

ABSTRACTS

Behavior Genetics Association Abstracts

Nelson Adams,¹ W. N. Peterson,¹ and R. C. Colley.¹ **Social Behavior in Maudsley Reactive and Nonreactive Rats.** Although there is a large literature on the Maudsley inbred rat strains, there are few data on the social behaviors of these rats. The present investigation examined the development of social behavior in juvenile Maudsley Reactive (MR/Har) and Nonreactive (MNRA/Har) and the expression of offensive aggressive behavior in adult males of these strains. Experiment 1 sampled the behavior (25 to 30 time samples/week) of eight colonies of each strain between 33–35 and 53–55 days of age. Each colony was composed of 4 males and 2 females marked for individual identification. Whereas there were no overall general activity differences (time spent outside of the nestboxes), the MNRA rats were more exploratory and engaged in more play behavior and in more play fighting (pinning). Sex differences and decreases in play fighting across ages were consistent with other studies of rat social play. Experiments 2 and 3 investigated adult aggression through resident-intruder designs where MR and MNRA males (4–6 months of age) were exposed to either intruders of their own strain (Expt 2) or a standard opponent (Expt 3) on 3 or more consecutive days. Various measures of offensive behavior in residents (e.g., latency and duration of attack behavior) and defeat behavior in intruders suggested that MR males were more aggressive than MNRA males. Differences in social behavior across these strains may provide valuable information for the Maudsley model.

V. Elving Anderson² and M. Leppert.³ **Mapping the Gene for Benign Familial Neonatal Convulsions.**⁴ The epilepsy syndrome known as benign familial neonatal convulsions (BFNC) has a unique developmental pattern. By the fifth day of life there are up to 15 seizures per day, each lasting a few minutes, and often with additional episodes of cyanosis. These usually stop by 3 weeks of life (in most cases by 3 months). In 10–14% of cases there are seizures later in life. The condition follows an autosomal dominant inheritance pattern. The risk to siblings and offspring is 42%, as compared with the expected 50% (indicating high penetrance). In one large family with 19 affected members the gene for BFNC has been localized to the long arm of chromosome 20 (M. Leppert *et al.*, *Nature* 337:647–648, 1989. Two polymorphic DNA loci are tightly linked to the disease locus. (Joint analysis of the three loci gave a lod score of 5.64.) The issue of genetic heterogeneity is being studied by testing additional families with the two markers. Attention then can be directed towards a search for the gene and an explanation for the distinctive developmental pattern of the seizures.

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J. Michael Bailey.⁵ A Test of the Maternal Stress Hypothesis for Human Male Homosexuality. A growing body of evidence suggests a biological and, particularly, a neurohormonal etiology for human male homosexuality. In contrast to most other traits, there is a rather strong a priori argument against the likelihood of substantial heritability for sexual orientation, due to natural selection. The discovery that prenatal stress behaviorally feminizes male offspring in rats (I. Ward, *Science* 175:82–84, 1972) provides an environmental model, plausible for humans, which could account for the neural feminization required by the neurohormonal theory of male homosexuality. Dorner (*Exp Clin. Endocrinol.* 81:83–87, 1983) has presented evidence supporting a strong maternal stress effect for human male homosexuality; however, his methodology was grievously flawed. We tested the maternal stress hypothesis using mothers' retrospective reports of event during pregnancy. A within-family analysis was also done, as mothers also rated stress for their pregnancies with one heterosexual sibling for each subject. Results of both between- and within-families analyses were strikingly negative. However, stress-proneness of mothers (as measured by personality scales) correlated positively with childhood effeminacy of male offspring, thus providing some support for a modified maternal stress hypothesis. Because of the overall failure to confirm the maternal stress hypothesis and because homosexuality is familial (replicated in the present study), it is recommended that genetic explanations be pursued more vigorously. Different genetic models for homosexuality are discussed, as well as potential tests for the models.

Cindy S. Bergeman⁶ and H. M. Chipuer.⁶ A Twin/Adoption Study of the "Little Three" of the "Big Five" Personality Traits: Openness to Experience, Agreeableness, and Conscientiousness.⁷ The focus of the present study is to assess genetic and environmental influences on the three components of the five-factor model of personality that have not received as much attention as Extraversion and Neuroticism: Openness to Experience, Agreeableness, and Conscientiousness. An abbreviated version of the Openness to Experience, Agreeableness, and Conscientiousness scales from the NEO Personality Inventory was administered to 82 pairs of identical twins reared apart (MZA), 132 pairs of identical twins reared together (MZT), 171 pairs of fraternal twins reared apart (DZA), and 167 pairs of fraternal twins reared together (DZT) as part of the Swedish Adoption/Twin Study of Aging (SATSA). The average age of the sample at the time of testing was 59 years. Estimates of genetic and environmental effects for Openness to Experience and Conscientiousness were similar to those found in studies of Extraversion and Neuroticism: genetic influence was substantial and there was little evidence of shared rearing environment. However, results for Agreeableness were different: genetic influence accounted for only 12% of the variance and shared rearing environment accounted for 21% of the variance.

Cindy S. Bergman⁸ and P. Wamboldt.⁸ Environmental Influences on Twin Resemblance for Personality Across the Life Span.⁹ Environmental influences on development are likely to

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be "poly-environmental" and pleiotropic and difficult to pinpoint using specific measures of the environment. Behavioral genetic model-fitting designs can estimate the relative importance of several types of environmental influences on personality development which contribute to twin resemblance: shared rearing environment, correlated environments, and MZT assimilation or DZT contrast effects. The effects of shared rearing environments make twins growing up together more similar than twins reared apart in uncorrelated environments. Most studies have concentrated on this type of environmental influence. Another type, correlated environments, assesses similarity for twins beyond resemblance due to heredity and shared rearing environment. This includes adult contact as well as the effects of selective placement. In addition, a special type of shared rearing environmental effect, specific to twin studies, is an MZT assimilation or DZT contrast effect which violates the equal environments assumption of the twin method. Recent data from the Swedish Adoption/Twin Study of Aging (SATSA), with twins reared together and apart, provide estimates of the relative contributions of these environmental influences on personality development across the life span.

Joseph Berta¹⁰ and James R. Wilson.¹⁰ Selection in Mice for Alcohol Withdrawal Seizures.¹¹

In a previous selection study, replicate high (Severe Ethanol Withdrawal: SEW₁, SEW₂), low (Mild: MEW₁, MEW₂), and control (CEW₁; CEW₂) lines of mice were selected for 23 generations using as a selection index a weighted sum of 7 behavioral and physiological indicators of alcohol withdrawal severity. The limits to selection seem to have been reached at generation 14 and the mice are now being inbred within line. Although the lines differ significantly, the differences are not large. They do show interesting characteristics: All 6 lines now voluntarily consume 150–200% more ethanol in their liquid diet than did the base population and all lines reach surprisingly high BACs when administered ethanol in an inhalation chamber (Crabbe, personal communication). We are now developing another mouse model of the alcohol withdrawal syndrome, based on a simpler selection index that we expect will lead to larger between-line differences. Beginning with 372 heterogeneous stock (HS/ibg) mice, each mouse was fed a mixture of liquid diet (AIN76) and ethanol for 11 days. On Days 1–2 the mice received 10% ethanol-derived calories (e.d.c.) in their liquid diet; on Days 3–4, 20% e.d.c.; on Days 5–6, 30% e.d.c.; and on Days 7–11, 32% e.d.c. Tap water was available at all times. On Day 12, the ethanol diet was withdrawn at 7 AM and replaced with alcohol-free diet and lab chow. At 7, 9, 11, 1, and 3 o'clock, each mouse was tested for seizures using the Goldstein–Pal index. Using the sum of the seizure scores as the selection index, replicate high (HA₁, HA₂), low (LA₁, LA₂), and control (CA₁, CA₂) lines were formed, with 10 pairs per line. Results of testing the first-generation offspring indicate a heritability of 0.14 (averaged across lines) for the new "area under the seizure curve" selection index. If success in selection continues, a valuable new model for studying the alcohol withdrawal syndrome will be available.

Aksel Bertelsen.¹² Beyond the Usual Strategies in Psychiatric Genetics: Offspring of Dual-Mating Psychiatric Inpatients and Offspring of Discordant Identical Twins.¹³ The advances in our understanding of the genetic aspects of major mental disorders such as schizophrenia and affective psychoses have resulted from careful family, twin, and adoption studies conducted since 1916. New strategies to complement such information are now possible through

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the use of the Danish National Psychiatric Register to identify all psychiatric inpatients who have had offspring by other psychiatric inpatients and to follow such offspring well into the risk periods for major mental disorders. This strategy is analogous to the diallel cross methods of plant and animal genetics for mendelian traits except that the parents in dual-matings have complex phenotypes and all combinations are observed ranging from schizophrenia X schizophrenia to severe personality disorder X reactive psychosis. The combination of the Psychiatric Register with the Twin Register permits the observation of the disorders, if any, in the offspring of identical twins affected with schizophrenia or manic-depressive disorder and their normal cotwins. Data are thus revealed about the complexities of gene expression for complex traits. Strategic implications, difficulties, and initial results are presented from this work conducted in Denmark with I. I. Gottesman.

Dorret I. Boomsma,¹⁴ P. C. M. Molenaar¹⁵ and N. G. Martin.¹⁶ Genetic Analysis of Large Numbers of Variables: Application of the Karhunen–Loeve Expansion to EPQ Data. A method is presented for the genetic analysis of (very) large numbers of variables. The proposed analysis yields estimates of the portion of genetic variance to the total variance in addition to estimates of underlying genetic and environmental covariance structures. This approach is a generalization of the Karhunen–Loeve expansion (P. C. M. Molenaar and D. I. Boomsma, *Behav. Genet.* 17:229–242, 1987) that involves the decomposition of a number of correlated observations into uncorrelated projections on the eigenvectors of the correlation function. These new uncorrelated variables enable the use of univariate techniques to obtain estimates of the proportion of genetic and environmental variance associated with each eigenvector. For each eigenvector any plausible genetic model can be tested including genetic, within- and between-family environmental, or dominance components and the corresponding covariance matrices can be obtained. We present a simulation study where the observed phenotypic and the underlying genetic and environmental factor structures in the data are different and an application to Eysenck's EPQ. Genetic and environmental covariance matrices (90×90) were constructed using the Karhunen–Loeve expansion. PCA of these matrices followed by varimax rotation showed 3 common genetic factors explaining about 43% of the genetic variance in both sexes with loadings corresponding to E, N, and L, respectively.

John D. Boughter,¹⁷ M. J. Burek,¹⁷ R. G. Burrigh,¹⁷ and P. J. Donovick.¹⁷ Intermale Aggression and Behavioral Laterality: Is There a Relationship in Binghamton Heterogeneous Stock Mice?¹⁸ Collins selected mice for degree of paw preference in food retrieval; he found also that there were differences in levels of, or sensitivity to, testosterone. For instance, mice from the Collins' LO line, demonstrating very weak paw preference, have more nonreproductive mating pairs, smaller litters, and more females per litter than mice from the HI line (strong, directional paw preference). Furthermore, in female, but not in male, mice line differences were demonstrated in intensity and duration of agonistic behavior (J. P. Scott, D. Brandt, and R. L. Collins, *Aggress. Behav.* 12:41–44, 1986). Using Binghamton Heterogeneous (HET) stock mice, we have assessed the relationship of paw preference to other directional behaviors in a water maze, a spatial maze, and the righting reflex (Burrigh, Scheer, Doring, and Donovick, *Behav. Genet.* 17:618, 1987). In the present study we ex-

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amined the intensity, frequency, and duration of intermale aggression between groups expressing different degrees of paw preference in food retrieval. In keeping with the findings of Scott *et al.*, (1986), we failed to find a relationship between degree of paw preference and intermale aggression in Binghamton HET stock mice.

Julia M. Braungart,¹⁹ Genetic Influence in Infant Temperament: Comparison of Twin and Sibling Adoption Results.²⁰ MZ and DZ correlations for tester ratings on the Infant Behavior Record at 1 and 2 years of age indicate substantial genetic influence in a sample of about 85 MZ and 50 DZ pairs (A. P. Matheny, Jr., *Child Dev.* **51**:1157–1167, 1980). The same measure was used in the Colorado Adoption Project (R. Plomin, J. C. DeFries, and D. W. Fulker, in *Nature and Nurture During Infancy and Early Childhood*, 1988) for about 95 pairs of nonadoptive siblings and 80 pairs of adoptive siblings in the first sibling adoption analysis of temperament in infancy. Although correlations for nonadoptive siblings exceeded those for adoptive siblings, estimates of genetic influence from the sibling adoption design are somewhat lower than the twin estimates. Because the nonadoptive sibling correlations are similar to the fraternal twin correlations, we conclude that either nonadditive genetic variance or an MZ assimilation effect is responsible for the different results from the twin and sibling adoption designs. Adoptive sibling correlations were near zero, indicating no evidence for shared environment. Model-fitting analyses supported the results.

John C. S. Breitner,²¹ K. Magruder-Habib,²¹ C. M. Churchill,²² K. M. Welsh,²¹ C. Owens,²¹ and C. Priolo.²¹ Pilot Study of Alzheimer's Disease in the NAS Twin Registry.²³ In a pilot study of Alzheimer's disease (AD) in the National Academy of Sciences Registry of aging twin veterans, we attempted to ascertain AD cases among the 442 Registry pairs listed in 1984 as both alive and resident in North Carolina or four nearby states. Fifteen members (1.7%) refused by mail, 54 (6%) had died since 1984, 88 (10%) could not be located or contacted with the limited resources available, and 49 (6%) refused to be interviewed. There was substantial pairwise concordance on response ($p < .00001$). A brief telephone interview for cognitive status was administered to the 678 respondents. Of these, 125 scored below a (very sensitive) cutoff point and were further evaluated by a telephone interview of their spouses or other informants. Eighteen subjects with symptoms suggesting AD were offered comprehensive in-person clinical assessment. Most (85%) qualified for diagnoses of Probable/Possible AD (NINCDS Criteria) or had mild but progressive cognitive dysfunction not yet evident as dementia. Examination of cotwins revealed several "screen-negative" monozygotic cotwins with neuropsychological changes suggesting early AD. These results suggest that the above telephone/clinical assessment protocol is practical for ascertainment of AD in large, geographically disperse populations and that over 2% of the NAS Registry have a disorder that can be followed as "presumptive AD" pending further observation. A twin study of the full NAS Registry should therefore be feasible and should yield substantial new insights into the causes of AD.

