A Graph Theoretical Analysis of Functional Brain Networks Related to Memory and Healthy Aging

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Brigham Young University

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A Graph Theoretical Analysis of Functional Brain Networks

Related to Memory and Healthy Aging

Ty Alvin Bodily

A thesis submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of

Master of Science

Christopher B. Kirwan, Chair
Jonathan J. Wisco
Michael D. Brown

Neuroscience Center
Brigham Young University

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ABSTRACT

A Graph Theoretical Analysis of Functional Brain Networks Related to Memory and Healthy Aging

Ty Alvin Bodily
Neuroscience Center, BYU
Master of Science

The cognitive decline associated with healthy aging begins in early adulthood and is important to understand as a precursor of and relative to mild cognitive impairment and Alzheimer disease. Anatomical atrophy, functional compensation, and network reorganization have been observed in populations of older adults. In the current study, we examine functional network correlates of memory performance on the Wechsler Memory Scale IV and the Mnemonic Discrimination Task (MST). We report a lack of association between global graph theory metrics and age or memory performance. In addition, we observed a positive association between lure discrimination scores from the MST and right hippocampus centrality. Upon further investigation, we confirmed that old subjects with poor memory performance had lower right hippocampus centrality scores than young subjects with high average memory performance. These novel results connect the role of the hippocampus in global brain network information flow to cognitive function and have implications for better characterizing and predicting memory decline in aging.

Keywords: aging, resting state, fMRI, memory, graph theory, centrality, hippocampus
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According to recent work, cognitive decline due to aging begins in early adulthood at an age of 20-30 years old (Salthouse, 2011). The aging and cognitive decline incident to so-called “healthy aging” (the focus of this paper) are accompanied generally by global structural atrophy in the brain, including decreased cortical thickness, decreased white matter integrity, and reduced brain volume (Goh & Park, 2009). Interestingly, these changes have been observed to correlate only loosely with cognitive measures, indicating that maintenance-oriented or compensatory neurological changes are at least somewhat effective (Goh & Park, 2009).

In addition to widespread structural changes, studies of the medial temporal lobe (MTL), a group of brain regions associated with episodic memory have observed specific anatomical changes in healthy aging. For instance, studies have observed that the hippocampus, its subfields, and other MTL regions seem to shrink increasingly rapidly with age (Abe et al., 2008; Fjell & Walhovd, 2010; Murphy et al., 2010; Sullivan & Pfefferbaum, 2006), and some studies show that hippocampus size correlates with memory performance in aging (Salthouse, 2011).

Functional imaging studies have observed a pattern of decreased brain activity in MTL regions and increased activity in regions of the PFC associated with cognitive preservation in aging during encoding and retrieval tasks, and some studies show a reversed trend of increased hippocampal activity in older adults with relatively large memory deficits (Grady, 2008; Miller et al., 2008; Tromp, Dufour, Lithfous, Pebayle, & Després, 2015; Yassa, Lacy, et al., 2011). These findings—along with task-based memory studies showing increased connectivity between the hippocampus and PFC with decreased connectivity between the hippocampus and MTL to posterior and occipital regions in aging—play an important role in current cognitive models of
aging. One such model, the compensation-related utilization of neural circuits hypothesis (CRUNCH), posits that observed brain function changes in aging are compensatory for regional atrophy, decreased network processing efficiency, or a decrease in network input (Reuter-Lorenz & Cappell, 2008). For instance, a decrease in memory network input could result from MTL atrophy, memory circuit processing efficiency, or from the deteriorating quality of sensory information as sensors and sensory relays age.

Another model of cognitive aging, the scaffolding theory of aging and cognition (STAC), also incorporates compensation as a key model component. Broadly, STAC describes an ongoing readjustment or compensation, or “scaffolding,” that occurs in brain networks in aging (Park & Reuter-Lorenz, 2009). Scaffolding consists of network recruitment and reorganization such that many older adults maintain remarkably good cognitive function despite apparent brain deterioration. Importantly, this model emphasizes the compensation of the prefrontal cortex for deficient hippocampal/parahippocampal activity in aging. This model additionally accounts for relatively high default mode network (DMN) activity during task performance associated with poor performance on cognitive tasks.

