Otto Hahn Research Group on Associative Memory in Old Age

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Research Team 2014–2016

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Overview

The Otto Hahn Research Group on Associative Memory in Old Age led by Yvonne Brehmer explores mechanisms contributing to individual differences in associative binding among older adults. Typical research questions are: Which cognitive, social, health, and lifestyle factors contribute to individual differences in associative binding? What are the genetic as well as functional and structural brain characteristics of older adults who show well-preserved associative binding skills?

This group was established in December 2012 and is funded by the Otto Hahn Award of the Max Planck Society, which was presented to Yvonne Brehmer for her dissertation on episodic memory plasticity across the lifespan. Nina Becker joined the group in August 2013 as a predoctoral fellow. The group's work is primarily based on data from the Swedish National Study on Aging and Care (SNAC-K), which is coordinated by the Aging Research Center (ARC) at the Karolinska Institutet in Stockholm, Sweden.

Memory for associations, such as linking a name to a face, is of fundamental importance for individuals' well-being, independence, and mental health in old age. However, older adults often show disproportionate difficulties in remembering associative information. We investigate the mechanisms underlying between-person differences in associative memory in old age. The basic questions we pose are: Why are some older adults quite good at remembering associative information while others are not? What are the (a) structural and functional brain correlates; (b) cognitive, social, and lifestyle factors; and (c) genetic markers accounting for interindividual differences in associative memory functioning? Is there a relationship

Key Reference

Becker, N., Laukka, E. J., Kalpouzos, G., Naveh-Benjamin, M., Bäckman, L., & **Brehmer, Y.** (2015). Structural brain correlates of associative memory in older adults. *NeuroImage, 118,* 146–153. doi:10.1016/j.neuroimage.2015.06.002

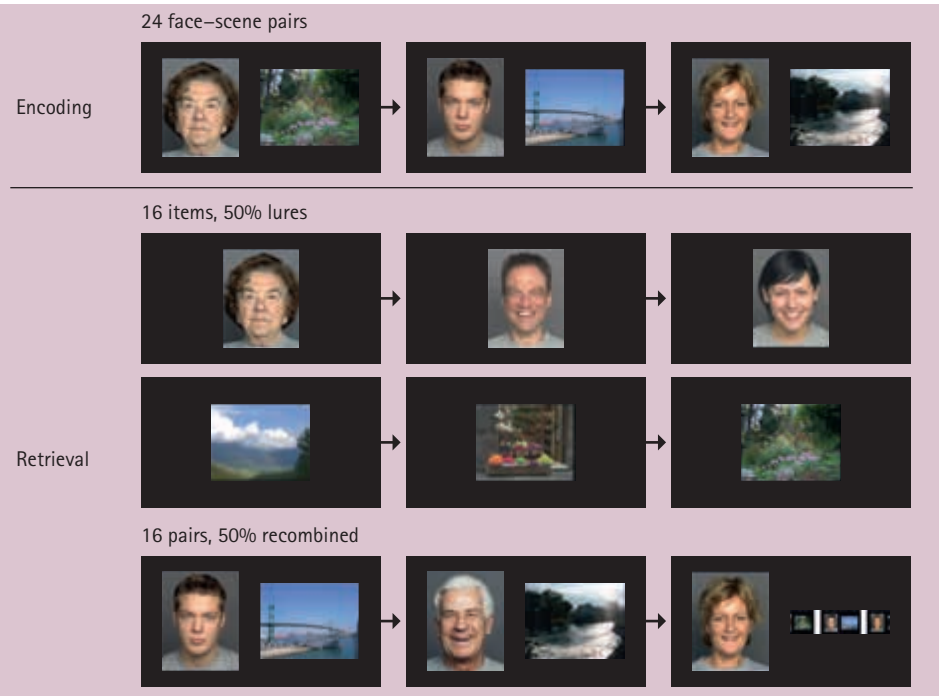

Figure 1. Experimental design and exemplar trials from the item-associative memory task. During encoding, 24 face–scene picture pairs were presented for 4 seconds each. Participants were instructed to memorize both the single pictures and the combinations. At retrieval, three self-paced recognition tasks were administered. In the item memory tasks, subjects saw 16 single pictures; half of the pictures had been studied and the other half served as novel lures. In the associative memory task, subjects saw 16 face–scene pairs. All stimuli had been studied, but half of the pairs were intact and the other half were recombined. Participants were told to indicate whether they had studied a particular item or item pair by pressing the buttons "yes" or "no" on a computer keyboard (adapted from Becker et al., 2015).