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F. Robert Brush,²⁴ Mickey D. Isaacson,²⁴ Louis J. Pellegrino,²⁴ Irene M. Rykaszewski,²⁵ and Carolyn Nagase Shain.²⁶ Characteristics of the Pituitary-Adrenal System in the Syracuse High and Low Avoidance Rat strains.²⁷ After many generations of selective breeding, rats of the high avoidance strain (SHA) average 67% avoidance responses in a two-way shuttle box, whereas those of the low avoidance strain (SLA) average 0%. Adrenal gland weights, both absolutely and relative to body weight, are 40–50% greater in adult SLAs than SHAs. Females of both strains have larger adrenal glands than males. The strain difference occurs as early as 21 days of age, whereas the sex differences appears only after puberty. Morphometry revealed that the difference in adults is entirely in the three cortical zones. Genetic determination of size of the adrenal glands is suggested by the finding that B_L (low backcross) animals have larger glands than those of F₂ animals, which have larger glands than those of B_H (high backcross) animals. Despite having the smaller glands, SHAs have higher basal adrenal and plasma concentrations of corticosterone than SLAs. Following ether stress, SHAs also show higher adrenal, but not plasma, concentrations of corticosterone than do SLAs. These results suggest that the genes determining adrenal size and function are fairly closely linked to those determining the avoidance phenotypes. The reduced steroidogenesis of the large adrenals of SLAs suggests an enzymatic defect of genetic origin in those animals.

Lon R. Cardon²⁸ and D. W. Fulker.²⁸ Developmental Analysis of Sibling Cognitive Data from the Colorado Adoption Project.²⁹ The main thrust of the Colorado Adoption Project (CAP), an ongoing longitudinal study of genetic and environmental influences on behavioral development, involves comparisons between parents and children in adoptive and nonadoptive families. However, a small sample of adoptive siblings and nonadoptive siblings has been added to the study since its inception. To date there are 103 families in which an adopted child can be paired with either another adopted child or a natural child of the adoptive parent and 113 families in which there are pairs of natural full siblings. General cognitive ability data are available for some or all of these sibling pairs at ages 1, 2, 3, 4, and 7 years (Bayley Scales of Infant Development at 1 and 2, Stanford Binet at 3 and 4, and WISC-R at 7). A multivariate analysis involving a Cholesky decomposition of genetic and environmental covariance components of phenotypic resemblance between sibling pairs over the five age points was undertaken for the general mental ability scores. A maximum-likelihood pedigree approach was necessary, in view of incomplete data, in order to utilize efficiently all the available information. Both shared environmental and genetic influences were in evidence, although the power to detect the former was weak. The Cholesky decomposition of the genetic influences indicated that most of the genetic variance at years 1 and 2 accounted for that at ages 3, 4, and 7, supporting the notion of continuity of genetic expression during development. A similar pattern was observed for shared environmental influences but with years 1, 2, and 3 accounting for most of the variation at ages 4 and 7. Specific environmental influences, which include error of measurement, indicated considerable unique variance at all five ages. Additional models were evaluated in order to arrive at a more parsimonious description.

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Gregory Carey.³⁰ Behavioral Genetic Models of Cultural Transmission and Evolution.³¹ To examine the evolution of cultural transmission (as the term is most often used in behavioral genetics), fitness functions were applied to data analysis models. Results were as follows: (1) in the absence of genetic variation, cultural transmission achieves a mean population fitness equal to optimal fitness only under a very restricted parameter range; (2) in the presence of genetic variation, even small amounts of cultural transmission can increase population fitness and the rapidity with which the population moves to optimal fitness; (3) in most cases, a locus that improves cultural transmission is superior to one of equal effect that improves learning from the idiosyncratic environment; (4) cultural transmission can have a very important effect on a mean while accounting for only a small proportion of phenotypic variability; (5) path coefficients typically referred to as indicating "parent-offspring cultural transmission" can be confounded with other effects; and (6) incorrect assumptions about development and age effects can invalidate tests of cultural transmission. Results are applied to data on intelligence, substance abuse, and suicide, and some ways to improve tests for cultural transmission are suggested.

Michele Carlier³² and P. L. Roubertoux.³² Y Chromosome and Intermale Aggression in Mice. I. Genetic Analysis. NZB (N) males attack more frequently than CBA/H (H) males in a dyadic encounter test (P. L. Roubertoux, and M. Carlier, *Behav. Genet.* 18:175-184, 1988). These differences were analyzed using a full Mendelian design and neo-Mendelian crosses. Partial results have been previously presented at BGA meetings suggesting a Y-chromosome effect interacting with strain background. Several genetic models are tested taking all the data into account. The model that fits best with the data assumes that at least three segregating units are involved: one autosomal and two Y-associated (one on the X-Y pairing region and one on the specific part of the Y). Moreover, maternal effects exist.

Crista M. Carmichael³³ and D. T. Lykken.^{33,34} Marital Resemblance for Self-Reported Personality: An Analysis of Twins and Their Spouses.³⁵ The existence of assortative mating for personality traits has been established in the literature (S. G. Vanderberg, *Behav. Genet.* 2:127-157, 1972), with correlations being small and positive, typically between .10 and .20. The present study examined 573 MZ and 487 DZ twin pairs and their spouses in an attempt to discover the genetic and environmental influences upon marital resemblance. Personality trait data were collected from the couples via mailouts of the Multidimensional Personality Questionnaire (A. Tellegen, *Brief Manual for the Differential Personality Questionnaire*, Unpublished manuscript, University of Minnesota, 1978/1982) as part of their participation in the Minnesota Twin Registry. Twin-cotwin, twin-spouse, twin-cotwin's spouse, and spouse-spouse correlations computed separately for males and females within each zygosity were analyzed in order to examine the underlying genetic and environmental influences on marital resemblance. For most of the scales, the twin-spouse correlations are similar to those found previously in the literature; they range from 0 to .35, with most falling between .10 and .20. One exception is the Traditionalism scale, for which the marital correlations are approximately .50.

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Heather M. Chipuer.³⁶ Home Observation for Measurement of the Environment: A Nonshared and Shared Environmental Approach. No objective nonshared environment measure has been developed for use in infancy and early childhood. This study uses sibling differences in the Colorado Adoption Project to construct a nonshared and a shared version of the most widely used measure of the home environment, the Home Observation for Measurement of the Environment. Approximately one-quarter of the items showed no significant sibling resemblance but a significant test-retest reliability. Sibling resemblance was observed for both adopted and nonadopted siblings and for same-sex and different-sex siblings. The items that showed no sibling resemblance were used to construct a measure of Nonshared Environment (NSE) at 12 and 24 months of age. A measure of Shared Environment (SE) was made with the items which showed significant sibling resemblance. To assess genetic influence on NSE and SE, a comparison of the correlations for adoptive and nonadoptive siblings on these two scales is presented. In addition, correlations between these two scales and mental development are examined.

Nancy E. Colley³⁷ and K. Schlesinger.^{37,38} Differences in Learning Ability of Mice Selectively Bred for High Activity. The bidirectional selection study for activity, initiated by J. C. DeFries (J. C. DeFries and J. P. Hegmann, in *Contributions to Behavior-Genetic Analysis: The Mouse as a Prototype*, pp. 23-56, 1970), was landmark for the use of controls and replicated lines. Both the high lines (H_1 and H_2) were selectively bred for high activity in an open-field arena. In this study, however, these lines differ significantly in their ambulation during two 10-min periods. In exploratory behavior, measured from 0 to 10 min, H_1 differ from H_2 mice, and in motor behavior, measured from 30 to 40 min, H_1 females differ from all other groups. Mice were tested in a Morris water maze for spatial, nonspatial, and place learning, as well as ability to learn a t-maze. For the Morris maze, there is a significant line-by-sex interaction due to the inability of H_1 females to learn, while H_2 males learn the task better than any other group. In H_1 females there is a positive correlation between motor ambulation and latencies in the Morris maze, while in H_2 males there is a negative correlation. No significant correlations were found in H_1 males or H_2 females. Preliminary evidence suggests that these differences will be replicated in a t-maze with positive reinforcement. The correlations observed are likely due to random drift and/or fixation of alleles due to the inbreeding which has been implemented for the last 16 generations. The fact that these correlated responses are not found in all groups of the high-activity lines demonstrates the utility of a replicate design in determining whether correlated responses are related genetically to selected responses.

Hilary Coon.³⁹ Environmental Transmission in Adoptive Families: Alternative Models.⁴⁰ Alternative models of environmental transmission from parent to child are explored using data on cognitive ability taken from the Colorado Adoption Project (CAP). First, because the parental phenotype that a child imitates is in part determined by parent's age, the effects of environmental transmission from parent to child may be underestimated when age corrections are used in adoption data. The major association between age and parental cognitive ability in CAP does not appear to be a developmental change for adoptive and control parents. Rather, educational level and cognitive ability determine age of parenting (or adoption) and, hence, age of entry into the study. In this case, scores unadjusted for age are the appropriate measures for analysis. A second model uses a different categorization of parents

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based on which parent obtained higher cognitive scores, independent of gender. The model investigates transmission from parents categorized in this manner as opposed to a categorization of parents by gender. Trends were found in the data showing that the offspring was more likely to resemble the parent with the lower scores.

I. Damez-Kinselle and J.-M. Guastavino.⁴¹ Behavioral Pleiotric Effects of the Hot-Foot Murine Mutation: Example on Sexual Behavior. The neurological hot-foot mutation affects the cerebellum of the mouse and causes impairment of the gait and of the posture. This study demonstrates that the effects of the mutation in the C57BL/6 strain widely overcomes the frame of the locomotor abnormality. In fact, the reproductive behavior is severely altered too. *Homozygous females ho/ho*: They all bred, although the latency before copulation was longer and the survival rate of the pups at weaning time (compared to the normal females) was reduced. *Homozygous males ho/ho*: They never bred, although they were provided with several experimental breeding conditions. This differential alteration, males-females, has been observed with other neurological mutants and it was not possible to reduce the causes of this alteration to the only motor deficit.

Christopher M. de Fiebre⁴² and A. C. Collins.⁴² Classical Genetic Analysis of Ethanol and Nicotine Sensitivity in Long-Sleep (LS) and Short-Sleep (SS) Mice.⁴³ The LS and SS mouse lines, which were selectively bred for differential "sleep-time" following ethanol administration (G. E. McClearn and R. Kakihana, *Behav. Genet.* 3:409-410, 1973), also differ in sensitivity to nicotine (C. M. de Fiebre, L. J. Medhurst, and A. C. Collins, *Alcohol*, 4:493-501, 1987). In the present study, a classical genetic analysis has been used to test whether common genes may regulate the sensitivity of the LS and SS mice to these two drugs. LS and SS mice, as well as crosses derived from these mice (F₁, F₂, and backcross generations), were tested for sensitivity to ethanol-induced "sleep-time" (dose range, 50-100 mmol/kg). Other mice of these same generations were tested for sensitivity to nicotine via a battery of behavioral and physiological tests. Respiration, startle response, Y-maze activity, heart rate, and body temperature were measured following injection with 0.0 to 2.0 mg/kg nicotine. Sensitivity to nicotine-induced seizures was measured following injection with 2.0 to 7.0 mg/kg nicotine. Initial analysis of the data indicates that the genetic segregation is similar for responsiveness to both these drugs. Furthermore, inheritance of sensitivity to these drugs appears to be primarily additive. This finding is consistent with the hypothesis that common genes regulate sensitivity to these two drugs; however, further studies must be conducted to ascertain this with certainty.

Douglas K. Detterman⁴⁴ and L. A. Thompson.⁴⁴ Heritability Within Low- and High-IQs Groups.⁴⁵ With respect to intelligence, there are a number of empirical differences that are observed between the low end of the distribution and the high end. For example, low-IQ subjects show greater within-subject variability than high-IQ subjects; low-IQ subjects demonstrate higher levels of reliability for IQ measures than high-IQ subjects; and low-IQ sub-

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jects show *higher* intercorrelations among subtests of the WISC and WAIS. Given these differences, it would not seem unreasonable to examine the question of whether heritability of IQ varies for high- and low-IQ subjects. Preliminary data from the Western Reserve Twin Project, currently consisting of approximately 86 pairs of MZ and 55 pairs of DZ twins, were analyzed by forming a composite of subtests of the WISC-R, WRAT, PPVT, and Metropolitan Achievement test. A first effort to assess differences across ability was to compute intraclass correlations for this composite by splitting the group at the mean. The analysis suggested that heritability was higher for low-ability subjects ($h^2 = 1.00$) than for high-ability subjects ($h^2 = .49$). However, intraclass correlations were unstable and failed to yield stable results because of covariance differences produced by selection. A regression method developed by LaBuda, DeFries, and Fulker was used to solve the covariance adjustment problem. Though dividing the sample into bands produced bias, Monte Carlo methods showed the regression methodology was robust. The results of the regression analysis provide evidence for differences in both heritability and environmentality across groups. Differences between groups suggest that low-ability MZ twins are much more similar than high-ability MZ twins when compared to expectations. This suggests higher heritability of mental abilities at lower ability levels.

Michael J. Dewey.⁴⁶ Transgenic Mice: An Overview of Research Applications. Recent years have witnessed great strides in our ability to isolate and manipulate the genes controlling specific hereditary traits. Simultaneously the technology has been developed to use these same genes to alter the basic hereditary make-up of living organisms. Animals that contain and transmit experimentally introduced genetic material are termed transgenic. They are a potent and important new tool for modern biological research and should provide new avenues to benefit studies of the genetic basis of behavior. Transgenic mice are ideally suited to provide two general types of information. First, they are an excellent system in which to define genetic elements responsible for tissue-specific and temporal expression of genes. The transgenic mouse system also offers potential in the exploration of gene function by providing the opportunity to alter the tissue profiles and expression levels of individual genes. Phenotypic consequences of such alterations will then lead to *in vivo* information as to the function of that particular gene.

Scott R. Diehl,⁴⁷ E. J. Stanek,⁴⁸ and R. J. Prokopy.⁴⁹ A Quantitative Genetic Analysis of Oviposition Preference Behavior and Larval Survival Ability in the Fruit Fly *Rhagoletis pomonella* (Diptera: Tephritidae).⁵⁰ Previous studies have demonstrated that flies infesting apples consistently differ from those infesting hawthorn fruit in several behavioral and ecological assays. In order to evaluate whether there is a genetic basis to these differences, crosses were made between the two "strains" of fly in a paternal half-sibling design. The analysis of these experiments is complicated by the fact that (i) many of the variables of interest are binary responses (e.g., accept or reject a fruit for oviposition or survive or die in different types of fruit) and (ii) the strong influence of measured environmental factors (e.g., ambient temperature) that need to be incorporated into the statistical analysis as covariates. Results of a preliminary statistical analysis using the logistic regression model and weighted least-squares methods for repeated measurements are presented.

