

perhaps they were legitimate and not to be feared as symptoms. He hoped to fully embrace and enjoy these feelings, yet the cool hand of caution kept them in partial check.

I have known Irving Gottesman for many years. The weight of his scholarship is evident, perhaps best demonstrated by his receipt of the 1997 *Lifetime Achievement Award* in Psychiatric Genetics from the International Society for Psychiatric Genetics — the only such honor ever received by a psychologist. Like Gottesman, I would, however, go beyond the obvious to note that no one has grasped the texture of science, the culture of the field or the rules of research better than he has — he is a master at it. In conclusion, I would urge him to relish the recogni-

tion accorded him by Festschrift attendees; the crowd of colleagues, students and friends knew his feelings were/are legitimate.

Additional information about the life and work of Professor Irving Gottesman can be found in the references listed at the end of this article and on his homepage: <<http://www.people.virginia.edu/~iig>>

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# Abstracts from the Festschrift — Foreword

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The purpose of this Festschrift was to honor the distinguished scientific career of Dr. Irving I. Gottesman, whose work on schizophrenia and the behavior genetics of personality and psychopathology, primarily through twin research, has permeated the thinking of both the scientific community and the public at large. The Festschrift was held in Minneapolis, MN, on June 8<sup>th</sup> and 9<sup>th</sup>, 2001, and brought together a remarkable group of researchers whose work has been touched, both directly and indirectly, by Dr. Gottesman over the past 35 years. The title of the Festschrift reflects the many areas of research in which Dr. Gottesman has been actively involved. Speakers came from all over the world to present research and to re-establish ties with each other and with Dr. Gottesman. The conference was held in Minneapolis because, following his retirement this spring from the

University of Virginia, Dr. Gottesman returned to the University of Minnesota where he was formerly a Professor of Psychology. He will have appointments at the Psychiatry Department at the University of Minnesota School of Medicine and at the Veterans Administration Hospital in Minneapolis, where he will continue his research and collaborations.

The presenters at the Festschrift were Dr. Gottesman's students, colleagues, and friends. They included Drs. Aksel Bertelsen (Aarhus Psychiatric Hospital, Denmark), Thomas J. Bouchard, Jr. (University of Minnesota), Greg Carey (University of Colorado), David DiLalla (Southern Illinois University), Niki Erlenmeyer-Kimling (Columbia University), Anne Farmer (King's College London), H. Hill Goldsmith (University of Wisconsin), Matt McGue (University of Minnesota), Peter McGuffin (Kings College London), Hans Moises (Kiel University

Hospital, Germany), Susan Trumbetta (Vassar College), and Eric Turkheimer (University of Virginia). The symposia discussants were Drs. Lisabeth DiLalla (Southern Illinois University School of Medicine), Dan Hanson (University of Minnesota), William Iacono (University of Minnesota), Sandra Scarr (Emerita, University of Virginia), and S. Charles Schulz (University of Minnesota School of Medicine). Lunch discussion group leaders were Drs. Sheri Berenbaum (Southern Illinois University School of Medicine), Leonard Heston (Emeritus, Univ. of Washington School of Medicine), Ann Masten (University of Minnesota), Vishwajit Nimgaonkar (University of Pittsburgh), Susan Resnick (National Institutes of Health), and Nancy Segal (California State University, Fullerton).

Dr. Gottesman is internationally renowned for his extensive and innovative work in many areas of psychopathology, most notably his twin

research on schizophrenia. He recently was awarded the Distinguished Scientific Contributions Award from APA. Receipt of this Award reflects the committee consensus that he is “at the absolute top of the field”. His research focuses on genetic principles and the many ways that genetic factors interact with and augment environmental influences that lead to psychopathology. His innovative work with twin populations, including the study of identical twin pairs discordant for schizophrenia and other psychopathologies, has greatly influenced much of the behavior genetics literature. Dr. Gottesman’s impact on the field is evident not only through his own work, but also through the work of the large number of students whom he has mentored and who have gone on themselves to make major contributions to the fields of psychology and psychopathology. Included at the Festschrift were both students and colleagues who fall into this category, many of whom currently conduct leading edge research on twins as a direct result of their interactions with Dr. Gottesman. Drs. Goldsmith, McGue, and Carey were graduate students of Dr. Gottesman’s at the University of Minnesota in the 1970’s. Dr. Bouchard is a self-proclaimed mentee of Dr. Gottesman from their shared faculty time at the University of Minnesota. Drs. Farmer and McGuffin were post-doctoral fellows at Washington University in St. Louis when Dr. Gottesman was on faculty there, and they became students, collaborators, and friends. Drs. Erlenmeyer-Kimling, Moises, and Bertelsen met Dr. Gottesman through research avenues and became close collaborators and friends, publishing together over a large number of years. Drs. L. DiLalla, D. DiLalla, and Trumbetta were graduate students of Dr. Gottesman’s at the University of Virginia in the 1980’s and 1990’s. Dr. Turkheimer was recruited by Dr. Gottesman to the University of Virginia, where they have been compatriots in behavior genetic work in the clinical department of Psychology.

