HEB 2100

Diet and Exercise

Mondays 1:00-4:00 PM
Peabody Museum 52H

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Course description

This seminar considers evolutionary factors underlying how variations in diet and exercise affect the human body. Weekly readings and discussion will be used to explore how ancestral diets and forms of physical activity have shaped human anatomy and physiology, and how differences between past and present diets and forms of exercise may contribute to illness, mortality, and variations in reproductive success. In doing so, we challenge popular conceptions of what it means to be "healthy."

Course structure

Each week we will meet to discuss selected readings on core topics, organized around questions. Because we aim to use evolutionary theory and data to explore and critique some big, important questions, it is imperative that you read and think about these readings before class. Come prepared to not just discuss these ideas but also to debate them! To encourage you to think broadly and to stimulate debate, during class we will randomly assign you to advocate and defend one or another point of view. We anticipate learning as much from one another as we do from the readings, and so we encourage you to leverage your own research and expertise in assessing these topics. However, to assist others in internalizing and evaluating your contributions, please be prepared to share citations for any points you raise that are not covered in the assigned readings.

Course requirements

- Informed, engaged, and thoughtful participation in class (40%)
- Mid-term paper (approximately 2,500 words) due March 20 (20% of final grade):
  What did we evolve to eat? What physical activities did we evolve to do?
- Final paper (approximately 5,000 words) due May 1 (40% of final grade):
  Using an evolutionary perspective, what is your prescription for optimal diet and exercise? Critique your prescription.

Required readings are indicated under the weekly headings below. Readings are available on the course website, unless otherwise noted, and must be reviewed in advance of the meeting for which they are listed.

Class Policies

Collaboration

In this course, we hope that you learn as much from each other as you do from the readings. Therefore, you are encouraged to discuss class topics, readings, and assignments outside of class. However, your contributions in class discussions and the written work that you submit for evaluation must reflect your own efforts. In addition, we draw your attention to the Faculty of Arts and Sciences policy on the proper crediting of sources:

> "It is expected that all homework assignments, projects, lab reports, papers, theses, and examinations and any other work submitted for academic credit will be the student's own. Students should always take great care to distinguish their own ideas and knowledge from information derived from sources. The term "sources" includes not only primary and secondary material published in print or online, but also information and opinions gained directly from other people. Quotations must be placed properly within quotation marks and must be cited fully. In addition, all paraphrased material must be acknowledged completely. Whenever ideas or facts are derived from a student's reading and research or from a student's own writings, the sources must be indicated." (Except from the Student Handbook)

Attendance

You are expected to attend all class meetings, except in extraordinary circumstances. If you cannot attend class due to illness or an emergency, you must notify the instructors in advance. You may be offered the opportunity to receive participation credit for the missed seminar by completing an opinion piece that will be shared with the entire class and graded for quality.

Grading

Grades will be assigned based on FAS guidelines, as follows:

A: "excellent quality; full mastery of subject"
B: "good comprehension of course material; and good commandment of skills"
C: "adequate and satisfactory; basic requirements met"
D: "unsatisfactory with minimal commandment of material"

Weekly Questions and Readings

Week 1 (January 23). The modern problem.

- What is health? Is it different under clinical, individual and evolutionary perspectives?
- How have patterns of morbidity and mortality changed over historical and evolutionary time?
- What is the state of health and healthcare today?
- How do we evaluate different lines of evidence about health and evolution? What are the strengths and weaknesses of different study designs?

Readings *(skim those marked with an asterisk*)*

Huber M et al. (2011) How should we define health? *BMJ* 343: d4163.

Finch CE (2010) Evolution of the human lifespan and diseases of aging: roles of infection, inflammation, and nutrition. *PNAS* 107: 1718–1724.

*Gurven M, Kaplan H (2007) Longevity among hunter-gatherers: a cross-cultural examination. *Population and Development Review* 33: 321-365.

*GBD 2015 Mortality and Causes of Death Collaborators (2016) Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet* 388: 1459-1544.

*GBD 2015 DALYs and HALE Collaborators (2016) Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet* 388: 1603-1658.

Makary M, Daniel M (2016) Medical error – the third leading cause of death in the US. *BMJ* 353.i2139. See also: http://jamanetwork.com/journals/jama/fullarticle/2544638.

