adulthood: a cohort study

Feitong Wu, Markus Juonala, Niina Pitkänen, Antti Jula, Terho Lehtimäki, Matthew A. Sabin, Katja Pahkala, Nina Hutri-Kähönen, Mika Kähönen, Tomi Laitinen, Jorma S. A. Viikari, Costan G. Magnussen & Olli T. Raitakari

Annals of Medicine

Published online: 07 Nov 2017

10.1080/07853890.2017.1399446

Abstract

Objectives: To determine whether vitamin D status in childhood and adolescence (herein collectively referred to as youth) and the long-term status from youth to adulthood is associated with risk of developing type 2 diabetes mellitus (T2DM) and impaired fasting glucose (IFG) in adulthood.

Materials and methods: This was a 31-year follow-up study of 2300 participants aged 3–18 years. Multinomial logistic regression was used to assess the association of both (a) baseline 25-hydroxyvitamin D (25OHD) levels and (b) the mean of baseline and the latest follow-up 25OHD levels (continuous variable and quartiles) with incident T2DM and IFG (cut-off = 5.6 mmol/L) in adult life.

Results: High serum 25OHD levels in youth and also mean values from youth to adulthood were associated with reduced risk of developing T2DM in adulthood (odds ratio, 95% confidence interval= 0.73, 0.57–0.95 and 0.65, 0.51–0.84, respectively, for each SD increment in 25OHD). Compared to Q1, a dose-dependent negative association was observed across other quartiles of youth 25OHD, while the strongest association was found in the Q3 for the mean 25OHD levels. Neither youth nor the mean 25OHD was associated with IFG.

Conclusions: High serum 25OHD levels in youth, and from child to adult life, were associated with a reduced risk of developing T2DM in adulthood.

Database

Taylor & Francis Online Journals
Continuity of medication management among adults with schizophrenia and comorbid cardiometabolic conditions

Richard A. Hansen, Natalie Hohmann, Matthew L. Maciejewski, Marisa E. Domino, Neepa Ray, Nirosha Mahendraratnam and Joel F. Farley

Journal of Pharmaceutical Health Services Research

Volume: Version of Record online: 20 NOV 2017

Doi: 10.1111/jphs.12201

Abstract

Objectives
Adults with schizophrenia and cardiometabolic conditions (CMCs) may be good candidates for comanagement by primary care prescribers (PCPs) and specialists. Associated risks for discontinuity in medication management have not been well studied. This study examines whether medication adherence, inpatient admissions and emergency department (ED) visits vary by the number and types of prescribers seen by adults with schizophrenia and CMCs.

Methods
This study used a retrospective cohort of 4223 adult Medicaid enrollees with schizophrenia and hypertension, hyperlipidemia and/or diabetes from three states in 2009–2010. Logistic regression models were run on outcome variables reflecting medication adherence, ED utilization and inpatient admissions as a function of the number and types of prescribers.

Key findings
Increases in number of psychiatric specialists were associated with better antipsychotic adherence, but decreasing statin adherence. Increases in number of psychiatric specialists were also associated with a higher probability of inpatient admission and ED visits, while increases in number of PCPs were associated with increases in the probability of ED visits.

Conclusions
Greater antipsychotic adherence for adults receiving prescriptions from multiple psychiatric specialists was counteracted by lower statin adherence and greater risk of ED and inpatient utilization. This may help inform optimal care models for these complex individuals.

Database
Wiley Online Library
**Title:** Extracellular adenosine-induced Rac1 activation in pulmonary endothelium: molecular mechanisms and barrier-protective role

