



ERIMETER LETTER 8.2.05

*In a recent 4-week crossover trial of 47 children with ADHD, those homozygous for the 9-repeat variant of the dopamine transporter 3'-untranslated region variable number tandem repeat (VNTR) allele (n=6), relative to children with at least one 10-repeat allele (n=41), had less response to scheduled increases in the dose of Concerta, as assessed by the ADHD Rating Scale (*Neuropsychopharmacology*. 2005 Jul;30:1374-82). Interestingly, boys with a SWAN ADHD score over the 90th percentile (n=55) compared to boys with a score below the 10th percentile (n=64) had an odds ratio 2.4 (95%CI 1.1 to 5.0) of being homozygous for the 10-repeat allele of the dopamine transporter gene (DAT1) versus having one or two 9-repeat alleles; and, after linear regression, there appeared to be an association between the homozygous 10-repeat genotype and response inhibition (*Mol Psychiatry*. 2005 Jul;10:686-98). Furthermore, neuroimaging of patients with ADHD, unaffected siblings, and healthy subjects revealed prefrontal gray matter volume reduction in 34 individuals homozygous for the 4-repeat variant of the dopamine D4 receptor gene (DRD4) versus 36 carriers for this variant (effect size $d=0.6$, 95%CI 0.1 to 1.1) as well as caudate nucleus volume reduction in 40 individuals homozygous for the 10-repeat variant of DAT1 versus 32 carriers for this variant ($d=0.6$, 95%CI 0.1 to 1.1) (*Mol Psychiatry*. 2005 Jul;10:678-85). Abstinent methamphetamine users (n=35) had reduced regional cerebral glucose metabolism in right superior frontal white matter and increased errors on the Wisconsin Card Sort Test compared to healthy subjects (n=21) and there was a correlation between the two findings (Pearson's $r=-0.45$, $p<0.01$) (*Neuropsychopharmacology*. 2005 Jul;30:1383-91). Regarding another stimulant, mice expressing a mutant NR1 subunit of the NMDA receptor channel that reduces calcium flux did not show increased ambulation with chronic administration of cocaine, unlike the locomotor sensitization seen in wild-type mice, and they showed less preference for the location of repeated cocaine administration compared to wild-type mice (*J Neurosci*. 2005 Jul 13;25:6651-7). In another investigation of hedonic reinforcement, rats learning to obtain food after an auditory cue, with 28 trials per day, showed increased latency to response after receiving a D1 receptor antagonist versus receiving a placebo on day 3 of training, but not after receiving a D1 receptor antagonist on days 7 or 17 of training or after receiving the D2 antagonist raclopride, despite persistent ability of the D1 and D2 receptor antagonists to reduce general locomotion (*J Neurosci*. 2005 Jul 20;25:6729-33).*

*Unexpectedly, real-time quantitative reverse transcriptase-PCR of the adenomatous polyposis coli gene (APC) in leukocytes showed increased expression in schizophrenic patients (n=59) versus healthy control subjects (n=30) ($d=0.6$, 95%CI 0.2 to 1.1) and 3 APC single-nucleotide polymorphisms were pinpointed by transmission disequilibrium test analysis of 163 schizophrenic parent-child trios (*Mol Psychiatry*. 2005 Jul;10:669-77). The auditory cortex of the superior temporal gyrus is recruited when people imagine hearing music, according to this review (*Neuron*. 2005 Jul 7;47:9-12). Functional MRI revealed reduced correlations between low-frequency blood oxygen level-dependent fluctuations in anterior cingulate cortex and limbic areas, viz.,*

pallidostriatum, medial thalamus, and amygdala, in 12 unmedicated depressed patients versus 11 matched healthy subjects while they viewed positive and negative pictures and at rest; but after 6 weeks of sertraline the depressed patients showed increased correlations, relative to baseline, between anterior cingulate cortex and limbic areas while viewing positive pictures and at rest (*Neuropsychopharmacology*. 2005 Jul;30:1334-44). In another approach to affective disorders, doses of estradiol that produced physiological plasma levels in ovariectomized rats, compared with placebo and lower and higher doses of estradiol, reduced anxiety (open field and elevated plus maze tests) and depressive (forced swim test) behaviors and reduced corticosterone levels, whether or not rats experienced a 20-minute restraint stressor before testing (*Neuropsychopharmacology*. 2005 Jul;30:1288-301). Examining time to therapeutic onset, chronic administration of escitalopram and citalopram to rats initially decreased the firing rate of dorsal raphe serotonergic neurons, but firing rate returned to baseline after 2 weeks of escitalopram and 3 weeks of citalopram, with an attendant desensitization of 5-HT_{1A} inhibitory autoreceptors (*Neuropsychopharmacology*. 2005 Jul;30:1269-77). Glycogen synthase kinase-3 (GSK-3) appears to be an important mediator of the therapeutic effects of lithium and most other psychotropics, according to this review (*Neuropsychopharmacology*. 2005 Jul;30:1223-37).

