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Personalized learning: From neurogenetics of behaviors to designing optimal language training

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ABSTRACT

Variability in drug responsivity has prompted the development of Personalized Medicine, which has shown great promise in utilizing genotypic information to develop safer and more effective drug regimens for patients. Similarly, individual variability in learning outcomes has puzzled researchers who seek to create optimal learning environments for students. "Personalized Learning" seeks to identify genetic, neural and behavioral predictors of individual differences in learning and aims to use predictors to help create optimal teaching paradigms. Evidence for Personalized Learning can be observed by connecting research in pharmacogenomics, cognitive genetics and behavioral experiments across domains of learning, which provides a framework for conducting empirical studies from the laboratory to the classroom and holds promise for addressing learning effectiveness in the individual learners. Evidence can also be seen in the subdomain of speech learning, thus providing initial support for the applicability of Personalized Learning to language.

1. Introduction

Research in educational sciences and related clinical disciplines has strived to identify the most efficacious educational and interventional programs. Results from numerous high-quality empirical studies provided converging evidence for many areas of best educational practices, ranging from early childhood cognitive development to mathematics, sciences and literacy. In asking what factors and interventions predict and produce the best learning outcomes, high-quality research in educational science often focuses on learners as a group. More recently, research has begun to examine the impact that individual differences and learning-centered factors may have on responsivity to a given intervention.

This review discusses **Personalized Learning**, a translational line of inquiry that stands in parallel with pharmacogenomics and Personalized Medicine (Wang et al., 2011). The concept of using genetic information to improve patient outcomes has already been established by pharmacogenomic research. This concept has great potential to be extended to developing personalized educational practices as well as personalized treatment of behavioral disorders, communication disorders and learning disabilities (see also Gabrieli et al., 2015). Recent advances in genomics have expanded beyond understanding of the molecular genetics of cellular functions and diseases (McCormack et al., 2011; Pare et al., 2010) directly relevant to drug therapies and have begun to also shed light onto the genetic basis of higher order human functions, including executive functions and memory (Papassotiropoulos and de Quervain, 2011) as well as domain-specific behaviors, such as motor learning (Adkins et al., 2006). Exploring how genetic, neural and behavioral predictors can be used to customize learning paradigms across various modalities of learning would lay the foundation for optimizing both learning and behavioral treatment to the individual, a shift away from learning paradigms that focus on cognitive training at the group level. After briefly reviewing Personalized Medicine, the framework for Personalized Learning will be discussed, followed by an example of personalized learning in speech learning and general considerations for implementations.

2. Personalized medicine

Recognizing individual variability in drug responsivity and safety, researchers and clinicians in fields of medicine have begun to seek ways to tailor medical treatments to patients on an individual level. Often termed Individualized Medicine, Personalized Medicine and more recently Precision Medicine (Collins and Varmus, 2015), this new area of intensive research has resulted in a number of treatment strategies

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that have shown great promise in improving patient outcomes (Ma and Lu, 2011; Wang et al., 2011). Facilitated by recent developments and reduced costs in human genomics, researchers have demonstrated that in the pharmacological treatment of certain diseases, genetic variation contributes to differences in patients' responses to medication (Mallal et al., 2008). A well-studied example of genetic polymorphisms affecting treatment response in Personalized Medicine is warfarin, an anticoagulant whose responsivity is associated with variants of *CYP2C9*, a group of genes that encode enzymes that are responsible for the metabolic clearance of warfarin, and *VKORC1*, which encodes for an enzyme involved in recycling vitamin K-, a cofactor necessary for the formation of various clotting factors. These discoveries have led to FDA approval of clinical tests for genetic variants and labeling changes on medication that provide considerations of *CYP2C9* and *VKORC1* polymorphisms in deciding on a dosing regimen (Schwarz et al., 2008). Other pharmacological therapies that have shown similar successes in treatment responses include abacavir (Mallal et al., 2008), gefitinib (Lynch et al., 2004), clopidogrel (Mega et al., 2010; Pare et al., 2010), carbamazepine (McCormack et al., 2011; Phillips and Mallal, 2011), and hepatitis C treatments (Thomas et al., 2009). These successes in Personalized Medicine can potentially be extended to domains of learning.

3. Personalized learning: the framework

Personalized Learning depends on three conditions. First, individual differences in learning need to be identified, demonstrating that not every person learns optimally under the same training paradigm. Second, genotypic, endogenotypic (neural) and/or behavioral (e.g., cognitive-perceptual) factors that are predictive of individual differences in learning should be determined. Third, these predictors should be used to place learners into the most optimal training conditions, individualized to their specific learning needs.

