

Temporal Dynamics of Brain Activity in Human Memory Processes

Stephen J. Guastello,^{1,4} Kristy A. Nielson,^{1,2} and Thomas J. Ross³

We propose a line of study by which Functional Magnetic Resonance Imaging (fMRI) can be used together with nonlinear dynamics concepts as a medium for the study of brain organization. The concentration is on (a) the complex behavior of elementary neural circuits, and how they interact over brief spans of time to produce cognition and memory; and (b) the change in circuit patterns associated with aging. The method of orbital decomposition appears to be ideally suited for these objectives and for determining how they integrate into hierarchical processes. The adapted procedure begins with a 3-D fMRI matrix of metabolic activity. Recurring patterns within a matrix row are identified and matched across rows and across depth slices. These hierarchical patterns are then compared over time for further recurrences. The computational procedure identifies the optimal pattern length over time, the patterns, and the largest Lyapunov for the system of patterns. Computations are assisted by statistical tests for the extent to which the isolated patterns represent the underlying data.

KEY WORDS: fMRI; neural circuit; memory; topological entropy; Lyapunov exponent; symbolic dynamics.

MESO-LEVEL NEURODYNAMICS AND COGNITION

Most of the early landmarks in the understanding of brain physiology were derived from a simple but general hypothesis that localized functions are associated with specific brain regions. The discoveries of Broca's area and

¹Department of Psychology, Marquette University, Milwaukee, Wisconsin.

²Foley Center for Aging and Development, Medical College of Wisconsin, Wisconsin.

³Department of Psychiatry, Medical College of Wisconsin, Wisconsin.

⁴Correspondence should be directed to Stephen J. Guastello, PhD, Department of Psychology, Marquette University, P.O. Box 1881, Milwaukee, Wisconsin 53201-1881.

the sensory and motor cortices are examples that inevitably reinforced that line of thinking. Other major discoveries have emanated from a microlevel focus on the synaptic organization of the brain.

More contemporary research, however, has shifted the focus to meso-levels of brain organization. The visual system is now understood as containing many possible components which act in combination to produce a particular perceptual result (Grigsby & Stevens, 2000). Similarly, there is reason to believe that memory is a distributed process that involves many groupings of neurons that are relatively small, and that the temporal patterns of neuron firing contain a substantial amount of information about memory storage processing (Freeman, 2000; Grigsby & Stevens, 2000; Kohonen, 1989). Working from the micro end of hierarchical organization, patterns of neuron firing are studied productively as neural networks (see Vickers & Lee, 1998 for review). The temporal patterns of neuronal activation are chaotic over time and the partial result of the combination of simple activation and inhibition responses of neurons in a cluster or pathway (Freeman, 2000; Kohonen, 1989). Furthermore, neuronal activation patterns differ for novel stimuli compared to familiar stimuli. The formation of activation patterns for familiar stimuli amounts to the formation of an *attractor* in the nonlinear dynamics sense. Attractor structures are then thought to remain stable, or shift, in the course of a lifespan.

The temporal dynamics of memory experiments can be analyzed for two broad classes of information. Intertrial analyses would indicate whether and how the response to one experimental trial would impact on the subsequent responses. While intertrial response times have been traditionally regarded as random or probabilistic processes, dynamical analyses indicates that is not the case, and that modicum of structure and long-term patterning is evident (Clayton & Frey, 1996, 1997). On the other hand, the meaning of those patterns is yet to be revealed. Intra-trial analyses of memory experiment data would provide information on the cue encoding, retrieval, and decision processes.