Dr. Gottesman is one of the world’s leading experts on the genesis of schizophrenia. His constructs of the development of psychopathology have become accepted models for the ways in which genes and environment interact. For example, Dr. Gottesman (in 1967, with James Shields) was the first

to apply polygenic/threshold models of inheritance to the field of psychopathology. Their threshold model neatly describes the mechanism by which behavior varies from normal to abnormal, positing that genetic and environmental risks for psychopathology exist, and that an accumulation of sufficient risks can push an individual over the threshold from normal behavior to psychopathology. Fewer risks may result in sub-threshold manifestations of unusual behavior, but not in overt psychopathology. A second model of development is his reaction range concept (Gottesman, 1963), more recently elaborated into a reaction threshold model (Turkheimer, Goldsmith, & Gottesman, 1995). This model elegantly describes the ways that genetic and environmental influences separately create limits for the expression of behavior, resulting in behaviors that are multiply determined, but have upper and lower limits as a function of both genetic and environmental influences. Dr. Gottesman first introduced this concept from the genetics literature into psychology, and now it is included in nearly every introductory psychology textbook.

Dr. Gottesman’s treatment of his research topics is impressive in its mixture of science and compassion. He has always been sensitive to issues of genetic determinism and has been clear about the importance of both genetic and environmental influences on behavior. Even when there is evidence of a genetic effect on a disorder, he is a strong advocate for individual personal rights. For example, in a recent NAMI (The Nation’s Voice on Mental Illness) pamphlet on Schizophrenia and Genetic Risks (Gottesman & Moldin, 1999), the authors answer the question of whether schizophrenics should have children, with the following statement: “A simple ‘yes’ or ‘no’ answer cannot do justice to this very personal and delicate question that goes to the heart of personal liberty and civil rights in a democratic society.” Dr. Gottesman’s research has combined a compassionate treatment of the rights of individuals with a rigorous scientific approach to psychopathology, resulting in a career worthy of commemoration. This Festschrift provided the appropriate forum for such a celebration. The atmosphere was informal enough that

everyone had a chance to contribute by either presenting, asking questions, or interacting one-on-one. This was a chance not only for old friends to meet again, but also for students to meet some of the people they had only read about. The gathering mixed scientists from every rank, from students through emeriti, and provided us with a wonderful opportunity to learn, to teach, and to think. Further information about the Festschrift can be found on the web page at <[www.siumed.edu/iigfest](http://www.siumed.edu/iigfest)>.

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## Presentation Abstracts

### ■ Developmental Behavior Genetics Symposium

#### TEMPERAMENT AND CHILDHOOD BEHAVIORAL DISORDERS

H. Hill Goldsmith, Ph.D., *Leona Tyler Professor, Department of Psychology, University of Wisconsin.*

Research on childhood behavioral disorders has historically proceeded without sufficient reference to the growing body of work on the nature of typical emotional development and temperament. Reviewing data from several studies, we consider experiential, biological and genetic factors as providing causal input to typical developmental variation in fearfulness, pleasure, irritability and other temperamental traits during infancy and early childhood. Longitudinal behavioral methods, psychophysiological measures, and a behavior-genetic framework are used to approach these issues. Twin study results implicate, for instance, moderately strong genetic influences on different facets of temperamental fearfulness as well as

childhood anxiety symptoms. Then we consider the distinction between normal range temperament and childhood behavioral symptoms from a quantitative genetic perspective. Biological correlates (cortisol, asymmetric frontal EEG activation, cardiac reactivity) of inhibited behavior are considered as related endophenotypes for anxiety. In a non-genetic analysis, we report the prediction of internalizing problems during kindergarten from earlier temperament and earlier basal cortisol measures. Our review highlights connections between behavioral indicators and various putative endophenotypes and the fuzzy boundary between normal-range temperament and childhood behavioral disorders.

#### DEVELOPMENTAL BEHAVIORAL GENETIC PERSPECTIVES ON ADOLESCENT SUBSTANCE USE AND ABUSE

Matt McGue, Ph.D., *Professor, Department of Psychology, University of Minnesota.*

Behavioral genetic studies of substance use and abuse in adult samples implicate a strong influence of genetic factors. Nonetheless, we know relatively little about the how genetic influences on substance use disorders combine with or are modulated by environmental factors. We will describe longitudinal behavioral genetic research aimed at identifying the determinants of initial use of alcohol and other substances in early adolescence, the transition to regular patterns of substance use in late adolescence, and the progression to substance abuse and dependence in early adulthood.

#### HEALTH HABITS, MARRIAGE, AND DIVORCE DURING THE GREATEST GENERATION'S MIDDLE AGE

Susan Trumbetta, Ph.D., *Assistant Professor, Department of Psychology, Vassar College.*

Social causation and social selection hypotheses have been offered to explain persistent positive relationships between marriage and physical health observed in both clinical and epidemiological studies. This study evaluates the strength of these hypotheses in light of data from the National Academy of Sciences-National Research Council's World War II Veteran Twin Registry. Using data from the 1972 and 1985 health questionnaires, we examine phenotypic associations between marital status and

health risk behaviors, including consistency and changes in each over the period studied. We also examine the degree to which genetic and environmental factors implicated in health risk behaviors may contribute to the heritability of divorce risk and of risk for never marrying.