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Scott R. Diehl^{51,52} Ying Su,⁵¹ Charles J. MacClean,⁵² Dermot Walsh,⁵³ Aileen O'Hare,⁵³ Mary McGuire,⁵⁴ and Kenneth S. Kendler.^{51,52} **Linkage Studies of Schizophrenia Using Polymorphic DNA Markers.**⁵⁵ We are conducting linkage studies using RFLP markers on a large number of multiplex pedigrees segregating for schizophrenia that are being ascertained in Ireland. We seek to capitalize on the unique attributes of these pedigrees that include (i) a relatively homogeneous ethnic composition of the population, which might reduce problems due to genetic heterogeneity; (ii) enhanced ability to determine optimal diagnostic criteria and estimates of gene frequency and penetrance necessary for linkage analyses by using data obtained from a large-sample, epidemiologically based family study nearing completion in the west of Ireland; and (iii) the close genetic relationship between Ireland and both Iceland and England, the source of families that have previously provided significant evidence of linkage to chromosome 5. We have initiated the genotyping of currently available pedigrees using chromosome 5 markers. Our long-term plan is to type highly variable markers from throughout the genome, with a special emphasis on "candidate" genes such as the recently cloned D₂ dopamine receptor (provided by O. Civelli). We will employ multipoint linkage analysis and a variety of other statistical methods to utilize these data fully.

David L. DiLalla,⁵⁶ Irving I. Gottesman,⁵⁷ G. P. Vogler,⁵⁸ and J. W. Kneesevich.⁵⁹ **Personality and Psychopathology: Selection Models for Dimensions of the MMPI.**⁶⁰ When twin probands are selected for psychopathology, the distribution of personality variables for probands deviates from the population distribution when the personality traits are related to the pathological phenotype. Distributions for cotwins also differ to the extent that the trait is familial and state effects in probands are small. MZ and DZ cotwins show smaller deviations than selected probands, and for heritable factors, DZ twins regress farther than MZs toward the population mean. This selection model allows testing of hypotheses about the relationship of personality to psychopathology. We identify two selection hypotheses: (1) personality traits (e.g., neuroticism) directionally increase liability for illness; and (2) selection heterogeneity exists (e.g., some diagnoses have personality trait distributions that resemble the population while others are associated with selection). For both models, the degree of deviation from the general population in proband and MZ and DZ cotwin means and variances can be predicted from heritable and environmental effects on personality traits. Given adequate normative data, this both provides a powerful test of the models and allows some resolution of state versus trait effects. These principles are illustrated with data from the Minnesota Multiphasic Personality Inventory (MMPI) and the Washington University Twin Series.

Lisabeth Fisher Dilalla⁶¹ and David W. Fulker.⁶¹ **Infant Measures as Predictors of Later IQ: The Twin Infant Project (TIP).**⁶² The Twin Infant Project (TIP) is an attempt to assess the

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usefulness of a number of infant measures as indicators of later intelligence. Rather than the traditional longitudinal approach, this project utilizes mid-parent scores as approximations of the infants' later IQ scores, thus circumventing the need for a 20-year follow-up. The predictability of the infant measures for adult IQ is assessed by regressing mean twin (midtwin) score on mean parent (midparent) IQ. This short-cut approach will be validated if the infants' scores which predicted parental IQ are correlated with the infants' IQ scores in childhood. Two hundred fifty-two pairs of twins and their parents were tested on the TIP battery. Twins were tested at 7 and 9 months in their homes on a number of measures including the Fagan Test of Infant Intelligence. At 8 months twins were tested in the laboratory on a visual anticipation measure, and their parents were administered two IQ measures, the Wechsler Adult Intelligence Scale (WAIS-R) and the Hawaii Family Study of Cognition's (HFSC) battery of specific cognitive abilities tests (J. C. DeFries *et al.*, *Behav. Genet.* 9:23-43, 1979). Four measures consistently showed high midparent-midtwin correlations: the Fagan test, a measure of visual anticipation, the number of types of vocalizations, and Bayley IBR factor scores. These measures also tended to predict children's IQ scores at ages 1, 2, and 3 years. Thus, several infant measures have been identified which are related to IQ, and some support has been provided for this midparent-midtwin approach.

Thomas C. Doetschman.⁶³ **Targeted Gene Modification of the HPRT Gene in Mouse Embryonic Stem Cells.** Blastocyst-derived embryonic stem (ES) cells can be maintained in culture in the embryonic stem cell state, can be genetically modified in a site-directed manner, and can reconstitute a mouse when introduced into a blastocyst-stage embryo. Together, these characteristics will enable us to make predetermined genetic alterations in specific genes of living animals. To demonstrate the feasibility of targeted gene modification in ES cells, the hypoxanthine phosphoribosyl transferase (HPRT) gene, which is involved in the purine salvage pathway, was chosen as the target gene because it is X linked and because it can be selected for or against in cell culture. In one set of experiments an HPRT deletion mutation was corrected by an homologous recombination event in which the missing sequences were inserted into the mutant gene following electroporation of the cells in the presence of the targeting DNA sequences. The targeted cells were selected for in HAT medium in which only cells with functional HPRT could survive. In another set of experiments a normal HPRT gene was disrupted by the insertion of foreign DNA sequences into the HPRT gene. The ES cells were electroporated in the presence of the targeting sequences, and the targeted cells were selected for by 6-thioguanine, a purine analogue which poisons cells when utilized by HPRT as a substrate. In both sets of experiments, about one in a million electroporated cells were targeted. Experiments in which ES cells were used to make transgenic mice are also described, and ES cell-derived mouse models for the Lesch-Nyhan syndrome (HPRT deficiency) are discussed.

Laura J. Draski and D. J. Nash.⁶⁴ **Motor Activity, Response to Amphetamine, and Learning in the Ataxic Mouse Mutant, Hotfoot.** The autosomal recessive mouse mutation, hotfoot (*ho*), provides a unique model for studying the complex effects of single genes on brain and behavior. Homozygous recessive animals are visibly discernible after approximately the third postnatal week by a body tremor at rest and a striking ataxia involving primarily the hindlimbs. However, an examination of the development of motor anomalies in hotfoot mice suggests profound disturbances in activity as early as postnatal day 10 and a progressive loss of activity in adults. For example, after being placed 10-12 cm from their home nests, hotfoot pups took a significantly longer time to return to their nest than phenotypically normal mice at postnatal day 11. In a separate study, hotfoot and phenotypically normal

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mice were given an amphetamine dose of either 0 or 4 mg/kg prior to being tested in an open field either at postnatal day 10 or 30 or as adults. While hotfoot mice receiving 0 mg/kg of amphetamine did not differ significantly from phenotypically normal mice at 10 or 30 days of age, hotfoot mice given 4 mg/kg amphetamine crossed significantly fewer squares and reared significantly less than phenotypic controls at each age. Adult hotfoot mice crossed fewer squares and reared less than normal mice in the absence of amphetamine, and administration of this drug did little to alter hotfoot behavior. In addition, hotfoot adults failed to learn a black–white discrimination task in a water maze after four days of testing. These results suggest multiple effects of the hotfoot mutation on brain and behavioral development and support the consideration of hotfoot as a potential model for human hereditary ataxia.

Lindon J. Eaves.⁶⁵ Resemblance of Personality Test Scores in Twins and Their Relatives. A shortened form of the EPQ was administered by mail to adult U.S. twins and their parents, spouses, siblings, and children ($N = 23,000$). Large-sample correlations for psychoticism, extraversion and neuroticism (P, E, and N) were computed. The resemblance of MZ twins is consistently greater than that for DZs. Siblings are no more or less alike than DZ twins. For E and N, the parent–offspring correlation is the same as that for siblings and DZ twins. For P, the parent–offspring correlation was significantly lower than the DZ twin correlation. Spousal correlations are virtually zero for E and N and slightly positive for P. There is no indication of a shared environmental effect on E or N, but strong evidence of genetic non-additivity. In the case of neuroticism the nonadditivity is apparently confined to males.

Lee Ehrman.⁶⁶ Effects of Lifelong Experience on the Rare-Male Mating Advantage in *Drosophila pseudoobscura*.⁶⁷ The numbers of observed matings participated in by *Drosophila pseudoobscura* females isolated from contact with all other flies before mate selection are shown in Table I. Total number of observed matings = 3050, with more planned.

Bruce Elder⁶⁸ and Carol B. Lynch.⁶⁸ Genetic Architecture of Nest-Building in a Northern and a Southern Population of *Mus domesticus*.⁶⁹ We employed two triple-test crosses (TTC) to compare genetic architecture of nest-building within a population of mice originating from Maine (M) and one originating from Florida (F). If there had been stronger selection due to colder temperatures in the M population, we would expect less additivity and more dominance for nesting in the M than in the F population. The “tester” population came from lines of mice divergently selected to their limits for nest-building. The “tested” mice consisted of males from the two populations, each harem-mated to three tester females: high nesting, low nesting, and the F_1 between them. The analysis was based on males that produced at least two male and two female offspring from all three tester females in four blocks. This resulted in 13 M sires producing 624 offspring and 18 F sires producing 864 offspring. Nesting was measured at 21 and 5°C. For nesting at both temperatures in both sexes the additive genetic variance component was larger in the M than in the F population. Dominance variance was significant for both nesting measures only in the M males. As a result, heritabilities of nesting were generally lower in the M than in the F mice. Epistatic variance was not significant. The lack of epistasis and the fit of the results to the prediction (more northern mice seem to have been the more strongly selected) indicate that laboratory mice were adequate testers for the wild populations, i.e., essentially the same genes which result in high and low nesting in laboratory mice also influence nesting in wild populations.

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Table I. Numbers of Observed Matings^a

| Female karyotype | Isolated as | Rare males | Number of matings with males at 1:4 ratios | | χ^2 |
|------------------|-------------|------------|--|--------------|----------|
| | | | Rate males | Common males | |
| 1. AR/AR | Eggs | AR | 20 | 80 | .00 |
| | Eggs | CH | 23 | 52 | 5.34* |
| | 1st instars | AR | 26 | 74 | 2.25 |
| | 1st instars | CH | 15 | 35 | 3.13 |
| | 2nd instars | AR | 30 | 120 | .00 |
| | 2nd instars | CH | 10 | 40 | .00 |
| | 3rd instars | AR | 18 | 57 | .75 |
| | 3rd instars | CH | 10 | 40 | .00 |
| | Pupae | AR | 4 | 21 | .25 |
| | Pupae | CH | 11 | 189 | 26.28** |
| 2. CH/CH | Eggs | AR | 98 | 327 | 2.49 |
| | Eggs | CH | 25 | 75 | 1.56 |
| | 1st instar | AR | 65 | 185 | 5.63* |
| | 1st instar | CH | 11 | 64 | 1.34 |
| | 2nd instar | AR | 82 | 143 | 38.03** |
| | 2nd instar | CH | 12 | 38 | .50 |
| | 3rd instar | AR | 47 | 103 | 12.04** |
| | 3rd instar | CH | 31 | 94 | 1.80 |
| | Pupae | AR | 30 | 45 | 18.75** |
| | Imagoes | AR | 49 | 101 | 15.04** |
| Imagoes | CH | 36 | 64 | 16.00** | |
| 3. AR/CH | 2nd instar | AR | 40 | 110 | 4.16* |
| | 2nd instar | CH | 25 | 125 | 1.04 |
| 4. CH/AR | 2nd instar | AR | 27 | 73 | 3.06 |
| | 2nd instar | CH | 12 | 38 | .50 |

^a AR, arrowhead inversion; CH, Chiricahua inversion. See P. Parsons and L. Ehrman (*Behavior Genetics* 11:127-133, 1981) for all methodological details and L. Ehrman (*Genetical Research* 11:135-140, 1968) for data concerning the behavior of normally raised *D. pseudoobscura* in the same circumstances.

* Significant at $p = .05$.

** Significant at $p = .01$.

Elizabeth E. Epstein,⁷⁰ B. E. Ginsburg,⁷⁰⁻⁷² V. M. Hesselbrock,⁷² and J. C. Schwarz.⁷⁰ **Personality, Psychopathologic, and Demographic Characteristics of Male Substance Abusers with and without a Family History of Substance Abuse.** Substance abuse can be conceptualized as a heterogeneous disorder which may be fractionated into a taxonomy of subtypes and of sets of covarying factors associated with each. If measures which predict inclusion in certain

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subtypes can be replicated reliably, "at-risk" individuals could be identified. Implications for treatment, preventative intervention, and for researching modes of transmission are discussed. Data are presented on 83 male inpatients (ages 18–45) in substance abuse or dual-diagnosis treatment programs. Research Diagnostic Criteria and Family History Research Diagnostic Criteria were used to obtain diagnoses of alcoholism, drug abuse, Antisocial Personality Disorder, and depressive disorders in the proband, as well as uni- or bilineal family history of alcoholism and drug use disorder. The sample is divided into subtypes based on uni- or bilineal family history of alcoholism and/or drug abuse; subtypes are compared on (1) a variety of personality measures, particularly those measuring sensation, thrill and novelty seeking, anxiety, psychopathy, and depression; (2) demographic information; (3) psychopathology; and (4) patterns of substance abuse.

Debbie Finkel⁷³ and David Lykken.⁷⁴ Personality Data from Twin Families: Support for Emergence?⁷⁵ Tellegen *et al.* (*Journal of Personality and Social Psychology* 54:1031–1039, 1988) found evidence of nonadditive genetic effects on personality using data from reared-apart and reared-together twins. The present study attempted to replicate these findings using twin family data. The Multidimensional Personality Questionnaire (MPQ) was administered to a sample consisting of 235 young adult twin pairs, 65 male and 170 female, 50 same-sex siblings of these twins, and 201 fathers and 222 mothers, 195 of which were parent pairs. Genetic and environmental contributions for each of the 11 scales and 3 superfactors of the MPQ were estimated using a biometrical model-fitting procedure. Comparing parent–offspring correlations to sibling correlations failed to suggest any support for dominance. Comparing sibling correlations to DZ twin correlations suggested a strong trend for DZ twins to be more similar than ordinary siblings. Investigation of nonadditive genetic effects found significant nonadditive effects for two factors: Social Potency and Control. The nonadditivity of these two factors does not appear to be due to dominance, only. This study is a partial replication of Tellegen *et al.*, who found epistasis for on these two factors as well as for Positive Emotionality.

C. Gentsch,⁷⁶ Lichtsteiner,⁷⁶ B. Siegfried,⁷⁷ H. R. Frischknecht,⁷⁷ and P. Driscoll.⁷⁸ Novelty-Induced Analgesia (NIA) in Roman High- and Low-Avoidance (RHA/Verh and RLA/Verh) Rats. Exposing rats to a novel environment results in a mild analgesia, as measured by tail-flick latencies (TFLs) (Siegfried *et al.*, *Behav. Neurosci.* 101:436, 1987). TFLs were measured in RHA/Verh and RLA/Verh rats immediately before, and 2 min after, exposure to an open field or their home cages. The resulting NIA measurements, i.e., (post-open field minus pre-open field TFLs) minus (post-home cage minus pre-home cage TFLs), were more than twice as high in the RHA/Verh rats, because RLA/Verh rats had already shown a significant elevation in TFLs upon reexposure to their home cages (i.e., a handling-stress effect). RHA/Verh rats were more active, and reared more, in the open field compared to RLA/Verh rats, which, in turn, defecated and groomed themselves much more often. The latter indices of emotionality paralleled the freezing behavior seen in the RLA/Verh rats when tested in the shuttle box 1 week later, where they averaged 1% avoidance behavior in a session of 60 trials (the RHA/Verh rats scored 71%, by comparison). In another study, however, ip injections of 0, 2, 4, or 10 mg/kg morphine resulted in no significant genetic differences in TFLs, but only in a pronounced, dose-dependent increase in analgesia for both lines of rats. The exact opioid role in NIA, therefore, remains to be determined.