FMRI AND MEMORY

FMRI technology is capable of detecting localized event-related changes in MR signal over time. Its principal advantages over other non-invasive methods are its excellent spatial and temporal resolution and, as no isotopes are required, a virtually unlimited number of scanning sessions can be performed on a given subject, making within-subject designs feasible. FMRI has the ability to detect increases in cerebral blood volume, flow (Kwong, Belliveau, & Chesler, 1992), and oxygenation (Bandettini, Wong, Hinks, &

Tikofsky, 1992; Kwong et al., 1992; Ogawa, Lee, Kay, & Tank, 1992) that locally occur in association with increased neuronal activity. A widely used fMRI method for following human brain activity is based upon blood oxygenation level dependent contrast (Ogawa, Lee, Nayak, & Glynn, 1990).

fMRI has several inherent properties that enhance its utility for functional brain mapping. The relatively small size of fMRI voxels (typically 2–4 mm) results in favorable image quality and spatial localization characteristics. In addition, functional data can be registered with very high resolution standard MRI images acquired during the same scan session, giving the ability to associate functional loci with specific anatomic landmarks. Third, a large number of activation procedures can be performed in each subject during a single session, enabling improved signal-to-noise ratios, exploration of a wider variety of different functional systems in a given individual, and virtual elimination of order effects in the experimental design.

Currently, the prevalent uses of neuroimaging in neuropsychology have been centered on localization and show, for instance that certain regions, such as the hippocampus and the prefrontal cortex, are simply involved in memory (e.g., Abdullev & Posner, 1997; Gabrieli et al., 1996; LeBar & Phelps, 1998). Medial temporal lobe damage, and specifically damage to the hippocampus and adjacent structures, has been shown to result in severe anterograde amnesia and lesser degrees of retrograde amnesia (e.g., Mishkin, 1978; Scoville & Milner, 1957; Zola-Morgan, Squire, & Amaral, 1986). Other regions, such as prefrontal cortex are also important for memory functions, especially in episodic and “working” memory tasks (e.g., Goldman-Rakic, 1990; McIntosh, Grady, Haxby, Ungerleider, & Horwitz, 1996). Neuroimaging studies using a variety of techniques support these findings. For example, medial temporal lobe and hippocampal activation occurs during encoding of visuospatial stimuli (Haxby et al., 1996; Tulving, Markovitsch, Craik, Habib, & Houle, 1996), as well as during retrieval of verbal (Nyberg, McIntosh, Houle, Nilsson, & Tulving, 1996; Schacter, Alpert, Savage, Rausch, & Albert, 1996) and nonverbal stimuli (Schacter et al., 1995). The prefrontal cortex shows asymmetric activation during memory processing such that the left is active during encoding and the right during retrieval (Tulving, Kapur, Craik, Moscovitch, & Houle, 1994; Nyberg, Carbeza & Tulving, 1996). Finally, other regions in temporal and parietal cortex have also been shown to activate during either encoding or retrieval processes (Haxby et al., 1996). The foregoing work does not show, however, how and when those regions interact to produce a memory or the successful retrieval of a memory.

Relatively few functional neuroimaging studies have been published examining cognition in aging. However, most demonstrate differences between older and young subjects in the functional areas or extent of activation,

suggesting more diffuse activation in aging (Grady, 1998). Neuroimaging studies of working memory in aging have also begun to surface. Using PET, Jonides et al. (1998) reported greater bilateral frontal activation in aged than young subjects in both verbal and spatial working memory tasks. It has been suggested that the differences in activation exhibited in older subjects are evidence of recruitment of additional processing areas (Cabeza, McIntosh, Tulving, Nyberg, & Grady, 1997; Jonides, Smith & Marsheutz, 1998) or reorganization of processing (Grady, 1998). Recently, we have done studies of cognitive processes in older adults, which support the idea that older adults must recruit additional processing areas to perform at a comparable level to young adults (Nielson, Langenecker, & Garavan, in press; Nielson, Garavan, Langenecker, Stein, & Rao, 2001).