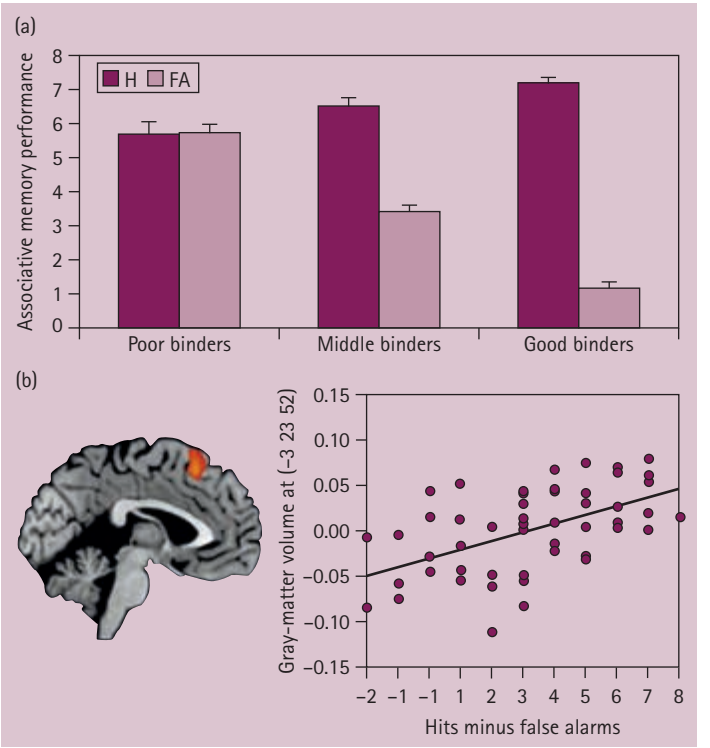

Figure 2. (a) Hit (H) and false-alarm (FA) rates in the associative memory task across performance groups (poor binders, middle binders, good binders). Error bars represent standard errors around the means. (b) Gray-matter volume correlates of associative memory performance in left dorsolateral prefrontal cortex (BA 8). With increasing hit minus false-alarm rates, gray-matter volume at brain coordinates –3 23 52 increases linearly. BA = Brodmann area (adapted from Becker et al., 2015).

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between associative memory functioning and successful aging? Are older adults with good associative memory performance more similar to younger adults regarding their performance and brain structure/function than older adults with clear associative deficits?

Most of the group's work has been conducted using SNAC-K, an existing large-scale population-based data set that was established at the Aging Research Center, Karolinska Institutet, Stockholm, Sweden (Laukka et al., 2013). A newly established cohort within SNAC-K is of special importance for the group. It consists of 550 60-year-old adults who performed a memory task that allows the separation of associative memory from item memory performance (see Figure 1; Old & Naveh-Benjamin, 2008). In addition, the data set includes (a) data from an extensive cognitive test battery; (b) a large range of demographic, social, and health information; (c) genotyping of 103 specific single nucleotide polymorphisms (SNPs) related to cognition, vascular disease, longevity, and dementia; and (d) magnetic resonance imaging (MRI) data for a subset of participants.

