

1. Mayo Clin Proc. 2014 Aug;89(8):1030-2. doi: 10.1016/j.mayocp.2014.07.001.

The Chairman's Curse: Lethal Sitting.

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PMID: 25092363 [PubMed - in process]

2. Am J Clin Nutr. 2014 Jul 30. pii: ajcn.079822. [Epub ahead of print]

Effect of dietary adherence on the body weight plateau: a mathematical model incorporating intermittent compliance with energy intake prescription.

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BACKGROUND: Clinical weight loss in individuals typically stabilizes at 6 mo.

However, validated models of dynamic energy balance have consistently shown weight plateaus between 1 and 2 y. The cause for this discrepancy is unclear.

OBJECTIVE: We developed 2 mathematical models on the basis of the first law of thermodynamics to investigate plausible explanations for reaching an early weight plateau at 6 mo.

DESIGN: The first model was an energy-expenditure adaptation model and was applied to determine the degree of metabolic adaptation required to generate this plateau. The second model was an intermittent lack-of-adherence model formulated by using a randomly fluctuating energy intake term accounting for intermittent noncompliance in dietary intake to reach this plateau. To set model variables, validate models, and compare free-living weight-loss patterns to in-residence supervised programs, we applied the following 4 different studies: The US NHANES 1999-2004, Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE) weight-loss study, the Bouchard Twin overfeeding study, and the Minnesota Starvation Experiment.

RESULTS: The metabolic adaptation model increased final weight but did not affect the predicted plateau time point. The intermittent lack-of-adherence model generated oscillating weight graphs that have been frequently observed in weight-loss studies. The model showed that a 6-mo weight-loss plateau can be attained despite what can be considered as high diet adherence. The model was programmed as a downloadable application. **Conclusions:** An intermittent lack of diet adherence, not metabolic adaptation, is a major contributor to the frequently observed early weight-loss plateau. The new weight-loss prediction software, which incorporates an intermittent lack of adherence, can be used to

guide and inform patients on realistic levels of adherence on the basis of patient lifestyle. The CALERIE study was registered at clinicaltrials.gov as NCT00099151.

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3. Diabetes. 2014 Jun 26. pii: DB_140619. [Epub ahead of print]

Reducing RIP140 expression in macrophage alters ATM infiltration, facilitates white adipose tissue browning and prevents high fat diet-induced insulin resistance.

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Adipose tissue macrophages (ATMs) recruitment and activation play a critical role in obesity-induced inflammation and insulin resistance (IR). Mechanism regulating ATM activation and infiltration remains unclear. In this study, we found Receptor Interacting Protein 140 (RIP140) can regulate the dynamics of ATM that contributes to adipose tissue remodeling. A high fat diet (HFD) elevates RIP140 expression in macrophage. We generated mice with RIP140 knockdown in macrophages using transgenic and bone marrow transplantation procedures to blunt HFD-induced elevation in RIP140. We detected significant white adipose tissue (WAT) browning and improved systemic insulin sensitivity in these mice, particularly under a HFD feeding. These mice have decreased circulating monocyte population and altered ATM profile in WAT (a dramatic reduction in inflammatory M1 and expansion in M2 macrophage), which could improve HFD-induced IR. These studies suggest that reducing RIP140 expression in monocytes/macrophages can be a new therapeutic strategy in treating HFD-induced and inflammation-related diseases.

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4. Int J Environ Res Public Health. 2014 Jun 25;11(7):6653-65. doi: 10.3390/ijerph110706653.

Using sit-stand workstations to decrease sedentary time in office workers: a randomized crossover trial.

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OBJECTIVE: This study was conducted to determine whether installation of sit-stand desks (SSDs) could lead to decreased sitting time during the workday among sedentary office workers.

METHODS: A randomized cross-over trial was conducted from January to April, 2012 at a business in Minneapolis. 28 (nine men, 26 full-time) sedentary office workers took part in a 4 week intervention period which included the use of SSDs to gradually replace 50% of sitting time with standing during the workday. Physical activity was the primary outcome. Mood, energy level, fatigue, appetite, dietary intake, and productivity were explored as secondary outcomes.

RESULTS: The intervention reduced sitting time at work by 21% (95% CI 18%-25%) and sedentary time by 4.8 min/work-hr (95% CI 4.1-5.4 min/work-hr). For a 40 h work-week, this translates into replacement of 8 h of sitting time with standing and sedentary time being reduced by 3.2 h. Activity level during non-work hours did not change. The intervention also increased overall sense of well-being, energy, decreased fatigue, had no impact on productivity, and reduced appetite and dietary intake. The workstations were popular with the participants.

CONCLUSION: The SSD intervention was successful in increasing work-time activity level, without changing activity level during non-work hours.

PMCID: PMC4113835

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5. Arch Gerontol Geriatr. 2014 May-Jun;58(3):314-9. doi: 10.1016/j.archger.2014.01.004. Epub 2014 Jan 15.

"Go4Life" exercise counseling, accelerometer feedback, and activity levels in older people.

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Older people are more sedentary than other age groups. We sought to determine if providing an accelerometer with feedback about activity and counseling older subjects using Go4Life educational material would increase activity levels. Participants were recruited from independent living areas within assisted living facilities and the general public in the Rochester, MN area. 49 persons aged 65-95 (79.5±7.0 years) who were ambulatory but sedentary and overweight participated in this randomized controlled crossover trial for one year. After a baseline period of 2 weeks, group 1 received an accelerometer and counseling using Go4Life educational material (www.Go4Life.nia.nih.gov) for 24 weeks and accelerometer alone for the next 24 weeks. Group 2 had no intervention for the first 24 weeks and then received an accelerometer and Go4Life based counseling

for 24 weeks. There were no significant baseline differences between the two groups. The intervention was not associated with a significant change in activity, body weight, % body fat, or blood parameters ($p>0.05$). Older (80-93) subjects were less active than younger (65-79) subjects ($p=0.003$). Over the course of the 48 week study, an increase in activity level was associated with a decline in % body fat ($p=0.008$). Increasing activity levels benefits older patients. However, providing an accelerometer and a Go4Life based exercise counseling program did not result in a 15% improvement in activity levels in this elderly population. Alternate approaches to exercise counseling may be needed in elderly people of this age range.

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6. FASEB J. 2014 Mar;28(3):1499-510. doi: 10.1096/fj.13-239806. Epub 2013 Dec 16.

Altered regulation of energy homeostasis in older rats in response to thyroid hormone administration.

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Hyperthyroidism causes increased energy intake and expenditure, although anorexia and higher weight loss have been reported in elderly individuals with hyperthyroidism. To determine the effect of age on energy homeostasis in response to experimental hyperthyroidism, we administered 200 μg tri-iodothyronine (T3) in 7- and 27-mo-old rats for 14 d. T3 increased energy expenditure (EE) in both the young and the old rats, although the old rats lost more weight (147 g) than the young rats (58 g) because of the discordant effect of T3 on food intake, with a 40% increase in the young rats, but a 40% decrease in the old ones. The increased food intake in the young rats corresponded with a T3-mediated increase in the appetite-regulating proteins agouti-related peptide, neuropeptide Y, and uncoupling protein 2 in the hypothalamus, but no increase occurred in the old rats. Evidence of mitochondrial biogenesis in response to T3 was similar in the soleus muscle and heart of the young and old animals, but less consistent in old plantaris muscle and liver. Despite the comparable increase in EE, T3's effect on mitochondrial function was modulated by age in a tissue-specific manner. We conclude that older rats lack compensatory mechanisms to increase caloric intake in response to a T3-induced increase in EE, demonstrating a detrimental effect of age on energy homeostasis.

PMCID: PMC3929673 [Available on 2015/3/1]

PMID: 24344330 [PubMed - indexed for MEDLINE]

7. Work. 2014;48(1):47-51. doi: 10.3233/WOR-131708.

Increasing physician activity with treadmill desks.

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BACKGROUND: Prolonged sitting has been shown to increase mortality and obesity.

OBJECTIVE: We sought to determine whether physicians would use a treadmill desk, increase their daily physical activity and lose weight.

PARTICIPANTS: 20 overweight and obese physicians aged 25 to 70 with Body Mass Index > 25.

METHODS: Participants used a treadmill desk, a triaxial accelerometer, and received exercise counseling in a randomized, cross-over trial over 24 weeks. Group 1 received exercise counseling, accelerometer feedback, and a treadmill desk for 12 weeks and then accelerometer only for 12 weeks. Group 2 received an accelerometer without feedback for 12 weeks followed by exercise counseling, accelerometer feedback, and the treadmill desk for 12 weeks.

RESULTS: Daily physical activity increased while using the treadmill desk compared to not using the desk by 197 kcal per day ($p=0.003$). The difference in weight during the two 12 week periods was 1.85 kg ($p=0.03$). Percent body fat was 1.9% lower while using the treadmill desk ($p=0.02$). There were no differences in metabolic or well-being measures.

CONCLUSIONS: This study suggests that physicians will use a treadmill desk, that it does increase their activity, and that it may help with weight loss. Further studies are warranted.

PMID: 24004766 [PubMed - in process]

8. Diabetes Technol Ther. 2013 Sep;15(9):751-7. doi: 10.1089/dia.2013.0044. Epub 2013 Aug 12.

Comparison of physical activity sensors and heart rate monitoring for real-time activity detection in type 1 diabetes and control subjects.

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BACKGROUND: Currently, patients with type 1 diabetes decide on the amount of insulin to administer based on several factors, including current plasma glucose value, expected meal input, and physical activity (PA). One future therapeutic modality for patients with type 1 diabetes is the artificial endocrine pancreas (AEP). Incorporation of PA could enhance the efficacy of AEP significantly. We compared the main technologies used for PA quantitation.

SUBJECTS AND METHODS: Data were collected during inpatient studies involving healthy control subjects and type 1 diabetes. We report PA quantified from accelerometers (acceleration units [AU]) and heart rate (HR) monitors during a standardized activity protocol performed after a dinner meal at 7 p.m. from nine control subjects (four were males, 37.4 ± 12.7 years old, body mass index of 24.8 ± 3.8 kg/m²), and fasting plasma glucose of 4.71 ± 0.63 mmol/L) and eight with type 1 diabetes (six were males, 45.2 ± 13.4 years old, body mass index of 25.1 ± 2.9 kg/m²), and fasting plasma glucose of 8.44 ± 2.31 mmol/L).

RESULTS: The patient-to-patient variability was considerably less when examining AU compared with HR monitors. Furthermore, the exercise bouts and rest periods were more evident from the data streams when AUs were used to quantify activity.

Unlike the AU, the HR measurements provided little insight for active and rest stages, and HR data required patient-specific standardizations to discern any meaningful pattern in the data.

CONCLUSIONS: Our results indicated that AU provides a reliable signal in response to PA, including low-intensity activity. Correlation of this signal with continuous glucose monitoring data would be the next step before exploring inclusion as input for AEP control.

PMCID: PMC3757536 [Available on 2014/9/1]

PMID: 23937615 [PubMed - indexed for MEDLINE]

9. Diabetes. 2013 Jul;62(7):2223-9. doi: 10.2337/db12-1759. Epub 2013 Feb 27.

Diurnal pattern of insulin action in type 1 diabetes: implications for a closed-loop system.

Hinshaw L(1), Dalla Man C, Nandy DK, Saad A, Bharucha AE, Levine JA, Rizza RA, Basu R, Carter RE, Cobelli C, Kudva YC, Basu A.

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Comment in

Diabetes. 2013 Jul;62(7):2173-4.

We recently demonstrated a diurnal pattern to insulin action (i.e., insulin sensitivity [SI]) in healthy individuals with higher SI at breakfast than at dinner. To determine whether such a pattern exists in type 1 diabetes, we studied 19 subjects with C-peptide-negative diabetes (HbA1c $7.1 \pm 0.6\%$) on insulin pump therapy with normal gastric emptying. Identical mixed meals were ingested during breakfast, lunch, and dinner at 0700, 1300, and 1900 h in randomized Latin square of order on 3 consecutive days when measured daily physical activity was equal. The triple tracer technique enabled measurement of glucose fluxes. Insulin was administered according to the customary insulin:carbohydrate ratio for each participant. Although postprandial glucose excursions did not differ among meals, insulin concentration was higher ($P < 0.01$) and endogenous glucose production less suppressed ($P < 0.049$) at breakfast than at lunch. There were no differences in meal glucose appearance or in glucose disappearance between meals. Although there was no statistical difference ($P = 0.34$) in SI between meals in type 1 diabetic subjects, the diurnal pattern of SI taken across the three meals in its entirety differed ($P = 0.016$) from that of healthy subjects. Although the pattern in healthy subjects showed decreasing SI between breakfast and lunch, the reverse SI pattern was observed in type 1 diabetic subjects. The results suggest that in contrast to healthy subjects, SI diurnal pattern in type 1 diabetes is specific to the individual and cannot be extrapolated to the type 1 diabetic population as a whole, implying that artificial pancreas algorithms may need to be personalized.

PMCID: PMC3712033

PMID: 23447123 [PubMed - indexed for MEDLINE]

10. Obesity (Silver Spring). 2013 Apr;21(4):705-11. doi: 10.1002/oby.20121.

Treadmill desks: A 1-year prospective trial.

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OBJECTIVE: Sedentariness is associated with weight gain and obesity. A treadmill desk is the combination of a standing desk and a treadmill that allow employees to work while walking at low speed.

DESIGN AND METHODS: The hypothesis was that a 1-year intervention with treadmill desks is associated with an increase in employee daily physical activity (summation of all activity per minute) and a decrease in daily sedentary time (zero activity). Employees (n = 36; 25 women, 11 men) with sedentary jobs (87 ± 27 kg, BMI 29 ± 7 kg/m²), n = 10 Lean BMI < 25 kg/m², n = 15 Overweight 25 < BMI < 30 kg/m², n = 11 Obese BMI > 30 kg/m²) volunteered to have their traditional desk replaced with a treadmill desk to promote physical activity for 1 year.

RESULTS: Daily physical activity (using accelerometers), work performance, body composition, and blood variables were measured at Baseline and 6 and 12 months after the treadmill desk intervention. Subjects who used the treadmill desk increased daily physical activity from baseline 3,353 ± 1,802 activity units (AU)/day to, at 6 months, 4,460 ± 2,376 AU/day (P < 0.001), and at 12 months, 4,205 ± 2,238 AU/day (P < 0.001). Access to the treadmill desks was associated with significant decreases in daily sedentary time (zero activity) from at baseline 1,020 ± 75 min/day to, at 6 months, 929 ± 84 min/day (P < 0.001), and at 12 months, 978 ± 95 min/day (P < 0.001). For the whole group, weight loss averaged 1.4 ± 3.3 kg (P < 0.05). Weight loss for obese subjects was 2.3 ± 3.5 kg (P < 0.03). Access to the treadmill desks was associated with increased daily physical activity compared to traditional chair-based desks; their deployment was not associated with altered performance. For the 36 participants, fat mass did not change significantly, however, those who lost weight (n = 22) lost 3.4 ± 5.4 kg (P < 0.001) of fat mass. Weight loss was greatest in people with obesity.

CONCLUSIONS: Access to treadmill desks may improve the health of office workers without affecting work performance.

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PMID: 23417995 [PubMed - indexed for MEDLINE]

11. Chest. 2013 Jul;144(1):79-86. doi: 10.1378/chest.12-2829.

Effects of experimental sleep restriction on caloric intake and activity energy expenditure.