3.1. Individual differences in learning

Research on cognition and across domains of learning has shown individual degrees of success in learning vary, even under the same learning paradigms. Widespread individual differences have been found in learning achievement across mathematics, science and reading literacy (Halberda et al., 2008; Martin and Mullis, 2013), from the learning of facts to the acquisition of skill (Ackerman, 2007), in explicit forms as well as implicit forms of learning (Kaufman et al., 2010). Individual differences exist in how fast children normally acquire their native language (Bates et al., 1995) and in native language attainment (Street and Dąbrowska, 2010). Compared to first language acquisition, individual differences are even more pervasive in second language acquisition (Birdsong, 2004). In clinical populations, treatment outcomes have also demonstrated variability. For example, children who are severely or profoundly deaf and have received cochlear implants have shown extensive variability in speech-and-language outcomes (Peterson et al., 2010).

It is worth mentioning that the identification of individual differences in learning outcomes is not the sole focus of Personalized Learning. It is important to consider *what* is being learned and *how* learning occurs. In this regard, individual differences in learning outcomes per se may be less useful for the goals of Personalized Learning than individual differences in the determinants (i.e., predictors) of learning (see next section). This is because the existence of individual differences in learning outcomes suggests that not everyone learns optimally under certain conditions, but these differences alone give little information as to why some learners do not succeed. Individual differences in predictors of learning are important because these differences can further elucidate the learning conditions that may impede or facilitate learning. Such differences can ultimately be used to improve learning. Important questions arise: To what extent can individual differences in learning be predicted? Are there available objective predictors that do not require extensive testing of individual performance? Can predictors be used to modify approaches to individual learning?

3.2. Predictors of learning

In Personalized Medicine, genetic polymorphisms (genetic variations across individuals) have been shown to be predictive of patient responsivity to certain pharmacological treatments (Pare et al., 2010). These genomic advances have also extended beyond life-threatening diseases that have clear molecular origins. In learning and higher-level functions, numerous studies have emerged that demonstrate the predictive ability of individual genetic differences on learning and cognition. Individual differences in episodic memory have been found to be associated with a cluster of genes related to the glutamate system (de Quervain and Papassotiropoulos, 2006; Papassotiropoulos and de Quervain, 2011). Individual differences in various aspects of procedural learning have been tied to polymorphisms of genes in the dopaminergic D2 receptor and striatal systems (Frank et al., 2009; Klein et al., 2007). Individual differences in working memory have also been linked to polymorphisms of dopaminergic D1 receptor genes (Egan et al., 2001; Rybakowski et al., 2005), such that homozygous carriers of the G allele of *DRD1* seemed to show worse performance. Not suprisingly, some of these genes have recently been found to be associated with cognitive and psychiatric disorders (Bilder et al., 2011). As cognitive functions are strongly linked across domains of learning (Klahr et al., 2011), these cognition-related genes are likely to be predictive of aspects of learning although future studies are required to examine their actual predictive power.

Despite numerous cases of success (e.g., Franke et al., 2008; Gateva et al., 2009; Soronen et al., 2010), it is important to point out the enormous challenges in finding genetic predictors. For example, many previously identified associations based on genome-wide association studies (GWAS) have failed to replicate (Campa et al., 2012; Cousin et al., 2011; Molendijk et al., 2012). Even the best examples of replications explain only a small proportion of phenotypic variance (Queitsch et al., 2012). In a recent study, Harlaar et al. (2014) used a genome-wide association approach to identify genetic variants associated with individual differences in receptive language in a sample of 2329 children. No associations were found that survived the conventional statistical significance threshold correcting for multiple comparisons; it was suggested that larger sample sizes and newer sequencing methods are required for future studies.

As finding genetic predictors will continue to be challenging, Personalized Learning also aims to incorporate other predictors outside of genetic markers for successful learning. Among non-genetic markers, having been shown to have predictive powers across diverse areas of learning are general cognitive factors such as psychometric intelligence (Neisser et al., 1996), executive functioning (Bull et al., 2008) and working memory (Alloway and Alloway, 2010). For example, fluid intelligence measured at age 11 could predict academic achievement at age 16 across an extensive list of school subjects, from mathematics and sciences (physics, chemistry, biology) to arts and humanities that included native and foreign languages (Deary et al., 2007). Based on past behavioral studies, in addition to executive functioning and working memory, candidate markers of language learning may include measures of ability to learn specific associations between stimuli (Ellis, 2008) and also declarative memory (Ullman, 2005), implicit learning of sequential regularities (Kaufman et al., 2010) and also procedural memory (Ullman, 2005), and perceptual sensitivity such as pitch contour perception (Wong and Perrachione, 2007). Electrophysiological and neuroimaging studies further suggest that event-related negative response seen in younger infants can serve as a predictor of later language development (Kooijman et al., 2013) while volumes in the left Heschl's gyrus and white matter connectivity