Wisconsin Twin Panel: Current Directions and Findings

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The Wisconsin Twin Panel is based on the population of all twins born in the state of Wisconsin, United States. Our research focus is the etiology and developmental course of early emotions, temperament, childhood anxiety and impulsivity, the autism spectrum, auditory and tactile sensory sensitivity, and related psychobiological and behavioral phenotypes. We employ a range of research methods including structured interviews with caregivers, observer ratings, child self-report, home-based behavioral batteries, biological measures of basal and reactive cortisol, palm prints, birth records, genotyping, cognitive testing, and questionnaires. Reported results highlight the utility of employing multiple modes of assessment when studying child development and psychopathology.

The Wisconsin Twin Panel (WTP) is a statewide, birth register-based twin sample used for a set of related studies. The WTP is located in the Waisman Center at the University of Wisconsin-Madison. The WTP is one of many research studies contained within the Waisman Center's Social and Affective Processes Unit. Aspects of the research are conducted at the University of Wisconsin-Madison's Department of Psychology. Funding for the project is currently provided by grants from the National Institute of Mental Health, the University of Wisconsin-Madison, the Wallace Foundation, and, indirectly by Waisman Center core services supported by the National Institute of Child Health and Human Development.

The general research strategy of the panel is to screen a large, representative sample of young twins and identify early factors related to both risk and resilience during infancy, childhood, and early adolescence. A variety of research methods are employed, tapping both typical and atypical behavioral development.

Recruitment of the Panel

Wisconsin is located in the North Central portion of the United States. Residents are of predominantly German (42.7%), Irish (10.9%), Polish (9.3%), and Norwegian (8.5%) ancestry (United States Census Bureau, 2000). The total population is largely Wisconsin native (95.8%). Wisconsin ranks second in the United States for per cent employment in manufacturing industries (22.2%), and it is also well known for agriculture. The state of Wisconsin is a blend of rural and metropolitan communities, with 67.7% of the population living in metropolitan areas.

All families with twins are identified through state birth records. The WTP staff recruited families with twin births in Wisconsin from 1989 through 2004. Beginning with the 2005 twin births, the Waisman Center Research Participation Core assumed responsibility for recruitment. Recruitment guidelines are set by the state and approved by Institutional Review Boards. The names and addresses of 500 to 525 twin families are received every 6 months; no other information from birth records is provided. All families are sent an initial recruitment letter and join the project by responding with an enclosed reply card. Six weeks after an initial recruitment letter, a second letter reminds parents of the recruitment and encourages their reply. About 76% of families respond to the recruitment letters; of those families, about 89% respond favorably. Recruitment is ongoing.

Data Storage and Linking

The WTP laboratory maintains a small local area network connecting Pentium-based IBM-compatible computers. Data are currently stored in the Access database, with a custom-built front-end utility written in Java. The utility was built for data entry, customized computations, and data maintenance procedures and is compatible with other database programs.

Research Projects and Methodology

The panel currently supports five studies: (1) behavioral screening of toddlers at age 2 to 3 years, (2) a longitudinal study of the genetics of emotional

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ontogeny (GEO) from 3 months to 3 years of age, including a follow-up at age 7 years, (3) a study of child psychopathology at age 7 years, with a planned follow-up in early adolescence, (4) a multiage study of childhood sensory defensiveness, and (5) a study of the autism spectrum. One of the hallmark approaches of the WTP is detailed assessment from multiple methods and informants. Different assessments and informants often provide varying and unique perspectives on developmental processes and psychopathology. A comprehensive summary of the measures included in each of the studies is provided in Table 1.

Behavioral Screening at 2 to 3 Years

Families are recruited for an assessment of the base population when the twins are 2 to 3 years old. Participation includes a 35-minute telephone interview with the twins' primary caregiver concerning each twin's socioemotional development, sensory sensitivities, features of autism, zygosity and family demographics. A mailed questionnaire completed by both parents includes a measure of each twin's temperament and language development. Approximately 65% of families in the panel participate in this phase of the research, and data have been collected on over 5750 twins and their families as of May, 2006.

