How do I remember things?
two main processes

How good are DMRs in old age & AlzD?

Working Memory – WM

7 ± 2 items, effortful, evanescent.

But is WM other processes? much, much more?

Daily Memory Records - DMRs

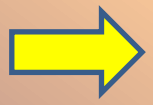
thousands of items, effortless, enduring, one-trial

Other Memory Terms: Declarative (incl. enduring EM, Autobiograph, Knowledge) all derived from DMRs

context is NOT repeated and context (generally) DISAPPEARS over time

Episodic Memory

initial EM
aka DMRs



Declarative Memory

including enduring EMs

see notes on dichotomy; SAMs retain ~ DMRs

LTM = long term memory, **STM** = short term

Annu Rev Psychol. 2015 January 3; 66: 115–142.

2015: now on CANVAS

THE COGNITIVE NEUROSCIENCE OF WORKING MEMORY

= WM ≈ *STM*

… or How the Brain Works!

Mark D'Esposito[1] and **Bradley R. Postle**[2]

Mark D'Esposito: despo@berkeley.edu; Bradley R. Postle: postle@wisc.edu

[1]Helen Wills Neuroscience Institute and Department of Psychology, University of California, Berkeley, Berkeley, CA 94720

[2]Department of Psychology and Psychiatry, University of Wisconsin-Madison, Madison, WI 53719

Abstract

highlights: "info not present", allocation, fMRI DATA

For over 50 years, psychologists and neuroscientists have recognized the importance of a "working memory" to coordinate processing when multiple goals are active, and to guide behavior with information that is not present in the immediate environment. In recent years, psychological theory and cognitive neuroscience data have converged on the idea that information is encoded into working memory via the allocation of attention to internal representations – be they semantic long-term memory (e.g., letters, digits, words), sensory, or motoric. Thus, information-based multivariate analyses of human functional MRI data typically find evidence for the temporary representation of stimuli in regions that also process this information in nonworking-memory contexts. The prefrontal cortex, on the other hand, exerts control over behavior by biasing the salience of mnemonic representations, and adjudicating among competing, context-dependent rules. The "control of the controller" emerges from a complex interplay between PFC and striatal circuits, and ascending dopaminergic neuromodulatory signals.

PFC:

🡐 decisions are WTA operations

This is an expanded scope of WM, *way beyond* e.g. remembering phone numbers!
and it smears into LTM, fuzzying up the LTM/STM distinction. ***Brief 2019 Essay below***

some essays have been incorporated into SNCD, 2021, but perhaps still convenient below

What was OLD has become NEW

Who is John Galt?...no...

Soon thereafter, Pribram and colleagues (1964) posited that the neural machinery supporting working memory may include the prefrontal cortex (PFC). They did so on the basis of the deficits that PFC lesions were known to produce on various tests that imposed a delay between the target stimulus and the subsequent target-related response (or, in the case of delayed alternation, between the execution of one action and the execution of a subsequent action that depended on the former).

The most enduring conceptualization of working memory, however, has been that of the multicomponent model, introduced in 1974 by experimental psychologists Alan Baddeley and Graham Hitch (1974). The model was developed to address two factors in the literature of the time. First, Baddeley and Hitch's assessment that contemporary models of short-term memory (STM) did not capture the fact that mental operations performed on information in conscious awareness can be carried out independent of interaction with, or influence on, long-term memory (LTM); for example, maintenance rehearsal had recently been shown not to enhance encoding into LTM. And second, their own work indicated that performance on each of two tasks under dual-task conditions could approach levels of performance under single-task conditions if the two engaged different domains of information, specifically verbal and visuospatial. Thus, the original version of their model called for two STM buffers (dubbed the "phonological loop" and the "visuospatial sketchpad," respectively) that could operate independently of each other and independently of LTM, although both under control of a separate system that they dubbed the "central executive" (Baddeley 1986).

from Mark and Brad, page 1

Who is Karl Pribram? rhetorical, see notes

PFC and WM: linkage derived from lesions
WM ≈ STM (short term memory)

Baddeley: WM is independent of LTM
WM does not (easily) transfer ➔LTM
Why not? **DQ:** What ***does yield*** transfer?

Badd. & Hitch: "2 independent stores"
- phonological loop
- visuospatial sketchpad
- under control of Central Executive
- superseded? not so fast . . .

BUT FIRST, an EXPERIMENT…

WM = working memory [***rehearsal*** does not → enduring EM (w/ any great efficacy; see notes)
WM ≈ STM (short-term memory): it's the same store, but WM implies manipulation by some accounts
LTM = long-term memory aka **declarative memory** / knowledge
LTM includes **EM** (episodic) and ABM (autobiograph.) and **KAs** (knowledge architectures)
LTM derived from **DMRs** - Daily Memory Records ~ Transient Episodic Memory (0 in PubMed)
ALL LTM is derived from our initial episodic/DMR store [**thoughts** are part of our DMR]

To understand the *breakdown of neural circuits* due to age and neuropathology, we first have to understand the *Neural Circuits!*

aside: outrageous embrace of patent stupidity: not good

WORKING MEMORY

(aka WM) **1950 - 2019**

Pribram's theories of **Holographic Memory Storage** (HMS) and a role for Gabor / Fourier Functions still lurk within the broader context of Conscious Experience, yet all that we really know about WM stems from our conscious experience of our working memory stores. Pribram was active until 2015, and had worked with renowned Memory Engram Researcher, Karl Lashley (1890-1958). Pribram argued that interference patterns in neocortical dendrites helped explain the "non-locality" of memory storage. ***Fast-forward 70 years and what have we accomplished?*** Suffice to say that I cannot unequivocally rule out HMS as a neural mechanism of WM. [but I did ask Adam Reeves (NU Psych Prof. Emeritus) about Gabor functions and V1 visual information processing: see notes]

more intro notes: WM enables adept actions to achieve multiple, syncopated goals; this fits with WM thesis in ***Rise of the Homo Sapiens*** (Coolidge and Wynn)
Disordered behavior (w/ age, injury; ADLs) is associated with WM deficits

p.s. play Hominids 101 at firstmaze.com

Central Executive **(multicomponent) model achieved** buffering and coordinating so p. 2

is to be able to maintain and successfully carry out multiple behavioral goals simultaneously. In 1986, Baddeley summarized it as "the temporary storage of information that is being processed in any of a range of cognitive tasks" (p. 34). The following year, Goldman-Rakic (1987) echoed these ideas in an influential synthesis of cognitive and neurobiological perspectives, stating that "the evolution of a capacity to guide behavior by [mnemonic] representation of stimuli rather than by the stimuli themselves introduces the possibility that concepts and plans can govern behavior"(p. 378) Thus, "the ability to guide behavior by representations of discriminative stimuli rather than by the discriminative stimuli themselves is a major achievement of evolution" (p. 378). What is captured in each of these seminal writings is that working memory underlies the successful execution of complex behavior, regardless of the cognitive domain or domains being engaged. When working memory fails, so too does the ability to carry out many activities of daily living. It

Patricia Goldman Rakic was seminal player in exploring memory states of PFC neurons. Her data show some ***mammals*** can hold a representation "in mind" and make decisions based upon ***stored*** representation (vs. live sensory input)

ExCrQ: which mammals? lots of monkey studies, but ***which other mammals***? UP notes below

consciousness, C. access and subconscious storage = huge tar baby

WM = regularly accessed consciously. DMR = never or almost never

Conscious Record Memory (Gioioso & O'Malley, 2009) changed to DMR to avoid C.

"**Multicomponent Model" of WM** = 14 hits in PubMed despite "40 year history"

Mark & Brad advocate "state based model" vs. "slots" model [*see notes*]

Any implications for breakdown of Exec. Functioning in normal aging or late-AlzD?

I said WM is stored in PFC but. . . it's complicated…

SYMBOLS, PERCEPTS and ATTENTION

Multi-Component Model **is just another name for Slots Model**

COGNITIVE MODELS OF WORKING MEMORY

p. 3

As we write this review, the multicomponent model of working memory is marking its fortieth anniversary, and from roughly 1985 through 2005—what one might consider the first 20 years of the cognitive neuroscience study of working memory—this was the dominant theoretical framework. More recently, however, what might be called state-based models have taken on increased prominence. As a class, these models assume that the allocation of attention to internal representations—whether semantic LTM (e.g., letters, digits, words), sensory, or motoric—underlies the short-term retention of information in working memory. These models conceptualize information being held in working memory as existing in one of several states of activation established by the allocation of attention. ???

Our brief review of state-based models is organized into two categories: activated LTM models and sensorimotor recruitment models. Although these two types of models have arisen within different literatures, the principal difference between them seems to be simply the class of stimuli for which each has been proposed. That is, activated LTM models have by and large been articulated for, and tested with, symbolic stimuli typically considered to be semantic (e.g., letters, words, digits). Sensorimotor recruitment models, however, have typically been invoked for classes of stimuli considered to be perceptual (e.g., visual colors and orientations, auditory pitches, tactile vibrational frequencies). Despite these surface-level differences, however, both of these classes of state-dependent models of working memory are grounded in the idea that the attentional selection of mental representations brings them into working memory and that the consequences of attentional prioritization explain such properties as capacity limitations, proactive interference from no-longer-relevant items, etc.

The Multicomponent Model

- entails storage "slots"
- 7 +/- 2 (possibly less)

State-Based Models of WM

- entails *allocation of attention*
- targets *internal representations*
- includes **symbolic**, *perceptual*
  letters, digits, words, places in LTM
  sensory stim: color, freq., locations
- **but why 7-item limit?**
  Lisman: 7 gamma on theta
  this paper: nada?

Sternberg Effect: reaction time increases with the number of items currently held in WM.
-an additional *intrusion* effect persists for 5 seconds after some items are "ruled out" ???

newest model: multiple "activated" items from LTM with smaller Focus of Attention (FoA)
FoA has 4 items (or chunks, can be complex), held in WM via top-down/PFC controls
p. 4 "activated LTM has no capacity limit" beyond interference from binding/other items

dmo: the older 7 +/-2 rule might subsume FoA story; further variants discussed might reflect a gradient of losses (decays) and interferences and be f(salience). imho.

ask me about faster T-pass purchases: also, the Sternberg Effect is, in a sense: mimicked by age (cognitive slowing)

Capacity Limits of Visual Working Memory

3 to 4 slots **p. 5**

A focus of intensive investigation for sensorimotor recruitment models has been the factors that explain capacity limitations. Much of this work has followed from Luck & Vogel's (1997) experiments with a change detection task in which a target array of colored squares (varying across trials from a single square to 10 or more) is presented for a few hundred milliseconds, followed by a brief (roughly 1-second) blank delay, followed by a probe array containing the same number of items but presenting one item in a different color on half of the trials (a yes/no recognition procedure). By applying a simple algebraic formula to the results, investigators estimated that subjects had a visual STM capacity of between three and four items. They found that an individual's capacity did not change with the number of features used to individuate objects, up through objects defined by conjunctions of four features. This observation led them to hypothesize that the capacity of visual STM is constrained by a finite number of hypothetical slots, each one capable of storing an object representation, regardless of the complexity of any single object (Vogel et al. 2001).

