MCKNIGHT BRAIN RESEARCH FOUNDATION

October 3, 2010

(Russell Board Room, JW Marriott Hotel)
Washington, DC

AGENDA

Sunday, October 3, 2010		
12:00 pm. – 12:30 p.m.	Call to Order/Lunch	Teresa Borcheck
12:30 p.m. – 1:00 p.m.	Approval of Minutes from Board Meeting August 10-11, 2010	Teresa Borcheck
	Minimum Distribution Calculation	
1:00 p.m. –2:00 p.m.	Investment and IPS Review	Michael Hill *(Via teleconference)*
2:00 p.m. – 2:15 p.m.	Break	
2:15 p.m. – 3:30 p.m.	Upcoming Dates & Events	Teresa Borcheck

- ❖ University of Arizona Site Visit/ Board of Trustees Meeting
  Tucson, AZ--October 25-26, 2010
- ❖ Society for Neuroscience 2010 McKnight Poster Session
  San Diego, CA--November 14, 2010
- ❖ Board of Trustees Meeting
  February, 2011--University of Alabama Site Visit?
- ❖ Inter-Institutional Meeting
  Miami, FL--May 1-3, 2011--Estimated Expenses
- ❖ University of Miami Gift Agreement
- ❖ Strategic Planning/Tag Line Follow up

3:30 p.m. – 4:00 p.m.	Grant Inquiries (Columbia University)	Teresa Borcheck
4:00 p.m. – 5:00 p.m.	Columbia University	Dr. Scott Small & Amelia Alverson, VP for Development, Columbia, University
5:00 p.m.	Adjournment	
6:15 p.m.	Dinner at Restaurant 1789	

Monday, October 4, 2010
8:30 a.m. – 5:00 p.m. Cognitive Aging Summit 2010
(Breakfast at 7:30 a.m., Reception at 6 p.m.)

Tuesday, October 5, 2010
8:30 a.m. – 4:00 p.m. Cognitive Aging Summit 2010
(Breakfast at 7:30 a.m., Executive Session at 1:30 p.m.)

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION
BOARD OF TRUSTEES MEETING
August 10-11, 2010

August 10, 2010
The quarterly Trustee's meeting of the McKnight Brain Research Foundation (MBRF) was called to order at 12:30 p.m. on August 10, 2010 on the 16th floor of the Lincoln Plaza Building, Orlando, Florida.

The following members were present:
Dr. John Clarkson, Trustee
Dr. J. Lee Dockery, Trustee
Dr. Nina Ellenbogen Raim, Trustee
Dr. Judith Salerno, Trustee
Mrs. Teresa Borcheck, Corporate Trustee
SunTrust Bank Institutional Investment Solutions

Others attending:
Mr. Henry H. Raattama, Jr., Legal Counsel
Mr. Michael Hill, Managing Director, SunTrust Institutional Investment Advisors
Mr. Dan Ledbetter, Product Manager, Lighthouse Partners
Ms. Tiffany Ahlfield, SunTrust Bank, Foundation & Endowments Specialty Practice
Mr. Mike Batts, CPA, Batts, Morrison, Wales & Lee, P.A.
Ms. Michele Wales, CPA, Batts, Morrison, Wales & Lee, P.A.

Via teleconference:
Ms. Shelly Simpson, Asset Allocation Analyst, SunTrust Institutional Investment Advisors
Mr. Harry B. Leggat, Associate Director of Private Markets, Hammond Associates
Mr. Michael LeVar, Co-Director of Hedge Funds, Hammond Associates

1. Approval of Minutes

The minutes of the April 28, 2010 meeting of the McKnight Brain Research Foundation were reviewed. The minutes were approved as presented (Attachment 1).

Action Item 1: The trustees approved the minutes of the April 28, 2010 meeting as presented (Attachment 1).

