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# Pittsburgh Registry of Infant Multiplets (PRIM)

Melissa Strassberg<sup>1</sup>, Katherine Peters<sup>1</sup>, Mary Marazita<sup>1,2,3,7</sup>, Jennifer Ganger<sup>4</sup>, Margaret Watt-Morse<sup>5</sup>, Lenn Murrelle<sup>6</sup>, Ralph Tarter<sup>7</sup>, and Michael Vanyukov<sup>1,7</sup>

<sup>1</sup> Department of Human Genetics, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

<sup>2</sup> Cleft Palate-Craniofacial Center, School of Dental Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

<sup>3</sup> Department of Oral and Maxillofacial Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

<sup>4</sup> Department of Psychology, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

<sup>5</sup> Magee-Womens Hospital, Pittsburgh, Pennsylvania, USA

<sup>6</sup> Mid-Atlantic Twin Registry, Virginia Commonwealth University, Richmond, Virginia, USA

<sup>7</sup> Center for Education and Drug Abuse Research (CEDAR), Department of Pharmaceutical Sciences, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

This paper describes the Pittsburgh Registry of Infant Multiplets (PRIM; Pittsburgh, Pennsylvania), the results of pilot research conducted in this registry, and the plans for future studies. The main focus of the registry is on psychological development and the risk for behavioral disorders. Particularly, characteristics associated with antisociality and the risk for substance use disorders (e.g., aggressivity, hyperactivity/impulsivity), as well as language development and other traits (e.g., dental health) are among the research targets.

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The Pittsburgh Registry of Infant Multiplets (PRIM) was created in 1996. The goal of this project was to establish a registry of multiplets based upon multiple births occurring at Magee-Womens Hospital, a high-risk obstetrics center in Pittsburgh, PA. This registry will serve as a resource for research performed at the University of Pittsburgh, the University of Pittsburgh Medical Center, and Magee-Women's Hospital. A large proportion of all Allegheny county births occur in this facility.

## Recruitment

All subjects are included in the registry prospectively. Currently, a part-time graduate student researcher serves as the project coordinator. This individual goes to the Labor and Delivery Center at Magee-Womens Hospital each day and reviews the births records from the previous day. Upon identifying a multiple birth, the researcher approaches the infants' mother to solicit participation. At that time, the mother is given a detailed explanation of the goals of the registry and her consent to be listed in the registry and contacted at a later date for participation in a research project is requested. The mother is assured that participation in the registry is voluntary and is given contact information to use if she has any questions. Upon obtaining consent, the family's information is entered in a database. No remuneration is given for participation in the registry.

In cases in which a multiple birth event is missed, (i.e., the family is discharged prior to contact), Magee-Womens Hospital contacts the mother, upon our request, asking for permission for PRIM to contact her. Once permission is

received, a letter explaining the registry, a brochure explaining the goals and methods of the registry, and the consent form are sent to the mother. Currently, there are 228 sets of multiplets enrolled in the registry.

## Data Collection

The co-investigators of the registry send out sets of questionnaires related to the health and behavior of twins and their parents. These questionnaires are age-appropriate and completed by the mothers or fathers of the twins. All data are entered into a Microsoft Access™ database maintained by the project coordinator. The database is password-protected and maintained on a local area network server located in the Center for Education and Drug Abuse Research (CEDAR), University of Pittsburgh. Only the PI and the project coordinator have access to personally identifiable data, which are maintained separately from the research data.

To obtain zygosity information, a questionnaire consisting of 15 items ascertaining physical similarity between the twins is sent to the mother after discharge, to be completed at home. This questionnaire is based on the Nicholls and Bilbro (1966) study, and its zygosity determination algorithm, developed by Eley and her collaborators for the Twins Early Development Study (TEDS) in London (personal communication), has an accuracy of correct assignment of zygosity of 94%. The questionnaire was transformed into BasicScript for TELEform Version 6.1, with each question coded as an item and each available response to a question given a numeric value. Responses from study participants are scanned and scored via the TELEform (1999) software. TELEform converts paper forms into online coded information for database systems. The algorithm for scoring was recoded from the original SAS script used by Mid-Atlantic Twin Registry, Virginia Commonwealth University, and scored using SPSS syntax.

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*Address for correspondence: Michael Vanyukov, University of Pittsburgh, 707 Salk Hall, Pittsburgh, PA 15261, USA. Email: mmv@pitt.edu*

A parental demographic data form is also sent to the enrolled families. This demographic questionnaire consists of a total of 20 items regarding marital status, ethnicity, and religious preference for each parent, as well as items regarding height, weight, and age for each parent and child. Additionally, items regarding the mother's pregnancy history, medical history, alcohol, cigarette and caffeine use are included.

