

ABSTRACT

Long Distance Running: Our Evolutionary Past, and its Mismatch With the Modern Environment

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When compared to other mammals, bipedal humans are unique in their capacity for endurance walking and running. Recent discoveries in the fossil record provide solid evidence for our transformation from tree dwellers to elite runners. In addition to our unique structural adaptations, the human body contains an elaborate pain regulation system. This biochemical system supports and encourages our ability to scavenge over many miles. Unfortunately, modern society differs drastically from the one we evolved in. This mismatch produces many negative effects including dramatic changes in our mood, and our propensity for injuries while engaging in physical activity. Through a better understanding of our evolutionary origins, we can begin to make changes to our approach to running that allow it to be more enjoyable, and less injurious

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LONG DISTANCE RUNNING: OUR EVOLUTIONARY PAST,
AND ITS MISMATCH WITH THE MODERN ENVIRONMENT

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CHAPTER ONE

The Origins of Bipedalism

Since Charles Darwin, explanations for the rise of *Homo sapiens* have been on the minds of many evolutionary biologists. How is it that humans managed to surpass nearly every organism on the planet despite being slower and weaker than almost all of its competition? Only the fastest humans can exceed 20 mph for more than 30 seconds, while horses and goats can surpass those speeds for minutes at a time. Additionally, despite being 30 to 40 pounds lighter than humans, chimps can lift two times what the strongest human is capable of (Lieberman, 2013). In *The Descent of Man*, Darwin argues that man's dominion emerged from the freeing of his hands from locomotion. By becoming bipedal, humans sacrificed physical prowess for the ability to defend themselves and hunt using hand crafted tools (Darwin, 1871/1981). Although this explanation was generally accepted for decades, archeological findings have found that the simplest stone spears only appeared 500,000 years ago, while the bow and arrow only 100,000 years ago. These innovations appear much later than the divergence between our last common ancestors (LCA) with chimpanzees some 5 to 8 million years ago (Lieberman, 2013). Recently, an alternative argument has emerged based on evidence present in the fossil record. Evidence points towards bipedalism originating from evolutionary pressure that led to physical adaptations that allowed our ancestors to walk and run long distances in a unique manner that outclasses all other mammals. The answer began to emerge after evolutionary biologists first compared us to our closest genetic

relative, the chimpanzee, to determine the largest differences between their biology and ours.

While humans as habitual bipeds travel almost exclusively on two limbs, chimps as occasional bipeds travel either by climbing in trees, or walking on all fours. The manner in which chimps move on four limbs, termed knuckle walking, involves resting their arms on the middle digits of their hands (Lieberman, 2013). Since other African great apes such as gorillas and bonobos also knuckle walk, evolutionary biologists infer that the human-chimp LCA must have knuckle walked as well. When on the ground knuckle walking is the preferred method of movement 98 percent of the time (Barak et al., 2013). Upon comparison with human bipedal locomotion, knuckle walking is 4 times as energetically costly to move the same distance when measured as a function of oxygen consumption. This dramatic difference in energy expenditure helps explain why chimps only travel an average of 1 to 2 miles a day while humans travel an average of 5 to 8 miles; it simply costs too much energy (Lieberman, 2013). It is true however, that chimps are capable of bipedal locomotion. When compared to humans, the absence of several key adaptations prevents its use as a viable locomotion strategy.

Chimpanzee bipedalism is similar to knuckle walking in that it costs nearly 4 times as much energy to travel the same distance as a human. Bipedal chimps move forward by dramatically tilting their body from side to side with widespread legs, landing on the outside of their feet (Lieberman, 2013). Additionally, their bent knees and hips have allowed for the categorization of their bipedalism as bent-hip and bent-knee gait (BHBK). This is contrasted by the extended-knee and extended-hip gait (EHEK) of

humans (Barak et al., 2013). The BHBK gait's increased metabolic cost arises from the increased activation of the back, hip and thigh muscles to keep the chimp upright (Lieberman, 2013). These constraints on chimp bipedalism originate from anatomical characteristics of the hips, foot, spine, and skull.

The first major anatomical difference between chimpanzees and humans is the shape of the upper section, the ilium, of the pelvis. In chimps, the ilium is much taller and wider than its human counterpart. The chimp's ilium also faces backwards as opposed to the sideways facing human ilium. This crucial adaptation allows the gluteal muscles to stabilize the upper body while one foot is planted on the ground. By adding the ability to slightly sway their hips as they walk, the majority of energy expended moves the body forward, as opposed to chimps who expend much more energy on stabilizing their upper body than they do on forward movement (Lieberman, 2013).

Another major anatomical difference lies in the shape of the foot and toes. Chimpanzee's feet lack the longitudinal arch found in humans that allows the foot to stiffen when support one's body. This forces chimps to walk on the outside of their foot as they wobble back and forth (Lieberman, 2013). The shape of the toes is also dramatically different between these two species. The toes of a chimp are much longer and curvier when compared to humans. While this configuration makes climbing much easier, it increases the metabolic costs associated with stabilizing the toes during the stance phase of walking (Rolian, Lieberman, Hamill, Scott, & Werbel, 2008). Also, the lack of alignment between the big toe and the ball of the foot in chimps prevents the use of this toe during the push off phase of walking (Lieberman, 2013).

Differences between the spines and skulls of chimpanzees and humans are the final major differences between the two species. When upright the spine of chimps forms one continuous curve in a C-like shape. Upright humans however, have an S-like shape to their spine with the addition of a lumbar curve formed by the addition of several wedge shaped lumbar vertebrae. This additional curve allows for the spine to insert into the human skull from below, rather than from behind as seen in chimps. This allows for a fully upright human to orient its skull forward and downward naturally while chimps find it more difficult to observe what is in front of and below them while standing on two legs (Lieberman, 2013). Without these crucial postural adaptations, chimps are unable to observe their surroundings while upright.

Once these adaptations for bipedalism missing in chimpanzees were identified, the next step in discovering the origins of bipedalism lies in the fossil record. Two of the earliest identified human ancestors are *Ardipithecus ramidus*, nicknamed Ardi, and *Sahelanthropus tchadensis*. While fossils from these two species are rare, they provide the earliest glimpse at changes in skeletal structure that point toward emerging bipedalism. Thought to have lived 4.5 to 4.3 million years ago, Ardi displays intriguing differences in the skeletal structure of its hips and foot when compared to modern chimps. The pelvis of Ardi displays a shortened and more sideways-facing ilium that differentiates it from modern chimps. This change is the first step seen toward fixing the stabilization problem seen in chimps (Lieberman, 2013). Ardi's foot also is unique in its markers for the presence of a longitudinal arch, and shorter toe joints better suited for push off during bipedal locomotion (Lieberman, 2013). *Sahelanthropus tchadensis*, believed to have lived

6 to 7.5 million years ago, has a spinal insertion into its skull that allowed for a human-like orientation of the head when walking on two limbs (Lieberman, 2013). This is the first indicator we have found of changes in spinal and cranial anatomy that favors bipedalism. Taken together, these early indicators of bipedalism point toward a divergence between the human-chimp LCA that must have been adaptive toward evolutionary fitness. One theory on the reason for this evolutionary pressure points toward climate changes during this period and its effect on the diet of the early hominids.

Despite frequent fluctuations in global temperatures, around 5 million years ago a major cooling period corresponds with the presumed date of our divergence from the human-chimp LCA. On the African continent, the changes most likely involved a dramatic reduction of rainforest in favor of woodland habitats. This change would have proved particularly troubling for early primates, as their diet consisted mainly of fruit obtained by climbing trees (Lieberman, 2013). With this source of easily available food on the decline, these primates would resort to eating so-called fallback foods. Consisting of fibrous stems, leaves, and bark, fallback foods are caloric sources of last resort that help primates survive in times of low fruit availability. Because of the relative lack of calories when compared to fruit, more of these fallback foods would be required to meet the caloric needs of primates. This would result in early primates being forced to walk and travel longer distances in order to obtain the greater quantities of this food required to survive (Lieberman, 2013). The increased reliance on fallback foods is a powerful source of evolutionary pressure; an organism's ability to obtain fallback foods during food shortages is strongly correlated with its ability to survive. Any advantage these early

primates possessed in traveling to obtain these foods dramatically increased their chance to pass on their genes (Lieberman, 2013). The importance of this dietary based evolutionary pressure is most strongly demonstrated in the skeletal remains of the genus *Australopithecus*.