Longitudinal GEO project

Families who live within a 50-mile radius of Madison, Wisconsin, are invited to participate in the in-depth longitudinal GEO project. GEO explores the nature, sources, and functional consequences of emotional individuality from birth to age 3 years using multimodal, comprehensive assessments of emotion and temperament, as well as selective assessment of cognition, motor development, physiology, social interaction, and the home environment. The project incorporates an unusually broad set of methods (Table 1). Assessment periods include 3 months of age (home visit), 6 months (laboratory visits), 9 months (home visit), 12 months (laboratory visits), four laboratory visits spaced across the second year, and 36 months (laboratory visits). A site recently established in Milwaukee, Wisconsin, allowed expanded recruitment of ethnic minorities. The final sample size will be approximately 500 twin pairs.

The GEO twins are then followed up at 7 years of age with a home visit including observational assessment of temperament, basal and reactive salivary cortisol, and questionnaire assessment of temperament, health, and the family environment. Some twin pairs also participate in a psychophysiology laboratory visit including measures of central (EEG) and peripheral (cardiac) nervous system measures during a series of videotaped emotion-eliciting episodes.

Follow-Up of Twins at Risk for Child Psychopathology

When the panel twins are 7 years of age, families are again contacted by phone to screen for the broad dimensions of internalizing, externalizing, and inattentive-hyperactive psychopathology. Each twin is classified as (1) at-risk for one or more dimensions of psychopathology; (2) a control for all psychopathology; or (3) an unselected individual. Currently, the full (unselected) sample comprises 8.4% twins identified as internalizing, 6.9% as externalizing, 3.1% as inattentive, 9.3% as comorbid, and 14.9% as controls. As of May 2006, over 2270 twins have completed the screening process. If either twin is identified as at-risk or control, the pair is followed up in an in-depth study of child psychopathology. The psychopathology follow-up utilizes multiple modes of assessing risk for psychopathology by including additional measures of the child, parents, siblings, family environment, and biological factors (see Table 1), with several hours of videotaped observational data collected in the home. Preliminary work has begun on single nucleotide polymorphism (SNP) genotyping. The genes that are currently being typed are SERT (a promoter of the serotonin transporter), DAT1 (dopamine transporter 1), and COMT (catechol-O-methyl-transferase), with plans to type additional candidate genes in the future.

This study provides an important foundation for additional extensive assessment at adolescence when the twins have lived through more of the risk period for the onset of disorders.

Childhood Sensory Defensiveness

Twins are initially screened for tactile and auditory sensory defensiveness (i.e., reacts strongly to sensations/sounds that most people do not notice) in the behavioral screening of toddlers. A sample of those scoring in the top 5% have been rescreened for a more detailed follow-up study (including observational assessment in the home) of sensory defensiveness at age 4 to 5 years. The rescreened sample included 282 twins; full follow-up data have been collected on 78 twin pairs and their families. In addition, sensory defensiveness is included in the screening assessment of all 7-year-old twins; data have been collected on over 750 twins at age 7.

Study of Childhood Autism

The twin study on autism began as case finding throughout Wisconsin for any twins under the age of 18 years with an autism spectrum diagnosis (autism, Aspergers, or pervasive developmental disorders not otherwise specified). An initial telephone screening assesses for behaviors in the autism spectrum. As of May, 2006, 222 twins (including those with a possible diagnosis and their co-twins) have been identified through the case-finding approach, and a second-stage screen of these pairs has begun. Individuals participate in a follow-up home-based behavioral assessment that includes assessment of co-occurring but nondiagnostic behavioral phenotypes. We also assess behavioral strengths of autistic individuals, the 'broader autism phenotype' in family members, and psychosocial functioning of the families. In the future, structural and functional MRI studies are planned.

