Twin Research and Human Genetics (2020), **23**, 94–95
doi:10.1017/thg.2020.41

CAMBRIDGE UNIVERSITY PRESS

Article

A Brief History of the Collaboration between Dr Nathan Gillespie and Professor Nick Martin Including Personal Reflections

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Abstract

This article describes Dr Nathan Gillespie's PhD training and supervision under Professor Nick Martin and their ongoing collaborations. Drs Gillespie and Martin have collaborated on numerous biometrical genetic analyses applied to cross-sectional and longitudinal twin data, combined molecular and phenotypic modeling, as well as genomewide meta-analyses of psychoactive substance use and misuse. Dr Gillespie remains an active collaborator with Professor Martin, including ongoing data collection, analysis and publications related to the Brisbane Longitudinal Twin Study.

Keywords: Nick Martin; Nathan Gillespie; biometrical genetic; twin modeling; genomewide association scan; Brisbane Longitudinal Twin Study

(Received 20 February 2020; accepted 14 April 2020; First Published online 26 May 2020)

I first met Nick Martin almost 21 years ago when he took me on as a PhD student in his Genetic Epidemiology unit in what was then simply known as the Queensland Institute of Medical Research (QIMR). Before meeting Nick, all I knew was that he was a biologist, but it became quickly apparent that his intellectual curiosity was extremely broad and encompassed many clinical and nonclinical phenotypes. Looking back over the last two decades, it is clear to me that his success at ascertaining large twin samples, his emphasis on broad but high-quality phenotyping and repeated sampling, his foresight to begin collecting genotypes and maintain genotyping efforts, his obtaining the resources for data storage and facilitating data access, his investment in his students, his ability to attract the experts in genetics, his constant encouragement and his collaborative and convivial spirit have provided the launchpad for many scientific careers, including my own. Moreover, his contributions to science have given us all an invaluable resource and treasure trove of genetically and environmentally informative human data with which to tackle some of the most compelling questions regarding our natures.

Present during my first meeting with Nick was his colleague and long-time collaborator, Professor Ian Hickie. They were both keen to explore the genetic etiology of somatic distress and its relationship to internalizing symptoms and needed a student to do the work. Under Nick's supervision, my first manuscript explored the internalizing symptoms of the Duke Social Support Index and Symptom Checklist scales from which we extracted the factors of somatic distress, anxiety and depression (Gillespie et al., 1999). Applying the Classic Mx software program to the summary polychoric correlations, we were able to show using weighted least squares that while there was significant genetic overlap between these three dimensions, there was still evidence of distinct genetic influences in somatic distress (Gillespie et al., 2000). The broader implication of these findings was that for individuals suffering from chronic fatigue syndrome, their symptoms of somatic distress were not entirely the same as those of depression. Several years later, Nick and I modeled the direction of causation between these same internalizing dimensions and measures of parental bonding. It was and remains a novel use of twin data, which demonstrates how under certain conditions, cross-sectional data can be effectively used to test competing causal hypotheses. The results when published (Gillespie et al., 2003) earned us the 2003 Fulker Award and a 'very nice bottle of wine' (which Nick selected!) at the Behavior Genetics meeting in Aix-en-Provence. Thanks to Nick, my interest in modeling causality has persisted along with my preference for pricey Châteauneuf-du-Papes.

Not only do longitudinal data trump cross-sectional for testing causal hypotheses, but such data provide opportunities for testing compelling developmental hypotheses. The methods for modeling genetic and environmental changes over time have been well described by Eaves et al. and others (Eaves et al., 1989). However, thanks to Nick's decades-long and persistent efforts to ascertain and resample his twin cohorts, we were in a position to begin applying and testing developmental hypotheses to well-powered samples with repeated measures. Using data from his Brisbane Longitudinal Twin Study, we were able to demonstrate the emergence of different genetic and environmental influences in adolescent and teenage personality at ages 12, 14 and 16 years (Gillespie, Evans et al., 2004). Using the repeated measures from his two adult twin cohorts, we demonstrated that the genetic risks in nonclinical symptoms of depression and anxiety at age of 20 years were, by and large, enduring well into an individual's 70s (Gillespie, Kirk et al., 2004). Incidentally, we also identified 'innovative' or additional sources of genetic variance in those in their 30s and 40s for anxiety and depression, respectively.

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Cite this article: Gillespie NA. (2020) A Brief History of the Collaboration between Dr Nathan Gillespie and Professor Nick Martin Including Personal Reflections. *Twin Research and Human Genetics* **23**: 94–95, https://doi.org/10.1017/thg.2020.41

Regarding the genetics of depression, it was Nick who alerted me to Caspi et al.'s (2003) report investigating the interaction between stressful life events and the serotonin transporter genotype as a predictor of major depression. Nick realized that he had isomorphic data to validate this landmark finding using his Australian adult twins and we immediately set to work. Regardless of whether our results were based on binary logistic or ordinal regression analyses, we were the first to find no corroborating evidence supporting a main effect of 5-HTTLPR, or an interaction between the 5-HTTLPR genotype and stressful life events on major depression (Gillespie et al., 2005). In the decade that followed, the field entirely recalibrated its views toward candidate genes and candidate gene-by-environmental interactions concerning complex behaviors (Duncan & Keller, 2011).

In 2004, I left Nick's laboratory at QIMR for what was to be a brief 2 year's visit to the Virginia Institute for Psychiatric and Behavior Genetics in Richmond, Virginia, where Nick himself had worked during the early 80s with the likes of Lindon Eaves, his PhD supervisor, Kenneth Kendler, Michael Neale, John Hewitt and Andrew Heath, among others. And although 2 years have somehow (and very quickly) turned into 16 years, I have had the great fortune of maintaining my collaboration with Nick on grant applications, numerous projects and many more publications. Perhaps the greater fortunes include the many meals I have had at the Martin household dinner table or better still, his being my best man at my wedding in 2017. I am deeply indebted to his support, confidence in me and abiding friendship. I will remain forever grateful for the opportunities that his tutelage, which has never really stopped, continues to give me.

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https://doi.org/10.1017/thg.2020.41 Published online by Cambridge University Press