Structural Brain Correlates of Associative Memory in Older Adults

Little is known about how volumetric differences in the medial temporal lobe (MTL) and prefrontal cortex (PFC) might contribute to individual differences in associative memory. We investigated regional gray-matter volumes related to individual differences in associative memory in the aforementioned SNAC-K subsample of healthy older adults (n = 54; Becker et al., 2015). To differentiate item memory from associative memory, participants intentionally learned face–scene picture pairs before performing a recognition task that included single faces, scenes, and face–scene pairs (see Figure 1). Gray-matter volumes were analyzed using voxel-based morphometry region-of-interest (ROI) analyses. To examine volumetric differences specifically for associative memory, item memory was controlled for in the analyses. Behavioral results revealed large variability in associative memory that mainly originated from differences in false-alarm rates (see Figure 2a). Moreover, associative memory was independent of the individuals' ability to remember single items. Older adults with better associative memory showed larger gray-matter volumes primarily in regions of the left and right lateral PFC (see Figure 2b). These findings provide evidence for the importance of PFC in intentional learning of associations, likely because of its involvement in organizational and strategic processes that distinguish older adults with good, from those with poor, associative memory.

Dopamine Receptor Genes and Associative Memory in Old Age

In another study on the SNAC-K sample, we investigated to what extent associative memory deficits in old age may be due to disadvantageous genetic predispositions. Animal and human data suggest that dopaminergic modulation may be particularly relevant for associative binding (Li, Naveh-Benjamin, &

Lindenberger, 2005; Papenberg et al., 2017). In this case, we investigated the influence of dopamine (DA) receptor genes on item and associative memory in 525 participants using the same face–scene recognition task as described above (see Figure 1). The effects of SNPs of DA receptor genes D1 (DRD1; rs4532), D2 (DRD2/ANKK1/Taq1A; rs1800497), and D3 (DRD3/Ser9Gly; rs6280) were examined and combined into a single genetic score. Individuals carrying more beneficial alleles, likely associated with greater DA receptor efficacy, performed better on associative memory than older adults with less beneficial genotypes (see Figure 3a). There were no effects of these gene variants on item memory or other cognitive measures, such as short-term memory, executive functioning, fluency, or perceptual speed, indicating a selective association between DA genes and associative memory. By contrast, genetic risk for Alzheimer's disease (AD) was associated with lower item and associative memory, indicating adverse effects of the APOE ε4 gene, which encodes the protein apolipoprotein E, and of a genetic risk score for AD (PICALM, BIN1, CLU) on episodic memory in general (see Figures 3b and 3c). These results confirm that DA may be particularly important for associative memory and that AD-related genetic variations may also influence overall episodic memory in older adults without dementia.

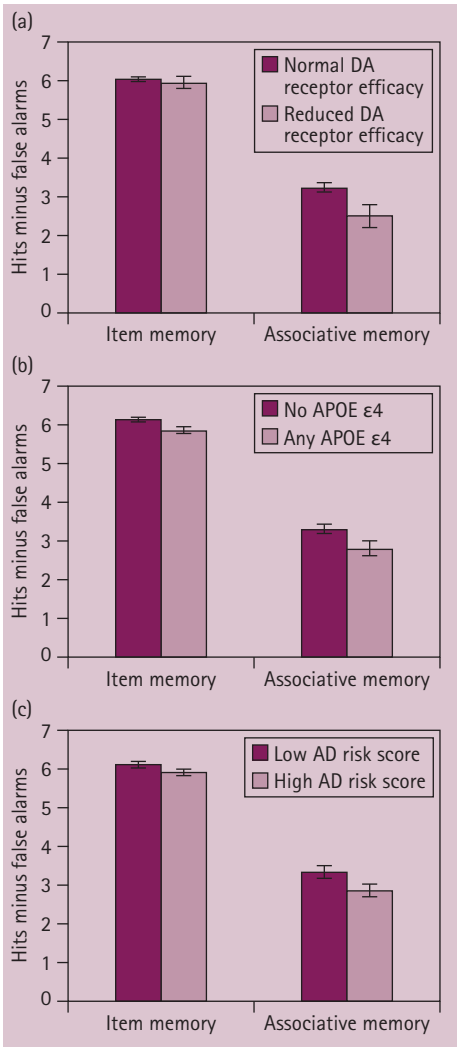

Figure 3. Item and associative memory performance for (a) carriers of genetic predispositions for normal and reduced dopamine (DA) receptor efficacy, (b) noncarriers and carriers of the APOE ε4 allele, and (c) persons with a low and high risk score for Alzheimer's disease (AD) (adapted from Papenberg et al., 2017).