2. Investment Review

Mr. Hill presented the investment review and commented on key economic and investment factors for the second quarter (Attachment 2). Equities continued to rally through most of

April as companies reported strong first quarter earnings and economic data was above expectations. In just two months, however, those gains were erased as new concerns arose over Europe's debt crisis and slowing US economic activity arose. Consequently, the fear of the euro zone fiscal crisis spreading to the rest of the globe caused stocks to correct sharply. Mr. Hill stated the European fiscal crisis will not be resolved quickly; however, it is believed it will only moderately affect growth in the US.

The decline in equities has been greater than the marginal weakening in fundamentals and the slight equity overweight and moderately positive investment outlook remains unchanged. The drivers of corporate profits all remain in place. Corporate balance sheets are flush with cash, rates are low, and the yield curve steep. Inflation should remain low, affording the Federal Reserve Board with flexibility on monetary policy. The zero interest rate policy will likely remain in place for several more quarters.

Sluggish bank lending appears to be holding back the recovery in the small business and services sectors. Passage of the financial services regulatory reform bill will ease, but not alleviate the regulatory and tax policy uncertainty which we believe is also impeding the recovery. The problems in Europe have provided an important alert for other countries to get their fiscal houses in order, a longer term positive effect.

Action Item 2: The trustees received the Investment Review for information (Attachment 2).

3. Efficient Frontier

Ms. Shelly Simpson presented the annual Asset Allocation Analysis/Strategic Allocation Solutions (SAS) update. Ms. Simpson explained to the Trustees that the capital market assumptions for various bond and stock indexes, as well as non-traditional asset classes, are below last year's estimated returns. This is because equity markets generally post a substantial rebound the year after a market crash, then contract over the next 3-5 years; therefore, equity returns are expected to be below their historical averages over the next 3-5 years. The same is also true for bonds since the assumption would include the currently low yields and slowly rising rates in the future. Mid-cap and small-cap stocks have slightly higher returns mostly due to an M&A (mergers and acquisitions) premium as companies look for ways to take market share and create synergies. International developed equities have had a higher return than domestic. The difference is mostly due to U.S. dollar weakness, although most advanced economies are hampered by high debt to Gross Domestic Product (GDP) and huge deficit spending. Emerging markets economies, especially in Asia and Latin America, look much more attractive in terms of economic growth and in terms of their debt to GDP ratios.

Ms. Simpson then discussed how the estimated investment return work is factored into the proposed portfolio. First, the overall portfolio returns are lower than the current portfolio. Again, the markets were up strongly last year, while this year the markets have been more volatile. In the proposed portfolio, overall cash is taken down, the alternatives sector is

reduced and the funds have been moved into private equities. The fixed income portion remains the same.

The current international bond allocation is transferred moved over to core fixed income. Large cap stock allocations will remain about the same as in the current portfolio. For the Mid-Cap sector, Russell Mid-Cap Growth has been added to the proposed portfolio. This area could continue to be an attractive place for investment in light of continued mergers and acquisitions activity. The Small-Cap equity allocation remains the same. In the international equities sector, both developed markets and emerging markets have been added, but emerging markets is the more attractive asset class. U.S. domestic equities have outperformed the developed equity markets over the last year by a wide margin and also over the last three years. Therefore, the fund has benefited from the lower weight in developed equity markets (as measured by MSCI EAFE Index). To hedge the probabilities, it is proposed that 2% of the portfolio be added to the international developed position. The allocation to Emerging Markets has been raised by 2.5%. This asset class has the best return potential out of all the asset classes, although it can be volatile.

In the Alternatives section, investments in Real Estate Investment Trusts (REITs) were removed from the portfolio last year since there were concerns over commercial real estate mortgages and the amount of debt that would need to be rolled over. Currently, valuations for REITs are extremely high and other more attractive investment opportunities exist in funding a private equity position. For the hedge fund positions, the Lighthouse L/S fund is still favored for performance and liquidity reasons.

Mr. Hill also discussed selling the Lighthouse Credit Opportunities fund, taking advantage of its good performance over the last year, and funding a diversified hedge fund allocation by possibly using Hammond's hedge fund of funds. He also proposed reducing Lighthouse's Diversified fund by half to fund a private equity position, possibly using Hammond's private equity fund of funds. Hammond's hedge fund of funds would give the portfolio more diversification in terms of managers, although the withdrawal terms appear to be stricter than Lighthouse's. Private equity was added to provide the fund with a higher return potential in order to meet funding goals and objectives over time. The private equity investment, however, would require funding over time. Therefore, completing a fully funded position could take a number of years since the portfolio would benefit by vintage diversity – which would mean that funding would be split among a series of "private equity funds" over several years.