In a genetic rescue, the excessive aggression and abnormal forebrain and ocular structure seen in mice lacking the nuclear receptor 2E1 gene were not present when such mice carried the human NR2E1 gene and its promoter and regulatory regions (*J Neurosci*. 2005 Jul 6;25:6263-70). Lactating rats bred for high anxiety behavior, compared with lactating rats bred for low anxiety behavior, showed more aggression toward an intruder and this aggression correlated positively with oxytocin levels in the paraventricular nucleus of the hypothalamus ($r^2=0.6$, $p=0.005$) and the central nucleus of the amygdala ($r^2=0.7$, $p=0.004$); and infusion of an oxytocin receptor antagonist into the paraventricular nucleus or the central amygdaloid nucleus reduced aggression in high-anxiety lactating rats (*J Neurosci*. 2005 Jul 20;25:6807-15). Elucidating another aspect of anxiety, increased magnitude of hippocampal theta-frequency oscillations was observed in mice lacking the serotonin 1A receptor gene while they underwent a test of anxiety, viz., the elevated plus maze, but not while in a familiar environment or during REM sleep, when compared with wild-type mice (*J Neurosci*. 2005 Jul 13;25:6509-19). Orexin neurons in the hypothalamus of rats were most active while animals were awake and moving and were quiescent during sleep, including REM sleep (*J Neurosci*. 2005 Jul 13;25:6716-20). In an attempted rescue of Alzheimer's, mice overexpressing a mutant amyloid precursor protein gene had no accumulation of β -amyloid peptides or amyloid plaques when their presenilin 1 gene was chronically inactivated, and inactivation of presenilin 1 in these transgenic mice was associated with responses on cognitive testing (contextual memory and serial spatial learning tasks) that matched the responses of wild-type mice, but only in the short term (*J Neurosci*. 2005 Jul 20;25:6755-64).



UKE RESEARCH

GENETICS

Genetic counseling for fragile x syndrome: updated recommendations of the national society of genetic counselors.

McConkie-Rosell A, Finucane B, Cronister A, Abrams L, Bennett RL, Pettersen BJ.
J Genet Couns. 2005 Jul;14:249-70.

MED-PSYCH

Loving-kindness meditation for chronic low back pain: results from a pilot trial.

Carson JW, Keefe FJ, Lynch TR, Carson KM, Goli V, Fras AM, Thorp SR.
J Holist Nurs. 2005 Sep;23:287-304.

Positive emotion and health: going beyond the negative.

Richman LS, Kubzansky L, Maselko J, Kawachi I, Choo P, Bauer M.
Health Psychol. 2005 Jul;24:422-9.

A dyadic investigation of exercise support between cardiac patients and their spouses.

Hong TB, Franks MM, Gonzalez R, Keteyian SJ, Franklin BA, Artinian NT.
Health Psychol. 2005 Jul;24:430-4.

PSYCHOLOGY

Decision making as coping.

Luce MF.
Health Psychol. 2005 Jul;24:S23-8.

TOXICOLOGY

Developmental and behavioral effects of embryonic exposure to the polybrominated diphenylether mixture DE-71 in the killifish (*Fundulus heteroclitus*).

Timme-Laragy AR, Levin ED, Di Giulio RT.
Chemosphere. 2005 Jul 18

BIOLOGY

An Akt/beta-Arrestin 2/PP2A Signaling Complex Mediates Dopaminergic Neurotransmission and Behavior.

Beaulieu JM, Sotnikova TD, Marion S, Lefkowitz RJ, Gainetdinov RR, Caron MG.
Cell. 2005 Jul 29;122:261-73.

Dopamine-Independent Locomotor Actions of Amphetamines in a Novel Acute Mouse Model of Parkinson Disease.

Sotnikova TD, Beaulieu JM, Barak LS, Wetsel WC, Caron MG, Gainetdinov RR.
PLoS Biol. 2005 Aug 2;3:e271



FIGURE OF THE WEEK



J Neurosci. 2005 Jul 6