**Author:** Anita Kovacs-Kasa, Kyung Mi Kim, Mary Cherian-Shaw, Stephen M. Black, David J. Fulton and Alexander D. Verin

**Journal:** Journal of Cellular Physiology

**Volume:** Accepted manuscript online: 23 NOV 2017

**Doi:** 10.1002/jcp.26281

**Abstract**

We have previously shown that Gs-coupled adenosine receptors (A2a) are primarily involved in adenosine-induced human pulmonary artery endothelial cell (HPAEC) barrier enhancement. However, the downstream events that mediate the strengthening of the endothelial cell (EC) barrier via adenosine signaling are largely unknown. In the current study we tested the overall hypothesis that adenosine-induced Rac1 activation and EC barrier enhancement is mediated by Gs-dependent stimulation of cAMP-dependent Epac1-mediated signaling cascades. Adenoviral transduction of HPAEC with constitutively-active (C/A) Rac1 (V12Rac1) significantly increases transendothelial electrical resistance (TER) reflecting an enhancement of the EC barrier. Conversely, expression of an inactive Rac1 mutant (N17Rac1) decreases TER reflecting a compromised EC barrier. The adenosine-induced increase in TER was accompanied by activation of Rac1, decrease in contractility (MLC dephosphorylation), but not Rho inhibition. Conversely, inhibition of Rac1 activity attenuates adenosine-induced increase in TER. We next examined the role of cAMP-activated Epac1 and its putative downstream targets Rac1, Vav2, Rap1 and Tiam1. Depletion of Epac1 attenuated the adenosine-induced Rac1 activation and the increase in TER. Furthermore, silencing of Rac1 specific guanine nucleotide exchange factors (GEFs), Vav2 and Rap1a expression significantly attenuated adenosine-induced increases in TER and activation of Rac1. Depletion of Rap1b only modestly impacted adenosine-induced increases in TER and Tiam1 depletion had no effect on adenosine-induced Rac1 activation and TER. Together these data strongly suggest that Rac1 activity is required for adenosine-induced EC barrier enhancement and that the activation of Rac1 and ability to strengthen the EC barrier depends, at least in part, on cAMP-dependent Epac1/Vav2/Rap1-mediated signaling.

**Database**

Wiley Online Library
Abstract

Two pharmacologic approaches that are currently at the forefront of treating advanced cancer are those that center on disrupting critical growth/survival signaling pathways within tumor cells (commonly referred to as “targeted therapies”) and those that center on enhancing the capacity of a patient’s immune system to mount an antitumor response (immunotherapy). Maximizing responses to both of these approaches requires an understanding of the oncogenic events present in a given patient’s tumor and the nature of the tumor-immune microenvironment. Although these 2 modalities were developed and initially used independently, combination regimens are now being tested in clinical trials, underscoring the need to understand how targeted therapies influence immunologic events. Translational studies and preclinical models have demonstrated that targeted therapies can influence immune cell trafficking, the production of and response to chemokines and cytokines, antigen presentation, and other processes relevant to antitumor immunity and immune homeostasis. Moreover, because these and other effects of targeted therapies occur in nonmalignant cells, targeted therapies are being evaluated for use in applications outside of oncology.
Effects of long-term weekly iron and folic acid supplementation on lower genital tract infection – a double blind, randomised controlled trial in Burkina Faso

Loreta Brabin, Stephen A. Roberts, Sabine Gies, Andrew Nelson, Salou Diallo, Christopher J. Stewart, Adama Kazienga, Julia Birtles, Sayouba Ouedraogo, Yves Claey, Halidou Tinto, Umberto d’Alessandro, E. Brian Faragher and Bernard Brabin

BMC Medicine

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Abstract

Background: Provision of routine iron supplements to prevent anaemia could increase the risk for lower genital tract infections as virulence of some pathogens depends on iron availability. This trial in Burkina Faso assessed whether weekly periconceptional iron supplementation increased the risk of lower genital tract infection in young non-pregnant and pregnant women.

Methods: Genital tract infections were assessed within a double blind, controlled, non-inferiority trial of malaria risk among nulliparous women, randomised to receive either iron and folic acid or folic acid alone, weekly, under direct observation for 18 months. Women conceiving during this period entered the pregnancy cohort. End assessment (FIN) for women remaining non-pregnant was at 18 months. For the pregnancy cohort, end assessment was at the first scheduled antenatal visit (ANC1). Infection markers included Nugent scores for abnormal flora and bacterial vaginosis (BV), T. vaginalis PCR, vaginal microbiota, reported signs and symptoms, and antibiotic and anti-fungal prescriptions. Iron biomarkers were assessed at baseline, FIN and ANC1. Analysis compared outcomes by intention to treat and in iron replete/deficient categories.

Results: A total of 1954 women (mean 16.8 years) were followed and 478 (24.5%) became pregnant. Median supplement adherence was 79% (IQR 59–90%). Baseline BV prevalence was 12.3%. At FIN and ANC1 prevalence was 12.8% and 7.0%, respectively (P < 0.011). T. vaginalis prevalence was 4.9% at FIN and 12.9% at ANC1 (P < 0.001). BV and T. vaginalis prevalence and microbiota profiles did not differ at trial end-points. Iron-supplemented non-pregnant women received more antibiotic treatments for non-genital infections (P = 0.014; mainly gastrointestinal infections (P = 0.005), anti-fungal treatments for genital infections (P = 0.014) and analgesics (P = 0.008). Weekly iron did not significantly reduce iron deficiency prevalence. At baseline, iron-deficient women were more likely to have normal vaginal flora (P = 0.016).

Conclusions: Periconceptional weekly iron supplementation of young women did not increase the risk of lower genital tract infections but did increase general morbidity in the non-pregnant cohort. Unabsorbed gut iron due to malaria could induce enteric infections, accounting for the increased administration of antibiotics and antifungals in the iron-supplemented arm. This finding reinforces concerns about routine iron supplementation in highly malarious areas.

Database

BMC Medicine