Ding D et al. (2016) The economic burden of physical inactivity: a global analysis of major non-communicable diseases. *The Lancet* 388: 1311-1324.

Valero-Elizondo J et al. (2016) Economic impact of moderate-vigorous physical activity among those with and without established cardiovascular disease: 2012 Medical Expenditure Panel survey. *Journal of the American Heart Association* 5: e003614.

Other references and resources

http://thelancet.com/gbd

Blurton Jones NG et al. (1992) Demography of the Hadza, an increasing and high density population of Savanna foragers. *American Journal of Physical Anthropology* 89: 159-181.

Paulsen HE (2009) Why epidemiological and clinical intervention studies often give different or diverging results? *Life* 61: 391-393.

Concato J, Shah N, Horwitz RI (2000) Randomized, controlled trials, observational studies, and the hierarchy of research designs. *New England Journal of Medicine* 342: 1887-1892.

Kaplan HS et al. (2000) A theory of human life history evolution: diet, intelligence, and longevity. *Evolutionary Anthropology* 9: 156-183.

Hawkes K, Smith KR, Robson SL (2009) Mortality and fertility rates in humans and chimpanzees: how within-species variation complicates cross-species comparisons. *American Journal of Human Biology* 21: 578-586.

Week 2 (January 30). Mismatch.

- What is mismatch?
- How do you test hypotheses of mismatch?
- How do modern and Paleolithic diets and activity levels differ, and do they cause mismatches?
- What is the quality of evidence on mismatch?

Readings

Lieberman DE (2013) "Chapter 7: Progress, Mismatch and Dysevolution" in *The Story of the Human Body: Evolution, Health and Disease*. Pantheon Books: New York.

Ludwig DS (2011) Technology, diet, and the burden of chronic disease. *JAMA* 305: 1352-1353.

Eaton SB, Konner M (1985) Paleolithic nutrition: a consideration of its nature and current implications. *New England Journal of Medicine* 312: 283-289.

Konner M, Eaton SB (2010) Paleolithic nutrition: twenty-five years later. *Nutrition in Clinical Practice* 25: 594-602.

Jabr F (2013) How to really eat like a hunter-gatherer: why the Paleo diet is half-baked. *Scientific American*. Available at: https://www.scientificamerican.com/article/why-paleo-diet-half-baked-how-hunter-gatherer-really-eat/.

COMPARE

Lieberman DE (2015) Is exercise really medicine? An evolutionary perspective. *Current Sports Medicine Reports* 14: 313-319.

Raichlen DA et al. (2016) Physical activity patterns and biomarkers of cardiovascular disease risk in hunter-gatherers. *American Journal of Human Biology*, doi: 10.1002/ajhb.22919.

Pontzer H et al. (2015) Energy expenditure and activity among Hadza hunter-gatherers. *American Journal of Human Biology* 27: 628-637.

O'Keefe JH et al. (2010) Organic fitness: physical activity consistent with our hunter-gatherer heritage. *The Physician and Sports Medicine* 4: 1-8.

Other references and resources

Cordain L et al. (1998) Physical activity, energy expenditure and fitness: an evolutionary perspective. *International Journal of Sports Medicine* 19: 328-335.

Week 3 (February 6). Does sugar make us fat?

- How much and in what way has sugar consumption changed?
- How are fructose and glucose digested differently?
- How much sugar is too much and what are the consequences?

Readings

Hardy K et al. (2015) The importance of dietary carbohydrate in human evolution. *Quarterly Review of Biology* 90: 251-268.

Lieberman DE (2013) "Chapter 10: The Vicious Cycle of Too Much" in *The Story of the Human Body: Evolution, Health and Disease*. Pantheon Books: New York.

Brand JC et al. (1985) Food processing and the glycemic index. *American Journal of Clinical Nutrition* 42: 1192-1196.

Siervo M et al. (2014) Sugar consumption and global prevalence of obesity and hypertension: an ecological analysis. *Public Health Nutrition* 17: 587-596.

COMPARE

Bray GA, Popkin BM (2014) Dietary sugar and body weight: have we reached a crisis in the epidemic of obesity and diabetes? Health be damned! Pour on the sugar. *Diabetes Care* 37: 950-956.

