

DR. HYMAN+

LESSONS FROM OUR PAST on HOW to LIVE BETTER and LONGER in OUR FUTURE

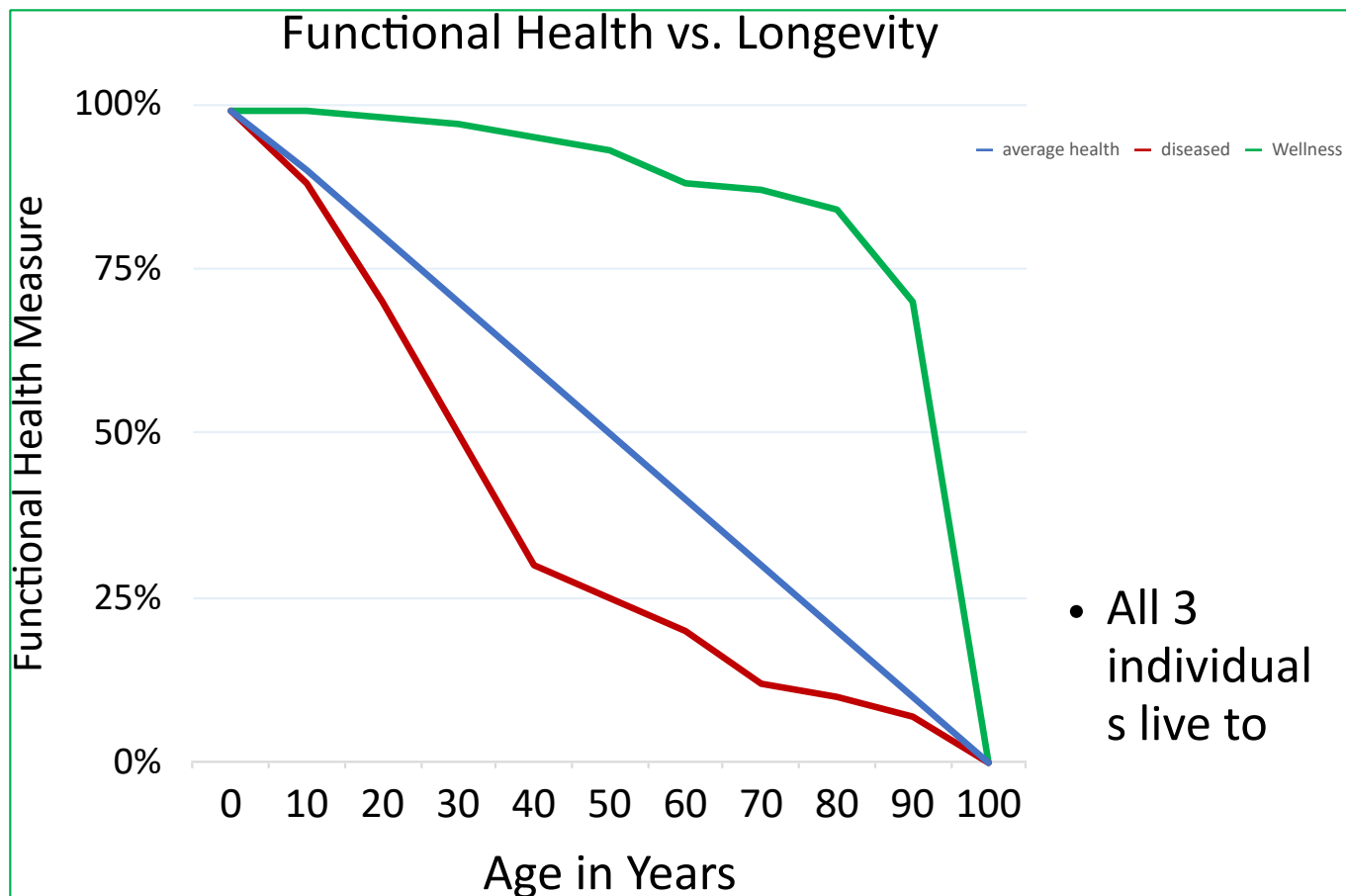
**Elizabeth M. Board, MD
DABA, IFMCP, ABIHM**



Living BETTER and Living LONGER

“The only way you can quantify Health is through its function.

Physical
Metabolic or Physiological
Cognitive
Psychological or Behavioral”
-2019 Jeff Bland, PhD