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Papenberg, G., **Becker, N.,** Ferencz, B., Naveh-Benjamin, M., Laukka, E. J., Bäckman, L., & **Brehmer, Y.** (2017). Dopamine receptor genes modulate associative memory in old age. *Journal of Cognitive Neuroscience, 29,* 245–253. doi:10.1162/jocn_a_01048

The Role of Encoding Instructions

Evidence from neuroimaging studies suggests a critical role of the hippocampus and inferior frontal gyrus in the encoding of associations versus items. The influence of study-specific factors such as task instruction on neural substrates of associative memory has not yet been investigated. In this study of younger adults ($n = 51$; $M_{age} = 25$ years), we investigated similarities and differences in functional brain correlates for associative and item memory as a function of encoding instruction (Becker, Kalpouzos, Persson, Laukka, & Brehmer, 2017). Participants received either incidental encoding instructions (being asked to judge the animacy of a visually presented item) or intentional instructions (being asked to memorize it), while functional MRI was employed during the encoding of associations (object combinations) and items (single objects). In a subsequent recognition task, memory performance of the participants who received intentional encoding instructions was higher than that of those receiving incidental instructions. Participants remembered more items than associations, regardless of instruction type. Greater brain activation in the left anterior hippocampus was observed for intentionally compared to incidentally encoded associations, although activity in this

Key Reference

Becker, N., Kalpouzos, G., Persson, J., Laukka, E. J., & **Brehmer, Y.** (2017). Differential effects of encoding instructions on brain activity patterns of item and associative memory. *Journal of Cognitive Neuroscience, 29,* 545–559. doi:10.1162/jocn_a_01062

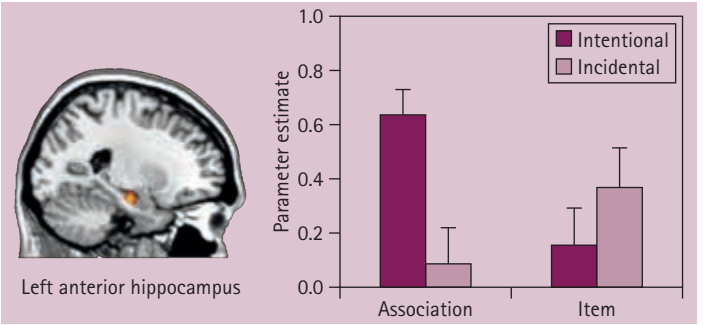

Figure 4. Region in the left anterior hippocampus showing a significant task-by-instruction interaction indicating the role of the left anterior hippocampus when intentionally encoding associations, but not when incidentally encoding associations or encoding single items under either instruction type. Mean subject-specific weights of voxels within this region are plotted separately for encoding groups and experimental conditions. Error bars represent standard errors around the means (adapted from Becker, Kalpouzos, Persson, Laukka, & Brehmer, 2017).

region was not modulated by instruction type for encoded items. Further, greater activity in the left anterior hippocampus and left inferior frontal gyrus was observed during intentional associative compared to item encoding. The same regions were related to subsequent memory of intentionally encoded associations and were thus task-relevant (see Figure 4).

Similarly, connectivity of the anterior hippocampus to the right superior temporal lobe and inferior frontal gyrus was uniquely linked to subsequent memory of intentionally encoded associations. Our study demonstrates differential involvement of the anterior hippocampus in intentional relative to incidental associative encoding. This finding likely means that the intent to remember triggers a specific binding process accomplished by this region.

Outlook

In future studies, we will investigate age-related differences in structural correlates of associative memory functioning in younger and older adults as well as cognitive, social, health, and lifestyle factors contributing to individual differences in associative binding. The investigation of individual differences in associative memory in older adults is likely to provide useful information for the development of individualized memory training programs that would allow people to make better use of their latent potential, as manifested in larger training gains and transfer effects (e.g., Brehmer, Kalpouzos, Wenger, & Lövdén, 2014).

Publications 2014–2016

(last update: Spring 2017)

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