What is as yet unclear is how and when the multiple brain regions involved in memory processes interact. Understanding how this occurs may be critical to understanding both memory processes per se and how they change during aging. That is, their relative interactions may be more important than simply the magnitude of regionally specific activation. We know this is true to some degree by examining the processes by which some events are made more memorable than are others. Specifically, while medial temporal lobe structures are important for memory formation, there are some structures and responses for which changes in activation leads to enhancement or impairment of memory consolidation (McGaugh, 2000). Emotion and arousal, mediated in part by amygdala activity and systemic catecholamine levels, are two such factors that influence memory (McGaugh, 2000; Nielson, Czech, & Laubmeier, 1999; Nielson & Jensen, 1994; Nielson, Radtke, & Jensen, 1996). These factors are ever present but also vary in magnitude over time and with internal conditions, thereby affecting the strength of memories and our ability to retrieve them. Another factor, inhibition, the ability to suppress irrelevant or competing stimuli, is also critical to memory formation and retrieval, and changes with age. Indeed it has been proposed that inhibitory decline is responsible for age-related memory changes (Hasher & Zacks, 1988). As such, evaluation of the dynamical systems involved in the larger process of "memory" will improve our understanding of memory itself, and the sources of change and rehabilitation during aging.

GO/NO-GO MEMORY TASK

We have developed a Go/No-go task that exploits the temporal (and cognitive) specificity of event-related fMRI to identify the neuroanatomical bases of inhibition (Garavan, Ross, & Stein, 1999). Subjects were presented

with a stream of letters presented serially every 500 msec with no inter-stimulus interval. They made a button response whenever certain target letters (X or Y) were presented. An additional alternation rule stipulated that the target had to be different than the preceding target (e. g., X–Y). Consequently, subjects had to occasionally inhibit responding to a target if it was identical to the preceding target (e.g., X–X). These nonresponse targets (lures) were presented on average every 20 seconds and valid targets every 3.5 seconds. A minimum of 15 seconds (30 letters) separated consecutive lures. Prepotency to respond to the targets was established by prior training in which no lures were presented, by including six times more valid targets than lures during the scanning session, and through instructions that stressed fast responding. Subjects completed four runs with 250 letters per run. In total there were 150 valid targets and 25 lures.

All data processing was conducted with the software package AFNI v2.2 (Cox, 1996). In-plane motion correction and edge detection algorithms were applied first. Functional images were time-locked to the lures and averaged to obtain a mean signal response for each voxel. These time-series averages were modeled with a gamma-variate function using a nonlinear regression (NLR) optimization procedure (Ward et al., 1992), believed to effectively model the hemodynamic response (Cohen, 1997). The exponential parameters of the gamma-variate function were constrained to a range similar to previously published estimates (Cohen, 1997), the onset times were constrained to occur within 4 seconds of the lure event, and the magnitude parameter of the model was free to vary. The NLR procedure thus arrived at the best-fitting function for each voxel time-series whilst retaining a hemodynamic waveform. Area under the curve for each voxel was expressed as a percentage of area under the baseline. The percentage area-under-the-curve (%AUC) maps were converted to a standard stereotaxic coordinate system (Talairach & Tournoux, 1998), and spatially blurred using a 4.2 mm full-width-at-half-maximum isotropic Gaussian filter.

A one-sample t-test (against H_0) was performed voxel-by-voxel on the %AUC measure separately for the subjects in each group, with a cluster analysis to preserve only clusters of contiguous non-zero voxels $\geq 100\mu\text{l}$. A false-positive statistical threshold level was established with an identical analysis sequence but with randomly selected time-series averaging points. The time-series images were time-locked and averaged as above, preserving any auto-correlation and drift trends in the data. A threshold ($p = .0001$) served as a false-positive cut-off for the real data.