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Jilla Ghodsian-Carpey⁷⁹ and L. A. Baker.⁷⁹ Genetic and Environmental Sources of Mother-Child Interaction.⁸⁰ Parental behavior has traditionally been viewed by psychologists as a major source of influence in child socialization. Recently it has been suggested that parental behavior itself may be influenced by children's genotype. The present study investigated the genetic and environmental etiologies of mother's behavior toward her preschool-aged twins and the relationship between her behavior and differences in social behaviors of the children using observational data. Fifty-nine pairs of twins ([29 monozygotic-(MZ); 30 dizygotic(DZ)] between 3 and 6 years of age were observed with their mothers during problem-solving tasks. Frequencies of several mother and child behaviors were recorded and combined to create composite scores Warmth and Control for the mother and Positive Affect, Negative Affect, and Task Orientation for the child. Significant correlations between mother's behavior and child's behavior were found. The twin who received more warmth from the mother demonstrated less negative affect and more task orientation. Likewise, the one who received more controlling behavior was rated to be lower on positive affect. Multivariate biometrical analyses revealed relatively high estimates of common environments for mother behavior and specific environments for child behavior. Low heritabilities were found for both mother and child behavior, but correlations between these measures were primarily genetically mediated, as indicated by high genetic correlations. The results underscore the need to consider both genetic and environmental factors in studying mother-child interaction.

Jacquelyn J. Gillis⁸¹ and J. C. DeFries.⁸¹ Multiple Regression Analysis of Reading Performance Data from Reading-Disabled Twins.⁸² DeFries and Fulker (*Behav. Genet.* 15:467-473, 1985) developed a multiple regression analysis of selected twin data which predicts a cotwin's score (C) from that of a proband (P; i.e., the member of a twin pair selected because of a deviant score on a continuous variable) and the coefficient of relationship (R). Two models were presented: (1) a basic model in which the partial regression of C on R is a function of h_g^2 (a measure of the extent to which the deficit exhibited by the probands is due to heritable influences) and (2) an augmented model containing an interaction term between P and R that yields direct estimates of within-group heritability (h^2) and the proportion of variance due to environmental influences shared by members of twin pairs (c^2). A comparison of h_g^2 and h^2 can be used to test the hypothesis that the etiology of extreme scores may differ from that of variation within the normal range. Subsequently, DeFries and Fulker (*Acta Genet. Med. Gemellol.* 37:205-216, 1988) noted that transformation of the twin data prior to multiple regression analysis facilitates direct estimates of h_g^2 and h^2 , as well as a test of their difference. Analysis of reading performance data obtained from 88 identical and 70 fraternal twin pairs in which at least one member of each pair was reading disabled yields estimates of $h_g^2 = .51$ ($p < .001$) and $h^2 = .84$ ($p < .05$), a nonsignificant difference ($p > .40$). Although the power to detect a difference between h_g^2 and h^2 is relative low, results of this analysis suggest that probands may constitute the lower tail of a normal distribution of individual differences in reading performance.

B. E. Ginsburg,⁸³ N. D. Szajnberg,⁸⁴ and R. Buck.⁸⁵ The Primacy of Affect in Modulating Phenotypic Expression in Social Systems.⁸⁶ Social systems of vertebrates are characterized

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by affinities, often hierarchically structured, that include various levels of bonding ranging from those involved in mating, parenting, and peer coalitions to the more complex affinities central to the formation and maintenance of socially cohesive groups. The affective dimension, if perturbed, disrupts the potential for species-typical social behavior and impairs the communication underlying such behavior. In restoring disrupted behaviors to an approximation of normality, the affective dimension is seen as primary. Genetic variations in personality profiles are assessed in relation to vulnerability for behavioral variations using canids, primates, inbred mouse strains, and human twins. Three major arguments are made: (1) that there are genetic set-points characterizing the individual and the species that are robust and can be attained even where serious developmental disruptions have occurred; (2) that the phenotypic readout for an individual can be changed during vulnerable periods in development by behavioral means that serve to regulate which encoded genes come to expression; and (3) that the capacity for communicative behavior requires an affective foundation or, if impaired, an affective approach to its remediation which precedes the cognitive.

R. Godijns,⁸⁷ E. Thiery,⁸⁷ R. Vlietinck,⁸⁸ C. Derom,⁸⁸ M. Thiery,⁸⁹ and R. Derom.⁸⁹ Linguistic Components of Language Acquisition in Mono- and Dizygotic Twins.⁹⁰ To sort out the genetic and acquired dimensions of the auditive synthesis capacity we investigated a group of forty-one 9-year-old twin pairs (21 monozygotic, 20 same-sex dizygotic) from the East Flanders Prospective Twin Survey (R. Vlietinck, *Determination of the Zygosity of Twins*, Thesis, Leuven, 1986). A Dutch adaptation of the Illinois Test of Psycholinguistic Abilities was used. Statistical analysis of the data allows us (1) to estimate the genetic impact versus the influence of the environment, (2) to compare the performances of our group of twins with singleton controls, and (3) to relate the performance to the degree of schooling. Our study points out that the auditive synthesis capacity is relatively more determined by genetic predispositions than the insight in presuppositions and appears to be more sensitive to unfavorable environmental conditions. The effect of schooling on both proficiencies can be called identical for singletons and twins.

H. H. Goldsmith,⁹¹ J. J. McArdle,⁹² and B. Thompson.⁹² Longitudinal Twin Analyses of Childhood Temperament.⁹³ Using twin data from the Collaborative Perinatal Project, we extend our common factor model for multivariate biometric analyses (J. J. McArdle and H. H. Goldsmith, *Behavior Genetics*, in press) to the longitudinal case. We estimate genetic and environmental influences on continuity and change in latent variables from 4 to 7 years of age using both autoregressive and difference score models. From psychologists' ratings during mental testing sessions, we identify two factors, fit invariant factor loadings at each age, and interpret the factors in temperamental terms as "reactivity" and "persistence." From the autoregressive perspective, the persistence factor showed greater phenotypic stability. Genetic differences influenced both factors at age 4 and accounted for essentially all the phenotypic stability in both latent factors. Genetic differences affected residual variance at 7 years in reactivity, but not persistence. From the difference score perspective, genetic differences were relatively less influential on change from 4 to 7 years. Shared environmental variance was minimal in all cases. The results suggest that different ways of conceptualizing

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change can yield different answers about the genetic architecture of developmental change and continuity.

Grazyna Gora-Maslak.⁹⁴ Molecular Biology Techniques Applicable to Behavioral Genetic Research. This presentation is designed for behavioral geneticists with little or no background in molecular biology. It introduces—in simple terms—the most commonly used methods: cloning and preparation of probes, labeling, hybridization, and Southern, Northern, and dot-blot analysis. The presentation includes restriction fragment length polymorphisms (RFLPs).

Irving I. Gottesman.⁹⁵ Interfacing the Old and the New in Psychiatric Genetics. The purpose of this symposium is to showcase the advances in methodological sophistication in psychiatric genetic aspects of such major mental disorders as schizophrenia, major affective disorders, Alzheimer disease, and alcoholism even before the burgeoning application of molecular genetic techniques. Family and twin designs (McGuffin and McGue) with depression and alcoholism continue to provide fundamental, if unexpected, information about both genetic and environmental contributions to such multifactorial disorders informed by path analysis and refinements in the measurement of phenotypes. New strategies involving the offspring of dual-mating psychiatric inpatients (analogous to “diallel crosses” for complex phenotypes) and the offspring of discordant identical twins (Bertelsen) provide new evidence about gene expression and genotype interactions. With the advent of positron emission tomography (PET) and its applications to Alzheimer disease and schizophrenia (Resnick), new endophenotypes are available for exploring the genetic aspects of subcomponent contributions to psychiatric disorder. A brisk, eyes-open walk toward embracing the use of RFLPs for linkage analyses, clearly important for single gene disorders, rather than a frantic race, may result from the consideration of complex disorders.

J.-M. Guastavino and I. Damez-Kinselle.⁹⁶ Hot-Foot Murine Mutation: Light Cerebellar Alterations and Severe Gait Abnormalities. We entered upon the behavioral study of a new neurological mutant that appeared in our laboratory on the C57BL/L strain of mice: the hot-foot. This recessive mutation is located on chromosome 6. An abnormal posture (body lying flat on the ground, hind legs widely open) and an abnormal locomotion (backward gait and jerky movements of the hind legs) are the most obvious characteristics of the mutation. The neuroanatomical analysis of the cerebellum shows abnormalities linked to the Purkinje cells whose ectopic spines lack presynaptic innervation. This clearly illustrates the connection between the deficiency of the cerebellum and the abnormal gait. However, the small importance of the anatomical deficiencies can hardly explain the serious impairment of the behavioral phenotype.

Lynn Gynther,⁹⁷ G. Carey,⁹⁷ and J. Knesevich.⁹⁸ A Twin Study of Drug Use.⁹⁹ Except for alcohol, little is known about familial aggregation for substance abuse. Here we report twin resemblance for nonalcohol substance abuse in the Washington University Twin Series, a

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consecutive series of 295 twin pairs with probands admitted to psychiatric facilities in the St. Louis area. From case history ratings and blind diagnostic summaries, a five-point substance abuse scale was constructed with values anchored by "never used drugs" (1) to "drug dependence" (5). Scores were standardized by race and sex in probands and cotwins, and a regression analysis was used to predict cotwin use by proband use in order to estimate the effects of heritability and common environment. Year of birth was the most powerful predictor of drug use—younger twins scored far higher than older twins. It was necessary to include either heritability or common environment in the model to avoid a significant drop in explained variance, but which of the two was more important could not be resolved. The correlation for identical twins exceeded that for fraternal twins, suggesting the possibility of a heritable factor.

Martin E. Hahn,¹⁰⁰ R. Benno,¹⁰⁰ L. Szobota,¹⁰⁰ and K. Repola.¹⁰⁰ Degree of Expression of Laterality in Mice Bred for High and Low Brain Size. Relative brain weight may be significantly related to degree of paw preference. One study (B. Cassells, R. L. Collins, and D. Wahlsten, *Abstracts, Society for Neuroscience* 1987) 13: Paper 18.15, showed a significant (positive) relationship between brain weight and degree of paw preference. The current study investigated the degree of laterality in Fuller Brain Weight Selected (Fuller BWS) mice. Animals ($N = 92$) from Fuller BWS high and low lines were evaluated on the basis of three behaviors. The number of left and right paw reaches were recorded and compared with results of turning behavior in a water T-maze and direction of rotation in aerial righting. Interestingly, no significant correlations were found between any of the three behaviors. A 2×2 analysis of variance indicates a line effect (.63 vs. .47), with low line animals expressing a greater strength of laterality in paw reaches. There were no other significant effects. This finding appears to be opposite to that of Cassells *et al.*

Martin E. Hahn,¹⁰¹ J. K. Hewitt,¹⁰² L. Weinreb,¹⁰¹ and A. Henry.¹⁰¹ A Diallel Analysis of Ultrasonic Calls in 3-Day-Old Mouse Pups. Ultrasonic call production by rodents was discovered in the 1950s. Though the calls of rodents of different species and ages have been compared, genetic analysis has rarely been used to explore this behavior. One genetic study (M. E. Hahn, J. K. Hewitt, M. Adams, and T. Tully, *Behav. Genet.* 17:155–166, 1987) used a Mendelian cross of two inbred strains to study several aspects of ultrasounds from 5-day-old pups and discovered directional dominance for the rate of calling. The present study extends the first by studying aspects of ultrasonic calls in male and female 3-day-old pups from a diallel cross of 4 inbred strains. A total of 246 mice was observed. Each mouse was placed on a cool cotton pad in a quiet, dark chamber and its vocalizations were recorded. The recordings analyzed for rate, length, and beginning, ending, highest, and lowest frequencies with a Kay Elemetrics digital sonagraph. The results indicate that hybrids exhibit more and longer calls of a generally lower frequency but with a greater range than do inbreds. A Hayman analysis of the data indicates significant additive and directional dominant components for rate of calling and length of calls and probably for all the frequency characteristics.

Richard J. Haier.¹⁰³ Position Emission Tomography Determination of Brain Metabolism and Intelligence. Position emission tomography (PET) is a technique that allows the survey of functional activity throughout the brain. By combining PET with sophisticated cognitive

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and psychometric assessment, the relationship between brain metabolism in specific areas and psychological performance can be determined. We used PET to study glucose metabolism during abstract reasoning (RAPM) in eight normals. Regional findings indicate left posterior cortex involvement but strong negative correlations are found between overall glucose use and test performance ($r = -.77, -.67,$ and $-.75$ for three slice levels). Similar correlations are not found during a test of attention (CPT). Two other PET reports confirm inverse correlations between glucose use and intelligence measures. This inverse relationship suggests that neuronal efficiency instead of number of neurons activated may underlie complex problems solving ability or general intelligence. Individual differences in "neural pruning" during the normal course of brain development may underlie this "efficiency."

Marie Claude Hass,¹⁰⁴ P. L. Roubertoux,¹⁰⁵ M. Carlier,¹⁰⁵ and H. Degrelle¹⁰⁴ **Y Chromosome and Intermale Aggression in Mice. II. Use of a Marker on the X-Y Pairing Region (XY-PR).** Carlier and Roubertoux's paper (Y Chromosome and Intermale Aggression in Mice) suggested that some genetic correlates of intermale aggression in NZB (N) and CBA/H (H) could be located on the Y. The results from two strains congenic for the Y (N-YH and HY-N, respectively) showed that the level of attack behavior in the two congenics are those expected under an autosomal or pseudoautosomal correlate hypothesis. To test the linkage between attack behavior and XY-PR, the first step was to look for a polymorphism between N and H for the XY-PR. Steroid sulfatase (STS) activity was determined on homogenized and sonicated liver using as substrate ³H-estrone sulfate, previously purified by partition chromatography. The radioactive estrone was extracted by petroleum ether and counted. The enzymatic activity was expressed as picomoles per minute per milligram of protein. The N and H strains differ for STS (being STS+ and STS-, respectively). Moreover N-YH males are STS+, and H-YN males are STS-. These results pave the way to linkage detection between STS and attack behavior.