#### Genetic Influences on Personality Symposium

##### PERSONALITY AND PSYCHOPATHOLOGY

Gregory Carey, Ph.D., *Associate Professor, Department of Psychology, and Faculty Fellow, Institute for Behavioral Genetics, University of Colorado.*

David DiLalla, Ph.D., *Associate Professor, Department of Psychology, Southern Illinois University.*

In this paper, we analyze two models for the genetic association between personality and psychopathology. The first is a mediation model whereby genes influence phenotypic personality traits which subsequently influence liability to psychopathology. The second model assumes that genes influence common biological pathways for both personality and psychopathology. In general, mediation models explain observed twin data more poorly than do common biological pathway models. We discuss potential reasons for this phenomenon.

##### GENETIC INFLUENCE ON SOCIAL ATTITUDES: ANOTHER CHALLENGE TO PSYCHOLOGISTS FROM BEHAVIOR GENETICS

Thomas J. Bouchard, Jr., Ph.D., *Professor, Department of Psychology, and Director of the Minnesota Center for Twin and Adoption Research, University of Minnesota.*

There is now a sufficient body of empirical evidence to support the conclusion that within modern industrial societies measures of social attitudes manifest significant variance due to genetic factors. This genetic variance cannot be explained by supposed nuisance variables such as general cognitive ability or personality. These findings challenge the belief that family rearing environment and straightforward learning models of attitude formation and acquisition found in psychology textbooks are sufficient to explain kin similarity in attitudes. The evidence in support of this conclusion, based on twin, adoption and family studies, will be reviewed and its implications for future research explicated.

#### Genetic Influences on Psychopathology Symposium

##### GENETIC AND ENVIRONMENTAL RISK FACTORS FOR MAJOR DEPRESSION

Anne Farmer, MD FRCPSych, *Professor of Psychiatric Nosology at the Institute of Psychiatry and Director of Medical Education at the Maudsley Hospital London.*

Major technological advances have ensured that molecular genetics has dominated research activity in psychiatric disorders and behavioural traits over the past 2 decades. Some researchers have focused all their attentions on "genes" and seem to regard "the environment" as that proportion of the variance in liability (to develop a particular disorder or trait) that is "left over" in calculations of the contribution of genetic risk factors, and therefore something that can be "ignored". One reason for this lack of interest is that for the most part, environmental risk factors for many disorders and traits are unknown. Also, those that are recognised make relatively small contributions to the variance compared to genetic risk factors (Jablensky & Eaton, 1995). In contrast to those who ignore the environment, Professor Irving Gottesman, whose life's work we are celebrating, has always emphasised the importance of environmental risk factors and their interaction and co-action with genes in relation to both disorders and behavioural traits. (Gottesman, 1991).

In recognition of Professor Gottesman's major contribution to research in this area, I will discuss recent studies examining both genetic and environmental risk factors in major depression, where the causal role of certain types of life event is well-recognised (Brown & Harris, 1978). In particular, I will present recent findings from the Cardiff Depression Study, a sib-pair study of life events and depression in depressed probands, their nearest aged siblings, healthy control probands and their siblings (Farmer et al., 2000). Unlike some twin studies (Kendler et al, 1994) where a self-report checklist method has been used to assess whether particular events have occurred, in the Cardiff study, life events were recorded following a detailed interview, the Life Events and Difficulties Schedule (Brown & Harris, 1978). In addition, measures of personality, cognitive and attributional style were also administered. The study design has enabled us to examine the

relationship between the familiarity of depression, reporting an excess of certain types of events and aspects of personality and cognition. For example, do individuals with high scores on measures of sensation seeking have more life events due to their propensity for “hazard prone” behaviour? An alternative hypothesis is that those with high scores for Aneuroticism@ exaggerate the impact of life events, and are thereby “threat perceiving”.

#### CONTRIBUTIONS OF THE DANISH TWIN REGISTER TO UNDERSTANDING PSYCHOPATHOLOGY

Aksel Bertelsen, M.D., *Institute of Psychiatric Demography, Aarhus Psychiatric Hospital, Risskov, Denmark*

Denmark has been an *eldorado* for research in psychiatric epidemiology and genetics due to its thoroughly registered population. The nation-wide population register (the Central Person Number Register), the Central Psychiatric Register, and the twin, adoption, and criminal registers together with an until recently homogenous and easily accessible population have allowed and at the same time been an obligation to do extensive research in psychiatric genetics. During the last 30 years, Irving Gottesman has been our initiator, collaborator, and mentor in a number of studies: A twin study on criminality, a twin study of schizophrenia and particularly in its extension in a study on the offspring of discordant monozygotic schizophrenic twins, a twin study on manic-depressive disorder, and most lately, a dual mating study on the offspring of two psychiatric in patients. The survey of the results from these studies will be mentioned in their contributions to psychopathology and psychiatric genetics will be discussed.