This slots model has been challenged from at least two perspectives and, at the time of this writing, the nature of visual STM capacity limits remains a topic of vigorous debate. One open question is that of the influence of object complexity—contrary to the findings of Vogel et al. (2001), others have found that visual STM capacity declines with increasing object complexity (e.g., Alvarez & Cavanagh 2004). A second challenge arises from the perspective that visual STM capacity may not depend on a finite number of slots but instead on a single attentional resource. Evidence for this latter view is marshaled when the procedure for testing visual STM is changed from recognition to recall. This procedural change allows researchers to estimate the precision of a mnemonic representation by measuring the error in the recall response. With STM for the orientation of one or more line segments, for example, the average error in recalling the orientation of the probed stimulus is larger when subjects are remembering several stimuli simultaneously, in comparison to when they are remembering just one stimulus (Bays & Husain 2008). That is, mnemonic precision (the inverse of recall error) declines monotonically as a function of memory set size, an outcome that one would expect if STM were supported by a limited resource that must be apportioned ever more thinly as the number of items in the memory set increases. Slots models have been modified to allow for variable representational precision within a slot, but one

"the functions we label as attention, intention and retention may be treated identically in the brain" p. 7. VALID?

How bad is it if we cannot even agree if WM holds 3 or 9 items?

Sensory or Sensorimotor Recruitment mechanisms

attention is placed on processed sensory input e.g. color, orientation, frequency, spatial layout **but** motor ***intentions*** and sensory WM are coupled-you need a "task" to test for WM contents and ongoing motor tasks disrupt sensory WM

Visual WM Capacity

100 msec presentation of colored blocks w/ subsequent recog. test ➔ WM store of 4 items. capacity NOT affected by complexity of items

***my old view*:** seemed to better fit with slots models

4 slots, independent of item complexity

vs. at left: "single attentional resource"

Also, ***recall*** is totally different from ***recognition***!

Has the question of why 4 (or 7) but not 2 or 13 been materially addressed in this paper?

Nice Reply from Mark: "shrug" & forward; **but** the "thinly apportioned resource" lacks merit, imho.

Bottom Line: the literature does not seem to have a clue re: disparity btw WM and DMR store size, beyond Lisman's γ-on-θ.

email exchange:

The Mark and Brad Show

On Mar 31, 2018, at 4:30 PM, O'Malley, Donald <d.omalley@northeastern.edu> wrote:

Hi Dr. D'Esposito,

I am using your 2015 Working Memory review (in Ann. Rev. Psych) in my Systems Neurobiology of Cognitive Decline course (60 students). It is a great paper and the links between working and long-term memory (LTM) quite intriguing.

.

I have been interested for some years in our Day-long Memory Records, from which all LTM is excerpted. What is most curious is that the DMR store holds perhaps thousands of items (for a day or so), while WM holds only 7 +/- 2 (or less). To my knowledge there is no compelling explanation for this dramatic difference, but I would welcome any thoughts/speculation/refs you might have on this question.

.

I had spoken with John Lisman (and also a bit with Howard Eichenbaum) on this topic and nothing definitive came out of these chats, as enjoyable as they were.

.

I greatly appreciate the care and detail you put into this nice review.

Best Regards, Don

You can write anyone, any time, for any reason:

when you're a savage, *the world* is your playground

From: Mark D'Esposito <despo@berkeley.edu>
Sent: Wednesday, April 11, 2018 5:39 PM
To: O'Malley, Donald
Cc: Charan Ranganath
Subject: Re: Working Memory query

Hi Don,

Sorry for the delay in getting back to you. Really tough question without an easy answer! The person that has the best work on the relationship between WM and LTM is Charan Ranganath at UC Davis. I've cc'ed him on this email, perhaps leading to some exchange between us. Charan, what's your thoughts?

Mark

2021 *update*: SCIP-working memory ≠ conscious WM stores because "language"/SNOPs. ck glossary

Let me tell you a story…about *slots* and MVPA and … fMRI decoding of WM stores

The Neural Plausibility of State-Based Accounts of Working Memory **p. 6**

State-based models of working memory have gained prominence in recent years because cognitive neuroscience research indicates that they accommodate neural data well. They have been particularly successful since investigators began to apply multivariate pattern analysis (MVPA) techniques to human functional neuroimaging data (these techniques have been summarized in many places; e.g., Lewis-Peacock & Postle 2012). To explore temporary activation of LTM, for example, Lewis-Peacock & Postle (2008) employed the following method. First, they scanned subjects with functional magnetic resonance imaging (fMRI) while the subjects made judgments that required them to access information from LTM: the likability of famous individuals; the desirability of visiting famous locations; the recency with which they had used a familiar object. Next, outside the scanner, they taught subjects arbitrary paired associations among items in the stimulus set. Finally, they scanned subjects a second time but while subjects performed delayed recognition of paired associates (i.e., see one item from the LTM memory set at the beginning of the trial and indicate whether the trial-ending probe was paired specifically with that item). These researchers found that multivariate pattern classifiers trained on data from the first scanning session, when subjects were accessing and thinking about information from LTM, could successfully decode the category of information that subjects were holding in working memory in the second scanning session. Such an outcome was possible only if the working memory task and the LTM task drew on the same neural representations. **MVPA was used to decode "second" scans, next slide**

In contrasts to "slots" models Mark and Brad advocate "state-based" models and touts an fMRI statistical approach: MVPA (see above). But MVPA seems to say little about ***Store Capacity*** or neuronal mechanisms of WM. Aside from this, article provides a wonderful review of WM & major concepts central to our cognitive capabilities relevant to decision making, orientation and more.

5 "Neural Mechanisms" that likely contribute to WM Operations

GREAT!

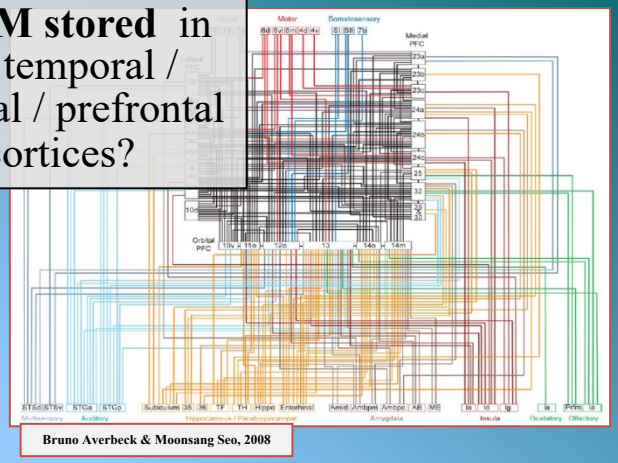
Persistent Neural Activity/PNA: neural oscillators like in spinal cord, AANs + ΔW_{ij}
Hierarchical Representations in PFC: specializations, gradients and GOLF rules!
Top-Down Signaling from PFC: e.g. visual search for a friend in a crowd
Long Range Connectivity: do long-range oscillations enable WM? unclear at present
Brainstem Neuromodulators: ACh, 5HT, NorEpi but mainly DA (dopamine)

THIS IS YOUR BRAIN!

Multi-Variate Madness

Your Path to Statistical Mayhem

Is WM stored in the temporal / parietal / prefrontal cortices?



The Mark and Brad MVPA Show:

MVPA = **Multi-Variate Pattern Analysis** - Herein:

- record fMRI **voxel activation patterns -- VAPs**
  [likability of famous people, desirable places, …]
- train the MVPA classifier on the VAP dataset
- rescan subjects and cue recall of earlier items
- MVPA can now decode VAPs, determine category

Does this approach have the *granularity* to tell us anything conclusive about the locus, mech or capacity of WM?

MVPA/Machine Learning: also applied to VAPs in paper on n. dediff. (used Ridge Regression). "The fidelity with which they can discriminate btw two cogn. conditions" reveals VAP distinctiveness (Abdulrahman, 2017).

HELP WANTED: prof. in need of statistical makeover; OK w/ Shannon Info Theory, Bayesian Inference & Poisson Process Neurons but dim. WORK STUDY / summer research opportunities.

Neural Plausibility Section: uses MVPA classifiers to decode fMRI signals and determine nature of stimulus. IMHO: one step above witchcraft. **However, they do report:** localization of fMRI signals e.g. motion in Area MT, visuospatial in parietal cortex, objects / faces /scenes in ventral occipitotemporal cortex. Does this go beyond confirming known neocortical specializations? no info is provided on nature of WM storage mechanisms.

METHOD likely relates to VBM in Cogn. Slowing slide set. Also see notes!

MVPA evidence dropped to zero, but item remained in WM (see notes):

re: the second retrocue. This finding has been replicated in an EEG study, thereby discounting the possibility that the unattended memory item may be transferred to an oscillatory code to which fMRI is insensitive (LaRocque et al. 2013). These findings, therefore, highlight the intriguing possibility that persistent neural activity may not be necessary to maintain representations held in working memory. Indeed, this possibility has also been explored by researchers working at other levels of investigation, including computational modeling, in vitro electrophysiology, and extracellular recordings in the behaving monkey. Computationally, information can likely be sustained over brief intervals via rapid shifts in synaptic weights. In such a scenario, the encoding of the sample stimulus would be accomplished via a transient reconfiguration of synaptic weights in the networks engaged in its initial processing. The contents of working memory could then be read out when the network was activated by a subsequent sweep of activation through this network (Itskov et al. 2011, Mongillo et al. 2008, Sugase-Miyamoto et al. 2008). Empirical evidence consistent with such a mechanism has been recorded from the ventral temporal cortex (Sugase-Miyamoto et al. 2008) and the PFC (Stokes et al. 2013) in monkeys. Which mechanism could support the short-term synaptic facilitation that would be needed to implement such a scheme? Theoretically, Mongillo et al. (2008) proposed residual presynaptic calcium levels. Empirically, Erickson et al. (2010) demonstrated that an associative short-term potentiation is GluR1-dependent in an in vitro preparation. Clearly, the relative contribution of persistent neural activity versus other mechanisms that do not rely on above-baseline activity to sustain working memory representations should be a high priority for future research.

Whether working memory representations are maintained via persistent neural activity, synaptic mechanisms, or some combination of both, these storage mechanisms are consistent with state-based models of working memory, which eliminate the need for currently relevant representations to be transferred to a limited number of dedicated, specialized buffers (D'Esposito 2007, Postle 2006). In neural terms, any population of neurons can serve as a buffer. Moreover, the ability to exhibit persistent neural activity, or a shift in synaptic weights, is likely a property of all neurons, from primary cortex to the multimodal association cortex. In sum, networks of neurons located anywhere in the brain can potentially store information that can be activated in the service of

Further Search for the WM "core"

CONVOLUTED TEXT --fMRI, EEG data suggest that active WM store is not evident as PNA (e.g. w/in population of neural oscillators) but might instead entail rapid changes in synaptic weights (Wij) that can be read out from ***memory cores*** (my term) as they are scanned. Fits with "slot' model?

Aside: **HOW MANY active neurons are required to trigger reliable EEG or fMRI signal? Or drive behavior?**

Mark and Brad: critique slots model mainly b/c of declining sensibility of having a few specialized, dedicated, buffers. Indeed, it makes sense that all neurons can do PNA and/or rapid ΔWij – whichever truly underlies WM.
transfer into slots: relevant to SNOPs-L

None of This: offers any compelling *rationale* for the size of WM store.

But a Context-Free WM store constrained by 7-item γ/θ does!
[new *March 2019* theory below]

Why only ONE "7-slot" at a time?