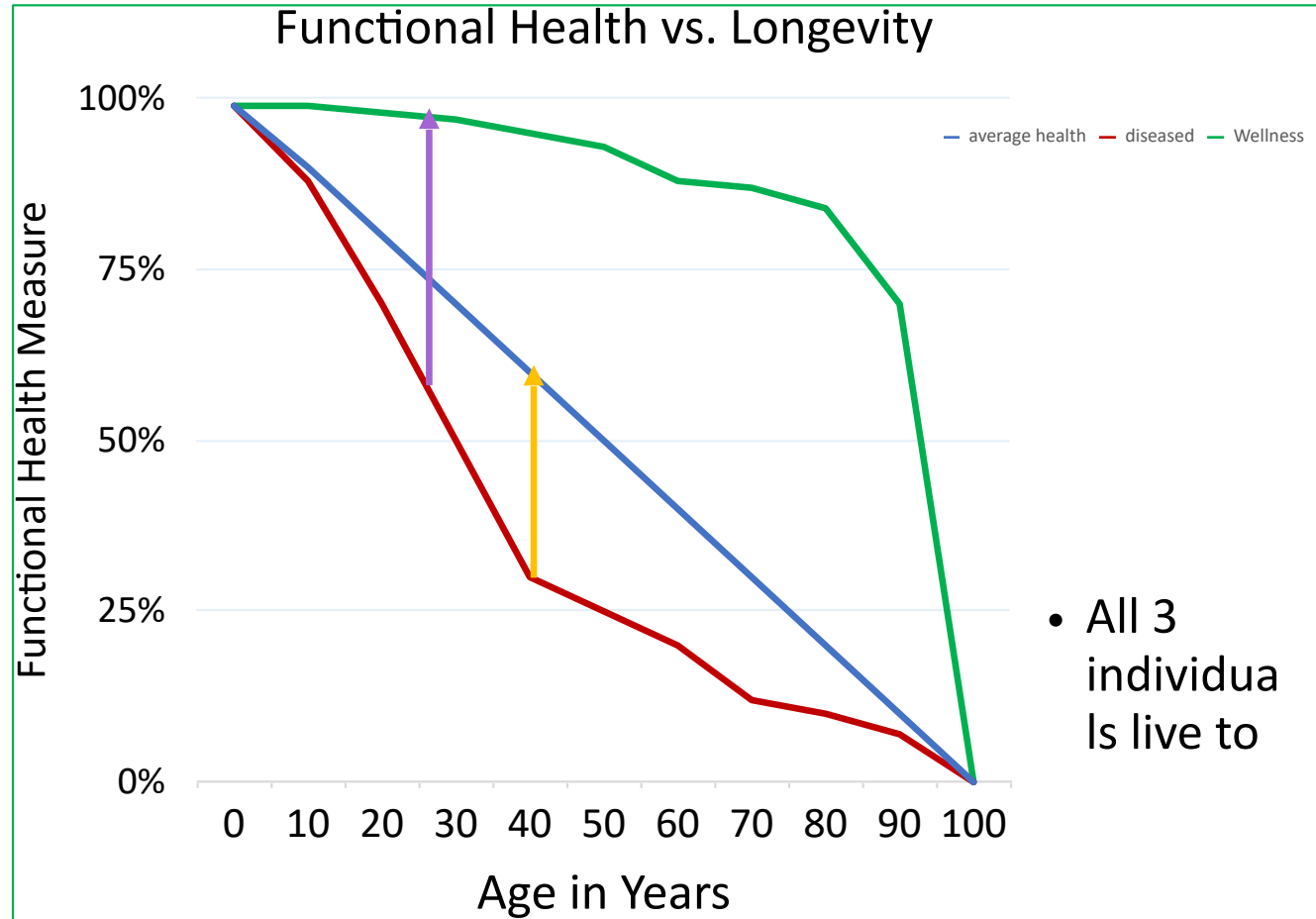
Living BETTER and Living LONGER

How can we move the patient from the red line to the blue line?

“Health Recovery”

How can we move the patient from the red line to the green line?

“Health Resiliency”



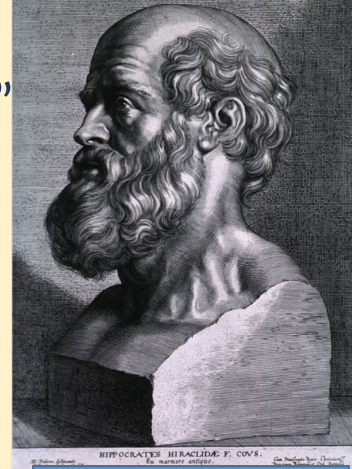
The wise learn from the lessons of the past.

“Foolish the doctor who despises the knowledge acquired by the ancients.”
-Hippocrates

PSALM 139:14 “I praise you, for I am fearfully and wonderfully made.
Wonderful are your works; my soul knows it very well.”

Why not apply principles of successful human evolution to improve our
health and well being today.

“EVOLUTIONARY MEDICINE” or “Darwinian Medicine”



TOUR GUIDE

- ❖ **Evolution:** change in the heritable characteristics of biological populations over successive generations due to natural selection, genetic drift, resulting in **biodiversity** at every level of biological organization
- ❖ **Natural Selection:** heritable variations allow competition for resources resulting in more successful reproduction
- ❖ **Genetic Drift:** frequency of different genotypes in a small population owing to chance disappearance or random failure to reproduce
- ❖ **Fitness:** relative ability to survive and transmit genes
- ❖ **Adaptation:** useful feature that promotes survival and reproduction

Today's Diseases in Evolutionary Medicine

Disease Categories

- Extrinsic cause
- Intrinsic cause
 - Adverse effects of host defenses
 - Disordered homeostasis
 - Age-related loss of maintenance
 - Genetic, genomic and chromosomal
 - Maternal, paternal, fetal genetic conflict disorders

Examples

- Infection, trauma, malnutrition & toxins
- Autoimmune diseases, asthma, allergies
- Diabetes type II, atherosclerosis, hypertension
- Neurodegeneration, sarcopenia, renal failure, osteoporosis, cancer
- Mendelian disease, trisomies, Turner
- Eclampsia, gestational diabetes, autism

Brunham RC. *CMAJ* 2018 Feb12;190:E162-6.

RESEARCH ARTICLE

Open Access

The status of evolutionary medicine education in North American medical schools

Brandon H Hidaka^{1*}, Anila Asghar², C Athena Aktipis³, Randolph M Nesse³, Terry M Wolpaw⁴, Nicole K Skatelyn J Bennett⁵, Matthew W Beyrouy⁵ and Mark D Schwartz⁵

Only 39% of North American Medical Schools responded to the survey

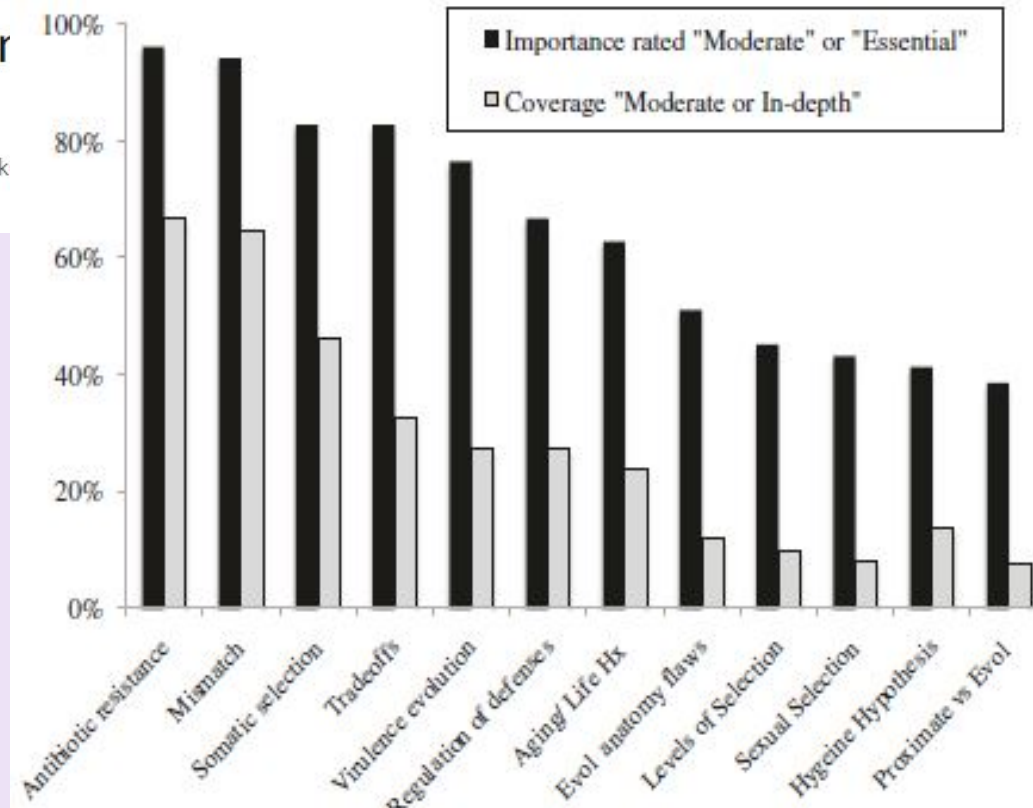
Most Important Topics:

Antibiotic Resistance

Environmental Mismatch Diseases

Somatic Selection in Cancer

Tradeoffs



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The status of evolutionary medicine education in North American medical schools

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10 years later:

Coverage increased most in these topics:

Environmental Mismatch

Tradeoffs

Aging/Life-history

Defense Regulation

Table 2 The change in evolutionary medicine resources and instruction over 10 years in North American medical schools

	2003	2013	Difference
Having any evolutionary biologists on the faculty	16%	43% ^a	+27%
Devoting any curriculum hours to teaching evolution	80%	97% ^b	+17%
Reporting that adding evolutionary content to the curriculum would arouse controversy	11%	48% ^c	+38%
% Reporting coverage of... ^d			
Antibiotic resistance	94%	98% ^e	+4%
Environmental mismatch	30%	94% ^e	+64%
Tradeoffs	26%	90% ^e	+74%
Pathogen virulence	83%	88% ^e	+5%
Aging/Life-history theory	19%	82% ^f	+63%
Defense regulation	20%	80% ^e	+60%
Levels of selection	51%	70% ^f	+19%
Anatomical flaws from path dependence	17%	67% ^e	+50%
Proximate vs. evolutionary explanations of disease	5%	57% ^e	+52%

Antagonistic Pleiotropy*

Pleiotropy: when a single gene locus impacts multiple unrelated phenotypes

- a survival mechanism that benefits us when we are young that is kept through evolution because this far outweighs any problems it may cause when we get older
- “Genes that help us reproduce when we are young don’t just become less helpful as we age, they actually come back to bite us when we are old.”
- WHY? “Our ancestors bred as fast as biology allowed, which was only slightly faster than the death rate.”

“tradeoffs”

*evolutionary theory of aging
proposed by George C. Williams

Sinclair, David A. (2019) *Lifespan Why We Age and Why We Don't Have To*. Pgs 11.152

Practical Utility of Evolutionary Medicine

Dr Naugler favors teaching family physicians an evolutionary perspective in med school

- carriers of **sickle cell trait** have greater than 90% protection against severe malaria.
- glucose-6-phosphate dehydrogenase deficiency, pyruvate kinase deficiency, α -thalassemia, hemoglobin C disease, hemoglobin E disease: all offer advantages against Malaria
- **Hemochromatosis** gene mutation C282Y may represent an adaptation that occurred when prehistoric humans switched from a Paleolithic hunter-gatherer diet rich in red meat to a Neolithic mostly cereal grain diet
- Randolph Ness: Evolutionary Psychiatry: stress and depression

PROPOSED EVOLUTIONARY EXPLANATION	DISORDERS
Heterozygote advantage	Sickle cell disease ⁷ Cystic fibrosis ⁸ Phenylketonuria ⁹
Antagonistic pleiotropy; adaptation to ancestral environment	Hemochromatosis ^{10,11}
Antagonistic pleiotropy	Gout ¹² Atherosclerosis ¹³ Prostatic hypertrophy ¹⁴ Alzheimer disease ¹⁵
Adaptation to ancestral environment	Obesity ¹⁶ Type II diabetes ^{17,18} Essential hypertension ¹⁴ Drug abuse ¹⁹ Female reproductive cancers ²⁰

Naugler, CT. *Can Fam Physicians* 2008 Sep;54(9):1265-9.

Milestones in 10 Million Years of Human Evolution

10 million

Bipedalism



5 million

Australopithecus



4 million

First stone tools



3 million

Homo habilis

Homo erectus

2 million

Signs of camps & meat eating
Use of fire



1 million

Environment of Evolutionary Adaption

700,000

Homo sapiens

Advanced tools

200,000

Homo sapiens sapiens

- modern humans

100,000



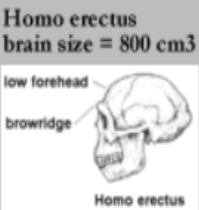
Cave painting about 20,000 years old

40,000

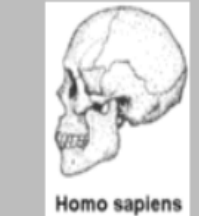
10,000

150

Industrial revolution



Homo erectus brain size = 800 cm³



Homo sapiens sapiens brain size = 1700 cm³

“Transitions” our story

1st 6 mill: Three species Bipedal primates:

Sahelanthropus: upright footprints, smaller canines, enamel, short bodies, big guts, small brain (6-7 mill)

Orrorin: thickened femur (upright bipedal walking)

Ardipithecus: (5.8-5.2 mill); ALL ate mostly fruit, climate change favored these “tree and land” hominids

2nd 4 mill Genus *Australopithecus* “Lucy” who “expanded her palate” ranging open habitats, sacrificed an opposable toe & long arms for better bipedalism (endures 3 mill y)

Increasing the variety of foods

[Australopithecus afarensis - V](#)