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Table 1

Overview of Wisconsin Twin Panel Studies and Measures

Overview of Measures

Behavioral screening of toddlers at age 2 to 3 years

1. Zygosity Questionnaire for Young Twins: Mother
2. Family demographics: Mother
3. Brief Infant–Toddler Social and Emotional Assessment: Mother
4. Sensory sensitivity items from Infant–Toddler Social and Emotional Assessment: (ITSEA) Mother
5. Autism screening items: Mother
6. Toddler Behavior Assessment Questionnaire — Revised: Mother and Father
7. MacArthur Communicative Development Inventory: Mother

Birth-to-3 Study of the Genetics of Emotional Ontogeny (GEO) and age 7 follow-up

Temperament and emotion for twins

1. Laboratory Temperament Assessment Battery (Lab-TAB)
2. Bayley Scales of Infant Development (2nd edition) — Behavior Rating Scale Record Form: Observer
3. Infant Behavior Questionnaire: Mother and father
4. Infant Irritability Questionnaire: Mother
5. Toddler Behavior Assessment Questionnaire (TBAQ-R): Mother and father
6. Child Behavior Questionnaire: Mother and father
7. Social smile, separation anxiety, stranger anxiety, self-conscious emotions onsets: Observer and mother
8. Emotion checklists: Mother every two weeks over first year
9. Nursing Child Assessment Teaching Scales: Observer, used to code feeding, bathtime, bedtime parent–child interactions
10. Child Behavior Checklist: Mother

Physical development, cognition and play for twins

11. Visual Expectation Paradigm
12. Bayley Scales of Infant Development (2nd edition) — Observer
13. Language sample: Observer
14. MacArthur Communicative Development Inventory — Words and Gestures: Mother
15. MacArthur Communicative Development Inventory — Words and Sentences: Mother
16. Diaries of motoric, language, and play milestones, laterality, tooth eruptions: Mother every 2 weeks over first year

'Biological' measures

17. Zygosity Questionnaire for Young Twins: Mother or father
18. Pediatric update: Mother or father
19. Lab-TAB with EEG and cardiac measures
20. Multiday basal cortisol and reactive cortisol (3X) during the lab assessment for twins
21. Hand Usage Questionnaire: Mother and father

Parent psychopathology and personality

22. Center for Epidemiological Studies — Depression Scale: Mother
23. Multidimensional Personality Questionnaire: Mother and father
24. Positive and Negative Affect Schedule: Mother and father

Family emotions, stress and relationships

25. Demographic Information Questionnaire: Mother or father
26. Family Expressiveness Questionnaire: Mother
27. Parenting Stress Index: Mother and father
28. Living Environment Observation Scale: Observer
29. Child Rearing Practices Report: Mother
30. Sibling Conflict Questionnaire: Mother

Age 7 follow-up

1. Temperament Assessment Battery: 20 behavioral measures tapping affective style; videotaped and coded.
2. Children's Behavior Questionnaire: Mother and father
3. Health and Behavior Questionnaire including siblings aged 6–18: Mother
4. Hand Usage Questionnaire: Mother and father
5. Multiday basal cortisol and reactive cortisol (4X) during the home assessment for twins
6. Living Environment Observation Scale: Observer
7. Life Experiences Survey: Mother
8. Family Assessment Device: Mother and father

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Table 1 (CONTINUED)

Overview of Wisconsin Twin Panel Studies and Measures

Overview of Measures

Age 7 study of child psychopathology

Psychopathology for twins

1. Berkeley Puppet Interview: Twin
2. Child Depression Inventory: Mother and father
3. Diagnostic Interview Schedule: Mother
4. Obsessions and Compulsions Measure: Mother and father
5. Observer ratings of behavior symptoms.
6. Sensory Over-Responsivity Inventory: Mother
7. Symptom scales, Health and Behavior Questionnaire: Mother and father

Temperament for twins

8. Temperament Assessment Battery: 20 behavioral measures tapping affective style; videotaped and coded.
9. Children's Behavior Questionnaire: Mother and father
10. Positive and Negative Affect Schedule: Observer
11. Revised Bayley Observer ratings of reactivity and regulation