PFC: WM / Executive Functions (ExecFx) Rule the Neocortical Landscape

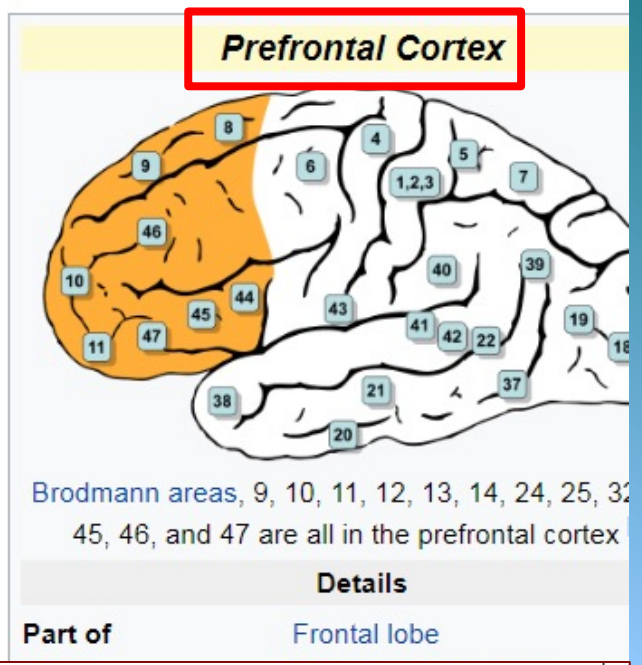
Anatomical details (see notes): granular layer 4 distinguishes PFC from motor cortices (M1, SMA)

In mammalian brain anatomy, the **prefrontal cortex** (**PFC**) is the cerebral cortex which covers the front part of the frontal lobe. The PFC contains Brodmann areas 8, 9, 10, 11, 12, 13, 14, 24, 25, 32, 44, 45, 46, and 47.[1]

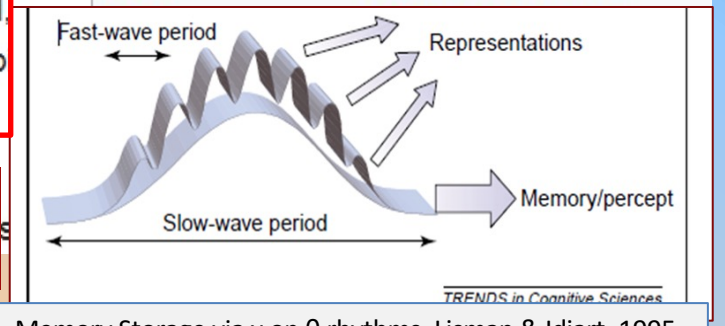
Many authors have indicated an integral link between a person's will to live, personality, and the functions of the prefrontal cortex.[2] This brain region has been implicated in planning complex cognitive behavior, personality expression, decision making, and moderating social behavior.[3] The basic activity of this brain region is considered to be orchestration of thoughts and actions in accordance with internal goals.[4]

The most typical psychological term for functions carried out by the prefrontal cortex area is executive function. Executive function relates to abilities to differentiate among conflicting thoughts, determine good and bad, better and best, same and different, future consequences of current activities, working toward a defined goal, prediction of outcomes, expectation based on actions, and social "control" (the ab to suppress urges that, if not suppressed, could lead to socially unacceptable outcomes).

Frontal cortex supports concrete r



↑↑ **GREAT summary of ExecFx. WM might use γ-on-θ ➔**



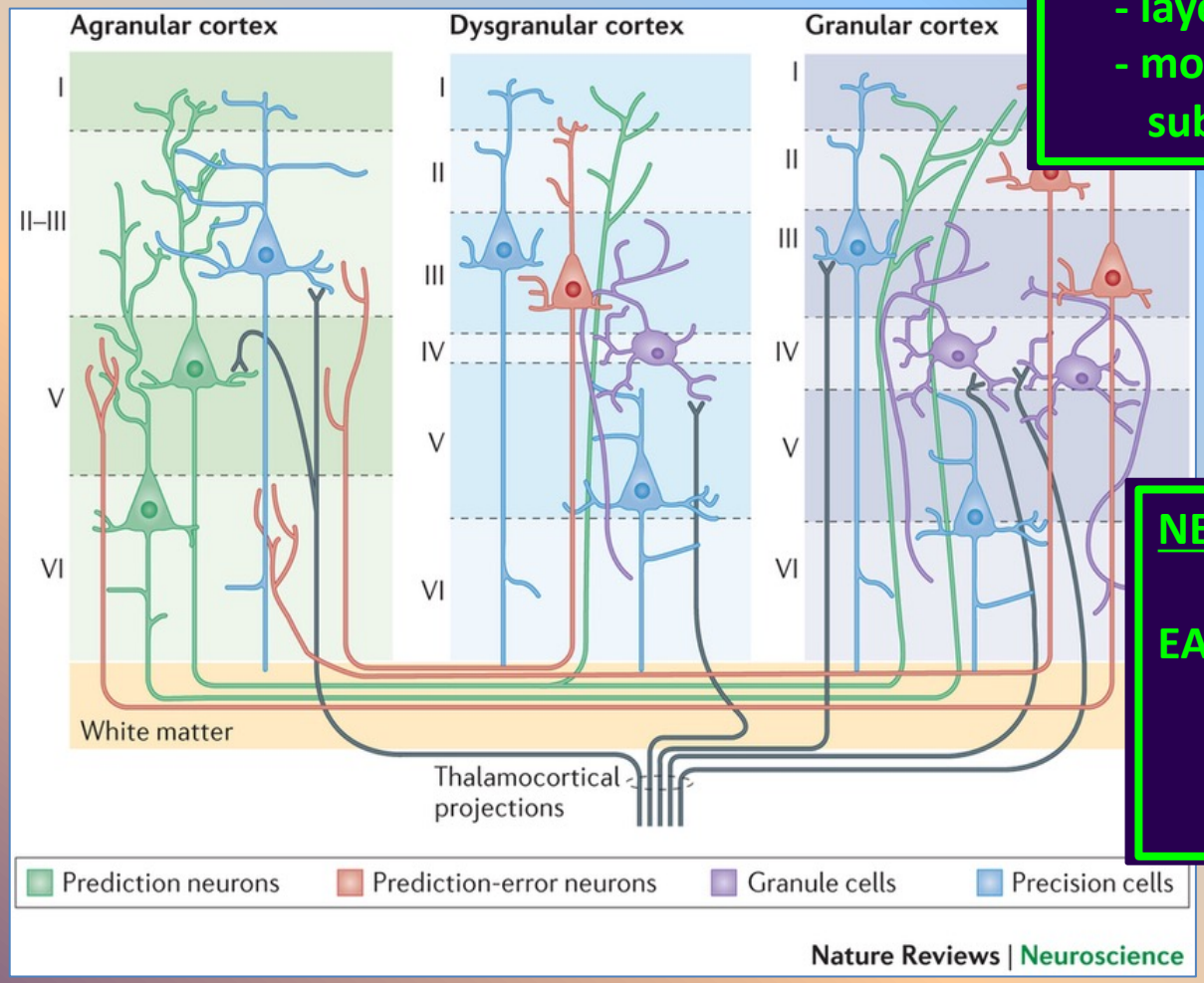
Memory Storage via γ on θ rhythms, Lisman & Idiart, 1995

PFC is the shining star of Mammalian Evolution: found within is a cognitive (primate) capacity that transcends ancient ERC-hippo circuits. PFC enables WM/ExecFx.

see below for Supplemental, Arcane and granular Notes on the History of PFC, orbitofrontal and granular cortex

PFC as “granular cortex”

PFC = “granular cortex”
w/ layer 4 granule cells
M1, SMAs = agranular cortex
- layer 4 is “missing”
- motor areas do not need subcortical inputs?



NEXT 6 SLIDES:
look kinda “the same” but
EACH addresses WM aspect
hierarchical, top-down
long-range connectivity
neuromodulators

source: G-Image, granular cortex hit: “Intracortical architecture and Intercortical connectivity” see notes on preceding slide: **history of PFC**

Hierarchical Representations in PFC

Studies examining population coding of lateral PFC delay activity have also found information about stimuli (Stokes et al. 2013), rules (Riggall & Postle 2012), and object categories (Meyers et al. 2008) throughout the delay period of working memory tasks. In fact, Rigotti and colleagues (2013) have recently demonstrated that neuronal activity within the PFC is tuned to mixtures of multiple task-related variables, suggesting that PFC representations exhibit high-dimensionality. That is, many dimensions are needed to characterize the distinct (multivariate) patterns that can be taken on by the sampled population of neurons across various experimental conditions. Moreover, this dimensionality is predictive of the animal's behavior: The population of PFC neurons exhibited a decrease in dimensionality on error trials. The authors of the very first reports of persistent activity within the PFC offered interpretations that are in line with many current models. For example, Fuster & Alexander (1971) wrote,

FUSTER, 1971:

The temporal pattern of firing frequency observed in prefrontal and thalamic units during cue and delay periods suggest [sic] the participation of these units in the acquisition and temporary storage of sensory information which are implicated in delay response performance. Their function, however, does not seem to be the neural coding of information contained in the test cues, at least according to a frequency code, for we have not found any unit showing differential reactions to the two positions of the reward. It is during the transition from cue to delay that apparently the greatest number of prefrontal units discharge at firing levels higher than the intertrial baseline…. We believe that the excitatory reactions of neurons in MD [nucleus medialis dorsalis] and granular frontal cortex during delayed response trials are specifically related to the focusing of attention by the animal on information that is being or has been placed in temporary memory storage for prospective utilization. (p. 654)

STM/WM: it is not simply a matter of holding an item in memory

PFC Notes: exhibits "coarse selectivity for items and features in WM" perhaps better encodes task rules, contingent motor responses and stimulus response mappings and categories, OR mixtures of variables ➔ *High D/dimensionality*

- *Fuster's 1971 single unit recordings* provide evidence not obtainable w/ EEG, fMRI, TMS.

Neocortical AAN's are High-D Devices:

- they can operate as neural oscillators w/ PNA and store any kind of pattern
- their dimensionality = # distinct inputs e.g. an object could have a color, size use, composition, softness, sheen, etc.
- neurons can have 1000, 10,000, 200k inputs; requires "Calculus of 10K-conn"

Fuster-1971 fits w/ **"flexible 7-slots model":** see notes: relates to Binding & Consciousness

Aging Brains SHOULD gradually lose *the capabilities ascribed to PFC…* based upon our course readings. How reliable is this depiction?

Top-Down Signaling (prequel comments)

These empirical findings are consistent with the original theoretical notions put forth by Fuster (1990), and Miller & Cohen (2001) that integrated representations of task contingencies and rules are maintained in the PFC, which is critical for the mediation of events separated in time but contingent on one another. This formulation of PFC function places less emphasis on a storage role and instead emphasizes its role in providing top-down control over all other brain regions where information is actually stored (D'Esposito et al. 2000, Petrides 2000, Smith & Jonides 1999). Thus, the sustained activity in the PFC does not reflect the storage of representations per se; it reflects the maintenance of high-level representations that provide top-down signals to guide the flow of activity across brain networks (see also Sreenivasan et al. (2014) and Postle (2014). This idea is explored further in the next section. However, we must consider first the nature of the information represented within the PFC about the functional organization of the PFC as a whole.

