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Review article

Adolescent transitions in reflexive and non-reflexive behavior: Review of fear conditioning and impulse control in rodent models

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ABSTRACT

Adolescence is a time of critical brain changes that pave the way for adult learning processes. However, the extent to which learning in adolescence is best characterized as a transitional linear progression from childhood to adulthood, or represents a period that differs from earlier and later developmental stages, remains unclear. Here we examine behavioral literature on associative fear conditioning and complex choice behavior with rodent models. Many aspects of fear conditioning are intact by adolescence and do not differ from adult patterns. Sufficient evidence, however, suggests that adolescent learning cannot be characterized simply as an immature precursor to adulthood. Across different paradigms assessing choice behavior, literature suggests that adolescent animals typically display more impulsive patterns of responding compared to adults. The extent to which the development of basic conditioning processes serves as a scaffold for later adult decision making is an additional research area that is important for theory, but also has widespread applications for numerous psychological conditions.

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1. Introduction

Characterized by novel alterations in behavior, growth, and structural remodeling of the brain (Brenhouse and Andersen, 2011; Caballero and Tseng, this volume; Juraska et al., 2013; Stevens, this volume; Smith et al., 2015; Spear, 2000), adolescence may represent a unique period in cognitive development, different from prior and later life stages. This can be contrasted to a view of adolescence as reflecting a more linear transition to adulthood, when learning and other cognitive processes become progressively, and monotonically, more mature. However, isolating and characterizing adolescent-unique patterns of development is made complex given that there are many distinct components to learning and memory (e.g., encoding, maintenance, retrieval), as well as different forms of learning ranging, for example, from simple reflexive classical conditioning to more complex non-reflexive processes of complex choice behavior and decision-making. The present review brings focus to these latter different dimensions of cognitive function and behavior, namely, classical conditioning and decision making.

Although not well integrated in the literature there are important connections between these two areas. Many processes recognized as critical to more complex aspects of cognition such as decision making are also known to be affected by classical conditioning, including attention (Pearce and Hall, 1980), learning (Rescorla and Wagner, 1972), value representation (Holland and Rescorla, 1975), response selection (Bolles, 1970; Fanselow, 1994; Miller and Matzel, 1988) and inhibition (Pavlov, 1927; Rescorla, 1969). Our review of classical conditioning and decision making in adolescents will be presented in separate sections. As we suggest later, a significant future research area is how variation in the development of basic associative learning processes affects decision making. The first section of this review considers behavioral plasticity, specifically learning, involved in classical fear conditioning. The second section considers more complex aspects of cognition, specifically, impulse control in decision making. Thus, the two sections of review span reflexive and non-reflexive dimensions of behavior in adolescence. It is noteworthy that the extensive and analytical review of adolescence by Spear (2000) in this journal over 15 years ago acknowledged and cited the limited nature of available evidence for adolescent-unique performance in basic fear learning tasks (the first section of the present review; in Spear, 2000; see p. 423 "Cognitive development" section). Since that time there have important advances we highlight in this review. We equally highlight significant remaining gaps in current literature. Our review expands upon basic findings on adolescence from conditioning experiments to also include issues of impulse control in decision making. Given the paucity of data available on these topics from studies comparing adolescent animals to other age groups our review will be intentionally focused. An overall summary of the literature discussed in this review is presented in Table 1 which is intended as a useful aggregate of available findings.

2. Defining adolescence in rodent models

In its broadest sense, adolescence refers to a transitional period between the parental dependence of childhood and the independence and sexual maturity of adulthood. Adolescence can be considered in many ways (e.g., social, emotional, cognitive, hormonal and neural) and, depending upon the specific question being asked, adolescence may be defined in a more restrictive sense that is based upon the observation of a specific behavior or measure (Adriani and Laviola, 2004; Juraska et al., 2013; Spear, 2000). Within the adolescent period there can be further distinctions spanning early, middle-, to late-adolescence.

In rodents (rats and mice), this transitional period between maternal dependence and adulthood occurs between the time of typical laboratory weaning (postnatal day [PD] 21) and the attainment of sexual maturity (PD 60 or even up to approximately PD 70, cf. Smith et al., 2015). Many researchers, however, may use a more limited range of ages, based on the age-specific behavior of interest, to define adolescence (e.g. Juraska et al., 2013; Smith et al., 2015; Spear, 2000), sometimes discriminating between early (PD 24–35, Adriani et al., 2002; centered around PD 30, Juraska et al., 2013) middle, (PD 37–48, Adriani et al., 2002) and late adolescence (PD 50–61, Adriani et al., 2002) although it is recognized there are no strict age-limits defining these phases (Adriani and Laviola, 2004). Thus the operational age range of PD 21 to PD 60 includes the adolescent period. However, given our desire to capture more of the limited available literature characterizing adolescent performance in basic conditioning and decision making (i.e., operant choice tasks), some papers reviewed vary from this range. As seen throughout this journal volume, the specific age range used to capture a rodent adolescent period also varies across laboratories. Nonetheless, most investigators would agree that PD 30–35 is part of the adolescent period and the majority of studies in this review include animals in this age range. We will also include discussion of data from younger and older subjects, when available, placing the adolescent within broader developmental context.

2.1. Defining fear: procedures for induction and measurement

Fear is a central emotional state that confers advantage in the face of threat. The fear state elicits reflexive behaviors that are protective and enhance survival and has been preserved both phylogenetically and ontogenetically (Bolles, 1970; Bolles and Fanselow, 1980; Hunt and Campbell, 1997). Decades of animal research, primarily with rodents (rats and mice), together with more recent human neuroimaging data, serve to highlight the fact that the neural systems regulating fear, and the variety of ways in which fear is expressed, have also been conserved (Cain et al., 2013; Craske et al., 2006; Davis et al., 2010; Debiec and LeDoux, 2009). There is also a clear similarity between fear studied in animals and human anxiety (Craske et al., 2006; Perusini and Fanselow, 2015). Both humans and animals show conditioned fear potentiation of the startle reflex (in rats, Davis et al., 1993; in humans, Grillon and Davis, 1997), contextual modulation of startle (in rats, McNish et al., 1997; in humans, Ameli et al., 2001), conditioned fear modulation of heart rate (in rats, Hunt et al., 1997; Iwata and LeDoux, 1988; in humans, Hamm et al., 1993), and blood pressure (in rats, LeDoux, 2000; in humans, De Leon, 1972, see also Reiff et al., 1999). Other common measures related to fear and anxiety include conditioning of skin conductance in humans (Hamm et al., 1993; Öhman, 1974) and freezing in rodents (Bolles, 1970; Fanselow, 1994). Thus, findings and conclusions based on research with animal subjects can, to some extent, generalize to human fear and anxiety. Furthermore, fear conditioning can be used to address fundamental questions regarding the mechanisms underlying learning and memory formation across species and ages (e.g. Dumas and Rudy, 2010; LeDoux, 2000; Pattwell et al., 2012; Powell et al., 1997; Richardson and Hunt, 2010; Sullivan et al., 2010).

Fear can be studied in the lab using well-controlled experiments employing classical conditioning paradigms (Cain et al., 2013; Davis et al., 2010; Maren, 2001; Perusini and Fanselow, 2015). In classical conditioning, a neutral stimulus (conditioned stimulus, CS) such as a tone or light is followed by the onset of an aversive stimulus (unconditioned stimulus, US) such as a brief footshock or loud noise. During this training procedure, the subject learns not only about the predictive nature of the CS, but also about the context in which the CS-US pairings occur. Upon presentation of the CS or context during test, animals display a variety of observable or measurable changes