Action Item 3: The trustees unanimously approved the recommended changes to the asset classes and the allocations in the MBRF Portfolio.

4. Lighthouse Partners

Mr. Ledbetter presented an update on the three Lighthouse funds held in the MBRF portfolio. The Diversified Fund is currently using the least amount of leverage since inception and was down .31% through June, with a cumulative rate of return of 46.99% since May of 2002. The

Global Long Short Fund was down 1.39% through June with a cumulative rate of return of 22.70% since October of 2005. This fund managed to do well amid continuing market volatility and was able to find attractive investment opportunities in select market sectors by utilizing their long short strategy. The Credit Opportunities Fund, which was added to the MBRF portfolio in June 2008, was up 3.58% for the year with a negative cumulative rate of return of 13.94%.

Action Item 4: The trustees received the Lighthouse presentation for information.

5. Hammond Associates

Mr. Harry Leggat, Associate Director of Private Markets and Mr. Michael LeVar, Co-Director of Hedge Funds from Hammond Associates gave an overview of their private equity offering via teleconference.

Action Item 5: The trustees received the Hammond Associates presentation for information (Attachment 3).

6. Investment Policy Review

After the investment review, a discussion of the recommendations of the Efficient Frontier analysis, Lighthouse Partners and teleconference with representatives from Hammond Associates, the Amended and Restated Investment Policy was reviewed and several changes were made as follows:

-Page 7-Appendix A
    -The 3.5% Allowance for Inflation should be changed to 3.1%.

-Page 8-Appendix B
    -Large Cap Equity should be changed to 37.1%
    -Mid Cap Equity should be changed to 7.1%
    -Small Cap Equity should be changed to 4.8%
    -International Equity should be changed to 15.6%
    -Hedge Funds should be changed to 20%
    -Private Equity should be changed to 5%
    -Fixed Income should be changed to 9.4%
    -Cash should be changed to 1%

The Amended and Restated Investment Policy Statement was approved as amended (Attachment 4).

Action Item 6: The Amended and Restated Investment Policy Statement was approved as amended (Attachment 4).

7. Tax Update

Mr. Mike Batts and Ms. Michele Wales from Batts, Morrison, Wales & Lee, P.A. met with the Trustees to provide them with an update on their progress (Attachment 5):

1. Summary of services provided by BMWL to date
   a) Analysis of IRS notices received for multiple years related to Forms 990-PF and 990-T confirmed that IRS properly refunded approximately $14,000 to MBRF.
   b) Preparation of Form 990-PF and Form 990-T for the FYE 6/30/2009.
   c) Amendment of prior years' Forms 990-T to claim 50% charitable contribution deduction and to correct reporting of long-term capital gains, which are taxed at lower rates.
      i. 6/30/2006 and 6/30/2008 amendments have been filed - resulting in refund claims totaling approximately $37,000
      ii. 6/30/2007 year to be filed (after research completed on potential net operating loss carry back discussed further below) - resulting in a refund claim of approximately $50,000.
   d) Identified Form 990-T filing requirement for 6/30/2003 and 6/30/2004 tax years, which were subsequently prepared by KPMG at the instruction of SunTrust.

2. Items still in process by BMWL
   a) Potential carry back of net operating loss in 6/30/2009 tax year arising from partnership investments - potential additional refunds of approximately $28,000
      i. Research regarding passive activity loss limitations in progress
   b) State tax return filing requirements - initial research indicates that a Florida return, and possibly other state returns, should be filed in connection with Forms 990-T filed by MBRF. Pending additional information from partnership regarding state activity for 6/30/2009 year.