The PFC is a heterogeneous region covering a significant amount of territory in the brain. In this review we are focusing on the lateral PFC and not the medial or the orbital PFC regions, which likely have distinct yet complementary functions (Cummings 1993). Any understanding of the nature of the representations stored and maintained in the PFC that are necessary for goal-directed behavior must consider subregional differences in both cellular makeup and connectivity. Numerous neuropsychological, physiological, imaging studies support the general idea that as one moves rostral (anteriorly) in the frontal cortex, from the premotor cortex to the frontopolar cortex, the processing requirements of these regions for planning and selection of action are of higher order (Burgess et al. 2007, Christoff et al. 2003, Ramnani & Owen 2004). Koechlin and colleagues (2003) have put forth a hypothesis that the frontal cortex may be organized from rostral to caudal in a hierarchical fashion en route to action (see also Fuster 2004 for earlier formulation of a similar idea). Specifically, Koechlin & Summerfield (2007) propose a cascade model that predicts that competition among alternative action representations is resolved on the basis of mutual information with various contextual information, termed control signals. Using fMRI in healthy subjects, Koechlin and colleagues (2003) found support for their predictions by demonstrating that as contextual information required to select a response was more abstract and relevant over a longer temporal interval, fMRI activation progressed from caudal to more rostral regions of the frontal cortex.

p. 11

a LOT is going on in PFC

it **SAYS PFC DOES NOT STORE INFO** but instead exerts control over what stored information is used and accessed. The section on *Top-Down* processing begins on p. 14 of M&B, but THIS IS IT!

PFC DETAILS: focus here is on lateral PFC (not medial, orbital).

Local details of cell physiology and connectivity may be undetectable by fMRI, PET, EEG, MEG, TMS, etc.

Front to Back gradient of hierarchical controls is suggested, fits with fMRI data.

Are PFC neurons *more vulnerable* **to damage of neuronal aging or is there a** *better explanation* **of Exec Fx'g decline?**

e.g. greater *demand* **reveals vulnerability?**

Top-Down Signaling (2nd paragraph of section)

We have used fMRI and evoked-related potentials (ERP) in humans to investigate such top-down mechanisms (Gazzaley et al. 2005). In this study, during each trial of a working memory task participants observed sequences of two faces and two natural scenes presented in a randomized order. In separate blocks of trials, subjects were required to remember faces and ignore scenes, remember scenes and ignore faces, or passively view faces and scenes without attempting to remember them. Because each trial had equivalent bottom-up visual information (e.g., faces and scenes), we could directly determine if top-down signals were engaged. Moreover, the inclusion of a passive baseline allowed for the dissociation of possible enhancement and suppression mechanisms. With both fMRI and ERP, we obtained activity measures from areas of the visual association cortex specialized in face and scene processing. For fMRI, we used an independent functional localizer to identify both stimulus-selective face regions [within the fusiform face area (FFA); Kanwisher et al. 1997] and scene regions [within the parahippocampal place area (PPA); Epstein & Kanwisher 1998]. For ERP, we utilized a face-selective ERP, the N_{170}, a component localized to posterior occipital electrodes, which reflect visual association cortex activity with face specificity (Bentin et al. 1996). Our fMRI and ERP data revealed top-down modulation of both activity magnitude and processing speed that occurred above and below the perceptual baseline, depending on task instruction. That is, during the encoding period of the delay task, FFA activity was enhanced, and the N_{170} occurred earlier, when faces had to be remembered as compared with a condition where they were passively viewed. Likewise, FFA activity was suppressed, and the N_{170} occurred later, when faces had to be ignored compared with a condition where they were passively viewed. These results suggest that there are at least two types of top-down signals: One serves to enhance task-relevant information, and the other serves to suppress task-relevant information. By generating contrast via enhancing and suppressing activity magnitude and processing speed, top-down signals can bias the likelihood of successful representation of relevant information in a competitive system (Corbetta et al. 1990, Hillyard et al. 1973, Moran & Desimone 1985). p.14

Enhance & Suppress

claims PFC imposes BIAS signal to suppress extraneous info, e.g. when selecting face from a crowd.
FFA = fusiform face area in ITC.
PPA = parahippocampal (gyrus) place area--also discussed

ERP = EEG Event Related Potentials

- ERP complements fMRI
- their study used faces and scenes
- when storing scenes in WM they see
  FFA signal is suppressed
  "face-selective" N170 ERP is delayed
- concludes that PFC top-down signals can enhance targets and suppress extraneous info
- *this "bias" signal is another* example of WTA processing aka vertebrate decision making

Why should *techniques* matter to us?

when distracting stimuli are presented during the delay period, the amplitude of the ERP recorded from posterior electrodes was markedly increased in patients with frontal lesions compared with controls. Investigators interpreted that these results demonstrated disinhibition of sensory processing, which supports a role for the PFC in suppressing the representation of task-irrelevant stimuli. Recently, we investigated the causal role of the PFC in the modulation of evoked activity in the human extrastriate cortex during the encoding of faces and scenes (Miller et al. 2011). We employed two experimental approaches to disrupt PFC function: TMS of the PFC in healthy subjects and focal PFC lesions in stroke patients. We then investigated the effect of disrupted PFC function on the selectivity of category representations (faces or scenes) in the temporal cortex. Different object categories, such as faces and scenes, are represented by spatially distributed yet overlapping assemblies in the extrastriate visual cortex (Haxby et al. 2001). Thus, we reasoned that disruption of PFC function would lead to higher spatial correlations between scene- and face-evoked activity in the extrastriate cortex, suggesting a decrease in category selectivity. Consistent with our predictions, following disruption of PFC function (i.e., TMS session versus baseline, or lesion versus intact hemisphere in stroke patients), stimulus-evoked activity in the extrastriate cortex exhibited less distinct category selectivity to faces and scenes (more spatial overlap). In a follow-up study (Lee & D'Esposito 2012), we further demonstrated that the decreased tuning of the extrastriate cortex response coincided with decrements in working memory performance. This work extended the findings of Fuster and colleagues (1985) from monkeys to humans and suggests that the PFC may sharpen the representations of different object categories in the extrastriate cortex by increasing the distinctiveness of their distributed neural representations. These findings are also consistent with other recent combined TMS/fMRI and TMS/EEG studies demonstrating decreased attentional modulation of stimulus-selective visual regions following PFC disruption (Feredoes et al. 2011, Higo et al. 2011, Zanto et al. 2011). Together, such causal evidence clearly supports the notion that the PFC is the source of top-down signals that act via both gain and selectivity mechanisms.

p. 15

A key to understanding the role of the PFC in cognition likely rests in its connectivity with other regions (Yeterian et al. 2012). Any top-down signal from a particular PFC region, representing a particular goal, could have a different influence and behavioral consequence depending on which brain regions receive these signals. For example, PFC top-down signals could enhance internal

modulating **Top-Down Signaling**

bringing the Cudgel to PFC: inactivation of PFC via lesions, cooling were used to reveal PFC's role in top-down control. **TMS** (trans-cranial magnetic stimulation) has finer temporal control, but is spatially coarser than cooling. *Optogenetics* would be better, but not yet practical in humans.

Frontal Lesion Effects

- ↑ in posterior ERP suggests "disinhibition of sensory processes", but perhaps this is neural recruitment--aka "scaffolding".
- leads to ↓ category-selectivity in extra striate cortex (e.g. faces, scenes), suggests "PFC may sharpen the representations of different object categories".
- but how do Top-Down PFC signals know which activities to enhance unless this is already known?
- see *Yeterian-2012*. Any goal specific pathways?

more "slots and FoA" data! the number of control signals that can emanate at any one time (e.g. 7) is limited by PFC mechanism.

← **targets matter**

"extra striate" ≈ V2, V3, V4, V5/MT

Long-Range Connectivity (and neural oscillators!)

Distributed synchronized activity could occur via synaptic reverberations in recurrent circuits (Durstewitz et al. 2000a, Wang 1999) or synchronous oscillations between neuronal populations (Buzsáki & Draguhn 2004, Fries 2005, Singer 2009). In humans, EEG, magnetoencephalographic (MEG), and electrocorticographic (ECoG) recordings have been used to investigate which particular frequencies of oscillations may be related to working memory. Activity in low and high frequencies in the theta (4–7 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (30–200 Hz) ranges was modulated during working memory tasks (for a comprehensive review of 26 studies, see Roux & Uhlhaas 2014). Roux & Uhlhaas (2014) have proposed a different functional role for each of these frequency bands. They propose that gamma-band oscillations are specifically involved in the active maintenance of working memory information, theta-band oscillations are specifically involved in the temporal organization of working memory items, and alpha-band oscillations are involved in the inhibition of task-irrelevant information. These notions are based on studies that have demonstrated amplitude modulation of neural oscillations presumably emanating from particular brain regions involved in working memory. For example, during a delayed match-to-sample task while recording human EEG, investigators observed that occipital gamma and frontal beta oscillations were sustained across the retention interval. Moreover, as this delay interval lengthened, these oscillations decreased in parallel with decreased performance on the task (Tallon-Baudry et al. 1999). In a recent study, Anderson et al. (2014) showed that the spatial distribution of power in the alpha frequency band (8–12 Hz) tracked both the content and the quality of the representations stored in visual working memory. These empirical findings support the notion that neural oscillations are critical for working memory maintenance processes.

Long-range synchronization of these oscillations between brain regions likely also plays an important role in working memory function (Crespo-Garcia et al. 2013, Sauseng et al. 2005). For example, in a human MEG study, synchronized oscillations in the alpha, beta, and gamma bands were observed between frontoparietal and visual areas during the retention interval of a delayed match-to-sample visual working memory task. Moreover, these observed synchronized oscillations were sustained and stable throughout the delay period of the task, were memory load dependent, and were correlated with an individual's working memory capacity (Palva et al. 2010). Monkey

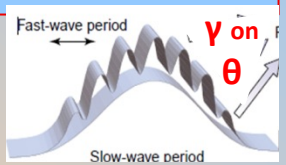
do θ α β and γ matter?
boost, enhance, suppress

neural oscillators at work: nice "bands" overview. "Recurrent Circuits" means circuits with feedback (ala AAN) or reciprocal connections (ala spinal oscillators). WM tasks modulate different oscillations frequency bands.

note: ***PNA*** aka Persistent Neural Activity is often presumed to be local-circuit oscillators, but binding across neocortex seems to require slower frequency oscillations e.g. alpha, beta (although *gamma* is included)

Oscillations and WM

MEG aka Magnetoencephalography seems to detect synchrony between frontal and parietal cortex during delay period (of WM task); it is sustained and memory-load dependent.



top of p. 16: *Top Down signals emanate from* PFC hippocampus, parietal cortex and basal ganglia

NEUROMODULATORS

Brain stem neuromodulators. In many models of cognition, neuromodulators such as dopamine, serotonin, norepinephrine, or acetylcholine play a limited role, if any role at all. Yet, given that brain stem neuromodulatory neurons send projections to all areas of the brain, their influence on cognitive function is without question. Abundant evidence from both animal and human studies indicates that dopaminergic modulation of frontostriatal circuitry in particular is critical for working memory function (Cools & D'Esposito 2009).