#### ■ Genetic Influences on Schizophrenia Symposium

##### LONGITUDINAL PREDICTION OF SCHIZOPHRENIA IN A PROSPECTIVE HIGH-RISK STUDY

Niki Erlenmeyer-Kimling, Ph.D., *Chief of Medical Genetics, New York State Psychiatric Institute, and Professor, Departments of Psychiatry and Genetics and Development, College of Physicians and Surgeons, Columbia University.*

A goal of high-risk research studies, such as the New York High-Risk Project (NYHRP), has been the identification of neurobiological variables that may be both predictors of future

psychopathology and early phenotypic indicators of the genetic liability to schizophrenia and related disorders. In the NYHRP, two samples ( $N = 324$ ) of offspring of schizophrenic, affectively ill, and psychiatrically normal parents have been followed from the age of 7–12 years old (in 1971–72 or 1977–79) to mid-adulthood in search of this goal. Although all of the offspring were free of major psychiatric disorders in childhood, 14%, 5% and 0.6% of the three parental diagnostic groups, respectively, have later developed adulthood schizophrenia or related psychoses (SRP).

In a childhood test-battery, deficits in three neurobehavioral measures — assessing global attention, gross motor skills, and short-term verbal memory— emerge as moderate to strong predictors, respectively, of adulthood SRP, but not other psychiatric disorders, in the group with schizophrenic parents. These deficits, however, were rare or absent in the offspring of affectively ill and normal parents, thus suggesting that they may be expressions of specific schizophrenia-susceptibility genes. The extensive data bank of the NYHRP is under analysis to identify other neurobehavioral, social, clinical, environmental and family variables, collected over the longitudinal course of the project, that may be potentiators interacting to enhance the effect of such susceptibility genes. Different patterns of variables are also under investigation in offspring who have developed affective, rather than schizophrenia-related, psychoses.

##### GENES AND NEURODEVELOPMENT IN SCHIZOPHRENIA

Hans W. Moises, Ph.D., *Director, Molecular Genetics Laboratory, Department of Psychiatry, Kiel University Hospital, Kiel, Germany.*

Genetic and neurodevelopmental hypotheses are currently the two most widely accepted models to explain the distal etiology of schizophrenia. The polygenic model of schizophrenia by Gottesman and Shields (1967) has been confirmed by numerous family, twin, adoption, and linkage studies while the developmental hypothesis of the disorder is able to explain such divergent findings as obstetric complications, congenital dermatoglyphic abnormalities, neurological soft signs, and structural brain abnormalities, as

well as cognitive and behavioral dysfunction which appear long before the onset of the illness. Findings of studies will be reviewed suggesting an involvement of neurodevelopmental genes in the susceptibility to schizophrenia.

#### ■ Molecular Genetics and the Future of the Field Symposium

##### NULL HYPOTHESIS SIGNIFICANCE TESTING AND THE MOLECULAR GENETICS OF COMPLEX BEHAVIOR

Eric Turkheimer, Ph.D., *Associate Professor and Director of Graduate Studies, Psychology Department, University of Virginia.*

This paper examines an ironic contrast between two of the most important trends in contemporary social science. On the one hand, after 75 years of domination by ritualistic null hypothesis significance testing (NHST), the field has at last begun to question the utility of its reliance on  $p < .05$  methodology, and begun to turn in the direction of effect size estimation, careful consideration of statistical power, Bayesian approaches, and meta-analysis. On the other hand, exponential advances in molecular genetic technology has made it possible to conduct ever-widening scans of the genome in a search for associations between specific alleles and complex behavior. And at the bottom of the statistical methodology on which this new technology is based, we find Y. NHST, complete with familiar discussions of appropriate  $p$  values, Type-I error corrections, appropriate levels of statistical power, and the relative advantages of parametric and nonparametric approaches.

There are only two ways to resolve this apparent paradox. Either the molecular genetics of complex behavior is better suited to NHST than routine social science, or it is following a methodological blind alley already thoroughly explored by several generations of social scientists. Choosing between these alternatives requires an explanation of an aspect of the NHST problem that remains poorly understood: why has the practice of NHST hung on so long (and it's not dead yet) despite almost universal opposition to it on theoretical grounds? The answer, I will suggest, is that although NHST was designed as a method for distinguishing true scientific signals from sampling

error, sampling error has turned out not to be the most important source of noise in social science. Instead, noise in social science arises from the ineluctable contextual embedding of behavior. What we learn about a complex psychological phenomenon in one setting does not, in general, apply to the same phenomenon in a different setting. The persistence of NHST is explained by the fact that it seems to offer the frustrated social scientist a statistical and methodological remedy for the context-dependent variability of behavior, but unfortunately it doesn't work. The final question is whether linkage and association studies of complex behavior are as context-dependent as traditional social science. Consideration of this question leads to conclusions about the possibilities and limitations of genetic explanation in psychology.

#### BEHAVIOURAL GENOMICS: WHERE MOLECULAR GENETICS IS TAKING PSYCHIATRY AND PSYCHOLOGY

Peter McGuffin, M.D., Ph.D., *Director of the Social, Genetic, and Developmental Psychiatry Research Centre, Institute of Psychiatry, King's College London.*

Both the promise and the frustrations of applying molecular genetic methods in the study of behaviour are well exemplified by schizophrenia. Although it is clear from twin and adoption studies that schizophrenia is highly heritable (with most estimates suggesting that genetic factors account for about 80% of variance), linkage studies have produced conflicting and, at times, confusing results. This almost certainly reflects on the fact that schizophrenia, as predicted by Gottesman and Shields (1967), is a polygenic disorder where many genes of small effect combine to produce a liability. For example, a systematic scan using nearly 200 families containing affected sib pairs (Williams et al., 1999) excluded a gene, conferring a relative risk of three from over 80% of the whole genome. However, some chromosomal regions have been replicated in more than one study and it seems likely that a combination of linkage and association approaches will identify at least some of the genes involved in the foreseeable future. Meanwhile, recent linkage studies have produced replication in disorders where the genetic basis has, in the past, been disputed, such as autism (Hanson & Gottesman, 1982).