Emerging during the Pliocene era 5.3 million years ago, the genus *Australopithecus* represent one of the most studied of our early ancestors. While earlier fluctuations in global climate may have triggered the early adaptations seen in *Ardipithecus ramidus* and *Sahelanthropus tchadensis*, the dramatic cooling during this period manifested in a dramatic change in the diet, and consequently the skulls, of australopiths. While chimpanzees have long faces with sharp teeth ideal for eating fruit, australopiths have shorter faces with large flat molars ideal for chewing tough fibrous foods. This reliance on tougher foods was successful through the discovery of underground storage organs (USO) such as roots and tubers which are plentiful in drier woodland climates. These USOs contain more calories than fruit, so their presence in the diet of australopiths increases their chance of survival (Lieberman, 2013). Support in the fossil record of this transition consists of skulls from australopiths such as *Australopithecus africanis* and *Australopithecus boisei* that contain flatter, thicker teeth, and shorter faces with thicker jawbones (Lieberman, 2013). While these changes allowed for an increase in the consumption of fibrous foods, additional skeletal characteristics of australopiths indicate that in order to obtain sufficient quantities of these foods, they had to walk farther distances.

While a complete example of an australopith's pelvis has yet to be found, the

discovered remains indicate a human like shape with a shorted ilium and a sideways orientation. This adaptation, as discussed earlier, is crucial in the development of an EHEK gait seen in human. The preserved Laetoli footprints made by several bipeds, most likely australopiths, 3.6 million years ago, could only have been made by organisms walking with an EHEK gait (Lieberman, 2013). This change in pelvic structure is the first important adaptation needed for bipedalism. Dramatic changes in foot structure also appear in australopiths. Muscle insertion points in the foot indicate the presence of a longitudinal arch that stiffens under the pressure of walking. The toes of australopiths are also shorter and straighter, allowing for their effective use during the push-off phase of walking (Lieberman, 2013). Additionally, the spines of species such as *Australopithecus africanus* and *Australopithecus sediba* distinctly display the curved lumbar spine seen in humans (Lieberman, 2013). Finally, CT scans of australopith ankles demonstrate human-like bone density. In contrast to chimpanzee ankles, the location of denser areas in the ankle indicates a need for structural support in line with the EHEK gait of modern humans. This finding indicates additional anatomical adaptations developed in australopiths to facilitate bipedal motion (Barak et al., 2013). While australopiths retained some anatomical adaptations for climbing, the changing climate during their existence resulted in the reduction of these characteristics for those favoring bipedalism. This trend towards walking longer distances begins to transition to running said distances in the next evolutionary link, *Homo erectus*.

Emerging in Africa 1.9 million years ago, *Homo erectus* spread as far as Indonesia, China, and even Europe by 1.2 million years ago. Bearing proportions similar

to modern humans including long legs, modern pelvises, and completely modern feet, these anatomical characteristics allowed Homo erectus to traverse continents (Lieberman, 2013). With longer legs compared to australopiths, Homo erectus was able to walk with an EHEK gait that may have been twice as efficient. Preserved footprints made 1.5 million years ago discovered in Kenya display footprints nearly indistinguishable from modern humans. This further supports the presence of a human-like arch in Homo erectus necessary for walking long distances to scavenge for food. Finally, the lower limbs continued the trend seen in australopiths favoring thicker, more robust bone shafts and joints in order to withstand the stress of bipedal movement (Lieberman, 2013). The progression of these anatomical adaptations to support bipedal motion was likely accelerated by another dramatic change in diet for Homo erectus; the introduction of a steady supply of meat.

Sites of animal bones with cut marks indicating the use of simple stone tools dated to 2.6 million years ago indicate that our ancestors began to acquire and process large quantities of meat. Despite the presence of simple stone tools to process the acquired meat, actual stone tipped spears only become common 500,000 years ago. When hunting, Homo erectus most likely was limited to sharpened wooden spears (Lieberman, 2013). To overcome these technological limitations, hunters began to use unique characteristics of bipedal motion to hunt and exhaust their prey. This method, known as persistence hunting, depends on the ability of Homo erectus to run after its prey in such a way that results in its incapacitation through hyperthermia. Unlike most quadrupeds, which rely on a bellows-like effect when running to obtain oxygen utilizing the

diaphragm and locked into a one stride/one breath relationship, modern humans, and most likely Homo erectus as well, can comfortably maintain a stride/breath relationship of 2:1, 3:1, or even 4:1. This dramatic difference emerges as a result of the bipedal gait that both humans and Homo erectus display (Daley, Bramble, & Carrier, 2013). While a quadruped can only cool down by panting, an action it is incapable of performing during a gallop, a bipedal gait allows for cooling through its breathing pattern over a wide range of speeds. Comparable to the fable of the tortoise and the hare, the quadrupedal prey of Homo erectus might race ahead of hunters and stop in an attempt to cool itself, but its bipedal hunters would be close behind inciting it to run again before fully recovering. After enough repetitions, the exhausted quadruped collapses, allowing Homo erectus to dispatch its mobilized prey with its simple wooden spears (Lieberman, 2013).

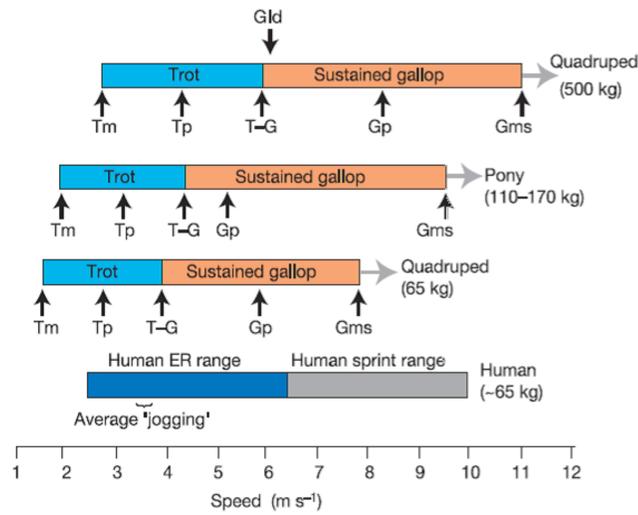


Figure 1: Bramble, and Lieberman (2004) describing the breathing patterns between humans and quadrupeds

This dependence on running may seem like a poor investment of energy, but, in

reality, running is not as large of an energy sink as many believe. Running is only 30 to 50 percent more costly than walking, and an equal number of calories is required to run at a 7 minute per mile pace as a 10 minute per mile pace. Under these energetic parameters, bipedal running is an efficient method of transportation that could effectively be used to persistence hunt (Lieberman, 2013). The efficiency of bipedal running is attributable to several unique adaptations in the anatomy of *Homo erectus* that reduces this cost through spring-like mechanisms in the leg and foot. Evidence for these mechanisms comes from skeletal characteristics of *Homo erectus* that indicate their aptitude for running.

The completely human-like arch seen in *Homo erectus* allows for the storage of elastic energy during running. While the australopiths had a partial arch, it was neither as convex nor as stable as the arch seen in *Homo erectus*. The arch of the foot is not fully necessary for simple walking, but during running it can lower the energetic cost by up to 17 percent (Lieberman, 2013). Another important spring-like mechanism is the Achilles tendon. While apes have an Achilles less than a centimeter long, modern humans have an Achilles more than 10 centimeters long. Analysis of the insertion point of this tendon in the heel bones of australopiths indicate a similar length to apes. It was not until *Homo erectus* that the Achilles began to lengthen. The Achilles tendon stores and returns nearly 35 percent of the mechanical energy during running, and like the arch of the foot, undergoes little usage under walking conditions (Lieberman, 2013). The relative importance of these two spring-like mechanisms when comparing their function in running and walking is indicative of a strong evolutionary driving force favoring efficient running over long distances.

Several other adaptations began to emerge during the time of *Homo erectus* that contributed to their ability to run. The first of these is the increased size of the gluteal muscles. One of the largest muscles in the human body, the gluteus maximus serves as a balancing mechanism for the human torso during running. By contracting forcefully during footstrike to prevent toppling forward, the gluteus maximus is essential for efficient running. Just like the arch of the foot and the Achilles tendon, this muscle shows very little activity under walking conditions, but strongly activates during running (Lieberman, Raichlen, Pontzer, Bramble, & Cutright-Smith, 2006). The gluteus maximus of apes is much smaller in comparison with a humans. Signs of its expansion begin to emerge in australopiths, but it wasn't until *Homo erectus* that it achieved a size comparable to humans (Lieberman, 2013).