Finally, HAROLD (hemispheric asymmetry reduction in older adults) is a model similarly built on compensation, though its focus is on hemispheric asymmetries within the PFC across a variety of tasks and conditions, including episodic and working memory (Cabeza, 2002). PASA (posterior-anterior shift in aging) likewise describes a compensatory process focused on the PFC, though it emphasizes a shift from posterior, occipital activity to frontal activity during task completion (Davis, Dennis, Daselaar, Fleck, & Cabeza, 2008). It is significant to note that most of these models include dedifferentiation as an explanatory component. Used to describe a
dispersal of task completion brain activity from a bounded ROI to multiple or bilateral ROIs, dedifferentiation plays an important role in these models of cognitive aging.

The above models and referenced studies focus largely on region-specific or pair-wise brain changes in aging and memory. More broadly however, the brain can be considered to be a complex network or graph in which each brain region is a node and each functional connection between brain regions is an edge. Graph theory is a mathematical approach to analyzing the properties of such networks that is becoming increasingly common in functional imaging (Bullmore & Sporns, 2009).

Graph theory-based studies of healthy neural aging broadly have shown a decrease in network modularity and global efficiency with age as well as decreases in average local clustering/efficiency, though some results differ between studies, likely due to parcellation, thresholding, or preprocessing methods. (Achard & Bullmore, 2007; Geerligs, Renken, Saliasi, Maurits, & Lorist, 2014; Sala-Llonch et al., 2014; Song et al., 2014). In one recent study using this approach to study memory in the context of aging and brain, the authors report an association between memory performance and decreased clustering in memory circuits, including the DMN and hippocampus (Sala-Llonch et al., 2014). Decreased global clustering can be thought of as representing a dispersion of relatively local processing of information by recruitment of other ROIs and/or circuits. This finding indicates that predicted compensatory dedifferentiation and compensation in memory circuits is observable from a whole-brain network perspective.

One so far unexplored aspect of brain networks in aging is their relationship with performance on memory tasks like the Mnemonic Similarity Task (MST) (Kirwan & Stark, 2007). A visual object recognition and discrimination task, the MST is thought to tax
hippocampal pattern separation. In this task, participants encode a series of every-day objects for a later memory test. At test, participants are shown exact repeats (targets), completely novel foils, or lure stimuli that are conceptually and perceptually similar to the previously-viewed targets. Discrimination of the lures from the targets has been shown to be compromised in hippocampal amnesia (Kirwan et al., 2012). Additionally, healthy older adults consistently perform worse on lure discrimination in the MST than younger controls (Doxey & Kirwan, 2015; Toner, Pirogovsky, Kirwan, & Gilbert, 2009; Yassa, Lacy, et al., 2011). Given that this task is sensitive to small neurocognitive changes associated with aging, one goal of our study is to discover which of these neurocognitive changes are observable in a whole-brain network analysis approach.

To further explore complex network properties associated with memory in aging by utilizing brain network metrics relating to global connectivity, clustering, and efficiency, we will test the following hypotheses: (a) older adults will have decreased global efficiency and increased global clustering as measured by graph theory analysis of their resting-state functional MRI; (b) memory-related brain regions in the MTL and DMN will have higher global connectivity and lower clustering in subjects with better memory performance; and, (c) older adults with better memory performance will have higher global efficiency and lower global clustering overall.
Methods

Participants

Twenty-five younger (mean age=22.4 yrs; 11 males; mean years of education=14.4) and fourteen older adults (mean age=73.8 yrs; 6 males; mean years of education=16.3) were recruited for this study from the university and surrounding neighborhood. Participants were screened to include ages 18-30 for the younger adults and 60-90 for the older adults as well as only right-handed participants without any history of psychiatric or neurological disorders. All older adults underwent the Brief Cognitive Status Exam from the Wechsler Memory Scale (WMS) IV and scored in the normal range. The study was approved by the Brigham Young University Institutional Review Board (IRB), and all subjects gave informed consent before participating.