A. C. Heath.¹⁰⁶ Genetic Nonadditivity and the Structure of Personality.¹⁰⁷ Multivariate genetic analysis was applied to the responses of 2903 adult Australian twin pairs (N. G. Martin and R. Jardine, in S. Modgil and C. Modgil, eds., *Hans Eysenck: Consensus and Controversy*, Falmer Press, London, 1986), to items of the Extraversion and Neuroticism scales of the EPQ. In male pairs, conventional analysis of scale scores had revealed both additive and nonadditive (e.g., dominance or epistatic) genetic effects on both E and N (Martin and Jardine, 1986). A two-factor model, which constrained the dominance genetic loadings to be a constant multiple of the corresponding additive genetic loadings, for each factor, was fitted to the E and N items. Genetic nonadditivity was found only for the first latent factor, which had loadings consistent with Gray's Anxiety dimension (J. A. Gray, in H. J. Eysenck, ed., *A Model for Personality*, Springer-Verlag, New York, 1981), i.e., contrasting Neurotic Introverts and Stable Extraverts. The second, purely additive, genetic factor, had loadings consistent with Gray's Impulsivity dimension, contrasting Neurotic Extraverts and Stable Introverts. In female pairs, genetic nonadditivity was associated with an Extraversion dimension, and the second, orthogonal Neuroticism dimension exhibited purely additive genetic inheritance. Reasons for this inconsistency are discussed.

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Norman D. Henderson.¹⁰⁸ Genetic Influences on Infant Behavior of *Mus domesticus*: Possible Mediating Effects of Litter Size and Dam's Weight.¹⁰⁹ The genetic architecture of nipple attachment latencies of 1-day-old mice was found to be highly similar in two 6×6 diallel crosses, one using inbred parent strains of diverse origins and the second using inbred parents derived from a common population (N. D. Henderson, *Behav. Genet.*, **19**:554–574, 1989). In both cases latencies exhibited complete genetic dominance favoring rapid attachment to the mother. Subsequent analysis produced positive phenotypic correlations between speed of attachment and both litter size and the mother's body weight. The current report describes the degree to which the original genetic results were mediated by these two factors. Results indicate that the pattern of directional dominance remains after adjustments but that genetic and environmental paths both exist between dam's weight, litter size, and speed of nipple attachment. The strength of the environmental paths appears greater for genotypes derived from a common base population than for the diverse established strains from the Jackson Laboratory.

J. K. Hewitt,¹¹⁰ L. J. Eaves,¹¹⁰ M. Mosteller,¹¹⁰ and R. Schieken.¹¹¹ Can Increases in Mean Heart Rate During Aerobic Exercise Be Accounted for by Scalar Increments in the Effects of Genes that Control Individual Differences?¹¹² Dolan *et al.* (*Behav. Genet.* **18**:714, 1988; *Behav. Genet.* **19**:51–62, 1989) have presented an approach to modeling the means of set of measurements in terms of the same genetic and environmental influences that determine individual differences. Their approach implies a strong hypothesis about the action of the genes and/or the environment and about the scale of measurement. This strong hypothesis is unlikely to be confirmed in practice for psychological data. Where it is confirmed, however, it is extremely informative. An exception to the anticipated general lack of instances may be found in the study of cardiovascular variables observed under conditions of increasing stress. This paper presents some modifications to Dolan's model to make it more generally applicable and reports the results of an analysis of heart rate reactivity data from the MCV twin project. Implications for the scaling of measurements are also discussed.

J. K. Hewitt¹¹³ and M. C. Neale.¹¹³ A Simple Simulation Procedure for Exploring Genetic Models.¹¹⁴ The simulation of data sets under different assumptions about genetic and environmental control is an important tool in behavior genetics. It enables us to check on the sensitivity of our model fitting procedures and the power of our experimental designs in situations where a direct analytic approach is difficult or intractable. Simulations are an important tool in developing more formal theory, where "knowing what the answer should look like" is often of considerable heuristic value. Simulated data sets can give us a very good idea of what the world can look like under a particular hypothesis, and working from simulated data to discover how they were generated is of great didactic value. There are lots of ways of doing simulations and lots of programs are in use. Here we set out one extremely simple approach of considerable flexibility using SAS. Illustrative applications show how simple it is to translate a path diagram into a data simulation program, to simulate the effects of "soft" selection or variable age of onset on family correlations (Neale, M. C., Eaves, L. J., Kendler, K. S., and Hewitt, J. K., *Behav. Genet.* **19**:163–169, 1989; Neale,

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M. C., Eaves, L. J., Hewitt, J. K., Meyer, J. M., MacLean, C., and Kendler, K. S., *Am J. Human Genet.*, in press), and to simulate the control of age of onset under a gamma process survival time model (Meyer, J. M., and Eaves, L. J., *Genet. Epidemiol.* 5:265–275).

Jerry Hirsch,¹¹⁵ K. Lofdhal,¹¹⁶ D. Hu,¹¹⁷ and J. Belkhir.¹¹⁶ Homogamy Within, Partial Reproductive Isolation and Isozyme Differences Between Nonregressing *Drosophila melanogaster* Laboratory Populations Formerly Divergently Selected (Intermittently) for Positive or Negative Geotaxis. We describe the measurement of partial reproductive isolation and isozyme differences between the two *D. melanogaster* populations formerly (since 1958) divergently selected (intermittently), one for negative and the other for positive geotaxis, but which now (since 1978) no longer show regression on relaxation of selection even though not homozygous, as shown by their response to reverse selection.

Ronald C. Johnson¹¹⁸ and C. T. Nagoshi.¹¹⁹ Influences on Marital Status and on Within- vs. Across-Group Marriage of Hawaii Family Study of Cognition (HFSC) Offspring. We report data from the follow-up of HFSC offspring, assessing the association of personality, cognition, family background, and own attainment with marital status for the two sexes separately. For those offspring who are married we report variables associated with marriage within vs. across racial/ethnic groups.

Byron C. Jones,¹²⁰ J. M. Connell,¹²⁰ and V. G. Erwin.¹²⁰ Isolate Housing Affects Sensitivity to Ethanol in Long-Sleep and Short-Sleep Mice.¹²¹ Sensitivity to the anesthetic effects of ethanol differentiates in response to selective breeding and is well characterized in housemice (G. E. McClearn and R. Kakahana, *Behav. Genet.* 3:409–410, 1973). The lability of this selected ethanol sensitivity to environmental events in LS and SS mice, however, is less well-known. One study reported circadian cycle as an important covariate in brain tissue sensitivity to ethanol, especially in LS mice (D. M. Gilliam and A. C. Collins, *Pharmacol. Biochem. Behav.*, 18:803–808, 1983). To characterize further the role of environmental influences on ethanol sensitivity, we recently completed a study comparing the effects of individual vs. group housing on ethanol sensitivity in LS and SS mice. In two separate replicate experiments, male mice were assigned to individual housing at 45 days of age. Control animals were allowed to remain housed with 3 or 4 littermates until both groups were tested at 65–66 days of age. Compared with control mice isolate-housed LS showed significant decreases in sensitivity to ethanol as measured by sleep time, hypothermia and blood ethanol content (BEC) at regain of righting response. Changes seen in SS mice followed the same pattern as with LS mice, the exception being no significant change seen in BEC.

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Laura Karkowski-Shuman¹²² and G. E. McClearn.¹²² **The Effects of Short-Term Food Restriction and Realimentation on Behavior in C57BL/6 Mice.**¹²³ Following growth retardation due to dietary restriction, realimentation results in "catch-up growth." Catch-up growth is basically an accelerated growth response to a level approximating the expected value had dietary intervention never been imposed. Food restriction also has an apparent effect of "slowing" aging processes, in that it increases mean and maximum life spans and decreases the incidence or delays the onset of disease in certain experimental settings. The current research assesses the possibility of a process of "catch-up aging," analogous to "catch-up growth." Two types of food restriction were applied in this study: (1) everyother-day feeding for 200 days or (2) restriction to 60% of an *ad libitum* group for 60 days. The subjects were C57BL/6 female mice that were either 3 or 7 months at the beginning of the study. Putative biomarkers of aging were activity and autonomic reactivity (defecation and urination) in a File apparatus and on a dowel rod and hang time and autonomic reactivity on a tight wire. Tail tendon fiber break time, a measure of collagen cross-linkage known to increase with chronological age, was also measured. It was determined that restriction regimen 1 had effects on collagen cross-linkage and body weight, and regimen 2 affected squares and rears in the File apparatus as well as activity on the rod, tight wire hang time, and body weight, most of which were in a direction consistent with the interpretation that the rate of biological aging was reduced. After realimentation, the restricted groups converged on control values for most variables. Evaluating effects mediated by body weight change produced complex outcomes which are illustrated.

Kevin A. Kelley.¹²⁴ **Neuronal Expression of a Thy-1/*lacZ* Fusion Gene in Transgenic Mice.** The production of transgenic mice offers a unique system for examining gene regulation *in vivo*. Several isolated neuron-specific genes have been successfully expressed in the central nervous system (CNS) of transgenic mice, including the human light-neurofilament gene (J.-P. Julien *et al.*, *Genes Dev.* **1**:1085–1095, 1987), mouse myelin basic protein (C. Readhead *et al.*, *Cell* **48**:703–712, 1987), and human and mouse Thy-1 (J. W. Gordon *et al.*, *Cell* **50**:445–452, 1987; G. Kollias *et al.*, *Proc. Natl. Acad. Sci. USA* **84**:1492–1496, 1987). In an attempt to identify the Thy-1 regulatory sequences which are required for CNS expression and to produce a novel neuronal marker, we fused the protein-coding region from bacterial β -galactosidase (*lacZ*) to the mouse Thy-1.2 promoter. Five transgenic mice were produced from this fusion gene, and offspring were examined for the presence of transgene mRNA in various tissues. Expression was observed in only two of the five lines and was restricted to the CNS. The Thy-1.2 regulatory sequences that were used in this hybrid gene were sufficient to direct CNS expression; however, transcription appears to be integration dependent since only two of the lines express the transgene, suggesting that the Thy-1.2 5' sequences may contain a weak neuron-specific promoter/enhancer. The bacterial protein was easily detected in most neurons throughout the CNS, with particularly high levels observed in hippocampal area CA1 neurons, septal nucleus neurons, large neurons of most cranial nerve nuclei, and spinal cord motoneurons. Interestingly, the transgene-encoded bacterial protein is also expressed in the developing CNS (as early as embryonic day 10); the entire ventricular zone containing the neuronal precursors which migrate into the sub-cortical region of the developing brain produces very high levels of the bacterial protein. These results demonstrate the feasibility of using isolated CNS-specific regulatory elements to direct neuronal expression of heterologous proteins; the presence of bacterial β -galactosidase in the CNS of transgenic mice provides a novel marker for examining neuronal lineages during CNS development.

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Elizabeth A. Laffan¹²⁵ and C. B. Lynch.¹²⁵ Thermoregulatory Nesting in *Mus domesticus*: An Analysis of the Selection Limits.¹²⁶ Replicated, bidirectional selection for thermoregulatory nesting in *Mus domesticus* for over 40 generations has resulted in more than a 30-fold difference between high-nesting (H) and low-nesting (L) lines, and both H and L lines appear to have plateaued. To investigate the factors responsible for this plateau, relaxed and reversed selection was started at generation 36 in both replicates of the H and L lines. After 10 generations there has been a significant response to reversed selection in both H lines, demonstrating the presence of residual genetic variability. The data implicate heterozygote advantage as a source of selection limits in the H lines. In contrast, in the L lines only one of the replicates has responded to reversed selection; the other L line appears to be fixed. This is consistent with a relative ease of fixation of recessive alleles at loci influencing nesting. The relaxed lines differed from the H or LO lines, but not significantly; thus there does not appear to be strong opposing natural selection in either direction. While the two H lines are responding similarly to selection; they show a different pattern of correlated responses both in body weight and fertility. All lines responding to reversed selection for nesting in the warm also respond in a similar manner to nesting in the cold, indicating that these correlated responses are still firmly coupled.

Dasen Luo¹²⁷ and L. A. Thompson.¹²⁷ Memory Abilities in School-Age Twins.¹²⁸ Twin data were used to assess genetic and environmental influences on memory abilities. Memory measures included the Immediate and Delayed Names and Faces and the Immediate and Delayed Picture Memory subtests from the Colorado Specific Cognitive Abilities battery and the WISC-R Digit Span subtest. The tests were administered to 121 twin pairs, 76 MZ and 45 DZ, ranging in age from 7 to 12 years. Analyses were conducted for the entire sample, for different subgroups selected for a proband scoring either low or high on the first unrotated principal component of the memory tests, and for a high or low score on the individual memory tests. A regression model (DeFries and Fulker, *Behav. Genet.* 15:467-473, 1985) was used to test for genetic and environmental influences in the different proband groups. In addition, LISREL was used to test for genetic and environmental influences using between- and within-pair mean cross-product matrices from the total sample. The LISREL model for the whole sample could not determine whether genetic or shared family environmental influences were more important for structuring the observed relationships among the three memory measures. The regression analyses did not find heritability to be significant in any of the proband groups. However, for the WISC-R Digit Span subtest, some evidence for increased heritability was found in the low proband group.

G. Robert Lynch,¹²⁹ W. Puchalski,¹²⁹ and C. B. Lynch.¹²⁹ Selection for Photoresponsiveness in Djungarian Hamsters Affects Circadian Function.¹³⁰ The Djungarian hamster, *Phodopus sungorus sungorus*, exhibits multiple physiological and behavioral adjustments in response to chronic short-day exposure (9 h light:15 h dark). However, not all individuals respond to short-day conditions; this phenotypic difference has a genetic basis (G. R. Lynch, C. B. Lynch, and R. M. Kliman, *J. Comp. Physiol.* 164A:475-481, 1989). By using replicated bidirectional selection, we are developing genetically distinct lines for high and low photoresponsiveness. Since the circadian clock is an integral component of photoperiod time measurement in this species, one use of these genetic lines is to examine which aspects of

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circadian function are associated with photoresponsiveness. After three generations of bi-directional selection, the mean (\pm SE) period of the free-running activity rhythm in constant dark (DD) is shortest in responsive hamsters from the high lines (23.89 ± 0.05 h; $n = 24$), followed by the control lines (23.94 ± 0.03 ; $n = 25$) and then the low lines (24.24 ± 0.04 ; $n = 21$). Thus, even in individuals that respond to short days, selection for differences in photoresponsiveness has simultaneously altered circadian function. At this point in selection, pronounced differences in the duration of activity under DD (14.7 ± 0.5 , 15.3 ± 0.4 , and 15.4 ± 0.5 h, respectively) and response of activity onset to 15-min flashes of light (=phase response curve) have not been observed in responsive hamsters.