3. Opportunity area - Classification of MBRF as a supporting organization
Mr. Batts explained that by being classified as a supporting organization, the MBRF would be exempt from paying the 2 percent excise tax on net investment income reported on the Form 990-PF. This could potentially save the Foundation up to $60,000 per year.

The Trustees advised Mr. Batts to continue further research in coordination with the corporate trustee (Teresa Borcheck) and MBRF legal counsel (Henry H. Raattama, Jr.) to determine the whether the MBRF would be eligible for classification as a "support organization" and the ramifications of doing so.

8. Minimum Distribution Calculation

The trustees reviewed the projected Minimum Distribution Calculation for information (Attachment 6).

9. Grant Inquiries-Medical College of Georgia

The proposal submitted by Ricardo Azziz from the Medical College of Georgia was reviewed and it was decided that the trustees are not currently able to consider the program because of prior grant commitments through 2013. Mrs. Borcheck will send the Medical College of Georgia a letter congratulating Dr. Joe Tsien and his team on their advancements, as well as inform them of the trustees' decision to decline funding the proposal.

Action Item 7: Mrs. Borcheck will send the Medical College of Georgia a letter with the trustees' decision to decline funding the proposal (Attachment 7).

10. Cognitive Aging Summit II

The Second Cognitive Aging Summit will be held on October 3-5, 2010 at the JW Marriott in Washington, DC. The trustees will arrive on the morning of October 3, 2010 and meet in the afternoon, beginning with lunch at 12:00. The Board meeting will begin immediately following lunch. The Summit will begin the morning of October 4, 2010 running through lunch on October 5, 2010. An executive session involving the program participants, the trustees and the respective staff from the National Institute on Aging (NIA) and the Foundation for the National Institutes of Health (FNIH) will be held in the afternoon of October 5, 2010. The reports from the grant recipients awarded through the Research Partnership on Cognitive Aging between the MBRF and the NIA will be reviewed on October 6, 2010.

Dr. J. Lee Dockery provided the agenda and an update on the status of the arrangements for Summit. He informed the trustees that flash drives will be used in place of binders in an effort to use a more agile, electronic approach to sharing the speakers PowerPoint presentations. The suggestion was made to have the wording, "McKnight Brain Research Foundation" imprinted on each of the flash drives. The trustees also thought the idea of posting the slides on the FNIH web site with a link to the MBRF web site would be beneficial and hope it will be possible without violating the 508 compliance requirements of the NIA.

Action Item 8: Dr. J. Lee Dockery will contact Julie Wolf-Rodda at the FNIH to finalize the arrangements for the Cognitive Aging summit II.

11. University of Arizona

The trustees discussed the board meeting that will be held October 25-26, 2010 in Tucson, AZ in conjunction with a site visit at the University of Arizona. The site visit, hosted by Dr. Carol Barnes, will begin at 1:00 PM on the afternoon of Monday, October 25th followed up with a reception and dinner and continued discussions that evening. The board meeting will begin the morning of October 26th and conclude not later than 12:00 noon.

12. Society for Neuroscience 2010 McKnight Poster Session

The event is a MBRF sponsored and hosted event for graduate students and faculty who will be attending the meeting from each of the four institutions to which the MBRF provides funding. The trustees are invited to attend the event, which will be held on Sunday,

November 14, 2010 from 6:30-8:30 pm at the San Diego Marriott Ballroom in San Diego, CA and will feature scientific poster displays from each of the four institutions.

13. University of Miami Gift Agreement

Mrs. Borcheck and Mr. Raattama advised the Trustees that there is still some confusion at the University of Miami regarding the spendable dollars for the Center from the unfunded (unmatched) portion of the endowment. Mr. Raattama and Mrs. Borcheck will continue to work with the University to resolve the issue.

Action Item 9: Mr. Raattama and Mrs. Borcheck will continue to work with the University of Miami (UM) to resolve the understanding and the commitment by the University of Miami regarding the investment return and spendable dollars for the unmatched portion of the MBRF gift to the University of Miami.