Kahn R, Sievenpiper JL (2014) Dietary sugar and body weight: have we reached a crisis in the epidemic of obesity and diabetes? We have, but the pox on sugar is overwrought and overworked. *Diabetes Care* 37: 957-962.

Other references and resources

Bray GA et al. (2004) Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. *American Journal of Clinical Nutrition* 79: 537-543.

Lustig RH, Schmidt LA, Brindis CD (2012) The toxic truth about sugar. *Nature* 482: 27-29.

Malik VS et al. (2010) Sugar-sweetened beverages, obesity, type 2 diabetes mellitus, and cardiovascular disease risk. *Circulation* 121: 1356-1364.

Week 4 (February 13). When does sugar lead to insulin resistance?

- Why do some people but not others become insulin resistant?
- What accounts for healthy obese and diabetic thin people?
- Is insulin resistance a mismatch condition?

Readings *(skim those marked with an asterisk*)*

Marlowe FW et al. (2014) Honey, Hadza, hunter-gatherers, and human evolution. *Journal of Human Evolution* 71: 119-28.

O'Dea K (1984) Marked improvement in carbohydrate and lipid metabolism in diabetic Australian aborigines after temporary reversion to traditional lifestyle. *Diabetes* 33: 596-603.

Ibrahim MM (2010) Subcutaneous and visceral adipose tissue: structural and functional differences. *Obesity Reviews* 11: 11-18.

Mann S et al. (2014) Changes in insulin sensitivity in response to different modalities of exercise: a review of the evidence. *Diabetes/Metabolism Research and Reviews* 30: 257–268.

Kuzawa CW et al. (2008) "Chapter 19. Evolution, Developmental Plasticity, and Metabolic Disease" in *Evolution in Health and Disease*, 2nd Edition, eds. Stearns SC, Koella JC. Oxford University Press: Oxford.

Wells JCK (2011) The thrifty phenotype: an adaptation in growth or metabolism? *American Journal of Human Biology*: 23: 65-75.

*Koren O et al. (2012) Host remodeling of the gut microbiome and metabolic changes during pregnancy. *Cell* 150: 470-480.

*Cani PD et al. (2007) Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes* 56: 1761-1772.

*Suez et al. (2014) Artificial sweeteners induce glucose intolerance by altering the gut microbiota. *Nature* 514: 181-186.

Other references and resources

Neel JV (1962) Diabetes mellitus: A "thrifty" genotype rendered detrimental by "progress"? *American Journal of Human Genetics* 14: 353-362.

Hales CN, Barker DJ (1992) Type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. *Diabetologia* 35: 595-601.

Gaggini M, Saponaro C, Gastaldelli A (2015) Not all fats are created equal: adipose vs. ectopic fat, implication in cardiometabolic diseases. *Hormone Molecular Biology and Clinical Investigation* 22: 7-18.

Crittenden AN (2011) The importance of honey consumption in human evolution. *Food and Foodways* 19: 257-273.

Week 5 (February 27). Does fat make us fat?

- How has fat consumption changed over time?
- How good/bad are different fats?
- Can high-fat diets (e.g. Atkins, Inuit, ketogenic) really help people lose weight?

Readings

Cordain L et al. (2002) Fatty acid analysis of wild ruminant tissues: evolutionary implications for reducing diet-related chronic disease. *European Journal of Clinical Nutrition* 56: 181-191.

Baum SJ et al. (2012) Fatty acids in cardiovascular health and disease: a comprehensive update. *Journal of Clinical Lipidology* 6: 216-234.

Tobias DK et al. (2015) Effect of low-fat diet interventions versus other diet interventions on long-term weight change in adults: a systematic review and meta-analysis. *Lancet Diabetes Endocrinology* 3: 968-79.

Astrup A, Larsen TM, Harper A (2004) Atkins and other low-carbohydrate diets: hoax or an effective tool for weight loss? *The Lancet* 364: 897-899.

COMPARE

Fumagalli M et al. (2015) Greenlandic Inuit show genetic signatures of diet and climate adaptation. *Science* 349: 1343-1347.

