Empirical Evaluation of the Genetic Similarity of Samples From Twin Registries in Australia and the Netherlands Using 359 STRP Markers

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One way to achieve the large sample sizes required for genetic studies of complex traits is to combine samples collected by different groups. It is not often clear, however, whether this practice is reasonable from a genetic perspective. To assess the comparability of samples from the Australian and the Netherlands twin studies, we estimated $F_{st}$ (the proportion of total genetic variability attributable to genetic differences between cohorts) based on 359 short tandem repeat polymorphisms in 1068 individuals. $F_{st}$ was estimated to be 0.30% between the Australian and the Netherlands cohorts, a smaller value than between many European groups. We conclude that it is reasonable to combine the Australian and the Netherlands samples for joint genetic analyses.

The cohorts were ascertained from twin registries in Australia and the Netherlands following an extreme discordant and concordant design (Boomsma et al., 2000; Kirk et al., 2000). DNA samples were extracted using standard methods from whole blood in the Australian sample and from buccal epithelial brushings in the Netherlands sample. A genome-wide linkage panel (Weber16, 402 short tandem repeat polymorphisms [STRP] markers; Ghebranious et al., 2003) was genotyped in all samples by the Mammalian Genotyping Service (Marshfield Clinic Research Foundation, Marshfield, WI, NHLBI contract N01-HV-48141). Following cleaning and quality control checks, 359 STRP markers were available for analysis on 1068 individuals (519 from the Australian cohort and 549 from the Netherlands cohort) who were either genotyped pedigree founders or, if there were no genotyped founders, a randomly selected individual from that pedigree.

We used AMOVA in Arlequin (v3.01; Schneider et al., 2001) to estimate $F_{st}$ (Weir & Hill, 2002). $F_{st}$ is the proportion of total genetic variability attributable to the genetic differences between cohorts. Based on 359 STRPs in 1068 individuals, $F_{st}$ was estimated to be 0.30% between the Australian and the Netherlands cohorts. Figure 1 places this finding in context of multiple worldwide cohorts (Rosenberg et al., 2002). Empirically, the variability between the Australian and the Netherlands cohorts was smaller than for all other samples including an European cohort (0.7%). Based on these findings, we conclude that it is reasonable to combine the Australian and the

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Netherlands samples for joint genetic analyses. This finding is not unexpected given the population history of Australia, whose large-scale colonization in the past 250 years was overwhelmingly via immigrants from northern European (mainly from Britain and Ireland) as well as prior empirical results (Stankovich et al., 2006).

An essential caveat is that results such as these do not provide proof the comparability of cohorts, nor do they provide protection against all forms of bias. For example, across cohorts, there may be systematic differences in etiologically relevant environmental exposures, phenotypic assessments, or laboratory procedures. In addition, even if STRP marker patterns are relatively similar in closely related cohorts, empirical data suggest that population stratification can still exert a profound impact at least in some instances (Campbell et al., 2005; Marchini et al., 2004).

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References