MRI Data Acquisition and Preprocessing

All participants were scanned with a Siemens 3T Tim Trio scanner using a 32-channel head coil at the BYU MRI Research Facility. Standard-resolution structural images were acquired using a T1-weighted MPRAGE sequence with the following parameters TR = 1900 ms; TE = 2.26 ms; slices = 176; flip angle = 9 degrees; FOV = 250 mm; matrix size = 256x215 mm; slice thickness = 1 mm; voxel size = 1 mm³. Resting state functional MRI (fMRI) data were acquired using a multi-band EPI sequence with the following parameters: multi-band factor = 4; TR = 1800 ms; TE = 42 ms; slices = 72; voxel size = 1.8 mm³; flip angle = 90 degrees; total acquisition time = 10 min. The first five volumes were discarded to allow for T1 equilibration. During the resting state scan, participants were instructed to lie still with their eyes open.

MRI preprocessing was performed using AFNI and ANTs software (Avants, Tustison, Song, & Gee, 2009; Cox, 1996). Preprocessing steps included the following: within-scan functional alignment; structural-to-functional scan alignment; registration of structural scan to a
template; warping of functional scan to template space; extraction of white matter (WM),
cerebrospinal fluid (CSF), and global signals; noise regression of motion parameters with first
derivatives, CSF, WM, and global signals; bandpass filtering from 0.008 to 0.08 Hz; and
censoring of TRs with motion exceeding 0.5 mm displacement.

**Graph Theory Analysis**

ROI definitions were taken from the AAL template with a new orbitofrontal cortex
parcellation, which were resampled to match the resting-state scan resolution (Rolls, Joliot, &
Tzourio-Mazoyer, 2015; Tzourio-Mazoyer et al., 2002). Time courses for each ROI were
extracted from individual subject scans in template space and were used to create functional
connectivity matrices with Pearson correlation coefficients representing functional connectivity
between ROI pairs. We used a relative threshold and preserved the strongest ten percent of all
possible edges in our binary connectivity matrices. We chose a ten percent threshold because
sparse thresholds have been shown to be most physiologically relevant and in order to maintain
comparability with previous studies (Sala-Llonch et al., 2014). We utilized implementations of
the MATLAB brain connectivity toolbox from (Rubinov & Sporns, 2010) to calculate graph
theory measures.

**Behavioral Testing**

We administered the WMS-IV subtests of Visual Reproduction (VR) I and II, Logical
Memory (LM) I and II and symbol span through the Q-Interactive iPad administration route,
with the older adults completing the older adult variants where applicable. The visual
reproduction task consisted of immediate and delayed (20-30 minutes) recall of presented visual
figures. The logical memory task included immediate and delayed (20-30 minutes) recall of two
different stories. The symbol span task is a visual working memory task that requires participants
to remember the identity and order of a series of symbols in order to select them from a new set of symbols on a subsequent screen. WMS IV data from 3 younger adults were lost in a technical error.

A mnemonic similarity task (MST) was also administered. Participants were presented with 128 color pictures of common objects (2 seconds each with 0.5 second inter-stimulus-interval) and were asked to respond to each by labelling it an “indoor” or an “outdoor” item. After a short delay, participants were given a recognition memory task. Sixty-four target, 64 lure, and 64 foil objects were presented. Participants were instructed to respond “old” to exact repeats (targets), “similar” to items that were similar to, but not identical with, previously-seen items (lures), and “new” to never-before-seen items (foils). We calculated a bias-corrected lure discrimination index (LDI) as follows: \[p(\text{“Similar”}|\text{Lure}) - p(\text{“Similar”}|\text{Foil})\]. Similarly, our bias-corrected recognition score was calculated as: \[p(\text{“Old”}|\text{Target}) - p(\text{“Old”}|\text{Foil})\]. Responses of 3 older adults were excluded because of incomplete or missing data due to failure to follow instructions.

Tests and Statistics

Statistical analyses were performed using SPSS (v25 SPSS Inc, Chicago, IL, USA). Analyses comparing young and old groups included years of education as a covariate.

Behavioral

A memory composite score was created from a subset of behavioral measures of interest from the WMS-IV. The following were included after conversion into z-scores for equal weighting: VR II, the delayed score from the LM story that was common across young and old groups, and SS. Partial correlations were calculated between the above-mentioned behavioral measures as well as with MST Lure discrimination scores while correcting for age. In addition,
one-tailed t-tests were performed on behavioral measures of interest to examine mean performance differences between young and old groups.