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Comment in

Chest. 2013 Aug;144(2):711.

Chest. 2013 Aug;144(2):711-2.

BACKGROUND: Epidemiologic studies link short sleep duration to obesity and weight gain. Insufficient sleep appears to alter circulating levels of the hormones leptin and ghrelin, which may promote appetite, although the effects of sleep restriction on caloric intake and energy expenditure are unclear. We sought to determine the effect of 8 days/8 nights of sleep restriction on caloric intake, activity energy expenditure, and circulating levels of leptin and ghrelin.

METHODS: We conducted a randomized study of usual sleep vs a sleep restriction of two-thirds of normal sleep time for 8 days/8 nights in a hospital-based clinical research unit. The main outcomes were caloric intake, activity energy expenditure, and circulating levels of leptin and ghrelin.

RESULTS: Caloric intake in the sleep-restricted group increased by +559 kcal/d (SD, 706 kcal/d, $P=.006$) and decreased in the control group by -118 kcal/d (SD, 386 kcal/d, $P=.51$) for a net change of +677 kcal/d (95% CI, 148-1,206 kcal/d; $P=.014$). Sleep restriction was not associated with changes in activity energy expenditure ($P=.62$). No change was seen in levels of leptin ($P=.27$) or ghrelin ($P=.21$).

CONCLUSIONS: Sleep restriction was associated with an increase in caloric consumption with no change in activity energy expenditure or leptin and ghrelin concentrations. Increased caloric intake without any accompanying increase in energy expenditure may contribute to obesity in people who are exposed to long-term sleep restriction.

TRIAL REGISTRATION: ClinicalTrials.gov; No.: NCT01334788; URL: www.clinicaltrials.gov.

PMCID: PMC3707179

PMID: 23392199 [PubMed - indexed for MEDLINE]

12. J Alzheimers Dis. 2013;34(2):501-7. doi: 10.3233/JAD-121270.

Caloric intake, aging, and mild cognitive impairment: a population-based study.

Geda YE(1), Ragosnig M, Roberts LA, Roberts RO, Pankratz VS, Christianson TJ, Mielke MM, Levine JA, Boeve BF, Sochor O, Tangalos EG, Knopman DS, Petersen RC.

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In a population-based case-control study, we examined whether moderate and high caloric intakes are differentially associated with the odds of having mild cognitive impairment (MCI). The sample was derived from the Mayo Clinic Study of Aging in Olmsted County, Minnesota. Non-demented study participants aged 70-92 years (1,072 cognitively normal persons and 161 subjects with MCI) reported their caloric consumption within 1 year of the date of interview by completing a Food Frequency Questionnaire. An expert consensus panel classified each subject as either cognitively normal or having MCI based on published criteria. We conducted multivariable logistic regression analyses to compute odds ratios (OR) and 95% confidence intervals (95% CI) after adjusting for age, gender, education, depression, medical comorbidity, and body mass index. We also conducted stratified analyses by apolipoprotein E $\epsilon 4$ genotype status. Analyses were conducted in tertiles of caloric intake: 600 to <1,526 kcals per day (reference group); 1,526 to 2,143 kcals per day (moderate caloric intake group); and >2,143 kcals per day (high caloric intake group). In the primary analysis, there was no significant difference between the moderate caloric intake group and the reference group (OR 0.87, 95% CI 0.53-1.42, $p = 0.57$). However, high caloric

intake was associated with a nearly two-fold increased odds of having MCI (OR 1.96, 95% CI 1.26-3.06, $p = 0.003$) as compared to the reference group. Therefore, high caloric intake was associated with MCI but not moderate caloric intake. This association is not necessarily a cause-effect relationship.

PMCID: PMC3578975

PMID: 23234878 [PubMed - indexed for MEDLINE]

13. Surg Obes Relat Dis. 2012 Sep-Oct;8(5):501-6. doi: 10.1016/j.soard.2012.08.001. Epub 2012 Aug 3.

Nonexercise activity thermogenesis: a way forward to treat the worldwide obesity epidemic.

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PMID: 22986115 [PubMed - indexed for MEDLINE]

14. Endocr Pract. 2012 Nov-Dec;18(6):834-41. doi: 10.4158/EP12094.OR.

Population-based study of hypoglycemia in patients with type 1 diabetes mellitus requiring emergency medical services.

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OBJECTIVE: To report the population burden of hypoglycemia necessitating emergency medical services (EMS) and the long-term outcomes in patients with type 1 diabetes mellitus (T1DM) receiving different insulin treatments.

METHODS: We retrieved all EMS calls because of hypoglycemia in patients with T1DM in Olmsted County, Minnesota, between January 1, 2003, and December 31, 2009, and reviewed the related medical records.

RESULTS: During the 7-year study period, 531 EMS calls were made involving 208 patients with T1DM (112 men, 96 women; mean age 47 ± 13 years). Of the 208 patients, 137 (66%) were receiving multiple daily insulin (MDI) injections, 50 (24%) were receiving continuous subcutaneous insulin infusion, 15 (7%) were receiving simple insulin (SI), 4 (2%) were treated with metformin + MDI, and 2 (1%) were not receiving treatment for diabetes (after pancreas transplantation). The last 2 groups were excluded from further analysis because of small sample size. The remaining 3 treatment groups differed by age ($P < .02$), with the oldest patients receiving SI. Repeated calls, emergency department transportation (EDT), and hospitalization had a 33%, 49%, and 18% frequency, respectively, and did not differ among the treatment groups. In a multivariate model, mortality was significantly associated with treatment type (the SI group had a higher risk for mortality than did the MDI group [$P = .03$] after exclusion of 27 patients who changed treatment during follow-up), age ($P < .0001$), and EDT ($P = .04$).

CONCLUSION: The population burden of EMS-requiring hypoglycemia in patients with T1DM is high. Medical resource utilization was similar among the 3 treatment groups. Mortality was higher in the SI group (limited by small sample size) and among patients requiring EDT and increased with advancing age. Further research could be directed toward understanding the effect of expert evaluation of high-risk patients on long-term outcomes.

PMID: 22784848 [PubMed - indexed for MEDLINE]

15. Diabetes. 2012 Nov;61(11):2691-700. doi: 10.2337/db11-1478. Epub 2012 Jun 29.

Diurnal pattern to insulin secretion and insulin action in healthy individuals.

Saad A(1), Dalla Man C, Nandy DK, Levine JA, Bharucha AE, Rizza RA, Basu R, Carter RE, Cobelli C, Kudva YC, Basu A.

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Comment in

Diabetes. 2013 Jul;62(7):2173-4.

Evaluation of the existence of a diurnal pattern of glucose tolerance after mixed meals is important to inform a closed-loop system of treatment for insulin requiring diabetes. We studied 20 healthy volunteers with normal fasting glucose (4.8 ± 0.1 mmol/L) and HbA(1c) ($5.2 \pm 0.0\%$) to determine such a pattern in nondiabetic individuals. Identical mixed meals were ingested during breakfast, lunch, or dinner at 0700, 1300, and 1900 h in randomized Latin square order on 3 consecutive days. Physical activity was the same on all days. Postprandial glucose turnover was measured using the triple tracer technique. Postprandial glucose excursion was significantly lower ($P < 0.01$) at breakfast than lunch and dinner. β -Cell responsivity to glucose and disposition index was higher ($P < 0.01$) at breakfast than lunch and dinner. Hepatic insulin extraction was lower ($P < 0.01$) at breakfast than dinner. Although meal glucose appearance did not differ between meals, suppression of endogenous glucose production tended to be lower ($P < 0.01$) and insulin sensitivity tended to be higher ($P < 0.01$) at breakfast than at lunch or dinner. Our results suggest a diurnal pattern to glucose tolerance in healthy humans, and if present in type 1 diabetes, it will need to be incorporated into artificial pancreas systems.

PMCID: PMC3478548

PMID: 22751690 [PubMed - indexed for MEDLINE]

16. J Diabetes Sci Technol. 2012 Jan 1;6(1):65-73.

Population-based study of severe hypoglycemia requiring emergency medical service assistance reveals unique findings.

Parsaik AK(1), Carter RE, Pattan V, Myers LA, Kumar H, Smith SA, Russi CS, Levine JA, Basu A, Kudva YC.

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OBJECTIVE: The objective is to report a contemporary population-based estimate of hypoglycemia requiring emergency medical services (EMS), its burden on medical resources, and its associated mortality in patients with or without diabetes mellitus (DM, non-DM), which will enable development of prospective strategies that will capture hypoglycemia promptly and provide an integrated approach for prevention of such episodes.

METHODS: We retrieved all ambulance calls activated for hypoglycemia in Olmsted County, Minnesota, between January 1, 2003 and December 31, 2009.

RESULTS: A total of 1473 calls were made by 914 people (DM 8%, non-DM 16%, unknown DM status 3%). Mean age was 60 ± 16 years with 49% being female. A higher percentage of calls were made by DM patients (87%) with proportionally fewer calls coming from non-DM patients (11%) (chi-square test, $p < .001$), and the remaining 2% calls by people with unknown DM status. Emergency room transportation and hospitalization were significantly higher in non-DM patients compared to DM patients ($p < .001$) and type 2 diabetes mellitus compared to type 1 diabetes mellitus ($p < .001$). Sulphonylureas alone or in combination with insulin varied during the study period ($p = .01$). The change in incidence of EMS for hypoglycemia was tracked during this period. However, causality has not been established. Death occurred in 240 people, 1.2 (interquartile range 0.2-2.7) years after their first event. After adjusting for age, mortality was higher in non-DM patients compared with DM patients ($p < .001$) but was not different between the two types of DM.

CONCLUSIONS: The population burden of EMS requiring hypoglycemia is high in both DM and non-DM patients, and imposes significant burden on medical resources. It is associated with long-term mortality.

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PMCID: PMC3320823

PMID: 22401324 [PubMed - indexed for MEDLINE]

17. J Pediatr Endocrinol Metab. 2011;24(9-10):689-95.

The energy expenditure of an activity-promoting video game compared to sedentary video games and TV watching.

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BACKGROUND: In the present study we investigated the effect of television watching and the use of activity-promoting video games on energy expenditure in obese and lean children.

METHODS: Energy expenditure and physical activity were measured while participants were watching television, playing a video game on a traditional sedentary video game console, and while playing the same video game on an activity-promoting video game console.

RESULTS: Energy expenditure was significantly greater than television watching and playing video games on a sedentary video game console when children played the video game on the activity-promoting console. When examining movement with accelerometry, children moved significantly more when playing the video game on

the Nintendo Wii console.

CONCLUSION: Activity-promoting video games have shown to increase movement, and be an important tool to raise energy expenditure by 50% when compared to sedentary activities of daily living.

PMCID: PMC3900116

PMID: 22145458 [PubMed - indexed for MEDLINE]

18. Work. 2011;40(4):473-7. doi: 10.3233/WOR-2011-1258.

Productivity of transcriptionists using a treadmill desk.

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OBJECTIVE: Time spent sitting increases all-cause mortality. Sedentary occupations are a major contributor to the obesity epidemic. A treadmill desk offers the potential to increase activity while working; however, it is important to make sure that productivity does not decline. The purpose of this study is to evaluate productivity while using a treadmill desk.

PARTICIPANTS: Eleven experienced medical transcriptionists participated in the study.

METHODS: Transcriptionists were given 4 hours training in the use of a treadmill desk. They were asked to transcribe tapes for 8 hours both while sitting and while using the treadmill desk. Speed and accuracy of transcription were compared as were the average expended calories per hour.

RESULTS: The accuracy of transcription did not differ between sitting and walking transcriptions. The speed of transcription was 16% slower while walking than while sitting ($p < 0.001$). The transcriptionists expended 100 calories per hour more when they transcribed while walking than when they transcribed while sitting ($p < 0.001$).

CONCLUSION: The treadmill desk offers a way to reduce sedentariness in the workplace and has potential to reduce employee obesity and health care costs. However, more than 4 hours of training will be necessary to prevent a significant drop in employee productivity.

PMID: 22130064 [PubMed - indexed for MEDLINE]

19. Urban Stud. 2011;48(11):2417-27.

Non-exercise physical activity in agricultural and urban people.

Levine JA(1), McCrady SK, Boyne S, Smith J, Cargill K, Forrester T.

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(1)Mayo Clinic.

With evidence that urbanisation is associated with obesity, diabetes, hypertension and cardiovascular disease, this article compares daily physical activity between rural and urban dwellers. Specifically, it examines habitual daily activity levels, non-exercise activity thermogenesis (NEAT) and energy

expenditure in agricultural and urban Jamaicans and urban North Americans. Ambulation was 60 per cent greater in rural Jamaicans than in the urban dwellers (4675 ± 2261 versus 2940 ± 1120 ambulation-attributed arbitrary units (AU)/day; $P = 0.001$). Levels of ambulation in lean urban Jamaicans were similar to those in lean urban North Americans, whereas obese urban dwellers walked less than their lean urban counterparts (2198 ± 516 versus 2793 ± 774 AU/day; $P = 0.01$). The data with respect to daily sitting mirrored the walking data; obese Americans sat for almost four hours more each day than rural Jamaicans (562 ± 78 versus 336 ± 68 minutes/day; $P < 0.001$). Urbanisation is associated with low levels of daily activity and NEAT.

PMID: 22073428 [PubMed - indexed for MEDLINE]

20. J Biol Dyn. 2011 Nov;5(6):579-599.

A Simple Model Predicting Individual Weight Change in Humans.

Thomas DM(1), Martin CK(2), Heymsfield S(3), Redman LM(2), Schoeller DA(4), Levine JA(5).

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Excessive weight in adults is a national concern with over 2/3 of the US population deemed overweight. Because being overweight has been correlated to numerous diseases such as heart disease and type 2 diabetes, there is a need to understand mechanisms and predict outcomes of weight change and weight maintenance. A simple mathematical model that accurately predicts individual weight change offers opportunities to understand how individuals lose and gain weight and can be used to foster patient adherence to diets in clinical settings. For this purpose, we developed a one dimensional differential equation model of weight change based on the energy balance equation is paired to an algebraic relationship between fat free mass and fat mass derived from a large nationally representative sample of recently released data collected by the Centers for Disease Control. We validate the model's ability to predict individual participants' weight change by comparing model estimates of final weight data from two recent underfeeding studies and one overfeeding study. Mean absolute error and standard deviation between model predictions and observed measurements of final weights are less than 1.8 ± 1.3 kg for the underfeeding studies and 2.5 ± 1.6 kg for the overfeeding study. Comparison of the model predictions to other one dimensional models of weight change shows improvement in mean absolute error, standard deviation of mean absolute error, and group mean predictions. The maximum absolute individual error decreased by approximately 60% substantiating reliability in individual weight change predictions. The model provides a viable method for estimating individual weight change as a result of changes in intake and determining individual dietary adherence during weight change studies.

PMCID: PMC3975626

PMID: 24707319 [PubMed]

21. Obesity (Silver Spring). 2011 May;19(5):897-9. doi: 10.1038/oby.2010.281.

Federal health-care reform: opportunities for obesity prevention.

Levine JA(1), Koepp GA.

Author information:

(1)Mayo Clinic, Rochester, Minnesota, USA. Levine.james@mayo.edu

PMID: 21519335 [PubMed - indexed for MEDLINE]

22. Health Serv Manage Res. 2011 May;24(2):69-74. doi: 10.1258/hsmr.2010.010015.

Scalable office-based health care.