'Biological' measures

12. Zygosity Questionnaire for Young Twins: Mother
13. Twin height, weight, and head circumference; still photo
14. Palm and finger print asymmetries (index of possible prenatal insults)
15. Neonatal Morbidity Scale
16. Obstetrical and Neonatal Complications Scales
17. Multiday basal cortisol for all family members and reactive cortisol (4X) during the home assessment for twins
18. Buccal swabs for collection of cells for DNA extraction — all family members

Cognition for Twins

19. Block Design subtest of the WISC-III: Twin
20. Peabody Picture Vocabulary Test — Revised: Twin

Family Psychopathology and Personality

21. Beck Depression Inventory: Mother and Father
22. Diagnostic Interview Schedule: Mother and Father
23. Health and Behavior Questionnaire for siblings aged 6–18: Mother
24. Composite International Diagnostic Interview: Mother and father
25. Multidimensional Personality Questionnaire: Mother and father

Family stress

26. Confusion, Hubbub, and Order Scale: Mother
27. Demographics: Mother and father
28. Differential Treatment: Mother and father
29. Dyadic Adjustment Scale: Mother
30. Family Assessment Device: Mother and father
31. Family Conflict Scale: Mother and father
32. Life Experiences Survey: Mother
33. Living Environment Observation Scale: Observer
34. Parenting Stress Index: Mother

Parenting

35. Behavior Management Self-Assessment: Mother and father
36. Child Rearing Practices Report: Mother and father
37. Discipline Measure: Mother and father
38. Parent/twin triadic interactions (videotaped and coded using manual)

Peer and social relations

39. Berkeley Puppet Interview: Twin
40. Sibling Relationship Questionnaire: Parent and twin
41. Twin dyadic interactions (videotaped and coded using manual)

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Table 1 (CONTINUED)

Overview of Wisconsin Twin Panel Studies and Measures

Overview of Measures

Multiage Study of Childhood Sensory Defensiveness

1. Sensory Defensiveness subscale of the TBAQ-R: Mother
2. Sensory Responsivity Scale Assessment: Mother
3. ITSEA Sensory Sensitivity Scale: Mother
4. Health and Behavior Questionnaire: Mother
5. Multidimensional Personality Questionnaire: Mother
6. Sensory Over-Responsivity Inventory: Mother for self and twins
7. Short Sensory Profile: Mother
8. Adolescent/Adult Sensory Profile: Mother
9. Miller's Sensory Responsivity Scale Assessment Record Form: Child tester and observer

Multiage Study of the Autism Spectrum

Temperament for Twins

1. Children's Behavior Questionnaire: Mother
2. Health and Behavior Questionnaire: Mother
3. Berkeley Puppet Interview: Twin
4. Infant Toddler Social Emotional Assessment: Mother
5. Early Adolescent Temperament Questionnaire — Revised: Mother

Family Stress

6. Coping Orientations to Problems Experienced Questionnaire: Mother
7. Demographics: Mother
8. Dyadic Adjustment Scale: Mother
9. Family Relations Index: Mother
10. HOME inventory: Observer

Interventions

11. Interventions Questionnaire: Mother

Parent Affect

12. Profile of Mood States: Mother
13. Center for Epidemiological Studies-Depression: Mother

Sensory Sensitivity

14. Short Form of the Sensory Profile: Mother

Autism Spectrum Disorder

15. Social Communication Questionnaire: Mother
16. Social Responsivity Scale: Mother
17. Autism Diagnostic Observation Schedule: Observer

Praxis

18. Praxis Test of the Boston Diagnostic Aphasia Exam — 3rd Edition: Twin
19. Kaufman Speech Praxis Test for Children: Twin