14. MBRF Endowment to University of Alabama (UAB)

The MBRF Trustees discussed the second of five $1,000,000 payments, plus the second and last payment of $500,000 for operational costs by the MBRF, due on October 1, 2010, to fund the MBRF Endowment to the UAB. The trustees unanimously agreed to make the second payment on schedule. Mrs. Borcheck will prepare a letter notifying Dr. Shirley Salloway Kahn, vice president for development, alumni and external relations at the UAB of the MBRF's intentions to make the second payment on schedule (Attachment 8).

Action Item 10: Mrs. Borcheck will prepare a letter notifying Dr. Shirley Salloway Kahn, vice president for development, alumni and external relations at the UAB of the MBRF's intentions to make the second payment on schedule (Attachment 8).

15. Tag Line to Accompany the MBRF Logo

The trustees reviewed a list of suggested tag lines suggested by a faculty member at the University of Miami to be printed in conjunction with the MBRF logo (Attachment 9). Each of the trustees submitted votes for their first three choices and requested Ms. Borcheck and Ms. Ahlfield to perform and informal survey among the SunTrust employees to determine a favorite tag line among individuals representing the Public.

Examples: McKnight Brain Research Foundation, *Preserving Memory Through Research.* Or: *Preserving Memory, Enhancing Life* **General Electric**: *"We light up your life."*

Action Item 11: The Corporate trustee will tabulate the choices of the trustees for a tag line to accompany the MBRF logo, seek public reaction among the employees of SunTrust and report the findings at a future meeting of the MBRF.

There being no further business, the meeting adjourned at 6:15 p.m.

Summary of Action Items:

Action Item 1: The trustees approved the minutes of the April 28, 2010 meeting as presented (Attachment 1).

Action Item 2: The trustees received the Investment Review for information (Attachment 2).

Action Item 3: The trustees unanimously approved the recommended changes to the asset classes and the allocations in the MBRF Portfolio.

Action Item 4: The trustees received the Lighthouse presentation for information.

Action Item 5: The trustees received the Hammond Associates presentation for information (Attachment 3).

Action Item 6: The Amended and Restated Investment Policy Statement was approved as amended (Attachment 4).

Action Item 7: Mrs. Borcheck will send the Medical College of Georgia a letter with the trustees' decision to decline funding the proposal (Attachment 7).

Action Item 8: Dr. J. Lee Dockery will contact Julie Wolf-Rodda at the FNIH to finalize the arrangements for the Cognitive Aging summit II.

Action Item 9: Mr. Raattama and Mrs. Borcheck will continue to work with the University of Miami (UM) to resolve the understanding and the commitment by the University of Miami regarding the investment return and spendable dollars for the unmatched portion of the MBRF gift to the University of Miami.

Action Item 10: Mrs. Borcheck will prepare a letter notifying Dr. Shirley Salloway Kahn, vice president for development, alumni and external relations at the UAB of the MBRF's intentions to make the second payment on schedule (Attachment 8).

Action Item 11: The Corporate trustee will tabulate the choices of the trustees for a tag line to accompany the MBRF logo, seek public reaction among the employees of SunTrust and report the findings at a future meeting of the MBRF.

Respectfully Submitted,

Teresa W. Borcheck
SunTrust Bank, Corporate Trustee

McKnight Brain Research Foundation
Minimum Distribution Calculation
Fiscal years 2000 - 2010

Market Value Dec 1999 -$69,126,583	*Tax Year*	*Distributable Amount*	*Qualifying Distributions*	*Excess Distributions Carryover*	*Undistributed Income*
$45,973,696	7/1/02 - 6/30/03	$1,954,735	$148,481	$5,953,272	$0.00
$51,867,213	7/1/03 - 6/30/04	$2,352,435	$1,665,404	$5,266,241 (last year we could carryover gift to UF	$0.00
$51,898,266	7/1/04 - 6/30/05	$2,450,345	$3,026,049	$575,704	$0.00
$55,777,369	7/1/05 - 6/30/06	$2,620,008	$2,036,659	$0	$7,645.00
$62,782,831	7/1/06 - 6/30/07	$2,843,725	$3,299,931	$448,561	$0.00
$54,753,484	7/1/07 - 6/30/08	$2,817,569	$3,110,508	$292,939	$0.00
$39,447,094	7/1/08-6/30/09	$2,016,762	$2,517,340	$500,578	$0.00
$39,991,364	7/1/09-6/30/10	$2,034,286 (estimate)	$3,855,267 (estimate)	$1,820,981 (estimate)	$0.00
$40,700,866 (estimated)	7/1/10-6/30/11	$2,004,517 (estimate)	$3,724,222 (estimate)	$1,719,703 (estimate)	$0.00
			$38,605,719	$4,782,762	(estimated total excess carryover)