Lieberman, D.E. (2013). *The Story of the Human Body*. New York: Vintage Books

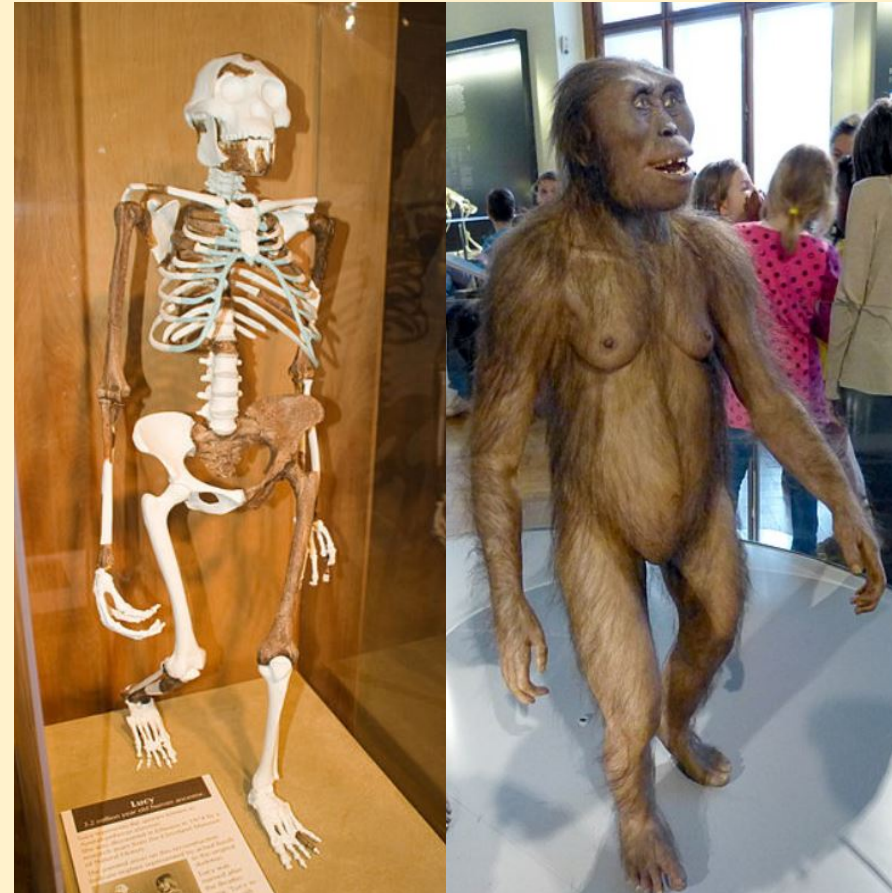
“Transitions” our story

3rd 2.5 mill Genus *Homo* Hunters/gatherers, brains getting bigger, communication, cooperation, adaptations: for running and throwing, heat (leaner), taller, pelvis changed, earlier births.

2 mill: tools, labor division, prey

4th Fire use began 800,000 yrs ago; by 300,000 yrs regular use of fire enabled *Homo* to eat greater variety of foods, especially meat. **Brains grew rapidly**, gut shrank, and body size stalled.

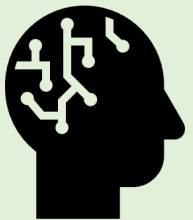
Fire: protection and **connection**



[Australopithecus africanus - wikipedia](#)

Lieberman, D.E. (2013). *The Story of the Human Body*. New York: Vintage Books

- *Homo erectus* “upright man” origin Eastern Asia would survive 2 mill years
 - *Homo rudolfensis*, *Homo ergaster*, *Homo florensis*, *Homo soloensis*, etc. die out
- *Homo neanderthalensis* “man from Neander valley” 500,000 yr Europe & Western Asia. Colder climate: more subcu fat, bulkier, bigger brains, thicker bones, testosterone, hunters, cared for ill, used medicinal plants, used tools, hearth for cooking, wore clothing.
- *Homo sapiens* evolves 250,000 yr ago in East Africa: proficient hunter-gatherers, adv. social skills, bigger brains.



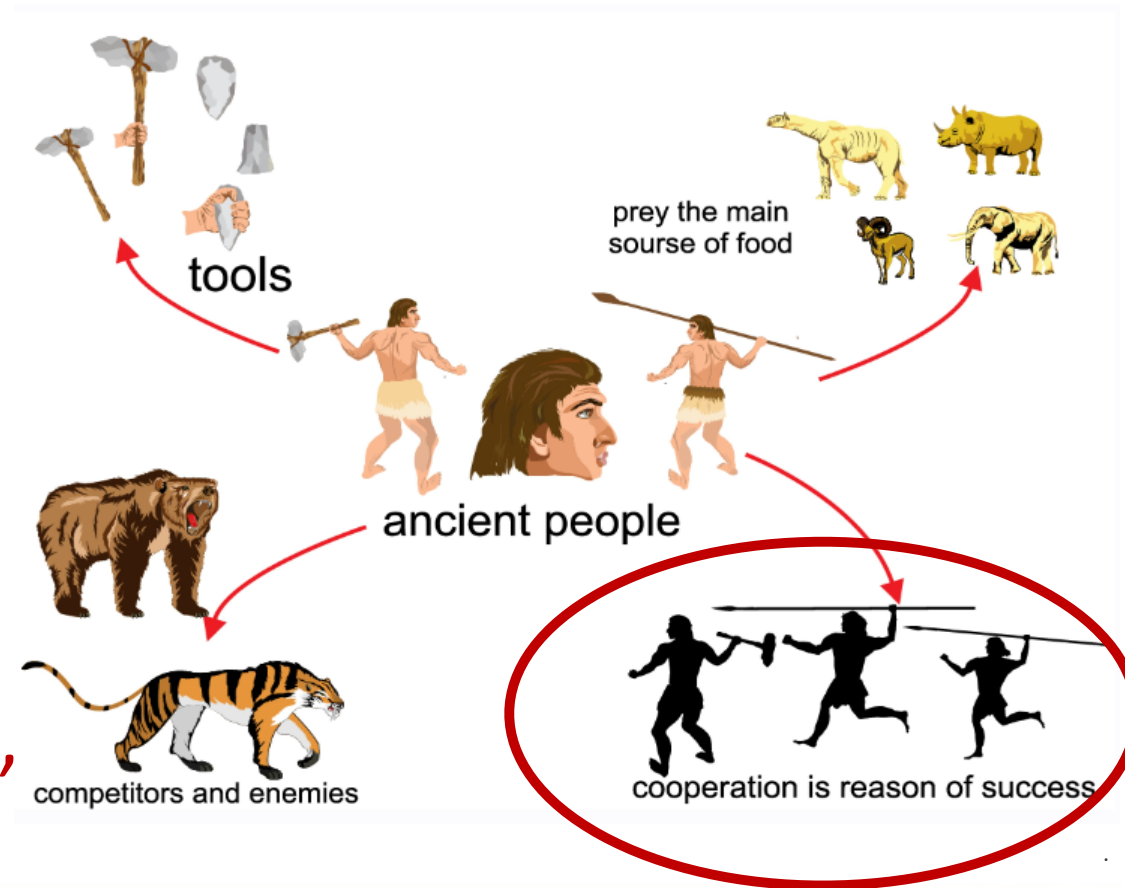
Harari, YN (2015). *Sapiens A Brief History of Humankind*. New York: HarperCollins
 Weyrich, LS et al. *Nature*. 2017 Apr 20;544(7650):357-361.