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The goal of health care is to provide high-quality care at an affordable cost for its patients. However, the population it serves has changed dramatically since the popularization of hospital-based health care. With available new technology, alternative health care delivery methods can be designed and tested. This study examines scalable office-based health care for small business, where health care is delivered to the office floor. This delivery was tested in 18 individuals at a small business in Minneapolis, Minnesota. The goal was to deliver modular health care and mitigate conditions such as diabetes, hyperlipidaemia, obesity, sedentariness and metabolic disease. The modular health care system was welcomed by employees - 70% of those eligible enrolled. The findings showed that the modular health care deliverable was feasible and effective. The data demonstrated significant improvements in weight loss, fat loss and blood variables for at risk participants. This study leaves room for improvement and further innovation. Expansion to include offerings such as physicals, diabetes management, smoking cessation and prenatal treatment would improve its utility. Future studies could include testing the adaptability of delivery method, as it should adapt to reach rural and under-served populations.

PMCID: PMC3919052

PMID: 21471576 [PubMed - indexed for MEDLINE]

23. J Phys Act Health. 2010 Nov;7 Suppl 3:S307-12.

Scalable Obesity Solutions (S.O.S.).

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Author information:

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The know-how is available to reverse the obesity epidemic. Reversing obesity is a societal necessity because it is the predominant contributor to chronic ill health in developed countries and a growing precipitant of illness in middle and

low-income countries. In the United States, for example, obesity is the chief driver of health care costs in a country that can no longer afford health care. Although some might advocate population-wide medication use to mitigate the effects of obesity on health, the more direct response is to end obesity. The goal of this paper is explain how mass-scalable obesity containment can be designed, built, and disseminated. Scalable Obesity Solutions (S.O.S.) are discussed from concept through deployment.

PMID: 21116015 [PubMed - indexed for MEDLINE]

24. Diabetes. 2010 Nov;59(11):2715-6. doi: 10.2337/db10-1042.

Health-chair reform: your chair: comfortable but deadly.

Levine JA.

Author information:

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Comment on

Diabetes. 2010 Nov;59(11):2732-4.

Diabetes. 2010 Nov;59(11):2717-25.

Diabetes. 2010 Nov;59(11):2790-8.

PMCID: PMC2963525

PMID: 20980469 [PubMed - indexed for MEDLINE]

25. Expert Rev Med Devices. 2010 Mar;7(2):201-7. doi: 10.1586/erd.09.73.

Integrated electronic platforms for weight loss.

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Author information:

(1)Endocrine Research Unit, Mayo Clinic, Rochester, MN 55905, USA.

What can be done to build effective weight loss solutions for the 1.5 billion people with obesity? It is self-evident that no one good solution exists for people who are overweight or obese, otherwise it would have been applied across the people who need it worldwide. There is, therefore, an urgent need for approaches that will afford weight loss; what is more, such approaches need to be scalable. For that reason, it is attractive to consider electronic platforms as an avenue for scalable weight loss solutions. Such platforms often do not require substantial investments but rather the integration of pre-existing off-the-shelf components. In this article we explore the concepts and design challenges for electronic platforms that precipitate weight loss.

PMCID: PMC2897161

PMID: 20214426 [PubMed - indexed for MEDLINE]

26. J Phys Act Health. 2009 Nov;6(6):781-9.

An accelerometer-based earpiece to monitor and quantify physical activity.

Manohar C(1), McCrady S, Pavlidis IT, Levine JA.

Author information:

(1)Endocrine Research Unit, Mayo Clinic, Rochester, MN, USA.

BACKGROUND: Physical activity is important in ill-health. Inexpensive, accurate and precise devices could help assess daily activity. We integrated novel activity-sensing technology into an earpiece used with portable music-players and phones; the physical-activity-sensing earpiece (PASE). Here we examined whether the PASE could accurately and precisely detect physical activity and measure its intensity and thence predict energy expenditure.

METHODS: Experiment 1: 18 subjects wore PASE with different body postures and during graded walking. Energy expenditure was measured using indirect calorimetry. Experiment 2: 8 subjects wore the earpiece and walked a known distance. Experiment 3: 8 subjects wore the earpiece and 'jogged' at 3.5 mph.

RESULTS: The earpiece correctly distinguished lying from sitting/standing and distinguished standing still from walking (76/76 cases). PASE output showed excellent sequential increases with increased in walking velocity and energy expenditure ($r_2 > .9$). The PASE prediction of free-living walking velocity was, 2.5 +/- (SD) 0.18 mph c.f. actual velocity, 2.5 +/- 0.16 mph. The earpiece successfully distinguished walking at 3.5 mph from 'jogging' at the same velocity ($P < .001$).

CONCLUSIONS: The subjects tolerated the earpiece well and were comfortable wearing it. The PASE can therefore be used to reliably monitor free-living physical activity and its associated energy expenditure.

PMCID: PMC2813462

PMID: 20101922 [PubMed - indexed for MEDLINE]

27. Work. 2009;34(3):359-64. doi: 10.3233/WOR-2009-0934.

Description and clinical studies of a device for the instantaneous detection of office-place stress.

Levine JA(1), Pavlidis IT, MacBride L, Zhu Z, Tsiamyrtzis P.

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Occupational stress is universally experienced and is emerging as a major risk factor for physical and mental illness and a key factor in poor work performance and low job satisfaction. However, the technology does not currently exist to unobtrusively measure occupational stress in real-time. Here, we describe the design and clinical validation of an automated high-definition thermal imaging system that can be used to quantify human stress, remotely and instantaneously. Healthy human subjects underwent a computer-based version of the Stroop-color conflict test, which is a validated stress provocation test, in an experimental office facility. In separate experiments, the same subjects completed a mental arithmetic challenge. The thermal signal associated with stress provocation is near-instantaneous corrugator warming. The stress response was detected in all subjects for all stress-events compared to the respective baselines. Furthermore,

there was remarkable inter-individual preservation of the corrugator signal with stress $R(2) = 0.96$, $P < 0.001$). High-definition thermal imaging can be used for real-time detection of stress provocation. This technology may prove to be of help in ameliorating office-place stress.

PMID: 20037251 [PubMed - indexed for MEDLINE]

28. PLoS One. 2009 Jun 12;4(6):e5869. doi: 10.1371/journal.pone.0005869.

Endurance capacity, not body size, determines physical activity levels: role of skeletal muscle PEPCK.

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Some people remain lean despite pressure to gain weight. Lean people tend to have high daily activity levels, but the source of this increased activity is unknown. We found that leanness cannot be accounted for by increased weight-corrected food intake in two different types of lean rats. As previously reported in lean people, we found that lean rats had higher daily activity levels; lean rats also expended more energy. These lean rats were developed through artificial selection for high aerobic endurance capacity. To test whether our findings extended to a human population, we measured endurance capacity using a $VO(2max)$ treadmill test and daily activity in a group of non-exercising individuals. Similar to lean rats selectively bred for endurance capacity, our study revealed that people with higher $VO(2max)$ also spent more time active throughout the day. Hence, endurance capacity may be the trait that underlies both physical activity levels and leanness. We identified one potential mechanism for the lean, active phenotype in rats, namely high levels of skeletal muscle PEPCK. Therefore, the lean phenotype is characterized by high endurance capacity and high activity and may stem from altered skeletal muscle energetics.

PMCID: PMC2690400

PMID: 19521512 [PubMed - indexed for MEDLINE]

29. Obesity (Silver Spring). 2009 Nov;17(11):2103-5. doi: 10.1038/oby.2009.117. Epub 2009 Apr 23.

Sedentariness at work: how much do we really sit?

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Author information:

(1)Endocrine Research Unit, Mayo Clinic, Rochester, Minnesota, USA.

Sedentariness is associated with obesity. We examined whether people with sedentary jobs are equally inactive during their work days and leisure days. We enrolled 21 subjects of varying weight and body fat (11 men:10 women, 38 +/- 8 years, 83 +/- 17 kg, BMI 28 +/- 5 kg/m², 29 +/- 11 fat kg, 35 +/- 9% fat). All subjects continued their usual work and leisure-time activities whilst we

measured daily activity and body postures for 10 days. The data supported our hypothesis that people sit more at work compared to leisure (597 +/- 122 min/day cf 484 +/- 83 min/day; $P < 0.0001$). The mean difference was 110 +/- 99 min/day. Similarly, work days were associated with less standing (341 +/- 97 min/day; $P = 0.002$) than leisure days (417 +/- 101 min/day). Although the walking bouts did not differ significantly between work and leisure (46 +/- 9 vs. 42 +/- 9 walking bouts/day); the mean free-living velocity of a walk at work was 1.08 +/- 0.28 mph and on leisure days was 0.94 +/- 0.24 mph ($P = 0.03$) and the average time spent walking was 322 +/- 91 min on work days and 380 +/- 108 min on leisure days ($P = 0.03$). Estimates of the daily energetic cost of walking approximated 527 +/- 220 kcal/day for work days and 586 +/- 326 kcal/day for leisure days ($r = 0.72$, $P < 0.001$). Work days are associated with more sitting and less walking/standing time than leisure days. We suggest a need to develop approaches to free people from their chairs and render them more active.

PMCID: PMC2783690

PMID: 19390526 [PubMed - indexed for MEDLINE]

30. Obesity (Silver Spring). 2009 Aug;17(8):1493-8. doi: 10.1038/oby.2009.91. Epub 2009 Apr 2.

Daily intraparaventricular orexin-A treatment induces weight loss in rats.

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The neuropeptide orexin (hypocretin) increases energy expenditure partially through increasing spontaneous physical activity. The ability of exogenous orexin to alter body weight has never been established, however. We sought to determine whether orexin-A microinjected into the paraventricular nucleus of the hypothalamus (PVN) induced weight loss in rats. Chronic guide cannulae were implanted into rats, aimed at the PVN. Rats were given daily microinjections of orexin (0.5 nmol) or vehicle into the PVN for 6 days; food intake and body weight were measured daily. In a separate group of rats, we injected orexin-A and vehicle intra-PVN and measured daily activity levels. Daily orexin treatment induced weight loss: orexin-A-treated rats lost significantly more weight than their vehicle-injected counterparts without a significant difference in food intake. Rats were significantly more active after intra-PVN orexin compared to vehicle. These results support the concept that orexinergic agents have the potential to produce negative energy balance through increasing physical activity. This presents a promising, untapped potential resource for weight loss.

PMCID: PMC2717187

PMID: 19343016 [PubMed - indexed for MEDLINE]

31. J Pediatr. 2009 Jun;154(6):819-23. doi: 10.1016/j.jpeds.2009.01.009. Epub 2009 Mar 25.

Activity-promoting video games and increased energy expenditure.

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OBJECTIVES: To test the hypothesis that both children and adults would expend more calories and move more while playing activity-promoting video games compared with sedentary video games.

STUDY DESIGN: In this single-group study, 22 healthy children (12 +/- 2 years; 11 male, 11 female) and 20 adults (34 +/- 11 years; 10 male, 10 female) were recruited. Energy expenditure and physical activity were measured while participants were resting, standing, watching television seated, sitting and playing a traditional sedentary video game, and while playing an activity-promoting video game (Nintendo Wii Boxing). Physical activity was measured with accelerometers, and energy expenditure was measured with an indirect calorimeter.

RESULTS: Energy expenditure was significantly greater than all other activities when children or adults played Nintendo Wii (mean increase over resting, 189 +/- 63 kcal/hr, $P < .001$, and 148 +/- 71 kcal/hr, $P < .001$, respectively). When examining movement with accelerometry, children moved significantly more than adults (55 +/- 5 arbitrary acceleration units and 23 +/- 2 arbitrary acceleration units, respectively, $P < .001$) while playing Nintendo Wii.

CONCLUSION: Activity-promoting video games have the potential to increase movement and energy expenditure in children and adults.

PMCID: PMC2683894

PMID: 19324368 [PubMed - indexed for MEDLINE]

32. Pediatrics. 2009 Jan;123(1):e127-31. doi: 10.1542/peds.2008-1908.

Pedometer accuracy for children: can we recommend them for our obese population?

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OBJECTIVE: In this study, we investigated the accuracy of measuring walking steps with commercially available pedometers and an accelerometer-based step-counter in normal and overweight children. Our primary hypothesis was that commercially available pedometers are not an accurate measure of walking steps in normal and overweight children while walking. Our secondary hypothesis was that the accelerometer-based step-counter provides an accurate measure of walking steps in normal and overweight children.

METHODS: Thirteen boys (11 +/- 1 years) and 14 girls (11 +/- 1 years) who ranged in BMI from 15 to 27 kg/m² (16 normal and 11 overweight or obese) were recruited. Each child wore 4 pedometers at the waist and 1 accelerometer-based step-counter on each ankle. Steps were manually counted and energy expenditure was measured while the child walked on the treadmill at 0.5, 1.0, 1.5, and 2.0 mph, each for 5 minutes. The step-counting devices were also validated while children walked on level ground at a self-selected pace.

RESULTS: For the commercially available pedometers at the lowest speed of 0.5 mph, the percentage error approximated 100% for both of the pedometers. At the fastest speed of 2.0 mph, the percentage error approximated 60%. Conversely the accelerometer-based step-counter showed a percentage error of 24% +/- 22% (mean

+/- SD) at 0.5 mph; however, as walking speed increased, the error declined to 5% +/- 8% at 1.0 mph, 4% +/- 5% at 1.5 mph, and 2% +/- 2% at 2.0 mph. The relationship between steps counted and walking energy expenditure showed good linear correlation.

CONCLUSIONS: Commercially available pedometers are less accurate for measuring walking and require discretion in their use for children. The accuracy of the accelerometer-based step-counter enables it to be used as a tool to assess and potentially promote physical activity in normal and overweight children.

PMCID: PMC2678845

PMID: 19117834 [PubMed - indexed for MEDLINE]

33. J Am Coll Radiol. 2008 Nov;5(11):1130-6. doi: 10.1016/j.jacr.2008.05.003.

Feasibility of using a walking workstation during CT image interpretation.

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Comment in

J Am Coll Radiol. 2009 Mar;6(3):213; author reply 213-4.

OBJECTIVE: Two-thirds of the US population is overweight or obese. Sedentary lifestyles and occupations are one factor in the development of obesity. Methods to help reduce sedentary work environments may help reduce obesity. The purpose of this study was to determine the feasibility of using a walking workstation during computed tomographic image interpretation.

METHODS: Two radiologists reinterpreted 100 clinical computed tomographic examinations they had previously interpreted, each while walking at 1 mph on a treadmill using an electronic workstation. Ten cases were reviewed per session. The time period between the initial conventional interpretations and the reinterpretations was greater than one year, to reduce recall bias. Discrepant findings were ranked according to a classification system based on clinical importance on a scale ranging from 1 to 6. Discrepant findings classified as greater than or equal to 3 were considered significant. Detection rates for the initial interpretations and reinterpretations were determined for each reviewer and compared using a paired t-test.

RESULTS: A total of 1,582 findings were reported (825 by reviewer 1 and 757 by reviewer 2). There were 459 findings with clinical importance of 3 or higher. For reviewer 1 (91 cases of at least one important finding), the mean detection rates were 99.0% for the walking technique and 88.9% for the conventional interpretations ($P = .0003$). For reviewer 2 (89 cases with at least one important finding) the mean detection rates were 99.1% for the walking technique and 81.3% for the conventional interpretations ($P < .0001$).

CONCLUSION: The use of a walking workstation for the interpretation of cross-sectional images is feasible. Further studies are needed to assess the potential impact on diagnostic accuracy.