Campbell T (2015) Masai and Inuit high-protein diets. A closer look. Center for Nutrition studies. Available at: http://nutritionstudies.org/masai-and-inuit-high-protein-diets-a-closer-look/.

Bjerregaard P, Young TK, Hegele RA (2003) Low incidence of cardiovascular disease among the Inuit – what is the evidence? *Atherosclerosis* 166: 351-357.

Other references and resources

Dyerberg J (1989) Coronary heart disease in Greenland Inuit: a paradox. Implications for western diet patterns. *Arctic Medical Research* 48: 47-54.

Mozaffarian D, Aro A, Willett WC (2009) Health effects of trans-fatty acids: experimental and observational evidence. *European Journal of Clinical Nutrition* 63: S5-S21.

Hooper L et al. (2012) Effect of reducing total fat intake on body weight: systematic review and meta-analysis of randomized controlled trials and cohort studies. *BMJ* 345: e7666.

Week 6 (March 6). Can diet and/or exercise prevent heart disease?

- To what extent do diet versus exercise influence the risk of heart disease?
- How heart-unhealthy are “bad” cholesterols?
- What does blood cholesterol measure?
- Can a person exercise too much?

Readings *(skim those marked with an asterisk*)*

COMPARE

Mozaffarian D, Micha R, Wallace S (2010) Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: a systematic review and meta-analysis of randomized controlled trials. *PLoS Medicine* 7: e1000252.

Chowdhury R et al. (2014) Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. *Annals of Internal Medicine* 160: 398-406.

Nordestgaard BG. (2016) Triglyceride-rich lipoproteins and atherosclerotic cardiovascular disease: new insights from epidemiology, genetics, and biology. *Circulation Research* 118: 547-563.

*Yang Q et al. (2014) Added sugar intake and cardiovascular diseases mortality among US adults. *JAMA Internal Medicine* 174: 516-524.

*Koeth RA et al. (2013) Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis. *Nature Medicine* 19: 576-585.

COMPARE

Levine BD (2014) The benefits of competitive endurance training for cardiovascular structure and function. *Circulation* 130: 987-991.

La Gerche A, Heidbuchel H (2014) You can get too much of a good thing. *Circulation* 130: 992-1002.

Chakravarty EF et al. (2008) Reduced disability and mortality among aging runners: a 21-year longitudinal study. *Archives of Internal Medicine* 168: 1638-1646.

*Kim JH, Baggish AL (2016) Physical activity, endurance exercise, and excess—Can one overdose? *Current Treatment Options in Cardiovascular Medicine* 18:68.

Other references and resources

Tang WHW et al. (2013) Intestinal microbial metabolism of phosphatidylcholine and cardiovascular risk. *New England Journal of Medicine* 368: 1575-1584.

Johnson RK et al. (2009) Dietary sugars intake and cardiovascular health: a scientific statement from the American Heart Association. *Circulation* 120: 1011-1020.

Mozaffarian D et al. (2014) Global sodium consumption and death from cardiovascular causes. *New England Journal of Medicine* 371: 624-634.

O’Donnell M et al. (2014) Urinary sodium and potassium excretion, mortality, and cardiovascular events. *New England Journal of Medicine* 371: 612-623.

Week 7 (March 20). Why do so many diets fail?

- What percentage of diets actually fail, over what time period, and why?
- How does weight loss affect energy expenditure?
- How does weight loss affect food intake?

Readings

Dombrowski SU et al. (2014) Long-term maintenance of weight loss with non-surgical interventions in obese adults: systematic review and meta-analyses of randomized controlled trials. *BMJ* 348: g2646.

MacLean PS et al. (2015) NIH working group report: innovative research to improve maintenance of weight loss. *Obesity* 23: 7-15.

COMPARE

Ochner CN et al. (2013) Biological mechanisms that promote weight regain following weight loss in obese humans. *Physiology & Behavior* 120: 106-113.

Ebbeling CB et al. (2012) Effects of dietary composition on energy expenditure during weight-loss maintenance. *JAMA* 307: 2627-2634

Sumithran P et al. (2011) Long-term persistence of hormonal adaptations to weight loss. *New England Journal of Medicine* 365: 1597-1604.