J. J. McArdle¹³¹ and Carol A. Prescott.¹³¹ Biometric Analyses of Changes over Age.¹³² This report discusses structural equation models for the biometric analysis of age related changes in psychometric scores. We use a structural equation approach to model the change over time in longitudinal twin data. Using this model we examine the overlapping contribution of age variation and genetic components. We extend this model to account for both longitudinal (intraperson) and cross-sectional (interperson) changes over age. This model also allows the separation of components of training (or retest) from other components of change, and we test hypotheses about the invariance of the biometric patterns of cross-sectional and longitudinal changes over age. We illustrate these models using mathematical data based on prior studies of cognitive data from adult twins. We discuss the importance of chronological age as a variable within both cross-sectional and longitudinal analyses of biometric data.

Christine M. McCauley.¹³³ Predicting the Child Behavior Checklist at 7 Years of Age from Infant Home Environment: The Role of Heredity. Is the relationship between the home environment during infancy and problem behavior in childhood genetically mediated? This question was explored by predicting problem behavior at 7 years of age from measures of the home environment (FES and HOME). As part of the longitudinal Colorado Adoption Project, data for 263 adopted and nonadopted children were analyzed. Correlations between environmental measures at 1 year of age and the Child Behavior Checklist (CBC) at 7 years of age were compared for adopted and nonadopted children to explore possible genetic effects. The nonadopted children's multiple correlations generally exceeded the adopted children's multiple correlations. For example, the multiple correlation of the CBC on the FES and the HOME measures at 1 year of age was .04 for adopted children and .16 for nonadopted children.

Gerald E. McClearn.¹³⁴ The Aspects of Team-Yoking Molecular and Quantitative Genetics. The astonishing successes of molecular genetics raised the prospect that the "old" Mendelian, population and quantitative genetics could be reduced to the "new" molecular genetics in the full theoretical sense. Whether such reduction will eventually be possible is the subject of current lively debate in the philosophy of science, with a positive position pointing to the enormous successes to date and with a contrary position arguing that there

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are emergent phenomena, particularly at the population and quantitative levels, that are not deducible from the molecular level of explanation. Even if full theoretical reduction is possible, it seems likely that efficiency in dealing with many population and quantitative genetic issues will still require concepts from those levels. Whatever the ultimate outcome, therefore, it seems likely for the foreseeable future that both the old and the new genetics will be required in the attempt to understand the bases of behavior individuality. However, the prospects are not just for continuation of parallel but separate approaches to the genetics of behavior. Opportunities are rapidly developing for using molecular genetics in the service of quantitative genetics methods, and converse developments are reasonably to be expected. These nascent methods have important implications for research strategies, and may dramatically affect the field of behavioral genetics.

Matt McGue¹³⁵ and T. J. Bouchard, Jr.¹³⁵ Genetic and Environmental Determinants of Information Processing and Special Mental Abilities: A Twins Reared Apart Analysis. A battery of information processing and special mental ability tests was administered to 49 sets of monozygotic and 25 sets of dizygotic reared-apart and adult twins. Significant genetic influences were observed on the composite, but not component, measures of speed of processing as well as on the psychometric measures of verbal reasoning, spatial ability, and perceptual speed and accuracy. Environmental influences for these traits appeared to be largely nonfamilial. Multivariate analyses aimed at associating the genetic and environmental influences on the psychometrically assessed abilities with measured differences in speed of processing and quality of the rearing environment were completed. Results of these analyses are presented and discussed within the broader context of the developmental behavioral genetics of human cognitive ability.

Matt McGue,¹³⁶ R. W. Pickens,¹³⁷ and D. S. Svikis.¹³⁸ Sex Differences in the Inheritance of Alcoholism.¹³⁹ Adoption studies suggest that the heritability of alcoholism is lower in females than in males. However, the results of the only published twin study of alcoholism to include a female sample of alcoholics are equivocal. Pickens *et al.* (1989) recently completed a twin study of alcoholism which, by virtue of its inclusion of relatively large samples of male ($N = 189$ pairs), female ($N = 90$), and opposite-sexed ($N = 96$) twin pairs, is especially informative with respect to sex differences in transmission. Alcohol-related problems were diagnosed using DSM-III criteria for Alcohol Abuse and/or Dependence from information obtained through mail survey. Analysis of the twin concordances under a multifactorial threshold model revealed reduced genetic transmission in females relative to males. Nonetheless, there is significant cross-sex transmission and the reduced genetic loading in females could be accounted for largely by differences in the diagnostic composition of the male and female proband groups. Results are discussed in relation to hypotheses concerning heterogeneity in the inheritance of alcoholism.

Peter McGuffin.¹⁴⁰ Genes, Environment, and Depression. There is no doubt that affective illness is more common in the relatives of depressed subjects than in the population at large.

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This is most marked for severe disorders so that the average lifetime risk of major affective disorder in first-degree relatives of patients with bipolar illness is about 20%, while for first-degree relatives of patients with unipolar disorder the risk is about 10%. In general, the risks are lower in relatives where the proband has a neurotic pattern of disorder but here the data from family studies are somewhat inconsistent, probably due to variation in the way the phenotype has been defined. Twin and adoption studies indicate that genes account for most of the familial aggregation of severe depression whereas twin studies of non endogenous depression suggest that common family environment may be a more important factor. Studies which focus on the relationship between life events, family loading, and depression have revealed an intriguing pattern. There is little to support the old dichotomy between neurotic/reactive and endogenous/nonreactive depression. Subjects whose onset of depression follows a threatening life event are just as likely to have affected relatives as those whose illness arises "out of the blue." Indeed, it appears that not only is depression familial but so also is the propensity to encounter (or to report) threatening life events. These tendencies are inextricably bound together and no simple model provides an adequate explanation at present. However, it is tempting to suggest that familial depressive cognitions play an important role.

Peter McGuffin.¹⁴¹ **Molecular Biology and Mental Illness: Problems and Possibilities.** Studies of major psychiatric disorders using restriction fragment length polymorphisms (RFLPs) as genetic linkage markers have provoked much recent interest. In particular, there have been reports of linkages between markers on chromosome 21q and Alzheimer-type dementia, a marker on chromosome 11p and manic depressive illness, and markers on chromosome 5q and schizophrenia. Unfortunately all of these findings have suffered from problems of non-replication. The most common explanation of reported linkage in one center but not in others has been that there is heterogeneity. This seems reasonable given that we are dealing with conditions which are common and show considerable clinical variability. However, the lack of consistency in linkage study findings might also lead us to the less optimistic view that the positive results so far are due either to chance or to some systematic sources of error. The major obstacle in applying linkage strategies in mental illness is that the mode of inheritance of the disease is always unknown. Furthermore, any proposed major gene models must allow that penetrance is incomplete. Although not insurmountable, these facts together with the inherent classification difficulties of psychiatric phenotypes and the problems of heterogeneity at the molecular level greatly tax the would-be researcher. Molecular genetics holds great promise for advance of our understanding of mental illnesses and other behavioral phenotypes but cannot be regarded as an easy panacea. If we are to capitalize properly on new and powerful tools, we must not expect them to provide simple solutions to old and intrinsically complex problems.

Joanne M. Meyer.¹⁴² **Exploring the Dimensionality of the Smoking Habit.**¹⁴³ In studying genetic and environmental influences on the smoking habit, a critical question is whether the adoption of the habit and the quantity consumed are transmitted independently or as part of a single liability continuum. To address this question, we used nonmetric multidimensional scaling and parametric model-fitting procedures on smoking data from 1335 pairs of like-sex monozygotic and dizygotic twins. Multidimensional scaling was applied to similarity matrices derived from 2-way contingency tables cross classifying the smoking responses of each member of a twin pair; parametric models were fitted directly to the observed tables. Results from both analyses indicate that the adoption of the smoking habit and the quantity smoked are inherited independently of each other. We suggest using nonmetric procedures

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for exploratory analyses of the dimensionality of additive behaviors but caution that parametric model fitting must be used to test hypotheses rigorously.

Craig T. Nagoshi,¹⁴⁴ R. C. Johnson,¹⁴⁵ and K. A. M. Honbo.¹⁴⁵ Parent-Offspring Resemblances in Cognitive Abilities of Offspring Assessed in Adolescence and Young Adulthood.¹⁴⁶ Caucasian and Japanese American offspring from the Hawaii Family Study of Cognition (HFSC) originally assessed on a battery of cognitive abilities tests between 1973 and 1976, when subjects were between 13 and 20 years of age, were retested in 1988 on those same measures. The biological parents of these offspring were also tested in 1976. Parent-offspring resemblances were compared between the earlier and the later offspring testing to examine whether such resemblances would change as these subjects approached the age of their parents at the time the parents were tested.

Donald J. Nash¹⁴⁷ and L. J. Draski.¹⁴⁷ Genotypic and Age Differences in the Mouse Staircase Test. The mouse staircase test has been found to be a sensitive test for the detection of the antianxiety activities of different clinical anxiolytic drugs. The test measures the ability of mice to negotiate an enclosed staircase containing five steps. The present study examined genotypic and age differences in the staircase test. Mice homozygous for the hotfoot (ho) mutation and their phenotypically normal sibs as well as mice from a random-bred stock were used. Hotfoot is an autosomal recessive mutation and produces a syndrome of progressive neuromuscular disability of the hindlegs. Subjects were tested at ages from 1 month to over 1 year. Testing consisted of placing a naive mouse in the staircase and observing the number of steps climbed and the number of rearings made in a 3-min period. The two behaviors measured are indicators of the locomotor activity and the anxiety state of the mouse. Both genotypic and age differences were observed. Many homozygous hotfoot mice, for example, did not climb any stairs at all, and those that did averaged considerably less than did their normal sibs. In general, all genotypes showed a decline in activity with age. Results indicate that the stairclimb test may be used as a sensitive measure of locomotor activity as affected by genotype and age.

M. C. Neale.¹⁴⁸ A Latent Variable Model of Assortative Mating.¹⁴⁹ Traditional treatments of multivariate assortative mating assume that mate selection occurs on the basis of measured phenotypes. In this context, correlation between mates may arise through direct assortment (primary homogamy) or through correlation with another variable for which there is assortment (secondary homogamy). In addition, there may be cross-assortment such that one variable in males may be associated with another in females. Although the full form of this model fit perfectly to any set of marital correlations, it may be difficult to obtain a parsimonious account of spouse resemblance. An alternative model that specifies a simple structure of assortment between latent variables is presented. Within spouses, each latent variable may cause variation in each observed variable. The saturated model is equivalent to canonical correlation analysis with predictor variables for one spouse and criterion variables

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for the other. It is shown that this model gives a more parsimonious account of anthropometric data (K. Pearson and A. Lee, *Biometrika* 2:357–396, 1903) than does the direct phenotypic homogamy model. Implications for the genetic consequences of assortative mating are discussed.

Jenae M. Neiderhiser,¹⁵⁰ Between- and Within-Litter Variance in Inbred Strains of Mice as Evidence of Shared and Nonshared Environment. Nonshared environmental influences in the development of personality recently has become a focus of research in human behavioral genetics. However, a review of animal research reveals that nonshared environment has received little attention. The literature indicates variance within inbred strains of mice, although rarely is variance between and within litters compared. Between-litter variance can be viewed as shared environment and within-litter variance may be interpreted as nonshared environment. An analysis of shared and nonshared environmental influences on behavior in inbred mice points to a substantial role for nonshared environment in mice as well as in humans.

Marika Nosten-Bertrand,¹⁵¹ P. Signore,¹⁵¹ and M. Chaoui.¹⁵¹ Involvement of the Major Histocompatibility Complex in Handedness in Mice. According to Geschwind (*Archives of Neurology* 42:428–459, 1985), the major histocompatibility complex (MHC; HLA in man) would be involved in cerebral and behavioral asymmetry via the sensitivity to testosterone. First, in mice it has been demonstrated that animals exhibit a reliable paw preference (Collins, *Journal of Heredity* 60:117–119, 1988; Nosten *et al.*, *Behavior Genetics* 18:727, 1988). Second, the MHC (H-2 in mice) is involved in sensitivity to testosterone (Ivanyi, *Nature* 238:280–281, 1972). Third, association between testosterone sensitivity and paw preference has been demonstrated using the Tfm mutation (Nosten *et al.*, *Journal of Endocrinology* in press. A hypothesis implicating the MHC in behavioral asymmetry is tested here using congenic strains for H-2 which present the same genetic background but differ for the H-2 haplotype. Significant differences for strength of lateralization are observed for six strains C57BL/10, congenic for H-2 (a, b, d, f, k, and s). A strain/haplotype interaction is observed using three H-2 haplotypes transferred on two inbred strains BALB/cJ and C57BL/10J. These results are in line with an effect of the MHC on behavioral asymmetry, and possible interaction with segregating units located on others chromosomes is discussed.

Mary L. Oster-Granite,¹⁵² A. Mjaatvedt,¹⁵² S. Fisher,¹⁵² J. Bennett,¹⁵² R. Reeves, and J. D. Gearhart.¹⁵² Recent Studies of Mice Transgenic for the Gene Encoding Amyloid Precursor Protein. The neuropathologic stigmata of Alzheimer's disease—neurofibrillary tangles, neuritic plaques, and granulovascular degeneration—are also found in the brains of adults with Down syndrome (trisomy 21). The neuritic plaques observed in both these conditions contain a 42-amino acid peptide, the A4 or B amyloid peptide, encoded as a portion of a larger precursor molecule by the gene *amyloid precursor protein* (*APP*). Not only are the mouse and human forms of this gene very similar in sequence, but also several alternative splicing forms of the precursor protein exist in mice and humans. *APP* is located on human chromosome 21 and on mouse chromosome 16, in a region of known genetic synteny with human chromosome 21. Mice with trisomy 16 exhibit elevated expression of *App* message in their

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brains at very early developmental stages. Unfortunately, these mice do not survive into the postnatal period and, thus, are not amenable to studies of the results of overexpression of *App* on continued development or survival of cells in the central nervous system. Mice transgenic for all or portions of this gene may provide useful insights into the role overexpression of *APP* plays in normal developmental processes and, particularly, to its role, if any, in the pathogenesis of alterations that occur in the brain in trisomy 16 mice. Using various promoters and portions of the sequence encoding the precursor forms of *App*, we have constructed transgenic mice designed to exhibit overexpression in many tissues and others designed to exhibit overexpression only in neurons. Results of our studies indicate that overexpression of the last portion of the gene (involving the A4 sequence) is associated with limited pre- and postnatal survival of such transgenic mice.

Susan F. Parlour¹⁵³ and Patricia A. Broen.¹⁵³ Familial Risk for Articulation Disorder: a 25-Year Follow-Up.¹⁵⁴ This study provides a better understanding of the genetic and environmental factors that contribute to the etiology of functional speech articulation (sound pronunciation) disorders. Subjects were drawn from a group of approximately 400 individuals who participated in a longitudinal study of speech and academic development conducted at the University of Minnesota between 1960 and 1972. These individuals are now 32–34 years of age, and most of them have families. Two groups were identified from the original study: (1) a proband group ($N = 24$), consisting of individuals who displayed significant and persistent articulation problems in childhood; and (2) a control group ($N = 29$), selected from individuals who performed above average on articulation measures when they were children. The current speech and language skills, child-rearing practices, and educational and occupational status of these two groups were compared, as were the speech and language skills of their spouses and offspring. Results demonstrate the extent to which articulation and related disabilities aggregate in families with a parent who had a documented articulation disorder as a child. If familial aggregation occurs, this suggests that having a parent with a positive history of articulation disorder is a significant factor in predicting risk for communication impairment in children.