PMID: 18954813 [PubMed - indexed for MEDLINE]

34. Chin Med J (Engl). 2008 Jun 5;121(11):1043-50.

Obesity in China: causes and solutions.

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Author information:

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PMID: 18706257 [PubMed - indexed for MEDLINE]

35. Diabetes. 2008 Jul;57(7):1784-5. doi: 10.2337/db08-0108.

The Pol-e-pill finally arrives.

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PMCID: PMC2453630

PMID: 18586910 [PubMed - indexed for MEDLINE]

36. Arch Phys Med Rehabil. 2008 Jul;89(7):1380-5. doi: 10.1016/j.apmr.2007.11.053.

Energy expenditure and activity of transfemoral amputees using mechanical and microprocessor-controlled prosthetic knees.

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OBJECTIVE: To quantify the energy efficiency of locomotion and free-living physical activity energy expenditure of transfemoral amputees using a mechanical and microprocessor-controlled prosthetic knee.

DESIGN: Repeated-measures design to evaluate comparative functional outcomes.

SETTING: Exercise physiology laboratory and community free-living environment.

PARTICIPANTS: Subjects (N=15; 12 men, 3 women; age, 42+/-9 y; range, 26-57 y) with transfemoral amputation.

INTERVENTION: Research participants were long-term users of a mechanical prosthesis (20+/-10 y as an amputee; range, 3-36 y). They were fitted with a microprocessor-controlled knee prosthesis and allowed to acclimate (mean time, 18+/-8 wk) before being retested.

MAIN OUTCOME MEASURES: Objective measurements of energy efficiency and total daily energy expenditure were obtained. The Prosthetic Evaluation Questionnaire was used to gather subjective feedback from the participants.

RESULTS: Subjects demonstrated significantly increased physical activity-related energy expenditure levels in the participant's free-living environment (P=.04) after wearing the microprocessor-controlled prosthetic knee joint. There was no significant difference in the energy efficiency of walking (P=.34). When using

the microprocessor-controlled knee, the subjects expressed increased satisfaction in their daily lives ($P=.02$).

CONCLUSIONS: People ambulating with a microprocessor-controlled knee significantly increased their physical activity during daily life, outside the laboratory setting, and expressed an increased quality of life.

PMCID: PMC2692755

PMID: 18586142 [PubMed - indexed for MEDLINE]

37. J Endocrinol. 2008 Sep;198(3):599-605. doi: 10.1677/JOE-08-0179. Epub 2008 Jun 19.

Metabolic consequences of pregnancy-associated plasma protein-A deficiency in mice: exploring possible relationship to the longevity phenotype.

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Mice born with the deletion of the gene for pregnancy-associated plasma protein-A (PAPP-A), a model of reduced local IGF activity, live approximately 30% longer than their wild-type (WT) littermates. In this study, we investigated metabolic consequences of PAPP-A gene deletion and possible relationship to lifespan extension. Specifically, we determined whether 18-month-old PAPP-A knockout (KO) mice when compared with their WT littermates have reduced energy expenditure and/or altered glucose-insulin sensitivity. Food intake, and total energy expenditure and resting energy expenditure as measured by calorimetry were not different between PAPP-A KO and WT mice when subjected to the analysis of covariance with body weight as the covariate. However, there was an increase in spontaneous physical activity in PAPP-A KO mice. Both WT and PAPP-A KO mice exhibited mild insulin resistance with age, as assessed by fasting glucose/insulin ratios. Oral glucose tolerance and insulin sensitivity were not significantly different between the two groups of mice, although there appeared to be a decrease in the average size of the pancreatic islets in PAPP-A KO mice. Thus, neither reduced 'rate of living' nor altered glucose-insulin homeostasis can be considered key determinants of the enhanced longevity of PAPP-A KO mice. These findings are discussed in the context of those from other long-lived mouse models.

PMCID: PMC2593875

PMID: 18566100 [PubMed - indexed for MEDLINE]

38. Obesity (Silver Spring). 2008 Aug;16(8):1849-53. doi: 10.1038/oby.2008.282. Epub 2008 May 29.

Changing the school environment to increase physical activity in children.

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Comment in

Obesity (Silver Spring). 2009 Apr;17(4):631; author reply 631.

We examined the hypothesis that elementary school-age children will be more physically active while attending school in a novel, activity-permissive school environment compared to their traditional school environment. Twenty-four children were monitored with a single-triaxial accelerometer worn on the thigh. The students attended school in three different environments: traditional school with chairs and desks, an activity-permissive environment, and finally their traditional school with desks which encouraged standing. Data from the school children were compared with another group of age-matched children ($n = 16$) whose physical activity was monitored during summer vacation. When children attended school in their traditional environment, they moved an average (mean \pm s.d.) of 71 ± 0.4 m/s². When the children attended school in the activity-permissive environment, they moved an average of 115 ± 3 m/s². The children moved 71 ± 0.7 m/s² while attending the traditional school with standing desks. Children moved significantly more while attending school in the activity-permissive environment compared to the amount that they moved in either of the traditional school environments ($P < 0.0001$ for both). Comparing children's activity while they were on summer vacation (113 ± 8 m/s²) to school-bound children in their traditional environment showed significantly more activity for the children on summer vacation ($P < 0.0001$). The school children in the activity-permissive environment were as active as children on summer vacation. Children will move more in an activity-permissive environment. Strategies to increase the activity of school children may involve re-designing the school itself.

PMCID: PMC2690697

PMID: 18535550 [PubMed - indexed for MEDLINE]

39. Int J Eat Disord. 2008 Apr;41(3):280-3.

Measurement of daily activity in restrictive type anorexia nervosa.

Harris AM(1), McAlpine DE, Shirbhate R, Manohar CU, Levine JA.

Author information:

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OBJECTIVE: The assessment of daily activity in patients with restrictive type anorexia nervosa is limited by an absence of accurate and precise technology. We wanted to test a daily activity detecting device named, the physical activity monitoring system (PAMS).

METHOD: Women participants with restrictive type anorexia nervosa ($n = 8$, 36 ± 11 years, 17 ± 2 kg/m²) and healthy women participants ($n = 8$, 30 ± 11 years, 27 ± 7 kg/m²) were asked to lie, sit, and stand motionless, and walk at 0.5, 1.0, 1.5, 2.0, 2.5, and 3.0 mph while wearing PAMS.

RESULTS: For all restrictive type anorexia nervosa and healthy participants, body posture was correctly detected for all measurements (300/300). There was excellent correlation of an individual's body acceleration with walking velocity and walking energy expenditure ($r(2) > .99$).

CONCLUSION: The PAMS technology could serve as a tool for lending insight into the pathophysiology of restrictive type anorexia nervosa; and potentially measuring compliance with activity recommendations for medical professionals

treating individuals with restrictive type anorexia nervosa.

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PMCID: PMC2705949

PMID: 18004719 [PubMed - indexed for MEDLINE]

40. Diabetes. 2008 Mar;57(3):548-54. Epub 2007 Nov 14.

The role of free-living daily walking in human weight gain and obesity.

Levine JA(1), McCrady SK, Lanningham-Foster LM, Kane PH, Foster RC, Manohar CU.

Author information:

(1)Endocrine Research Unit, Mayo Clinic, Rochester, MN 55905, USA. jim@mayo.edu

OBJECTIVE: Diminished daily physical activity explains, in part, why obesity and diabetes have become worldwide epidemics. In particular, chair use has replaced ambulation, so that obese individuals tend to sit for approximately 2.5 h/day more than lean counterparts. Here, we address the hypotheses that free-living daily walking distance is decreased in obesity compared with lean subjects and that experimental weight gain precipitates decreased daily walking.

RESEARCH DESIGN AND METHODS: During weight-maintenance feeding, we measured free-living walking using a validated system that captures locomotion and body movement for 10 days in 22 healthy lean and obese sedentary individuals. These measurements were then repeated after the lean and obese subjects were overfed by 1,000 kcal/day for 8 weeks.

RESULTS: We found that free-living walking comprises many (approximately 47) short-duration (<15 min), low-velocity (approximately 1 mph) walking bouts. Lean subjects walked 3.5 miles/day more than obese subjects (n = 10, 10.3 +/- 2.5 vs. n = 12, 6.7 +/- 1.8 miles/day; P = 0.0009). With overfeeding, walking distance decreased by 1.5 miles/day compared with baseline values (-1.5 +/- 1.7 miles/day; P = 0.0005). The decrease in walking that accompanied overfeeding occurred to a similar degree in the lean (-1.4 +/- 1.9 miles/day; P = 0.04) and obese (-1.6 +/- 1.7 miles/day; P = 0.008) subjects.

CONCLUSIONS: Walking is decreased in obesity and declines with weight gain. This may represent a continuum whereby progressive increases in weight are associated with progressive decreases in walking distance. By identifying walking as pivotal in weight gain and obesity, we hope to add credence to an argument for an ambulatory future.

PMID: 18003759 [PubMed - indexed for MEDLINE]

41. Conf Proc IEEE Eng Med Biol Soc. 2007;2007:2659-63.

Design of posture and activity detector (PAD).

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In recent years, there has been much research and development of wearable devices using accelerometers for studying physical activity. Previously, we have described the development of the Posture and Activity Detector (PAD). After demonstrating success with PAD, we were motivated to improve the design by taking the device one step further and implementing all of these components on a single printed circuit board, adding a few additional features to make the system more flexible, and custom-designing an outer case. We have continued our efforts in improving PAD with respect to software development as well as making PAD more physically robust and mass producible. In this paper, the specifications for PAD will be outlined including its hardware and software components, and clinical research applications.

PMID: 18002542 [PubMed - indexed for MEDLINE]

42. J Neuroendocrinol. 2007 Dec;19(12):923-40.

Central neural and endocrine mechanisms of non-exercise activity thermogenesis and their potential impact on obesity.

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The rise in obesity is associated with a decline in the amount of physical activity in which people engage. The energy expended through everyday non-exercise activity, called non-exercise activity thermogenesis (NEAT), has a considerable potential impact on energy balance and weight gain. Comparatively little attention has been paid to the central mechanisms of energy expenditure and how decreases in NEAT might contribute to obesity. In this review, we first examine the sensory and endocrine mechanisms through which energy availability and energy balance are detected that may influence NEAT. Second, we describe the neural pathways that integrate these signals. Lastly, we consider the effector mechanisms that modulate NEAT through the alteration of activity levels as well as through changes in the energy efficiency of movement. Systems that regulate NEAT according to energy balance may be linked to neural circuits that modulate sleep, addiction and the stress response. The neural and endocrine systems that control NEAT are potential targets for the treatment of obesity.

PMID: 18001322 [PubMed - indexed for MEDLINE]

43. Gait Posture. 2007 Oct;26(4):489-93. Epub 2007 Sep 14.

Gait and balance of transfemoral amputees using passive mechanical and microprocessor-controlled prosthetic knees.

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Comment in

Gait Posture. 2009 Jan;29(1):161-2; author reply 163-4.

BACKGROUND: Microprocessor-controlled knee joints appeared on the market a decade ago. These joints are more sophisticated and more expensive than mechanical ones. The literature is contradictory regarding changes in gait and balance when using these sophisticated devices.

METHODS: This study employed a crossover design to assess the comparative performance of a passive mechanical knee prosthesis compared to a microprocessor-controlled knee joint in 15 subjects with an above-knee amputation. Objective measurements of gait and balance were obtained.

RESULTS: Subjects demonstrated significantly improved gait characteristics after receiving the microprocessor-controlled prosthetic knee joint ($p < 0.01$). Improvements in gait were a transition from a hyperextended knee to a flexed knee during loading response which resulted in a change from an internal knee flexor moment to a knee extensor moment. The participants' balance also improved ($p < 0.01$). All conditions of the Sensory Organization Test (SOT) demonstrated improvements in equilibrium score. The composite score also increased.

CONCLUSIONS: Transfemoral amputees using a microprocessor-controlled knee have significant improvements in gait and balance.

PMID: 17869114 [PubMed - indexed for MEDLINE]

44. Br J Sports Med. 2008 Mar;42(3):225-8; discussion 228. Epub 2007 Aug 23.

Feasibility of a walking workstation to increase daily walking.

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OBJECTIVE: The number of calories expended in the workplace has declined significantly in the past 75 years. A walking workstation that allows workers to walk while they work has the potential to increase caloric expenditure. We evaluated whether employees can and will use walking workstations while performing their jobs.

METHODS AND PROCEDURES: We studied nurses, clinical assistants, secretaries and appointment secretaries using the StepWatch Activity Monitor System (which accurately measures steps taken at slow speeds) while performing their job functions in their usual fashion and while using the walking workstation.

RESULTS: Subjects increased the number of steps taken during the workday by 2000 steps per day ($p < 0.05$). This was equivalent to an increase in caloric expenditure of 100 kcal/day. Subjects reported that they enjoyed using the workstation, that it could be used in the actual work arena and that, if available, they would use it.

DISCUSSION: Walking workstations have the potential for promoting physical activity and facilitating weight loss. Several subjects in this study expended more than 200 extra calories daily using such a system. Further trials are indicated.

PMID: 17717060 [PubMed - indexed for MEDLINE]

45. Brain Res. 2007 Sep 12;1169:57-68. Epub 2007 Jul 13.

Sensitivity of the hypothalamic paraventricular nucleus to the locomotor-activating effects of neuromedin U in obesity.

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Obesity is associated with a decrease in energy expenditure relative to energy intake. The decrease in physical activity associated with obesity in several species, including humans, contributes to decreased energy expenditure. Several hormones and neuropeptides that affect appetite also modulate physical activity, including neuromedin U (NMU), a peptide found in the gut and brain. We have demonstrated that NMU microinjected into the hypothalamic paraventricular nucleus (PVN) in rats increases the energy expenditure associated with physical activity, called non-exercise activity thermogenesis (NEAT). Here we examined whether obesity in rats is related to decreased sensitivity of the PVN to the locomotor-activating effect of NMU. Diet-induced obese (DIO) rats and lean, diet-resistant (DR) rats were given PVN microinjections of increasing doses of NMU both before and after 1 month on a high-fat diet. We found that NMU increases physical activity, energy expenditure, and NEAT in a dose-dependent manner in both DR and DIO rats, both before and after 1 month on the high-fat diet. Before high-fat feeding, the obesity-prone and lean rats showed similar levels of physical activity after intra-PVN microinjections of NMU. After 1 month of the high-fat diet, however, the obesity-resistant rats showed significantly more NMU-induced physical activity compared to the obese DIO rats. Taken together with previous studies, these results suggest that obesity may represent a state associated with decreased central sensitivity to neuropeptides such as NMU that increase physical activity and therefore energy expenditure.

PMCID: PMC2735201

PMID: 17706946 [PubMed - indexed for MEDLINE]

46. J Intern Med. 2007 Sep;262(3):273-87.

Nonexercise activity thermogenesis--liberating the life-force.

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Obesity occurs when energy intake exceeds energy expenditure over a protracted period of time. The energy expenditure associated with everyday activity is called NEAT (Nonexercise activity thermogenesis). NEAT varies between two people of similar size by 2000 kcal day⁻¹ because of people's different occupations and leisure-time activities. Data support the central hypothesis that NEAT is pivotal in the regulation of human energy expenditure and body weight regulation and that NEAT is important for understanding the cause and effective treatment for obesity.

