Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

Brain Research

Research Report

BDNF val66met polymorphism affects aging of multiple types of memory

*Kristen M. Kennedy**, *Elizabeth D. Reese*, *Marci M. Horn*, *April N. Sizemore*, *Asha K. Unni*, *Michael E. Meerbrey*, *Allan G. Kalich Jr.*, *Karen M. Rodrigue*

Center for Vital Longevity, School of Behavioral and Brain Sciences, The University of Texas at Dallas, 1600 Viceroy Dr., Ste 800, Dallas, TX 75235, United States

ARTICLE INFO

Article history:
Accepted 19 September 2014
Available online 28 September 2014

Keywords:
Aging
BDNF val66met polymorphism
Prospective memory
Associative memory
Subjective memory
Episodic memory

ABSTRACT

The *BDNF* val66met polymorphism (rs6265) influences activity-dependent secretion of brain-derived neurotrophic factor in the synapse, which is crucial for learning and memory. Individuals homozygous or heterozygous for the met allele have lower BDNF secretion than val homozygotes and may be at risk for reduced declarative memory performance, but it remains unclear which types of declarative memory may be affected and how aging of memory across the lifespan is impacted by the *BDNF* val66met polymorphism. This cross-sectional study investigated the effects of *BDNF* polymorphism on multiple indices of memory (item, associative, prospective, subjective complaints) in a lifespan sample of 116 healthy adults aged 20–93 years. Advancing age showed a negative effect on item, associative and prospective memory, but not on subjective memory complaints. For item and prospective memory, there were significant age × *BDNF* group interactions, indicating the adverse effect of age on memory performance across the lifespan was much stronger in the *BDNF* met carriers than for the val homozygotes. *BDNF* met carriers also endorsed significantly greater subjective memory complaints, regardless of age, and showed a trend ($p < .07$) toward poorer associative memory performance compared to val homozygotes. These results suggest that genetic predisposition to the availability of brain-derived neurotrophic factor, by way of the *BDNF* val66met polymorphism, exerts an influence on multiple indices of episodic memory – in some cases in all individuals regardless of age (subjective memory and perhaps associative memory), in others as an exacerbation of age-related differences in memory across the lifespan (item and prospective memory).

This article is part of a Special Issue entitled Memory & Aging.

Contents

*Corresponding author.
E-mail address: Kristen.kennedy1@utdallas.edu (K.M. Kennedy).

http://dx.doi.org/10.1016/j.brainres.2014.09.044
0006-8993/

1. Introduction

Human memory can be classified into several different types, and each shows differential susceptibility to the effects of aging across the adult lifespan (Brickman and Stern, 2009; Craik and McDowd, 1987; Nilsson, 2003). For example, declarative, or episodic memory has been shown to decrease with increasing age (Verhaeghen et al., 1993), as opposed to procedural, or more nondeclarative types of memory (Light, 1991). Within the realm of declarative memory, there are further distinctions between memory types based upon the mnemonic process being utilized. Memory for items or lists, for example, can be distinguished from memory for associations, the latter of which requires binding of at least two items, along with accompanying contextual information (Naveh-Benjamin, 2000; Old et al., 2008; Spencer and Raz, 1995). Both item memory and associative memory performance decrease with age (Chalfonte and Johnson, 1996; Naveh-Benjamin et al., 2004). There has also been a recent surge of research interest in the ability to remember to do things in the future, referred to as prospective memory (Einstein and McDaniel, 1990). Prospective memory can be divided into two basic categories: time-based and event-based prospective memory cues. During time-based tasks, participants are asked to carry out tasks at a specific time in the future, and event-based tasks require the participant to respond to a particular environmental cue. Meta-analysis studies have indicated that both types of prospective memory decline with advancing age (Henry et al., 2004; Uttl, 2008). Finally, subjective assessment of one's own memory performance – a kind of meta-memory – has been referred to as subjective memory assessment or subjective memory complaints (Gilewski et al., 1990; McDonald-Miszczak et al., 1995). Subjective memory has been studied in aging populations, with varied findings regarding its age-sensitivity (Hertzog and Pearman, in press; Pearman et al., forthcoming).

These age-sensitive aspects of human memory are so vulnerable to the aging process, putatively because they are served by brain systems whose components show a high rate of change with age (Buckner, 2004; Raz and Kennedy, 2009; Rodrigue and Kennedy, 2011). There is also, however, great variability in individual memory performance, even within the aging process, and thus there is unexplained variance in memory performance that is due in large part to individual differences. One known aspect of such individual differences is genetic predisposition to different availability of neurotransmitter levels, neurotrophic factors and other neurobiological factors (Raz and Lustig, 2014).

Research focused on understanding factors that contribute to individual differences in memory ability has highlighted the fact that memory performance, like other cognitive abilities, is partly under genetic control (Payton, 2006). The study of candidate genes associated with cognitive and brain aging has been enabled by recent developments in assaying variants in specific genes, or single nucleotide polymorphisms (SNPs). One such candidate genetic polymorphism that is of special interest to the study of declarative memory is *BDNF* val66met, a valine to methionine substitution at codon 66 of the *BDNF* gene on chromosome 11 (Egan et al., 2003). The *BDNF* gene regulates activity-dependent secretion of brain-derived neurotrophic factor and met carriers of the *BDNF* gene show reduced secretion of this growth factor compared to val carriers. BDNF as a growth factor is crucial to learning and memory, likely through its regulation of LTP (long-term potentiation) and LTD (long-term depression), and its role in synaptic plasticity, neuronal differentiation, proliferation of dendritic arbor, and axonal sprouting (Binder and Scharfman, 2004; Egan et al., 2003; Kojima et al., 2001; Murer et al., 2001). BDNF expression is fairly ubiquitous throughout the brain (Barbacid, 1994; Zhang et al., 2007), at least in rodents and primates, but by far the most research attention has been directed to BDNF expression in the hippocampus.