**fMRI**

We compared global graph theory measures between young and old subjects, including global efficiency, global clustering, and global modularity. Global efficiency is defined as the average for all pairs of ROIs of the inverse of the shortest path between an ROI pair. Global clustering is the average of the local clustering coefficients, where the clustering coefficient represents the proportion of a node’s neighbors that are connected to each other. Global modularity is a measure which represents how well a brain graph divides into distinct non-overlapping modules. One way ANCOVAs with age group as a fixed factor were performed for these measures to test for age effects while correcting for education level.

In addition, we defined a subset of memory-relevant ROIs for more specific testing of network effects. We selected DMN regions due to previous studies indicating that DMN function alters with age in regards to memory (Andrews-Hanna et al., 2007; Sala-Llonch et al., 2014; Wang et al., 2010). Our DMN network definition within the AAL atlas came originally from (Rosazza & Minati, 2011), with application to the AAL atlas by (Van Dellen et al., 2013). Here the DMN is defined as including precuneus, posterior cingulate gyrus, inferior parietal gyrus, and medial prefrontal gyrus (all bilateral). In addition, we included the classically memory-related MTL subregions of the bilateral hippocampus and parahippocampal gyrus. In order to address the question of differential effects of aging on local graph structure, we performed partial correlation analyses on the old and young adult groups separately of WMS composite and lure discrimination memory scores with the local graph theory metrics of clustering coefficient, degree, and centrality from each predefined ROI while correcting for education level. An ROI’s
degree is its number of connections with other nodes in the graph, and the centrality of an ROI is a hub measure defined as the proportion of shortest paths in the graph which pass through it. We corrected for multiple comparisons by using a partial Bonferroni stepdown at $p \leq 0.005$. 
Results

Behavioral

A partial correlation analysis of behavioral measures revealed significant correlations between the WMS composite score and the other WMS sub-test scores (VR II, LM II, SSP; p<.0001), as well as between the WMS composite score and the MST lure discrimination score (p<.05). In addition, the LM II score significantly correlated with the lure discrimination score (p<.05).

Table 1 Behavioral Partial Correlation Matrix.
Matrix representing partial correlations for WMS-IV and MST behavioral scores while correcting for age. Correlation corresponds to Pearson’s r, and significance corresponds to the p-value of the significance test. Abbreviations: VR2, delayed visual reproduction score; SSP, symbol span; LM2, logical memory delayed score; PS score, pattern separation score. ( * p<0.05, *** p<0.001)

<table>
<thead>
<tr>
<th></th>
<th>VR2</th>
<th>SSP</th>
<th>Composite</th>
<th>LM2</th>
<th>PS score</th>
</tr>
</thead>
<tbody>
<tr>
<td>VR2</td>
<td>1.000</td>
<td>.054</td>
<td>.521</td>
<td>-.085</td>
<td>.120</td>
</tr>
<tr>
<td></td>
<td>Significance</td>
<td>.385</td>
<td>.001***</td>
<td>.325</td>
<td>.261</td>
</tr>
<tr>
<td>SSP</td>
<td>Correlation</td>
<td>.000</td>
<td>.576</td>
<td>.029</td>
<td>.185</td>
</tr>
<tr>
<td></td>
<td>Significance</td>
<td></td>
<td>.0003***</td>
<td>.438</td>
<td>.160</td>
</tr>
<tr>
<td>WMS</td>
<td>Correlation</td>
<td></td>
<td>1.000</td>
<td>.625</td>
<td>.376</td>
</tr>
<tr>
<td></td>
<td>Significance</td>
<td></td>
<td></td>
<td>.0009***</td>
<td>.019*</td>
</tr>
<tr>
<td>LM2</td>
<td>Correlation</td>
<td></td>
<td></td>
<td>1.000</td>
<td>.325</td>
</tr>
<tr>
<td></td>
<td>Significance</td>
<td></td>
<td></td>
<td></td>
<td>.037*</td>
</tr>
<tr>
<td>PS score</td>
<td>Correlation</td>
<td></td>
<td></td>
<td></td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>Significance</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</table>

T-tests across group of age-dependent differences in memory scores show that the young group outperformed the old group on all measures of interest except for the logical memory subtest. (Table 2; p<.001).
Table 2: Descriptive Statistics and T-test Results for Behavioral Scores. The young group scored significantly better on all tests and subtests except for the logical memory subtest of the WMS-IV (**p<.001).  

