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Review

Linking neurogenetics and individual differences in language learning: The dopamine hypothesis

Patrick C.M. Wong [a,b,d,*], Kara Morgan-Short [c], Marc Ettlinger [a] and Jing Zheng [b,d]

[a] Roxelyn and Richard Pepper Department of Communication Sciences & Disorders, Northwestern University, Evanston, IL, USA
[b] Department of Otolaryngology, Head & Neck Surgery, Northwestern University, Chicago, IL, USA
[c] Departments of Hispanic & Italian Studies and Psychology, University of Illinois at Chicago, IL, USA
[d] Knowles Hearing Center, Northwestern University, Evanston/Chicago, IL, USA

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ABSTRACT

Fundamental advances in neuroscience have come from investigations into neuroplasticity and learning. These investigations often focus on identifying universal principles across different individuals of the same species. Increasingly, individual differences in learning success have also been observed, such that any seemingly universal principle might only be applicable to a certain extent within a particular learner. One potential source of this variation is individuals' genetic differences. Adult language learning provides a unique opportunity for understanding individual differences and genetic bases of neuroplasticity because of the large individual differences in learning success that have already been documented, and because of the body of empirical work connecting language learning and neurocognition. In this article, we review the literature on the genetic bases of neurocognition, especially studies examining polymorphisms of dopamine (DA)-related genes and procedural learning. This review leads us to hypothesize that there may be an association between DA-related genetic variation and language learning differences. If this hypothesis is supported by future empirical findings we suggest that it may point to neurogenetic markers that allow for language learning to be personalized.

1. Introduction

Research on the neuroscience of learning has been dominated by investigations of neuroplasticity that consider questions such as what aspects of the brain can change, under what conditions can they change, and at what age is change still be possible (e.g., Hubel and Wiesel, 1970; Merzenich et al., 1984; Recanzone et al., 1992). This research has informed our most fundamental understanding of learning and the brain. Increasingly, researchers are now paying close attention to the fact that large individual differences also exist in learning (e.g., Golestani and Zatorre, 2009; Wong et al., 2007). Therefore it is crucial that research on the neuroscience of learning should begin to examine the origins of these individual differences, including neurogenetic contributions. In this article, we will focus on a type of learning that shows large individual differences especially when learning begins in adulthood, namely language learning (e.g., Donyei, 2005;

* *Corresponding author*. Department of Communication Sciences & Disorders, School of Communication, 2240 Campus Dr, Evanston, IL 60208, USA.
E-mail address: pwong@northwestern.edu (P.C.M. Wong).
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Johnson and Newport, 1989). Language is arguably a defining characteristic of humans (e.g., Donald, 1991; Jerison, 1973; Lewin, 1993), and its relationship with the brain has been extensively studied (e.g., Friederici et al., 2002; Hickok and Poeppel, 2007; Ullman, 2004). Language learning is therefore ideally suited for examining the biological bases of individual differences in learning. We will focus on the learning of grammar, an aspect of language that has been shown to be very difficult to acquire to native-like proficiency (Abrahamsson and Hyltenstam, 2009; Weber-Fox and Neville, 1996) and that has a relatively clear neurophysiological basis.

Numerous factors have been found to relate to success in language learning, including environmental and neural factors such as musical experience (Wong & Perrachione, 2007; Slevc and Miyake, 2006), the type of training (Morgan-Short et al., 2010, 2012; Norris and Ortega, 2000; Peach and Wong, 2004), working memory (Miyake and Friedman, 1998), and neuroanatomy (e.g., Golestani et al., 2007 Wong et al., 2008; Warrier et al., 2009). Although these studies have identified some sources of variability in language learning success, none have focused on genetics. The complexity of both language and the genome makes it challenging to identify specific genes that contribute to language learning, especially genes related to our focus of normal variation in learning (see gene *ASPM* for the perception of lexical tone, Wong et al., in press; see genes *ROBO1*, Hannula-Jouppi et al., 2005; *FOXP2*, Lai et al., 2003; *CNTNAP2*, Whitehouse et al., 2011 for work on communicative impairments and developmental delay). Fortunately, several characteristics of the dopaminergic system have been established, including relevant genes, brain systems, domain-general (e.g., cognitive) functions, and language functions. These characteristics can form the basis for developing informed hypotheses concerning the genetic basis of grammar learning. For example, studies have attributed grammar learning (and non-linguistic rule learning) to domain-general functions such as the procedural (implicit) memory system (e.g., Ullman, 2004), as well as to brain systems such as structures within the frontostriatal pathway (especially Broca's area) (e.g., Opitz and Friederici, 2003).

