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Editorial

Early ontogeny as a unique developmental epoch for learning, memory and consequences of alcohol exposure: A Festschrift to honor the work of Dr. Norman E. Spear

1. Introduction to the Special Issue

The developmental concepts of critical and sensitive periods for brain development—and the mechanisms by which early development defines both opportunities and vulnerabilities for an organism's future—have permeated the literature across all taxonomic orders. Indeed, pioneering studies that have identified early ontogeny as a unique developmental period cross a wide range of seemingly disparate fields. Though our interest in many cases lies in furthering our understanding of the human condition, substantive milestones have been accomplished through the use of preclinical (particularly rodent) models, whose brain and behavioral development can be readily aligned with that of humans (see Fig. 1). For instance, brain development during the first postnatal week in rat is considered to be the developmental equivalent of the third trimester in humans based on brain maturation processes ongoing at that time. Whereas the first week or so after weaning is often considered to be the juvenile period in rat, early manifestations of adolescence begin to emerge at around P28 and subside around P65. Rats are considered to be fully mature, young adults starting about P70–P90, and at this point investigators often switch from a focus on early developmental processes toward examination of aging and lifespan-related issues. Thus, rats aged 9–15 months probably correspond to middle-aged humans of about 40–60 years old, whereas 18 months often demarcates early stages of senescence in the laboratory rat. There are, of course, notable species and strain differences in neurobehavioral development that might cause these age boundaries to "slide" somewhat across rodent model systems. Nevertheless, the developing rodent provides a superb model through which cross-sectional and longitudinal studies can be performed readily, thereby underscoring the value of rodent models for advancing our understanding of brain–behavior relationships in a diverse range of research areas.

Regardless of the species/strain being studied, developmental models have taught us that sophisticated analyses of sensory/perceptual, cognitive, and behavioral processes require extraordinary attention to innate differences in how developing organisms transduce, perceive, and encode environmental and social experiences throughout the lifespan. Furthermore, developmental research has illustrated that the building blocks of early experience give rise to neural rubrics which guide early behavior and often persist, even if in latent form, for a lifetime. Today, advances in our understanding of molecular physiology have extended many of these "programming" effects into altered genomic function that can even endure across generations.

Several guiding principles have emerged from the study of early life experiences and form the common parlance of developmentally oriented psychologists and neurobiologists. For instance, early exposure to enriched environments appears to confer competitive advantage relative to individuals from impoverished environments. Similarly, adverse early life experiences (social or nutritional deprivation, harsh rearing conditions, or hostile environments) appear to engrain long-lasting health and disease vulnerabilities throughout life. Together, the relative balance of enrichment (opportunity) versus adversity (threat) has shaped not only the development of the organism exposed to such circumstances, but also the major questions being asked in the field of developmental psychobiology.

There have been many pioneers who have identified early ontogeny as a unique developmental epoch during which experience (or lack thereof) hard-wires behavior and brain function across the lifespan. The work presented in this Special Issue of *Physiology & Behavior* pays special tribute to one such pioneer in developmental psychobiology who has shaped the thinking of generations of scholars: our friend and colleague, Dr. Norman E. "Skip" Spear (see Fig. 2). As such, this Special Issue is organized into "epochs" that resemble areas related to Skip's work, whose contributions over nearly 50 years as an independent investigator gave birth to a wide range of basic and translational studies. This Special Issue evolved from a symposium held in May, 2014 to honor and recognize the contributions of Dr. Spear. Present at the symposium were many former students, long-term collaborators, and colleagues (Fig. 3), and we are pleased to dedicate the work presented in this Special Issue to him. Not only has Skip contributed significantly to all of the research areas contained in this collection, but he has also shaped the intellectual development and scholarly achievements for many of the authors in this issue. In this way, it seems fitting to distinguish the work of a pioneer in developmental psychobiology with a developmentally-themed Special Issue.

In the first section, you will find a series of articles examining developmental differences in basic aspects of cognitive function, and how these developmental differences are altered by early alcohol exposure. For instance, Revillo et al. (in this issue) [1] reviewed the literature on context learning as a means to better understand cognitive development in both rodents and humans. This article presented a summary of two, often competing, hypotheses regarding the acquisition of cognitive abilities across early development. Whereas some studies seem to support a gradual accumulation of cognitive abilities that corresponds with neuronal maturation (particularly in the hippocampus for context learning effects), other studies seem to support the hypothesis that

