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Abstract title: Adequate Prenatal Choline May Mitigate The Negative Impact of Marijuana Use During Pregnancy On The Developing Child

Background: Anxiety, nausea, pain, and mood are the most common reasons why pregnant women report continuing marijuana use during pregnancy despite recommendations against its use due to adverse effects on the child's subsequent cognition and behavior. Prenatal choline has positive effects on the (neuro)development of the offspring of healthy women and in women with mental illness, early pregnancy infection, and alcoholism. Choline targets acetylcholine receptors on fetal cerebro-cortical inhibitory neurons whose development is, conversely, impeded by cannabis blockade of their cannabinoid 1 (CB1) receptors.

Objective: The objective of this study was to assess whether higher maternal choline levels mitigate the adverse effects of prenatal marijuana use on fetal brain development when mothers refuse to stop use, as measured by newborn cerebral inhibition and 3-month behavioral ratings.

Study Design/Methods: Self-report of marijuana use and urine toxicology were obtained during pregnancy from 162 women who ultimately brought their infants for study. Planned outcomes were fetal development of cerebral inhibition measured electrophysiologically in the newborns and subsequent attention and related behavior using the Infant behavioral questions (IBQ) at 3 months of age. Mothers were informed that drug use would be assessed as part of a study of stressors during pregnancy and informed about dietary choline and other nutrients, but not specifically in regard to marijuana use. Choline levels were measured at 16 weeks gestation. All women were advised by research and clinical personnel to cease marijuana use as per clinical standards.

Results: Forty percent (64) of mothers used marijuana at conception. Women who stopped before 10 weeks gestation had infants who were similar to infants whose mothers had never used. Continued use at 10 weeks gestation and later by 15% of mothers was correlated with decreased inhibition of evoked potentials to repeated sounds ($d' = 0.55$, $P < 0.05$). This effect was ameliorated in women with higher gestational levels of choline ($r_s = -0.50$, $P = 0.011$). At 3 months of age, infants whose mothers continued gestational marijuana use for 10 weeks or more had poorer self-regulation ($d' = -0.79$, $P < 0.05$). This effect was also ameliorated in mothers with higher gestational levels of choline ($r_s = 0.54$, $P = 0.013$). Higher maternal choline levels correlated with the infant's improved attention, cuddliness and bonding with parents.

Conclusions: Marijuana use continuing through 10 weeks gestation or later adversely affects fetal brain development and subsequent behavioral self-regulation, a precursor to more serious attention and social problems in later childhood. These effects were prevented by stopping marijuana use before 10 weeks gestation. However, many mothers continued use, because of their familiarity with marijuana and belief in its safety and efficacy. Higher maternal choline levels mitigated some of marijuana's

adverse effects on the fetus/infant. As choline appears to act as a buffer of fetal brain development from adverse exposures (known and unknown, it should be recommended to pregnant women as part of their routine prenatal supplement regimen.