



Commentary

The Organizational Hypothesis: Reflections on the 50th anniversary of the publication of Phoenix, Goy, Gerall, and Young (1959)

Kim Wallen

Department of Psychology, Emory University, Atlanta, GA 30322, USA

ARTICLE INFO

Keywords:

Sexual differentiation
Androgens
Activation
Organization
Masculinization
Defeminization

ABSTRACT

The 1959 publication of “Organizing action of prenatally administered testosterone propionate on the tissues mediating mating behavior in the female guinea pig” by Charles H. Phoenix, Robert W. Goy, Arnold A. Gerall, and William C. Young transformed how sex differences in mating behavior were thought to develop. Previous work provided extensive evidence that steroid hormones activated patterns of male and female sexual behavior, but only activated the behavioral patterns typical of a given sex. The 1959 paper explained this phenomenon by arguing that androgens, or their metabolites, acting at specific time(s) during development sexually dimorphically organized the tissues mediating mating behavior, which were activated by appropriate hormonal stimulation in adulthood. Thus, exposure to steroids at specific time(s) permanently altered the structure or function of the organism. The exact hormone, exact timing, exact mechanism, and exact tissues were unspecified in the article. The last two paragraphs of the discussion illustrate the investigators’ unresolved views. The first proposes that the ‘organization’ was likely to be functional and not evident in visible structure, whereas the next paragraph argues that behavioral change implies structural change and thus structural changes are the likely consequence of steroid actions. These unresolved issues have produced extensive work in the intervening 50 years. The papers in this issue mark the 50th anniversary of this landmark paper and reflect the scope and relevance of the issues raised in the original paper and demonstrate the progress that has been made in understanding the Organizational Hypothesis and its impact on sexual differentiation.

© 2009 Elsevier Inc. All rights reserved.

Fifty years hold no special place in the life of an idea, yet an idea that remains relevant for a half century reflects an endurance few ideas achieve. The Organizational Hypothesis, which was not referred to as such by its authors, is an idea whose impact is hard to overstate. In the 50 years since its publication it has transformed common views of the actions of hormones on the nervous system. The notion that hormones could permanently alter the structure of the nervous system, radical when it was first published, is currently taught in high school and undergraduate classes in psychology and neuroscience. It has become the dominant explanation for the genesis of behavioral sex differences. A testament to its importance is that this paper has been cited 648 times by others and in each succeeding decade since its publication it has been cited more often than it was in the decade before (Fig. 1). No other idea in behavioral neuroendocrinology, has so transformed how we think about the genesis of masculine and feminine behavior. The notion that hormones at circumscribed times in life predictably and permanently alter the function, and we now know, the structure, of a living being to become phenotypically male, is one of the truly powerful ideas of the 20th century. Yet it is an idea, for all of its power, which is sometimes misunderstood, likely

reflecting unresolved issues in its original description in the 1959 paper authored by Charles H. Phoenix, Robert W. Goy, Arnold A. Gerall, and William C. Young.

The exact genesis of the 1959 study is lost, but we know that it came from a desire on W.C. Young’s part to complete a study which would have a lasting a lasting impact on the field of hormones and behavior. Young, a survivor of one bout with cancer, was convinced that the cancer would return and that he had a short time to leave a lasting mark on the field which he had, essentially, created (Gerall, 2009). Whether the resulting study met or exceeded Young’s hopes is unknown, but we do know that with its publication, controversy and conflict, as well as a reevaluation of the function of hormones, particularly steroid hormones, in sexual differentiation followed.

It is somewhat surprising that in the 1950s Young would be seeking a study to cement his impact on the field since his pioneering work in the 1930s (Young et al., 1935, 1937; Boling, Young and Dempsey, 1938; Collins et al., 1938) had established the underpinnings what would become behavioral neuroendocrinology. Dissuaded by his mentor as a graduate student from investigating the behavioral effects of hormones, Young, as a new professor at Brown University, pursued for the first time how ovarian hormones regulated female sexual behavior in guinea pigs (Goy, 1967). The work of his team at Brown established that hormones could produce changes in female sexual

E-mail address: kim@emory.edu.

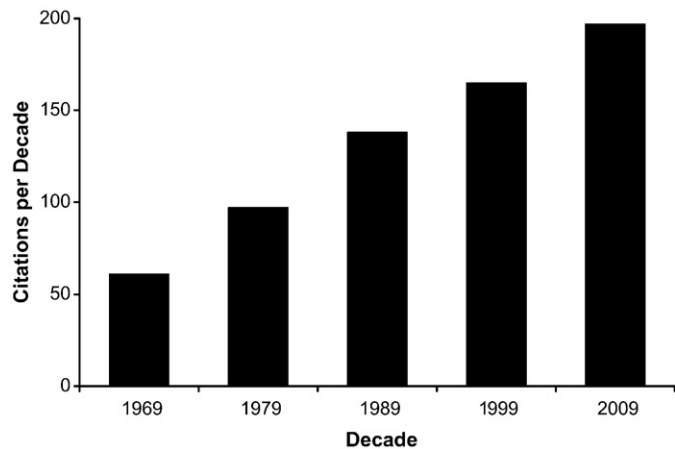


Fig. 1. Total citations of Phoenix et al. (1959) by decade since publication. Citations have increased in every decade with no evidence of slowing down. In the 50 years since publication, 2008 had the greatest number of citations (34) of all years. 1962 had the least citations when the paper was never cited.

behavior, which, contrary to his mentor's contention that behavior was too unpredictable to study, were highly predictable and followed the hypothesized patterns of endogenous ovarian hormone secretion.

