

Article

The Genetics of Reading and Language

Michelle Luciano and Timothy C. Bates

Department of Psychology, University of Edinburgh, UK

Abstract

Recounts how our collaboration with Nick Martin was shaped over two decades, leading to the first studies of predictions from the ‘Dual Route Cascaded’ computational model of reading in twins, and extending into the molecular work, first linkage, fine mapping of genes identified in pedigree studies, into now the genomewide association study era and the first polygenic risk scores for reading and their potential in early clarifying causality and validating interventions, as well as for future global collaborations in improving these predictors and identifying causal variants. We highlight Nick’s warm, future-focused optimism, support and inclusive approach without which none of this would have been possible. The circle of Nick asking, over half a century ago, ‘What genes do you think make some kids get better grades?’ has built a diverse scientific legacy involving thousands of papers and collaborations. The (heritable) traits of curiosity, boldness, warmth, interest in societally important questions, openness to new methods, ambition and collaborative skill to bring into being the infrastructure and samples needed for this research are rare, and we are grateful.

Keywords: Reading; dyslexia; GWAS; SNP; genetics; prediction; education; gratitude

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One of us (Bates) first met Nick Martin at the Behavior Genetics Association meeting in Sydney, Australia. I was a student with no status in BG, but Nick’s personal warmth and gregariousness welcomes all-comers. This would have its first concrete effect a dozen years later when, working in Sydney, we successfully applied for a modest National Health and Medical Research Council grant to study the genetics of reading, testing predictions from the leading ‘Dual Route Cascaded’ computational model of reading. We had proposed collecting our own twin sample: As most reading this will be aware, to ascertain, zygosity test, and phenotype 500 pairs of twins was a daunting prospect (though not to Nick, who had done just this for his — wait for it — undergraduate thesis in Adelaide!). An email became a phone call, and a trip up to Brisbane, which soon morphed into our training the professional testers who Nick had assembled on the subtleties of assessing nonword pronunciation over the telephone! Soon enough the first twin study from this project was published (Bates et al., 2004). It addressed, with key collaborators Anne Castles and Max Coltheart, aspects of the Dual Route Cascade model of reading and showed that the genetic factor structure mimicked the phonological and lexical pathways to reading aloud and not a connectionist model that was also popular in cognitive science (Bates, Castles et al., 2007; Castles et al., 2006). With a grant far too small to accomplish our goals, Nick, through his generosity, encouragement, smooth management systems, efficient and warm personal relations and the support of the large team of researchers, assistants, postdocs, and PhDs, all of whom lent a hand, made it possible not just to deliver on our goal, but to get ahead and overdeliver as a series

of analyses emerged. This leads us naturally into the molecular phase of the longer term project.

The other of us (Luciano) had been lucky enough to receive Nick’s red pen marks on her thesis chapter drafts despite him not being an official PhD supervisor. Nick has forever been provocative, sharp-minded and extremely helpful, and none more so as when he encouraged me as a recent PhD graduate from his lab to get involved in a new study on the genetics of reading and language — something that I am still active in today. With data collection now complete, the reading project began to take on a different, more Queensland Institute of Medical Research-aligned direction. While cognitive scientists are interested in the models, well Nick, he was interested in the genes, and, with the human genome project beginning to pay off, this was a great time to realize that interest. Nick had been successful in attaining funding for microsatellite genotyping in the twin adolescent sample, and so onto linkage analysis we went. Now with my own funding as a research fellow on the project, I performed my first (and reading ability’s first) linkage analysis! Just as Nick was helpful in guiding me through twin analyses during my PhD, he continued to provide support in this new postdoc period. Nick wasn’t helping with the finer details of the analysis, but he was (and still is) always on top of the latest research developments in statistical genetics (he will point you to the right paper!). Our linkage study (Bates, Luciano et al., 2007) was the first of reading ability in an unselected sample, and while we did not expect too much in way of significant results, we contributed to quite a number of replications of candidate dyslexia genes and quantitative trait loci in our sample (Bates et al., 2010; Luciano et al., 2007; Lind et al., 2009). One of our findings was that evidence for replication was always stronger when we removed IQ variance from our reading measure.

Nick, who always looked to the future and kept pace with technological advances, soon had funding for genomewide single

Author for correspondence: Michelle Luciano, Email: michelle.luciano@ed.ac.uk

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nucleotide polymorphism (SNP) genotyping. And next, came the first genomewide association study (GWAS) of reading ability in an unselected sample — well, two samples actually. Nick always encouraged collaboration and with that in mind, we got Avon Longitudinal Study of Parents and Children on board to contribute to a GWAS meta-analysis of reading, spelling and language traits (Luciano et al., 2013). Again, the sample size was relatively small, and we did not find much. GWAS samples of children are always, by comparison, going to be smaller than those of adults, so why not study reading and language in adults (see Luciano et al., 2018). Which is exactly what we have recently done with Nick's ongoing support, another successful phone interview study on Australian twins that is supporting a proof-of-principle that GWAS of adult reading and language phenotypes will help us understand their disorder in development (Doust et al., 2020). We collected educational attainment data in this study, but could not collect IQ data (controlling for nonverbal IQ allows the reading and language measures to be much more sensitive to genetic effects — it seems that not everything is IQ, Nick). Where we have come to date in this ongoing story is not possible to compress into a single trait — not even one as 'general' as IQ, which both of us worked on with Nick. Nor either, it seems to us, is it simply high ability that led Nick to ask all those years ago 'What genes do you think make some kids get better grades?' and build this into a diverse scientific legacy involving hundreds of papers and collaborations across topics as diverse as attitudes, methods, Alzheimer's, baldness, twinning and skin cancer. This operating, poetry and essay reading, adventurous, bon vivant manages to combine curiosity, boldness, warmth, interest in both big societally important questions, the openness to adopt new methods, ambition and collaborative skill to bring into being the infrastructure and samples needed for this research. It is all too rare, and we are grateful: Thank you Nick, for these, and for many more years to come!

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