Dopaminergic neurons in the human brain are organized into several major subsystems (mesocortical, mesolimbic, and nigrostriatal). The mesocortical and mesolimbic dopaminergic systems originate in the ventral tegmental area of the midbrain and project to the frontal cortex, the anterior cingulate, the nucleus accumbens, and the anterior temporal structures such as the amygdala, hippocampus, and entorhinal cortex (Bannon & Roth 1983). Across the cerebral cortex, the concentration of dopamine is highest within the frontal cortex (Brown et al. 1979, Williams & Goldman-Rakic 1993). However, there is also a strong dopaminergic input into the hippocampus (Samson et al. 1990), and abundant evidence from both animal and human studies shows that dopamine is involved in hippocampal-dependent LTM (for a review of this topic, see Shohamy & Adcock, 2010).

p. 17

The functional importance of dopamine to working memory and PFC function has been demonstrated in several ways. First, in monkeys, depletion of PFC dopamine or pharmacological blockade of dopamine receptors induces working memory deficits (Brozoski et al. 1979, Sawaguchi & Goldman-Rakic 1991). These deficits are as severe as those in monkeys with PFC lesions and are not observed in monkeys in which other neurotransmitters, such as serotonin, are depleted. Furthermore, dopaminergic agonists administered to monkeys with dopamine depletion reverse working memory deficits (Arnsten et al. 1994, Brozoski et al. 1979). Likewise, numerous studies have shown that administration of dopamine receptor agonists to healthy young human subjects improves working memory performance (Kimberg et al. 1997, Kimberg & D'Esposito 2003, Luciana & Collins 1997, Muller et al. 1998). An important feature of the dopaminergic system is that it exhibits a U-shaped dose-response curve: Specific doses of dopaminergic drugs produce optimal performance on working memory tasks (Arnsten 1997, Kimberg et al. 1997; reviewed in detail in Cools & D'Esposito 2011). These observations illustrate that more is not better; rather,

Neuromodulators: DA plays major role in WM.
- ACh plays a role in Hippo. encoding/retrieval.
- serotonin (5HT) and norepinephrine-more nuanced
- The nucleus accumbens and ventral tegmental areas are part of a parallel "basal-ganglia like" circuit with VTA supplying DA to multiple sites.
- PFC has highest [DA] in neocortex

Brainstem nuclei such as the VTA, raphe and locus coeruleus have relatively small numbers of neurons which project over large swaths of neocortex, other places and can enhance or inhibit (modulate) ongoing neural activity in those targets. Perhaps their smaller numbers makes these systems more vulnerable to damage.

Dopamine (DA) Depletion
- yields WM deficits as substantial as PFC lesions **agrees w/ Hedden/Gabrieli (chap. 5)**
- taking DA boosts WM (don't try this at home!)

DA also part of Dedifferentiation Theory (tba)

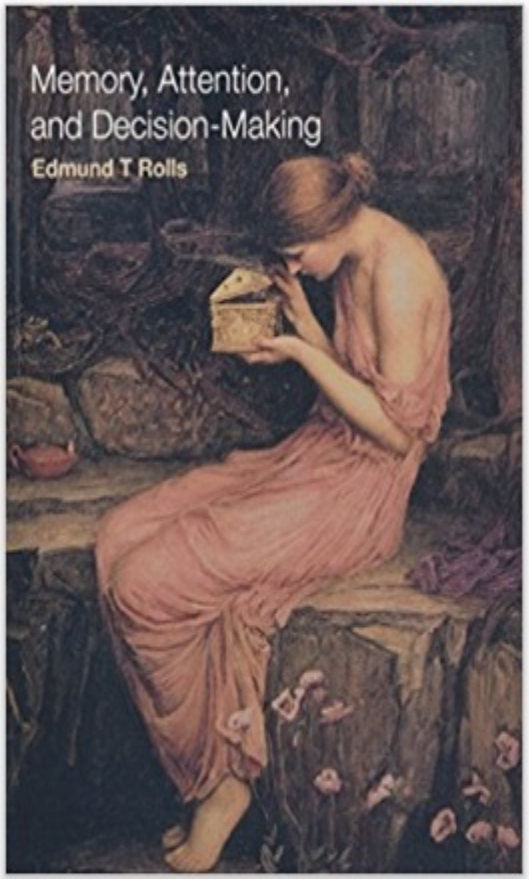
regarding: U-shaped Curve *& effects of specific DA doses:* is this not true of all neurotransmitter systems?

Memory, Attention, and Decision-Making: A unifying computational approach

Edition

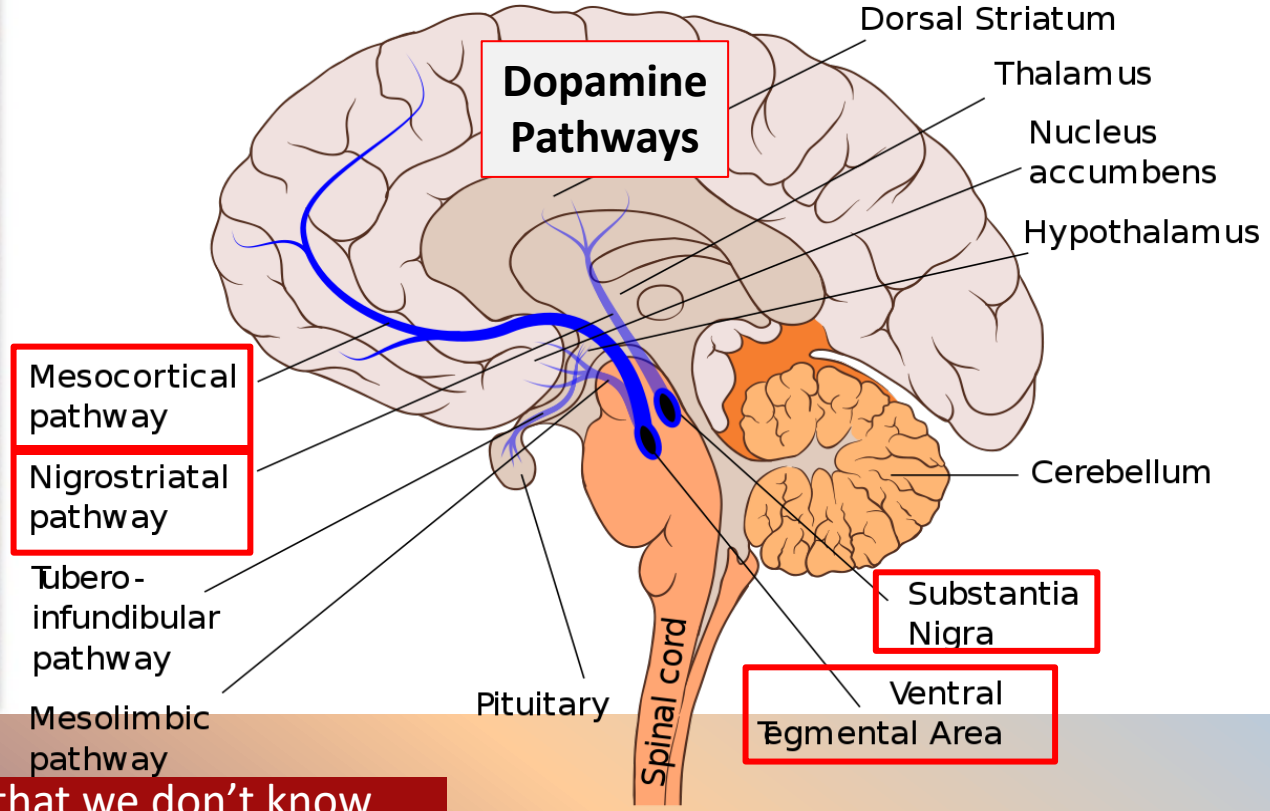
by Edmund Rolls (Author)

Why 7 +/- 2 items?



At SFN one year, I asked Edmund Rolls how it could be that DMRs hold thousands of items, but WM only 7?

← He said to go read a chapter in this book.



As soon as we start denying that we don't know things, we close our minds to learning new things.

p.s. it's a great book!

Is cognitive slowing part of WM?
Is WM part of fluid intelligence?

EM = Episodic Memory
EM is derived from DMRs

Fluid Intelligence = WM related, *Cognitive Manipulation*

Crystallized Intelligence = Declarative Memory (DM), experiences, strategies and associated skills aka **LTM**

AlzD – lose ability to add to DM (part of crystal-I)
Fluid-I is OK very early on in AlzD (not 1st symptom)
Research Topic: can they add new skills, capabilities?
requires little new DM, uses neocortex

Normal Aging – 1st declines are in Fluid-I
b/c normals have cogn. slowing, WM, PFC issues

Who is Endel Tulving? Tulving coined the term/concept of Episodic Memory but Mr. EM, later got sucked into a list-learning rabbit hole, morphed into calling that EM. Hate to contradict Mr. EM, but no, list-learning is more related to WM-like processes. EM comes from DMRs which are 1-trial, effortless, not list learning. *very strange*. ET born 1927. *93 years old!*

SUMMARY -- The Cognitive Neuroscience of Working Memory, Annual Rev. Psych, 2015

1. An enduring principle of the multiple-component model of working memory (Baddeley and Hitch, 1974) is that the short-term retention of information **(a.k.a. "working memory storage") and the control of how that information is used to guide behavior are subserved by distinct processes.** With regard to the former, however, earlier ideas of specialized buffers have been challenged by state-based models.

2. Although state-based models of working-memory storage are often categorized as "activated LTM" models or "sensorimotor recruitment" models, all are grounded in the idea that **the attentional selection of mental representations (AANs?) brings them into working memory,** and that the consequences of attentional prioritization explain such properties as capacity limitations, proactive interference from no-longer-relevant items, and so on.

3. Recent research applying multivariate pattern analysis (MVPA) to **fMRI and EEG data has provided indirect neural evidence for state-based models of working memory storage.** [but there is a gap btw fMRI and neural operations]

4. Some recent findings from computational modeling, extracellular electrophysiology, fMRI, and EEG, suggest that working memory storage may depend on **the transient reorganization of synaptic weights, rather than on sustained, elevated activity**.

5. The PFC likely represents higher-order information, such as task rules, goals, or abstract representations of categories, as compared to feature- and stimulus-specific representations in posterior cortex. Moreover, a critical mechanism for working memory function is the **synchronization of PFC activity with activity** in other brain regions.

6. One reported dimension of functional organization of PFC is **a hierarchical caudal-to-rostral gradient of increasing level of abstraction** of the rules and goals that guide behavior. [*possibly a red herring?]*

7. Top-down control signals emanating from PFC likely take at least two forms: signals that modulate gain by either enhancing task-relevant information or suppressing task-irrelevant information, and signals that can modulate the selectivity of information represented in posterior cortical regions. (+ TD/bottom up collisions)

8. Dopamine plays a critical role in working memory function. The complex interplay of midbrain dopamine in prefrontal and striatal circuits reportedly underlies "tonic maintenance" and "phasic gating" functions that govern the balance between cognitive flexibility and stability.

NOTES: It is the **PFC mechanism** that is 7 +/- 2 limited! There are no "anatomical" slots . . .