30,000 yr ago extinction of *H. neanderthalensis*?

- Replacement Theory: *Sapiens* competition and possible genocide
- Interbreeding Theory: Offspring of both species of *homo*
- Both: presence of 1-4% Neanderthal DNA in middle east and Europe

By 10,000yr: lone survivor is:

Homo Sapiens, “wise man”



EVOLUTION OF HUMAN

Homo sapiens



Dated to 30,000-10,000
years ago

Homo neanderthalensis



Dated to 50,000
years ago

Homo erectus



Dated to 1,000,000
years ago

Australopithecus africanus Sahelanthropus tchadensis



Dated to 2,500,000
years ago



Dated to 7-6 million
years ago

*Bipedal

*Slightly fat (fertility)

*Furless

*Plentiful sweat glands

*Big Brained

*Smaller teeth

*Shorter GI tract

*Tool-dependent

*Crave sugar and fat

*Physically active

*Rest whenever
possible (fertility)

*Desire to be close

*Extended family to
care for "premature"

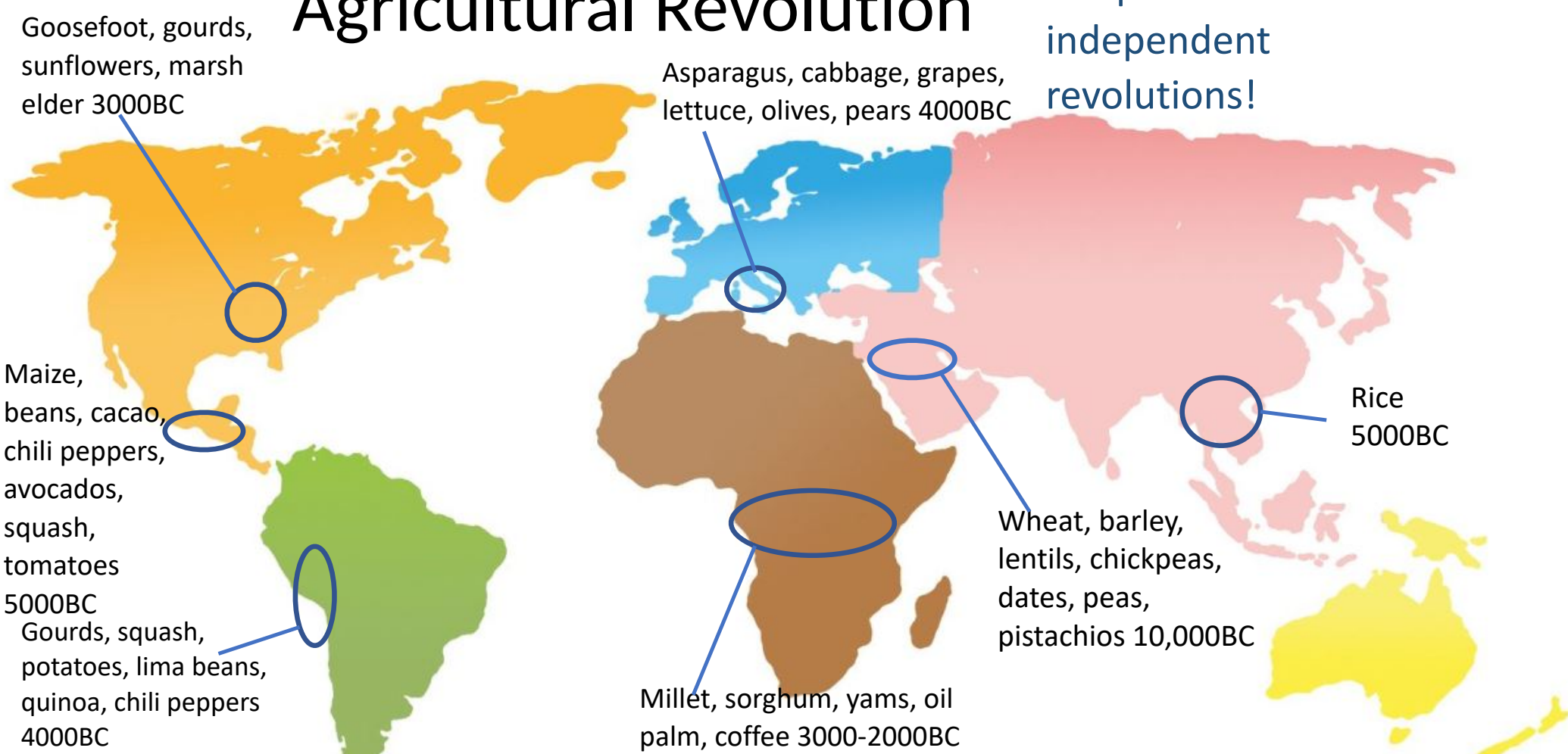
Key points 1st Revolution: Cognitive

- Variety of food
- Nutrition and gut connection to brain health
- Energy conservation increased body fat which increased reproductive capacity
- Need for community & cooperation
 - Raising offspring
 - Safety
 - Prevent starvation
- Communication and development of social skills (theory of *Homo sapiens* success and dominance)



Agricultural Revolution

7 separate and independent revolutions!