<table>
<thead>
<tr>
<th></th>
<th>Group</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>t</th>
<th>p</th>
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<tbody>
<tr>
<td>Lure Discrimination</td>
<td>Young</td>
<td>25</td>
<td>.43</td>
<td>.15</td>
<td>3.7</td>
<td>.0008***</td>
</tr>
<tr>
<td></td>
<td>Old</td>
<td>10</td>
<td>.22</td>
<td>.14</td>
<td></td>
<td></td>
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<tr>
<td>VR2</td>
<td>Young</td>
<td>22</td>
<td>35.13</td>
<td>6.44</td>
<td>4.77</td>
<td>.00004***</td>
</tr>
<tr>
<td></td>
<td>Old</td>
<td>13</td>
<td>23.69</td>
<td>7.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSP</td>
<td>Young</td>
<td>22</td>
<td>28.36</td>
<td>4.47</td>
<td>4.97</td>
<td>.00002***</td>
</tr>
<tr>
<td></td>
<td>Old</td>
<td>13</td>
<td>20.15</td>
<td>5.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LM</td>
<td>Young</td>
<td>22</td>
<td>14.86</td>
<td>3.75</td>
<td>1.26</td>
<td>.22</td>
</tr>
<tr>
<td></td>
<td>Old</td>
<td>13</td>
<td>13.00</td>
<td>4.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WMS Composite</td>
<td>Young</td>
<td>22</td>
<td>1.25</td>
<td>1.38</td>
<td>6.04</td>
<td>.0000009***</td>
</tr>
<tr>
<td></td>
<td>Old</td>
<td>13</td>
<td>-1.47</td>
<td>1.10</td>
<td></td>
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</table>

**Brain Networks and Memory in Aging**

A group-wise ANCOVA revealed that there were no differences between groups in global efficiency, clustering, or modularity whether or not we corrected for education level. We tested to see if any global graph theory metrics correlated with the WMS composite score or the MST lure discrimination score. We found no significant relationships between the WMS composite or lure discrimination score and the global graph theory metrics in a partial correlation analysis, including while correcting for education or age.

We tested for local graph structure interactions with age and memory as described above. We found that in the older but not younger adult group, lure discrimination score correlated significantly with the centrality of the right hippocampus (r=.837, p<.005). Since this finding appeared to be influenced by a subject in the older adult group with a particularly high lure discrimination score, we tested for a correlative relationship between lure discrimination and right hippocampus centrality across all subjects combined and confirmed the presence of this relationship in the broader subject pool (Figure 1; r=.463, p=.006).
To further investigate this effect, we separated the older adult group by median split on composite WMS score. We chose the WMS composite to separate the older adults by memory performance, because three of the older adults were missing useable MST results. We performed a one-way ANCOVA across these memory performance groups while correcting for education on right hippocampus centrality and observed a main effect of group. There was a significant effect of group on right hippocampus centrality ($p=.034$, $\eta^2_p=.196$; Figure 2).
Figure 2 One-way ANCOVA of Right Hippocampus Centrality by WMS composite groupings. There is a significant main effect of group on centrality with education as a covariate. Post-hoc t-tests show that this difference is driven by the significant difference between the Young and Older Poor Memory groups (* p<0.05).

Post-hoc comparisons showed that the young group (marginal mean=.011, SE=.002) and older poor memory group (marginal mean=.001, SE=.004) differed significantly in centrality (p=.034), whereas the other pair-wise comparisons between groups were not significantly different.
Discussion