Changes in Brain Network Efficiency and Working Memory Performance in Aging

Network Metrics of Aging WM

Matthew L. Stanley[1]*, Sean L. Simpson[1,2], Dale Dagenbach[1,3], Robert G. Lyday[1], Jonathan H. Burdette[1,4], Paul J. Laurienti[1,4]

1 Labo
United
Winstor
Univers
Forest

* stanl

2015, PLoS1

WM = 7 +/- 2 items

Abstract

Working memory is a complex psychological construct referring to the temporary storage and active processing of information. We used functional connectivity brain network metrics quantifying local and global efficiency of information transfer for predicting individual variability in working memory performance on an *n*-back task in both young ($n = 14$) and older ($n = 15$) adults. Individual differences in both local and global efficiency during the working memory task were significant predictors of working memory performance in addition to age (and an interaction between age and global efficiency). Decreases in local efficiency during the working memory task were associated with better working memory performance in both age cohorts. In contrast, increases in global efficiency were associated with much better working performance for young participants; however, increases in global efficiency were associated with a slight decrease in working memory performance for older participants. Individual differences in local and global efficiency during resting-state sessions were not significant predictors of working memory performance. Significant group whole-brain functional network decreases in local efficiency also were observed during the working memory task compared to rest, whereas no significant differences were observed in network global efficiency. These results are discussed in relation to recently developed models of age-related differences in working memory.

anything of interest here? [ExCred]

Assorted changes in *Global* and *Local* network efficiency were observed in aged populations performing an n-back task (e.g. recall an items two steps back in a sequence). **DQ: How reliable and significant might these results be?**

Local and Global Efficiency are Network Metrics, being applied here to fMRI

Local efficiency. Local efficiency is a measure of the average efficiency of information transfer within local subgraphs or neighborhoods and is defined as the inverse of the shortest average path length of all neighbors of a given node among themselves [67]. Local efficiency was first computed for each individual node *i* in the network by identifying the set nodes, or subgraph, to which node *i* is directly connected. After removing node *i* from the identified subgraph, the shortest path between all nodes in the subgraph was calculated. The inverse of the shortest path from each node formerly connected to node *i* to every other node formerly connected to node *i* was then summed across all nodes formerly connected to node *i*, and this summed quantity is normalized by taking into account the total possible number of connections that could exist among all nodes formerly connected to node *i*. Formally, local efficiency is calculated as

$$E_{local} = \frac{1}{N_{G_i}(N_{G_i} - 1)} \sum_{j,k \in G_i} \frac{1}{L_{j,k}}$$

where N_{G_i} represents the number of nodes in the subgraph G_i. Local efficiency is a scaled measure ranging from 0–1, with a value of 1 indicating maximum local efficiency in the network. In functional brain networks, high local efficiency suggests a topological organization indicative of segregated neural processing [2]. The local efficiency of the network reveals how effectively information is transferred among the first neighbors of node *i* when node *i* is removed from the network. Nodes in networks with high local efficiency tend to effectively share information within their immediate local communities, which provides a basis for effective segregated information processing in the network.

These are ***path-length metrics***, but they might say little about actual NIP (neuronal info processing). **Graph-Theory** requires node-to-node signaling, but ***voxel-activation patterns*** might mean something very different. stay tuned.

is this anything?

Local and Global Efficiency: Network Science vs. SNOPs

Analysis of fMRI data sets
. Manual Analysis
. ICA / seed based analysis
. other statistical (is MVPA diff.?)
. Network Science Metrics

Network Science Metrics
aka *Graph Theory*
. path length
. local efficiency
. global efficiency
. lots more

We've seen voxel-based analysis (CSS slides) and ROI-style analysis (ABM activity in cingulate, other brain regions. When you base analysis on regions, you might average out voxel-level signals and therefore weaken your analysis to more "diffuse" processes. But if you apply network science metrics at the voxel level you might end up with a mass of Network Spaghetti*.

**ala Brainbow's technicolor spaghetti*

The more facts you have to think with, the deeper you can think.

"morsel look-up" on Google / "smart"-phones good for superficial thinking

NU network science had a research symposium on Friday, October 25th: https://www.networkscienceinstitute.org/

Working Memory Performance and Brain Network Efficiency

The primary purpose of this study is to determine whether differences in local and global efficiency account for a substantial proportion of individual variability in working memory performance across age groups. In order to approach this research question, we conducted backward/forward stepwise linear regression analyses with Akaike's information criterion (AIC; [82–83]) and Adjusted R^2 as criteria to discover (1) whether individual differences in local and global efficiency are significantly predictive of working memory performance, and (2) whether local and global efficiency are dependent upon age-related differences in predicting working memory performance. Age was included as an independent variable and coded as a binary, categorical variable (0 = young, 1 = old). *d'* was used as the dependent variable in all regression analyses. We sought to quantify the relationship between working memory performance and each of the covariates, all possible interactions between those covariates, and all possible quadratic terms while controlling for the variability in working memory performance explained by the speed of responding (measured in milliseconds) and the number of volumes removed per participant due to excessive motion.

Table 1. Mean (SD) local and global efficiency for both resting and task states between age groups.

Condition	*Young Adults (n = 14, 48%)*		*Older Adults (n = 15, 52%)*	
	E_{local}	E_{global}	E_{local}	E_{global}
Rest	0.447 (.03)	0.243 (.03)	0.436 (.04)	0.243 (.04)
2-back	0.411 (.02)	0.251 (.03)	0.413 (.04)	0.236 (.04)

doi:10.1371/journal.pone.0123950.t001

main effect = ???

High *local efficiency* suggests segregated information processing in that nodes share info with their neighbors moreso than with distant nodes.

Performance on Working Memory (2-back) Task

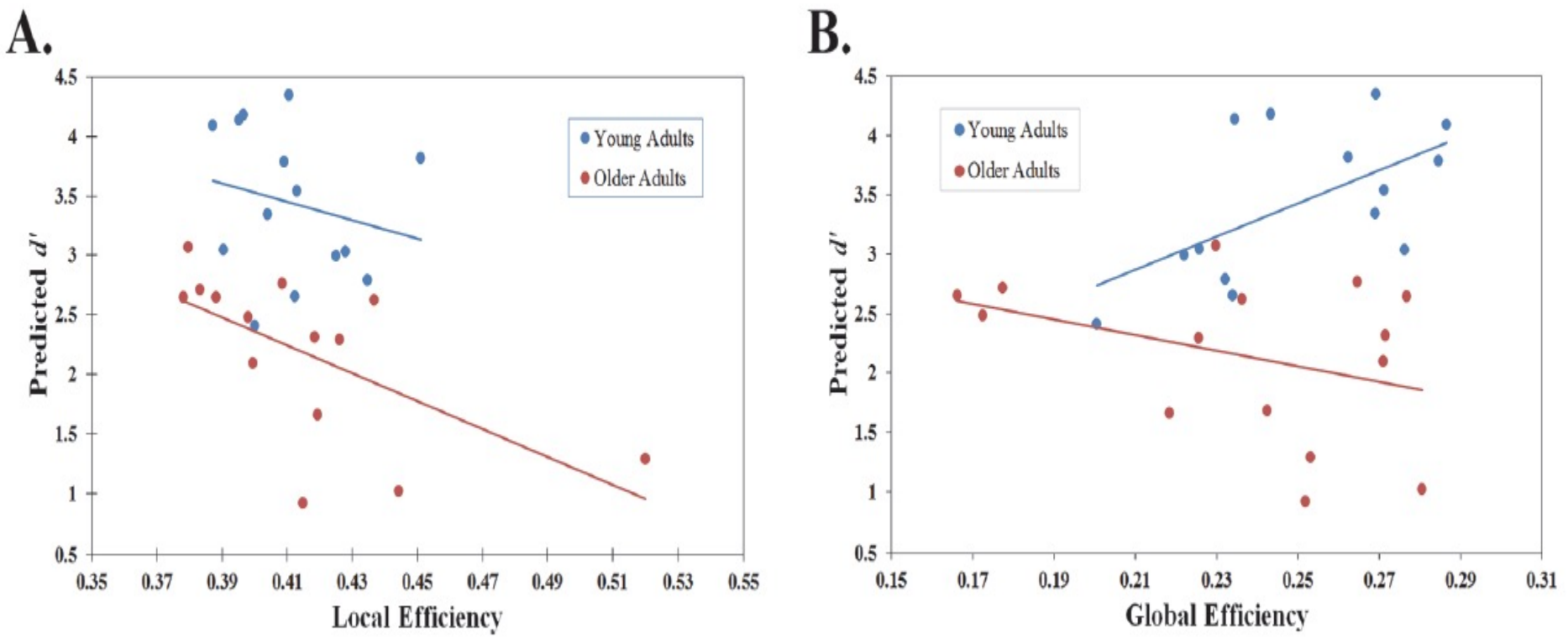
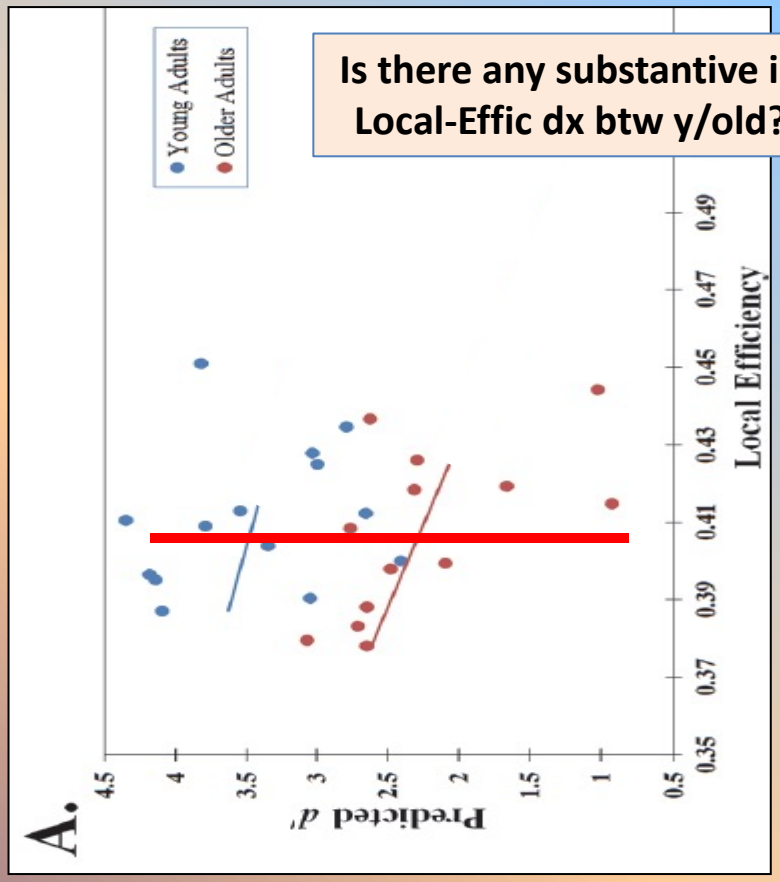
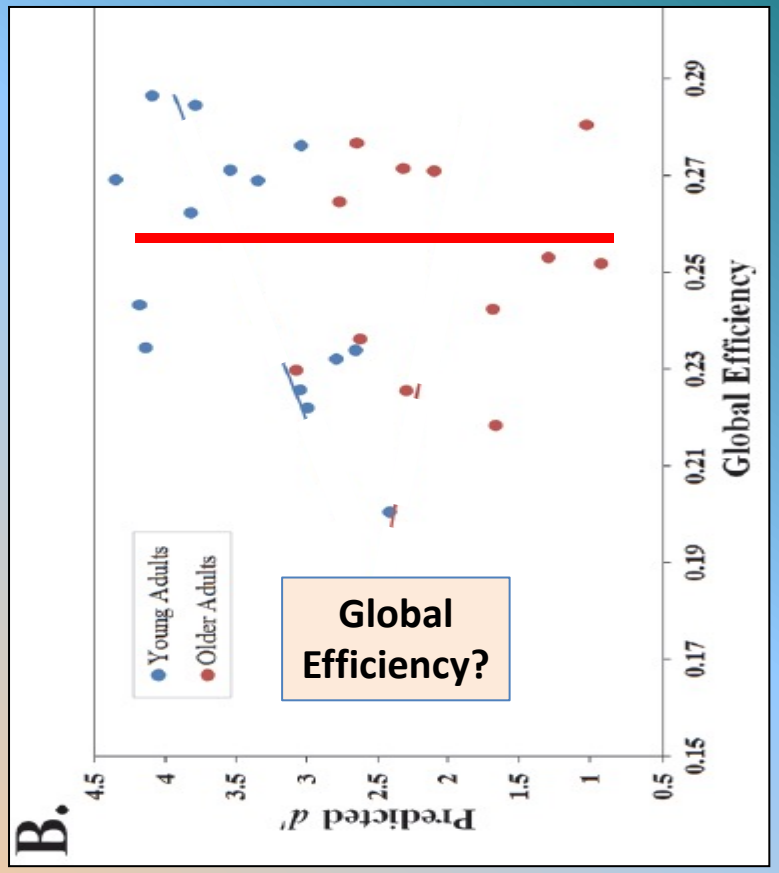