Two additional adaptations emerging first in *Homo erectus* served to stabilize our expanding craniums. The first of these, the Nuchal ligament, connects the back of the head to the arms. During footstrike of the running cycle, the arms on the same side as the footstrike pulls back to prevent the head from pitching forward (Lieberman, 2013). Seen primarily in other running adapted, known as cursorial, animals, such as horses and dogs, this ligament is absent in apes and australopiths, but first appears in *Homo erectus* (Lieberman, 2013). An example of convergent evolution, the Nuchal ligament shows that beginning with the *Homo* genus, running became vital to their ability to survive and prosper (Bramble & Lieberman, 2004). An additional support structure that developed in *Homo erectus* involved adaptations to the cochlear labyrinth to assist in balance during high speed movement. Unlike apes and australopiths, modern humans and *Homo erectus*

show enlargement of the anterior and posterior semicircular canals accompanied by a reduction in the lateral canal. These findings, produced through CT scans of recovered *Homo erectus* skulls, indicate that increased sensitivity to movement of the head in the sagittal and coronal planes became important to survival (Spoor, Wood, and Zonneveld, 1994). Both of these adaptations assisted in maintaining the integrity of the cranium of *Homo erectus* during its persistence hunts. Using its advantageous ability to travel and hunt over long distances, *Homo erectus* became the first intercontinental hominid. This feat was later repeated by our very own species, *Homo sapiens*, 100,000 years ago.

First appearing in Africa 300,000 to 200,000 years ago, *Homo sapiens* began to leave the continent 100,000 years ago. Traveling more extensively than their *Homo erectus* ancestors, humans reached Asia 60,000 years ago, Europe and Australia 40,000 years ago, and the Americas by way of the Bering Strait 30,000 years ago (Lieberman, 2013). When it comes to running, modern humans outclass all other primates. Many of the trends seen in their evolutionary ancestors such as the shortening of the toes, changes to the foot and ankle to increase energetic return, enlargement of the gluteal muscles, and unique manners of respiration are continued and made even more efficient. Continued shortening of the toes allows for less metabolic work performed by the muscles that flex the big toe during the push off phase of running. Among a group of human runners, those with longer toes required at least twice as much force to flex the toes during push off. This continues to highlight the fact that shorter toes immensely benefits endurance running (Rolian et al., 2008). Additional modifications in the calcaneus of modern humans increases the elastic return provided by the Achilles.

Studies investigating the correlation between calcaneus length and Achilles tendon performance in modern humans have found that the greater the calcaneus length, the greater the moment arm, the force exerted by the tendon perpendicular to the axis of rotation, of the Achilles. This increase in the moment arm results in a subsequent decrease in the energy that can be stored during footstrike. The impact of moment arm length is evident in a human study that found 64 percent of the variation in the energetic costs of running results from variance in its length (Raichlen, Armstrong, & Lieberman, 2011). Additionally, this relationship between the calcaneus length and Achilles elastic return can help explain another mystery of evolutionary biology; the survival of modern humans over neanderthals. Unlike their contemporary evolutionary cousins, neanderthals were bigger, stronger, and faster. Remains of neanderthals do reveal however, that they possessed a longer calcaneus than modern humans. This difference translates to an 11.4 percent increase in the energetic cost of running for neanderthals. Along with other characteristics that decreased the efficiency of endurance running in neanderthals like increased body weight and shorter legs, it is possible that their extinction was due in part to their inability to out distance their Homo sapien counterparts (Raichlen et al., 2011). A final note on the importance of the Achilles tendon comes from detailed computer simulations of human gait that allow for computational adjustments to the elasticity of the tendon. With elasticity in the normal ranges for humans, speeds of 5.6 meters per second are possible. When the elasticity of the tendon is removed, the model is only capable of achieving speeds of 3.6 meters per second. Additionally, the cost of locomotion with normal tendon elasticity was 1.1 Joules per kilogram meter, while inelastic tendons more

than triple this value to 3.8 Joules per kilogram meter (Sellers, Pataky, Caravaggi, & Crompton, 2009). Combined with even larger gluteal muscles than *Homo erectus* and the ability to couple breathing rates independent of stride, modern humans represent further refinement in their endurance running capabilities.

The pinnacle of human's ability to run long distances is the act of persistence hunting. While persistence hunting is rarely practiced today because of the advent of more versatile methods such as firearms, it has been observed in many modern hunter-gatherer societies such as the Kalahari bushmen, the Navajo and Paiutes of the Americas, Australian Aborigines, and the Tarahumara of northern Mexico (Lieberman, Bramble, Raichlen, & Shea, 2007). Persistence hunting in these cultures is a group effort that even the older male members can participate in and contribute to during its early stages. It has fallen out of favor because of its increased time demands and its need to adjust targets and strategies based on seasonal weather patterns. Despite this, when compared to hunting with a bow and arrow, persistence hunting has at least an equal, and possibly greater, success rate. Over a 46 day period observing hunts of the Kalahari bushmen, out of 41 hunting attempts with a bow and arrow, only two were successful. Additionally, clubs and spears were successful in 5 of 11 attempts. In contrast, of the two persistence hunts attempted, both were successful (Liebenberg, 2006). While this is a much smaller sample size than the other methods, it proves that it is indeed possible to run an animal down in a fashion that relies on almost no tools successfully. The continued practice of persistence hunting in hunter gatherer societies all over the world further supports the importance of running in our evolutionary history.

Our ability to walk and run long distances has been continually refined and improved over our evolutionary history. Culminating in our ability to hunt prey simply by chasing them, running has helped our species survive for many thousands of years. As we diverged from our LCA with chimps, the evolutionary pressure has led to our becoming the only fully bipedal primate on earth. Our relationship with endurance running is engraved in both our culture and our anatomy. By recognizing the origin of our heritage, we can better understand potential conflicts that result from our current environment's mismatch with the one in which we evolved in.

CHAPTER TWO

The Biochemical Support System of Running

The anatomical characteristics surrounding bipedalism are not the only contributing factors towards man's endurance running prowess. Modern humans also possess a sophisticated system of pain regulation that activates during long periods of physical activity. Often referred to as a runner's high, this biochemical support system generates subjective feelings of euphoria, time dilation, and feelings of peace. These sensations closely resemble those described during both sedative and hallucinogenic drugs, leading researchers to search for the biochemical basis behind these sensations. In order to objectively measure such sensations, Dietrich and McDaniel (2004) suggest a focus on quantitative measurements such as analgesia (pain reduction), sedation, and anxiolysis (anxiety reduction). If our anatomical structure is our motor, and the food we consume is our fuel, this biological support system is the oil that keeps us running smoothly despite accumulated damage to our body during endurance activity.

β -endorphins, the endogenous agonist of the μ -opioid receptors (MOR), have long been considered the leading suspect in the search for the origins of the runner's high, hereafter referred to as exercise induced analgesia (EIA). As a G_i/o protein, MORs inhibit the formation of adenylyl cyclase in cells to produce an inhibitory effect on cellular pathways. While evidence to support the endorphin hypothesis exists, two features of EIA are incompatible with this explanation. The first is the failure of this explanation to account for the cognitive effects of EIA. The majority of evidence supporting this

hypothesis comes from measurements of β -endorphins in the peripheral bloodstream. As large neuropeptides, β -endorphins experience difficulty in crossing the blood brain barrier to exert its central effects. An additional problem arises when considering the full effects that β -endorphins produce. Respiratory depression, inhibition of gastric functions, and pinpoint pupils are seen even in low activation of MOR, symptoms that are completely absent during EIA (Dietrich & McDaniel, 2004).

Recent research has focused on answering these doubts about the central activity of β -endorphins. To measure β -endorphin activity in humans, positron emission tomography (PET) scans were performed on 10 males both at rest, and after a 2 hour running session. To visualize the binding of endogenous β -endorphins, the dissociation of a tracer capable of binding to MOR, [18F]FDPN, was used. The dissociation of [18F]FDPN, indicates its displacement by endogenous β -endorphins (Boecker et al, 2008). When compared to baseline scans, the post run scans revealed that many cortical areas including the prefrontal cortex, cingulate cortex, and sensorimotor regions experienced significant [18F]FDPN dissociation. The increased release and binding of β -endorphins in these areas, each closely associated with emotional regulation/decision making and physical sensations, indicates that β -endorphins may play a larger role than expected in the affective components of EIA (Boecker et al., 2008). Additional research has shown that the activity of β -endorphins in the periaqueductal grey (PAG), one of the major pain centers of the central nervous system (CNS), is increased following running, but not walking. This indicates that β -endorphins are capable of exerting a central effect on the pain centers of the brain (Scheef et al., 2012). Finally, this helps focus the role of

this biochemical support system to that of high intensity endurance activities such running, but not walking.

