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Multiple independent appearances of the cecal appendix in mammalian evolution and an investigation of related ecological and anatomical factors

Multiples apparitions indépendantes de l'appendice du cæcum dans l'évolution des mammifères et une étude des facteurs écologiques et anatomiques pertinents

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ABSTRACT

Although the cecal appendix has been widely viewed as a vestige with no known function or a remnant of a formerly utilized digestive organ, the evolutionary history of this anatomical structure is currently unresolved. A database was compiled for 361 mammalian species, and appendix characters were mapped onto a consensus phylogeny along with other gastrointestinal and behavioral characters. No correlation was found between appearance of an appendix and evolutionary changes in diet, fermentation strategy, coprophagia, social group size, activity pattern, cecal shape, or colonic separation mechanism. Appendix presence and size are positively correlated with cecum and colon size, even though this relationship rests largely on the larger size of cecum and colon in taxa that have an appendix. The appendix has evolved minimally 32 times, but was lost fewer than seven times, indicating that it either has a positive fitness value or is closely associated with another character that does. These results, together with immunological and medical evidence, refute some of Darwin's hypotheses and suggest that the appendix is adaptive but has not evolved as a response to any particular dietary or social factor evaluated here.

RÉSUMÉ

Même si l'appendice du cæcum a été considéré comme un vestige sans fonction connue ou comme un reste d'organe digestif autrefois fonctionnel, son histoire évolutive demeure énigmatique. L'évolution de l'appendice, d'autres caractères du tractus gastro-intestinal, ainsi que de caractères comportementaux est étudiée à l'aide d'une nouvelle banque de données de 361 espèces de mammifères. Aucune corrélation n'est détectée entre l'apparition de l'appendice et des changements de régime alimentaire, de la stratégie de fermentation, de la coprophagie, de la taille du groupe social, du patron d'activité, de la forme du cæcum, ou du mécanisme de séparation du côlon. La présence et la taille de l'appendice sont

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positivement corrélées à la taille du côlon et du cæcum, même si cette relation semble provenir surtout de la plus grande taille du côlon et du cæcum chez les espèces pourvues d'un appendice. L'appendice est apparu au moins 32 fois, mais il a été perdu moins de sept fois, ce qui indique, soit une valeur sélective positive, soit une association étroite avec un caractère possédant une telle valeur sélective. Ces résultats, avec des données immunologiques et médicales, réfutent certaines hypothèses de Darwin et suggèrent que l'appendice est adaptatif, mais qu'il n'a pas évolué en réponse aux régimes alimentaires ou facteurs sociaux considérés dans cette étude.

1. Introduction

The cecal appendix has long been an anatomical structure of intrigue, with historically uncertain function and a well-earned reputation for inflammation that results in frequent surgical removal (MacFayden et al., 2000). Its interest to early anatomists is apparent in the numerous original publications on the subject (Arvy, 1972; Bockman, 1983; Bürgi, 1905; Cave, 1936; Eggeling, 1920; Gluckmann, 1939, 1947a, b; Jacobshagen, 1922; Keith, 1912; Kostanecki, 1913, 1926; Muthmann, 1913). Recent studies have revealed that the appendix has undergone a complicated evolution, which has not been easy to reconstruct (Laurin et al., 2011; Smith et al., 2009). It projects from the cecum, the most proximal section of the large intestine, which typically functions as a fermentation chamber involved in cellulose breakdown; as such, the appendix could be inferred to be affected by diet, cellulose content in the diet, cecal size and shape, and/or other anatomical characteristics of the gastrointestinal system.

The lack of evident function of this organ in humans was discussed by Charles Darwin in his famous *On the Descent of Man*... (Darwin, 1871). Darwin observed that humans, along with other apes, uniformly possess a cecal appendix, but that its size and structure render it incapable of participating to any notable degree in digestion, despite its location along the intestinal tube. Darwin posited that in extant hominoids (great apes), who are for the most part frugivorous, the shift from a predominantly folivorous ancestor to a descendent with diet requiring less fermentation led to a reduction in cecal size, which was in turn associated with the appearance of the appendix. During Darwin's time, the presence of a cecal appendix had not been documented in many nonhuman taxa, so the idea that this structure was a uniquely hominoid trait was entirely reasonable. Thus, for many decades, the idea that the cecal appendix was a synapomorphy of the Hominoidea predominated (Clark, 1971; Groves, 1986; Hill, 1972; Napier and Napier, 1985; Scott, 1980).

More recently, Fisher conducted a broad survey of published descriptions of the presence or absence of cecal appendices across primate species (Fisher, 2000). She discovered that the appendix is present in many more species than is traditionally recognized. It is found, at least variably, in several species of lorises, lemurs, New World monkeys, and Old World monkeys, and is found ubiquitously in all apes (Fisher, 2000). Based on these findings, Fisher argued that the appendix should be identified and defined as more than simply a distinct narrow-lumened apex projecting off the cecum, but that related characteristics such as a concentration of lymphoid tissue and a thickening of the cecal wall should also be considered (Fisher, 2000).

Although Darwin initially posited that the appendix lacked an important biological function, the idea that the appendix must have some important function has not been without support. For example, the observation that the vermiform appendix is associated with substantial amounts of gut-associated lymphoid tissue (GALT) was made more than a century ago (Berry, 1900), and suggested that the appendix may have an immune function. A few years later, Keith argued strongly, based on phylogenetic observations and other evidence, that the vermiform appendix probably did have a function, and in fact that appendicitis was due to changes in behavior associated with industrialization rather than a "degenerate" nature of the structure (Keith, 1912). Keith's ideas were supported by numerous others in the following decades (Barker et al., 1988; Boroda, 1961; Bremner, 1964; Burkitt, 1969, 1971; Gelfand, 1956; Janssens and de Muynck, 1966; Scott, 1980; Trowell, 1960; Walker et al., 1973), culminating with the identification of the vermiform appendix as a "safe-house" for beneficial bacteria with the capacity to re-inoculate the gut following depletion of the normal flora after diarrheal illness (Bollinger et al., 2007; Laurin et al., 2011). The identification of this function was based on old observations regarding the appendices' size, shape, location, and association with GALT, in combination with more recent findings that the immune system supports microbial biofilm growth in the large intestine (Everett et al., 2004; Sonnenburg et al., 2004; Thomas and Parker, 2010), and that intestinal biofilms are most abundant in the appendix (Bollinger et al., 2007).

The idea that the appendix is a safe-house for beneficial bacteria can be demonstrated by deduction (Bollinger et al., 2007). This function is consistent with a wide range of corroborating evidence (Laurin et al., 2011; Smith et al., 2009). First, the observation that the appendix is associated with a large amount of GALT (Berry, 1900) and the discovery that the immune system supports intestinal biofilms (Everett et al., 2004; Sonnenburg et al., 2004; Thomas and Parker, 2010) are consistent with this function as a safe-house. Second, the size and anatomical location of the appendix are well suited for inoculation of the gut and for avoidance of contamination by pathogens that might infect the main fecal stream (Laurin et al., 2011). Third, the newly recognized importance of the microbiome to human health (Cho and Blaser, 2012) and the high impact of diarrheal illness in developing countries (Guerrant et al., 1990) suggest that rapid recolonization of the gut following diarrheal disease may be important for survival. Fourth, a broad consideration of symbiotic relationships in biology indicates that

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