Fig 1. Graphical Summary of Results from Final Regression Model. The predicted *d'* values from the final model (the model containing local efficiency during task, global efficiency during task, age group, average RT, and an interaction between global efficiency during task and age group as parameters) are plotted against observed local efficiency (A) and global efficiency (B) values during the 2-back task, respectively, and split by age group.

decreased Local E associated with increased performance in 2-back task for both groups
for young'uns increased Global E associated with signif. better WM performance
we might revisit Age-Related differences in WM; not much here though…..BUT….

How *should* their data be displayed?





Decreases in *Local Efficiency* associated with better performance in all groups.
***Allegedly*!**

Increases in *Global Efficiency* associated with "much better" WM performance in young'uns.
***Allegedly*!**

What do the data really look like?

Performance on Working Memory: 2-back Task. How about a plot w/ performance?

A brief *Division of your Attention*. This work notes that ***memory for context*** is ravaged by age and addresses the "limited resources" hypothesis. While this tries to explain general impacts of Div. Attn., old folks had additional "associative" or MTL deficits.

Effects of Aging and Divided Attention on Memory for Items and Their Contexts

Fergus I. M. Craik
University of Toronto

Lin Luo
York University, Toronto

Yuiko Sakuta
Waseda University

How should we interpret the *Associative* Effects?

Psychology & Aging, 2010

It is commonly found that memory for context declines disproportionately with aging, arguably due to a general age-related deficit in associative memory processes. One possible mechanism for such deficits is an age-related reduction in available processing resources. In two experiments we compared the effects of aging to the effects of division of attention in younger adults on memory for items and context. Using a technique proposed by Craik (1989), linear functions relating memory performance for items and their contexts were derived for a Young Full Attention group, a Young Divided Attention group, and an Older Adult group. Results suggested that the Old group showed an additional deficit in associative memory that was not mimicked by divided attention. It is speculated that both divided attention and aging are associated with a loss of available processing resources that may reflect inefficient frontal lobe functioning, whereas the additional age-related decrement in associative memory may reflect inefficient processing in medial-temporal regions.

This PDF is not posted, ping me if you'd like me to add it to supplemental and/or if you have any questions.

that a disproportionate deficit in associative information is unique to aging and that dividing attention in young adults simply leads to a general decline in memory performance. In contrast, a study reported by Castel and Craik (2003) examining the same question showed that young adults under DA, like older adults, did show greater deficits in associative memory than in item memory. However, they also suggested that aging is associated with a second factor that is not simulated by DA, possibly a more extensive age-related associative deficit or an increased reliance on familiarity at the time of retrieval. *

DA = divided attn.

The question of whether DA in young adults impairs memory for context disproportionately is difficult to answer because the levels of performance in item memory often differ between an old group and a young DA group. Compared to young adults under full attention (FA), older adults typically show a considerable reduction in memory for context, but relatively little reduction in recognition memory for items. In contrast, DA in young adults substantially reduces both item and context memory. One example of this pattern was found in a study by Sanders (1985; also reported by Craik, 1989). In this experiment, participants encoded a series of words presented with colorful visual scenes (i.e., a garden, a beach scene, a kitchen, etc.). Six scenes served as the contexts for the 60 encoded words, with 10 words associated with each scene. After the encoding phase, participants were given an item recognition test for the words, followed by a context identification test in which the encoded words were presented, and the participants asked to make a forced-choice decision regarding the scene.

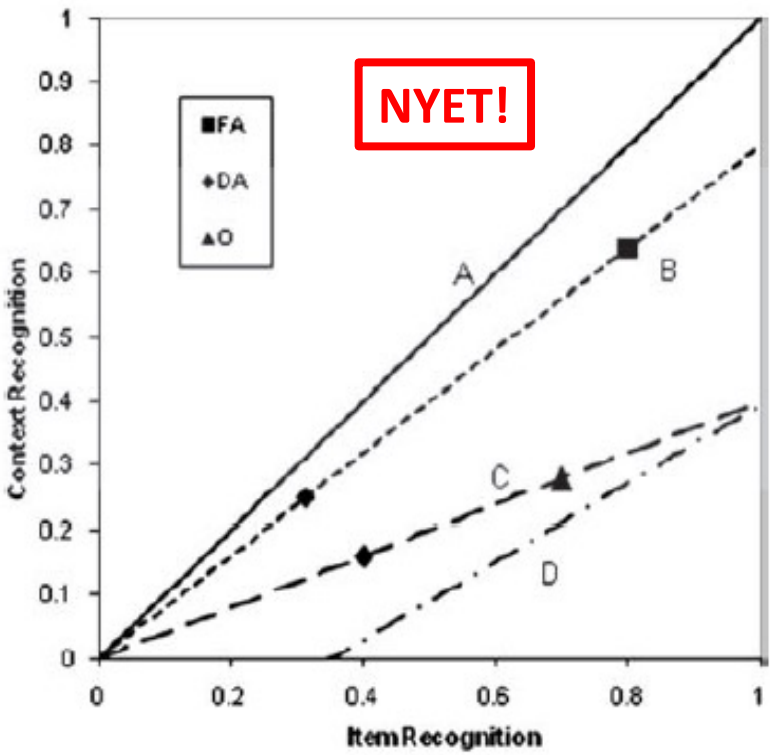


Figure 1. Hypothetical functions relating item and context recognition. Function A is the positive diagonal; in function D, item recognition is substantial when associative recognition is zero. Data points refer to hypothetical means in full-attention young groups (FA), divided-attention young groups (DA), and older groups (O), respectively. DA has two possible effects: decreasing item and context recognition equivalently (group mean for DA falls on the same function B as the FA group), or decreasing context recognition disproportionately (group mean for DA falls on function C with the O group).

* Sounds like *Object Recognition Memory*, ala Aude Oliva MIT, which extends to 1000's of objects; also increased reliance on familiarity which resonates with recalling gist, not details.

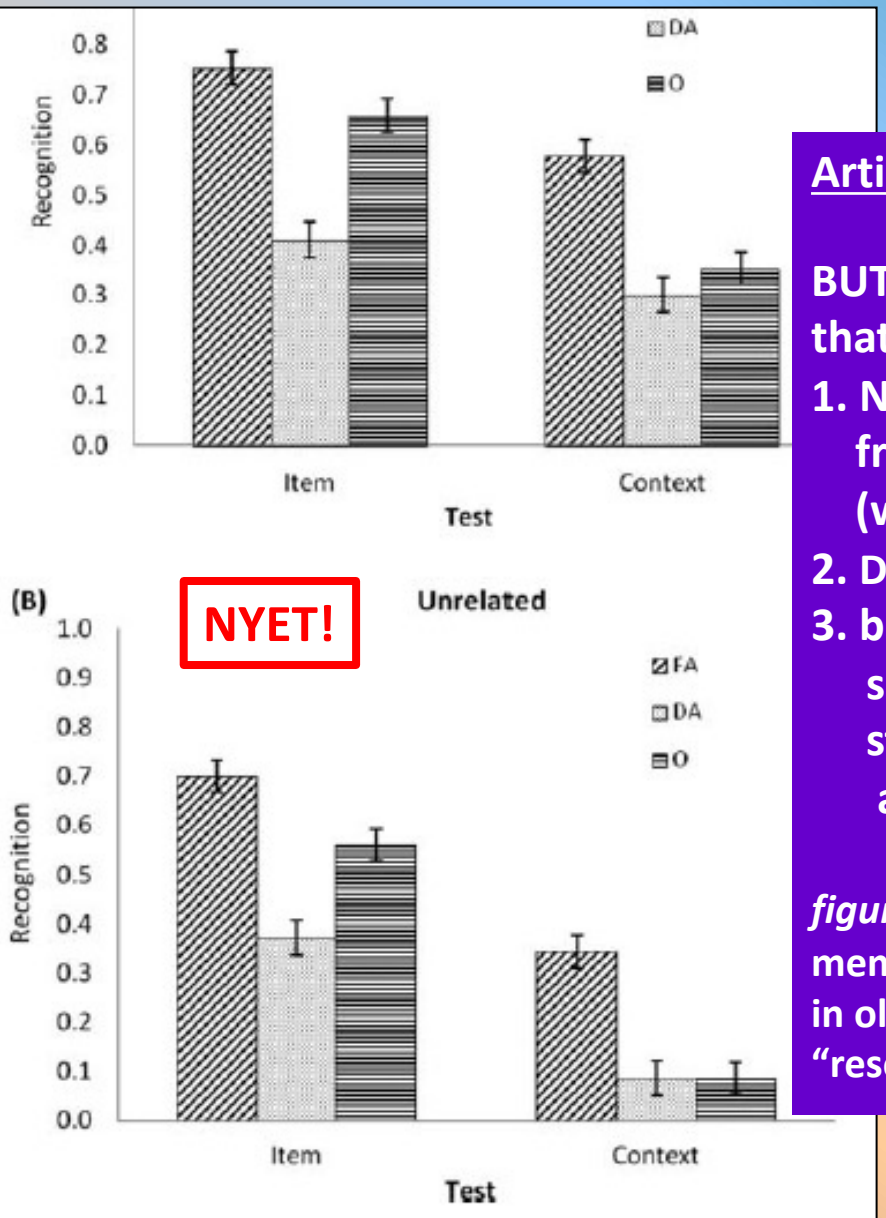


Figure 2. Mean item and context recognition rates for related (A) and unrelated (B) word-scene pairs in Experiment 1, collapsed over presentation rates (FA = younger adults, full attention; DA = younger adults, divided attention; O = older adults, full attention).

Article results are a bit incremental, vague

(don't worry about details of figures)

BUT: the gist of these network analyses are that:

1. **Normal Aging is doing something diff. from simply "overloading resources" (which is what DA, Divided Attn. is)**
2. **Deficit w/ DA is attributed to PFC overload**
3. **but experiments indicate that older subjects have difficulty specifically w/ storing contextual info: ala ERC/Hippo system!**

***figures show*: divided attn. degrades item memory in Young Uns, but context mem. is worse in old folks. the results do not fit with a simple "resource limitation"**

caution: DA is a very frequently used abbrev. for dopamine, but there is no **dopamine** in this paper, even though, dopamine is most important for WM and complex task performance!