In other childhood or developmental disorders such as ADHD and reading disability there are also promising findings. Current molecular genetic studies in behaviour focus not just on disorders but on traits that showed continuous variation in the population, such as personality and cognitive ability. Discovering genes involved in normal and abnormal behaviour and following through with functional studies of the effects of molecular variation is likely to have a profound influence on psychiatry and psychology. First, there are implications for a better understanding of the neurobiological underpinning of disorders such as schizophrenia and normal traits such as personality and intelligence. Second, behavioural genomics will drive the last nails into the coffins of those seemingly everlasting old phonies: "nature versus nurture" and "mind versus body". With this should come a third result, a change in attitude towards mental illness, not, as has sometimes been suggested, in the direction of increasing its stigma, but rather in the direction of reducing it. Fourth, there will be important spin-offs for drug discoveries in that molecular genetics will identify targets for new and more effective compounds, ultimately improving the lives of those with mental health problems.

#### Poster Abstracts

##### CAN THE MMPI AT AGE 15 PREDICT SCHIZOPHRENIA-TO-BE? REVISITING THE QUESTION

P. Kevin Bolinsky, Irving I. Gottesman, and Daniel R. Hanson, *University of Virginia, Charlottesville, VA, and University of Minnesota, Minneapolis, MN.*

Recent research has found evidence for a group of selected clinical and supplementary MMPI scales to differentiate premorbid schizophrenics from comparison groups. This research has focused on a group of scales comprising the Moldin-Gottesman Psychometric Index. The current study examined the validity of an index of six scales to predict future schizophrenia onset in the Hathaway-Monachesi ninth-grade normative participants who later developed the disorder. Twenty-three participants (14 males, 9 females) with valid MMPIs who later developed schizophrenia and their classroom-matched controls who developed no

psychiatric disorder comprised the groups in this study. T scores for each scale were entered into a discriminant function analysis (DFA) in which diagnosis served as the grouping variable. DFA correctly placed in diagnostic groups 19 future schizophrenics and 18 non-schizophrenics; overall accuracy of the function was 80.4% ( $\chi^2 = 18.8$ ,  $df = 6$ ,  $p < .005$ ). PPP for group placement was 79% and NPP was 82%. These results, considered along with other recent evidence, support the notion that there are premorbid processes that differentiate schizophrenics from non-schizophrenics, and, further, that the MMPI is effective in measuring those processes.

##### THE MULTIPLE DIMENSIONS OF SCHIZOTYPY IN THE FIRST DEGREE BIOLOGICAL RELATIVES OF SCHIZOPHRENIA PATIENTS

Monica E. Calkins, Clayton E. Curtis, William M. Grove, & William G. Iacono, *University of Minnesota, Minneapolis, MN.*

There has been considerable research aimed at identifying individuals who carry the latent predisposition for schizophrenia, with much effort devoted to the characterization of the personality characteristics of the biological relatives of schizophrenia patients. Although resource consuming interview methods of assessing schizotypal features in schizophrenia relatives have yielded promising results, investigators have long sought self-report measures that index genetic risk for schizophrenia. The Schizotypal Personality Questionnaire (SPQ) is a self-report measure that assesses the 9 major features of schizotypy as defined by the DSM. Previous work has indicated that three factors (social-interpersonal, cognitive-perceptual and disorganization) underlie the SPQ. The SPQ, modified to include validity scales, was administered to 135 non-psychotic first-degree relatives of schizophrenia patients and 112 healthy controls. Social interpersonal deficits best differentiated relatives from controls and thus may be the most important features associated with genetic vulnerability. Principal components analysis yielded three factors that correlated highly with previously reported factors. Inconsistent with the hypothesis that schizophrenia relatives are more defensive in responding to schizotypy questionnaires, relatives were significantly less defensive

than controls. The results demonstrate that a multidimensional paper-and-pencil measure can characterize schizotypal features in schizophrenia relatives and, as such, will be useful for the further delineation of the heritable schizophrenia spectrum phenotype.

#### INTERNALIZING AND EXTERNALIZING AS A FUNCTION OF RELATIONSHIP IN PRESCHOOL TWINS AND SIBLINGS

Rebecca A. Caraway & Lisabeth F. DiLalla, *Southern Illinois Univ. School of Medicine, Carbondale, IL*

Identical (MZ) twins, who spend much time with each other and are very much alike, may experience less diversity in their playmates than do fraternal (DZ) twins, who may experience less diversity than do other-age siblings. Therefore, developmental social genetics theory might predict that MZ twins will be more socially withdrawn than DZ twins, who will be more withdrawn than non-twin siblings. Conversely, MZ twins might be either more aggressive because of less experience with others or less aggressive because they are more inhibited. These hypotheses were assessed using the Child Behavior Checklist (CBCL) scales of withdrawn, aggressive, internalizing, and externalizing. Parents of 5-year-old twins and 5-year-old non-twin sibling pairs completed a packet of questionnaires, among them the CBCL. Thirty-two MZ twins, 68 DZ twins, and 51 siblings were rated on the CBCL. A MANOVA was performed on withdrawn, aggressive, internalizing, and externalizing scores, with zygosity group (MZ, DZ, or siblings) as the independent factor. There were significant group effects on the withdrawn scale ( $F(2,151) = 2.64, p < .08$ ) and internalizing ( $F(2,151) = 4.88, p < .01$ ), but not on aggression or externalizing. Siblings' withdrawn and internalizing scores were significantly higher than MZ scores. This does not support the developmental social genetics theory that experience with dissimilar peers may be important for reducing withdrawn behaviors in preschool children.