The absence of global graph differences between young and old groups is not unprecedented. While some studies have reported selective global differences correlating with aging (Achard & Bullmore, 2007; Onoda & Yamaguchi, 2013; Sala-Llonch et al., 2014; Song et al., 2014), others have observed no difference in specific tests (Meunier, Achard, Morcom, & Bullmore, 2009), and most studies have reported only a subset of global graph metrics, leaving uncertainty regarding reliable age differences in unreported metrics. In addition, inter-study differences such as group selection from different populations or differences in study protocol may be masking consistent results. These differences extend to analytical choices as well, since decisions regarding node selection, thresholding, and preprocessing methods have been shown to affect brain graphs non-trivially (Aurich, Alves Filho, Marques da Silva, & Franco, 2015; Gargouri et al., 2018; Zalesky et al., 2010). The lack of observed correlation between memory scores and global graph theory metrics may be attributable to limited locality of demand or effect. The demand that the MST places on hippocampal pattern separation and the difference with age in ability to meet this demand are possibly relatively focal to hippocampal subregions and functionally adjacent subnetwork that is small enough to not impact global graph theory metrics when altered (Yassa & Stark, 2011). If WMS-IV demands on brain networks are analogous, then both these scores and MST scores might be expected to correlate with network metrics only insofar as the metrics are as focal as the subnetwork demands.

In that context, it is not surprising that we observe a significant relationship between right hippocampus centrality and lure discrimination score in our older adult group and a stratification of right hippocampus centrality levels according to memory performance grouping. The significantly smaller right hippocampus centrality in older adults with poor memory suggests that
hippocampus integration in the broader brain network may play a role in determining lure discrimination memory performance and may interact with hippocampus subfield pattern separation processes. The centrality of the hippocampus in the brain graph represents part of its “hubness,” or its importance to global information flow within the graph. Recent studies exploring hub structures in the human brain have identified a set of brain regions that typically can be distinguished as structural or functional hubs, including the precuneus, cingulate gyrus, ventromedial frontal cortex and inferior parietal regions (Cole, Pathak, & Schneider, 2010; Tomasi & Volkow, 2010; van den Heuvel & Sporns, 2013; Zuo et al., 2011). While many of these studies do not classify the hippocampus as a major brain network hub, the hippocampus has been observed to act as a hub region in some settings (Mišić, Goñi, Betzel, Sporns, & McIntosh, 2014; van den Heuvel & Sporns, 2011). Misic et al. describe the nature of hippocampal connections in the Macaque brain using the CoCoMac database. Utilizing a computational model of brain communication dynamics, they predict a network funneling of information flow traffic through CA1. According to this model, despite its lack of observable hub characteristics when accounting for structural tract connectivity alone, CA1 is an effectual sink for network information flow after considering network communication dynamics. Van den Heuvel and Sporns found by DTI measures of structural connectivity that the hippocampus was among a set of “rich-club” brain regions, which have both high whole-brain connectivity and high intraconnectivity within their own rich-club subnetwork. These two studies indicate that the hippocampus may play an important role in whole-brain network dynamics as a hub region. The findings of the current study demonstrate that preservation of the hippocampus as a high centrality hub region contributes to maintenance of memory function in aging. These findings parallel those of other studies linking brain hub profiles with other neurocognitive traits such as
intelligence and personality (Adelstein et al., 2011; Bassett et al., 2009; Li et al., 2009; Tomasi & Volkow, 2011).

On a smaller scale, the pattern separation processes in the hippocampus that are thought to be associated with lure discrimination are specific to hippocampal subfields (Kirwan & Stark, 2007; Yassa, Mattfeld, Stark, & Stark, 2011; Yassa & Stark, 2011). Furthermore, deficits in lure discrimination in aging have been shown to be associated with increased CA3 and dentate gyrus activity and other memory deficits with increased hippocampus activity (Miller et al., 2008; Yassa, Lacy, et al., 2011). The coherence of this trend with the present study’s centrality findings is explored as follows. When integrated into the brain network in healthy young and cognitively preserved older adults, the hippocampus acts as a relative hub, functionally connected with sensory and association cortices in such a way as to be an efficient route for information flow. It could be that in older adults with decreasing memory capacity, the hippocampus and its subnetwork of functional connections undergo a functional reorganization as part of atrophy, scaffolding, and compensation processes, that ultimately leads to less efficient information flow through the hippocampal hub. Such an efficiency deficiency might lead to locally increased hippocampus activity as an attempt to compensate for broader network reorganization.