PMID: 17697152 [PubMed - indexed for MEDLINE]

47. Mayo Clin Proc. 2007 Jul;82(7):797-8.

Exercise: a walk in the park?

Levine JA.

PMID: 17605957 [PubMed - indexed for MEDLINE]

48. FASEB J. 2007 Nov;21(13):3629-39. Epub 2007 Jun 21.

The enzyme CD38 (a NAD glycohydrolase, EC 3.2.2.5) is necessary for the development of diet-induced obesity.

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Obesity is one of the major health problems of our times. Elucidating the signaling mechanisms by which high-fat caloric diet induces obesity is critical for the understanding of this condition and for the development of therapeutic strategies for its treatment. Here, we demonstrate a novel role for protein CD38 as a regulator of body weight during a high-fat diet. CD38 is a ubiquitous enzyme that catalyzes the synthesis of second messengers and has been implicated in the regulation of a wide variety of signaling pathways. We report that CD38-deficient mice are protected against high-fat diet-induced obesity owing to enhanced energy expenditure. In fact, calorimetric studies indicate that CD38-deficient animals have a higher metabolic rate compared to control mice. Analysis of the mechanism revealed that this resistance to diet-induced obesity is mediated at least in part via a NAD-dependent activation of SIRT-PGC1 α axis, a well-established cascade, involved in the regulation of mitochondrial biogenesis and energy homeostasis. Thus, together these results identify a novel pathway regulating body weight and clearly show that CD38 is a nearly obligatory component of the cellular cascade that led to diet-induced obesity.

PMID: 17585054 [PubMed - indexed for MEDLINE]

49. Br J Sports Med. 2007 Dec;41(12):903-7. Epub 2007 May 18.

An office-place stepping device to promote workplace physical activity.

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OBJECTIVE: It was proposed that an office-place stepping device is associated with significant and substantial increases in energy expenditure compared to sitting energy expenditure. The objective was to assess the effect of using an office-place stepping device on the energy expenditure of lean and obese office workers.

METHODS: The office-place stepping device is an inexpensive, near-silent,

low-impact device that can be housed under a standard desk and plugged into an office PC for self-monitoring. Energy expenditure was measured in lean and obese subjects using the stepping device and during rest, sitting and walking. 19 subjects (27+/-9 years, 85+/-23 kg): 9 lean (BMI<25 kg/m²) and 10 obese (BMI>29 kg/m²) attended the experimental office facility. Energy expenditure was measured at rest, while seated in an office chair, standing, walking on a treadmill and while using the office-place stepping device.

RESULTS: The office-place stepping device was associated with an increase in energy expenditure above sitting in an office chair by 289+/-102 kcal/hour ($p<0.001$). The increase in energy expenditure was greater for obese (335+/-99 kcal/hour) than for lean subjects (235+/-80 kcal/hour; $p = 0.03$). The increments in energy expenditure were similar to exercise-style walking.

CONCLUSION: The office-place stepping device could be an approach for office workers to increase their energy expenditure. If the stepping device was used to replace sitting by 2 hours per day and if other components of energy balance were constant, weight loss of 20 kg/year could occur.

PMCID: PMC2658993

PMID: 17513333 [PubMed - indexed for MEDLINE]

50. Br J Sports Med. 2007 Sep;41(9):558-61. Epub 2007 May 15.

The energy expenditure of using a "walk-and-work" desk for office workers with obesity.

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OBJECTIVE: For many people, most of the working day is spent sitting in front of a computer screen. Approaches for obesity treatment and prevention are being sought to increase workplace physical activity because low levels of physical activity are associated with obesity. Our hypothesis was that a vertical workstation that allows an obese individual to work while walking would be associated with significant and substantial increases in energy expenditure over seated work.

METHODS: The vertical workstation is a workstation that allows an office worker to use a standard personal computer while walking on a treadmill at a self-selected velocity. 15 sedentary individuals with obesity (14 women, one man; 43 (7.5) years, 86 (9.6) kg; body mass index 32 (2.6) kg/m²) underwent measurements of energy expenditure at rest, seated working in an office chair, standing and while walking at a self-selected speed using the vertical workstation. Body composition was measured using dual x ray absorptiometry.

RESULTS: The mean (SD) energy expenditure while seated at work in an office chair was 72 (10) kcal/h, whereas the energy expenditure while walking and working at a self-selected velocity of 1.1 (0.4) mph was 191 (29) kcal/h. The mean (SD) increase in energy expenditure for walking-and-working over sitting was 119 (25) kcal/h.

CONCLUSIONS: If sitting computer-time were replaced by walking-and-working, energy expenditure could increase by 100 kcal/h. Thus, if obese individuals were to replace time spent sitting at the computer with walking computer time by 2-3 h/day, and if other components of energy balance were constant, a weight loss of 20-30 kg/year could occur.

PMCID: PMC2465387

PMID: 17504789 [PubMed - indexed for MEDLINE]

51. J Therm Biol. 2006 Dec;31(8):634-638.

Does Non-Exercise Activity Thermogenesis Contribute to Non-Shivering Thermogenesis?

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We wanted to examine if spontaneous physical activity contributes to non-shivering thermogenesis. Ten lean, healthy male subjects wore a physical activity, micro-measurement system whilst the room temperature was randomly altered at two hourly intervals between thermoneutral (72°F), cool (62°F) and warm (82°F) temperatures. Physical activity measured during the thermoneutral, cooling and warming periods was not significantly different. Cooling, increased EE above basal and thermoneutral values 2061 ± 344 kcal/day ($p < 0.01$). Thus, the increase in energy expenditure associated with short-term environmental cooling in lean, healthy males does not appear to be due to increased spontaneous physical activity or fidgeting.

PMCID: PMC1847420

PMID: 17404604 [PubMed]

52. Am J Physiol Endocrinol Metab. 2007 Apr;292(4):E1207-12.

Nonexercise movement in elderly compared with young people.

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The association between free-living daily activity and aging is unclear because nonexercise movement and its energetic equivalent, nonexercise activity thermogenesis, have not been exhaustively studied in the elderly. We wanted to address the hypothesis that free-living nonexercise movement is lower in older individuals compared with younger controls matched for lean body mass. Ten lean, healthy, sedentary elderly and 10 young subjects matched for lean body mass underwent measurements of nonexercise movement and body posture over 10 days using sensitive, validated technology. In addition, energy expenditure was assessed using doubly labeled water and indirect calorimetry. Total nonexercise movement (acceleration arbitrary units), standing time, and standing acceleration were significantly lower in the elderly subjects; this was specifically because the elderly walked less distance per day despite having a similar number of walking bouts per day compared with the young individuals. The energetic cost of basal metabolic rate, thermic effect of food, total daily energy expenditure, and nonexercise activity thermogenesis were not different between the elderly and young groups. Thus, the energetic cost of walking in the elderly may be greater than in the young. Lean, healthy elderly individuals may have a biological drive

to be less active than the young.

PMID: 17401138 [PubMed - indexed for MEDLINE]

53. Mayo Clin Proc. 2007 Jan;82(1):93-101; quiz 101-2.

Treatment of obesity.

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For primary care physicians, obesity is one of the most challenging problems confronted in office practice. The disorder is increasing in prevalence despite the efforts of both patients and physicians. Treatment requires a multimodality approach that addresses diet, physical activity, and behavioral issues. Medication and surgical approaches may be appropriate as well. This review outlines the evidence for each approach, suggests how primary care physicians can best help obese patients, and provides practical tips for weight loss.

PMID: 17285790 [PubMed - indexed for MEDLINE]

54. Obesity (Silver Spring). 2007 Jan;15(1):32-9.

Galectin-3 stimulates preadipocyte proliferation and is up-regulated in growing adipose tissue.

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OBJECTIVE: Some cytokines and mediators of inflammation can alter adiposity through their effects on adipocyte number. To probe the molecular basis of obesity, this study determined whether galectin-3 was present in adipose tissue and investigated its effects on fat cell number.

RESEARCH METHODS AND PROCEDURES: In the first study, obesity-prone C57BL/6J mice were fed with high-fat (58%) diet. Epididymal fat pads were collected at Day 0, Day 60, and Day 120 after the start of high-fat feeding.

RESULTS: Levels of adipocyte galectin-3 protein, determined using Western blot analysis, increased as the mice became obese. Galectin-3 mRNA and protein were then detected in human adipose tissue, primarily in the preadipocyte fraction. It was found that recombinant human galectin-3 stimulated proliferation of primary cultured preadipocytes as well as DNA synthesis through lectin-carbohydrate interaction.

DISCUSSION: Galectin-3, which has been known to play a versatile role especially in immune cells, might play a role also in adipose tissue and be associated with the pathophysiology of obesity.

PMID: 17228029 [PubMed - indexed for MEDLINE]

55. Pediatrics. 2006 Dec;118(6):e1831-5.

Energy expenditure of sedentary screen time compared with active screen time for children.

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OBJECTIVE: We examined the effect of activity-enhancing screen devices on children's energy expenditure compared with performing the same activities while seated. Our hypothesis was that energy expenditure would be significantly greater when children played activity-promoting video games, compared with sedentary video games.

METHODS: Energy expenditure was measured for 25 children aged 8 to 12 years, 15 of whom were lean, while they were watching television seated, playing a traditional video game seated, watching television while walking on a treadmill at 1.5 miles per hour, and playing activity-promoting video games.

RESULTS: Watching television and playing video games while seated increased energy expenditure by 20 +/- 13% and 22 +/- 12% above resting values, respectively. When subjects were walking on the treadmill and watching television, energy expenditure increased by 138 +/- 40% over resting values. For the activity-promoting video games, energy expenditure increased by 108 +/- 40% with the EyeToy (Sony Computer Entertainment) and by 172 +/- 68% with Dance Dance Revolution Ultramix 2 (Konami Digital Entertainment).

CONCLUSIONS: Energy expenditure more than doubles when sedentary screen time is converted to active screen time. Such interventions might be considered for obesity prevention and treatment.

PMID: 17142504 [PubMed - indexed for MEDLINE]

56. J Appl Physiol (1985). 2007 Mar;102(3):1078-89. Epub 2006 Nov 16.

Impact of endurance training on murine spontaneous activity, muscle mitochondrial DNA abundance, gene transcripts, and function.

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We hypothesized that enhanced skeletal muscle mitochondrial function following aerobic exercise training is related to an increase in mitochondrial transcription factors, DNA abundance [mitochondrial DNA (mtDNA)], and mitochondria-related gene transcript levels, as well as spontaneous physical activity (SPA) levels. We report the effects of daily treadmill training on 12-wk-old FVB mice for 5 days/wk over 8 wk at 80% peak O₂ consumption and studied the training effect on changes in body composition, glucose tolerance, muscle mtDNA muscle, mitochondria-related gene transcripts, in vitro muscle mitochondrial ATP production capacity (MATPC), and SPA levels. Compared with the untrained mice, the trained mice had higher peak O₂ consumption (+18%; P <

0.001), lower percentage of abdominal (-25.4%; $P < 0.02$) and body fat (-19.5%; $P < 0.01$), improved glucose tolerance ($P < 0.04$), and higher muscle mitochondrial enzyme activity (+19.5-43.8%; $P < 0.04$) and MATPC (+28.9 to +32.4%; $P < 0.01$). Gene array analysis showed significant differences in mRNAs of mitochondria-related ontology groups between the trained and untrained mice. Training also increased muscle mtDNA (+88.4 to +110%; $P < 0.05$), peroxisome proliferative-activated receptor-gamma coactivator-1alpha protein (+99.5%; $P < 0.04$), and mitochondrial transcription factor A mRNA levels (+21.7%; $P < 0.004$) levels. SPA levels were higher in trained mice ($P = 0.056$, two-sided t-test) and significantly correlated with two separate substrate-based measurements of MATPC ($P < 0.02$). In conclusion, aerobic exercise training enhances muscle mitochondrial transcription factors, mtDNA abundance, mitochondria-related gene transcript levels, and mitochondrial function, and this enhancement in mitochondrial function occurs in association with increased SPA.

PMID: 17110513 [PubMed - indexed for MEDLINE]

57. J Neuroendocrinol. 2006 Aug;18(8):594-601.

Neuromedin U in the paraventricular and arcuate hypothalamic nuclei increases non-exercise activity thermogenesis.

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Brain neuromedin U (NMU) has been associated with the regulation of both energy intake and expenditure. We hypothesized that NMU induces changes in spontaneous physical activity and nonexercise activity thermogenesis (NEAT) through its actions on hypothalamic nuclei. We applied increasing doses of NMU directly to the paraventricular (PVN) and arcuate hypothalamic nuclei using chronic unilateral guide cannulae. In both nuclei, NMU significantly and dose-dependently increased physical activity and NEAT. Moreover, NMU increased physical activity and NEAT during the first hour of the dark phase, indicating that the reduction of sleep is unlikely to account for the increased physical activity seen with NMU treatment. As a positive control, we demonstrated that paraventricular NMU also significantly decreased food intake, as well as body weight. These data demonstrate that NMU is positively associated with NEAT through its actions in the PVN and arcuate nucleus. In co-ordination with its suppressive effects on feeding, the NEAT-activating effects of NMU make it a potential candidate in the combat of obesity.

PMID: 16867180 [PubMed - indexed for MEDLINE]

58. Obesity (Silver Spring). 2006 Apr;14(4):690-5.

Weekly changes in basal metabolic rate with eight weeks of overfeeding.

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OBJECTIVE: The contribution of basal metabolic rate (BMR) to weight gain susceptibility has long been debated. We wanted to examine whether BMR changes in a linear fashion with overfeeding. Our hypothesis was that BMR does not increase linearly with 1000-kcal/d overfeeding in lean healthy subjects over 8 weeks. The null hypothesis states that BMR increases linearly with 1000-kcal/d overfeeding in lean healthy subjects.

RESEARCH METHODS AND PROCEDURES: Initially, 16 lean healthy sedentary subjects completed 2 weeks of weight maintenance feeding at the General Clinical Research Center. The subjects were then overfed by 1000 kcal/d over 8 weeks. BMR was measured under standard conditions each week using indirect calorimetry.

RESULTS: Baseline BMR was 1693 +/- 154.5 kcal/d. BMR increased from 1711 +/- 201.3 kcal/d at week 1 of overfeeding to 1781 +/- 171.65 kcal/d at the second week of overfeeding ($p = 0.05$). BMR fell during the third week of overfeeding to 1729 +/- 179.5 kcal/d ($p = 0.05$). After 5 weeks of overfeeding, BMR reached a plateau. Thereafter, there was no further change. Comparison of BMR with weeks of overfeeding was significantly different compared with the linear model ($p < 0.05$).

DISCUSSION: Increases in BMR in lean sedentary healthy subjects with 1000-kcal/d overfeeding are not linear over 8 weeks. There seems to be a short-term increase in BMR in the first 2 weeks of overfeeding that is not representative of longer-term changes.

PMID: 16741271 [PubMed - indexed for MEDLINE]

59. Minn Med. 2005 Sep;88(9):54-7.

Role of nonexercise activity thermogenesis (NEAT) in obesity.

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Obesity develops when there is an imbalance between energy intake and energy expenditure, which can vary daily within and among individuals. High levels of energy intake and low levels of energy expenditure contribute to obesity, both together and independently. Energy expenditure from exercise associated with formal programs is encouraged for health and weight loss, but most individuals get very little formal exercise. Nonexercise activity thermogenesis (NEAT) is the cumulative energy expended through all other activities of daily living. It is highly variable among individuals; it is controlled by the environment and, possibly, neurobiologically. Mounting evidence suggests that NEAT is critical in determining a person's susceptibility to body fat deposition and is a major factor in human obesity. Recent research supported by the Minnesota Partnership for Biotechnology and Medical Genomics, a state-sponsored collaborative effort of the University of Minnesota and Mayo Clinic, is helping to define the complex brain regulation of NEAT and its role in obesity. This article reviews the evidence for NEAT and the impact of NEAT on obesity.