Despite the findings of a central role for β -endorphins during exercise, the results of studies showing peripheral increases in β -endorphins are yet to be fully explained. The search for additional biochemical factors behind EIA has led researchers to investigate the endocannabinoid system, the same system underlying the effects of marijuana. The human endocannabinoid system comprises two main receptors, the cannabinoid receptor type 1 (CB1) and cannabinoid receptor type 2 (CB2). Located centrally and peripherally respectively, these proteins are similar to MOR in that they inhibit formation of adenylyl cyclase, resulting in an overall inhibitory effect. Interestingly, these receptors are located pre-synaptically and their ligands undergo retrograde transmission in order to exert their effects. CB1 receptors are located on many pain sensing neurons including C-fibers, A β fibers, and A δ fibers (Dietrich & McDaniel, 2004). CB2 receptors are commonly located on cells in the immune system like B-cells, natural killer cells, and microglia (Merighi et al., 2012). The most common ligands for the CB1 and CB2 receptors produced by the human body are anandamide and 2-arachidonylglycerol (2-AG). The presence of CB1 receptors on pain sensing neurons was crucial in identifying the cannabinoid system as a potential influence in the development of EIA.

The first study directly implicating the endocannabinoid system in EIA involved 24 males whose blood was sampled and measured for anandamide and 2-AG following 45 minutes of either resting, running, or cycling. The results show that anandamide levels significantly increased during the running and cycling conditions, but not the resting

condition. Levels of 2-AG displayed a similar pattern, but their degree of increase wasn't statistically significant (Sparling, Giuffrida, Piomelli, Rosskopf, & Dietrich, 2003).

Regardless, these are the first results directly implicating an increase in endocannabinoid activity following exercise. Interestingly, these results are similar to that of Boecker et al. (2008) in which only intense activity showed an activation of the EIA response. This furthers the support of this response as critical in our ability to engage in endurance activities unlike any other primate.

Evidence for the role of the endocannabinoid system in the production of EIA was further provided in a study comparing the responses of two cursorial mammals, humans and dogs, with that of a non-cursorial species, in this case ferrets. Eight to 10 subjects from each species had their blood measured for anandamide levels before and after a running trial and walking on a treadmill for 30 minutes. Additionally, the human subjects completed a questionnaire before and after the running condition to determine positive mood states following their run (Raichlen, Foster, Gerdeman, Seiller, & Giuffrida, 2011). The results show that only in the cursorial animals do anandamide levels increase following the running condition. Additionally, none of the species show this increase following the walking trial. Finally, when the differences in the results of positive emotions questionnaire before and after the running condition were correlated with the difference in anandamide levels before and after the running condition, a linear relationship was uncovered (Raichlen et al., 2011). This indicates that increases in anandamide levels during intense exercise are closely related to the emotional components attributed to EIA. This study also supports the activation of the EIA system

exclusively during intense exercises like running as opposed to mild exertion activities like walking.

Unfortunately, a detailed examination of the biology underlying EIA in humans is not feasible ethically. As in many realms of study, a useful animal model can provide insight into potential structural and functional characteristics of biochemical systems. Thankfully, mice have been shown to be an adequate candidate for an animal model of EIA. The use of a running wheel, a common feature in many mouse habitats, allows for the relationship between the biochemical components isolated and observed in mouse biology and intense exercise to be studied.

The next step in determining the direct relationship between the endocannabinoid system and intense exercise was provided by Dubreucq, Koehl, Abrous, Mariscano, and Chaouloff (2010) in their study involving CB1 knockout mice. CB1 knockout mice lack the gene that codes for the CB1 receptor, and this results in the complete absence of the receptor throughout the body. These knockout mice were joined by a control group, and both groups lived for 6 weeks in a cage with unlimited access to a running wheel. The total distance traveled on the running wheels was monitored by computer (Dubreucq et al., 2010). After the 6 week period, the results showed that the CB1 knockout mice showed a decrease when compared to controls in every running variable measured; this includes total distance traveled, maximal running velocity, and total time spent running. An additional key finding of the study is that overall locomotion of the mice in their cages during periods between runs was no different between the two groups. The researchers conclude that these differences originate from dopamine based reward

mechanisms that are negatively affected by the lack of CB1 receptors (Debreucq et al. 2010). While one common component of EIA is its direct rewarding effects like euphoria and anxiolysis, the presence of CB1 receptors on pain fibers indicates that the CB1 knockout mice undoubtedly experienced reduced EIA. The lack of reduction in non-intensive forms of movement is also indicative of the activity of this system solely during endurance activities. Finally, these findings in mice indicate that they provide an appropriate model organism for investigations into EIA.

To begin to uncover the potential interactions between the endocannabinoid and opioid systems in the production of EIA, the interaction between the two systems could be either structural, involving co-localization on cells or anatomical location, or functional, direct modulation of receptor activity or ligand regulation. Structurally, the PAG is a site of high MOR density. Additionally, analgesia has been known to be produced by injections of both MOR and CB1 receptor agonists into the PAG, with this effect increasing synergistically with co-administration of the two agonists. To investigate the co-localization of these receptors on the same cells, the PAG from mouse brains were isolated and divided into multiple cross sections. These cross sections were then treated with immunofluorescent labels, anti-bodies that emit unique waves of light, to determine whether both CB1 and MOR labels appear together (Wilson-Poe, Morgan, Aicher, & Hegarty, 2012). The labeling experiments determined that CB1 and MOR were located throughout the PAG, and most densely in the dorsolateral and ventrolateral areas. More importantly, MOR and CB1 receptors were co-localized in 32 percent of the labeled cells. This points toward increased analgesia through increased adenylyl cyclate formation

inhibition in cells containing both CB1 and MOR receptors (Wilson-Poe et al., 2012).

Additional evidence for the close interaction of MOR and CB1 receptors in the PAG was provided by Wilson, Maher, and Morgan (2008). Male mice were outfitted with a cannula providing direct access for the injection of drugs into the PAG. The mice were then subjected to a hot plate test in which the latency between paw placement on a 52.5 degree Celsius plate and its subsequent removal was determined. Increased latency times are associated with increased analgesia. Injections of both morphine and HU-210, a CB1 receptor agonist, were performed into the PAG, and their effect on the hot plate tests were recorded. The study found that HU-210 injections increased the hot plate latencies when administered before morphine injections. Additionally, co-administration of HU-210 and morphine prevented the decline in morphine's effect associated with the development of tolerance to the effects morphine (Wilson et al., 2008). The results of this study further strengthen the claim that the co-localization of these receptors is vital to the production of analgesia, and particularly EIA. The effects generated by the co-administration of these two agonists indicate that their effect on the MOR and CB1 receptors located on the same cellular targets both increase the effect and duration of analgesia. The reduction of tolerance development is crucial as it ensures that EIA is capable of persisting throughout one's life without a decline in its effect.

A functional interaction between the opioid and cannabinoid system has also been observed. One source of their intertwined functionality comes from their shared activity on adenylyl cyclase. As metabotropic receptors, both the CB1 and MOR receptors act on adenylyl cyclase to inhibit the formation of cyclic AMP (cAMP), an important

intracellular messenger. The inhibition of cAMP formation results in both genetic and ionic effects on the cell. cAMP acts on MAP kinases, enzymes that stimulate the transcription of particular genes, to increase their activity. Inhibition of MAP kinases results in a dramatic shift in the transcription outcome of a cell, and could explain for the long lasting changes in tolerance to pain relieving chemicals seen in the previous study. This reduction in cAMP levels can also alter the ionic milieu of the cell. cAMP can bind to sites on ion channels inside the cell and close them. cAMP can bind to and close calcium channels; the closing of these channels results in a decrease in the resting potential of the cell, lessening its chance of firing. When co-localized on pain neurons, the increased inhibition of action potentials results in the reduction of pain sensations generated during intense exercise (Bushlin, Rozenfeld, & Devi, 2010).

