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A trade-off between cognitive and physical performance, with relative preservation of brain function

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Debate surrounds the issue of how the large, metabolically expensive brains of *Homo sapiens* can be energetically afforded. At the evolutionary level, decreased investment in muscularity, adiposity and the digestive tract allow for a larger brain. Developmentally, high neo-natal adiposity and preferential distribution of resources to the brain provide an energetic buffer during times of environmental stress. Through an experimental design, we investigated the hypothesis of a trade-off involving brain and muscle at the acute level in humans. Mental performance was measured by a free-recall test, and physical performance by power output on an indoor rowing ergometer. Sixty-two male student rowers performed the two tests in isolation, and then again simultaneously. Paired samples *t*-tests revealed that both power output and mental performance reduced when tested together compared to in isolation ($t(61) = 9.699$, $p < 0.001$ and $t(61) = 8.975$, $p < 0.001$). Furthermore, the decrease in physical performance was greater than the decrease in mental performance ($t(61) = -2.069$, $p = 0.043$). This is the first investigation to demonstrate an acute level trade-off between these two functions, and provides support for the selfish brain hypothesis due to the relative preservation of cognitive function over physical power output. The underlying mechanism is unclear, and requires further work.

Evolutionary and developmental implications of enhanced encephalization.

The development of an enlarged and elaborated brain is considered a defining characteristic of human evolution[1]. The evolution of the *Homo* clade has been accompanied by significant encephalization[2,3]. This facilitated the development of more complex social strategies[4,5], more effective food acquisition[6] and the ability to solve ecological problems through innovative means[7]. Each of these characteristics may have increased survival and reproductive success, giving a greater life expectancy at the age of first reproduction[8].

While the benefits of encephalization are numerous, the brain imposes significant metabolic costs on both the individual[9–11]. High levels of energetic expenditure are necessitated by the brain's responsibility for regulating the body's energy supply and controlling the function of many peripheral organs[12]. These functions require intense neuronal activity, giving the brain the highest metabolic demand relative to size of all organs[13].

The question of how larger brains can be metabolically afforded has remained a prominent problem in human evolution[11,14–17]. Life history theory states that as energy availability is finite, an organism has a limited energy budget. Energy allocated to one function cannot be used for another. Energy savings in other organs or tissues could allow for energetic diversion to the brain, without the need to increase overall metabolic expenditure[11,18]. Such a trade-off has been proposed with both digestive tract development[17] and adiposity[19].

Meeting the brain's metabolic requirements.

The immediate metabolic costs of the brain depend on its activation state. While the metabolic rate is low during sleep[20] increased energy consumption has been observed in response to a mental task[21], and following somatosensory, olfactory, visual and auditory stimulation[22–27]. The adult brain almost exclusively derives its energy from the metabolism of glucose[28]. This, coupled with its high energetic demand, ensure that the brain metabolises the most glucose of any organ[29,30]. The brain, however, is unable to store significant amounts of energy and hence buffer its high yet variable metabolic demand[31]. As such, the body is required to supply glucose to the brain quickly and effectively. The 'Selfish Brain Hypothesis'[12] posits that the brain prioritises its own glucose needs over those of the peripheral organs, such as skeletal muscle.

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	Protocol A (n = 62)		Protocol B (n = 62)		Protocol C (n = 62)	
	M	SD	M	SD	M	SD
Power output (W)	389.93	34.819	—	—	340.20	43.321
Free recall (words)	—	—	29.11	3.339	26.27	3.738

Table 1. Descriptive statistics for power output and free recall. Age M = 21.1 yrs, SD = 1.61; Weight M = 80.7 kg, SD = 4.46; Height M = 181.2cm, SD = 3.98.

	A: Power output	B: Recall	C: Power output	C: Recall	∆ Power	∆ Recall
A: Power output	—					
B: Recall	0.155	—				
C: Power output	0.484***	0.223	—			
C: Recall	0.102	0.758***	0.355**	—		
∆ Power output	−0.343**	0.105	0.656***	0.293*	—	
∆ Recall	−0.054	−0.203	0.234	0.485***	0.298*	—

Table 2. Correlation matrix. Note: Statistical significance: *p < 0.05; **p < 0.01; ***p < 0.001.

