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REVIEW

Bone biomechanical function and adaptation

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ABSTRACT

Biomechanical studies in biological anthropology rely on the principle of bone mechanical adaptation and that bone morphology reflects loading history. Although the cellular processes by which bone senses and adapts to loading are not fully understood, it is clear that mechanical adaptation may cause changes in bone mass and mineral density. Moreover, it is also clear that bone morphology at different scales and the mechanical properties of bone material and tissue are related to its mechanical function.

This paper reviews the general principles of bone mechanical adaptation and how bone structure and bone material properties are related to its mechanical function. Thus, it presents a general review of bone structure, bone mechanical properties and how bone adapts to loading.

Keywords: Biological anthropology; Biomechanics; Bone mechanical function; Bone mechanical adaptation.

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RESUMO

Os estudos de biomecânica em Antropologia Biológica baseiam-se no princípio da adaptação mecânica do osso e de que a morfologia óssea reflecte a sua história mecânica. Embora os processos celulares através dos quais o osso percepciona e se adapta à carga mecânica não sejam completamente conhecidos, está claramente demonstrado que o osso se adapta mecanicamente através de alterações na sua massa e na sua composição mineral. É igualmente claro que a morfologia dos ossos em diferentes escalas e as suas propriedades mecânicas estão relacionadas com a sua função mecânica.

O presente artigo revê os princípios gerais da adaptação mecânica óssea e a forma como a estrutura óssea e as suas propriedades mecânicas estão relacionadas com a sua função mecânica. É, assim, apresentada uma revisão genérica da estrutura óssea, das propriedades mecânicas do osso e da forma como se adapta a cargas mecânicas.

Palavras-chave: Antropologia biológica; Biomecânica; Função mecânica óssea; Adaptação mecânica óssea.

Introduction

Bones provide protection for the internal organs and a lever system that enables movement (Cael, 2010; Marieb, 1992; Lindsay, 1996; Larsen, 2002; Kerr, 2010). When loaded, bone experiences forces that stress and deform (strain) it in multiple ways, and as a living, dynamic and mechanosensitive tissue it adapts to the mechanical environment (Currey, 2006). Mechanical adaptation impacts on the material properties of bone, which are related to its micro and gross morphology (Ethier and Simmons, 2007; Cowin and Doty, 2007; Katz, 2008).

The principle of bone mechanosensitivity and mechanical adaptation has been the foundation for skeletal form-function studies and for the vast literature on biomechanical analysis in biological anthropology. Biomechanical studies of skull morphology commonly focus the impact of diet on the cranium and the mandible (González-José *et al.*, 2005; Carlson and Van Gerven, 1977; Von Cramon-Taubadel, 2011; Paschetta *et al.*, 2010). Ruff (2007) provides a review of biomechanical studies of the post-cranial skeleton, but examples include research on sexual dimorphism and the sexual division of labour (Wescott, 2006; Ruff, 1987), activity patterns and subsistence strategies (Bridges, 1989; Bridges *et al.*, 2000) and the influence of geographical context and mode of mobility on limb morphology (Ruff, 1999; Stock and Pfeiffer, 2001; Weiss, 2003).

Thus, this manuscript aims to provide a general review of the principles of bone mechanical adaptation. First it will provide an overview of the structure of bone, which impacts on bone material properties, mechanosensitivity and mechanical adaption.

It will then review bone mechanical properties and, lastly, how bone adapts to the mechanical environment.

Bone Structure

Bone is a connective tissue with an extracellular matrix composed of an organic phase (20%), mineral phase (70%) and water (10%) (Ethier and Simmons, 2007). The organic component, or osteoid, is secreted by osteoblasts in the first stage of ossification. Osteoid mainly comprises collagen, which is laid down in the form of fibrils that aggregate and form collagen fibres. In the second stage, the organic material mineralizes, by hydroxyapatite crystallization within the osteoid, thus forming the mineral component of bone (Lindsay, 1996; Junqueira and Carneiro, 2003). When the ossification process is rapid with haphazard secretion of collagen fibres, woven bone is formed. In contrast, lamellar bone is deposited slowly and formed by parallel arrays of collagen fibres arranged in layers (lamellae). Orientation of the collagen fibres is consistent within each lamella but different among layers, thus presenting a plywood-like organization (Giraud-Guille, 1988; Lieberman, 2011).