#### RECOGNITION MEMORY FOR FACES IN SCHIZOPHRENIA PATIENTS AND THEIR FIRST-DEGREE RELATIVES

Heather M. Conklin, Monica E. Calkins, Charles W. Anderson III, Thomas J. Dinzeo & William G. Iacono, *University of Minnesota, Minneapolis, MN*

It has consistently been shown that schizophrenia patients are impaired in

recognition memory for faces. However, studies have not examined the specificity of this deficit relative to other cognitive functions nor the relationship between this deficit and particular schizophrenia symptoms. In addition, no studies have examined recognition memory for faces in unaffected biological relatives of schizophrenia patients who likely share some of the genetic diathesis for this disorder without presenting the potential confounds of mentally ill study samples. The Faces subtests from the Wechsler Memory Scale -Third Edition were used to evaluate recognition memory for faces in 39 schizophrenia patients, 33 of their first-degree relatives and 56 normal controls. Both schizophrenia patients and their relatives were impaired, relative to control participants, in recognition memory for faces after controlling for group differences in simple attention or verbal memory. Further, recognition memory for faces was associated with positive symptoms in the schizophrenia group and schizotypal personality traits in the relative group. These findings may have important implications for reducing etiological heterogeneity among schizophrenia populations, identifying disorder susceptibility among their relatives and furthering understanding of disorder etiology.

#### WORKING MEMORY IMPAIRMENT IN SCHIZOPHRENIA PATIENTS AND THEIR FIRST-DEGREE RELATIVES

Heather M. Conklin, Clayton E. Curtis & William G. Iacono, *University of Minnesota, Minneapolis, MN*

There is accumulating evidence for the involvement of the prefrontal cortex in the genetic diathesis for schizophrenia. A primary function supported by the prefrontal cortex is working memory.

Neuroimaging studies increasingly suggest that working memory task characteristics, including stimuli type (e.g., verbal, spatial or object), as well as processing demands (e.g., storage, rehearsal/maintenance or executive processes such as task management) activate distinct neural regions thought to mediate performance. Given these findings, we evaluated the performance of schizophrenia patients, their first-degree relatives and nonpsychiatric controls on a battery of working memory tasks that varied in stimuli type and processing demands (digit span, letter-number sequencing, delayed response and self-ordered pointing tasks). Whereas

schizophrenia patients consistently demonstrated impaired performance across working memory measures, their first-degree nonpsychotic relatives demonstrated impairment only on a subset of measures. It may be that working memory impairment in these relatives is directly related to the degree to which executive processes are evoked, such that only tasks that require substantial manipulation of material within working memory or its protection from interference reveal impaired performance. These findings may begin to suggest which components of working memory are most effective at identifying individuals with genetic risk for schizophrenia and the corresponding candidate sites of neuropathology.

#### SACCADIC DISINHIBITION IN SCHIZOPHRENIA PATIENTS AND THEIR FIRST-DEGREE BIOLOGICAL RELATIVES: A PARAMETRIC STUDY OF THE EFFECTS OF INCREASING INHIBITORY LOAD

Clayton E. Curtis, Monica E. Calkins, & William G. Iacono, *University of Minnesota, Minneapolis, MN*

Several studies have reported that patients with schizophrenia and their relatives perform poorly on antisaccade tasks and have suggested that this deficit represents saccadic disinhibition. If this proposition is so, then varying task parameters that specifically increase the difficulty with which unwanted saccades can be inhibited should exacerbate deficits. Forty-two schizophrenia patients, 42 of their first-degree biological relatives, 21 psychotic affective disorder patients, and 38 non-psychiatric comparison subjects were administered fixation and antisaccade tasks. The introduction of distractors and the presence of visible fixation stimuli were parameters used to vary the difficulty in suppressing unwanted saccades (inhibitory load). It is known that the presence of a fixation stimulus at the time when a saccade must be inhibited results in fewer reflexive errors on antisaccade tasks. Performance on fixation tasks without (low load) vs. with distractors (high load) and antisaccade tasks that had fixation stimuli still visible (low load) vs. already extinguished (high load) at the time when the reflexive saccade must be inhibited was compared. The schizophrenia patients and their first-degree biological relatives showed evidence of increased saccadic disinhibition.

tion that was most pronounced during high inhibitory load conditions. These data indicate that dysfunctional inhibitory processes, at least in the oculomotor domain, are associated with the liability for schizophrenia. Results also suggest that this genetic liability may be related to dysfunctional prefrontal cortical areas that provide top-down inhibitory control over reflexive saccade generation.