The correlation of hippocampus centrality with lure discrimination score is present only in the right hippocampus. As cited above, increased activation specifically in the right hippocampus has been observed during lure discrimination portions of the MST (Yassa, Lacy, et al., 2011). Differences in the laterality of functional activity during the MST have been observed in at least one other study and were attributed to laterally distinct spatial or semantic information processing within the right and left hippocampus, respectively (Motley & Kirwan, 2012). The version of the MST used in the current study did not rely on stimulus sets using primarily
rotation as a method for producing similar stimuli, however, some of the lures nonetheless have a rotation component. If participants relied on these spatial cues to identify lure stimuli, then it is feasible that information flow through the right hippocampus particularly would affect MST task performance.

**Limitations and Future Directions**

The primary limitation of this study is its limited sample size. While relatively small sample sizes are sometimes well suited for efficiently observing large effects, they can also increase the chance of false positives. Such being the case, the findings of this study should be further explored with a larger dataset.

The interface of aging, memory, and brain networks remains relatively open for exploration. For instance, brain module composition or number may change differentially in aging with effects on memory performance. Other analysis routes include further characterization of the subnetworks underlying the observed hippocampus centrality differences between groups. A qualitative comparison of hippocampus subnetwork composition would shed light on the practical significance and implications of this study. Furthermore, the subnetwork of the hippocampus as elucidated by such a qualitative description could be explored as regions relevant to hippocampal pattern separation that have not yet been accounted for.
References


CURRICULUM VITAE
Ty Bodily
bodilyty@gmail.com

Education

Brigham Young University (BYU) Provo, UT
M.S. Neuroscience, expected August 2018

Brigham Young University Provo, UT
B.S. Neuroscience, B.A. Russian August 2016

Fellowships/Grants

BYU Departmental and University Travel Grants ($1,500)
October 2017

BYU Gerontology Program Research Grant ($10,000)
May 2017

Major Contributor—Sorenson Legacy Foundation Grant for an fMRI Study of Chronic Pain. P.I. David Busath. ($25,000)
November 2016

BYU Library Student Research Grant ($1,500)
October 2016

BYU MRI Facility Seed Grant for Chronic Pain Study. P.I. David Busath. ($5,000)
November 2015

BYU MRI Facility Seed Grand for Chronic Pain Study. P.I. David Busath ($5,000)
November 2014

Graduate Research

Research with Dr. Brock Kirwan, August 2016 - Present
Collect multimodal MRI and WMS-IV memory performance data from young and old adults. Extract and analyze functional brain graphs using AFNI, ANTS, and MATLAB to examine brain network correlates of memory in aging.

Research with Dr. David Busath June 2016 - Present
Lead planning and collection of resting-state fMRI and subjective pain report data in a treatment trial of two transcutaneous nerve stimulation (TENS) protocols. Analyze functional network data from an emotional network dysregulation standpoint.

Research with Drs. Ross Larsen and Jeff Jenkins August 2016 - Present
Examine respondent fatigue effects in computerized personality survey. Perform exploratory factor analysis on mouse cursor movement measures. Perform mixed model analysis to identify observable fatigue effects over time.

Undergraduate Research
Research with Drs. David Busath and Alonzo Cook August 2014 – August 2016
Perform dual whole-cell patch clamp in neuroblastoma cell cultures to monitor current flow through gap junctions. Run behavioral experiments on rodents.

Publications

Peer-reviewed Articles

Encyclopedia Entries


Poster Presentations


Service Experience

Reviewer—assisted Principle Investigator in article review
   Human Brain Mapping

Presidency of Science Policy Club
September 2016 – April 2017
   Promote pro-science legislative policy by facilitating contact between the student population and local legislators.

Technical Experience

Software and Programming
Analysis of Functional NeuroImages (AFNI)
   Build scripts for preprocessing structural and functional MRI images with emphasis on processing resting-state fMRI data. Perform univariate analyses of group effects and interactions in task-based fMRI.

Advanced Normalization Tools (ANTS)
   Build scripts for creating study-specific or broadly-purposed templates as well as skull stripping and subject-template warping during preprocessing.

MATLAB
   Build scripts for graph theory analyses of resting-state fMRI data, utilizing the Brain Connectivity Toolbox (BCT).

Other: R, JMP, Shell Scripts