Ossification gives rise to two macrostructurally different types of bone, compact (also referred to as cortical) and trabecular (or cancellous) (White and Folkens, 2005; Junqueira and Carneiro, 2003; Lindsay, 1996). Compact bone forms most of the external surface, or cortex, of bones and is covered by the *periosteum* on the outer surface, the *endosteum* on the inner surface and cartilage on the articular surfaces (White and Folkens, 2005). The most external layer of cortical bone is formed by the external circumferential lamellae, which are thin (+/- 5 µm thick) sheets of lamellar bone that cover the internal osteons. Osteons are cylindrical structures organized around a central (Haversian) canal and are made up of several concentric lamellae that have a maximum diameter of about 200 µm, a length of approximately 1 cm and are generally aligned with the long axis of the bone (Dechow *et al.*, 2008; Cowin and Doty, 2007). Osteons are populated by osteocytes, bone cells located in the lacunae among the lamellae. These bone cells are interconnected among themselves and with bone lining cells (located on bone surfaces) by processes that extend through canals known as *canaliculi*, forming a network throughout the bone (Cowin and Doty, 2007; Lindsay, 1996). The Haversian canals communicate with each other, the *periosteum* and the marrow cavity through the Volkmann's canals (Junqueira and Carneiro, 2003). Despite all these microstructures, on average cortical bone presents a level of porosity below 10%, although it is defined as bone with porosity below 30% (Ethier and Simmons, 2007).

Cancellous bone is mainly found in the extremities of long bones and vertebral bodies (Parkinson and Fazzalari, 2013). Like compact bone it has a lamellar structure in which the lamellae are generally, but not always, oriented parallel to the trabeculae (Ethier and Simmons, 2007), but usually lacks the osteonal structure (Guo, 2001). It is defined as being bone that presents a porosity level that ranges from 30% to 90%

(Cowin and Doty, 2007), with bony rod-like (trabeculae) and plate-like structures enclosing three dimensional interconnected open spaces, thus forming a cellular solid (Keaveny *et al.*, 2001). Trabecular bone is highly heterogeneous within and between bones and the proportions of plate-like structures and rod like trabeculae varies considerably. The most delicate architectures of trabecular bone, such as are found in deep parts of long bones, mainly present thin trabeculae that appear randomly oriented. At the other extreme, the most robust arrangements of cancellous bone are mainly found under articular surfaces, such as the head of the femur, and are made up of thick fenestrated plates (Singh, 1978) that are oriented according to the direction of habitually experienced loads (Currey, 2006).

Bone Mechanical Properties

Studies of bone material properties most commonly assess the ability of bone to resist deformation and failure due to applied forces at the micro and macrostructural levels. While extensive and thorough studies describe multiple material properties (for reviews see e.g. Cowin, 2001 and Currey, 2006) this section only presents a brief overview of some of those properties.

Bone is a linearly elastic, inhomogeneous, anisotropic, ductile material (Cowin, 2001; Currey, 2006; Humphrey and Delange, 2004). This complexity in material properties arises because bone is a highly intricate structure with several levels of organization (Katz, 2008). The organization of tropocollagen molecules in collagen and associated hydroxyapatite is denoted as the molecular level. The ultrastructural level is related to the assemblage of the collagen fibrils and hydroxyapatite into fibres. The microstructural level is associated with bone tissue, i.e., how collagen and hydroxyoapatite are arranged into woven or lamellar bone. The macrostructural level is concerned with the whole bone and its material properties, which are impacted by all levels of organization (Katz, 2008). Currey (2006) denotes bone material as the solid that forms bone (i.e. material that makes the trabeculae in cancellous bone) and bone tissue as the whole structure (i.e. bone material plus hollow spaces). This scheme is used throughout this manuscript.