PMID: 16475414 [PubMed - indexed for MEDLINE]

60. Arterioscler Thromb Vasc Biol. 2006 Apr;26(4):729-36. Epub 2006 Jan 26.

Non-exercise activity thermogenesis: the crouching tiger hidden dragon of societal weight gain.

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Non-exercise activity thermogenesis (NEAT) is the energy expenditure of all physical activities other than volitional sporting-like exercise. NEAT includes all the activities that render us vibrant, unique, and independent beings such as working, playing, and dancing. Because people of the same weight have markedly variable activity levels, it is not surprising that NEAT varies substantially between people by up to 2000 kcal per day. Evidence suggests that low NEAT may occur in obesity but in a very specific fashion. Obese individuals appear to exhibit an innate tendency to be seated for 2.5 hours per day more than sedentary lean counterparts. If obese individuals were to adopt the lean "NEAT-o-type," they could potentially expend an additional 350 kcal per day. Obesity was rare a century ago and the human genotype has not changed over that time. Thus, the obesity epidemic may reflect the emergence of a chair-enticing environment to which those with an innate tendency to sit, did so, and became obese. To reverse obesity, we need to develop individual strategies to promote standing and ambulating time by 2.5 hours per day and also re-engineer our work, school, and home environments to render active living the option of choice.

PMID: 16439708 [PubMed - indexed for MEDLINE]

61. Public Health Nutr. 2005 Oct;8(7A):1123-32.

Measurement of energy expenditure.

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Measurement of energy expenditure in humans is required to assess metabolic needs, fuel utilisation, and the relative thermic effect of different food, drink, drug and emotional components. Indirect and direct calorimetric and non-calorimetric methods for measuring energy expenditure are reviewed, and their relative value for measurement in the laboratory and field settings is assessed. Where high accuracy is required and sufficient resources are available, an open-circuit indirect calorimeter can be used. Open-circuit indirect calorimeters can employ a mask, hood, canopy or room/chamber for collection of expired air. For short-term measurements, mask, hood or canopy systems suffice. Chamber-based systems are more accurate for the long-term measurement of specified activity patterns but behaviour constraints mean they do not reflect real life. Where resources are limited and/or optimum precision can be sacrificed, flexible total collection systems and non-calorimetric methods are potentially useful if the limitations of these methods are appreciated. The use of the stable isotope technique, doubly labelled water, enables total daily energy expenditure to be measured accurately in free-living subjects. The factorial method for combining activity logs and data on the energy costs of activities can also provide

detailed information on free-living subjects.

PMID: 16277824 [PubMed - indexed for MEDLINE]

62. Med Sci Sports Exerc. 2005 Oct;37(10):1800-5.

Laboratory measurement of posture allocation and physical activity in children.

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PURPOSE: The purpose of this study was to validate the combined use of inclinometers and accelerometers to measure body posture and movement in children in a laboratory setting.

METHODS: We performed two separate experiments. In the first experiment, we tested the hypothesis that four inclinometers (tilt sensors) could be used to capture body posture in children. We observed and recorded body posture in eight healthy children (mean \pm SD; body mass index (BMI), $18 \pm 3 \text{ kg x m}^{-2}$) on 2880 occasions and compared these records with the inclinometer data. In the second experiment, the hypothesis was that two inclinometers could be used to determine whether 18 children (BMI, $21 \pm 5 \text{ kg x m}^{-2}$) were sedentary. We observed and recorded sedentariness (sitting/lying compared to standing) on 5575 occasions and compared these records with the inclinometer data. In both of these experiments, we also addressed the hypothesis that accelerometer output, when measured at varying velocities, correlated with walking energy expenditure.

RESULTS: In experiment 1, body posture was correctly identified in 2880 out of 2880 inclinometer measurements. In experiment 2, sedentary behavior was correctly identified in 5575 out of 5575 occasions. For the entire group, acceleration and body weight correlated well with energy expenditure ($r^2 = 0.84$).

CONCLUSION: The inclinometer-accelerometer system that we tested can be used to measure body posture and movement. We can measure sedentary behavior using two inclinometers instead of four inclinometers. This monitoring system may be useful for measuring energy expenditure, body posture, and physical activity in children.

PMID: 16260984 [PubMed - indexed for MEDLINE]

63. Am J Physiol Endocrinol Metab. 2006 Feb;290(2):E396-403. Epub 2005 Sep 27.

Central orexin sensitivity, physical activity, and obesity in diet-induced obese and diet-resistant rats.

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Nonexercise activity thermogenesis (NEAT), the most variable component of energy expenditure, can account for differential capacities for human weight gain. Also highly variable, spontaneous physical activity (SPA) may similarly affect weight balance in animals. In the following study, we utilized the rat model of obesity, the diet-induced obese (DIO) rat, as well as the diet-resistant (DR) rat strain,

to investigate how access to a high-fat diet alters SPA and the associated energy expenditure (i.e., NEAT). DIO and DR rats showed no differences in the amount of SPA before access to the high-fat diet. After 29 days on a high-fat diet, the DIO rats showed significant decreases in SPA, whereas the DR rats did not. Next, we wanted to determine whether the DIO and DR rats showed differential sensitivity to microinjections of orexin into the paraventricular nucleus of the hypothalamus (PVN). Unilateral guide cannulae were implanted, aimed at the PVN. Orexin A (0, 0.125, 0.25, and 1.0 nmol in 500 nl) was microinjected through the guide cannula into the PVN, then SPA and energy expenditure were measured for 2 h. Using the response to vehicle as a baseline, the DR rats showed significantly greater increase in NEAT compared with the DIO rats. These data indicate that diet-induced obesity is associated with decreases in SPA and a lack of increase in NEAT. A putative mechanism for changes in NEAT that accompany obesity is a decreased sensitivity to the NEAT-activating effects of neuropeptides such as orexin.

PMID: 16188908 [PubMed - indexed for MEDLINE]

64. *Prev Med.* 2005 Sep-Oct;41(3-4):778-83.

Precision and accuracy of an ankle-worn accelerometer-based pedometer in step counting and energy expenditure.

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BACKGROUND: Walking is a widely used approach to increase physical activity levels in obese patients. In this paper, we investigate the precision and accuracy of an ankle-worn dual-axis accelerometer (Stepwatch) and investigate its potential application as a predictor of energy expenditure.

METHODS: Twenty healthy subjects (10 lean, 10 obese) wore spring-levered (Accusplit), piezoelectric (Omron HF-100), and Stepwatch pedometers. Subjects walked on a treadmill at 1, 2, and 3 mph and in a hallway at 1 and 1.85 mph, during which energy expenditure was measured.

RESULTS: The Stepwatch counted 99.7 +/- 0.67% (mean +/- SEM) of the manual counts. In comparison, the Omron pedometer counted 61 +/- 3.3% and the Accusplit counted 26 +/- 2.8% of the manual counts at 1 mph although all pedometers were accurate (> 98% of counts) at 3 mph. In repeated measures, the Stepwatch produced negligible variance (SD = 0.36) over all speed whereas the other pedometers showed a large amount of variance at all speed (SD = 4-13). Stepwatch counts were predictive of walking energy expenditure corrected by weight ($r^2 > 0.8$).

CONCLUSION: The counts from the Stepwatch were virtually identical to the manual counts from a trained investigator and provided a reliable predictor of walking energy expenditure.

PMID: 16125760 [PubMed - indexed for MEDLINE]

65. *Acta Physiol Scand.* 2005 Aug;184(4):309-18.

NEAT--non-exercise activity thermogenesis--egocentric & geocentric environmental

factors vs. biological regulation.

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Non-exercise activity thermogenesis (NEAT) is the energy expenditure of all physical activities other than volitional sporting-like exercise. NEAT includes all those activities that render us vibrant, unique and independent beings such as going to work, playing guitar, toe-tapping and dancing. The factors that account for the 2000 kcal day⁻¹ variability of NEAT can be categorized as environmental or biological. The environmental determinants of NEAT can be viewed using one of two models. In the egocentric model we consider a single person as the focus, e.g. 'my job'. In the geocentric model we consider the 'environment' as the focus, e.g. well-lit and safe walk ways. These models provide us with a theoretical framework to understand NEAT and how best to intervene to promote NEAT. As well as environmental effectors of NEAT, there are also biological regulatory mechanisms that enable us to account for three-quarters of the biological variance in susceptibility and resistance to fat gain with human over-feeding. NEAT is likely to be regulated through a central mechanism that integrates NEAT with energy intake and energy stores so that NEAT is activated with over-feeding and suppressed with under-feeding. In conclusion, NEAT is likely to serve as a crucial thermoregulatory switch between energy storage and dissipation that is biologically regulated and influenced, and perhaps over-ridden, by environment. Deciphering the role of NEAT may lead to a better understanding of the pathogenesis, prevention and treatment of obesity.

PMID: 16026422 [PubMed - indexed for MEDLINE]

66. *Neurosci Lett*. 2005 Jul 22-29;383(1-2):99-104. Epub 2005 Apr 20.

Caloric restriction and physical activity in zebrafish (*Danio rerio*).

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Understanding the mechanism of energy flux may be critical for explaining how obesity has emerged as a public health epidemic. It is known that changes in caloric intake predictably alter physical activity levels (PA) in mammals. Here, our goal was to test the hypothesis that fasting induces a biphasic pattern of change in PA by measuring PA before and after long-term food deprivation in zebrafish. Compared to control-fed fish, food-deprived fish showed a significant increase in PA levels during the first 2 days of food deprivation. Subsequently, however, fasted fish showed a significant chronic decrease in PA compared to fish fed at weight-maintenance levels. These data are comparable to those seen with mammals, which also show a biphasic response of PA to caloric restriction. In a separate group of fish, long-term food deprivation, associated with decreases in PA, induced a significant increase in brain preproorexin mRNA levels compared to fed controls. No change in orexin mRNA was seen after 2 days of food deprivation. The finding that orexin mRNA expression is altered only after long-term

starvation suggests that orexin may be coupled with the changes in PA seen at this time. Thus, the association between negative energy balance and reductions in PA occurs across genera in biology and is associated with predictable neurological changes in brain gene expression.

PMID: 15936519 [PubMed - indexed for MEDLINE]

67. Science. 2005 Jan 28;307(5709):584-6.

Interindividual variation in posture allocation: possible role in human obesity.

Levine JA(1), Lanningham-Foster LM, McCrady SK, Krizan AC, Olson LR, Kane PH, Jensen MD, Clark MM.

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Comment in

Science. 2005 Jan 28;307(5709):530-1.

Obesity occurs when energy intake exceeds energy expenditure. Humans expend energy through purposeful exercise and through changes in posture and movement that are associated with the routines of daily life [called nonexercise activity thermogenesis (NEAT)]. To examine NEAT's role in obesity, we recruited 10 lean and 10 mildly obese sedentary volunteers and measured their body postures and movements every half-second for 10 days. Obese individuals were seated, on average, 2 hours longer per day than lean individuals. Posture allocation did not change when the obese individuals lost weight or when lean individuals gained weight, suggesting that it is biologically determined. If obese individuals adopted the NEAT-enhanced behaviors of their lean counterparts, they might expend an additional 350 calories (kcal) per day.

PMID: 15681386 [PubMed - indexed for MEDLINE]

68. Nutr Rev. 2004 Jul;62(7 Pt 2):S82-97.

Non-exercise activity thermogenesis (NEAT).

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Non-exercise activity thermogenesis (NEAT) is the energy expended for everything we do that is not sleeping, eating or sports-like exercise. NEAT can be measured by one of two approaches. The first approach is to measure or estimate total NEAT. Here, total daily energy expenditure is measured and from it, the basal metabolic rate-plus-thermic effect of food is subtracted. The second approach is the factorial approach whereby the components of NEAT are quantified and total NEAT calculated by summing these components. The amount of NEAT that humans perform represents the product of the amount and types of physical activities and the thermogenic cost of each activity. The factors that impact a human's NEAT are readily divisible in biological factors such as weight, gender and body composition and environmental factors such occupation or dwelling within a

"concrete jungle." The impact of these factors combined explains the substantial variance in human NEAT. The variability in NEAT might be viewed as random and unprogrammed but human data contradict this thesis. It appears that changes in NEAT accompany experimentally induced changes in energy balance and may be important in the physiology of weight change. NEAT and a sedentary lifestyle may thus be of profound importance in obesity.

PMID: 15387473 [PubMed - indexed for MEDLINE]

69. Am J Physiol Endocrinol Metab. 2004 May;286(5):E675-85.

Nonexercise activity thermogenesis (NEAT): environment and biology.

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Erratum in

Am J Physiol Endocrinol Metab. 2005 Jan;288(1):E285.

Nonexercise activity thermogenesis (NEAT) is the energy expended for everything that is not sleeping, eating, or sports-like exercise. It includes the energy expended walking to work, typing, performing yard work, undertaking agricultural tasks, and fidgeting. NEAT can be measured by one of two approaches. The first is to measure or estimate total NEAT. Here, total daily energy expenditure is measured, and from it "basal metabolic rate-plus-thermic effect of food" is subtracted. The second is the factorial approach, whereby the components of NEAT are quantified, and total NEAT is calculated by summing these components. The amount of NEAT that humans perform represents the product of the amount and types of physical activities and the thermogenic cost of each activity. The factors that impact a human's NEAT are readily divisible into environmental factors, such as occupation or dwelling within a "concrete jungle," and biological factors such as weight, gender, and body composition. The combined impact of these factors explains the substantial variance in human NEAT. The variability in NEAT might be viewed as random, but human and animal data contradict this. It appears that changes in NEAT subtly accompany experimentally induced changes in energy balance and are important in the physiology of weight change. Inadequate modulation of NEAT plus a sedentary lifestyle may thus be important in obesity. It then becomes intriguing to dissect mechanistic studies that delineate how NEAT is regulated into neural, peripheral, and humoral factors. A scheme is described in this review in which NEAT corresponds to a carefully regulated "tank" of physical activity that is crucial for weight control.

PMID: 15102614 [PubMed - indexed for MEDLINE]

70. Proc Nutr Soc. 2003 Aug;62(3):667-79.

Non-exercise activity thermogenesis.

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Non-exercise activity thermogenesis (NEAT) is the energy expended that is not from sleeping, eating or sports-like exercise. It ranges from the energy expended walking to work, typing, performing yard work, undertaking agricultural tasks and fidgeting. NEAT can be measured by one of two approaches. The first approach is to measure or estimate total NEAT. Here, total daily energy expenditure is measured and from it is subtracted BMR + thermic effect of food. The second is the factorial approach whereby the components of NEAT are quantified and total NEAT calculated by summing these components. The amount of NEAT that human subjects perform represents the product of the amount and types of physical activities and the thermogenic cost of each activity. The factors that affect the NEAT of a human subject are readily divisible into biological factors, such as weight, gender and body composition, and environmental factors, such as occupation or dwelling within a 'concrete jungle'. The combined impact of these factors explains the substantial variance in human NEAT. The variability in NEAT might be viewed as random but human data contradict this perception. It appears that changes in NEAT subtly accompany experimentally-induced changes in energy balance and are important in the physiology of weight change. NEAT and sedentariness may thus be important in obesity. It then becomes intriguing to dissect mechanistic studies that delineate how NEAT is regulated by neural, peripheral and humoral factors. NEAT may be a carefully-regulated 'tank' of physical activity that is crucial for weight control.