Skeletal muscle and encephalization. Skeletal muscle mass is an expensive tissue to maintain, accounting for approximately 20% of human male BMR[32,33], and may be compromised to partially offset the brain's high energy costs[11,34]. An adaptation to reduce muscle mass would thereby reduce metabolic demand, allowing for a reallocation of energy towards the central nervous system[35]. The glucose demands of skeletal muscle also increase significantly with activation[36–40]. In such circumstances, skeletal muscle thereby becomes a powerful competitor of the brain for glucose and oxygen[41].

High intensity exercise increases the metabolic demand of skeletal muscles and the brain[39,40,42–45], in proportion to degree of activation. At high levels of activation both are reliant upon glucose metabolism, and require a high rate of oxygen and glucose supply. Should both be challenged simultaneously, competition for these valuable yet limited resources may therefore develop, with one or both organs receiving an insufficient supply for optimal performance.

The concept of an antagonistic relationship between capacity to perform mental and physical work is not a new one[46]. As described by the idea of central fatigue, prior mental exertion may impair subsequent physical performance[47].

Despite the intuitive appeal of a trade-off between two competing functions, negative covariance in such traits are not frequently observed when phenotypic comparisons are made between individuals within a population[48,49]. This study seeks to experimentally investigate the possibility of a trade-off involving the brain at the acute, rather than at the evolutionary or developmental, level. It is hypothesised that, when both systems are challenged simultaneously, performance will be inferior to performance when each are challenged in isolation. It is further hypothesised that the relative decrease in muscle power output will exceed the relative decrease in cognitive function.

Results

A description of the samples is given in Table 1. Significant positive correlations were observed between rowing power output in both Protocols A and C ($r = 0.484$, $p < 0.001$), as well as recall performance in both Protocols B and C ($r = 0.758$, $p < 0.001$). This suggests that participants who row fast or recall many words do so irrespective of condition. Table 2 reports the correlation matrix (Pearsons product-moment correlation coefficients), with a significant negative correlation was observed between rowing power output in Protocol A and ∆power from Protocol A to C ($r = -0.343$, $p = 0.006$). No correlation was also observed between recall performance in Protocol B and ∆recall from Protocol B to C ($r = -0.203$, $p = 0.113$). This suggests that highly performing participants in Protocols A and B exhibit the greatest decline in performance when both tasks are performed together in Protocol C.

Paired samples t-tests revealed that power output (W) was significantly lower in Protocol C than in Protocol A (Protocol A M = 389.93, SD = 34.819; Protocol C M = 340.20, SD = 43.321; $t(61) = 9.699$, $p < 0.001$). Similarly, recall (correct words) was significantly lower in Protocol C than in Protocol B (Protocol B M = 29.11, SD = 3.339; Protocol C M = 26.27, SD = 3.738; $t(61) = 8.975$, $p < 0.001$). The percentage change in recall between Protocols B and C was significantly less than the percentage change in power output between Protocol A and C (∆recall M = −9.6740, SD = 8.62756; ∆power output M = −12.5535, SD = 9.81460, $t(61) = -2.069$, $p = 0.043$), see Fig. 1.

Discussion

We proposed that the simultaneous challenge of both cognitive and physical faculties would result in impaired performance in each task, compared to performance achieved when in isolation. This hypothesis has been supported. The observation that both tasks cannot be performed optimally at the same time suggests that a trade-off between mental and physical function does indeed exist. The secondary hypothesis was supported as concurrent challenge differentially affected each task; the decrease in brain function was significantly less than that of power output.

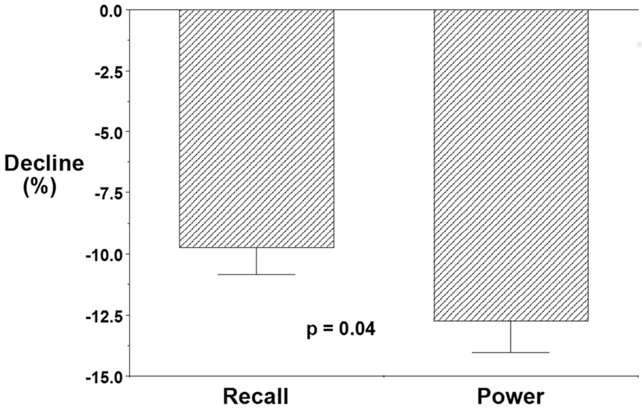

Figure 1. Bar graph showing the relative decrease in cognitive decrease and power output. Power output decreased significantly more than cognitive function.