When a force is exerted, bone, like any other structure, undergoes stress (σ) and deforms (strain, ε). Deformation is "sensed" by osteocytes and may trigger mechanical adaptation (see below). Stress is defined as the ratio of force (F) to the cross sectional area (A) of the bone to which it is applied ($\sigma = \frac{F}{A}$). When the direction of the force is perpendicular (normal) to a given plane, normal stresses develop (tensile when the structure is stretched, and compressive when compressed). When the force direction is parallel to the plane, shear stresses develop (Bird and Ross, 2012). Strain is measured in terms of the fractional changes in the dimensions of the bone due to loading and can be expressed as $\varepsilon = \frac{\Delta L}{L}$, where ΔL represents length after deformation and L equals original length. Like stress, strains can

be compressive, tensile and shearing. In compressive and tensile strains there are changes in form but none in the angle between the sides of the structure analyzed (Figure 1, A and B). In shearing strains there are changes in form and a change in the angle between two adjacent sides (Figure 1, C; Currey, 2006; Bird and Ross, 2012).

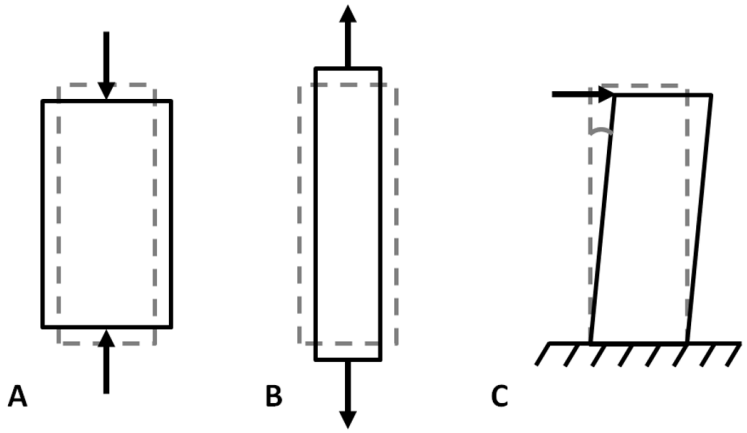

Figure 1 - Examples of form changes due to tension, compression and shearing. Black arrows represent forces applied, grey segmented forms original undeformed structures and solid black forms deformed structures due to loading.

Most deformations experienced by bone are small and do not cause permanent distortion, i.e. once the applied force is removed, bone returns to its original form. This change in morphology is termed elastic deformation (Bird and Ross, 2012), which is linear in bone within physiological ranges of deformation, and proportional to the applied force (Currey, 2006). However, if the force exceeds the elastic limit, then plastic deformation occurs and bone no longer recovers its original form. In plastic deformation there is no proportionality between applied force and deformation (Bird and Ross, 2012). Thus, bone is ductile in contrast to brittle materials, which present no plastic or post-yield deformation and so, fracture (Figure 2; Currey, 2006; Bird and Ross, 2012). The yield point marks the limit of the elastic deformation, at which plastic deformation begins. Before this point on the stress-strain curve it is linear. Its slope in this linear region gives the modulus of elasticity (Youngs modulus, denoted by *E*), and is expressed in Pascals (Pa), which are Newtons per square metre. The ultimate strength of a material is the highest point on the stress-strain curve, and this often does not coincide with the failure point (Bird and Ross, 2012).

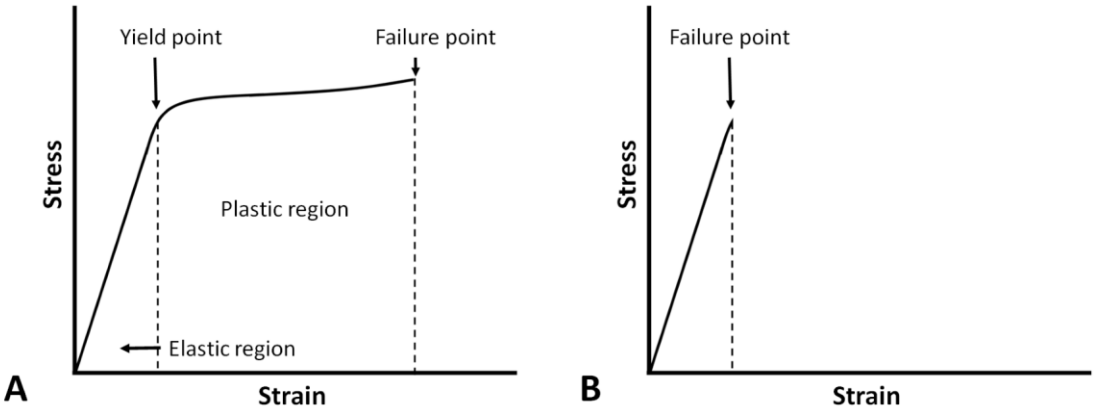

Figure 2 - Hypothetical stress-strain curves of a ductile (A) and a brittle material (B).