2nd Revolution: Agricultural

- Why those foods in those places?
- The plants and animals that were present were grown and were domesticated (oxen and pigs)
- At approximately 10,000 years ago consuming milk: goat
- Big Lie: Agricultural did not improve human health
- Hunter gatherers: more nutritional diversity, more fiber to slow digestion, minimal food storage.
- Eventually, average farmer:
 - poorer diet
 - more vulnerable to disease, more food storage (aflatoxins)
 - more carious teeth (<2% to 13%)
 - life span cut short
 - large quantity of food, lost the nutritional richness: **wheat**, rice, maize, potatoes, millet, and barley. Eventually sugar cane, sorghum, bananas.



Lack of **color** and
diversity

Harari, YN *Sapiens: A Brief History of Humankind*. 2015. p76-81

High Insulin Demand Foods

HIDDEN DANGER

These are all very high insulin demand foods:

Potatoes
Maize (corn)
Rice
Wheat
Barley
Sugar Cane
Bananas
Gourds

Insulin increases fat deposition

Increased body weight

Increased fertility, more offspring

More Agriculture

Kopp, W. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy* 2019;12 2221–2236

	Paleolithic	Agricultural Revolution	Industrial
Infant Mortality	30-50%	30-40%	<1% after PCN
Lifespan	60-80y	40-50y	70-80y
Height	5'8	5'4	5'10

Greatest drop in height occurred from the first farmers to second farmers era

Agricultural Revolution was also a Cultural Evolution

Social stratification

Landowners and slaves

Social hierarchy

Ease and comfort

Demand for Luxury items

Rapid expansion in population

Lieberman, D.E. (2013). *The Story of the Human Body*. New York: Vintage Books
 Harari, YN *Sapiens: A Brief History of Humankind*. 2015.



Great Plains of North America walk for 100s of miles and there would be no other plant except wheat!
Amount of wheat = 10x size of Britain.
Risk of crop failure deadly: led to famine
Wheat transformed man long before man transformed wheat!
Slipped discs, arthritis, hernias, osteoporosis
Cereal grains contain phytic acid which decreases zinc, iron, calcium, magnesium uptake.

Raboy, V *Plants*(Basel) 2020 Feb; 9(2): 140.

2nd big Cultural Evolution

HIDDEN DANGERS

- Industrial Revolution: farm population moves to cities for work
- Growth of cities: population compression, less movement, waste accumulation, cohabitation of animals with humans, pollution
- More infectious disease, Sulfa and PCN will eventually curtail
- Until HIV....
- And then CoVID 19

Behavioral Immune System

Sickness behavior mediated by cytokines IL-6, IL-1b, TNF-a

- decreased physical contact
- reduced contamination of shared environments
- advertised illness behavior, signaling



“By enabling infected people to travel widely and socialize, it interferes with a natural mechanism that prevents pathogen spread.” **HIDDEN DANGER**

Sickness behavior evolved to reduce the spread of an infection to immediate kin.

Evolved to experience “disgust” response when exposed to those infected.

Mitigation of these symptoms can reduce “sickness behavior” and could favor spread.

Shakhar, K et al. *PLoS Biol*, 2015 Oct;13(10): e1002276

Shakhar, K *Front Psychol* 2019 May3;10:1004.

POST AGRICULTURAL & INDUSTRIAL FOOD

- Last episodes of widespread starvation: soup kitchens in 1930s. Overabundance of food
- Mechanized food, stripped food, instant convenience food
- Canned, bagged and boxed transfer chemicals into food.
- Marketed for taste, texture, novelty → overeating.
- Chemicals to preserve shelf life.
- Removal of fiber speeds the digestive process reducing nutrient uptake. No time to feel full.
- Lack of variety of phytonutrients.
- Softer food led to changes in the shape and bone strength of the mandible. Obstructive sleep apnea.
- Medications given daily rob nutrients.

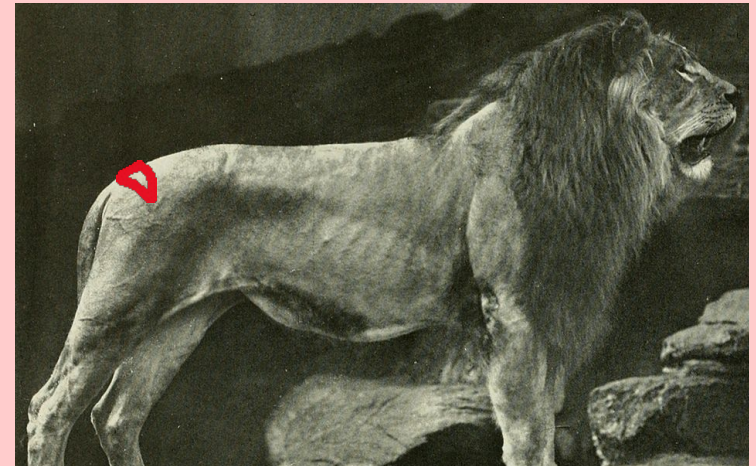
HIDDEN DANGERS

*Difficult to
practice
moderation*

Lack of movement. Preference for energy conservation.

Moving from all Fours to only Two

- Walking set us on a different evolutionary path.
- We sacrificed climbing for walking and running.
- Shorter arm span.
- Lengthened achilles tendon, arches in the feet
- Arm swing which balances us as we run.
- Shortened toes. Long toes would have prohibited us from running.
- Enlarged gluteal muscles. Even the king of the jungle lacks large butt muscles!
- Greater number of sweat glands, nearly hairless regulated our body temp.
- Running and head stabilization. How did we manage that?



Lieberman, DE (2013) *The Story of the Human Body*. New York: Vintage Books

What are the mechanisms of aging?

- Epigenetic alterations
- Genomic instability
- Telomere attrition
- Loss of proteostasis
- Deregulated nutrient sensing
- Mitochondrial dysfunction
- Cellular senescence
- Altered intercellular communication
- Stem Cell exhaustion
- Improves Stem Cell production which will assist cellular repair. As we age there is an impairment of muscle regeneration, sarcopenia

Exercise positively affects all of these!