Preferential allocation of glucose to the brain may be an evolved trait; a well-fuelled brain may offer better survival odds than well-fuelled muscles when facing an environmental challenge[31]. In such a situation, the body is able to buffer a muscle-fuel deficit by increasing supply of free fatty acids to fuel skeletal muscles[50,51]. High intensity physical activity considerably increases the metabolic needs of both the brain and skeletal muscle[28,38–40,42–44,52]. Competition for a limited supply of blood glucose and oxygen is a potential mechanism accounting for the fast-acting trade-off in brain and muscle function demonstrated here. The occurrence of glycogen supercompensation in the brain, as well as in skeletal muscles following exhaustive exercise, provides further support for this explanation[53].

Although the brain is normally dependent upon glucose for energy, it may also utilise the lactate produced by skeletal muscles during exercise. The brain takes up lactate in proportion to its arterial concentration, which increases with exercise intensity. This increased lactate utilisation contributes to the meeting of high cerebral energy demands, which result from increased neuronal activity during high intensity exercise[54]. The preferential uptake of lactate as the predominant oxidative substrate of neurones[55] has the effect of sparing glucose[56]. However, our results suggest that substrate competition between the brain and skeletal muscles is significant despite this.

Life history theory describes the competitive allocation of limited resources between physiological functions during development[57–60]. The optimal physiological distribution is determined by both the individual's life stage[61] and environment[62,63], and is achieved through phenotypic plasticity[64]. Hales & Barker extended life history theory to consider trade-offs between organs and tissues, such as brain and muscle, by proposing that nutritional stress during early development leads to certain tissues being prioritised over others[65]. This tactic allows the organism to endure conditions of energy deficit, but with the cost of decreased adaptability to varying ecological conditions later in life due to decreased investment in the development in other organs.

During neonatal development, the brain is most vulnerable to irregularities in energy supply. The high adiposity of humans at birth in comparison to other mammalian species[66] provides an energetic buffer[67], preserving cerebral metabolism despite high early-life energetic requirements. Furthermore, preferential distribution of resources is evident in undernourished foetuses, in whom some organs grow normally while others are underdeveloped[68]. For humans, the brain's development is spared[69], perhaps at the expense of muscle[70]. Low birth weight, indicative of foetal undernourishment, is associated with a negative relationship between development of brain and muscles[71]. The selfish nature of the brain has also been observed in the unique preservation of brain mass in individuals suffering from long-term malnutrition or starvation[51], in children born with intrauterine growth restriction[72,73] and in glucose-challenging situations such as fasting or hypo/hyper-glycaemia[74–76].

The evidence presented in this paper, which builds upon the existing body of research, indicates the possibility of an evolutionary trade-off between brain and muscle energetic demands.

Conclusion

This study has demonstrated an acute level trade-off between cognitive function and physical power output during simultaneous challenge. This supports the selfish brain hypothesis due to the relative preservation of cognitive function over physical power output. The underlying mechanism is unclear, and requires further investigation.

Methods

Sixty-two male rowers were recruited from the University of Cambridge, and testing was carried out in Cambridge, UK (mean age = 21.15 years, SD = 1.618 years). All participants were instructed in the risks and benefits of participating in the study and signed a written informed consent statement. The statement and the study was approved by the University of Cambridge Biology Ethics Committee (Application No: HBREC.2013.12), and the study was conducted in accordance with the approved methodology.

Participants completed three protocols (Table 3). Protocol A consisted of a maximum effort row for 3 minutes at free rate on a Concept 2 rowing ergometer (manufactured by Concept 2, Vermont, USA), and average power output (W) was recorded. Protocol B consisted of a mental free recall task, the number of words correctly recalled

Experimental protocol summary	
Protocol	**Description**
A	Physical task
B	Mental task
C	Physical and mental task

Table 3. Experimental protocols.

was recorded. Protocol C consisted of the same 3 minute row as A, but while simultaneously performing the mental task of Protocol B. Both average power output and number of words correctly recalled were recorded.