McKnight Brain Research Foundation

Average Fair Market Value Calculation
Estimate For Fiscal Year Ending 6/30/2011
As of September 21, 2010

July 2010	$39,804,849.85
August 2010	$38,789,117.77
September 2010	$40,981,643.32
October 2010*	$40,981,643.32
November 2010*	$40,981,643.32
December 2010*	$40,981,643.32
January 2011*	$40,981,643.32
February 2011*	$40,981,643.32
March 2011*	$40,981,643.32
April 2011*	$40,981,643.32
May 2011*	$40,981,643.32
June 2011*	$40,981,643.32

* Values from 10/01/10 - 6/30/2011 are estimated assuming a flat return over that 9 month period

Average Fair Market Value	**$40,700,866.74**

McKnight Brain Research Foundation

Projected Minimum Investment Return Calculations

(As of 9/21/2010 for fiscal year ending 6/30/2011)

Average Fair Market Value		$40,700,866.74
Less:		
	Cash held for charitable purposes (1 1/2 %)	($610,513.00)
Net value of non-charitable use assets		$40,090,353.73
Minimum Investment Return (5%)		$2,004,517.69

Net Minimum Investment Return Calculation:

Minimum investment return		$2,004,517.69
Less:		
**	Distributions as of 9/21/10	($2,000,000.00)
	UAB Grant Payment	($1,500,000.00)
sub total	Qualifying Distributions	($3,724,221.63)
		($1,719,703.94)
	Excess distribution carryover (actual for '07, '08, '09, estimated for '10)	$3,063,059.00
		$3,063,059.00
		$1,719,703.00
		$4,782,762.00

** ($1,000,000 FNIH, $1,000,000 U of A)

Grant Commitments Schedule

9/22/2010

Organization Request ID/Ref.	Grant Total	Paid Prior Years	Paid YTD	Scheduled Payments 2010	 2011	 2012	Remaining Balance
2009							
Foundation for the National Institutes of	$5,000,000.00	$1,000,000.00	$1,000,000.00 (paid 7/26/2010)	$0.00	$1,000,000.00	$1,000,000.00	$1,000,000.00
University of Alabama School of Medicine	$6,000,000.00	$1,500,000.00	$0.00	$1,500,000.00 (scheduled for 10/1/2010)	$1,000,000.00	$1,000,000.00	$1,000,000.00
Total 2009 (2 items)	$11,000,000.00	$2,500,000.00	$1,000,000.00	$1,500,000.00	$2,000,000.00	$2,000,000.00	$2,000,000.00
Grand Total (2 items)	$11,000,000.00	$2,500,000.00	$1,000,000.00	$1,500,000.00	$2,000,000.00	$2,000,000.00	$2,000,000.00

The Investment Review is under the Investment Information Folder

APPENDIX A

This Appendix A was adopted at the 8/10/2010 Board Meeting

Spending Policy of McKnight Brain Research Foundation

Expenses as Permitted	1.0%
Allowance For Inflation**	3.1%
Distribution From Foundation	5.0%
Target Total Return	9.1%

** Real inflation is Biomedical Research and Development Price Index ("BRDPI") published by the U.S. Bureau of Economic Analysis. .