Fothergill E et al. (2016) Persistent metabolic adaptation 6 years after "The Biggest Loser" competition. *Obesity* 24: 1612-1619.

Ochner CN et al. (2015) Treating obesity seriously: when recommendations for lifestyle change confront biological adaptations. *The Lancet Diabetes & Endocrinology* 3: 232-234.

Other references and resources

Mozaffarian D et al. (2011) Changes in diet and lifestyle and long-term weight gain in women and men. *New England Journal of Medicine* 364: 2392-2404.

Liou AP et al. (2013) Conserved shifts in the gut microbiota due to gastric bypass reduce host weight and adiposity. *Science Translational Medicine* 5: 178ra41.

Elfhag K, Rössner S (2005) Who succeeds in maintaining weight loss? A conceptual review of factors associated with weight loss maintenance and weight regain. *Obesity Reviews* 6: 67–85.

Westerterp-Plantenga MS et al. (2009) Dietary protein, weight loss, and weight maintenance. *Annual Review of Nutrition* 29: 21-41.

Week 8 (March 27). Does exercise help us lose weight?

- How does physical activity affect metabolic rate and energy allocation?
- Does physical activity affect appetite and energy balance?
- Is physical activity useful for losing weight?
- How do different types of physical activity affect ectopic versus subcutaneous fat utilization?

Readings

Pontzer H et al. (2012) Hunter-gatherer energetics and human obesity. *PLoS ONE* 7: e40503.

Pontzer H et al. (2016) Constrained total energy expenditure and metabolic adaptation to physical activity in adult humans. *Current Biology* 26: 410-417.

Church TS et al. (2011) Trends over 5 decades in U.S. occupation-related physical activity and their associations with obesity. *PLoS ONE* 6: e19657.

King NA et al. (2012) Exercise, appetite and weight management: understanding the compensatory responses in eating behaviour and how they contribute to variability in exercise-induced weight loss. *British Journal of Sports Medicine* 46: 315-322.

Hand GA, Blair SN (2014) Energy flux and its role in obesity and metabolic disease. *US Endocrinology* 10: 59–63.

Pavlou KN et al. (1989) Exercise as an adjunct to weight loss and maintenance in moderately obese subjects. *American Journal of Clinical Nutrition* 49: 1115–1123.

Slentz CA et al. (2011) Effects of aerobic vs. resistance training on visceral and liver fat stores, liver enzymes, and insulin resistance by HOMA in overweight adults from STRRIDE AT/RT. *American Journal of Physiology Endocrinology and Metabolism* 301: E1033-1039.

Other references and resources

Jeffery RW et al. (2003) Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? *American Journal of Clinical Nutrition* 78: 684-689.

Jakicic JM et al. (2003) Effect of exercise duration and intensity on weight loss in overweight, sedentary women: a randomized trial. *JAMA* 290: 1323-1330.

Ross R et al. (2000) Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men: a randomized, controlled trial. *Annals of Internal Medicine* 133: 92-103.

Week 9 (April 3). How do diet and exercise affect aging?

- Why do we age, get sick and die?
- Does caloric restriction and/or protein restriction slow aging? If so, how do we reconcile this with an adaptive view of energy allocation?
- How much does physical activity affect cardiovascular and/or skeletal aging?

Readings

Kirkwood TB, Austad SN (2000) Why do we age? *Nature* 408:233-238.

López-Otín C et al. (2016) Metabolic control of longevity. *Cell* 166: 802-821.

COMPARE

Colman RJ et al. (2009) Caloric restriction delays disease onset and mortality in rhesus monkeys. *Science* 325: 201-204.

Mattison JA et al. (2012) Impact of caloric restriction on health and survival in rhesus monkeys from the NIA study. *Nature* 489: 318-321.

Mirzaei H, Suarez JA, Longo VD (2014) Protein and amino acid restriction, aging and disease: from yeast to humans. *Trends in Endocrinology and Metabolism* 25: 558-566.

Lieberman DE (2013) Excerpt from "Chapter 11. Disuse" (pp. 293-303) in *The Story of the Human Body: Evolution, Health and Disease*. Pantheon Books: New York.