The rowing ergometer was used because it is an energetically demanding activity, and has been used in previous studies investigating extreme physical stress[77,78]. The mental task involved free recall. A large printed screen showing 75 words was clearly displayed in front of the participants' chair (Protocol B), or in front of the rowing ergometer (Protocol C), for a duration of 3 minutes. The participants were required to recall and write as many words as possible in any order from memory within 5 minutes (5 minutes immediately following the row in Protocol C)[79]. The words were selected from the Toronto Noun Pool[80]. Two 75-word lists were randomly created from the 150 words used by Kahana & Howard[81] and were counterbalanced across participants. Half of the participants were given List 1 for Protocol B and List 2 for Protocol C, with the other half being given List 2 for Protocol B and List 1 for Protocol C. This method ensured that each word was seen an equal number of times across participants, and each participant saw each word only once. Such counterbalancing ensured that any artefacts[82] were controlled for to reduce the likelihood of such artefacts[83].

The Protocols were completed at 1 week intervals. All participants refrained from extra exercise the day before, and the day of, each Protocol. The same machine was used for Protocols A and B, with the drag factor being consistent. The order in which the participants completed the three protocols was also counterbalanced, in order to control for any effects such as the development of memorising strategies.

References

1. Foley, R. & Lee, P. Ecology and energetics of encephalization in hominid evolution. *Philos Trans R Soc Lond B Biol Sci.* **334**(1270), 223–32 (1991).
2. Hawks, J., Hunley, K., Lee, S. H. & Wolpoff, M. Population bottlenecks and Pleistocene human evolution. *Mol Biol Evol.* **17**(1), 2–22 (2000).
3. Lee, S. & Wolpoff, M. The pattern of evolution in Pleistocene human brain size. *Paleobiology.* **29**(2), 186–96 (2003).
4. Byrne, R. & Corp, N. Neocortex size predicts deception rate in primates. *Proc Biol Sci.* **271**(1549), 1693–9 (2004).
5. Parker, S. & McKinney, M. Origins of intelligence: the evolution of cognitive development in monkeys, apes, and humans. (Johns Hopkins University Press, 1999).
6. Gibson, K. Cognition, brain size and the extraction of embedded food resources. *Primate Ontog Cogn Soc Behav.* **3**, 92–10 (1986).
7. Reader, S. & Laland, K. Social intelligence, innovation, and enhanced brain size in primates. *Proc Natl Acad Sci USA* **99**(7), 4436–41 (2002).
8. Barrickman, N., Bastian, M., Isler, K. & van Schaik, C. Life history costs and benefits of encephalization: a comparative test using data from long-term studies of primates in the wild. *J Hum Evol.* **54**(5), 568–90 (2008).
9. Mink, J., Blumenschine, R. & Adams, D. Ratio of central nervous system to body metabolism in vertebrates: its constancy and functional basis. *Am J Physiol Integr Comp Physiol.* **241**(3), R203–12 (1981).