#### RHEUMATIC DISEASES AND SCHIZOPHRENIA: AN AUTOPSY-BASED INVESTIGATION

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The neuropsychiatric consequences of streptococcal rheumatic disease have been well established for Sydenham Chorea and Obsessive-Compulsive disorder (PANDA syndrome). We revisit an older hypothesis that streptococcal rheumatic disease plays a role in psychoses including schizophrenia. We describe a collection of consecutive autopsies from Minnesota State Hospitals and present preliminary statistical findings. Among a population of 392 patients with psychoses, 14% had histories of streptococcal rheumatic disease. Clinical, epidemiologic, and neuropathological findings are discussed. In addition, we consider a simple rheumatic-epidemic model and propose a few conceptual issues or predictions that may be pertinent to future investigations. The tentative conclusion drawn from the current study implies that streptococcal infection may play a larger role in the genesis of schizophrenia than what has been generally appreciated.

#### THE STROOP INTERFERENCE EFFECT: READING, MENTAL ABILITY, AND PERSONALITY CORRELATES IN THE MINNESOTA STUDY OF TWINS REARED APART

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The Stroop Color-Word Test was administered to 50 pairs of monozygotic twins reared apart (MZA) and 37 pairs of dizygotic twins reared apart (DZA) in the Minnesota Study of Twins Reared Apart (MISTRA) as well as some spouses and other participants ( $N = 97$ ). These individuals also completed personality and special mental ability tests, two reading tests and one spelling test. There were no significant

correlations between the theoretically interesting Stroop Interference Score and the eleven Multidimensional Personality Questionnaire Scales nor with Full Scale WAIS IQ. Correlations with the reading tests were statistically significant but much lower than expected (.15 and .19). The correlation with spelling was not significant (.11). Various special mental ability tests (Pedigrees, a memory composite, Flexibility of Closure and Speed of Closure) correlated with the interference score to about the same extent as the reading tests (.21, .20, .17, .29). These findings suggest that the Stroop Interference Score is to a considerable degree independent of reading ability as well as mental ability and personality. The intraclass correlations for the MZA twins was .43, suggesting significant heritability for this trait.

#### HERITABILITY OF DEPRESSION SYMPTOMATOLOGY IN THE SECOND HALF OF LIFE: EVIDENCE FROM DANISH TWINS OVER 45

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The heritability of depression symptoms was investigated in a sample of 2,169 pairs of Danish twins (1,033 MZ and 1,136 same sex DZ) ranging in age from 45 to over 95. Twins completed an interview assessment that identified symptoms of depression, which were scored on Affective, Somatic, and Total scales. For the full sample, heritability estimates ( $h^2$ ) for the Affective ( $h^2 = .27$ ), Somatic ( $h^2 = .26$ ), and Total ( $h^2 = .29$ ) scales were all moderate, statistically significant, and similar to results from other studies (e.g. McGue & Christiansen, 1997). To assess possible variations in heritability across the wide age span, the sample was stratified into age groups in increments of five years. The magnitude of heritable influence did not vary significantly with age or sex, though there was some tendency for Affective scale heritability to increase with age and for Somatic scale heritability to decrease with age. In addition, Somatic scale heritability tended to be greater for females than for males. Bivariate model fitting produced a genetic correlation of .71 and a non-shared environmental correlation of .43 for the Affective and Somatic scales. The implications of

these findings for understanding the symptomatology of depression in the second half of life are discussed.

#### DEVELOPMENTAL INSTABILITY IN MZ TWINS CONCORDANT AND DISCORDANT FOR SCHIZOPHRENIA

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Although a major genetic component underlying the complex etiology of schizophrenia has been substantiated, concordance rates slightly less than 50% among monozygotic (MZ) twin pairs highlight the importance of epigenetic and environmental factors in etiology. Developmental instability represents the degree to which an individual's ontogenic program is perturbed by environmental and non-heritable genetic factors over time. Developmental instability is indexed by fluctuating asymmetry (FA) of bilaterally symmetrical morphometric traits, such as dermatoglyphics, and by minor physical anomalies, all of which reflect developmental integrity over the pre- and early post-natal periods. The present study examined levels of developmental instability, measured by a composite of dermatoglyphic FA and minor physical anomaly measures, in the Torrey, Gottesman and colleagues' sample of MZ twin pairs concordant ( $n = 20$ ) and discordant ( $n = 23$ ) for schizophrenia and spectrum disorders. While there was no difference in the level of developmental instability between discordant and concordant pairs, affected members of discordant pairs had substantially greater instability relative to their unaffected co-twins. These findings will be discussed in the context of developmental instability as an important framework from which to consider epigenetic processes in schizophrenia.