Previous research showed predominantly right prefrontal and parietal activation during this task in young adults (Garavan, et al., 1999). The current results show similarities and differences when comparing young and older groups. The coronal view of Fig. 1 shows that in the right hemisphere

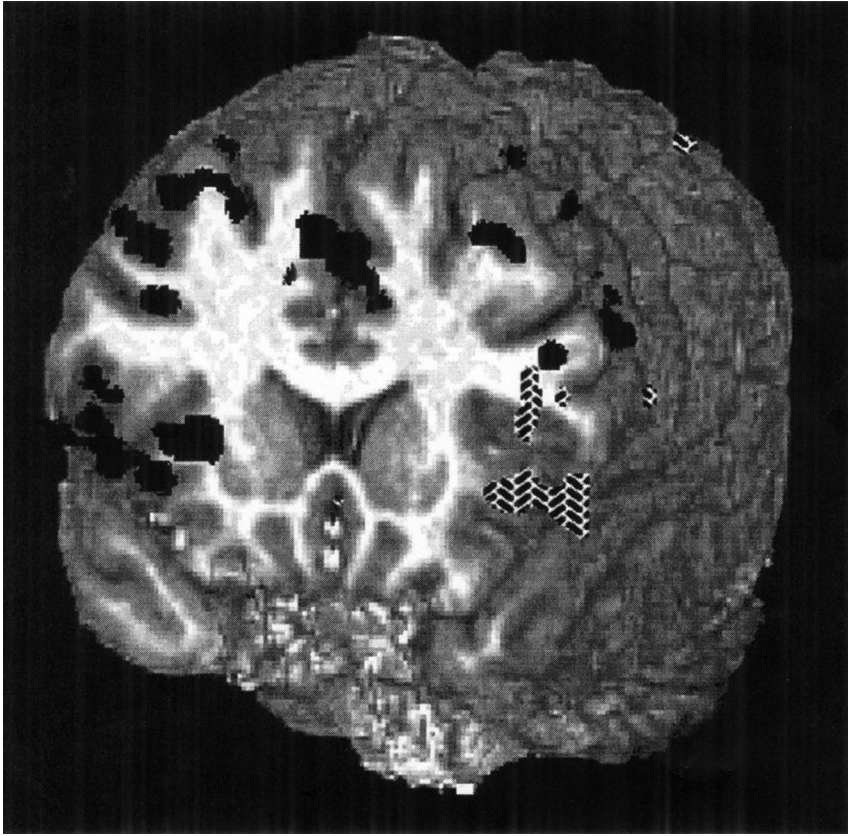


Fig. 1. Go/No-go task. Internal black areas: young and old subjects had equivalent, significant activation; herringbone areas: old subjects showed significantly greater activation than young subjects (Nielson et al., 1999).

prefrontal areas (on the left lower side of the picture) activation for the younger and older groups are equal (i.e., this area is needed for the task); on the left homologue, older subjects need to “recruit” more brain to perform equally. Note that these are maps for successfully inhibited trials for all subjects; no error trials are included, so performance is equal across groups. The center (right hemisphere) and right (left hemisphere) views are opposite sides in sagittal view. This additional frontal recruitment may reflect less specialized functioning in elderly subjects, as Cabeza et al. (1997) and Jonides et al., (1998) have reported for memory tasks. However, the reason and basis for this change in specialization is all but unstudied, but could be revealed through dynamical systems analysis.

ORBITAL DECOMPOSITION

The symbolic dynamics procedure requires three calculations in parallel: Shannon entropy (H_S), topological entropy (H_T), and a likelihood χ^2 test for strings of responses of varying length C . The calculations provide measures of dimensional complexity, the determination of an optimum behavior string length, a set of behavior strings with associated probabilities, and a chi-square test that provides a measure of fitness for the string structures (Guastello, 2000; Guastello, Hyde & Odak, 1998).

The calculation of topological entropy (H_T) is based on strings, or hypothetical orbits, of length C . C takes on a small range of integer values beginning with 1. For $C = 1$, a transition matrix, \mathbf{M}^C is created, which is square, and $r \times r$ in size. Each cell entry is binary, and indicates whether a particular behavior category is followed in time by any other behavior category. Its diagonal entries indicate whether an outcome is followed by itself in a consecutive period of time. Topological entropy is a function of the trace of \mathbf{M}^C :

$$H_T = \lim_{C \rightarrow \infty} (1/C) \log_2 \text{tr}(\mathbf{M}^C) \tag{1}$$

As the string length goes to infinity, H_T approaches the base-2 logarithm of the maximum Lyapunov exponent, which is, in turn, the largest eigenvalue of \mathbf{M}^C . Dimensionality is, therefore,

$$D_L = e^{H_T}. \tag{2}$$

The construction of \mathbf{M}^C is repeated for all $C > 1$, and Eqs. 2, and 3 are calculated for each. For $C = 2$, one axis of \mathbf{M}^C represents all possible pairs of categories, although some possible combinations might not actually appear in the data if their combinatorial probability is too low.