10. Bullmore, E. & Sporns, O. The economy of brain network organization. *Nat Rev Neurosci.* **13**(5), 336–49 (2012).
11. Isler, K. & van Schaik, C. P. Metabolic costs of brain size evolution. *Biol Lett.* **2**(4), 557–60 (2006).
12. Peters, A. *et al.* The selfish brain: competition for energy resources. *Neurosci Biobehav Rev.* **28**, 143–80 (2004).
13. Attwell, D. & Laughlin, S. An energy budget for signalling in the grey matter of the brain. *J Cereb Blood Flow Metab.* **21**(10), 1133–45 (2001).
14. Aiello, L. & Dunbar, R. Neocortex size, group size, and the evolution of language. *Curr Anthropol.* **34**(2), 183–93 (1993).
15. Byrne, R. The technical intelligence hypothesis: an additional evolutionary stimulus to intelligence? In *Machiavellian intelligence II: extension and evaluations* (eds Whiten, A., Byrne, R.) 289–311 (Cambridge University Press, 1997).
16. Isler, K. & van Schaik, C. Costs of encephalization: the energy trade-off hypothesis tested on birds. *J Hum Evol.* **51**(3), 228–43 (2011).
17. Aiello., L. & Wheeler, P. The expensive-tissue hypothesis the brain and the digestive evolution. *Curr Anthropol.* **36**(2), 199–221 (1995).
18. McNab, B. & Eisenberg, J. F. Brain size and its relation to the rate of metabolism in mammals. *Am Nat.* **133**(2), 157–67 (1989).
19. Navarrete, A., van Schaik, C. P. & Isler, K. Energetics and the evolution of human brain size. *Nature.* **480**(7375), 91–3 (2011).
20. Madsen, P. & Vorstrup, S. Cerebral blood flow and metabolism during sleep. *Cerebrovas brain met.* **3**(4), 281–96 (1990).
21. Madsen, P. *et al.* Persisent resetting of the cerebral oxygen/glucose uptake ratio by brain activation: evidence obtained with the Key-Schmidt technique. *J Cereb blood flow Metab.* **15**, 485–91 (1995).
22. Fox, P. & Raichle, M. Focal physiological uncoupling of cerebral blood flow and oxidative metabolism during somatosensory stimulation in human subjects. *Proc Natl Acad Sci USA* **83**, 1140–4 (1986).
23. Fox, P., Raichle, M., Mintun, M. & Dence, C. Nonoxidative glucose consumption during focal physiological neural activity. *Science.* **241**(4864), 462–4 (1988).
24. Sharp, F., Kauer, J. & Shepherd, G. Local sites of activity-related glucose metabolism in rat olfactory bulb during olfactory stimulation. *Brain Res.* **98**(3), 596–600 (1975).
25. Kennedy, C. *et al.* Metabolic mapping of the primary visual system of the monkey by means of the autoradiographic [14C] deoxyglucose technique. *Proc Natl Acad Sci USA* **73**(11), 4230–4 (1976).
26. Ginsberg, M. D., Dietrich, W. D. & Busto, R. Coupled forebrain increases of local cerebral glucose utilization and blood flow during physiologic stimulation of a somatosensory pathway in the rat: demonstration by double-label autoradiography. *Neurology.* **37**(1), 11–9 (1987).
27. Roland, P., Eriksson, L., Stone-Elander, S. & Widen, L. Does mental activity change the oxidative metabolism of the brain? *J Neurosci.* **7**, 2373–89 (1987).
28. Bélanger, M., Allaman, I. & Magistretti, P. Brain energy metabolism: focus on astrocyte-neuron metabolic cooperation. *Cell Metab.* **14**(6), 724–38 (2011).