Peter A. Parsons.¹⁵⁵ Behavioral Activity, Metabolic Rate, and Stress Tolerance. *Drosophila melanogaster* lines showing high desiccation resistance are resistant to many generalized environmental stresses because of a reduction in metabolic energy expenditure measured by oxygen consumption in the light and the dark (A. A. Hoffmann and P. A. Parsons, *Biol. J. Linn. Soc.* 1989, in press). Predictably the lines had reduced behavioral activity levels. Genotypes with low rates of metabolism may therefore be favored under stressful conditions.

T. Edward Reed¹⁵⁶ and A. R. Jensen.¹⁵⁷ Short-Latency Visual Evoked Potentials (VEPs), Visual Tract Speed, and Intelligence: Significant Correlations. Speed of information processing (SIP) should correlate positively with intelligence (IQ). This expectation is supported by the negative correlation observed between IQ and choice reaction *Time* (A. R. Jensen, in H. J.

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Eysenck, ed., *A Model for Intelligence*, Springer-Verlag, Heidelberg, 1982). A possible basis for variations in SIP has been suggested (T. E. Reed, *Behav. Genet.* 18:595–603, 1982); transmission speed of impulses along nerve axons (nerve conduction velocity; NCV) in the brain may vary appreciably among individuals. Persons with higher brain NCVs should have higher SIPs. One hundred forty-seven white male college students, ages 18–25 years, were tested for nonverbal problem-solving ability and for latencies of two VEPs, N70 and P100, recorded over the primary visual cortex. The mean latencies for N70 and P100 were 72.3 and 100.2 ms, respectively. Dividing each S's head length (uncorrelated with IQ) by his VEP latency gives a kind of visual tract speed, V:N70 and V:P100, which should be proportional to the true visual tract NCVs. Correlations (and two-tail *p*'s) of IQ score with N70 latency, P100 latency, V:N70, and V:P100 were $-.12$ (NS), $-.21$ ($<.05$), $+.18$ ($<.05$), and $+.25$ ($<.002$), respectively. Correcting for restriction of IQ range raises the last two correlations to $+.27$ and $+.37$, respectively. This finding may encourage other tests of these hypotheses.

Susan M. Resnick.¹⁵⁸ The Application of Genetic Strategies to Neuroimaging Studies of Neuropsychiatric Illness. Recent developments in neuroimaging provide a new group of phenotypic markers which can be examined in relation to normal and abnormal behavior. Magnetic resonance imaging (MRI) and computed tomography (CT) provide anatomic measures, while brain physiology is examined by positron emission tomography (PET), single photon emission computed tomography (SPECT), and the 133-xenon regional cerebral blood flow (rCBF) technique. The utility of these methods for the study of regional brain structure and function can be enhanced when they are used in combination with genetic methods. Twin studies, particularly studies of discordant identical twins, provide sensitive methods to identify and follow the progression of brain abnormalities and behavioral deficits. Family studies can be applied to examine dimensions of brain structure and function—e.g., ventricular size on MRI or CT, PET measures of anterior–posterior, subcortical–cortical, and laterality gradients of metabolism, or receptor density and affinity—which can be used as predictors of familial risk. Dimensions which predict familial risk may define homogeneous subtypes and indicate biologic markers for genetic forms of a disorder. Genetic approaches have been used in combination with neuroimaging methods to study a variety of neuropsychiatric disorders—including schizophrenia, Alzheimer's disease, and Tourette syndrome by our group and Huntington's disease by other investigators. Continued developments in genetics, improved resolution of neuroimaging techniques, and increasing availability of new radioligands for neurotransmitter receptor labeling will extend the utility of this approach.

Jo Etta Marie Roehl.¹⁵⁹ A Twin Study of Intelligence in Adults: Preliminary Findings.¹⁶⁰ Human intelligence is subject to developmental forces throughout the life span and there are no *prima facie* reasons to expect that hereditary factors maintain a constant degree of influence. Jarvik and colleagues (L. F. Jarvik, J. E. Blum, and A. O. Varma, *Behav. Genet.* 2:159–171, 1972) reported the results of a small 20-year follow-up study of twins first studied by Kallmann and associates in 1940 (F. J. Kallmann, L. Feingold, and E. Bundy, *Am. J. Hum. Genet.* 3:65–73, 1951), which seems to indicate that the heritability of intelligence is dynamic and decreases during the life span. Life-style factors have been posited as accounting for these changes in correlations. The WAIS-R was administered to a sample of monozygotic (MZ) and dizygotic (DZ) twins as part of the Minnesota Twin Study of Adult Development. The sample consisted of 94 MZ individuals and 104 DZ individuals with a mean age of 68.4 years. Correlations and heritabilities were obtained for the WAIS-R components. The relationship between WAIS-R components and several life-style factors were

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explored. Particular focus was placed on exploring the heritabilities and the relationship of life-style factors with those abilities felt to begin to decline, on average, as early as the third decade of life, and those that, on average, are stable or continue to increase throughout much of the adult life span.

Michael J. Rovine¹⁶¹ and H. M. Chipuer.¹⁶¹ Nonlinear Dependency on Sample Size of Maximum-Likelihood Solutions. Behavioral genetics analyses utilize multiple-group models to obtain estimates of genetic and environmental effects. Characteristics of the solutions of such models are dependent on the sample size of the subgroups. In certain circumstances, in particular when subgroup model equations present algebraically inconsistent information, it is possible to determine an optimal set of subgroup sample sizes that lead to an identified model. However, an optimal solution can mask an underlying problem based on the algebraically inconsistent data. LISREL outputs for the same set of input data with different sets of sample sizes are presented to illustrate the problem.

David C. Rowe and C. L. Britt.¹⁶² Continuity and Change in Self-Report Delinquency: A Behavioral Genetic Analysis of Siblings in the National Youth Survey. Self-report delinquency demonstrates considerable "within-person" stability during adolescence. Longitudinal models can test different theories about the determinants of behavioral stability and change. Three waves of data and 470 sets of siblings in the National Youth Survey (D. S. Elliott, D. Huizinga, and S. S. Ageton, *Explaining Delinquency and Drug Use*, Sage, Beverly Hills, Calif., 1985) were used in this analysis. Theories were stated as "structural equation" models containing (1) common factor parameters representing shared environment and/or heredity; (2) phenotypic continuity parameters, representing effects of earlier on later delinquency; and (3) sibling parameters, representing mutual interaction effects. Most delinquency covariation among occasions and across siblings was explicable in terms of the common factor. Interpreting the common factor as a genetic one suggests a heritability of about 40–50% for self-reported delinquency—in accord with a previous twin/sibling study (D. C. Rowe and J. L. Rodgers, in G. R. Adams, R. Montemayor, and T. P. Gullotta, eds., *Biology of Adolescent Development and Behavior*, Sage, Newbury Park, Calif., 1989).

Laura M. Sakai,¹⁶³ L. A. Baker,¹⁶³ and C. N. Jacklin.¹⁶³ Etiology of Individual Differences in Sex Steroids Present at Birth. Individual differences in sex-steroid hormones are believed to play an important role in behavioral development. Relationships have been found with some cognitive and personality traits in children (e.g., C. N. Jacklin, K. Thompson-Wilcox, and E. E. Maccoby, *Dev. Psychobiol.* 21:567–574, 1988; C. N. Jacklin, E. E. Maccoby, and C. H. Doering, *Dev. Psychobiol.* 16:163–168, 1983). The present study investigated genetic and environmental components of variation and covariation in levels of three sex steroids at birth: estradiol, progesterone, and testosterone. Radioimmunoassays were performed for each of these hormones in the umbilical cord blood samples of twin pairs. Preliminary multivariate biometrical analyses of 49 pairs indicated significant genetic effects for estradiol ($h^2 = .45$) and testosterone ($h^2 = .45$) and significant common environmental effects for progesterone ($c^2 = .57$). Thus maternal hormones may play a greater role in neonatal progesterone levels of offspring from multiple births, while differences in neonatal

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genotypes make a greater contribution to variation in estradiol and testosterone. However, correlational patterns among these three hormones varied for the two twin types, suggesting complicated interrelationships among estradiol, progesterone, and testosterone at birth. Additional analyses will be presented concerning these hormones and their relationship to novelty preference at 3 and 5 months after birth.

Marvin B. Seiger¹⁶⁵ and S. Swabb.¹⁶⁵ The Effect of the Motivation to Mate on Light Response in Three Sympatric Species of *Drosophila*. In studying the effects of various external environmental parameters on photobehavior in populations of *Drosophila*, we have found that a given stimulus will not always evoke the same light response when presented at different times. When an animal is motivated to behave in a specific way, perhaps to mate or oviposit, its internal environment is changed, which, in turn, may affect response to light (D. J. Wogaman and M. B. Seiger, *Can. J. Genet. Cytol.* **25**:370-377, 1983). This change in internal environment may be regarded as an internal variable affecting light response. While it would be difficult to study the internal variable directly, its effect on light behavior can be studied. The motivation to mate is used to generate the presumed internal variable. We determined any differences in light intensity preference for individuals who are not highly motivated to mate and for individuals who had been sexually deprived in three sympatric species of *Drosophila*. The results provide evidence that light intensity preferences for sexually sated and sexually deprived individuals differ within and between species. This could serve to reduce competition and maintain the integrity of the species.

B. Siegfried,¹⁶⁶ H. R. Frischknecht,¹⁶⁶ D. Lazega,¹⁶⁶ and P. Driscoll.¹⁶⁷ Morphine Effects on Body Temperature and Behavior in Roman High- and Low-Avoidance (RHA/Verh and RLA/Verh) Rats. Using low doses (up to 10 mg/kg, sc), Ushijima *et al.* (*Eur. J. Pharmacol.* **112**:331, 1985) have found a morphine-induced hyperthermia in nonstressed rats, vs. a morphine-induced hypothermia in stressed (immobilized) rats; 20 mg/kg resulted in hypothermia in both types of handling. In the present study, dose-dependent increases in body temperature (significant at 4 and 10 mg/kg, ip) were seen in RHA/Verh rats but not in RLA/Verh rats. This genetic difference may be mediated by mu opioid receptors, which show a greater CNS-binding capacity in RHA/Verh rats, especially in the striatum (1.7-fold). It has also been suggested that endogenous opioids and/or striatal mu receptors may be involved in locomotion and that they modulate striatal dopaminergic neurotransmission (e.g., George and Kertesz, *Peptides* **8**:487, 1987). RHA/Verh rats, which are generally more active than RLA/Verh rats, also have a higher turnover rate of dopamine in the striatum, corresponding to their greater binding capacity of mu receptors in that brain area. We have found an apparently stronger, dose-dependent effect of morphine on open-field behavior in RHA/Verh rats, especially on the number of rearings, than in RLA/Verh rats, but an accurate comparison has been impeded by the large baseline differences seen between the two selected lines, in both rearing behavior and locomotor activity.

Pierre Signore,¹⁶⁸ M. Chaoui,¹⁶⁸ P. Roubertoux,¹⁶⁸ and M. Nosten-Bertrand.¹⁶⁸ Handedness in Mice: Comparison of 11 Inbred Strains. Males and females from 11 inbred strains of mice (DBA/2J, CPB-K, BALB/cJ, NZB, BA, A/J, C57BL/6J, C57BL/10J, CBA/H, XL2, SWR/J) have been tested for handedness using Collins' paradigm (*Journal of Heredity* **60**:117-119, 1968). (1) We confirm that females are more strongly lateralized than males (either left or right). (2) Significant strain differences for strength of lateralization are observed. C57BL/

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6 and SWR/J strains for males and CPB-K and NZB strains for females exhibit the strongest contrasts, C57BL/6 and CPB-K, respectively, for males and females being the most lateralized. New results show significant differences for the direction of lateralization (right vs. left). For this variable, C57BL/10 and CPB-K strains for males and CBA/H and C57BL/6 strains for females exhibit the strongest contrasts, C57BL/10 and CBA/H, respectively, for males and females employing the right paw more frequently. (3) A sex-strain interaction is demonstrated for both variables.

Judy L. Silberg,¹⁶⁹ Sources of Variation in Depressive Symptoms in a General-Population Twin Sample.¹⁷⁰ To determine the etiology of depressive symptoms and their cooccurrence in the general population, multivariate genetic models were used to analyze the responses of 771 female twin pairs (463 MZ, 308DZ) to a 20-item epidemiological depression inventory (CES-D Scale) (Radloff, 1977). A model which contained one common genetic factor, one shared environmental factor, and four unique environmental factors provided the most parsimonious explanation of symptom covariation. The item loadings on the four common unique environmental factors were similar to those obtained from a phenotypic factor analysis of the CES-D scale. The first factor was interpretable as a "depressed affect" factor; the second, a "positive affect" factor; the third, a "somatic" factor; and the fourth, an "interpersonal sensitivity" factor. The common nonshared environmental factors accounted for the greatest proportion of variance in response to the CES-D scale, whereas the single common genetic factor explained substantially less of the variation in symptomatology. Consistent with previous findings (R. Jardine and N. G. Martin, *Genet. Epidemiol.* 1:89-107, 1984; K. S. Kendler, A. C. Heath, N. G. Martin, and L. J. Eaves, *Arch Gen. Psychiat.* 44:451-457, 1986) shared environmental influences played a relatively minor role in the report of depressive symptoms. These results suggest that while genetic factors do contribute to the covariation among symptoms of depression, it is largely nonshared environmental factors that account for the cooccurrence of symptoms in the general population.

Sandra M. Singer,¹⁷¹ M. J. Cosgrove,¹⁷¹ and L. A. DeVillez.¹⁷¹ A Dermatoglyphic Analysis of Autism. Good evidence exists that abnormal finger and palm prints are associated with such phenomena as chromosomal defects, prenatal exposure to rubella, and several forms of mental retardation. Other behavioral syndromes for which dermatoglyphic aberrations have been recently identified include a familial form of Alzheimer's disease and infantile autism. The studies that have analyzed the dermatoglyphic patterns of autistics suggest that several characteristics of finger and palm prints seem to be associated with this severe disorder of early childhood. Finger and palm prints of approximately 50 autistic children have been collected and analyzed. In keeping with other studies and our own preliminary data, an association seems to exist between the dermatoglyphic characteristic of palmar ridge dissociation and infantile autism. Photographs documenting these and other dermatoglyphic findings are presented.

