Contributors to and consequences of adolescent alcohol exposure: Studies in a rodent model

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Adolescents ingest more alcohol per occasion than do adults. This age effect is evident not only in human adolescents but also in laboratory animals undergoing this developmental transition, suggesting that such intakes may be partly biologically based. Work using rodent models of adolescence will be summarized that has revealed several potential contributors to these elevated intakes, as well lasting consequences of repeated ethanol (EtOH) exposure during adolescence.

Methods: Male and female Sprague-Dawley rats were either examined for their responses to acute EtOH challenge during early-mid adolescence (~postnatal day [P]25-45), or exposed every other day to 3.5 or 4 g/kg EtOH intragastrically during early/mid adolescence, late adolescence/ emerging adulthood (P45-65), or adulthood (P70) and examined later in adulthood.

Results: Adolescent rats were found to be more sensitive to the social facilitating and rewarding effects of relatively low doses of EtOH than mature rats, but were notably insensitive to motor-impairing, sedative, socially-impairing, aversive and hangover effects of higher doses of EtOH that likely serve as cues to moderate intake. These adolescent-typical EtOH sensitivities are not a function of age-related differences in pharmacokinetics but rather may reflect enhanced expression of acute (within session tolerance), along with apparent developmental differences in neural systems underlying various EtOH effects. Such adolescent-typical responses to acute EtOH are often atypically maintained into adulthood after repeated adolescent intermittent EtOH (AIE) exposure. Consequences of AIE sometimes differ in males and females and following exposure during early-mid adolescence versus later in adolescence with, for instance, early (but not late) AIE inducing replicable increases in social anxiety in males, but not females. AIE-induced decreases in choline acetyltransferase immunoreactivity in basal forebrain and in hippocampal neurogenesis were not evident after analogous EtOH exposure in adulthood.

Discussion: Although few comparable data are available among human adolescents, the findings which are available suggest that similar patterns of EtOH sensitivities may be evident in human youth. Such adolescent-typical enhanced sensitivities to EtOH's rewarding and social facilitatory effects combined with a relative resistance to intoxicating, intake-moderating consequences of EtOH may permit/encourage relatively high consumption of EtOH at this time, especially among adolescents who are at particular risk for elevated EtOH intake due to additional genetic or environmentally-associated insensitivities to EtOH intoxication. Such elevated exposures may lead to

adverse effects among at-risk adolescents that persist into adulthood. Indeed, our findings using a rodent model of adolescence have revealed certain long-lasting consequences of repeated exposure to EtOH during adolescence that are replicable, sex-specific and dependent on timing of the EtOH exposure, with early adolescence being perhaps an especially vulnerable period, and comparable exposures later in life not inducing similar effects.

Funding was provided by NIH grants P50 AA017823 and U01 AA019972 – NADIA project.