29. Reinmuth, O., Scheinberg, P. & Bourne, B. Total cerebral blood flow and metabolism archives of neurology. *Arch Neurol.* **12**(1), 49–66 (1985).
30. Peters, A. The selfish brain: Competition for energy resources. *Am J Hum Biol.* **23**(1), 29–34 (2011).
31. Beedie, C. & Lane, A. The role of glucose in self-control: another look at the evidence and an alternative conceptualization. *Personal Soc Psychol Rev.* **16**(2), 143–53 (2012).
32. Elias, M. Organ and tissue contribution to metabolic rate in *Energy metabolism: tissue determinents and cellular corollaries* (ed McKinney, J., Tucker, H.) 51–79 (Raven Press, 1992).
33. Snodgrass, J. J., Leonard, W. R. & Robertson, M. L. Interspecific variation in body composition and its influence on metabolic variation in primates and other mammals. *Am J Phys Anthropol.* **28**, 255 (1999).
34. Snodgrass, J. J., Leonard, W. R. & Robertson, M. L. The energetics of encephalization in early hominids in *The evolution of hominin diets*. 15–29 (Springer Netherlands, 2009).
35. Leonard, W. R., Robertson, M. L., Snodgrass, J. J. & Kuzawa, C. W. Metabolic correlates of hominid brain evolution. *Comp Biochem Physiol Part A Mol Integr Physiol.* **136**(1), 5–15 (2003).
36. Brooks, G. & Mercier, J. Balance of carbohydrate and lipid utilization during exercise: the "crossover" concept. *J Appl Physiol.* **76**(6), 2253–61 (1994).
37. Romijn, J. A., Gastaldelli, A., Horowitz, J. F., Endert, E. & Wolfe, R. R. Regulation in relation of endogenous fat and carbohydrate to exercise intensity and duration metabolism. *Am J Physiol.* **265**, 380–91 (1993).
38. McArdle, W., Katch, F. & Katch, V. Exercise physiology: energy, nutrition and human performance (Lippincott, Williams & Wilkins, 2001).
39. Wahren, J., Felig, P., Ahlborg, G. & Jorfeldt, L. Glucose metabolism during leg exercise in man. *J Clin Invest.* **50**(12), 2715–25 (1971).
40. Ahlborg, G., Felig, P., Hagenfeldt, L. & Hendler, R. Substrate turnover during prolonged exercise in man; splanching and leg metabolism of glucose, free fatty acids, and amino acids. *J Clin Invest.* **53**, 1080–90 (1974).
41. Fehm, H., Kern, W. & Peters, A. The selfish brain: competition for energy resources. *Prog Brain Res.* **153**, 129–40 (2006).
42. Holloszny, J. & Kohrt, W. Regulation of carbohydrate and fat metabolism during and after exercise. *Annu Rev Nutr.* **16**, 121–38 (1996).
43. Nybo, L. & Secher, N. H. Cerebral perturbations provoked by prolonged exercise. *Prog Neurobiol.* **72**(4), 223–61 (2004).
44. Ide, K., Horn, A. & Secher, N. Cerebral metabolic response to submaximal exercise. *J Appl Physiol.* **87**, 1604–8 (1999).
45. Dalsgaard, M., Ide, K., Cai, Y., Quistorff, B. & Secher, N. The intent to exercise influences the cerebral O2/carbohydrate uptake ratio in humans. *J Physiol.* **540**(2), 681–9 (2002).
46. Mosso, A. Fatigue. (Drummond M. & Drummond W. B., 1904).
47. Marcora, S. M., Staiano, W. & Manning, V. Mental fatigue impairs physical performance in humans. *J Appl Physiol.* **106**(3), 857–64 (2009).
48. Glazier, D. S. Trade-offs between reproductive and somatic (storage) investments in animals: a comparative test of the Van Noordwijk and De Jong model. *Evol Ecol.* **13**(6), 539–55 (2000).
49. van Noordwijk, A. & de Jong, G. Acquisition and Allocation of Resources: Their Influence on Variation in Life History Tactics. *Am Nat.* **128**(1), 137–42 (1986).
50. Houten, S. *et al*. Impaired amino acid metabolism contributes to fasting-induced hypoglycemia in fatty acid oxidation defects. *Hum Mol Genet.* **22**(25), 5249–61 (2013).
51. Wang, P. & Mariman, E. Insulin resistance in an energy-centered perspective. *Physiol Behav.* **94**(2), 198–205 (2008).
52. Maher, F., Vannucci, S. J. & Simpson, I. A. Glucose transporter proteins in brain. *FASEB J.* **8**(13), 1003–11 (1998).
53. Matsui, T. *et al*. Brain glycogen supercompensation following exhaustive exercise. *J Physiol.* **590**(Pt 3), 607–16 (2012).
54. Kemppainen, J. *et al*. High intensity exercise decreases global brain glucose uptake in humans. *J Physiol.* **568**(Pt 1), 323–32 (2005).
55. Bouzier-Sore, A. K., Voisin, P., Canioni, P., Magistretti, P. J. & Pellerin, L. Lactate is a preferential oxidative energy substrate over glucose for neurons in culture. *J Cereb Blood flow Metab.* **23**(11), 1298–306 (2003).
56. Quistorff, B., Secher, N. H. & Van Lieshout, J. J. Lactate fuels the human brain during exercise. *FASEB J.* **22**(10), 3443–9 (2008).