Judy Dean Foreman *Exercise is Medicine* 2019, Rand

Exercise

BMJ 2016

- Breast Cancer 14%
- Colon Cancer 21%
- Diabetes 28%
- Ischemic Heart Disease 25%
- Ischemic Stroke 26%



Increases flow mediated dilation

Increases angiogenesis

Improves endothelial function

Increases Insulin sensitivity

Increases adiponectin

Decreases inflammation

Increases the # of mitochondria in white adipose tissue

Increases mitochondrial biogenesis

Increases ATP production, increases energy

Increases skeletal muscle glucose disposal

Improves bowel function, increases vagal tone

Increases heart rate variability

Increases fibrinolysis, lowers fibrinogen & blood viscosity

Increases maximal oxygen consumption

Decreases blood pressure

Decreases TG and total cholesterol

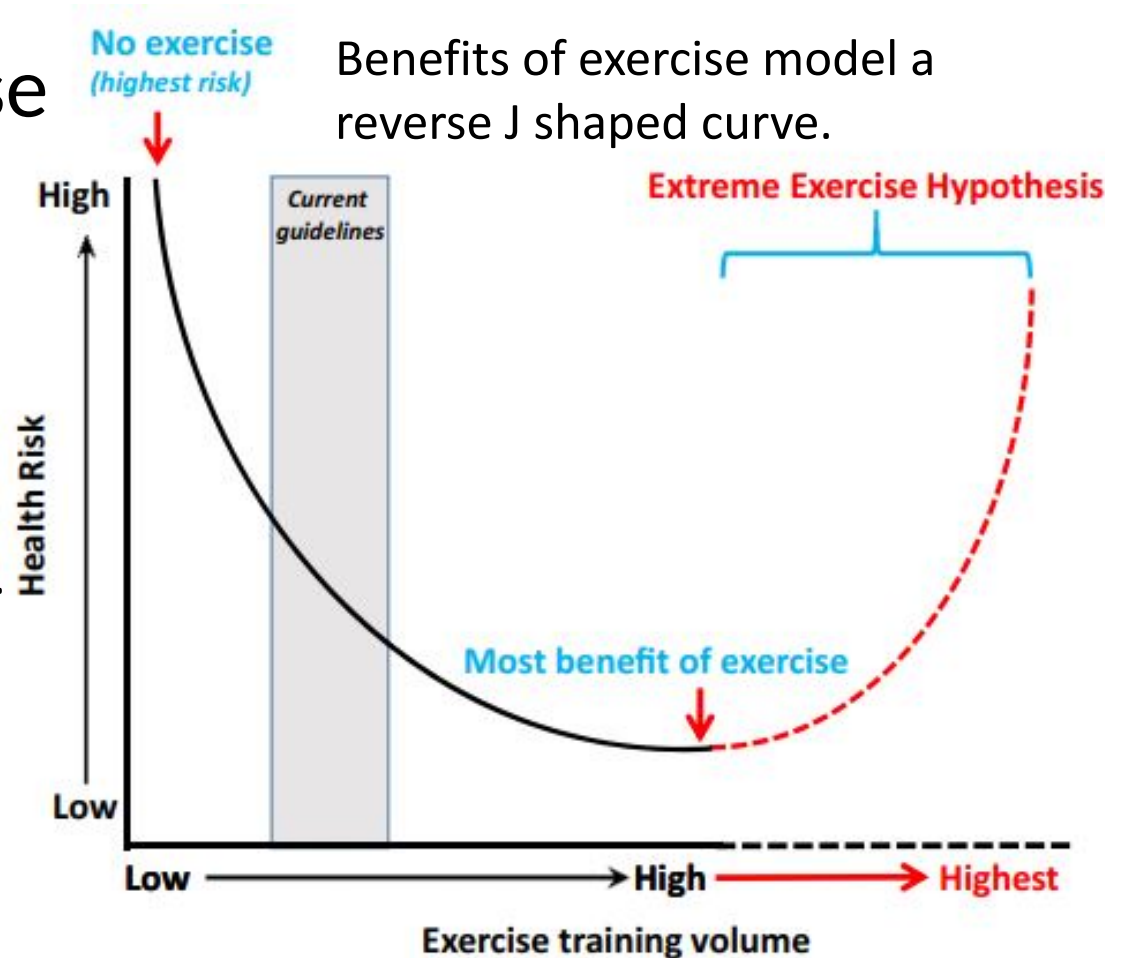
Decreases LDL and increases HDL

Increases BDNF

WHY it works

Risks of Excessive Exercise

- The act of moving itself transformed our bodies into what we are today.
- Increased risk of **atrial fibrillation** results from excessive exercise as stretched myocytes scar, & excessive oxidative stress damages mitochondria.
- Increased coronary artery calcification
- Animal models show elevated troponin acutely and eventually a dilated cardiomyopathy.



Eijsvogels, TMH, et al. *Curr Treat Options Cardio Med* (2018) 20: 84

BENEFITS OF MODERATE EXERCISE

- Research: Minimum of 112 min a week improved lipids, blood pressure and inflammation. Beyond 255 min a week those benefits were LOST!
- We evolved to avoid exercise.
- Dr. Lieberman studied the Hadza and south American runners of today
- Discovered: they never trained, they ran for fun and as a spiritual practice
- Movement was either necessary or it was for fun (spiritual).

Copenhagen City Heart Study: 25 year multivariable –adjusted life expectancy gains

Activity	Years gained
Tennis	9.7
Badminton	6.2
Soccer	4.7
Cycling	3.7
Swimming	3.4
Jogging	3.2
Health Club Activities	1.5

Schnor, P et al *Mayo Clinic Proc* 2018 Dec;93 (12):1775-1785.
Pontzer MID: 30511505

SLEEP and REST

Hunter Gatherers

- slept on the ground
- with children
- with noise

Modern sleep disruptors:

- Long work hours
- Blue light
- Loss of circadian rhythm
- High sugar foods
- Alcohol
- Stimulants

Ogilvie RP, et al. *Sleep Health*. 2017 Oct; 31 (5): 383-388



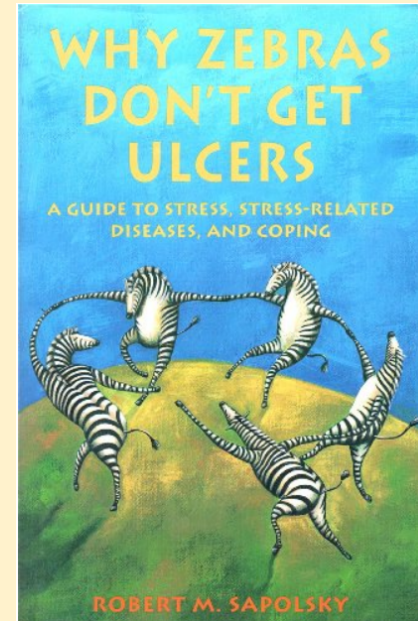
Painting of bison in Altimira, Northern Spain, first example of Stone Age cave art c 14,000BC.