The calculation of the χ^2 for goodness of fit, and it is carried out for each value of C used. The essential question posed by the test is whether the behavior strings observed in the data occur at rates different from chance, where chance is simply the combinatorial probability of each categorical element in the string. Optimal C is determined as the length of a string one step before the step at which H_T drops to 0.00. Having determined the optimal string length, it is possible to describe the contents and distribution of strings with that length; these were used as a basis of comparison with other conversations, along with the associated values of C , H_T and H_S . The array of strings identified at this stage could be analyzed for hierarchical dynamics using a repetition of the process just outlined.

H_T is an indicator of the amount of information produced by the underlying (neuronal) process. H_T decreases as C increases; it is the primary

indicator of the asymptotic limit of C . A comparison of the asymptotic H_T and C values across experimental conditions would indicate which neuronal processes are more complicated than others and how.

The original fMRI scans are $64 \times 64 \times 20$ voxel matrices containing continuously-valued entries. For the intended analyses, each fMRI cell will be calibrated in discrete units, based on z-score probabilities. Each cell entry would be a number ranging from 1–9 representing the degree and direction of metabolic activity, where 1 is an extreme positive, 9 is an extreme negative, and 5 is the nonsignificant region. The orbital decomposition analysis would treat each cell entry as a nominally coded (categorical) measurement. The actual matrix dimensions can be curtailed to those regions of the brain that were already found to be interesting, as shown in the fMRI scans obtained from experiments such as that depicted in Fig. 1. Figure 2 is an example of a prepared data matrix that was taken from an actual fMRI. *For purposes of a simple example, however*, an fMRI scan was recalibrated into larger areas so that the original area is blocked as an 8×8 matrix, where each cell represents an 8^2 voxel area.

5	5	2	1	1	2	2	1
5	2	3	3	2	2	1	1
1	1	2	2	3	2	2	1
2	2	3	5	5	5	5	3
5	8	8	9	9	9	9	5
5	8	9	9	9	9	9	0
5	8	9	9	9	9	9	5
5	0	8	8	8	7	0	5

Fig. 2. Sample matrix data entry for a single fMRI slice coded as 8^2 voxels.

For the intertrial data, a series of 4 scans can be used for each trial; they would represent the one-second time period immediately following the presentation of the stimuli. A *4-scan frame* should be taken for each stimulus. This set of frames will be separated as to whether the participant responded correctly (which was most of the time) or did not respond correctly. Next, in the case of set of correct responses, the frames from each sequential correct response can be stacked end to end in a continuous-appearing time series. For instance if there are 25 such stimuli, there would be a sequence of 100 matrices for orbital decomposition. Similarly, the frames from the incorrect responses can be stacked into a continuous-appearing time series and subjected to orbital decomposition.

Orbital decomposition will then be conducted on each participant's set of correct and incorrect responses. In other words, the set of 100 matrices will be pooled (stacked end-to-end) over the (approximately) 30 participants participating in an experimental condition. There will be four levels of hierarchical analysis. The first level concerns a row of a matrix. The sequence of 64 codes (*the 64 reduced to a smaller number representing interesting areas*) is analyzed for the frequency of its numerical combinations. Separate frequency distributions will be obtained for the first, second, third through eight rows of the matrix. These combinations will be less than the total number of rows. Each combination would be assigned a second-level letter code.