Because of the complexity at a microstructural level, variation in density, mineralization, and cortical and trabecular bone distribution and organization, bone is an inhomogeneous structure that presents regional variation in its material properties (Currey, 2006). As such, studies have reported differences in material properties within bone material (e.g. interstitial lamellae and secondary osteons; Rho *et al.*, 1999), within the same bone (e.g. mandible; Dechow *et al.*, 1993; Dechow *et al.*, 2008) and between bones (e.g. mandible, cranium and femur; Dechow *et al.*, 1993; Dechow *et al.*, 2008). Differences in material properties within and between bones have been associated with functional differences (Dechow *et al.*, 1993; Dechow *et al.*, 2008).

Another important material property of bone is anisotropy, thus presenting differences in strength according to the direction of the force applied (e.g. a long bone is stiffer if a force is applied along its shaft rather than perpendicular to it). Thus, a study using nanoindentation to measure modulus of elasticity reported values of 22.4 GPa in longitudinal loading of cortical bone tissue (average of osteons and interstitial lamellae) and of 16.6 GPa in transverse loading (Rho *et al.*, 1999). Bone anisotropy is associated not only with gross morphology but also with bone microstructure, namely the three dimensional orientation of osteons (Dechow *et al.*, 2008; Currey, 2006).

Lastly, bone is viscoelastic, i.e. its modulus of elasticity depends on the rate at which it is strained (strain-rate). It has been demonstrated that increases in strain rate result in increases in modulus of elasticity of bone but the increase is very small under normal physiological loading conditions (Currey, 2006; Mcelhaney, 1966).

It should be noted that the material properties reported for bone in different studies are not always consistent. This is has been attributed to two main factors,

differences in specimens tested and techniques used. Regarding the latter, two main approaches have been used, mechanical and ultrasonic. While mechanical testing directly assesses the elastic properties from resulting deformations, ultrasonic testing measures the velocity of sound waves travelling through bone and commonly reports higher modulus of elasticity (Kim and Walsh, 1992).

Despite differences in results due to methodology and specimen variability, it is clear that the material properties of a bone vary according to the scale at which it is examined. Microstructurally bone material, which includes trabecular and cortical material, has been characterized as a fibre-reinforced composite, with tensile strength and post-yield ductility provided by the collagen fibres and stiffness by the mineral component, hydroxyapatite (Ethier and Simmons, 2007; Guo, 2001). Even though both cortical and trabecular bone are lamellar, the latter is slightly less stiff than the former (e.g. the elastic modulus in cortical bone ranges from 16.6 to 25.7 GPa while in trabecular bone material ranges from 15 to 19.4 GPa; Rho *et al.*, 1999) due to structural and compositional differences (Guo, 2001). Trabecular bone material has lower density, higher water content and lower calcium content than cortical bone, thus making it less stiff (Guo, 2001). The compositional differences have been associated with a higher remodelling rate in trabecular bone and the fact that freshly remodelled bone is less mineralized (Guo, 2001). Furthermore, at a larger scale cortical bone and cancellous bone tissue (trabeculae and the spaces between them) have clearly different material properties due to the large differences in porosity and organization of the bone tissue (see above). The modulus of elasticity for bulk cortical bone is about 16GPa while that of cancellous tissue is about 1 GPa (Humphrey and Delange, 2004). These values are approximations and do not portray the complexity and regional variability that both cortical and cancellous bone tissue present (see above). The mechanical properties of the latter, as a bulk material, are a function of the arrangement of the trabeculae and of the apparent density (mass of dry bone divided by volume of specimen) (Keaveny *et al.*, 2001; Currey, 2006). Thus, studies have reported moduli of elasticity in human cancellous bone tissue that range from 4 to 350 MPa in the lower limb (Hodgskinson and Currey, 1992) and 3.5 to 125.6 MPa in the mandible (Misch *et al.*, 1999).