CONNECTION and Strong Social Support:

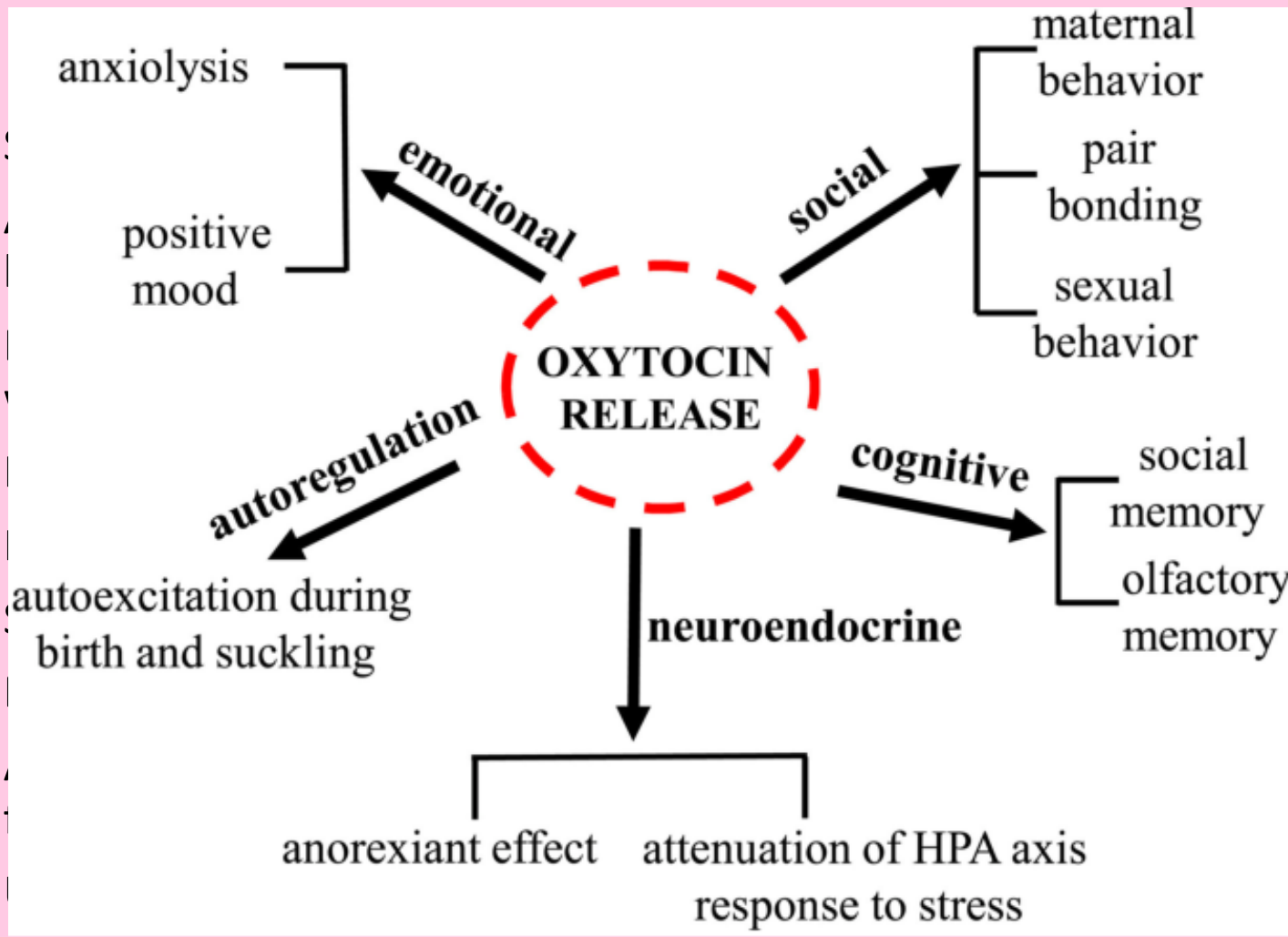
- Story of *Homo sapiens* out surviving *Homo neanderthalensis*
- Robert Sapolsky, PhD author “Why Zebras Don’t Get Ulcers”
Stress as a major risk factor in cardiovascular disease
- 4 of the 9 commonalities among centenarians of “The Blue Zones”, involve connection to family, community and purpose

“Natural forces within us are the true healers of disease.”
- Hippocrates

One of those forces is Dopamine...



Harari, YN *Sapiens A Brief History of Humankind*. 2015
Buettner, D and Skemp, *S Am J Lifestyle Med*. 206 Jul 7; 10(5):318-321.



social
 team,
 ry.
 release
 gastric

Oxytocin

Quintana, DS and Guastella, AJ. An Allostatic Theory of Oxytocin. *Trends in Cognitive Sciences*. July 2020, Vol 24. 7

DOPAMINE and the Dopaminergic Synapse

- Designed to keep us motivated to stay alive & reproductively successful
- An exaggerated risk-reward complex characterizes human cognitive differentiation, facilitated by microbiome derived bioactive compounds
- Host-microbe interactions: impacted human brain evolution & development
- Humans:Dopamine driven (social conformity); Primates:Acetylcholine driven
- Love and creativity = perfect recipe for passing on genes successfully
- Neurotransmitter of anticipated pleasure or reward and as such facilitates goal directed behavior
- Remain Flexible because the forces of cultural evolution can be overwhelming
 - Tobacco, alcohol, drugs, eating, etc. increase Dopamine
 - Smoking: decreases fertility and earlier menopause
 - Earlier menopause: shorter life expectancy

HIDDEN DANGER

Schnorr, SL et al. *Curr Opin Genet Dev.* 2016 Dec; 41:14-26.

Raghanti, MA et al. *Proc Natl Acad Sci USA* 2018 Feb 6; 115(6): E1108-E1116.