The second level of aggregation is the matrix slice level. We now have sets of 64 rows, each of which might contain a different sequence of row-codes. The 64-entry sequences of row codes will be analyzed for the frequency of the possible combinations. The resulting two-level sequences would be given a new set of letter codes, which would denote a matrix pattern. The third level of aggregation is over the 20 vertical slices (not shown in Fig. 2; again the 20 slices may be reduced to interesting areas).

The fourth level of aggregation is discerned through the orbital decomposition of the temporal sequences. We will, at this point, have matrix type codes and a series of matrices equal to 4 (frames per target stimulus) times the number of target stimuli. This series would then be analyzed using the computational procedure specified in Eqs. 1–2, along with the likelihood χ^2 and ϕ^2 coefficients. If a large number of patterns emerge, the temporal patterns would be labeled again and reanalyzed. At the present time, orbital decomposition has not been used often enough to offer a clear definition of “large” for this purpose. One likely pattern, however, would be that series of 4 matrices would be the optimal string length, corresponding to the 4 matrices of the frames surrounding the onset of a target stimulus. Those patterns would be coded again, therefore, and submitted to a further analysis through orbital decomposition.

The foregoing analyses would be conducted on data produced by each human participant in an experimental condition. The results of orbital decomposition for each participant would be compared for similarity, and the trends would be summarized, using relevant nonparametric statistics. The objective would be to determine whether different patterns were evident between people who were subjected to the same stimuli. Our expectation is that the similarities would be larger than the irregularities.

The difference between an intertrial analysis and an intra-trial analysis is a matter of degree. For the intra-trial analysis, the length of the frame would be extended as long as possible, although frames of equal length would be preserved. Comparisons between the results of intertrial and intra-trial patterns would show the immediate and longer-term unfolding of brain activity patterns. Intertrial analyses would indicate whether and how the response to one experimental trial would impact on the subsequent responses. Intra-trial analyses would provide information on the cue encoding, retrieval, and decision processes.

Once the patterns of matrix change (e.g., how data appearing in Fig. 2 change over time) have been identified, the particular patterns can be examined for their respective content. Feedback and feedforward loops can be discerned from the relative size of the subareas containing the extreme responses. The size of activity concentration give evidence of the feedback and feedforward activity (Kohonen, 1989). If a concentration is relatively large, then the positive feedback is dominant in the area. If a concentration is relatively small, then the negative feedback is dominant. Feedforward versus feedback would be discerned from the temporal patterns.

Recurring activity patterns that are identified from the orbital decomposition procedure represent limit cycle attractor structures, which could be hierarchically organized, according to Freeman (2000). The combination of recurring and non-recurring patterns creates a potential for adaptive responses, which change over the lifespan.

Ideally, the fMRI research program should include a variety of memory tasks. The orbital decomposition technique needs to be run on all data sets, and an efficient computer program needs to be written for orbital decomposition. The foregoing project for theory development assumed that we are working with dynamics that can be identified within the limits of the fMRI machine's cycle time. There may be other faster dynamics taking place that could elude current fMRI technology.

REFERENCES

- Abdullaev, Y. G., & Posner, M. I. (1997). Time course of activating brain areas in generating verbal associations. *Psychological Science*, 8, 56–59.