#### REUNITED TWINS VS. THEIR ADOPTIVE SIBLINGS: WHO DO THEY FAVOR?

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Perceptions of social closeness and familiarity between reunited monozygotic (MZA) and dizygotic (DZA) twins were compared via a detailed Twin Relationship Survey. This study is the first to systematically assess social relatedness in this special twin sample. Participants included 44 MZA and 33 DZA twin pairs, and several individual twins and triplets from the Minnesota Study of

Twins Reared Apart. A repeated measures ANOVA showed significantly greater closeness and familiarity among MZA and DZA twin pairs. In addition, MZA intraclass correlations significantly exceeded DZA correlations for current closeness and current familiarity ratings. Most revealing, twins' current closeness and familiarity scores for their newly found co-twins exceeded those for the unrelated siblings with whom they were raised. Other analyses showed that correlations between twins' perceptions of their current physical resemblance and current social closeness and familiarity were positive and statistically significant. However, most correlations between social relatedness ratings and contact time measures were non-significant. Some exploratory studies of associations between twins' social relatedness and similarities in personality traits, interests, values, and educational background were also conducted. The findings support various theoretical perspectives anticipating greater cooperation and affiliation among close relatives, compared to distant relatives and non-relatives.

#### DEFICIENT RECALL, INTACT RECOGNITION: ERP EVIDENCE REGARDING THE NATURE OF VERBAL MEMORY DEFICITS IN SCHIZOPHRENIA

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Although studies have consistently shown schizophrenia patients to manifest verbal memory deficits extending beyond a generalized cognitive dysfunction, the nature of these deficits remains unclear. In order to explore the basis for verbal memory dysfunction in schizophrenia we examined the behavioral responses and brain electrical activity (event-related potentials [ERPs]) of schizophrenia and control subjects completing verbal memory tasks. Across tasks schizophrenia patients performed worse than control subjects in recalling verbal material, but they performed similarly to control subjects in recognizing verbal material. Both schizophrenia patients and control subjects exhibited repetition priming effects on their reaction times. Analyses of ERPs to visually presented words revealed similar functional brain abnormalities during encoding, identification, and recognition in schizophrenia patients. Compared to control subjects, schizophrenia patients, exhibited diminished C1 and N1 amplitudes over

posterior brain regions, diminished P2 and late positive complex (LPC) components over prefrontal and frontal regions, and diminished P3 amplitudes over frontal, central, and parietal regions. Next, we examined ERPs associated with recall deficits. For control subjects failure to recall words was associated with diminished P2 and P3 components over frontal and central scalp regions during encoding. In contrast, schizophrenia patients failure to recall words was associated with diminished early negative components (80 to 250 msec after stimulus onset) over the posterior-temporal brain regions and diminished P2 amplitudes over the left frontal-temporal brain region during encoding. These findings are consistent with schizophrenia patients having encoding abnormalities during early processing by posterior-temporal brain regions and later processing by left frontal-temporal brain regions.

#### ATTENTION OR SUSTAINED ATTENTION DEFICIT? EVENT-RELATED POTENTIALS OVER THE COURSE OF A CONTINUOUS PERFORMANCE TASK IN SCHIZOPHRENIA

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It is unclear whether poor performance by schizophrenia patients on continuous performance tasks (CPT) is attributable to a specific deficit in sustained attention or an overall attentional impairment. In an attempt to identify functional brain abnormality associated with impaired sustained attention, we examined event-related potentials (ERPs) of schizophrenia and nonpsychiatric control subjects while they performed a degraded-stimulus CPT. During correct responses to target stimuli schizophrenia patients exhibited smaller P3 amplitudes than control subjects. Additionally, the P3 amplitudes for target and non-target stimuli were less differentiated for schizophrenia patients than for control subjects. To examine sustained-attention processes trials were divided into three time blocks (first third, middle third, last third) of 160 trials each. Across the three time blocks P3 amplitudes to target stimuli failed to decrement in either the schizophrenia or control subjects in the mid-parietal region. Amplitude differences between normal controls and schizophrenia patients decreased in the mid-central region. In

order to examine performance variability schizophrenia patients were divided into high and low scoring groups. The high scoring group performed as well as normal controls and appeared to have similar P3 amplitudes. Results support the contention that schizophrenia patients fail to exhibit greater performance decrement over the course of a degraded-stimulus CPT than control subjects. ERP analyses suggest that low-scoring schizophrenia patients may engage anomalous brain processes (as reflected by P3 amplitude) when performing visual target detection. This may differentiate them from high-scoring schizophrenia patients.

#### THE SIGNIFICANCE OF PROVERB INTERPRETATION IN SCHIZOPHRENIA

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In order to determine which phenomena in schizophrenia are closely tied to proverb interpretation, we examined the associations of proverb interpretation with domains of symptomatology and cognition in schizophrenia patients. Interpretations of proverbs by schizophrenia and comparison subjects were rated for abstraction, concreteness, and bizarre-idiosyncratic quality. Subjects also completed structured interviews and tests of cognition. Results showed schizophrenia subjects showed less abstract, more concrete and bizarre-idiosyncratic interpretation of proverbs than comparison subjects. For schizophrenia subjects abstraction in proverb interpretation was positively associated with overall intelligence, but no symptom measures. Concreteness in proverb interpretations by schizophrenia patients was negatively associated with overall intelligence, executive functioning, attention, and memory. Concreteness was also associated with bizarre behavior in schizophrenia patients. Finally, bizarre-idiosyncratic responses by schizophrenia patients during proverb interpretation failed to be associated with any cognitive functions; however, these responses were associated with positive formal thought disorder. The conclusion was that concreteness in proverb interpretation may reflect cognitive dysfunction in schizophrenia while bizarre-idiosyncratic aspects of interpretation may reflect positive formal thought disorder. ■