The dopaminergic system is tied to the frontostriatal pathway, among other brain structures (see Seamans and Yang, 2004 for a review), as well as to the procedural memory system (e.g., Shohamy and Adcock, 2010). In non-linguistic domains, the genes that encode dopamine (DA) receptors and transporters/catabolizers are tied to various types of procedural (rule) learning and brain responses (e.g., Karabanov et al., 2010). Based on the aforementioned facts about the dopaminergic system, we hypothesize that DA-related genes (and their interactions) may be associated with variation in grammar learning and functions of the frontostriatal pathway. This review provides our analysis and synthesis of the literature that led us to develop the above-stated hypothesis. It is our aim that this review and hypothesis will serve as a catalyst in generating new empirical research on the genetic bases of language learning.

Below, we will first discuss some basic facts about the DA system and its functions as they relate to procedural rule learning, reward, and cognition more broadly. We will specifically include studies that examine polymorphisms of DA-related genes and differences in performance on cognitive tasks. We will then focus the discussion on grammar learning, including the associated cognitive functions and brain systems. The relations among DA-related genes, procedural learning, grammar learning, and brain systems ultimately lead us to hypothesize that there may be a relationship between DA-genes and grammar learning.

2. The dopaminergic system and DA-related genes

Major divisions of the dopaminergic system contain neurons from the substantia nigra pars compacta and ventral tegmental area projecting to divisions of the striatum, cingulate cortex, amygdala, hippocampus, prefrontal cortex (PFC), and other regions (see Seamans and Yang, 2004 for a review). Once released presynaptically, DA interacts with one of five DA receptors D1, D2, D3, D4, and D5, encoded by genes *DRD1*, *DRD2*, *DRD3*, *DRD4*, and *DRD5* respectively. DA receptors are G protein-coupled receptors and are divided into two major classes: D1-like (D1 and D5) and D2-like (D2, D3 and D4). These receptors are distributed across regions of the central nervous system with different relative density levels. While very high densities of both classes of DA receptors are found in the striatum (across the caudate, putamen, and nucleus accumbens), a high density of D1, but not D2, receptors can be found in the frontal cortex (Camps et al., 1990; Khan et al., 2000; Little et al., 1995). In addition to interacting with DA receptors, once released, DA is eliminated extracellularly by the DA transporter (DAT) (encoded by gene *DAT1*) and the catabolizer enzyme Catechol-*O*-methyltransferase (COMT) (encoded by gene *COMT*), primarily in the striatum and frontal cortex, respectively (e.g., Cass and Gerhardt, 1995; Cragg et al., 1997; Sesack et al., 1998; Wayment et al., 2001). Thus, levels of DAT and COMT ultimately affect the impact of DA. DA and DA receptors modulate a number of different molecular and cellular processes, including (2-amino-3-(5-methyl-3-oxo-1,2- oxazol-4-yl)propanoic acid) (AMPA), N-methyl d-aspartate (NMDA), and γ-Aminobutyric acid (GABA) responses, which can lead to short- and long-term synaptic changes across different regions of the brain (see Seamans and Yang, 2004 for a review). One of these processes involves the DA-and-cAMP-regulated neuronal phosphoprotein (32 kDa) (encoded by gene *DARPP-32, also known as PPP1R1B*), which is found in the striatum (Ouimet et al., 1992) and affects functions and plasticity of DA receptors (e.g., Calabresi et al., 2000; Stipanovich et al., 2008). Over- and under-activation of DA receptors can lead to enhanced and/or impaired brain functions (e.g., Vijayraghavan et al., 2007; Zahrt et al., 1997).

It is worth noting that although our fundamental understanding of the dopaminergic system comes from animal research, and although substantial similarities exist between the non-human mammalian (especially primate) and human systems, there remain differences between the two systems. For example, a high density of D2 receptors can be found in the human hippocampal CA1/2 region but not in the monkey (Camps et al., 1990; Jiao et al., 2003; see Shohamy and Adcock, 2010 for a review). Therefore, when human functions (e.g., language) are examined, it is important to directly examine the human DA system. In our discussion below, we will focus on the human literature.