YNIMG-12649; No. of pages: 9; 4C: 3, 5, 6, 7

NeuroImage xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Behavioral correlates of changes in hippocampal gray matter structure during acquisition of foreign vocabulary

Martin Bellander [a,*], Rasmus Berggren [a], Johan Mårtensson [b], Yvonne Brehmer [a,c], Elisabeth Wenger [c], Tie-Qiang Li [d], Nils C. Bodammer [c], Yee-Lee Shing [c], Markus Werkle-Bergner [c], Martin Lövdén [a,*]

[a] Aging Research Center, Karolinska Institutet and Stockholm University, Stockholm, Sweden
[b] Department of Psychology, Lund University, Lund, Sweden
[c] Center for Lifespan Psychology, Max Planck Institute for Human Development, Berlin, Germany
[d] Department of Medical Physics, Karolinska Institutet, Stockholm, Sweden

ARTICLE INFO

Article history:
Accepted 8 October 2015
Available online xxxx

Keywords:
Experience-dependent plasticity
Gray matter
Foreign language learning
Associative memory
Hippocampus

ABSTRACT

Experience can affect human gray matter volume. The behavioral correlates of individual differences in such brain changes are not well understood. In a group of Swedish individuals studying Italian as a foreign language, we investigated associations among time spent studying, acquired vocabulary, baseline performance on memory tasks, and gray matter changes. As a way of studying episodic memory training, the language learning focused on acquiring foreign vocabulary and lasted for 10 weeks. T_1-weighted structural magnetic resonance imaging and cognitive testing were performed before and after the studies. Learning behavior was monitored via participants' use of a smartphone application dedicated to the study of vocabulary. A whole-brain analysis showed larger changes in gray matter structure of the right hippocampus in the experimental group ($N = 33$) compared to an active control group ($N = 23$). A first path analyses revealed that time spent studying rather than acquired knowledge significantly predicted change in gray matter structure. However, this association was not significant when adding performance on baseline memory measures into the model, instead only the participants' performance on a short-term memory task with highly similar distractors predicted the change. This measure may tap similar individual difference factors as those involved in gray matter plasticity of the hippocampus.

Introduction

Already in the 1960s it was shown that the macrostructure of the animal brain can change in response to experienced environmental changes (Bennett et al., 1964; Rosenzweig et al., 1962). Accumulating evidence over the last decade speaks for the same principle being true in humans (see Lövdén et al., 2013; May, 2011, for reviews). For example, a training intervention, such as practicing juggling, can result in increases of gray matter (GM) in task-relevant brain areas, as observed on T_1-weighted magnetic resonance (MR) images (Draganski et al., 2004).

The biological underpinnings of GM changes as measured by MR imaging are not known. Increases could for example reflect synaptogenesis, dendritic branching, increased vascularization, and an increase in number and size of glia (see Zatorre et al., 2012, for review). In some areas of the brain neurogenesis is sizable, such as in the dentate gyrus of the hippocampus (HC), which replaces 1.75% of its neurons annually in adulthood (Spalding et al., 2013). A study by Biedermann et al. (2014) compared groups of wheel running and sedentary mice, where half of the mice had received hippocampal irradiation to suppress neurogenesis. MR measures of HC GM were acquired, as well as a range of histological measures tapping into for example neurogenesis, gliogenesis, and vascularization. The main result of the study was that the best predictor of GM increase was new-born neurons. The results are correlational, but could mean that the birth of new neurons is able to cause volume increases visible on MR images. However, it should be kept in mind that other factors than neurogenesis likely play major parts in GM changes as measured my MR (Ho et al., 2013).

The behavioral correlates of GM changes are also largely unknown (Lövdén et al., 2013; May, 2011). The magnitude of changes could potentially reflect learning success, for example, measured as performance increase or amount of acquired knowledge. Alternatively, GM changes could also be use-related only, so that for example the effort or time spent training is the main driving force behind structural changes regardless of the amount of knowledge acquired. With few exceptions (Engvig et al., 2010; Landi et al., 2011), past studies have typically failed to observe associations between individual differences in the

* Corresponding authors at: Aging Research Center, Karolinska Institutet, Gävlegatan 16, 113 30 Stockholm, Sweden.
E-mail addresses: Martin.Bellander@ki.se (M. Bellander), Martin.Lovden@ki.se (M. Lövdén).

http://dx.doi.org/10.1016/j.neuroimage.2015.10.020
1053-8119/© 2015 Published by Elsevier Inc.

amount of training or magnitude of behavioral benefits and GM changes (see Lövdén et al., 2013, for review). Also, these two behavioral variables, which are often related such that time in training affects acquired knowledge or skill, have typically not been examined together. As an exception, Sampaio-Baptista et al. (2014) recently compared juggling training during six weeks of high and low intensity (30 min of training per day versus 15 min). They found an interaction effect between the average performance during juggling training and practice intensity on GM changes from baseline to the end of training in left motor cortex and DLPFC. Here the relation between performance and volume change was positive in the high intensity group, and negative in the low intensity group. However, these results are not generally obtained, for example, Driemeyer et al. (2008) did not find any correlation between GM changes and performance or exercise length when studying juggling training. In addition, Mårtensson et al. (2012) studied military interpreters learning a new language. After three months of intensive study, the interpreters showed GM increases relative to controls in several areas important to language: left middle frontal gyrus, inferior frontal gyrus, superior temporal gyrus, and right HC. The increases in left superior temporal gyrus and right HC were positively correlated with achieved language proficiency, whereas the increase in left middle frontal gyrus was related to how much they struggled with learning. This can be taken as both use and learning being related to the GM increases, although with differential consequences: those individuals talented in acquiring language may have more plastic temporal brain areas, whereas those that struggle need to recruit frontal regions more. However, because all interpreters studied extremely hard and a direct behavioral measure of talent (i.e., ability to acquire language) was not assessed, this interpretation remains speculative.