**Research**

Research based on the PRIM data, due to sample limitations, has so far been confined to pilot studies. One such study, part of Master's thesis research by one of the authors (K.P.), investigating behavioral traits of activity and aggression, employed the Child Behavior Checklist (CBCL) Survey (CBCL 1½ – 5) (Achenbach & Rescorla, 2000) and Dimensions of Temperament Survey — Revised (DOTS-R) (Windle & Lerner, 1986). These questionnaires were sent to mothers whose twins were within the age bracket of 1½ to 5 years of age. Twenty-five sets of returned questionnaires provided data on same-sex twins (12 female and 13 male pairs); the determination of zygosity was possible in 24 of them (11 MZ and 13 DZ pairs). The twins were 18 to 54 months old; the median age was 46 months.

We restricted this preliminary analysis to two variables, CBCL Aggression, and DOTS-R Activity. Considering the small number of twin pairs in this pilot sample, males and females were combined. Despite the small sample size, the data are consistent with results from numerous twin studies of behavioral traits, indicating a substantial contribution of genetic factors to variation in behavioral activity and aggression. Intraclass correlations for aggression in MZ and DZ pairs were 0.76 (95% CI: 0.32, 0.93) and 0.45 (-0.11, 0.79), respectively, consistent with the contribution of additive genetic and shared environmental variance to twin

similarity ( $2r_{DZ} > r_{MZ} > r_{DZ}$ ). The data for activity, however, indicated a closer fit to a high contribution of the dominance/nonlinear component, absence of shared environment influence, with a small contribution of non-shared environment to phenotypic variance: the MZ and DZ correlations were 0.92 (0.71, 0.98) and -0.08 (-0.59, 0.48), respectively. The low DZ correlation for activity might also indicate a rater-specific sibling contrast effect, a common finding for this type of maternal ratings of disruptive behavior disorder symptoms (Eaves et al., 2000). Obviously, these estimates have large errors and are far from being definitive.

Continuing PRIM research will allow application of the standard methods of behavior genetics (e.g., using structural equation modeling). The traits of interest include measures of temperament and personality, particularly those associated with antisociality and the risk for substance use disorders and possibly mediating, in part, their significant heritabilities (Vanyukov & Tarter, 2000). Language development research by one of the authors (J.G.) focuses on heritability of the learning of several grammatical constructions (passive voice, past tense, inflectional and derivational morphology), possible dissociation of grammatical processes from lexical ones using behavior genetic analysis (e.g., differences in heritability), and dissociation of specifically grammatical abilities from broader verbal abilities (e.g., verbal memory and verbal fluency) as well as broader non-verbal abilities (both measured using subtests of the McCarthy Scales of Children's Abilities). Tests are administered in person by two research assistants so that zygosity does not affect test administration. Studies of these and other behavioral development characteristics, such as dimensions contributing to liability to attention deficit/hyperactivity disorder and the risk for this disorder, are currently in progress.

**Table 1**  
Pittsburgh Registry of Infant Multiplets (PRIM)

Name of register	Pittsburgh Registry of Infant Multiplets (PRIM)
Country	US
Kind of ascertainment	Direct contact with the mother upon twins' birth; consecutive births at a major maternity hospital
Opposite sex twins (yes or no)	yes
Number of pairs (separated by birth range and sex)	1996–2002: 201 twins pairs (72 mm; 58 ff; 71 mf), 19 triplets (4 ff; 4ffm; 9 mmf; 2mmm), 1 quad (1 mmff)
Primary interest	behavioral and developmental traits, cleft lip/palate, language development, liability to substance use disorders
Variables measured (+number of pairs in total)	CBCL, DOTS-R, Demographic info, Zygosity information
DNA / blood samples (+number of pairs)	0
Contact	Michael Vanyukov, Ph.D.; Tanya Eble, B.S.
Institution	University of Pittsburgh/Magee Womens Hospital
Address	707 Salk Hall
Telephone	412-624-1071; 412-648-8469
Fax	412-624-1929
Email	mmv@pitt.edu
Web site	http://www.pitt.edu/~mmv/prim/prim.htm

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### References

- Achenbach, T. M., & Rescorla, L. (2000). *Manual for the Child Behavior Checklist for Ages 1½ – 5/LDR and 2000 Profile*. Burlington: University of Vermont, Department of Psychiatry.
- Eaves, L., Rutter, M., Silberg, J. L., Shillady, L., Maes, H., & Pickles, A. (2000). Genetic and environmental causes of covariation in interview assessments of disruptive behavior in child and adolescent twins. *Behavior Genetics*, *30*, 321–334.
- Nichols, R. C., & Bilbro, W. C. (1966). Diagnosis of twin zygosity. *Acta Genetica et Statistica Medica*, *16*, 265–275.
- Cardif Software, Inc. (1999). *TELEform Elite, Version 6.1*. Cardiff, Wales: Cardiff Software, Inc.
- Vanyukov, M. M., & Tarter, R. E. (2000). Genetic studies of substance abuse. *Drug and Alcohol Dependence*, *59*, 101–123.
- Windle, M., & Lerner, R. (1986). Reassessing the dimensions of temperamental individuality across the life span: The Revised Dimensions of Temperament Survey (DOTS-R). *Journal of Adolescent Research*, *1*, 213–230.