APPENDIX B

This Appendix B was adopted at the 8/10/2010 Board Meeting

McKnight Brain Research Foundation
Portfolio Guidelines

Asset Class	2010 Efficient Frontier	Range	Benchmark	Peer Group*
Large Cap Equity	37.1%	30% - 60%	S & P 500	Pure Large Cap Core
Mid Cap Equity	7.1%	5% - 14%	Russell Mid Cap	Mid Cap
Small Cap Equity	4.8%	0% - 15%	Russell 2000	Broad Small Cap
International Equity	15.6%	5% - 20%	MSCI - EAFE	Broad International Equity
Hedge Funds	20%	10% - 30%	HFR Fund of Funds Index	
Real Estate – U.S.	0%	0% - 10%	NAREIT Equity	
Real Estate – Non U.S.	0%	0% - 10%	DJW Global ex-U.S. Real Estate	
Private Equity	5%	0% - 10%	Cambridge Associates U.S. Private Equity	
Fixed Income	9.4%	0% - 10%	Barclays Agg Index	
Cash	1%			
	100%			

Static Benchmark #1

Russell 3000 Index	65%
Barclays U.S. Aggregate Index	35%
	100%

Spending Policy Benchmark

Distribution	5.0%
Expenses	1.0%
Inflation**	3.1%
	9.1%

* Mobius Group
M-Search Data Base System – Universes
Universes for peer group comparison – recommended by SunTrust and adopted by Trustees on 7/12/00. SunTrust advises there are no Alt/Hedge Fund, Real Estate or International Fixed Income Peer Groups.

** Real inflation is Biomedical Research and Development Price Index ("BRDPI") published by the U.S. Bureau of Economic Analysis. .

McKnight Brain Research Foundation

Upcoming Dates/Events (2010 - 2011)

2010

October 2010	November 2010
MBRF Board of Trustees Meeting ***University of Arizona Site Visit*** ***Tucson, AZ*** October 25-26, 2010	**Society for Neuroscience** ***2010 McKnight Poster Session*** ***San Diego, CA*** November 14, 2010 6:30-9:00pm

2011

February 2011	April 2011	July 2011
MBRF Board of Trustees Meeting February 2011 **Topics:** 1. Annual Compensation Review 2. Annual Reports from Institutions 3. 990 PF 4. UF 50/50 Deadline (11/3/2011)	***MBRF Board of Trustees Meeting*** University of Miami May 1-3, 2011 Inter-Institutional Meeting	***MBRF Board of Trustees Meeting*** July 2011 **Topics:** 1. Asset Allocation Analysis 2. Lighthouse Presentation 3. UAB Payment 4. Review Investment Policy

McKnight Inter-Institutional Meeting
May 1st, & 2nd, 2011
Estimated Expenses
Draft Budget 9/17/2010 Miami Beach Hotel and Spa

Hotel	# of rooms	# of nights	Cost per night	Tax (13%)	Resort Fee	Total	
University of Alabama	32	2	$129.00	$0.00	$12.00	$8,280.00	
University of Arizona	32	2	$129.00	$0.00	$12.00	$8,280.00	
University of Florida	32	2	$129.00	$0.00	$12.00	$8,280.00	
University of Miami	2	2	$129.00	$0.00	$12.00	$540.00	
	98					**$25,380.00**	**Estimated Total**

Flights	Number	Average Cost per flight		Total	
University of Alabama	32	$300.00		$9,600.00	
University of Arizona	32	$475.00		$15,200.00	
University of Florida	32	$735.00	Coach America $2000 each way	$4,000.00	**Estimate based on last year**
				$28,800.00	**Estimated Total**

Food Sunday May 1, 2011	# attending	Cost	Service (21%)	Tax (9.0%)	Total	
Trustee Lunch	10	$250.00	$52.50	$0.00	$302.50	
Reception (Full Fare)	150	$3,000.00	$630.00	$0.00	$3,630.00	
Wine and Beer	150	$2,000.00	$420.00	$0.00	$2,420.00	
Flowers	-	$250.00	-	-	$250.00	
Monday May 2, 2011						
Breakfast Buffet	175	$27.00	$992.25	$0.00	$5,717.25	
AM Break	175	$7.50	$275.63	$0.00	$1,588.13	
Buffet Lunch (per person)	175	$40.00	$1,470.00	$0.00	$8,470.00	****The 175 number**
PM Break	175	$10.00	$367.50	$0.00	$2,117.50	**includes local attendees**
Miami Beach Hotel	175	$70.00	$2,572.50	$0.00	$14,822.50	**Includes Cocktails for 1hr**
Wine and Beer	175	$18.00	$661.50	$0.00	$3,811.50	
Tuesday May 3, 2011						
Breakfast Buffet	125	$27.00	$708.75	$0.00	$4,083.75	
AM Break	175	$7.50	$275.63	$0.00	$1,588.13	
Boxed Lunch (per person)	125	$25.00	$656.25	$0.00	$3,781.25	
Meeting Rooms-Rental	125	$0.00	$0.00	$0.00	$0.00	
					$52,582.50	**Estimated Total**