A final functional interaction between the endocannabinoid and opioid systems come from a Manzanares et al. (1998) that looks at the effects of CB1 agonists on the precursors to enkephalins, an opioid agonist similar to β -endorphins. As neuropeptides, enkephalins are the final product of a long series of protein precursors. One of the first of these precursors to be produced is proenkephalin (PENK), a protein synthesized through translation of its mRNA by ribosomes. PENK then undergoes significant modifications to produce enkephalins. In this study, the levels of PENK before and after exposure to an analogue of anandamide, AM356, were measured using a radioactive oligonucleotide complementary to PENK mRNA. Mouse brains were obtained following 5 days of either AM356 injections or a control solution, and the cross sections were stained for PENK mRNA (Manzanares et al., 1998). When compared to the control, the brains exposed to

AM356 exhibited 49 percent higher levels of PENK mRNA in the PAG. This result indicates a functional interaction between the endocannabinoid system and the available levels of opioid receptor agonists (Manzanares et al., 1998). The increase of endocannabinoid agonists during intense exercise results in an increase of opioid activity over time that enhances the effects of EIA. The interaction of these two systems helps explain the relationship between the anxiolysis and analgesia associated with exercise and the increases seen in the circulating levels of the respective agonists of these systems.

In addition to the interaction between the cannabinoid and opioid systems, there are several unique functions served by the endocannabinoid system alone. The involvement of endocannabinoids has been implicated in the body's reaction to joint pain and inflammation. This relationship is important because inflammation and joint pain are often consequences of intense endurance exercise. The first such study involved mice lacking fatty acid amide hydrolase (FAAH). This enzyme breaks down endocannabinoids like anandamide, and mice lacking FAAH genes show elevated levels of the CB1 agonist. FAAH knockout mice were compared with wild type controls, and both groups were injected with collagen in their left paw to induce an animal model of arthritis. The mice were then examined for the severity of arthritis pain, and after they had been euthanized their joints were preserved and examined for damage (Kinsey, Naidu, Cravatt, Dudley, & Lichtman, 2011). The study found that the FAAH knockout mice showed less severe signs of arthritis pain when compared to controls. Additionally, the examined joints of the FAAH knockout mice displayed less bone and cartilage erosion. Of particular note, was

the finding that CB2 receptor antagonist SR144528 removed the improvements in arthritis severity seen in FAAH knockout mice, while CB1 antagonist rimonabant did not prevent the anti-arthritic phenotype (Kinsey et al, 2011). This indicates that the anti-arthritic properties of the endocannabinoid system are dependent on CB2 receptor activity, a finding supported by later studies as well.

Another study involving an animal model of joint pain and CB2 receptors involved the injection of monosodium iodoacetate (MIA) into the knee joints of wild type and both CB1 and CB2 knockout mice. Interestingly, mice containing a greater number of CB2 receptors, designated CB2xP, were also injected with MIA to produce joint pain. The severity of the joint pain resulting from the MIA injections was measured by observing the extent of mechanical allodynia, pain in response to normally non-painful touch, on areas of the body not directly injected with MIA (La Porta, Bura, Aracil-Fernández, Mansanares, & Maldono, 2012). Both CB1 and CB2 knockout mice showed increased allodynia on the side ipsilateral to the MIA injection, with the effect higher in the CB2 knockout mice. Additionally, the CB2 knockout mice also developed allodynia in the limbs contralateral to the MIA injection, while the CB1 knockout mice did not. The CB2xP mice also displayed even less allodynia than the wild type mice (La Porta et al., 2012). Taken together, these results add support to the role of CB2 receptors in the management of joint related pain. This activity would be especially important in EIA as the joints of the lower limb often experience forces up to 3 times one's body weight during each stride.

Additional insights into the role of CB2 receptors emerges from a review of the

literature on CB2 knockout mice by Buckley (2007). One of the most interesting findings from this review is the presence of CB2 receptors on osteoblasts and osteoclasts, the cells that deposit and degrade bone to shape it according to the body's needs. Also, mice completely lacking the CB2 receptor experienced accelerated age-related bone loss, indicating that CB2 receptors, while on both osteoblasts and osteoclasts, primarily contribute to the retention of bone density. The involvement of CB2 receptors in this system of bone remodeling applies to EIA in that bone reinforcement following the stress of intense endurance exercise is important to the prevention of skeletal stress injuries. The increase circulation of endocannabinoids seen during endurance exercise potentially serves to activate this system, contributing to bone reinforcement following intense endurance activities.

Another finding from this review is that the analgesic effects of CB2 receptors exert their effects locally at the site of the injury without producing CNS effects (Buckley 2007). This potentially provides solution for the problems encountered in the opioid hypothesis of EIA. When circulating levels of endocannabinoid rise during endurance exercise, the emotional effects associated with EIA are produced by the CB1 receptors located throughout the brain and the PAG, while the CB2 receptors modulate peripheral sources of pain and encourage repair mechanisms for skeletal tissue. Finally, CB2 receptors were also found to be important in the migration of cells involved to the inflammatory response to a chemical stimulant (Buckley 2007). This would also provide evidence towards its role in EIA, as muscle damage acquired during endurance exercise would trigger an inflammatory response to facilitate healing.

Further insight into the role of CB2 receptor in the inflammatory response comes from a study into the analgesic properties of CB2 agonists in an animal model of inflammation. This study compared CB2 agonist MT178 and CB2 antagonist AM 630 with CB1 agonist WIN 55,212-2 and CB1 antagonist AM 251 to isolate the role of the CB2 receptors in multiple inflammatory models. The model of most interest to the production of EIA involved a model based on acid-induced muscle pain. Mice were injected with saline (pH 4.0) directly into their calf muscle, and 5 days later a second saline injection was co-administered with the CB1 and CB2 agonists and antagonists mentioned above (Vincenzi et al., 2013). When measured for mechanical allodynia, MT178 was more effective than WIN 55,212-2 in reducing the extent of allodynia. Additionally, AM 630 injections resulted in pain tolerance below that of the control group, while AM 251 injections did not differ from the control group. This removal of the analgesic effect following injection of the CB2 receptor antagonist indicates that this response to inflammatory pain is mediated by the CB2 system (Vincenzi et al., 2013). This finding is important for EIA because it identifies another target of pain reduction, namely muscles facing a build-up of lactic acid, as dependent on the CB2 system. Elevated levels of endocannabinoids following exercise could activate this pain reduction in muscles in order to ensure that the organism will be willing to engage in another endurance activity as soon as possible.

The activity of the endocannabinoid system still remains an area of intense interest and research. While more studies with human subjects are required to make a definitive statement towards its role in EIA, the present data points toward its

contribution in the analgesia and euphoria associated with this state. Endocannabinoid receptor agonists have long been used by many cultures for its analgesic and anxiolytic effects. The underlying biochemistry of these effects seems to undergo significant activation following endurance exercise. Human's endurance abilities, particularly running, are exceptional, and this prowess is due in large part to the ability of this biochemical support system to manage potential injuries acquired during these activities. By keeping pain in check and producing positive affective states, running and other endurance activities have long been a source of both food and enjoyment for many cultures. Much of this success is due to our anatomical adaptations for these activities, but the importance of this biochemical support system cannot be ignored.

CHAPTER THREE

Running in a Modern Environment

Despite the finely crafted anatomical and biochemical support systems, many runners today face a gauntlet of injuries that often seem unpreventable. Each year, 37 to 56 percent of runners can expect to develop a musculoskeletal injury that prevents running for an extended period of time. In response to this epidemic in injuries, doctors in the 1980s began to recommend shoes with elevated, cushioned soles, and other features designed to provide motion control and stability. In their analysis of the scientific literature to determine the effectiveness of such prescriptions, Richards, Magin, and Callister (2008) refer to this style of footwear as Pronation control, Elevated Cushioned Heel (PECH). Despite continuing to be recommended to prevent running injuries, there exist no evidence based studies which demonstrate that PECH shoes are effective in preventing injury.

