
Pittsburgh Registry of Infant Multiplets (PRIM): An Update

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This article is an updated review of the Pittsburgh Registry of Infant Multiplets including recruitment methods, data collection, and results of pilot studies conducted in this registry. The main goal of the registry is to study psychological development. The risk for behavior disorders including substance use disorders, as well as language development and dental health are among research targets. Pilot data on the heritability of minor physical anomalies and neuropsychological characteristics (Continuous Performance Test) are reported.

This article is an update to a previous article that described the Pittsburgh Registry of Infant Multiples (PRIM; Strassberg et al., 2002). PRIM is a research registry, established in 1996, based on multiparous births in Magee-Womens Hospital, an obstetrics center in Pittsburgh, Pennsylvania. All mothers who give birth to multiples are invited to become part of the registry, which aims to serve as a database for future research involving twin studies. Researchers from the University of Pittsburgh and Magee-Womens Hospital use this registry as a resource for recruitment. All protocols and consent forms are approved by the University of Pittsburgh's Institutional Review Board. Additional information regarding PRIM is located in Table 1.

Recruitment

All subjects are included in the registry prospectively. A part-time graduate student researcher serves as the study coordinator. All births at the hospital are noted by pink or blue congratulatory tags placed outside of the mother's room — multiple births are identified by more than one of these tags, either of the same or different colors. Once a mother is found by the study coordinator via congratulatory tags, a nurse or other health care provider approaches and asks if she agrees to be approached by the coordinator. Approximately 90% of mothers agree to be approached. These

mothers are then given a detailed explanation of the goals and purpose of the registry, are assured of the confidentiality of the registry, and informed that they may withdraw from the registry at any time. If the mother then agrees to enrol, she is asked to sign a consent form that reviews the information described to her. She is then asked for general demographic information. Once consent is given, a letter reviewing the registry as well as a brochure reiterating the goals of the registry, and a copy of the consent form are sent to the mother. Another copy of the consent form is given to Magee-Womens Hospital Medical Records Department to be filed with the mother's medical records. No remuneration is given for participation in the registry. Currently there are over 600 sets of multiples enrolled in the registry.

Data Collection

Once consent is obtained, demographic and pregnancy information is entered and maintained in a Microsoft Access database. The database is password protected and maintained on a network server located at the University of Pittsburgh. As necessary, investigators associated with the registry send out age-appropriate questionnaires related to health and behavior to the parents of the twins (multiples). Additional demographic information is obtained by a 20 item questionnaire. Zygosity information is obtained through a 15-item questionnaire assessing similarity between the twins. This questionnaire is based on an earlier study by Nicholls and Bilbro (1966). Its zygosity determination algorithm, developed by T. Eley and colleagues. (personal communication, March 16, 1998), for the Twins Early Development Study in London, has an accuracy

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Table 1

Pittsburgh Registry of Infant Multiplets (PRIM)

Location	Pittsburgh, Pennsylvania, US
Kind of ascertainment	Direct contact with mothers of multiples born at Magee-Womens Hospital, major maternity hospital in Allegheny county
Opposite-sex twins	Yes
Number of pairs (separated by birth range and sex)	572 twin pairs (191 MM; 176 FF; 205 FM), 38 triplets (5 MMM; 6 FFF; 15 MMF; 12 FFM), 1 quadruplet (MMFF)
Focus of work	Behavior and developmental traits, cleft lip/palate, language development, liability to substance use disorder
Variables measures	Demographic information, zygosity information, CBCL, DOTS-R
Open to all types of collaboration	Yes
Contact	Michael Vanyukov, PhD
Institution	University of Pittsburgh; Magee-Womens Hospital
Address	707 Salk Hall, Pittsburgh, PA 15261
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Note: M = male, F = female; CBCL = Child Behavior Checklist, DOTS-R = Dimensions of Temperament Survey-Revised

of 94%. A subgroup of parents have also completed a Child Behavior Checklist adapted for children aged 18 months to 5 years (Achenbach & Rescorla, 2000), and a Dimensions of Temperament Survey — Revised (Windle & Lerner, 1986).

Results of Pilot Studies

Relationships Between Minor Physical Anomalies and Behavior and Physical Development.