- Bandettini, P.A., Wong, E.C., Hinks, R.S., Tikofsky, R.S., Hyde, J.S. (1992). Time-course EPI of human brain function during task activation. *Magnetic Resonance in Medicine*, 25, 390–397.
- Cabeza, R., McIntosh, A., Tulving, E., Nyberg, L., & Grady, C. (1997). Age-related differences in effective neural connectivity during encoding and recall. *NeuroReport*, 8, 3479–3483.
- Clayton, K. & Frey, B. F. (1996). Inter- and intra-trial dynamics in memory and choice. In W. Sulis & A. Combs, (Eds.), *Nonlinear dynamics in human behavior* (pp. 90–106). Singapore: World Scientific.
- Clayton, K. & Frey, B. F. (1997). Studies in mental “noise.” *Nonlinear Dynamics, Psychology, and Life Sciences*, 1, 174–180.
- Cohen, M. (1997). Parametric analysis of fMRI signal using linear systems methods. *Neuro-image*, 6, 93–103.
- Cox, R. (1996). AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Computers in Biomedical Research*, 29, 162–173.
- Freeman, W. J. (2000). *Neurodynamics: An exploration of mesoscopic brain dynamics*. New York: Springer-Verlag.
- Gabrieli, J. D. E., Desmond, J. E., Demb, J. B., Wagner, A. D., Stone, M. V., Vaidya, C. J., & Glover, G. H. (1996). Functional magnetic resonance imaging of semantic memory processes in the frontal lobes. *Psychological Science*, 7, 278–283.
- Garavan, H., Ross, T.J., & Stein, E.A. (1999). Right hemispheric dominance of inhibitory control: an event-related fMRI study. *Proceedings of the National Academy of Sciences USA* 96, 8301–8306.
- Goldman-Rakic, P.S. (1990). Cellular and circuit basis of working memory in prefrontal cortex of nonhuman primates. In Uylings, H.B.M., Van Eden, C.G., De Bruin, J.P.C., Corner, M.A., & Feenstra, M.G.P. (Eds.), *Progress in Brain Research*, Vol. 85 (pp. 325–336). Amsterdam: Elsevier.
- Grady, C. (1998). Brain imaging and age-related changes in cognition. *Experimental Gerontology* 33, 661–673.
- Grigsby, J., & Stevens, D. (2000). *Neurodynamics of personality*. New York: Guilford Press.
- Guastello, S. J. (2000). Symbolic dynamic patterns of written exchange: Hierarchical structures in an electronic problem solving group. *Nonlinear Dynamics, Psychology, and Life Sciences*, 4, 169–187.
- Guastello, S. J., Hyde, T., & Odak, M. (1998). Symbolic dynamic patterns of verbal exchange in a creative problem solving group. *Nonlinear Dynamics, Psychology, and Life Sciences*, 2, 35–58.
- Hasher, L. & Zacks, R. (1988). Working memory, comprehension and aging: A review and a new view. *Psychology of Learning and Motivation*, 22, 193–225.
- Haxby, J.V., Ungerleider, L.G., Horwitz, B., Maisog, J.M., Rapoport, S.I., & Grady C.L. (1996). Storage and retrieval of new memories for faces in the intact human brain. *Proceedings of the National Academy of Sciences USA*, 93, 922–927.
- Jonides, J., Reuter-Lorenz, P. A., Smith, E. E., Miller, A. C., Marshuetz, C., Hartley, A. A., & Koeppel, R. A. (1998). Age-related changes in the neural mechanisms of spatial and verbal working memory. *Society for Neuroscience Abstracts*, 24, 1252.
- Jonides, J., Smith, E., Marshuetz, C., Koeppel, R., & Reuter-Lorenz, P. (1998). Inhibition in verbal working memory revealed by brain activation. *Proceedings of the National Academy of Sciences of the United States of America*, 95, 8410–8413.
- Kohonen, T. (1989). *Self-organization and associative memory*. (3rd ed). NY: Springer-Verlag.
- Kwong, K. K., Belliveau, J.W., & Chesler, D. A. Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proceedings of the National Academy of Science*, 89, 5675–5679.
- LaBar, K. S. & Phelps, E. A. (1998). Arousal-mediated consolidation: Role of the medial temporal lobe in humans. *Psychological Science*, 9, 490–493.
- McGaugh, J. L. (2000). Memory—A century of consolidation. *Science*, 287, 248–251.
- McIntosh, A.R., Grady, C.L., Haxby, J.V., Ungerleider, L.G., & Horwitz, B. (1996). Changes in limbic and prefrontal functional interactions in a working memory task for faces. *Cerebral Cortex*, 6, 571–584.