Place Cells, Grid Cells, and Memory

2015 - CSHL

ERC/Hippocampal System: 2nd best studied system in the Mamm. Brain?

May-Britt Moser, David C. Rowland, and Edvard I. Moser

Centre for N
and Technol

The hippocampal system is critical for storage and retrieval of declarative memories, including memories for locations and events that take place at those locations. Spatial memories place high demands on capacity. Memories must be distinct to be recalled without interference and encoding must be fast. Recent studies have indicated that hippocampal networks allow for fast storage of large quantities of uncorrelated spatial information. The aim of the this article is to review and discuss some of this work, taking as a starting point the discovery of multiple functionally specialized cell types of the hippocampal–entorhinal circuit, such as place, grid, and border cells. We will show that grid cells provide the hippocampus with a metric, as well as a putative mechanism for decorrelation of representations, that the formation of environment-specific place maps depends on mechanisms for long-term plasticity in the hippocampus, and that long-term spatiotemporal memory storage may depend on offline consolidation processes related to sharp-wave ripple activity in the hippocampus. The multitude of representations generated through interactions between a variety of functionally specialized cell types in the entorhinal–hippocampal circuit may be at the heart of the mechanism for declarative memory formation.

see notes on dev amnesia

Updated:

This system is required for DMRs, consolidating information into LTM. Relative preservation of the WM system in AlzD suggests that ERC/hippo system isn't key to ongoing WM. Instead WM seems to utilize "consolidated" LTM that resides throughout neocortex, outside of ERC. I had described hippo as an "indexing" system to enable DMRs to be stored in neocortex (where representations are found) but more substantively is a contextualizing system that links space and time into a continuum or context where many items of potential relevance are bound b/c there are "strong representations" that are easily linked to the continuum. Mnemonic tricks can push items from WM into our DMRs (eventually into LTM) by engaging hippo processing resources that *normally do not play well* with evanescent contents of WM.

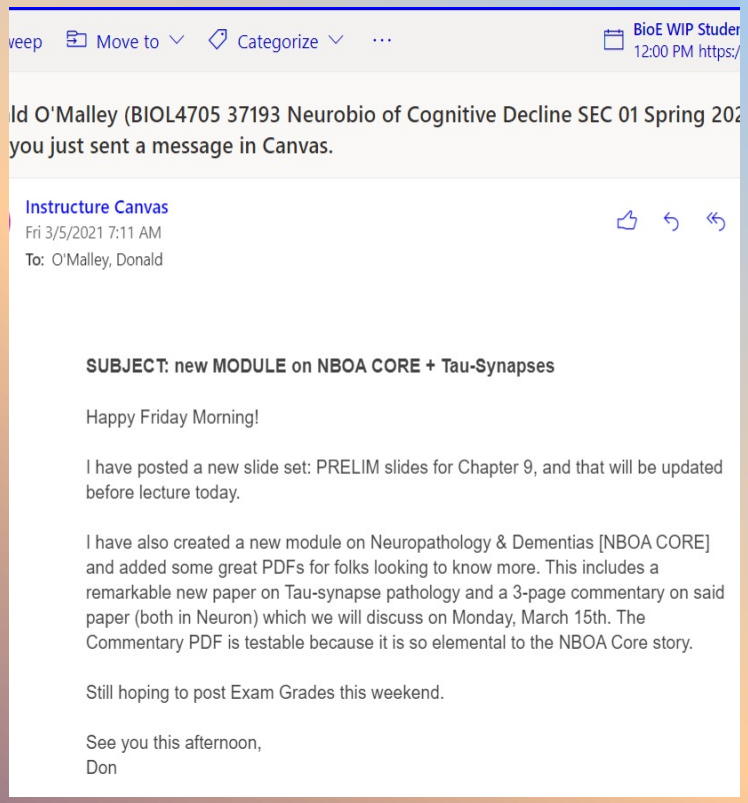
+ ADD
developmental
amnesia abstract

Meanwhile…

Learning by Analogy:
Hyena's on the Antelope
Thag's on the Fire (watch)
Grok's on the hand-axes (stone tools)

When Canvas Lies

I sez I sent email at 6:59 a.m.
am I demented? or just OCD?



veep Move to Categorize ··· BioE WIP Studer 12:00 PM https:/

ld O'Malley (BIOL4705 37193 Neurobio of Cognitive Decline SEC 01 Spring 202
you just sent a message in Canvas.

Instructure Canvas
Fri 3/5/2021 7:11 AM
To: O'Malley, Donald

SUBJECT: new MODULE on NBOA CORE + Tau-Synapses

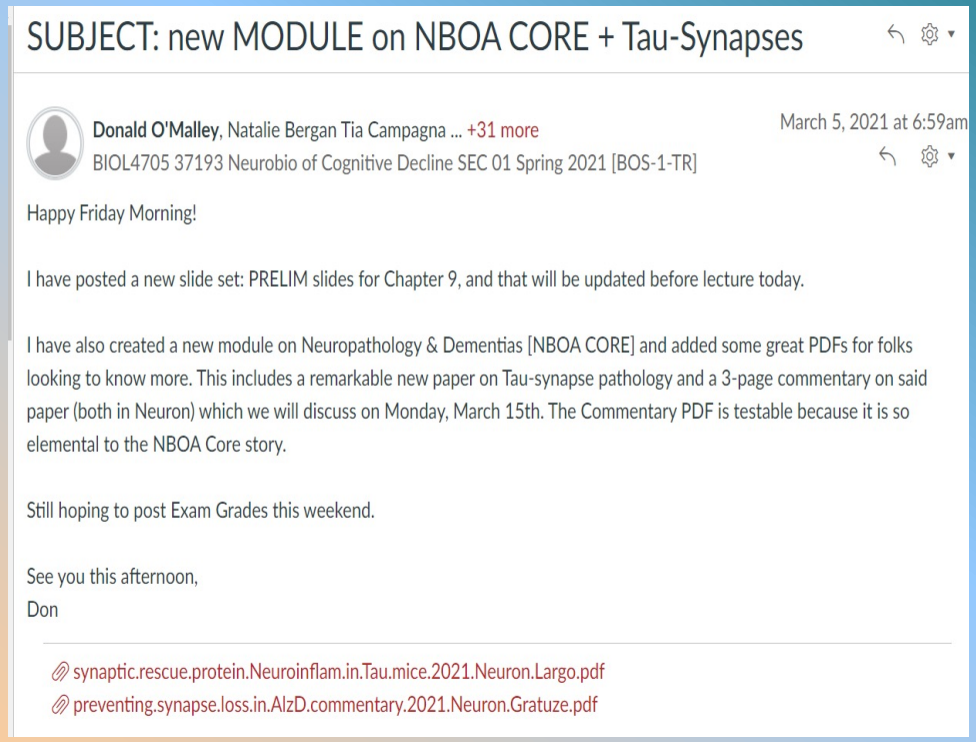
Happy Friday Morning!

I have posted a new slide set: PRELIM slides for Chapter 9, and that will be updated before lecture today.

I have also created a new module on Neuropathology & Dementias [NBOA CORE] and added some great PDFs for folks looking to know more. This includes a remarkable new paper on Tau-synapse pathology and a 3-page commentary on said paper (both in Neuron) which we will discuss on Monday, March 15th. The Commentary PDF is testable because it is so elemental to the NBOA Core story.

Still hoping to post Exam Grades this weekend.

See you this afternoon,
Don



SUBJECT: new MODULE on NBOA CORE + Tau-Synapses

Donald O'Malley, Natalie Bergan Tia Campagna ... +31 more
BIOL4705 37193 Neurobio of Cognitive Decline SEC 01 Spring 2021 [BOS-1-TR]
March 5, 2021 at 6:59am

Happy Friday Morning!

I have posted a new slide set: PRELIM slides for Chapter 9, and that will be updated before lecture today.

I have also created a new module on Neuropathology & Dementias [NBOA CORE] and added some great PDFs for folks looking to know more. This includes a remarkable new paper on Tau-synapse pathology and a 3-page commentary on said paper (both in Neuron) which we will discuss on Monday, March 15th. The Commentary PDF is testable because it is so elemental to the NBOA Core story.

Still hoping to post Exam Grades this weekend.

See you this afternoon,
Don

synaptic.rescue.protein.Neuroinflam.in.Tau.mice.2021.Neuron.Largo.pdf
preventing.synapse.loss.in.AlzD.commentary.2021.Neuron.Gratuze.pdf

Why this matters: I sent an email at 6:59. It did not arrive in my inbox until 7:11. [If this happens to you during an Exam, I can grant the missing time].
Canvas is Stupid and Lies, but I still LIKE the CANVAS program and interface!

Why Canvas is a Moron

it's NBOA, not Nboa, you idot!

me: **just OCD, and a tad persnickety**

This is what an EMAIL should look like

SUBJECT: new MODULE on NBOA CORE + Tau-Synapses

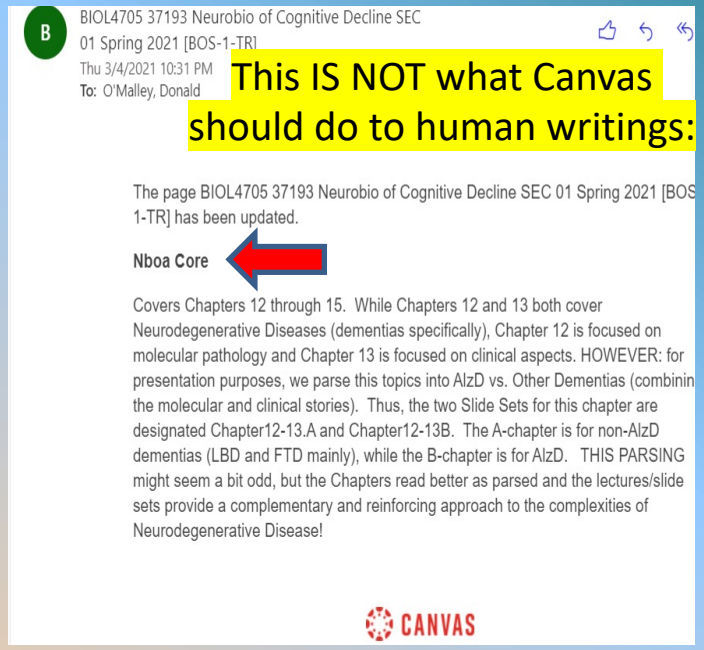
Happy Friday Morning!

I have posted a new slide set: PRELIM slides for Chapter 9, and that will be updated before lecture today.

I have also created a new module on Neuropathology & Dementias [NBOA CORE] and added some great PDFs for folks looking to know more. This includes a remarkable new paper on Tau-synapse pathology and a 3-page commentary on said paper (both in Neuron) which we will discuss on Monday, March 15th. The Commentary PDF is testable because it is so elemental to the NBOA Core story.

Still hoping to post Exam Grades this weekend.

See you this afternoon,
Don



While I am not demented, am almost certainly preclinical-AlzD and Amyloid positive: see Chapter 18. Boosting of *salience network* means I don't care.

preclinical ➔ aMCI ➔ AlzD (early, moderate, severe OR Braak stages)

prodromal-MCI

prodromal-AlzD

prodromal-being dead

prodromal = signs of a possible/likely impending illness ≠ the actual illness