This inconsistency first entered the public awareness with the publication of *Born to Run* by Christopher McDougall in 2009. Beginning with the question, “How come my foot hurts?” McDougall goes on a journey to answer this question by comparing how modern society and traditional hunter-gatherer societies run. Focusing on the Tarahumara tribes of the Sierra Madres, a tribe famed for its performance in ultramarathons, McDougall discovers that their running form differs dramatically from that of most modern runners. Running in no more than thin strips of rubber, these immensely skilled runners run by striking the ground with the ball of their foot. This running form, a

forefoot strike (FFS), stands in contrast to the rear foot strike (RFS) of most modern runners. In a RFS, the runner's foot first contact with the ground occurs with the heel of the foot, only possible in PECH footwear (McDougall, 2009). Evidence exists that points to a FFS and non-PECH footwear as useful practices to prevent running injuries. Recent research and legal events have arisen that contradict this relationship, but by examining the FFS through an evolutionary lens, the details of this running form, and when it can, and cannot be applied become clear.

First entering the market shortly before the running boom in the 1970s, the Nike Cortez, designed by Nike founder Bill Bowerman, was radically different from any running shoe seen before. Unlike the shoes of early running legends like Jesse Owens and Roger Bannister, which were flat and extremely thin, the Nike Cortez featured an elevated heel with rubber cushioning. These innovations were intended to reduce strain on the Achilles and allow the runner to increase one's stride length, in turn, shifting the foot's point of impact from the ball of the foot to the heel. By the 1972 Olympics, Nike's shoes had become so popular that they became the universal standard for participants of the jogging boom (McDougall, 2009). As the first example of a PECH shoe, the style of the Nike Cortez quickly became the shoe doctors recommended for preventing running injuries. As noted above, there exists no empirical evidence that such shoes are effective in preventing injury. Unfortunately, the timing of their emergence led to their establishment as the standard. This resulted in the formation of the null hypothesis that cushioned, elevated shoes and a RFS prevent injury. Until an alternative proved it was superior, RFS and PECH shoes would remain the standard method of running.

Despite its prevalence among casual runners, many elite running coaches began to question this established approach towards running form and footwear. Vin Lannana, the coach of multiple NCAA champion cross country and track teams, often has his runners train barefoot. He did this because he found that in doing so, his runners developed a FFS that led to faster times and fewer injuries (McDougall, 2009). Research with the goal of answering this relationship explores footstrike pattern, footwear, and injury rates in an attempt to uncover the forces underlying this assumption. A controlled study of 52 runners, 16 of which used a FFS, and 36 which used a RFS, found that both mild and moderate repetitive stress injuries were 2.5 times more likely in rear foot strikers as forefoot strikers. Additionally, moderate and severe injuries were 1.7 times more likely in rear foot strikers as forefoot strikers (Daoud et al., 2012). Another finding from this study found that different types of injuries also correlated with footstrike. At the outset of the study, Daoud et al. (2012) hypothesized that runners who RFS were more likely to suffer from injuries of the knee, hip, and lower back, while runners with a FFS would be more likely to suffer from Achilles tendon injuries and lower limb and foot stress fractures. On the contrary, while the injuries listed were found to be more common in RFS runners, the hypothesized injuries were not more common in FFS runners. The discrepancy between these results and the design of modern running shoes that encourage a RFS, highlights the design of PECH shoes as a potential source of common running injuries.

With the utility of PECH shoes in doubt, researchers began to examine the forces at play while running in PECH shoes as opposed to running in no shoes at all. The primary measurement under investigation is the ground reaction force (GRF). The GRF is

the collision force that the lower limbs experience upon impact with the ground. Approximately 1.5 to 3 times the runner's body weight, this force occurs with each foot strike, and is thought to contribute to the formation of repetitive stress injuries (Lieberman et al., 2010). Upon measurement of three conditions, barefoot RFS, shod RFS, and barefoot FFS, the following results were obtained.

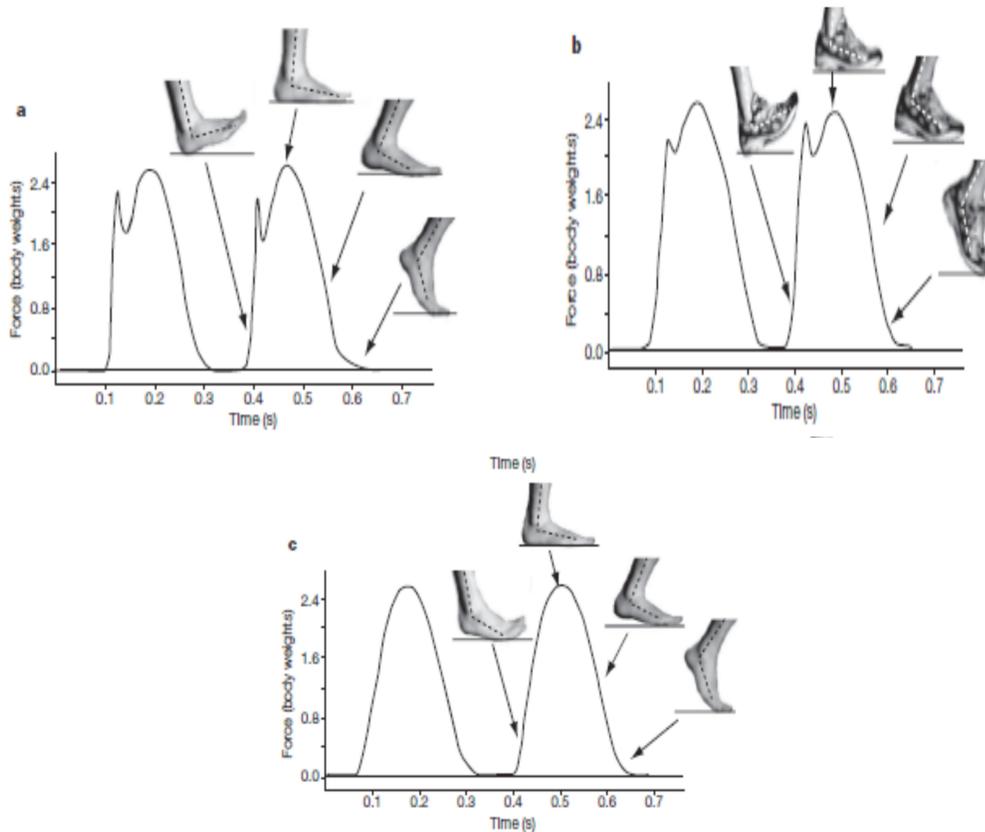


Figure 2: Liberman et al. (2010) showing the effect of stride on GRF

Despite the assumption that the wide, cushioned base of PECH shoe would spread the impact force out over a larger distance and time, these findings clearly show that the integral of these force curves are greater in the shod condition than either of the barefoot

conditions. Additionally, when comparing the RFS and the FFS, the large initial peak in the GRF coinciding with the initial impact of the heel is completely absent in the FFS. Finally, when comparing the barefoot conditions, it seems clear that if forced to run barefoot, one would prefer to adopt a FFS that prevents this painful initial contact (Lieberman et al. 2010).

The results of this and similar studies sparked intense debate over the benefits of shod versus un-shod running. Since at least 75 percent of modern runners are believed to RFS, the results of the VGRF data pointed to PECH shoes and the RFS as a possible culprit in the injury epidemic (Altman and Davis 2012). With the popularity of *Born to Run* and these intriguing findings, by 2012 an explosion of barefoot or minimalist shoes began to flood the market. Companies such as Vibram, makers of the colloquially known toe shoes, or Vibram Five Fingers, Nike, Saucony, and New Balance released shoes with a design opposite of PECH shoes meant to allow for a barefoot FFS running form while protecting one's feet from hazards on the ground (Altman et al. 2012). Many of these shoes were marketed with the claim that they would reduce and potentially even reverse running injuries resulting from PECH footwear and a RFS.

Many scientific studies attempting to understand the implications of a FFS in minimalist or no shoes at all began to examine the biomechanical consequences of this shift in running form. One of these studies examined the relationship between lower-limb stress fractures and the GRF. An analysis of the previous scientific literature on GRF and injuries by Zadpoor and Nikooyan (2010), revealed that the value of GRF itself is not correlated with the incidence of stress fractures. This study did find however, a

significant relationship between stress fractures and the vertical loading rate (VLR). The VLR is defined as the slope of the initial peak in the GRF versus time curve. Higher rates of VLR were correlated in a majority of the studies examined, with the remaining studies finding no significant difference between VLR and stress fractures. While not unanimous, the data still supports a significant statistical connection between higher VLR and stress fractures. This finding supports that of Liberman et al. (2010) when the data is examined with the above in mind. Since the VLR is measured as the slope of the GRF's initial impact peak, the initial spike seen in the RFS conditions coincides with a steeper VLR. With this in mind, running with a FFS would result in a reduced VLR, and possibly prevent the occurrence of stress fractures.

