



PERIMETER LETTER 8.9.05

Among 49 clinical research articles published from 1990 to 2003 and cited over 1000 times, 45 reported positive results, 16% of these were contradicted by later studies, 16% reported effects greater than in later studies, and randomized trials later contradicted or with greater effects had sample sizes in the hundreds compared to replicated or unchallenged trials, which had samples in the thousands (*JAMA*. 2005 Jul 13;294:218-28). There was no difference between groups in the combined rate of in-hospital major adverse cardiovascular events, 6-month readmission, and 6-month mortality when 748 patients receiving percutaneous coronary intervention or elective catheterization were randomized into 4 comparably sized groups to receive double-blinded off-site prayer versus none and on-site music, imagery, and touch therapy versus none (*Lancet*. 2005 Jul 16-22;366:211-7). In a randomized trial funded by Lilly, 431 of 543 enrolled patients with bipolar disorder who had a Young Mania Rating Scale (YMRS) below 12 and a Hamilton Depression Scale (HAMD) below 8 after treatment with both lithium and olanzapine for 6 to 12 weeks received either lithium ($n=214$) or olanzapine ($n=217$) for 52 weeks (171 completers), with 83 (39%) of the lithium patients and 65 (30%) of the olanzapine patients eventually experiencing YMRS or HAMD scores over 15 (NNT 11, 95%CI -6 to infinity), according to intention-to-treat analysis (*Am J Psychiatry*. 2005 Jul;162:1281-90). Forty-three children aged 6 to 16 with bipolar disorder who were assessed by MRI appeared to have smaller hippocampi than 20 healthy children and the effect may have been due to smaller total cerebral volume (effect size 1.1, $p<.001$), bipolar diagnosis (effect size 0.1, $p=.02$), or female sex (effect size 0.1, $p=.02$) (*Am J Psychiatry*. 2005 Jul;162:1256-65). The epidemiology, diagnosis, etiology, pathophysiology, and treatment of ADHD were reviewed (*Lancet*. 2005 Jul 16-22;366:237-48). Another review asserted that there are no known genes satisfying the criteria for causality in relation to a psychiatric disorder and that such genes will likely never be found (*Am J Psychiatry*. 2005 Jul;162:1243-52).

Of 20 children with abdominal injuries due to abuse and 52 with abdominal injuries due to a fall, 11 abused children versus 5 who had a fall sustained injury to the small bowel or stomach (odds ratio 11.5, 95%CI 3.2 to 41.1) (*Lancet*. 2005 Jul 16-22;366:234-5). In a study in Sudan of 99 women with primary infertility and 179 primigravid control subjects, 92 (93%) of the infertile women and 131 (73%) of the controls had the most severe form of genital mutilation, involving the labia majora, yielding an odds ratio of 4.7 (95%CI 1.5 to 19.7) between groups of having mutilation involving the labia majora versus lesser forms of mutilation or no mutilation, after adjusting for socioeconomic status, years in school, and seropositivity for gonorrhea or chlamydia (*Lancet*. 2005 Jul 30-Aug 6;366:385-91). Path analysis of the responses to several questionnaires of 72 children admitted for burns and their families during hospitalization and 3 months afterward revealed 2 sequences of risk factors: size of burn and degree of pain leading to separation anxiety leading to PTSD, and size of burn leading to dissociative symptoms leading to PTSD (*Am J Psychiatry*. 2005 Jul;162:1299-304). Similarly, among 156 children who reported sexual abuse and completed several questionnaires, path analysis suggested that avoidance, anxiety, and dissociation explained 57% of the variance in PTSD symptoms reported 7 to 36 months later (*Am J Psychiatry*. 2005 Jul;162:1305-10). A review discussed the neuroendocrine

pathophysiology of anorexia nervosa and exercise-induced hypothalamic amenorrhea, which includes low levels of leptin and low reproductive, thyroid, and growth hormones (*Lancet*. 2005 Jul 2;366:74-85). Linking data from the Swedish Military Service Conscription Register to data from other Swedish national registers revealed 3075 suicides among 1,299,177 men 18 to 49 years old followed for an average 15 years, and the hazard ratio for suicide for every 5-cm increase in height was 0.91 (95%CI 0.88 to 0.93) compared to the men within one-half a standard deviation from the overall mean height, after adjusting for age, birth year, conscription center, BMI, and parental socioeconomic index and education (*Am J Psychiatry*. 2005 Jul;162:1373-5).