Truswell AS, Hanson JDL. (1976) "Medical Research Amongst the !Kung" in *Kalahari Hunter-Gatherers*, eds. Lee RB, DeVore I. Harvard University Press: Cambridge, MA.

Cartee GD et al. (2016) Exercise promotes healthy aging of skeletal muscle. *Cell Metabolism* 23: 1034-1047.

Other references and resources

Williams GC (1957) Pleiotropy, natural selection, and the evolution of senescence. *Evolution* 11: 398-411.

Levine ME et al. (2014) Low protein intake is associated with a major reduction in IGF-1, cancer, and overall mortality in the 65 and younger but not older population. *Cell Metabolism* 19: 407-417.

Heintz C, Mair W (2014) You are what you host: microbiome modulation of the aging process. Cell 156: 408-411.

Gurven MD et al. (2016) Cardiovascular disease and type 2 diabetes in evolutionary perspective: a critical role for helminths? *Evolution, Medicine, and Public Health* 2016: 338-357.

Shave R et al. (in prep) Cardiovascular adaptations for endurance predispose sedentary humans to hypertensive heart disease.

Warden SJ et al. (2014) Physical activity when young provides lifelong benefits to cortical bone size and strength in men. *PNAS* 111: 5337-5342.

Week 10 (April 10). How do diet and exercise affect inflammation?

- What is inflammation and how important is it?
- Is systemic inflammation modulated by the gut microbiota?
- Why does exercise both elevate and depress systemic inflammation?
- Why and to what extent is visceral fat pro-inflammatory?

Readings *(skim those marked with an asterisk*)*

Groopman J (2015) Inflamed: The debate over the latest cure-all craze. The New Yorker. Available at: http://www.newyorker.com/magazine/2015/11/30/inflamed.

Minihane AM et al. (2015) Low-grade inflammation, diet composition and health: current research evidence and its translation. *British Journal of Nutrition* 114: 999-1012.

Cani PD et al. (2012) Involvement of gut microbiota in the development of low-grade inflammation and type 2 diabetes associated with obesity. *Gut Microbes* 3: 279-288.

*Chassaing B et al. (2015) Dietary emulsifiers impact the mouse gut microbiota promoting colitis and metabolic syndrome. *Nature* 519: 92-96.

Kasapis C, Thompson PD (2005) The effects of physical activity on serum C-reactive protein and inflammatory markers: a systematic review. *Journal of the American College of Cardiology* 45: 1563-1569.

Lavie CJ et al. (2011) Impact of physical activity, cardiorespiratory fitness, and exercise training on markers of inflammation. *Journal of Cardiopulmonary Rehabilitation and Prevention* 31: 137-145.

León-Latre M et al. (2014) Sedentary lifestyle and its relation to cardiovascular risk factors, insulin resistance and inflammatory profile. *Revista Española Cardiologia* 67: 449-455.

Other references and resources

Cani PD et al. (2009) Changes in gut microbiota control inflammation in obese mice through a mechanism involving GLP-2-driven improvement of gut permeability. *Gut* 58: 1091–1103.

Neves AL et al. (2013) Metabolic endotoxemia: a molecular link between obesity and cardiovascular risk. *Journal of Molecular Endocrinology* 2013: R51-R64.

Week 11 (April 17). How do exercise and diet affect the brain and behavior?

- How and why do exercise and diet affect mood and mental health?
- Why does exercise make you smart?
- How does the gut communicate with the brain?

Readings *(skim those marked with an asterisk*)*

Hillman CH, Erickson KI, Kramer AF (2008) Be smart, exercise your heart: exercise effects on brain and cognition. *Nature Reviews Neuroscience* 9: 58-65.

Raichlen DA, Polk JD (2013) Linking brains and brawn: exercise and the evolution of human neurobiology. *Proceedings of the Royal Society B* 280: 20122250.

Paillard T, Rolland Y, de Souto Barreto P (2015) Protective effects of physical exercise in Alzheimer's disease and Parkinson's disease: a narrative review. *Journal of Clinical Neurology* 11: 212-219.

Francis H, Stevenson R (2013) The longer-term impacts of Western diet on human cognition and the brain. *Appetite* 63: 119-128.