The negative effects of PECH shoes and a RFS were further elucidated in a study by Crowell and Davis (2011) that focused on methods to train runners to reduce the value of their VLR while receiving real time feedback on their tibial acceleration many training sessions. Over these eight weeks, runner's gait retraining consisted of advice to run with a softer stride while observing their tibial acceleration on a screen in front of them. This feedback was gradually reduced until the subjects assumed this new, lighter gate without conscious effort. For their one month follow up, their VLR was measured and found to have decreased an average of 7.6 percent. Of the four kinematic variables, the VLR experienced the greatest reduction. Although information on footwear and footstrike were absent from this study, this helps support the growing notion that footwear is secondary to running form when considering how to reduce biomechanical measurements associated with injuries like stress fractures. Interestingly, in *Born to Run*, McDougall receives

similar advice to lighten his stride during his transition from a RFS to a FFS. While not proof that these runners gait changed from a RFS to a FFS, it does suggest that this retraining encouraged a FFS that reduced the VLR.

Additional investigations into the relationship between footwear and injuries focused on the origin of knee pain, a common injury among modern runners. Fourteen subjects were examined while running barefoot on grass, and in five different PECH shoes on artificial turf. Infrared cameras designed to detect limb position monitored the angle of the knee during the six different running trials (Braunstein, Arampatzis, Eysel, and Brüggemann, 2010). Analysis of the strides in these six conditions found that the degree of flexion in the knee was greater in the barefoot condition than all five of the shod conditions. This increased extension of the knee in the shod condition is likely a result of the longer stride length often seen in rear foot strikers wearing PECH footwear. The authors of this study further conclude that this increased extension of the knee during shod running results in additional activation of the quadriceps femoris that places additional strain on the patella tendon (Braunstein et al., 2010). This additional strain to the knees of those who run in PECH shoes and RFS provides a reasonable explanation for the increased prevalence in knee injuries in those runners.

The relationship between knee biomechanics and running form was also investigated by Sinclair (2014) who monitored both the knee and Achilles tendon in runners wearing PECH footwear, minimalist footwear, or completely barefoot. In addition to using an infrared camera system to track the movement of the lower limbs, the 30 runners in the sample ran over a force plate. When combined together, this data

allowed for the calculation of forces acting on both the knee and the Achilles tendon. The results of these calculations are similar to that of Barunstein et al. (2010) in that the knee was extended more in the PECH condition than the minimalist or barefoot condition. The forces acting on the joint between the patella and the femur were also found to be greater in the PECH condition. Finally, the forces acting on the Achilles tendon were greater in the minimalist and barefoot conditions. The authors of the study interpret these results to indicate that a FFS in either minimalist or barefoot shoes results in less stress on the knee in exchange for increased load on the Achilles. Despite this, the finding that minimalist and barefoot shoes encourage a change in form that results in a reduction in knee stress is encouraging in the quest to support the claim that a FFS and non-PECH shoes can lead to a reduction in common knee injuries.

The tradeoff between forces acting on the Achilles and knee in FFS running was also examined by Almonroeder, Willson, and Kernozek (2013) in their examination of female barefoot runners using a variety of footstrikes. Runners were instructed to run over a 20 meter artificial surface while their limb movements were tracked using reflective markers, and their GRF was measured with a force plate. The forces acting on the Achilles were calculated using this data in a manner similar to the previous study. These calculations determined that subjects using a FFS experienced an 11 percent increase in the force experienced by the Achilles. They go on to determine that over the course of a mile, the Achilles tendon of these FFS runners will experience an additional 47.7 body weights worth of force. From this, the researchers caution that those who attempt to transition to a FFS will cause so much additional stress to their Achilles that it

may increase their chances of an Achilles tendonopathy (Almonroeder et al., 2013). Despite these words of caution, the findings of Daoud et al. (2012) contradict this hypothesis that FFS runners would experience increased Achilles injuries. An explanation to this contradiction is provided by an examination of the issue of a shod RFS versus a barefoot FFS through the lens of evolutionary biology.

The development of bipedalism in modern humans occurred over a period of millions of years. Only since the 1970s have PECH shoes become the normative equipment to use when running. Australopiths and *Homo erectus* certainly didn't wear such footwear, and even *Homo sapiens* didn't begin wearing simple moccasins and sandals until 45,000 years ago. All of the anatomical characteristics including the Achilles tendon, the arch of the foot, and impact resistant lower limb bones all provided the necessary equipment for efficient endurance running (Lieberman, 2013). Unlike today, when a running injury most likely means a few weeks of icing and rest, for early endurance based hominids, an injury as simple as an ankle sprain could likely prove fatal. Unable to hunt or defend themselves, any injured hominid most likely didn't survive and pass on their genetic legacy.

In order to prevent such a disaster from occurring, the biology of humans, and likely other early hominids, developed a repair system influenced by the external environment. This ability, dubbed phenotypic plasticity, allows for the body to adapt many observable anatomical parameters of the body based on input from the environment. This system exists so that early environmental experiences during childhood can better prepare the adult to survive and reproduce (Lieberman, 2013). The

skeletal system is more dependent on this process than most bodily systems. Loading of the skeleton at an early age is required in order to allow for osteoblasts, bone remodeling cells, to reinforce the skeleton in areas that undergo the most stress. This phenomenon is evident in the forearm bones of tennis players. Those who begin to play tennis at a young age have bones that are 40 percent thicker in their dominant tennis playing arm.

Additionally, children who walk more than their peers develop thicker legs bones (Lieberman, 2013). Unfortunately, these phenotypic alterations are lacking in modern society. This can be seen in the rise of osteoporosis among the elderly.

While osteoporosis leads to skeletal fractures in nearly one third of elderly women, such fractures were rare until recently. Elderly individuals, including women, most likely participated in the gather of food during mankind's existence as tribes of hunter-gatherers (Lieberman, 2013). Even today, elder men are able to run with their younger peers during the early stages of the persistence hunt (Liebenberg, 2006). This decrease in bone strength is most likely the result of decreased exposure to skeletal loading events during childhood. While bone density decreases in all individuals over time, this skeletal loading at a young age produces a higher peak value for the bone density. This means that an individual's bone density will never fall to levels that risk the development of osteoporosis (Lieberman, 2013).

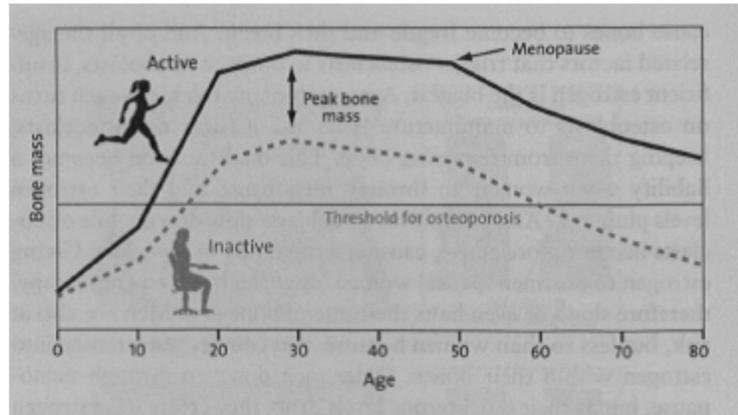


Figure 3: Lieberman (2013) describing the differences in bone density over the course of a lifetime between active and inactive individuals

Additional examples of phenotypic plasticity can be seen in differences between the incidence rates of flat feet in habitually shod versus habitually barefoot children. A survey of 2300 Indian children between the ages of 4 and 13, in which, 1555 wore footwear and 745 never wore footwear. Flat feet were present in 8.6 percent of those who wore shoes, while only 2.6 percent of those who were always barefoot had flat feet. This study also found that the incidence of flat foot was highest among the shod children who wore close toed shoes than those who wore slippers or sandals (Rao & Joseph, 1992). The results of this study all point to a weakening of the muscles of feet when shoes are worn. The arch of the foot provides a great deal of energetic return for each stride in a barefoot FFS gait. If the foot is not allowed to interact with the ground, this phenotypic plasticity that encourages the strengthening of the muscles is absent, and the foot's ability to absorb and release kinetic energy during running is impeded. PECH footwear places a rigid surface directly below the arch, preventing its ability to absorb and release kinetic energy, and impediments to this action can alter running mechanics in

a way that increases injury rates.