Research with PRIM data has continued to produce pilot studies. The most recent study, part of E. Jenkins's master's thesis (Jenkins, 2006), focused on behavior and physical development. The aim of this study was to determine whether minor physical anomalies (MPA) serve as a predictor for behavioral variation, and whether certain regions of the body are more likely to manifest anomalies related to behavioral problems. Twin pairs were recruited from PRIM and from the 2005 annual Twins Days Festival in Twinsburg, Ohio. The only inclusion criterion was that twin pairs were between 5 and 12 years of age. The Stroop Task and the Continuous Performance Test (CPT; Conners, 2000) were administered to assess attention and impulsiveness in the twin pairs. A 15- to 20-minute assessment for MPA using an expanded version of the standardized Waldrop Physical Anomaly Scale (Waldrop & Halverson, 1971) was performed by two investigators.

Significant differences were observed between monozygotic (MZ) and dizygotic (DZ) twins for the total number of head-related MPA (MPA head score), which was higher among the DZ twins (mean \pm SEM, 0.18 ± 0.068 vs. 0.49 ± 0.084 ; $p = .011$). Interestingly, variance for this score was also higher among DZ twins ($p < .00001$). Bearing in mind the preliminary character of the data, both differences are consistent with (intrauterine) sibling competition. Intraclass correlations

for the MPA head score were estimated in a set of twin pairs (17 MZ and 27 DZ). None was found to be significant, likely due to both small sample size and the rarity of the variant phenotypes.

Intraclass correlations for commission error scores of CPT, a measure of impulsivity, were significant in both MZ and DZ pairs, .638 (95% confidence interval [CI]: .179–.872; $p = .006$) and 0.337 (95% CI: $-.053$ –.640; $p = .044$), respectively, corresponding to a heritability estimate of .602. Whereas this estimate is within the range of heritabilities commonly estimated for psychological traits, direct comparison with results of other studies is difficult, because few of them have addressed neuropsychological characteristics, and the samples used have also predominately been small (Heiser et al., 2006; Holmes et al., 2002). The MPA head score did significantly correlate with the commission error rate ($r = .216$, $p < .01$), suggesting a possibility of common (not necessarily genetic) developmental mechanisms. Results indicate that MPA may not be useful as predictors for normal behavioral variation, but may be more applicable in relation to the risk for more severe conditions such as schizophrenia (Sivkov & Avabaliyev, 2003).

Language Development

Another pilot study concerned language development. The aim of this study (Ganger et al., 2005) was to determine whether different grammatical structures are associated with different levels of heritability during development, with the implication that those structures less influenced by heritability could potentially be influenced by environmental intervention to a greater extent. To participate, twins had to be between 3 and 6 years of age at the time of testing, and without diagnosed language or cognitive delay. Twins were administered three laboratory-developed tests of grammar (tests of past tense production, passive voice

comprehension, and word formation) as well as selected subtests of the McCarthy Scales of Children's Abilities (McCarthy, 1972).

Results for the passive voice measure, including 69 MZ and 117 DZ pairs recruited from PRIM and regional Mothers of Twins Clubs, were reported at the Society for Research in Child Development conference in 2005. Ganger et al. (2005) found significantly higher heritability for scores on nonactional passive items (e.g., 'The movie was watched by John') than for scores on actional passive items (e.g., 'The ball was kicked by John'). Results were $h^2 = .42$ (95% CI .13–.98), $c^2 = .03$ (95% CI .39–.40) and $h^2 = -.09$ (95% CI .61–.43), $c^2 = .45$ (95% CI .07–.83) respectively. These findings are consistent with two previous observations from the language development literature. First, actional passives are much more frequent in the input speech to children than nonactional passives, thus providing some environmental variation to work with, and driving up shared environment for actional passives (Gordon & Chafetz, 1990). Second, Borer and Wexler (1992) proposed that there is a fundamental difference between the two types of passives. Actional passives could be interpreted by children as adjectives, thus being understood without the use of a grammatical rule (Borer & Wexler, 1992; Babyonyshev et al., 2001), while nonactional passives require the use of a syntactic operation. The heritability difference, if it is maintained in a larger sample, is consistent with both of these theories and suggests a clear path for further experimental work to decide between them.

Future Directions

Future research utilising PRIM is planned to address the relationship between neuromaturation, behavioral and language development, and the risk for early onset behavioral disorders. The methodology to be applied in these studies is currently being tested in research in progress. The twin approach allows for genetic and environmental components of these relationships to be estimated. The particular candidate genes as well as measures of the environment can then be tested as mediators of these components. Understanding variation in early phenotypes of behavioral traits and other characteristics may be especially important from the prevention and intervention viewpoints.

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