Cognition, Speech and Language

20. Leiter International Performance Scale — Revised: Twin
21. Comprehensive Test of Phonological Processing: Twin
22. Peabody Picture Vocabulary Test-III: Twin
23. Test for the Reception of Grammar: Twin
24. Clinical Evaluation of Language Fundamentals — Revised: Twin

'Biological' measures

25. Zygosity Questionnaire for Young Twins: Mother
26. Palm & finger print asymmetries (index of possible prenatal insults)
27. Neonatal Morbidity Scale
28. Obstetrical and Neonatal Complications Scales
29. Multiday basal cortisol for all family members and reactive cortisol (4X) during the home assessment for twins
30. Buccal swabs for collection of cells for DNA extraction
31. Functional magnetic resonance imaging

Note: Sources for measures are available upon request.

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Sampling of Initial Results

Early Temperament

Early temperament involves substantial change, and generally the predictive utility of temperament is not realized until approximately age 3 years (Lemery et al., 1999). Further, genetically informative designs yield different patterns of genetic and environmental effects on temperament, depending on the measure (Goldsmith et al., 1997, 1999). In our sample of over 1000 pairs of twins ranging in age from infancy to 8 years, genes accounted for 53% of the variance in Difficult temperament and 72% of the variance in Unadaptable temperament, with no effects of the shared environment, sibling interaction or contrast, or sex and age (Lemery-Chalfant et al., 2006). Both additive and interactive genetic effects were important for Difficult and Unadaptable temperaments, and approximately 20% of the genetic influence on Difficult and Unadaptable temperament was shared.

Early Behavior Problems

Multiple rater models were utilized to explore the role of genetic and environmental influences on broad domains of social relatedness, general competency, and externalizing and internalizing behavior problems with a sample of 822 toddler-aged twin pairs (Van Hulle et al., 2006). In general, additive and nonadditive genetic factors explained the majority of variation in toddler behavior problems that was common to mothers' and fathers' reports. Broad-sense heritabilities ranged from .47 to .96, with nonshared environmental estimates ranging from .03 to .53. The relative contribution of genes and environment varied substantially across subscales of the externalizing and internalizing domains, with no significant shared environmental influences on any scale.

Early Language

Van Hulle et al. (2004) examined the genetic and environmental factors influencing expressive language development, in a sample of 386 toddler twin pairs from the toddler behavior screening. Using a sex-limitation model, heritability was higher for boys than for girls (20% vs. 8%) on productive vocabulary. However, heritability was higher for girls than for boys (28% vs. 10%) on word combination use. Overall, individual variation in both sexes was largely attributed to shared environment (54%–78%).

Multimethod Assessments of Impulsivity

The construct of impulsivity plays an important role in conceptualizing child psychopathology and is central to a diagnosis of ADHD. A multimethod, multisource assessment of impulsivity was conducted with a sample of 512 twins participating in Study 3, children at risk for psychopathology (Ruf et al., 2006). We examined 10 independent measures including scores from two home-based behavioral tasks, structured clinical interview, mother and father report of temperament, mother and father report of symptoms, behavioral ratings by two independent child examiners, and child self-report. Boys had higher impulsivity (using the first principal component as a composite) than girls, and impulsivity was significantly negatively correlated with family income, mother education, and IQ scores. Genetic model-fitting analyses identified a strong additive genetic and a nonshared environment effect for impulsivity.

Shyness and Low Positive Affect Differentiate Psychopathology Outcomes

Temperamental shyness increases the probability of the development of social anxiety and generalized anxiety disorders during childhood (Biederman et al., 2001; Goldsmith & Lemery, 2000; Goodwin et al., 2004; Hirshfeld et al., 1992), whereas low positive affect has been shown to increase the probability of developing depression (Durbin et al., 2005; Hayden et al., 2006; Shankman et al., 2003). A multimethod assessment was conducted with a sample of 862 twins participating in Study 3, children at risk for psychopathology (Krause et al., 2006). Controlling for age, sex, and social class, shyness significantly predicted symptoms of depression, social anxiety, and general anxiety, whereas low positive affect (controlling for shyness) predicted symptoms of depression.