The Achilles tendon is another likely target of environmental influences. The Achilles tendon owes its strength to collagen fibers that can be affected by phenotypic plasticity. While the study by Almonroeder et al. (2012) found increased stress on the Achilles tendon in FFS runners, it is likely that if this excess stress would be attenuated in runners with a greater history of Achilles tendon usage. Also, the findings of Sinclair (2014) that increased Achilles tendon stress removed forces acting on the knee, would be beneficial for runners hoping to avoid knee injuries. This is because differences in the repair mechanisms between the collagen fibers in the Achilles and cartilage in the knee would focus the stress of running on a tendon which can better respond to such damage. The Achilles also is designed to absorb and release kinetic energy generated by running, so an activation of this system by removing PECH shoes may result in a distribution of forces on the lower limbs less likely to cause injury.

Finally, adaptive input to the muscles of the lower limbs, defined as muscle tuning, also have an effect on phenotype. This novel approach to the role of impact forces states that during footstrike, the muscles of the leg interpret the forces experienced to adjust their output. Over many repetitions, the nervous system innervating these muscles adapts to ensure that the optimal pattern of activity is achieved. Modern PECH footwear prevents the activity of many muscles of the lower limb, reducing their ability to correctly adapt to the changing topography of the ground (Nigg, 2004). By preventing this muscles tuning from achieving the optimal pattern of muscles activation, injuries are likely to result from sub-optimal running form.

Despite the presence of evidence supporting the superiority of a FFS in either minimalist footwear or completely barefoot, many researchers still profess the advantages of PECH footwear. Many physicians discourage the use of minimalist footwear, and some claim that they observed an increase in foot injuries in these runners. One study attempted to measure the genesis of skeletal injuries in minimalist shoe runners through MRI imaging to detect bone marrow edema. Early indicators of skeletal stress injuries coincide with an increase in bone marrow edema (Ridge et al., 2013). Thirty six runners participated in this study, with half told to run in their preferred PECH footwear, and the other half instructed to transition into running with Vibram Five Fingers (VFF), a popular minimalist shoe, according to guidelines released by their manufacturer. After 10 weeks, MRI results showed that increased bone marrow edema was seen with much greater frequency in the feet and lower limbs of the VFF group. Ten VFF runners had levels of bone marrow edema high enough to be considered full blown stress reactions. This is in contrast to the 16 PECH runners of whom only one developed any kind of stress injury (Ridge et al., 2013). These findings seem to indicate that minimalist shoes would actually lead to a much greater risk of developing a running injury.

A study aimed to investigate injury rates between minimal and PECH wearing runners recruited 99 individuals and assigned them to three conditions; PECH footwear, partial minimalist footwear, and fully minimalist footwear. Following a one week period to adjust to their assigned footwear, over a 12 week period each runner followed a standardized training regimen in preparation for a 10K race. Following the race, each runner was assessed for any injuries and lower limb pain (Ryan, Elashi, Newsham-West,

& Taunton, 2013). At the end of twelve weeks, 23 injuries were reported. The injury rates of those in the partial and full minimalist conditions were respectively 160 percent and 310 percent higher than the PECH condition. Runners in the full minimalist conditions also reported higher incidences of shin and calf pain (Ryan et al., 2013). The findings of these two studies indicate that modern runners who attempt to transition to minimal footwear experience greater chances of serious repetitive stress injuries.

The increased incidence of injuries in many attempting to transition to a FFS using minimalist shoes such as VFFs came to a head in a class action suit against Vibram USA. Plaintiffs in the case argue that despite both implicit and explicit claims in the advertising material for VFF that they would reduce and prevent injuries using their product, the opposite occurred. They go on to argue that despite advertisements highlighting potential strengthening of the foot and lower legs to prevent injury, promotion and reinforcement of a natural gait, and improved posture, these claims were not backed by sufficient scientific proof (*Bezdek v. Vibram USA et al.*, 2013). The case was decided in favor of the plaintiffs, and Vibram was told to provide a \$3.75 million settlement fund to reimburse all purchasers of their VFF shoes from March 21, 2008 up to and including May 27, 2014.

Why then, despite the intertwined relationship between our running and our evolutionary history, do we produce conflicting information on the status of a barefoot FFS running form? Are we truly, as many doctors told Christopher McDougall, not designed to withstand the abuse of long distance running? The answer to these questions again lies in evolutionary biology. The environment that humans evolved to run in didn't

consist of concrete and asphalt; it consisted of grassy plains and dirt. Running on these softer surfaces decreased the magnitude of shock on their bones and joints when compared to running on harder, modern surfaces. Additionally, these early runners were much more active, requiring walking and running all day in order to procure the nutrients necessary to survive. Finally, this increased activity began at a much earlier age, resulting in phenotypic adaptations based on their experiences (Lieberman, 2013). The absence of these environmental experiences from an early age in the modern lifestyle has led to an evolutionary mismatch between our original environment and our current one. Those attempting to run in the same way as our ancestors without the anatomical reinforcements of our early experiences are fated to injure themselves if they ignore this discrepancy.

In regards to what can be done about this mismatch, the simple fact of that matter is that some people may be incapable of running either barefoot or in minimalist shoes with a FFS. Without sufficient bone density and muscle and tendon adaptations forged through high levels of activity as a child, running with this specific form may be unsustainable without injury for that individual. Anyone attempting to adjust their form away from a RFS they have practiced for many years must be aware of this potential insufficiency and adapt accordingly. Studies show that simply putting on minimalist shoes and running in them does not produce any major changes in footstrike and running form after 10 minutes, and the thought that a simple change in footwear can undo years of running with a RFS is foolish (Willy and Davis, 2014). Only through gradual, conscious effort like that seen in the study by Crowell and Davis (2011) can such a drastic change in running form occur successfully. Further, the prevalence of hard

artificial surfaces like concrete and asphalt may limit the areas in which this style of running can be practiced. The human body was not exposed to such surfaces during its development, and the style of running it developed may also be unsuited for its practice there.

The acknowledgment of this mismatch between a barefoot FFS gait and our modern environment is crucial to the success of an attempted transition. In order to increase the public perception of this mismatch, a change in the language surrounding this approach to running form must take place. Instead of a focus on the terms “barefoot” and “natural”, proponents of this style should focus on the FFS, its important biomechanical differences from a RFS, and the evolutionary origin of this form based on our ancient environment. Despite the poor experiences of many attempted transitions, the focus that this FFS movement has brought to the importance of running form and footwear is of unquestionable importance. By paying careful attention to one's previous rate of activity, body's reaction to any attempted changes, and their running form, every runner can apply the lessons highlighted by this evolutionary origin and mismatch to find their ideal running form.

CHAPTER FOUR

Concluding Remarks

In a sense, running in today's society is completely different from how it was approached for hundreds of thousands of years. Many view running as a chore; a daily trudge over a few miles in order to maintain their weight or prevent additional gains. For our ancestors, running was an act of joy; a way to feed one's family and to experience sensations otherwise unattainable. Remnants of this joyful approach to running can be seen in the history of America. Three times in American history, running has experienced a sudden surge in popularity. These surges occurred in the 1930s during the Great Depression, the 1970s during the Cold War and recession, and in the early 2000s one year following the attacks of September 11 (McDougall, 2009). When faced with emotional hardships, humans seek comfort in the joy that can always be experienced in the act of running.

When members from the Tarahumara tribe of northern Mexico participated in the ultramarathon the Leadville 100, Americans observing them were astounded by the joy that radiated from the faces of the runners as they raced over 100 miles of mountainous terrain (McDougall, 2009). To many Americans, the idea of running as a joyful act is completely counter to our approach to running. For many sports teams, running is used as a punishment for mistakes made during practices. This negative connotation is just as alien to modern hunter-gatherer tribes like that Tarahumara as ours is to their practice of joyful running. While remnants of this history remain throughout our culture, only a return to what running was evolved to do can we expect to reap its many benefits.

The evidence presented in this thesis hopes to dispel these common misconceptions. That humans are not adapted to run, that running is an experience characterized by pain and misery, and that running is inherently dangerous are all examples of these toxic conceptions. By acknowledging and gradually returning to what running meant to our ancestors, we too can experience this joy. This debt to our evolutionary heritage in providing both the physical means and the biochemical support for long distance running can be repaid through a methodical elimination of the current trends and environments that exist counter to these ideas.

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