PMID: 14692603 [PubMed - indexed for MEDLINE]

71. Am J Physiol Endocrinol Metab. 2004 Apr;286(4):E551-9. Epub 2003 Dec 2.

Orexin A (hypocretin 1) injected into hypothalamic paraventricular nucleus and spontaneous physical activity in rats.

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In humans, nonexercise activity thermogenesis (NEAT) increases with positive energy balance. The mediator of the interaction between positive energy balance and physical activity is unknown. In this study, we address the hypothesis that orexin A acts in the hypothalamic paraventricular nucleus (PVN) to increase nonfeeding-associated physical activity. PVN-cannulated rats were injected with either orexin A or vehicle during the light and dark cycle. Spontaneous physical activity (SPA) was measured using arrays of infrared activity sensors and night vision videotaped recording (VTR). O₂ consumption and CO₂ production were measured by indirect calorimetry. Feeding behavior was assessed by VTR. Regardless of the time point of injection, orexin A (1 nmol) was associated with dramatic increases in SPA for 2 h after injection (orexin A: 6.27 ± 1.95 × 10³ beam break count, n = 24; vehicle: 1.85 ± 1.13 × 10³, n = 38). This increase in SPA was accompanied by compatible increase in O₂ consumption. Duration of feeding was increased only when orexin A was injected in the early light phase and accounted for only 3.5 ± 2.5% of the increased physical activity. In a dose-response experiment, increases in SPA were correlated with dose of orexin A linearly up to 2 nmol. PVN injections of orexin receptor

antagonist SB-334867 were associated with decreases in SPA and attenuated the effects of PVN-injected orexin A. Thus orexin A can act in PVN to increase nonfeeding-associated physical activity, suggesting that this neuropeptide might be a mediator of NEAT.

PMID: 14656716 [PubMed - indexed for MEDLINE]

72. *Obes Res.* 2003 Oct;11(10):1178-81.

Labor saved, calories lost: the energetic impact of domestic labor-saving devices.

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OBJECTIVE: As the prevalence of obesity has increased, so has sedentariness. Progressive sedentariness has been attributed to greater use of labor saving devices, such as washing machines, and less nonexercise walking (e.g., walking to work). However, there is a paucity of data to support this conclusion. In this study, we address the hypothesis that domestic mechanization of daily tasks has resulted in less energy expenditure compared with performing the same tasks manually.

RESEARCH METHODS AND PROCEDURES: Energy expenditure was measured in four groups of subjects (122 healthy adult men and women total) from Rochester, Minnesota. Energy expenditure was measured using indirect calorimetry while subjects performed structured tasks such as cleaning dishes and clothes, stair climbing, and work-associated transportation, and these values were compared with the respective mechanized activity.

RESULTS: Energy expenditure was significantly greater and numerically substantial when daily domestic tasks were performed without the aid of machines or equipment (clothes washing: 45 +/- 14 vs. 27 +/- 9 kcal/d; dish washing: 80 +/- 28 vs. 54 +/- 19 kcal/d; transportation to work: 83 +/- 17 vs. 25 +/- 3 kcal/d; stair climbing: 11 +/- 7 vs. 3 +/- 1 kcal/d; $p < 0.05$). The combined impact of domestic mechanization was substantial and equaled 111 kcal/d.

DISCUSSION: The magnitude of the energetic impact of the mechanized tasks we studied was sufficiently great to contribute to the positive energy balance associated with weight gain. Efforts focused on reversing sedentariness have the potential to impact obesity.

PMID: 14569042 [PubMed - indexed for MEDLINE]

73. *J Comp Physiol B.* 2003 Nov;173(8):675-8. Epub 2003 Aug 19.

Differential effects of adrenocorticotrophic hormone on human and mouse adipose tissue.

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Adrenocorticotrophic hormone (ACTH) induces lipolysis in a dose-dependent fashion in rodent adipose tissue and adipocytes in vitro. The role of ACTH on lipolysis in human adipose tissue is less clear, however. In this study, we address the hypothesis that ACTH induces lipolysis in human adipose tissue. We used ex vivo organ culture to examine lipolysis in human and mouse adipose tissue. Adipose tissue fragments suspended in culture medium and human ACTH, isoproterenol (positive control), or insulin (negative control) was added in varying concentrations. Lipolysis was measured using glycerol appearance. ACTH receptor mRNA expression was assessed using reverse-transcription polymerase chain reaction (RT-PCR). In mouse adipose tissue, ACTH induced lipolysis in dose-dependent manner; 100 pmol/l ACTH induced 67 \pm 19% of isoproterenol-stimulated lipolysis and 500 pmol/l ACTH: 86 \pm 13%. In contrast, human adipose tissue shared no significant response to 100 pmol/l ACTH; ACTH was associated with 9 \pm 6% and 500 pmol/l of ACTH, 8 \pm 6% of isoproterenol-stimulated lipolysis. ACTH receptor mRNA was present in mouse adipose tissue, but undetectable in human adipose tissue. These results suggest lipolysis regulation differs between human and mouse adipose tissue in response to ACTH.

PMID: 12925881 [PubMed - indexed for MEDLINE]

74. Am J Physiol Endocrinol Metab. 2003 Dec;285(6):E1282-8. Epub 2003 Aug 12.

Regional uptake of meal fatty acids in humans.

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Two protocols were performed to study meal fatty acid metabolism. In protocol 1, 14 patients scheduled for elective intra-abdominal surgery (11 undergoing bariatric surgery for severe obesity) consumed a meal containing [³H]triolein in the evening before surgery. This allowed us to measure adipose tissue lipid specific activity (SA) in mesenteric and omental, deep and superficial abdominal subcutaneous adipose tissue. Intra-abdominal adipose tissue lipid SA was greater than subcutaneous lipid SA. There were no significant differences between mesenteric and omental or between deep and superficial abdominal subcutaneous adipose tissue. In protocol 2, meal fatty acid oxidation and uptake into subcutaneous and omental adipose tissue ([³H]triolein) were measured in six normal, healthy volunteers. Meal fatty acid oxidation (3H₂O generation) plus that remaining in plasma (approximately 1%) plus uptake into upper body subcutaneous, lower body subcutaneous, and visceral fat allowed us to account for 98 \pm 6% of meal fatty acids 24 h after meal ingestion. We conclude that omental fat is a good surrogate for visceral fat and that abdominal subcutaneous fat depots are comparable with regard to meal fatty acid metabolic studies. Using [³H]triolein, we were able to account for virtually 100% of meal fatty acids 24 h after meal ingestion. These results support the meal fatty acid tracer model as a way to study the metabolic fate of dietary fat.

PMID: 12915396 [PubMed - indexed for MEDLINE]

75. J Neurosurg. 2002 Dec;97(6):1460-71.

Vision of the future: initial experience with intraoperative real-time high-resolution dynamic infrared imaging. Technical note.

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High-resolution dynamic infrared (DIR) imaging provides intraoperative real-time physiological, anatomical, and pathological information; however, DIR imaging has rarely been used in neurosurgical patients. The authors report on their initial experience with intraoperative DIR imaging in 30 such patients. A novel, long-wave (8-10 microm), narrow-band, focal-plane-array infrared photodetector was incorporated into a camera system with a temperature resolution of 0.006 degrees C, providing 65,000 pixels/frame at a data acquisition rate of 200 frames/second. Intraoperative imaging of patients was performed before and after surgery. Infrared data were subsequently analyzed by examining absolute differences in cortical temperatures, changes in temperature over time, and infrared intensities at varying physiological frequencies. Dynamic infrared imaging was applied in a variety of neurosurgical cases. After resection of an arteriovenous malformation, there was postoperative hyperperfusion of the surrounding brain parenchyma, which was consistent with a loss of autoregulation. Bypass patency and increased perfusion of adjacent brain were documented during two of three extracranial-intracranial bypasses. In seven of nine patients with epilepsy the results of DIR imaging corresponded to seizure foci that had been electrocorticographically mapped preoperatively. Dynamic infrared imaging demonstrated the functional cortex in four of nine patients undergoing awake resection and cortical stimulation. Finally, DIR imaging exhibited the distinct thermal footprints of 14 of 16 brain tumors. Dynamic infrared imaging may prove to be a powerful adjunctive intraoperative diagnostic tool in the neurosurgical imaging armamentarium. Real-time assessment of cerebral vessel patency and cerebral perfusion are the most direct applications of this technology. Uses of this imaging modality in the localization of epileptic foci, identification of functional cortex during awake craniotomy, and determination of tumor border and intraoperative brain shift are avenues of inquiry that require further investigation.

PMID: 12507150 [PubMed - indexed for MEDLINE]

76. J Appl Physiol (1985). 2003 Jan;94(1):165-70.

Effect of hyperthyroidism on spontaneous physical activity and energy expenditure in rats.

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Thyroid hormone excess is associated with increased energy expenditure. The contributions of increases in spontaneous physical activity and nonexercise activity thermogenesis (NEAT) to this effect have not been defined. To address

the hypothesis that hyperthyroidism is associated with increased spontaneous physical activity and NEAT, we rendered rats hyperthyroid by using continuous infusion of high-dose triiodothyronine for 14 days and measured the effects on physical activity and NEAT. On day 14, in the hyperthyroid group the mean +/- SD triiodothyronine concentration was 755 +/- 137 (range 574-919) ng/dl and in the control group 59 +/- 0.5 (58-59) ng/dl. Over the 14-day treatment period, mean spontaneous physical activity increased in the hyperthyroid rats from 24 +/- 7 to 36 +/- 6 activity units (AU)/min; $P < 0.001$ but did not increase in the controls (23 +/- 7 vs. 22 +/- 4 AU/min). Also, over the 14-day period, daily NEAT increased in the hyperthyroid rats from 8.1 +/- 2.8 to 19.7 +/- 5.0 kcal/day ($P < 0.001$) but did not increase in the controls (8.7 +/- 3.5 cf 9.4 +/- 1.7 kcal/day; not significant). In conclusion, hyperthyroidism is associated with increased spontaneous physical activity and NEAT.

PMID: 12486020 [PubMed - indexed for MEDLINE]

77. Best Pract Res Clin Endocrinol Metab. 2002 Dec;16(4):679-702.

Non-exercise activity thermogenesis (NEAT).

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Non-exercise activity thermogenesis (NEAT) is the energy expended for everything we do that is not sleeping, eating or sports-like exercise. It ranges from the energy expended walking to work, typing, performing yard work, undertaking agricultural tasks and fidgeting. Even trivial physical activities increase metabolic rate substantially and it is the cumulative impact of a multitude of exothermic actions that culminate in an individual's daily NEAT. It is, therefore, not surprising that NEAT explains a vast majority of an individual's non-resting energy needs. Epidemiological studies highlight the importance of culture in promoting and quashing NEAT. Agricultural and manual workers have high NEAT, whereas wealth and industrialization appear to decrease NEAT. Physiological studies demonstrate, intriguingly, that NEAT is modulated with changes in energy balance; NEAT increases with overfeeding and decreases with underfeeding. Thus, NEAT could be a critical component in how we maintain our body weight and/or develop obesity or lose weight. The mechanism that regulates NEAT is unknown. However, hypothalamic factors have been identified that specifically and directly increase NEAT in animals. By understanding how NEAT is regulated we may come to appreciate that spontaneous physical activity is not spontaneous at all but carefully programmed.

PMID: 12468415 [PubMed - indexed for MEDLINE]

78. Obes Res. 2001 Nov;9(11):655-61.

Is there a role for gastric accommodation and satiety in asymptomatic obese people?

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Comment in

Obes Res. 2001 Nov;9(11):727-8.

OBJECTIVE: The relationships of gastric accommodation and satiety in moderately obese individuals are unclear. We hypothesized that obese people had increased gastric accommodation and reduced postprandial satiety. The objective of this study was to compare gastric accommodation and satiety between obese and non-obese asymptomatic subjects.

RESEARCH METHODS AND PROCEDURES: In 13 obese (body mass index [BMI] \geq 30 kg/m²; mean BMI, 37.0 \pm 4.9 kg/m²) and 19 non-obese control subjects (BMI $<$ 30 kg/m²; mean BMI, 26.2 \pm 2.9 kg/m²), we used single photon emission computed tomography to measure fasting and postprandial gastric volumes and expressed the accommodation response as the ratio of postprandial/fasting volumes. The satiety test measured maximum tolerable volume of ingestion of liquid nutrient meal (Ensure) and symptoms 30 minutes after cessation of ingestion.

RESULTS: Total fasting and postprandial gastric volumes and the ratio of postprandial/fasting gastric volume were not different between asymptomatic obese and control subjects. However, the fasting volume of the distal stomach was greater in obese than in control subjects. Maximum tolerable volume of ingested Ensure and aggregate symptom score 30 minutes later were also not different between obese and control subjects.

DISCUSSION: Asymptomatic obese individuals (within the BMI range of 32.6 to 48 kg/m²) did not show either increased postprandial gastric accommodation or reduced satiety. These data suggest that gastric accommodation is unlikely to provide an important contribution to development of moderate obesity.

PMID: 11707531 [PubMed - indexed for MEDLINE]

79. Science. 2001 Oct 26;294(5543):812.

The work burden of women.

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PMID: 11679660 [PubMed - indexed for MEDLINE]

80. Med Sci Sports Exerc. 2001 Sep;33(9):1593-7.

Validation of the Tracmor triaxial accelerometer system for walking.

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PURPOSE: Walking is likely to contribute substantially to nonexercise activity thermogenesis. The Tracmor triaxial accelerometer system (Maastricht, The Netherlands) is the most widely validated system for detecting body movement in free-living subjects. The aim of this study was to validate the Tracmor triaxial accelerometer system for estimating the energy expenditure of walking.

METHODS: Experiments were conducted in healthy subjects. First, baseline variability for Tracmor output was determined for subjects standing still.

Second, Tracmor output was compared for walking on a treadmill and on level ground. Third, both Tracmor output and energy expenditure were compared for walking on a treadmill and walking on level ground. Finally, the effect of gradient on Tracmor output and energy expenditure was compared for subjects walking on a treadmill.

RESULTS: The data demonstrated excellent reproducibility for comparing Tracmor output for standing (CV < 2%). There were excellent log-linear relationships between velocity and Tracmor output walking on a treadmill ($r = 0.998$) and on level ground ($r = 0.999$). Tracmor output and the energy expenditure of walking were inseparable for the two modalities of walking. However, the variance in response was such that to reliably derive the relationship between Tracmor output and energy expenditure, separate regression equations are needed for each subject. Finally, the Tracmor accelerometer did not detect the increased energy expenditure of walking that occurs as gradient increases.

CONCLUSION: The Tracmor triaxial accelerometer provides reproducible and reliable data on the body motion associated with walking regardless of whether a subject walks on a treadmill or level ground. Tracmor units can be used to predict the energetic cost of walking provided that separate regression equations are derived for each subject to convert Tracmor output to energy expenditure.

PMID: 11528350 [PubMed - indexed for MEDLINE]

81. Am J Clin Nutr. 2000 Dec;72(6):1451-4.

Energy expenditure of nonexercise activity.