Dermatoglyphic Asymmetries and Psychopathology Outcomes

We are interested in the role of nontransmissible environmental factors in the development of childhood disorders. Asymmetry between left and right hand dermal ridges might index exposure to maternal environmental stressors during the 3rd and 4th fetal months, when significant growth of the brain is also taking place. With a subsample from Study 3, children at risk for psychopathology, we identified 89 children with a difference of five or more ridges between the left and right palms, classified as asymmetric. These asymmetric children were significantly more impulsive, oppositionally defiant, aggressive and manic (Lemery-Chalfant et al., 2005). These palmar asymmetries were largely independent of maternal medications, smoking, alcohol, and drug use during pregnancy as well as recorded birth complications. Using the twin method, we verified that individual differences in palmar asymmetries were nonshared environmental rather than genetic in origin (i.e., all twin correlations were about zero), whereas the sum of ridge counts showed strong genetic effects. Thus, the genetic results are consistent with our hypothesis that palmar asymmetries, as a 'fluctutating asymmetry', might index effects of prenatal environmental stressors.

Family Similarity for Cortisol Levels

Schreiber et al. (in press) examined afternoon basal cortisol levels measured across 3 consecutive days in mothers and fathers and in multiple offspring for 233 families with twins from Study 3, children at risk for psychopathology. Data from a second, separate, longitudinal study of 321 families with singletons were also included (Smider et al., 2002). Modest family similarity

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was apparent for afternoon basal cortisol levels in both studies, with spouses' cortisol levels correlated. The twin data demonstrated family resemblance in afternoon cortisol was due to shared environment and not genetic similarity. Shared environment accounted for 62% of the variation in twin afternoon basal cortisol levels and 14% of the variation in parent afternoon basal cortisol levels. Using pooled data from the two studies, female offspring had higher cortisol levels than males, and family similarity persisted after accounting for parental depression, socioeconomic status, time of day, and offspring sex and age.

Sensory Defensiveness

Using mothers' reports of tactile and auditory defensiveness, temperament, and behavior problems for 1394 twins from the toddler behavioral screening, both auditory and tactile defensiveness were modestly associated with fearful temperament and anxiety, but they were relatively distinct from other common dimensions of childhood behavioral dysfunction (Goldsmith et al., 2006). Twin correlations for the full range of scores and concordance rates for the extremes suggested moderate genetic influences, with some indication that the tactile domain might be more heritable than the auditory domain. Our preliminary analyses suggest both stability and change in young children's sensory defensiveness. Fifty per cent (23/46) of the twins who were reported as auditory defensive at age 2 were still auditory defensive at age 4 to 5. Approximately 48% (27/56) of the twins who were reported as tactile defensive at age 2 were still tactile defensive at age 4 to 5.

Autism

Thus far, we have shown that the initial screening does in fact identify children on the autism spectrum. From the case-finding data, the concordance rate for the autism spectrum for monozygotic (MZ) twins is in the range of 50 to 70%, and for dizygotic (DZ) twins, 15 to 25% (Kees et al., 2005). The gender ratio was somewhat higher than the 4:1 male:female ratio most commonly reported in the literature. From the behavioral screening for toddlers, we examined 35 autism screening items for 2808 twins (mean age = 27 months). The items were divided into four subscales: speech, social behavior, restricted interests, and motor impairment. For twins with extreme scores (top 5%) on both the social and speech subscales, a proband-wise analysis revealed an MZ concordance rate in the .60s and a DZ rate in the .40s.

Future Directions

The WTP is still a relatively new resource, with sample sizes expanding for some years to come. We plan to continue our practice of intensive assessment, at the sacrifice of the larger sample sizes that other panels can provide. We also expect to focus more on behavioral challenges than on typical development in the future and to incorporate a wider range of affective neuroscience measures in study designs. We will continue to follow young twins longitudinally and use genetically informative growth modeling with our longitudinal data.

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