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Review

Heterochrony and developmental timing mechanisms: Changing ontogenies in evolution

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ABSTRACT

Heterochrony, or a change in developmental timing, is an important mechanism of evolutionary change. Historically the concept of heterochrony has focused alternatively on changes in size and shape or changes in developmental sequence, but most have focused on the pattern of change. Few studies have examined changes in the mechanisms that embryos use to actually measure time during development. Recently, evolutionary studies focused on changes in distinct timekeeping mechanisms have appeared, and this review examines two such case studies: the evolution of increased segment number in snakes and the extreme rostral to caudal gradient of developmental maturation in marsupials. In both examples, heterochronic modifications of the somite clock have been important drivers of evolutionary change.

Contents

1. Introduction

Development consists of a series of events that take place in a highly regulated spatial and temporal context. In most organisms there is a clear directionality to development as later events are commonly contingent on the proper completion of prior events. In animals at least, with a few exceptions such as regeneration and some processes that occur during metamorphosis there is rarely significant reversibility in developmental processes. In multicellular organisms, development proceeds from large scale patterning of the whole organism to events that are increasingly smaller in scale, and more modular and localized as individual parts differentiate and become more specialized. The field of developmental biology largely consists of the study of the mechanisms by which these intricate processes are controlled in space and time.

The process of timing and the role of changes in timing during development have been a strong focus of studies of comparative development and the interaction of development and evolution. The processes of development construct the organism and biologists have looked for ways that changes in developmental processes produce evolutionary change. Historically one kind of developmental change – the change in the timing of events – has received particular focus. Change in the timing of developmental events generally is termed heterochrony. The term heterochrony was initially coined to designate changes in the relative time of developmental processes between ancestors and descendants but in practice

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heterochrony is applied in a comparative sense to changes among taxa that are related at some level [1].

1.1. Historical perspective

The concept of heterochrony has evolved considerably over the past century. The term "heterochrony" was coined by Haeckel to denote certain deviations from his now discredited Biogenetic Law, which states that ontogeny recapitulates phylogeny. Haeckel believed that during development, an embryo repeated the, "...most important of the form changes which its ancestors traversed during the long and slow course of their paleontological evolution" [Haeckel quoted by 2]. Heterochrony indicated a shift in which a feature appeared at a different time in an organism's developmental sequence than which it appeared in the sequence of that organism's phylogeny [3,4]. Haeckel's definition stands in contrast to the contemporary definition in that it is a comparison of changing ontogenies across phylogeny rather than a comparison of an ontogenetic sequence in an individual species with its presumed evolutionary pattern.

In an effort to refute Haeckel's concept of recapitulation and join the fields of developmental biology, evolutionary biology and genetics, de Beer showed how timing changes during development could generate diversity among organisms [5–8]. He contended that heterochrony did not require an association with recapitulation; rather, de Beer used heterochrony to denote differences in the ontogenies of related taxa [9]. It is this comparative definition that is the principal one currently in use [3].

While de Beer's treatment of heterochrony is regarded as a valuable early effort to join development and evolution, Gould made heterochrony a well-known concept in the field of evolutionary biology [9,10]. His work, and that of his colleagues, defined the scope of heterochrony for many years. Gould's view of heterochrony, largely adopted by evolutionary biologists at the time, was characterized by a re-association of heterochrony with recapitulatory patterns and a focus on relative rates of growth rather than developmental sequences. Gould shifted the emphasis on heterochrony from the relative timing of developmental events to changes in the relationship between size and shape. In the 1980s and early 1990s, a surge of heterochrony studies focused nearly exclusively on size and shape changes such that the concept of heterochrony came to be practically synonymous with allometry [3].

In the late 1990s the application of Gould's definition of heterochrony was questioned. In certain instances "evolution by heterochrony" was invoked to explain a change in the relative proportion of any structure and often studies were so non-specific as to lack explanatory power. Attention was primarily on size and shape, and size was frequently used as a surrogate for time. In certain circumstances size can be a suitable proxy for age, but in other cases this exchange is inappropriate as rate of development, size and shape can evolve separate from one another [11–18]. Finally, the attention on size and shape restricted studies to global, organismal-level events and later processes in development [19,20]. Numerous variations among closely related species do result from growth heterochrony, but these methods cannot be used to examine a number of the most significant events in development: patterns of gene expression, cell and tissue specification and differentiation, induction and signaling cascades, and the emergence of segmental or regional identity, for example. Heterochronies in events such as these are absolutely critical in producing evolutionary change [3,19,21–25].

1.2. Heterochrony today

The study of heterochrony has been revitalized in the last two decades by a shift in focus from relative growth to relative timing of developmental events, and also an increasing focus on events at molecular and genetic levels. These studies focus on specific elements and increasingly on the underlying developmental mechanisms responsible for evolutionary change. New analytical tools now offer methods to analyze multiple events in many taxa, as well as to test hypotheses in a phylogenetic context. Thus the combination of modern developmental biological approaches using molecular and genetic data, with the renewed approach to heterochrony has brought new explanatory power to classic problems in evolutionary biology. Instead of emphasizing size and shape changes, modern heterochrony studies examine the basis for variation in an array of mechanisms and types of phenotypic modifications. Processes including shifts in critical periods, inductive events, and relative timing of gene expression have been studied; phenomena include patterning mechanisms, the timing of formation of organs and structures, alterations in life history phases, and morphological changes [3].

Most studies of heterochrony do not examine changes in timing mechanisms in the explicit sense – that is, the mechanisms that embryos use to actually measure time. This is partly due to the nature of development: many events in development are simply contingent on the completion of prior events. Within an embryo scheduling is often based on a sequence of events as opposed to clock time. The occurrence of many events depends on induction, cell and tissue interactions, and connections within signaling cascades. It is more appropriate to describe these types of control processes as scheduling rather than timing mechanisms. In addition, there appears to be no one mechanism organisms use for time assessment during development [26–41]. Diverse organisms at different stages of their life history use an array of mechanisms to track developmental time, complicating any evolutionary comparison of changes in timing mechanisms across taxa. However, our understanding of developmental timing mechanisms has increased dramatically in recent years, and heterochrony studies addressing the modification of timing mechanisms are beginning to emerge.

1.3. The somite clock

One such timing mechanism that has recently been the focus of heterochrony studies is the somite clock. Somites are transient structures in vertebrate embryos that are the first morphological sign of segmentation; they ultimately give rise to skeletal muscle, cartilage, tendons, endothelial cells, and dermis. Somites "bud off" from the anterior presomitic mesoderm, forming in rostral to caudal sequence. The most commonly referenced model for the mechanism of somitogenesis is that of the "Clock and Wavefront" [27,28,42,43]. The model posits that each cell in the presomitic mesoderm has its own internal clock, which oscillates between permissive and non-permissive states for formation of a segment boundary; cells are coupled so that oscillations within the presomitic mesoderm are synchronized. A wavefront travels rostro-caudal through the presomitic mesoderm, and after it has passed, cells are competent to form a segment boundary. In this fashion, a segment boundary is formed when the clock is in the permissive state and wherever the wavefront happens to be at that time. A large number of studies have detailed the specific molecular components of the Clock and Wavefront; these include members of the Notch, FGF, and Wnt signaling pathways [26–28,44]. While the identity of the clock pacesetter remains unknown, the readout of the clock can be seen in the periodic expression of members of the Notch, Wnt and Fgf signaling pathways in the presomitic mesoderm.

It is important to note that while an array of experimental evidence supports the Clock and Wavefront model, alternative models exist for which there is also experimental evidence, and not all models of the segmentation process rely on a clock mechanism [45,46].

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