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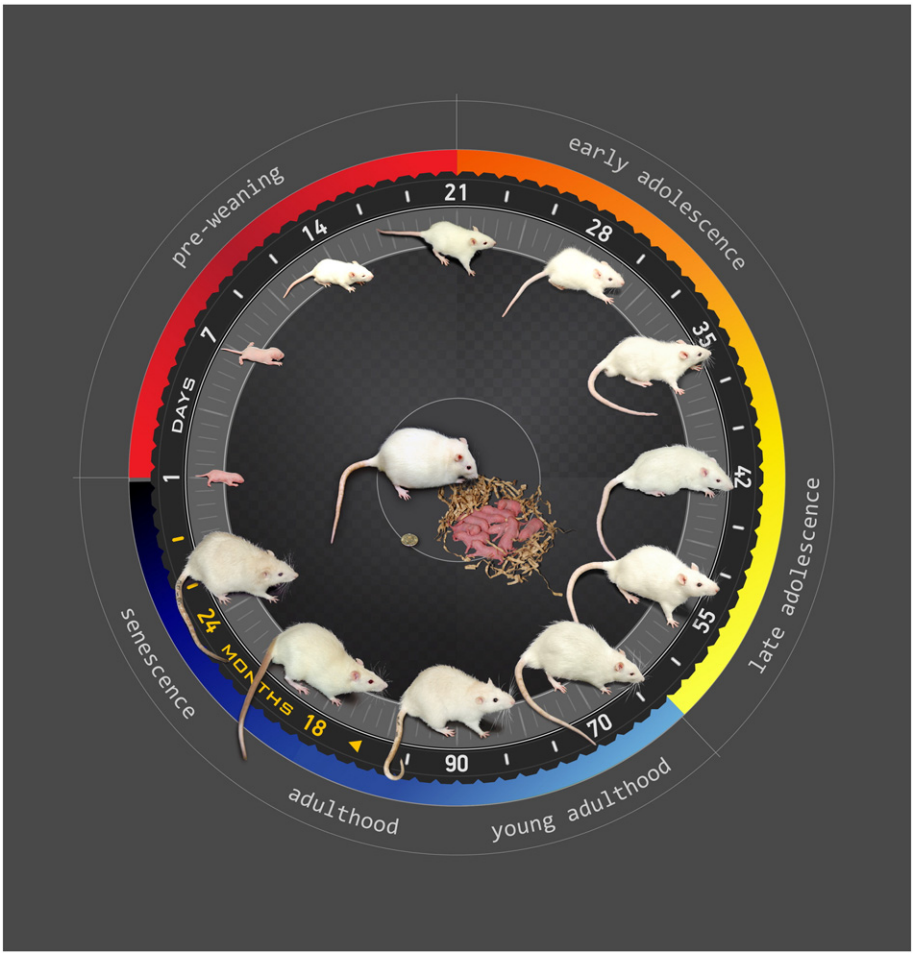

Fig. 1. Schematic illustration of developmental stages in the rat, from birth through senescence, which have often been the focus of early ontogenetic investigations in the field of developmental psychobiology (early postnatal/preweaning stage; early to late adolescence; young adulthood; adulthood; and senescence). The photos shown in this figure were taken by Anny Gano and Dr. Tamara Doremus-Fitzwater. We are grateful for the excellent illustration work contributed by Igor Khramov in the production of this graphic.

infants rely on distinct cues (relative to adults) and attentional processes that are optimized to their developing niche, but are not necessarily reflective of deficits in cognitive function per se (relative to adults). Robinson-Drummer and Stanton (in this issue) [2] utilized the well-established context pre-exposure facilitation effect (CPFE) in order to better understand differences in cognitive capacity as a function of early ontogeny. It was demonstrated that younger rats show weaker retention of the CPFE effect relative to older animals, with these findings extending what is already known about infantile amnesia and the gradual addition of complex cognitive abilities across early ontogeny. Chan et al. (in this issue) [3] assessed the role of glutamatergic signaling via the NMDA receptor using a fear conditioning procedure in preweanling rats. In addition to replicating previous findings showing that memories for fear conditioning erode rapidly when training occurs at an early age (training on P17, forgetting by P27), these data helped elucidate the role of NMDA-dependent and independent processes in the forgetting response.

Together, these fundamental, age-related differences offer important insight into the nature of cognitive development in preclinical models, and provide a foundation for better understanding alterations in cognitive development induced by other challenges, such as the response to early alcohol (ethanol) exposure. As a first example of this theme, Hunt and Barnet (in this issue) [4] examined the impact of early postnatal ethanol exposure (5 g/kg from P4–P9; a developmental period corresponding to the third trimester in humans) on trace conditioning deficits observed during early adolescence. Interestingly, the deficits in peri-adolescent trace conditioning produced by ethanol in this model were effectively reversed by dietary supplementation of choline or acute physostigmine at the time of conditioning, providing promising alternatives for rescuing cognitive deficits that may be characteristic of Fetal Alcohol Spectrum Disorders (FASD). In a highly relevant translational study, Infante et al. (in this issue) [5] examined ADHD symptomatology in 7–14 year old children with an established history of Prenatal Alcohol Exposure (PAE). Their findings supported the notion that inattention represents a core deficit in children prenatally exposed to ethanol, and may explain other cognitive deficits associated with FASD.

The second section includes a series of articles examining the impact of early sensory experience on preferences for, and acceptance of, odors and cues experienced early in life. For instance, Kamenetzky et al. (in this issue) [6] performed an interesting set of studies designed to assess how neonatal exposure to a novel odorant (within a few hours of birth) impacted consumption of either palatable or aversive tastants. They found greater consumption of an aversive solution (quinine), but not of a palatable one (saccharin) in the presence of the familiar odor cue, suggesting that neonatal rats were more accepting of (normally aversive) substances in the presence of familiar cues. Gaztanaga et al. [7] (in this issue) tested a similar hypothesis regarding how early sensory experiences via the chemical senses (odorant and tastant) impact later chemosensory preferences. They found that prenatal exposure to either vanilla or alcohol odor led to increased neonatal crawling behavior when rat pups were re-exposed to the same cue. Additionally, they found that the enhanced crawling behavior toward either vanilla or ethanol was blocked by mu opioid receptor antagonism, whereas kappa