57. Stearns, S. C. Trade-Offs in life-history evolution. *Br Ecol Soc.* **3**, 259–68 (1989).
58. Zera, A. J. & Harshman, L. G. The physiology of life history trade-offs in animals. *Ecology.* **32**, 95–126 (2001).
59. Leonard, W. R. Laboratory and field methods for measuring human energy expenditure. *Am J Hum Biol.* **24**(3), 372–84 (2012).
60. Stearns, S. C. The Evolution of Life Histories. (Oxford UnIversity Press, 1992).
61. Holliday, M. Body composition and energy needs during growth In: *Human growth: a comprehensive treatise* (Falkner, F., Tanner, J., ed) 101–17 (New York, NY, 1986).
62. McDade, T. W., Reyes-García, V., Tanner, S., Huanca, T. & Leonard, W. R. Maintenance versus growth: investigating the costs of immune activation among children in lowland Bolivia. *Am J Phys Anthropol.* **136**(4), 478–84 (2008).
63. Kramer, K. L., Greaves, R. D. & Ellison, P. T. Early reproductive maturity among Pumé foragers: Implications of a pooled energy model to fast life histories. *Am J Hum Biol.* **21**(4), 430–7 (2009).
64. Hill, K. & Hurtado, A. M. Ache life history. (Aldine de Gruyter, 1996).
65. Hales, C. & Barker, D. Type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. *Diabetologia.* **35**, 595–601 (1992).
66. Kuzawa, C. W. Adipose tissue in human infancy and childhood: an evolutionary perspective. *Am J Phys Anthropol.* **27**, 177–209 (1998).
67. Wells, J. C. K. The evolution of human fatness and susceptibility to obesity: an ethological approach. *Biol Rev Camb Philos Soc.* **81**(2), 183–205 (2006).
68. Widdowson, E. & McCance, R. A review: new thoughts on growth. *Pediatr Res.* **9**(3), 154–6 (1975).
69. Hofman, M. Energy metabolism, brain size and longevity in mammals. *Q Rev Biol.* **58**(4), 495–512 (1983).
70. Barker, D. J. The foetal and infant origins of adult disease. (BMJ Books, 1983).
71. Baker, J. *et al*. Brains versus brawn: an empirical test of Barker's brain sparing model. *Am J Hum Biol.* **22**(2), 206–15 (2010).
72. Latini, G. *et al*. Foetal growth of kidneys, liver and spleen in intrauterine growth restriction: "programming" causing "metabolic syndrome" in adult age. *Acta Paediatr.* **93**(12), 1635–9 (2004).
73. Grunewald, P. Chronic Fetal Distress and Placental Insufficiency. *Biol Neonate.* **5**, 215 (1963).
74. Oltmanns, K. M. *et al*. Insulin Resistance and the Cardiometabolic Syndrome: Adipose Tissue and Skeletal Muscle Factors Differential energetic response of brain vs. skeletal muscle upon glycemic variations in healthy humans. *Am J Physiol Regul Integr Comp Physiol.* **294**, 12–6 (2008).
75. Hilsted, J., Jensen, K., Thomsen, C., Larsen, S. & Henriksen, O. Maintenance of high-energy brain phosphorous compounds during insulin-induced hypoglycemia in men: 31P nuclear magnetic resonance spectroscopy study. *Diabetes.* **37**(6), 760–2 (1988).
76. Coker, R. & Kjaer, M. Glucoregulation during exercise. *Sport Med.* **35**(7), 575–83 (2005).
77. Hagerman, F., Connors, M., Gault, J., Hagerman, G. & Polinski, W. Energy expenditure during simulated rowing. *J Appl Physiol.* **45**(1), 87–93 (1978).
78. Golf, S. & Bender, S. On the Significance of Magnesium in Extreme Physical Stress. *Cardiovasc Drugs Ther.* **12**, 197–202 (1988).
79. Pesce, C., Crova, C., Cereatti, L., Casella, R. & Bellucci, M. Physical activity and mental performance in preadolescents: Effects of acute exercise on free-recall memory. *Ment Health Phys Act.* **2**(1), 16–22 (2009).

80. van der Helm, E., Gujar, N., Nishida, M. & Walker, M. Sleep-dependent facilitation of episodic memory details. *PLoS One.* **6**(11), e27421 (2011).
81. Kahana, M. & Howard, M. Spacing and lag effects in free recall of pure lists. *Psychon Bull Rev.* **12**(1), 159–64 (2005).
82. Friendly, M., Franklin, P., Hoffman, D. & Rubin, D. Methods & Designs, The Toronto Word Pool: Norms for imagery, concreteness, orthographic variables, and grammatical usage for 1,080 words. *Behav Res Methods Instrum.* **14**(4), 375–99 (1982).
83. Amichetti, N., Stanley, R., White, A. & Wingfield, A. Monitoring the capacity of working memory: Executive control and effects of listening effort. *Mem Cognit.* **41**, 839–49 (2013).

Author Contributions

D.L., J.C.K.W. and J.T.S. designed the experiments, D.L. performed the experiments, analysed the results and wrote the paper. All authors reviewed the manuscript.

Additional Information

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