*Maalouf M, Rho JM, Mattson MP (2009) The neuroprotective properties of calorie restriction, the ketogenic diet, and ketone bodies. *Brain Research Reviews* 59: 293-315.

Mayer EA, Tillisch K, Gupta A (2015) Gut/brain axis and the microbiota. *Journal of Clinical Investigation* 125: 926-938.

*Hsaio EY et al. (2013) Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. *Cell* 155: 1451-1463.

Other references and resources

Lutas A, Yellen G (2013) The ketogenic diet: metabolic influences on brain excitability and epilepsy. *Trends in Neurosciences* 36: 32-40.

Lopresti AL, Hood SD, Drummond PD (2013) A review of lifestyle factors that contribute to important pathways associated with major depression: diet, sleep and exercise. *Journal of Affective Disorders* 148: 12-27.

Ezenwa VO et al. (2012) Animal behavior and the microbiome. *Science* 338: 198-199.

Heijtz RD et al. (2011) Normal gut microbiota modulates brain development and behavior. *PNAS* 108: 3047-3052.

De Palma G et al. (2015) Microbiota and host determinants of behavioural phenotype in maternally separated mice. *Nature Communications* 6: 7735.

Foster JA, Neufeld KAM (2013) Gut–brain axis: how the microbiome influences anxiety and depression**.** *Trends in Neurosciences* 36: 305-312.

Cryan JF, Dinan TG (2012) Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour. *Nature Reviews Neuroscience* 13: 701-712.

O'Mahony SM et al. (2015) Serotonin, tryptophan metabolism and the brain-gut-microbiome axis. *Behavioural Brain Research* 277: 32-48.

Week 12 (April 24). Gene × environment interactions.

- What explains inter-individual differences in response to diet and exercise?
- How do we test for gene x environment interactions?
- How can knowledge of gene x environment interactions serve to improve human health?

Readings

Bouchard C (2011) Genomic predictors of the maximal O_2 uptake response to standardized exercise training programs. *Journal of Applied Physiology* 110: 1160-1170.

Kuzawa CW, Fried RL (2017) "Intergenerational memories of past nutritional deprivation: the phenotypic inertia model" (pp. 7-20) in *The Arc of Life: Evolution and Health Across the Life Course*, eds. Jasienska G, Sherry DS, Holmes DJ. Springer-Verlag: New York.

Povel CM et al. (2011) Genetic variants and the metabolic syndrome: a systematic review. *Obesity Reviews* 12: 952-967.

Ridaura VK et al. (2013) Gut microbiota from twins discordant for obesity modulate metabolism in mice. *Science* 341: 1241214.

Tang WHW, Hazen SL (2014) The contributory role of gut microbiota in cardiovascular disease. *Journal of Clinical Investigation* 124: 4204-4211.

Sonnenburg JL, Backhed F (2016) Diet-microbiota interactions as moderators of human metabolism. *Nature* 535: 56-64.

Other references and resources

Carmody RN et al. (2015) Diet dominates host genotype in shaping the murine gut microbiota. *Cell Host & Microbe* 17: 72-84.

Sommer F, Backhed F (2013) The gut microbiota – masters of host development and physiology. *Nature Reviews Microbiology* 11: 227-238.

Nicholson JK et al. (2012) Host-gut microbiota metabolic interactions. *Science* 336: 1262-1267.

Frayling TM et al. (2007) A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. *Science* 316: 889-894.

Rampersaud E et al. (2008) Physical activity and the association of common FTO gene variants with body mass index and obesity. *Archives of Internal Medicine* 168: 1791-1797.

Hancock AM et al. (2010) Human adaptations to diet, subsistence, and ecoregion are due to subtle shifts in allele frequency. *PNAS* 107: 8924-8930.

Chang CL et al. (2011) Identification of metabolic modifiers that underlie phenotypic variations in energy-balance regulation. *Diabetes* 60: 726-734.

Eriksson JG et al. (2003) Pathways of infant and childhood growth that lead to type 2 diabetes. *Diabetes Care* 26: 3006-3010.

Ameur A et al. (2012) Genetic adaptation of fatty-acid metabolism: a human-specific haplotype increasing the biosynthesis of long-chain omega-3 and omega-6 fatty acids. *Cell* 90: 809-820.