Leslie K. Smith¹⁷² and James R. Wilson.¹⁷² Stress and Mood Components of the Cigarette Withdrawal Syndrome.¹⁷³ Behavioral genetic analyses of smoking have been reported in several studies; apparently none, however, has examined cigarette withdrawal symptomatology in this way. We have recently undertaken such a study and here report preliminary

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results on level of stress, stress-related symptoms, "resistance resources," and mood change. During a 10-h testing day, we administer a large battery of physiological, motor, cognitive, personality, stress, and mood tests to a single individual two times while the individual continues to smoke, three times during withdrawal (maximum withdrawal 5–6 h), and once after resumption of smoking. For the BG design, MZ, DZ, and adoptee pairs are recruited. Preliminary findings from 33 individuals indicate for scale Stress smoker's mean = 19, compared to the general population mean of 17; smoker's Resources = 53.8, general population's = 61.7; and smoker's Symptoms = 22.3, general population's = 16.6. Subjects become more irritable, more confused, less accurate in their appraisal of time passage, and more likely to blame others for their condition. As the sample design is filled over the next 4 years, we anticipate that we will be able to partition the variance of specific symptoms (or symptom clusters) into additive genetic and environmental components, with a view to more specific amelioration of the uncomfortable symptomatology which seems to be an important factor in the difficulty of quitting smoking for many individuals.

Michael C. Stallings,¹⁷⁴ L. A. Baker,¹⁷⁴ and D. I. Boomsma.¹⁷⁵ Estimation of Cultural Transmission in Extended Twin Designs. Extended twin designs have recently gained in popularity in quantitative behavior genetics. The twin-family design is one extension of the basic twin design in that it incorporates additional information from the parents of the twins, thus allowing for the estimation of the effects of assortative mating and cultural inheritance on twin and family resemblance. However, some shortcomings of this model are now apparent. Specifically, the assumption of intergenerational equilibrium necessary for model identification may be too restrictive for many applications. When heritabilities differ in the parent and child generations, or when genetic effects at the two different age points are less than perfectly correlated, negative cultural transmission parameter values may result. Several researchers have attempted to interpret these parameters substantively when they may be better explained as artifacts of the inadequacies of the twin-family model under certain conditions. This paper demonstrates the shortcomings of the twin-family model using simulation data and suggests ways of improving the design by incorporating an additional sample of adult twins comparable in age to the parents of the child twins. Although some constraints on this model are still necessary, the inclusion of adult twins allows for the estimation of separate heritabilities in the two generations and provides additional information regarding some, but not all, cultural transmission parameters.

Patricia A. Szesulski¹⁷⁶ and L. A. Baker.¹⁷⁷ Resemblance on Word Recognition Processes Among Dyslexics and Their Parents. Two of the most consistent observations concerning developmental dyslexia are that (1) the disorder tends to cluster within families and (2) the fundamental problem shared by dyslexics is faulty word recognition skills. Central to the investigation was the assumption that word recognition skill is dependent upon the status of the development of phonological and orthographic processes. The goal of the present study was to determine whether dyslexic children and their parents evinced similar patterns of impairment in word recognition processes. Accordingly, 40 dyslexic children, both their biological parents, and 177 normal readers were administered multiple measures of phonological and orthographic processing. Processing deficits were defined in terms of deviations from the performance of normal readers matched on either chronological age or reading achievement level. A principal-components analysis conducted on the data identified two factors that were consistent with the two dimensions of reading ability posited by the dual-

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process theory of word recognition. In general, obtained patterns of familial correlations suggest that (1) individual differences among probands in both the phonological and the orthographic domains are associated with their parents' phonological ability, (2) familial relationships in the orthographic domain are stronger between father and proband than between mother and proband, and (3) there is good concordance between parents and probands in component processing ability despite the fact that there was virtually no relationship between parent and proband on the global word recognition measures.

L. A. Thompson¹⁷⁸ and D. K. Detterman.¹⁷⁸ Specific Cognitive Abilities and Achievement in School-Age Twins.¹⁷⁹ Genetic and environmental influences on the relationships among specific cognitive abilities and measures of school achievement are explored in a sample of same-sex twins ranging in age from 7 to 12. The current sample represents a normal range of intelligence (mean = 105, SD = 13.9; 86 MZ and 56 DZ twin pairs). Subjects were administered 8 of the subtests from the Colorado Adoption Project's battery of paper-and-pencil specific cognitive abilities tests and 4 composite scores were formed representing Verbal Ability, Spatial Ability, Perceptual Speed, and Memory. School achievement was assessed using the Metropolitan Achievement Test, which yields a Reading, Language, and Math score. At the phenotypic level, measures of achievement are moderately correlated with specific cognitive abilities. Heritabilities ranged from .29 to .75. Estimates of shared family environment ranged from .02 to .52. In general, shared family environment contributes more to twin similarity for achievement than for cognitive abilities. LISREL was used to fit a multivariate model to the data using MZ and DZ between- and within-mean cross-product matrices as detailed by Fulker *et al.* (1983). The model providing the best fit included one general factor and seven specific factors for each of the component matrices ($X^2 = 68.73$, $df = 70$, $p' = .52$). Genetic correlations among cognitive and achievement tests ranged from .60 to .76, shared environment correlations were essentially zero, and specific environment correlations were low (.06 to .22).

E. Turkheimer.¹⁸⁰ What Can We Learn from IQ Differences Between Separated Siblings? One of the more striking findings in the history of studies of genes and environment in the development of IQ is that siblings raised in contrasting environments show considerable differences in IQ, which are often interpreted as demonstrating directly the influence of the environment on mean levels of IQ. Beginning with the flawed but influential studies of Skodak and Skeels (e.g., M. Skodak and H. M. Skeels, *J. Genet. Psych.* 75:85-125, 1949), separated siblings have received renewed attention since the publication of Schiff and Lewontin's (*Education and Class: The Irrelevance of IQ Genetic Studies*, Clarendon Press, Oxford, 1986) report of dramatic differences among separated siblings in France. We consider the implications of the separated sibling design in light of a methodological analysis of group and individual effects in adoption studies, reanalyze the Schiff *et al.* data to demonstrate that attributing the IQ difference to the environment is not as simple as it appears at first and analyze a previously unreported sample of 28 pairs of separated siblings from the National Collaborative Perinatal Project. These new data demonstrate that although sibs raised in contrasting environments show IQ differences at 7 years, the magnitude of the difference is unrelated to all measured aspects of either sib's environment. Several methodological and substantive explanations of these findings are considered. The single most potent predictor of IQ at 7 years is a variable summarizing medical episodes during childhood.

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Philip A. Vernon¹⁸¹ and M. Mori.¹⁸¹ Intelligence, Reaction Times, and Nerve Conduction Velocity.¹⁸² Numerous studies have investigated the relationship between intelligence and reaction time measures of speed of information processing (P. A. Vernon, ed., *Speed of Information-Processing and Intelligence*, Ablex, Norwood, N.J., 1987). In the present study, conducted with 85 university students, subjects' nerve conduction velocity was measured in addition to their IQs and reaction times. The average correlation between full-scale IQ and eight reaction time tests was $-.44$, replicating previous work. Nerve conduction velocity, a pure physiological measurement involving no cognitive activity, also correlated significantly both with intelligence ($r = .42$) and with reaction times ($r = -.28$). In addition, the more g-loaded the subtests of the intelligence tests, the more highly correlated they were with nerve conduction velocity ($r = .46$). These results may, as Reed (*Nature* 311:417, 1984) hypothesized, be attributable to genetic variability in the structure and amount of transmission proteins (i.e., proteins involved in the transmission of impulses along nerve fibers and across synapses) which set limits on information-processing rates and, hence, on speed of processing and intelligence. The results are also compatible with those of other studies of physiological correlates of intelligence—such as evoked potentials and cerebral glucose metabolic rate—which indicate that subjects of higher intelligence possess more efficient and faster neural systems. We are currently administering the same tests to samples of adult MZ and DZ twins.

George P. Vogler,¹⁸³ Theodore Reich,¹⁸⁴ Paul van Eerdewegh,¹⁸⁴ John Rice,^{183,184} and Joe Mullaney.¹⁸⁴ Familial Nature of the Relationship Between Alcoholism and Major Depressive Disorder.¹⁸⁵ Previous research has established that there is familial transmission for both alcoholism and depression. This study examines the nature of the observed correlation between the two phenotypes within individuals. A bivariate model of familial resemblance in nonrandomly ascertained nuclear families was developed which subdivides transmissible factors into those which are common to both alcoholism and depression and those which are unique to each phenotype. Nontransmissible environmental factors can be correlated. Spouse resemblance and sibling shared environment are modeled both within and between traits. Secular trends are modeled by indexing relevant parameters to a logistic function of birth cohort. To handle qualitative family data, a rapid algorithm for integration of higher-order multivariate normal densities is implemented. Results indicate that there are no transmissible factors that are common to alcoholism and depression, whereas there is a substantial correlation of nontransmitted environmental influences which accounts for the observed phenotypic correlation. Secular trends occur for age of onset of both alcoholism and major depression, with earlier onset in younger cohorts.

Irwin D. Waldman,¹⁸⁶ Roy W. Pickens,¹⁸⁷ and Dace S. Svikis.¹⁸⁷ Sex Differences in Genetic and Environmental Components of Childhood Conduct Problems.¹⁸⁸ Data on childhood con-

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duct problems were gathered on 293 adolescent and adult same-sex twin pairs as part of a study on genetic and environmental factors in alcohol abuse and dependence. Four specific indices of childhood conduct problems were assessed; these included (1) playing hookey or being expelled from school; (2) frequently breaking rules at, or running away from, home; (3) stealing or destroying property; and (4) frequently starting or becoming involved in fights. A composite index of conduct problems was formed by summing these items; the internal consistency of this index was moderately high for both males and females ($\alpha = .77$ for both sexes). This index was moderately negatively correlated with current age, more strongly for females ($r = -.58$) than for males ($r = -.28$), indicating the possibility of cohort effects for reported conduct problems and of sex differences therein. Concordances and intraclass correlations for this composite were higher in female than in male same-sex twins. Hierarchical regression analysis was used to estimate the specific genetic and environmental components of the composite conduct problems index for each gender. For both sexes, twin similarity appeared to be mainly a function of genetic and nonshared environmental factors (males— $h^2 = .40 \pm .20$, $c^2 = .00 \pm .15$, $e^2 = .60$; females— $h^2 = .54 \pm .26$, $c^2 = .05 \pm .21$, $e^2 = .41$). Regression analyses incorporating current age were also performed to examine cohort differences in genetic and environmental components. For both sexes, MZ twin correlations remained similar, whereas DZ twin correlations decreased markedly as cohorts increased in age.

J. M. Warren,¹⁸⁹ No Gene–Environment Interaction in Maze Learning by BALB/cJ and CBA/J Mice and Their Hybrids. Groups of 15 inbred BALB/cJ(B) and CBA/J(C) mice and their BC and CB hybrids were trained on the Lashley III maze, at 60 or 180 days of age, with mouse chow, oatmeal, and cheese as incentives. Performance did not vary with incentives. The mice tested at 180 days made more errors than the 60-day mice; the relative rank of additive, maternal, and heterosis effects was the same at both ages. These findings contradict the observation (J. M. Warren, *Behav. Genet.* **18**:167–173, 1985) that C57B1/6J, DBA/2J, and their hybrids manifest different patterns of heritability as a function of incentives and age.

Jeanne M. Wehner,¹⁹⁰ M. Upchurch,^{190,191} and S. Sleight.¹⁹⁰ Correlation of Hippocampal Protein Kinase C Activity with Spatial Learning Ability.¹⁹² We have previously shown that spatial learning ability as measured by the Morris water task varies among inbred mice. C57BL/6Ibg mice are superior to DBA/2Ibg as measured by a spatial preference score. We have characterized aspects of cortical and hippocampal function in these two strains to determine whether neurochemical differences in these brain regions are related to their differential performance. Activity of hippocampal protein kinase C, an important enzyme mediating cholinergic and glutamatergic responses, was greater in the C57BL strain. To understand whether this biochemical difference was related to learning ability, 11 C57BL/6 × DBA/2 recombinant inbred strains (RIs) were tested on the Morris water task and cortical and hippocampal protein kinase C activities were determined. RIs varied on both measures and there was a significant correlation between the amount of hippocampal protein kinase C activity and a spatial preference score ($r = .81$, $p < .01$). There was no significant correlation with cortical activity. These results suggest that hippocampal protein kinase C activity has an important role in spatial learning performance in these strains.

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Lee Willerman,¹⁹³ R. Schultz,¹⁹³ J. N. Rutledge,^{193,194} and E. Bigler.^{193,195} **Magnetic Resonance-Imaged Brain Structures and Intelligence.** White college students with average or high SAT scores were administered an abbreviated Wechsler Adult Intelligence Scale-Revised. Forty right-handed students with prorated Full Scale IQs of ≤ 102 or ≥ 130 ($n = 20$) were selected for magnetic resonance imaging (MRI). Measures of brain size, cortical white matter, and cortical gray matter were obtained and correlated with average vs. high IQ classification. Based on observations that increases in relative brain size and cortical white matter volume are associated with evolutionary differences among species, it was predicted that these variables would correlate with IQ among humans. The discussion considers potential confounds and limitations in earlier studies of head circumference which have neglected head shape and regional differences in tissue growth in computing correlations with intelligence.

Joseph Yanai¹⁹⁶ and B.-G. Marcovici.¹⁹⁶ **High Concentration of Melanin in the CNS of the Black "Silkie" Domestic Fowl.** Progress in the study of Parkinson's disease can be accelerated if a better animal model were available in a species that is cheap and easy to raise, as well as sensitive to the Parkinson's syndrome inducing agent 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). It appears that neuromelanin is required for the MPTP to exert its toxic action on the dopaminergic neurons. Consequently, we have located, raised, and subjected to selection a breed of domestic fowl (*Gallus domesticus*), commonly called "Silkie" by the hobbyists, and established a breeding colony consisting of the animals selected for the highest level of pigmentation. The black pigmentation prevails in the skin, connective tissues, muscles, bones, and internal organs. Pigmentation in the meninges was also noticed. In our preliminary studies on the CNS, the brain of 6-week-old animals were cut, stained in hematoxylin and eosin, and examined for the presence of neuromelanin. The findings were verified in a few brains using enzymatic technique. Other brains were subjected to a bleaching procedure in order to verify that the pigment is neuromelanine. Black pigmentation prevailed throughout the brain in the meninges and around the blood vessels. Particularly heavy pigmentation could be seen in the choroid plexus. The bleaching results clearly suggest that the black pigmentation is indeed neuromelanine. No pigmentation could be found in the brains of control white (nonalbino) chickens. Presently we are studying the animal response to MPTP treatment on both the biochemical and the behavioral levels in order to obtain further insight into the relationships between neuromelanin and MPTP-induced Parkinsonism.

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