The existing literature is thus small and inconclusive, and it is still an open question whether GM changes, when they occur, reflect novel use, learning success, or both. Building on the findings of Mårtensson et al. (2012), we used vocabulary learning as a training paradigm for episodic memory in a randomized study with a larger sample of individuals that allows for investigating the associations among individual differences in GM plasticity and behavioral variables. Learning a new language is a complex task involving different processes, such as learning to understand and produce speech sounds, syntax, and vocabulary. Our focus is on the learning of written words in a foreign language as a paradigm of episodic memory training.

The acquisition of a new vocabulary is dependent on long-term memory functioning. The pairing of an unknown word with a semantic meaning bears close resemblance to the cognitive concept of associative memory (Davis and Gaskell, 2009). Associative memory mechanisms are thought critical for binding units of information into a coherent memory representation. Vocabulary acquisition also requires being able to form and retrieve distinct memory representations of words in the new language when there is interference from other similar words. Such types of associative memory are likely to involve the medial temporal lobe and the hippocampus. For example, a functional MR study of novel word learning found performance related activity change in the HC, where subjects who had a smaller decrease of HC activity over experiment blocks performed better (Breitenstein et al., 2005). Besides overall knowledge acquisition and time spent on task, and functionality of memory mechanisms might also impact GM plasticity — at least in the case of vocabulary learning. Specifically, individual differences in volume increase (i.e., plasticity; Lövdén et al., 2010) might be dependent on the individual's memory performance at baseline. This interpretation of plasticity would be akin to the ability (or talent) for acquiring a novel vocabulary.

In this study, we investigated GM change in the HC of participants training their episodic memory by learning a foreign vocabulary and modeled individual differences in GM change in relation to acquired vocabulary, time spent studying, and baseline memory performance (associative memory and formation of distinct memory representation) in a path-modeling framework.

Materials and methods

Participants

Healthy participants between 18 and 30 years of age were recruited through advertisement in a local newspaper (Metro) in Stockholm, Sweden, and by ads posted on the campuses of Stockholm University, Karolinska Institute, Royal Institute of Technology, and Södertörn University. To be eligible, participants had to report no history of any psychiatric or neurological disorders, no on-going or previous use of medication potentially influencing cognitive function, eligibility for MR imaging, being right-handed, being native Swedish speakers, and no prior knowledge of any of the Romance languages. We initially recruited 80 participants, who were randomly assigned with weighting (2 to experimental group and 1 to control group) to either a group learning the Italian vocabulary ($n = 54$) and an active control group ($n = 26$). Of these participants, 56 completed the entire study with complete data ($n_{\text{vocabulary learning}} = 33$; $n_{\text{control}} = 23$). Almost all dropouts occurred relatively fast after pre-test MR imaging, mostly due to realizing the amount of time required to complete the study, which is reflected in the disproportionally high dropout rate from the experimental condition (39% dropout in the experimental group vs. 11% in the control group). Background variables for the effective sample are reported in Table 1.

Dropouts from the experimental group had significantly worse associative memory, $t(42.7) = 2.33$, $p < .05$, and performance on a delayed match-to-sample (DMS) task, $t(35.1) = 2.88$, $p < .01$, than the participants in the experimental group completing the course (these tasks are described in the Behavioral measures section below). There was no significant difference in the number of languages mastered at entry between completers and dropouts, $t(52) = 1.84$, $p = 0.071$. We also calculated the dropout effect size with the formula $(M_C - M_F)/SD_F$ where M_C is the mean value of the experimental group completing the course, and M_F and SD_F is the mean and standard deviation of the full experimental group (including dropouts). The dropout effect was .24 SD for associative memory and .31 SD for DMS performance. Importantly, however, there were no significant baseline differences between the experimental and control group of the effective sample on either associative memory, $t(43.1) = 0.77$, $p = .44$, DMS performance, $t(46.8) = -0.67$, $p = .50$, or number of languages mastered at entry, $t(56) = 1.78$, $p = 0.081$.

Participants in both the experimental and the control group received 1000 SEK (roughly 100 Euro) for completing two MR sessions. Furthermore, those in the experimental group received an extra 60–650 SEK ($M = 260$, $SD = 130$) depending on their performance on an Italian vocabulary assessment at posttest. In addition, the top 50% on this vocabulary assessment test received an iPod.

Procedures

At pre-test and post-test the participants did MR imaging, and performed a series of computerized cognitive tasks.

Table 1
Background variables as a function of group.

Measure	Group				*P*
	Experimental		Control		
	M	*SD*	*M*	*SD*	
n	33	n/a	23	n/a	n/a
Age (years)	24.6	3.3	22.2	2.9	.008
% Women	.55	n/a	.61	n/a	.638
Education (years)	13.9	2.1	13.1	1.5	.119
Raven matrices	9.3	4.0	8.0	3.7	.247
Languages mastered at entry	1.77	.81	1.43	.51	.081

Note. *P*-values are reported for independent *t*-test of differences between groups, with an exception for the group difference in % women, which is tested with a χ^2-test. M = mean, SD = Standard deviation.

Please cite this article as: Bellander, M., et al., Behavioral correlates of changes in hippocampal gray matter structure during acquisition of foreign vocabulary, NeuroImage (2015), http://dx.doi.org/10.1016/j.neuroimage.2015.10.020