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BACKGROUND: We found recently that changes in nonexercise activity thermogenesis (NEAT) mediate resistance to weight gain with overfeeding in sedentary adults. A potentially important, yet seldom investigated, component of NEAT is the energy expenditure of fidgeting-like activities.

OBJECTIVE: Our goal was to measure changes in energy expenditure with fidgeting-like activities.

DESIGN: Energy expenditure was measured in 24 subjects (17 women and 7 men $x \pm$ SD body weight: 76 \pm 21 kg) while recumbent at rest, sitting motionless, standing motionless, partaking of self-selected fidgeting-like movements while seated and while standing, and walking on a treadmill at 1.6, 3.2, and 4.8 km/h (1, 2, and 3 mph). Measurements were performed by using a high-precision, indirect calorimeter connected to the subject via a transparent, lightweight facemask that enabled almost unrestricted movement.

RESULTS: Compared with metabolic rate in the supine position (5.4 \pm 1.5 kJ/min), energy expenditure increased while sitting motionless by 4 \pm 6%, while fidgeting while seated by 54 \pm 29% ($P < 0.0001$), while standing motionless by

13 +/- 8% (P: < 0.0001), while fidgeting while standing by 94 +/- 38% (P: < 0.0001), while walking at 1.6 km/h by 154 +/- 38% (P: < 0.0001), while walking at 3.2 km/h by 202 +/- 45% (P: < 0.0001), and while walking at 4.8 km/h by 292 +/- 81% (P: < 0.0001). There was a significant, positive correlation between changes in energy expenditure and body weight for fidgeting-like activities while standing (r = 0.43, P: = 0.02) but not while seated.

CONCLUSIONS: There is marked variance between subjects in the energy expenditure associated with self-selected fidgeting-like activities. The thermogenic potential of fidgeting-like and low-grade activities is sufficiently great to substantively contribute to energy balance.

PMID: 11101470 [PubMed - indexed for MEDLINE]

82. Int J Obes Relat Metab Disord. 2000 Sep;24(9):1153-7.

Body composition and resting energy expenditure in humans: role of fat, fat-free mass and extracellular fluid.

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OBJECTIVE: The objective of this study was to determine whether there are independent effects of extracellular fluid volume (ECF) and fat mass (FM) on resting energy expenditure (REE) relative to fat-free mass (FFM) in adult men and women.

METHODS: Multiple linear regression analysis was used to relate REE, as determined by indirect calorimetry, to FFM and FM (measured using dual energy X-ray absorptiometry) and ECF (measured using bromide space and/or the radiosulfate washout space) in 153 women and 100 men with varying amounts of body fat.

RESULTS: REE correlated significantly with FFM and FM in women (r=0.65 and r=0.63, both P<0.001) and men (r=0.62 and r=0.48, both P<0.001, FFM and FM, respectively). In a multiple linear regression analysis FFM, FM and age significantly contributed to the ability to predict REE in both genders. The models that were derived were not significantly different between women and men. In women the contribution to REE from FM was easier to detect when FM was greater. Adjustment of FFM for ECF did not improve the relationship between FFM and REE.

CONCLUSIONS: FFM, FM and age are significant, independent predictors of REE in both men and women. Adjustment of FFM for ECF does not improve the ability of FFM to predict REE, which suggests that ECF is a highly integrated component of FFM in healthy adults. Expressing REE relative to FFM alone will introduce errors when lean and obese populations are compared.

PMID: 11033984 [PubMed - indexed for MEDLINE]

83. Eur J Clin Invest. 2000 Sep;30(9):779-86.

Energy expenditure in chronic alcohol abuse.

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Comment in

Eur J Clin Invest. 2000 Sep;30(9):749-50.

BACKGROUND: In healthy subjects, alcohol decreases lipid oxidation favouring fat deposition. However, individuals who chronically abuse alcohol are not obese. To investigate this paradox, we measured energy expenditure (EE) and fuel utilization in chronic alcohol abusers in relation to their drinking behaviour.

METHODS: Resting and postprandial EE and nonprotein respiratory quotient (NPRQ) were measured using indirect calorimetry, in 36 alcohol abusers [mean (+/- SE) age 42 +/- 2 years; weight 67 +/- 2 kg; 21 with steatosis, eight with hepatitis; seven with cirrhosis] and in 36 gender-, age- and weight-matched healthy controls. Alcoholic patients were re-evaluated either after 14 days (n = 14) or on days 2, 4, 6, 8, 14 and 42 (n = 6) after abstinence.

RESULTS: When alcoholics were compared to healthy controls, mean energy intake was greater, 15 +/- 1 MJ day⁻¹ (38 +/- 2% from alcohol) cf. 9 +/- 1 MJ day⁻¹ (P < 0.001), resting EE increased, 82 +/- 2 cf. 65 +/- 2 W (P < 0.001) and NPRQ decreased, 0.75 +/- 0.02 cf. 0.82 +/- 0.01 (P < 0.001). The postprandial increases in EE and NPRQ were of similar magnitude in both groups. Abstinence from alcohol for 14 days was accompanied by reduced energy intake, 16 +/- 1 cf. 11 +/- 1 MJ day⁻¹ (P < 0.005) and decreased resting EE, 84 +/- 5 cf. 73 +/- 4 W (P < 0.05). The decrease in resting EE consistently occurred 4 days after abstinence from alcohol.

CONCLUSIONS: Chronic alcohol abuse is associated with energy wasting and inhibition of adipose tissue accumulation. This may explain why alcoholics are not obese despite high total energy intakes.

PMID: 10998077 [PubMed - indexed for MEDLINE]

84. J Appl Physiol (1985). 2000 Feb;88(2):452-6.

Measuring leg muscle and fat mass in humans: comparison of CT and dual-energy X-ray absorptiometry.

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Dual-energy X-ray absorptiometry (DEXA) is reported to be inferior to computed tomography (CT) to measure changes in appendicular soft tissue composition. We compared CT- and DEXA-measured thigh muscle and fat mass to evaluate the random and systematic discrepancies between these two methods. Thigh skeletal muscle area (single-slice CT) was suboptimally ($r(2) = 0.74$, $P < 0.0001$) related to DEXA-measured thigh fat-free mass (FFM). In contrast, thigh muscle and adipose tissue volumes (multislice CT) were highly related to DEXA-measured thigh FFM and fat (both $r(2) = 0.96$, $P < 0.0001$). DEXA-measured leg fat was significantly less than multislice-CT-measured leg adipose tissue volume, whereas multislice-CT-measured leg muscle mass was less ($P < 0.0001$) than DEXA-measured leg FFM. The systematic discrepancies between the two approaches were consistent with the 10-15% nonfat components of adipose tissue. In conclusion, CT and DEXA measures of appendicular soft tissue are highly related. Systematic differences between DEXA and CT likely relate to the underlying principles of the techniques.

PMID: 10658010 [PubMed - indexed for MEDLINE]

85. J Clin Endocrinol Metab. 1999 Aug;84(8):2751-4.

Leptin responses to overfeeding: relationship with body fat and nonexercise activity thermogenesis.

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Administration of leptin to rodents results in weight loss through decreased food intake and increased energy expenditure that occurs in part through increased spontaneous activity. In humans, low levels of spontaneous physical activity and below normal plasma leptin concentrations predict subsequent excess weight gain. We recently found that failure to increase nonexercise activity thermogenesis (NEAT) with overfeeding results in greater fat gain in humans, and subsequently evaluated whether changes in leptin are related to NEAT activation. We measured plasma leptin concentrations and adipose tissue leptin messenger ribonucleic acid together with the components of energy expenditure in 16 nonobese humans before and after overfeeding to assess the relationship between leptin responses to overfeeding and the changes in NEAT. Adipocyte leptin expression was up-regulated with overfeeding, and leptin concentrations increased. Leptin concentrations correlated with body fat before and after overfeeding. Changes in leptin with overfeeding were strongly related to changes in body fat, but not to changes in NEAT. Changes in NEAT correlated inversely with fat gain. It is, therefore, unlikely that leptin mediates activation of NEAT with overfeeding in nonobese humans; rather, leptin directly reflects body fat mass and fat mass gain.

PMID: 10443673 [PubMed - indexed for MEDLINE]

86. Science. 1999 Jan 8;283(5399):212-4.

Role of nonexercise activity thermogenesis in resistance to fat gain in humans.

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Comment in

Science. 1999 May 14;284(5417):1125-6.

Science. 1999 Jan 8;283(5399):184-5.

Humans show considerable interindividual variation in susceptibility to weight gain in response to overeating. The physiological basis of this variation was investigated by measuring changes in energy storage and expenditure in 16 nonobese volunteers who were fed 1000 kilocalories per day in excess of weight-maintenance requirements for 8 weeks. Two-thirds of the increases in total daily energy expenditure was due to increased nonexercise activity thermogenesis

(NEAT), which is associated with fidgeting, maintenance of posture, and other physical activities of daily life. Changes in NEAT accounted for the 10-fold differences in fat storage that occurred and directly predicted resistance to fat gain with overfeeding (correlation coefficient = 0.77, probability < 0.001). These results suggest that as humans overeat, activation of NEAT dissipates excess energy to preserve leanness and that failure to activate NEAT may result in ready fat gain.

PMID: 9880251 [PubMed - indexed for MEDLINE]

87. J Nutr Sci Vitaminol (Tokyo). 1998 Aug;44(4):569-72.

Adenoviral-mediated gene transfer to human adipocytes in vitro, and human adipose tissue ex vivo and rabbit femoral adipose tissue in vivo.

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Adenoviral-mediated gene transfer has proven useful in several organ systems to understand gene action and to provide a potential therapeutic modality for localized, organ-specific gene overexpression. However, the application of adenoviral-mediated gene transfer to adipocytes and adipose tissue has not been evaluated. We evaluated the feasibility of in vitro and ex vivo transfer of the beta-galactosidase gene to human adipocytes and adipose tissue by means of adenoviral vectors. The efficiency (percentage of cells transduced) of adenoviral-mediated gene transfer of the beta-galactosidase gene to human adipocytes in vitro and to human adipose tissue ex vivo was 21 +/- 3% and 14 +/- 3%, respectively. Adenoviral-mediated gene transfer in a rabbit femoral adipose tissue was also demonstrated in vivo. Adenoviral-mediated gene transfer may facilitate studies on understanding the biology of adipocytes and provide a potential tool for the modulation of adipocyte function in vivo and thereby for the treatment of obesity.

PMID: 9819717 [PubMed - indexed for MEDLINE]

88. Br J Cancer. 1998 Sep;78(5):579-81.

Preservation of macronutrient preferences in cancer anorexia.

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Indirect evidence suggests that cancer anorexia is associated with specific aversions to macronutrients. To investigate this, patients with cancer anorexia and hospitalized control subjects devised 3-day menus comprising foods that they wished to eat. These foods were then provided for 3 days and the intakes of each food carefully measured. As expected, patients with cancer anorexia consumed substantially less energy than hospitalized control subjects (6.0 +/- 0.9 MJ vs 9.5 +/- 0.5 MJ, P < 0.001). However, macronutrient composition was consistently

maintained in the patients with cancer anorexia. These data argue against cancer anorexia representing a state of macronutrient aversion.

PMCID: PMC2063064

PMID: 9744494 [PubMed - indexed for MEDLINE]

89. J Clin Invest. 1998 Apr 15;101(8):1557-64.

Adipocyte macrophage colony-stimulating factor is a mediator of adipose tissue growth.

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Adipose tissue growth results from de novo adipocyte recruitment (hyperplasia) and increased size of preexisting adipocytes. Adipocyte hyperplasia accounts for the severalfold increase in adipose tissue mass that occurs throughout life, yet the mechanism of adipocyte hyperplasia is unknown. We studied the potential of macrophage colony-stimulating factor (MCSF) to mediate adipocyte hyperplasia because of the profound effects MCSF exerts on pluripotent cell recruitment and differentiation in other tissues. We found that MCSF mRNA and protein were expressed by human adipocytes and that adipocyte MCSF expression was upregulated in rapidly growing adipose tissue that encircled acutely inflamed bowel and in adipose tissue from humans gaining weight (4-7 kg) with overfeeding. Localized overexpression of adipocyte MCSF was then induced in rabbit subcutaneous adipose tissue in vivo using adenoviral-mediated gene transfer. Successful overexpression of MCSF was associated with 16-fold increases in adipose tissue growth compared with a control adenovirus expressing beta-galactosidase. This occurred in the absence of increased cell size and in the presence of increased nuclear staining for MIB-1, a marker of proliferation. We conclude that MCSF participates in adipocyte hyperplasia and the physiological regulation of adipose tissue growth.

PMCID: PMC508735

PMID: 9541484 [PubMed - indexed for MEDLINE]

90. J Gen Intern Med. 1996 Dec;11(12):753-5.

Utility of a standardized sign-out card for new medical interns.

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Conscientious sign-out between medical interns is important for the continuity of care of hospitalized patients. We developed a standardized sign-out card that prompted the intern going off duty to transmit patient care information to the inter on call. The card was tested in a prospective, randomized, controlled trial in which one group of interns used the card, and another group did not. Any instance of poor sign-out was reported on a questionnaire completed by the intern who had been on call the previous night. The group using the sign-out cards

reported poor sign-out on 8 nights (5.8% of questionnaires), and the control group reported it on 17 nights (14.9% of questionnaires, $p = .016$). The card was time-effective and inexpensive, resulted in more complete data recording, and possibly decreased the morbidity associated with poor sign-out.

PMID: 9016423 [PubMed - indexed for MEDLINE]

91. Arthritis Rheum. 1996 Jan;39(1):169-70.

Splinter hemorrhages following arterial puncture.

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Splinter hemorrhages can be a feature of the antiphospholipid syndrome. We describe a patient in whom splinter hemorrhages developed following radial artery puncture. The implications of this findings in patients with the antiphospholipid syndrome are discussed.

PMID: 8546727 [PubMed - indexed for MEDLINE]

92. Am J Gastroenterol. 1995 Feb;90(2):290-4.

Brunner's gland hamartomas: clinical presentation and pathological features of 27 cases.

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OBJECTIVES: The aim of this study was to characterize the clinical presentation, pathological features, and outcome of a series of patients with Brunner's gland hamartomas.

METHODS: We reviewed the clinical and pathological features of 27 patients who presented with Brunner's gland hamartomas, and we obtained follow-up information.

RESULTS: Patients (12 men and 15 women) presented predominantly in the fifth and sixth decades of life either with gastrointestinal hemorrhage ($n = 10$) or obstructive symptoms ($n = 10$); there were also patients whose tumors were discovered as an incidental finding ($n = 7$). The tumors were generally pedunculated, were located in the first portion of the duodenum, and were in the range of diameter from 1 to 6 cm. Histologically, the hamartomas were characterized by the presence of nondysplastic, lobulated Brunner's glands with intervening bands of fibrous tissue and variable adipose and lymphoid tissue. Focal sclerosis was found in 93% of the hamartomas, possibly mimicking an adenocarcinoma. Whether managed surgically (24 patients) or endoscopically (three patients), the outcome was uniformly favorable. After a median period of 7-yr-follow-up, no tumors recurred, and no additional morbidity was identified.

CONCLUSIONS: Brunner's gland hamartomas are rare duodenal tumors occurring in middle age that present either with gastrointestinal hemorrhage, obstructive symptoms, or as an incidental finding. Surgical or endoscopic excision is

uncomplicated, and the long-term outcome is favorable.

PMID: 7847303 [PubMed - indexed for MEDLINE]