These early studies, of what became known after the 1959 paper as 'activational' effects of hormones, exemplified important aspects of Young's approach to understanding hormone action, which are evident in the 1959 paper. First, Young related naturally occurring events to experimental phenomena. Thus Young used the naturally occurring sequence of changes in the ovary to point the way to an effective hormonal procedure for inducing female sexual receptivity (Young et al., 1935). Secondly, his studies used the reliable occurrence of behavior to draw inferences about underlying physiology. For example, Young's demonstration that an injection of progesterone to an ovariectomized female guinea pig pretreated with estradiol was necessary to induce full sexual receptivity suggested that there was a preovulatory progesterone surge before any evidence existed for such an endogenous event (Boling, Young, and Dempsey, 1938). More than 30 years later the advent of hormone assays allowed Young's lab, after his death in 1966, to demonstrate the preovulatory progesterone surge in female guinea pigs (Feder, Resko, and Goy, 1968). A third aspect of Young's approach was that he believed that hormonal influences on behavior were the result of their actions on the 'soma' or the substrate upon which hormones act (Young et al., 1939). The soma was assumed to be neural (Young, Goy, and Phoenix, 1964), even though direct evidence of this was unavailable in the 1930s and would have to wait almost 10 years for its demonstration following the 1959 paper. The notion that the soma differed between males and females was not widely accepted, the more common view being that the brains of males and females were inherently bisexual (Phoenix et al., 1959). This view was irrevocably changed as a result of the 1959 paper and the studies that followed.

Soon after the publication of the 1959 paper other studies provided evidence that similar effects could be obtained in rats (Beach, Noble, and Orndoff, 1969) and that neonatal castration of rats, which deprived males of testicular secretions, resulted in males who were poorly masculinized and not defeminized (Feder and Whalen, 1965; Grady, Phoenix, and Young, 1965). Further studies in guinea pigs addressed the question of whether masculinity and femininity developed along a continuum, such that masculinization necessarily resulted in defeminization (Goy, Bridson, and Young, 1964). Still the notion that steroid hormones at certain times in life organized the tissues mediating mating behavior, most likely neural tissues, was

controversial. Frank Beach, in particular, strongly opposed the idea that the nervous system was altered by exposure to androgens during development arguing instead that the effects of steroids on sexual differentiation reflected peripheral effects on genital anatomy, which altered behavioral responsiveness (Beach, et al., 1969; Beach, 1971). Beach's student, Richard Whalen (1968), argued that the sexually differentiating effects of androgens were limited to altering adult sensitivity to the activational effects of steroids on mating behavior, a position that contradicted Beach's and was compatible with the notions proposed in Phoenix et al. (1959). Some of Beach's opposition to the Organizational Hypothesis may have come from his own earlier studies of androgens and male sexual differentiation.

In 1946, Beach neonatally castrated males and found that as adults they displayed reduced masculine copulatory behavior (Beach and Holz, 1946). This he attributed to an androgen-deficiency induced reduction in penile development producing a lack of appropriate penile sensory feedback resulting in reduced masculine sexual behavior. Since the neonatally castrated males were not tested for female receptive behavior, Beach was unaware that his neonatal castrates would not have been defeminized, an endpoint unlikely to be related to penile development and more compatible with alterations in the central nervous system. It has been suggested that Beach's opposition to the Organizational Hypothesis might have reflected a realization that his own data some 14 years earlier pointed in the same direction as did the Young Lab's data, but he had interpreted them as evidence of peripheral changes, not central nervous system changes (Baum, 1990). While this is a distinct possibility, it is also the case that Beach focused on the effects of hormones on genital structures as being important to masculine behavior, having demonstrated that post-castration changes in male penile anatomy paralleled the decline in masculine copulatory behavior in rats (Beach and Levinson, 1950). Thus Beach's interpretation of the effects of neonatal androgen deficiency as reflecting the consequences of steroid induced genital changes was consistent with his theoretical position. Had he looked at both masculine and feminine behavior in his neonatally castrated males he might have reached the same conclusion as did the Young Lab. When Beach discovered that urination posture, a behavior that is not hormonally activated, was masculinized in female dogs treated perinatally with testosterone, he conceded that androgens were capable of organizing the developing nervous system (Beach, 1975).

By contrast, Young was historically more focused on central effects of hormones on behavior. This likely reflected Young's early focus female sexual behavior, in contrast to Beach's on male sexual behavior, in which there was no discernable effect of hormonal influences on genital anatomy, or the lack thereof, that affected female sexual receptivity. Without an obvious peripheral explanation for the disappearance of sexual receptivity following ovariectomy, Young was left with an explanation in which the hormones that reinstated female sexual receptivity acted on the soma (Young 1961), which likely meant the neural tissues underlying sexual behavior. Young's demonstration that high drive and low drive male guinea pigs' sexual behavior was restored to their precastration levels, even when given suprphysiological levels of replacement androgens, suggested differences in the underlying neural substrate which determined the males' response potential to androgens (Grunt and Young, 1953). Similarly, Goy and Young (1957), in Young's lab, had demonstrated that the genetic constitution of inbred strains of guinea pigs predicted their responsiveness to steroids for the induction of sexual behavior; supporting the idea that hormones acted on different substrates in different genotypes or in males and females. Thus it is not surprising that Young's group turned to a central nervous system explanation for their findings in guinea pigs treated prenatally with testosterone.

The 1959 paper did not completely resolve whether hormones organize the nervous system or other tissues and if they do 'organize' neural tissues, the nature of such organization. The title of the paper

Download English Version:

<https://daneshyari.com/en/article/324134>

Download Persian Version:

<https://daneshyari.com/article/324134>

[Daneshyari.com](https://daneshyari.com)