Bone Mechanical Adaptation

Bone growth and development is influenced by epigenetic factors such as the mechanical loadings experienced during ontogeny (Moss, 1997a; Moss, 1997b; Carlson, 2005). Mechanical loading causes deformation (strain), which is detected at the cellular level, triggering a response that ultimately results in bone mechanical adaptation (Currey, 2006; Ruff *et al.*, 2006; Klein-Nulend and Bonewald, 2008).

Strain detection and mechanotransduction, i.e. the process by which stress/strain triggers electrical and/or bio-chemical signals

(Bonucci, 2009; Burger and Klein-Nulend, 1999), are not fully understood (Skerry, 2000; Robling *et al.*, 2006; Ethier and Simmons, 2007; Klein-Nulend and Bonewald, 2008; Burger and Klein-Nulend, 1999), however it is widely accepted that the osteocyte – bone lining cells – osteoblast network is fundamental in this process (Robling *et al.*, 2006; Klein-Nulend and Bonewald, 2008; Bonucci, 2009). Several mechanisms have been suggested for strain detection at the level of osteocytes, which include direct deformation of the cells along with bone, fluid flow and hydrostatic pressure with "measurement" of bulk and shear strains, electric and magnetic transduction, oxygen tension and osteocyte hypoxia (Robling *et al.*, 2006; Klein-Nulend and Bonewald, 2008; Bonucci, 2009). In response to stresses/strains a cascade of biochemical processes, that may include dedifferentiation of bone lining cells into osteoblasts, ultimately results in bone (re)modelling and bone mechanical adaptation (Klein-Nulend and Bonewald, 2008; Bonucci, 2009).

Regardless of the precise mechanotransduction mechanism, bone mechanical adaptation may arise through modelling or remodelling processes. Bone modelling, in which there is independent action of osteoblasts and osteoclasts, contrasts with remodelling, where these are coordinated (Robling *et al.*, 2006). Bone deposition or resorption may occur in the periosteal and/or endosteal surfaces and usually there is a change in bone size and/or shape (Currey, 2006). Bone modelling is age dependent and becomes much less marked once skeletal maturity is achieved (Robling *et al.*, 2006). Bone remodelling does not affect bone size or shape and occurs through the coupled action of osteoblasts and osteoclasts (Hall, 2005), which form the basic multicellular unit (Ortner, 2003; Robling *et al.*, 2006). In response to strains occurring in the bone matrix, osteocytes produce nitric oxide, thereby regulating bone deposition via the osteoblasts and bone resorption via the osteoclasts (Bacabac *et al.*, 2008). That bone deposition (Jones *et al.*, 1977; Kannus *et al.*, 1995) or bone resorption (Nordstrom *et al.*, 1996; Goodship *et al.*, 1998) occurs due to mechanical loading, thus changing bone mass, is clearly demonstrated. But bone adaptation may also occur via alterations in bone mineral content (Valdimarsson *et al.*, 2005; Kannus *et al.*, 1995) and in mineral density (Kerr *et al.*, 1996; Valdimarsson *et al.*, 2005). These bone mechanical adaptations occur throughout life, but the potential for adaptation to the mechanical environment decreases with age (Ruff *et al.*, 2006). This reduction may be due to diminished capacity of adult mesenchymal cells to differentiate into osteoblasts (Nishida *et al.*, 1999) and/or reduced sensitivity of osteoblasts and osteocytes to mechanical signals (Turner *et al.*, 1995; Stanford *et al.*, 2000). Metabolic, endocrine and dietary factors are also known to impact on bone biology (Aufderheide and Rodriguez-Martin, 1998; Ortner, 2003; Roberts and Manchester, 2005; Bilezikian *et al.*, 2008), and thus on "normal" mechanical adaptation.

Bone mechanical adaptation seems to occur when there are significant deviations from a "minimum effective strain" (Frost, 1987) or "optimum customary strain level"

(Skerry, 2000). In most sites of the skeleton, this is hypothesized to be in the range of 1500 - 2500 µE (Frost, 1987) to 3000 µE (Skerry, 2000). If deformations reach that threshold deposition of bone occurs. On the other hand, if strains are lower than a certain minimum, bone resorption occurs (Turner, 1998) (see Figure 3). However, peak strain is not the only variable that triggers bone adaptation. Other factors that have been demonstrated to cause bone adaptation include dynamic vs. static loading (Lanyon and Rubin, 1984; Turner, 1998), strain rate (Mosley and Lanyon, 1998) and strain frequency (Judex *et al.*, 2007).