- Mishkin, M. (1978). Memory in monkeys severely impaired by combined but not by separate removal of amygdala and hippocampus. *Nature*, *273*, 297–298.
- Nielson, K. A., Czech, D. A., & Laubmeier, K. K. (1999). Chronic administration of propranolol impairs inhibitory avoidance retention in the mouse. *Neurobiology of Learning and Memory*, *71*, 248–257.
- Nielson, K. A., Garavan, H., Langenecker, S. L., Stein, E. A., & Rao, E. A. (2001). Event-related fMRI of inhibitory control reveals lateralized prefrontal activation differences between healthy young and older adults. *Brain and Cognition*, *47*(1–2), 169–172.
- Nielson, K. A., & Jensen, R.A. (1994). Beta-adrenergic receptor antagonist antihypertensive medications impair arousal-induced modulation of working memory in elderly humans. *Behavioral and Neural Biology*, *62*, 190–200.
- Nielson, K.A., Langenecker, S., & Garavan, H. (in press). Differences in the functional neuroanatomy of inhibitory control across the adult lifespan. *Psychology and Aging*, *17*.
- Nielson, K. A., Radtke, R.C., & Jensen, R.A. (1996). Arousal-induced modulation of memory storage processes in humans. *Neurobiology of Learning and Memory* *66*, 133–142.
- Nyberg, L., Cabeza, R., & Tulving, E. (1996). PET studies of encoding and retrieval: the HERA model. *Psychonomic Bulletin Review*, *3*, 135–148.
- Nyberg, L., McIntosh, A.R., Houle, S., Nilsson, L.-G., & Tulving, E. (1996). Activation of medial temporal structures during episodic memory retrieval. *Nature*, *380*, 715–717.
- Ogawa, S., Lee, T. M., Kay, A. R., & Tank, D.W. (1992). Magnetic resonance imaging with contrast dependent on blood oxygenation. *Proceedings of the National Academy of Science. (USA)*, *87*, 9868–9872.
- Ogawa, S., Lee, T. M., Nayak, A. S., & Glynn P. (1990). Oxygenation sensitive contrast in magnetic resonance imaging of rodent brain at high magnetic field. *Magnetic Resonance in Medicine*, *14*, 68–78.
- Schacter, D.L., Alpert, N.M., Savage, C.R., Rauch, S.L., & Albert, M.S. (1996). Conscious recollection and the human hippocampal formation: evidence from positron emission tomography. *Proceedings of the National Academy of Sciences USA*, *93*, 321–325.
- Schacter, D.L., Reiman, E., Uecker, A., Polster, M.R., Yun, L.S. & Cooper, L.A. (1995). Brain regions associated with retrieval of structurally coherent visual information. *Nature*, *376*, 587–590.
- Scoville, W.B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery, and Psychiatry*, *20*, 11–21.
- Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. New York: Thieme.
- Tulving, E., Kapur, S. Craik, F.I.M., Moscovitch, M. & Houle, S. (1994). Hemispheric encoding/retrieval asymmetry in episodic memory: positron emission tomography findings. *Proceedings of the National Academy of Sciences USA*, *91*, 2016–2020.
- Tulving, E., Markowitsch, H.J., Craik, F.I.M., Habib, R., & Houle, S. (1996). Novelty and familiarity activations in PET studies of memory encoding and retrieval. *Cerebral Cortex*, *6*, 71–79.
- Vickers, D., & Lee, M. D. (1998). Dynamic models of simple judgments: I: Properties of a self-regulating accumulator model. *Nonlinear Dynamics, Psychology, and Life Sciences*, *2*, 169–194.
- Ward, B., Garavan, H., Ross, T., Bloom, A., Cox, R., & Stein, E. (1992). Nonlinear regression for fMRI time series analysis. In *4th International Conference on Functional Mapping of the Human Brain*, Montreal Canada.
- Zola-Morgan, S., Squire, L.R., & Amaral, D. G. (1986). Human amnesia and the medial temporal region: Enduring memory impairment following a bilateral lesion limited to field CA1 of the hippocampus. *Journal of Neuroscience*, *6*, 2950–2967.