When 205 of 400 eligible nursing home residents were randomized to receive an interview to determine their appropriateness for hospice care ($n=107$) versus not receiving an interview ($n=98$), more of those interviewed (20%) enrolled in hospice within 30 days than those not interviewed (1%) (NNT=5, 95%CI 4 to 9) (*JAMA*. 2005 Jul 13;294:211-7). When formulating an advance directive, attention should be paid to the affect of the patient and family members and to their treatment goals, instead of formulating a list of particular treatments based on contingency, according to this case study (*JAMA*. 2005 Jul 20;294:359-65). The modern hospice movement may have become too averse to death, according to this news story (*NY Times Magazine*. 2005 Aug 7). A news review described how pharmaceutical companies are struggling to find a drug for Alzheimer's disease (*Science*. 2005 Jul 29;309:731). Mice expressing A β 42 without A β 40 and without overexpression of amyloid β protein precursor developed amyloid plaques and angiopathy, which did not occur when only A β 40 was expressed; and amyloid deposits increased when A β 42 expression and amyloid β protein precursor overexpression were combined (*Neuron*. 2005 Jul 21;47:191-9). Historic atmospheric ^{14}C levels, which peaked during the nuclear bomb testing from 1955 to 1963, were measured in tree rings and compared with ^{14}C levels in the genomic DNA of occipital cortex neurons in 5 recently deceased persons born before 1955 and 5 born after 1963, thereby revealing that occipital neurons are as old as the person (*Cell*. 2005 Jul 15;122:133-43). A case of encephalomyelitis in an elderly man was discussed (*N Engl J Med*. 2005 Jul 21;353:287-95).

Two patients with marked medial temporal lobe lesions and complete anterograde amnesia were able to learn to discriminate a set of objects after months of trial and error even though, after a delay, they could not verbalize the task; but they were unable to perform immediately a similar task of sorting the objects (*Nature*. 2005 Jul 28;436:550-3). In a group of 36 white Americans and 37 black Americans, a conditioned fear response, as assessed by skin conductance, was acquired when pictures of white and black male faces were paired with a mild electric shock, but only pictures of the other race continued to elicit a fear response when pictures were repeatedly shown without being paired with an electric shock, thereby resisting extinction (*Science*. 2005 Jul 29;309:785-7). One hundred thirty-two new genes involved in synaptic function at the neuromuscular junction were found by screening particular *Caenorhabditis elegans* mutants for their resistance to an acetylcholine esterase inhibitor after being exposed to double-stranded RNAs that inactivated genes of interest by RNA interference (*Nature*. 2005 Jul 28;436:510-7). Evoked potentials in rat brain showed that D1 receptor activation promoted long-term potentiation in hippocampal projections to the nucleus accumbens but long-term depression in prefrontal cortical projections to the nucleus

accumbens, whereas D2 receptor inactivation promoted prefrontal long-term potentiation and hippocampal long-term depression in accumbal projections, and repeated cocaine administration altered these changes (Neuron. 2005 Jul 21;47:255-66). An author maintained that, to help patients quit smoking, clinicians should offer the 5 As – ask, advise, assess, assist, arrange – as well as nicotine replacement, bupropion, or both (JAMA. 2005 Jul 27;294:482-7). The tobacco company Philip Morris maintained secret ties to the research facility INBIFO, which chose not to publish results showing the harmful effects of secondhand smoke, according to this investigation (Lancet. 2005 Jul 2;366:86-92).



UKE RESEARCH

GENETICS

Psychiatric disease in the genomic era: rational approach.

Krishnan KR.

[Mol Psychiatry. 2005 Aug 2](#)

Identification of Significant Association and Gene-Gene Interaction of GABA Receptor Subunit Genes in Autism.

Ma DQ, Whitehead PL, Menold MM, Martin ER, Ashley-Koch AE, Mei H, Ritchie MD, DeLong GR, Abramson RK, Wright HH, Cuccaro ML, Hussman JP, Gilbert JR, Pericak-Vance MA.

[Am J Hum Genet. 2005 Sep;77:377-88.](#)

Maternal lineages and Alzheimer disease risk in the Old Order Amish.

van der Walt JM, Scott WK, Slifer S, Gaskell PC, Martin ER, Welsh-Bohmer K, Creason M, Crunk A, Fuzzell D, McFarland L, Kroner CC, Jackson CE, Haines JL, Pericak-Vance MA.

[Hum Genet. 2005 Aug 3;:1-8](#)

FORENSICS

Criminal records of homicide offenders.

Cook PJ, Ludwig J, Braga AA.

[JAMA. 2005 Aug 3;294:598-601.](#)

GERIATRICS

Declining prevalence of dementia in the U.S. elderly population.

Manton KC, Gu XL, Ukraintseva SV.

[Adv Gerontol. 2005;16:30-7.](#)

TOXICOLOGY

Alterations in central nervous system serotonergic and dopaminergic synaptic activity in adulthood after prenatal or neonatal chlorpyrifos exposure.

Aldridge JE, Meyer A, Seidler FJ, Slotkin TA.

[Environ Health Perspect. 2005 Aug;113:1027-31.](#)

Persisting behavioral consequences of prenatal domoic acid exposure in rats.

Levin ED, Pizarro K, Pang WG, Harrison J, Ramsdell JS.

[Neurotoxicol Teratol. 2005 Jul 26](#)

Marine and freshwater toxin impacts on neurobehavioral function.

Levin ED.

[Neurotoxicol Teratol. 2005 Jul 27](#)



FIGURE OF THE WEEK



NY Times Magazine. 2005 Aug 7