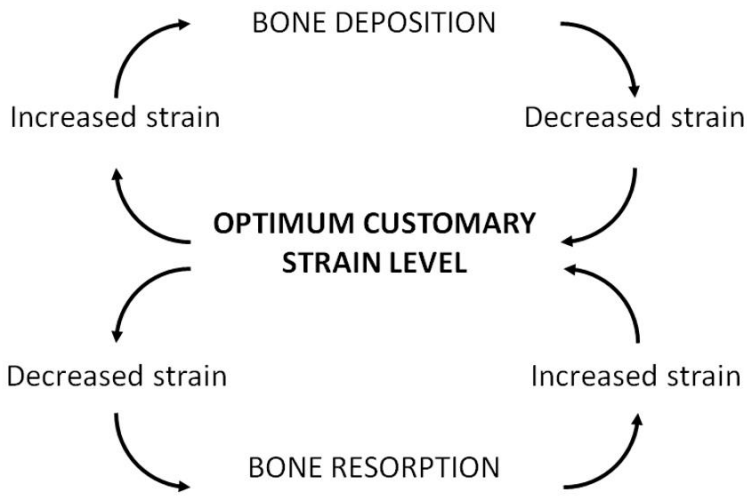

Figure 3 - Feedback model of bone function adaptation (adapted from Rubin and Lanyon, 1987).

Even though most sites in the skeleton share a similar optimal strain level, this threshold is hypothesized to be site-specific, based on differences in strain experienced by different skeletal elements. Recorded strains in the cranial vault appear to be 10 times lower than those in the long bones (Hillam *et al.*, 1995). If bone remodelling thresholds in the vault were similar to the remaining post-cranial bones this would result in severe osteoclasis. Thus, site-specific patterning information has been suggested, which would allow cells to adapt to site-specific loads (Skerry, 2000; Currey, 2006). This hypothesis is supported by studies that compared the calvarial and lower limb osteocyte morphology in rats and demonstrated differences in size, shape and orientation of these cells (Himeno-Ando *et al.*, 2012; Vatsa *et al.*, 2008). In the lower limb osteocytes are larger, longer and flatter than in the vault, where they are smaller and more spherical. Furthermore, in the lower limb osteocytes are aligned with the principal

direction of loading whereas in the vault, in which loads are multidirectional due to forces exerted by intracranial pressure and masticatory function, they show no consistent orientation. Because studies using osteocytes show that rounder cells are more mechanosensitive than flat ones these results support the hypothesis of site-specific osteocyte mechanosensitivity (Himeno-Ando *et al.*, 2012; Vatsa *et al.*, 2008; Bacabac *et al.*, 2008).

In contrast to these findings, using Finite Element Analysis, Witzel (2011) modelled a cranium as a homogenous solid in which the only details were the eye sockets, the nose cavity, the brain cavity and the form of the dental arcade. Forces were then applied that simulated biting and the acceleration of the brain. In accordance with principles of bone mechanical adaptation regions that experienced high stresses and strains were kept and regions that experienced low stresses and strains were removed. After several iterations of this algorithm simulating adaptation, the final result was a structure that clearly resembles a Neanderthal cranium (Witzel, 2011). In this study, and another that used the same approach but with a *Diplodocus* cranium (Witzel and Preuschoft, 2005), no site specific mechanosensitivity was assumed, and bone was removed throughout the cranium based on the same stress or strain level. Thus, these results seem to support a generalized threshold model.

Final Comments

Bone performs a mechanical function and has the ability to sense the mechanical demands to which it is subjected to at a cellular level. Furthermore, mechanosensitivity is coupled with a not yet fully understood mechanotransduction mechanism that enables bone to adapt to loading. Thus, bone structure, morphology and material properties reflect its loading history. This principle of bone mechanical adaptation has been the foundation for archaeological human bone biomechanical studies (Stock and Pfeiffer, 2001; Wescott, 2006; González-José *et al.*, 2005; Carlson and Van Gerven, 1977; Von Cramon-Taubadel, 2011; Paschetta *et al.*, 2010; Ruff *et al.*, 2006; Ruff, 2007; Ruff, 1987; Bridges, 1989; Bridges *et al.*, 2000; Ruff, 1999; Weiss, 2003).

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