Audio/Visual
Projector, Screen, Laptop, Power Strip, Tech Support - $1000 a day (+ fees) **$2,000.00** **Estimated Total**

Miscellaneous

Printing Fees	$1,500.00	**$1,500.00**	**Estimated Total**
Posterboards (moving expense)	$0.00	**$0.00**	
		$110,262.50	**ESTIMATED TOTAL**

Memorandum of Understanding

McKnight Brain Research Foundation Gift agreement
University of Miami Medical School

The purpose of this memorandum is to clarify the intent and understanding of the trustees of the Evelyn F. McKnight Brain Research Foundation ("Trustees") and the Evelyn McKnight Center for Age Related Memory Loss ("Center") at the University of Miami Miller School of Medicine ("UM") which has been fully operational since June, 2008.

The goal of the first amendment to the Gift Agreement dated July 29, 2008 was two-fold, 1. Insure that the unfunded portion of the endowment continued to grow at the same rate as the funded balance; 2. The Center will receive spendable income at the same rate of return on the unfunded balance as the rate received on the funded balance.

To implement the intent and understanding the Trustees and UM agree as follows:

Commencing for UM Fiscal Year 2010 and each fiscal year thereafter:

1. UM will distribute to the Center an amount equal to the "unmatched balance" multiplied by the UM Endowment Spending Policy Rate for the fiscal year in question and

2. If the average of the Endowment Investment Rate of Return for the fiscal year in question and the 2 immediately preceding years exceeds the UM Endowment Spending Policy Rate, an amount equal to the excess rate multiplied by the "unmatched balance" will be added to the MBRF Endowment.

UM shall pay amounts from sources other than the MBRF Endowment. The "unmatched balance" at 6/1/2010 is agreed to be $3,177,215.

Attached is a computation for the UM Fiscal Year 2010. It is agreed this computation accurately applies the above understanding and will be followed in future years.

Signatures: _____

_____

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_____

_____

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Date: _____

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August 11, 2010

Teresa W. Borcheck
Corporate Trustee
The McKnight Brain Research Foundation
c/o The SunTrust Bank
P.O. Box 620005
Orlando, Florida 32862–0005

Dear Ms. Borcheck:

We at Columbia University Medical Center are extremely grateful for The McKnight Brain Research Foundation's interest in partnering with us, to advance medical understanding of cognitive aging and related memory decline. As the population in the United States grows older, the importance of this research only becomes more urgent. My team and I continue to focus on learning why the brain ages, as well as how we can intervene to ameliorate this so-called "normal" cognitive decline, to improve the quality of life for aging people and their families.

Enclosed please find a proposal for the establishment of the Evelyn F. McKnight Brain Center at CUMC. We believe that Columbia is the optimal home for the Foundation's next brain center. With our high profile as a leader of the international academic medical community and our superior research infrastructure, CUMC has both the ability to draw attention to cognitive aging as a vital topic for investigation, and the means to conduct groundbreaking research. With these resources and your partnership, I believe we have the opportunity to make great strides.

The proposed vision for the Evelyn F. McKnight Brain Center adheres to three specific conditions: 1) its existence in a dedicated space on the Medical Center's campus; 2) my appointment as director of the Center; and 3) the provision of matching funds from CUMC, to supplement the Foundation's generosity.

I would be more than happy to speak with you in person about the proposed Evelyn F. McKnight Brain Center, or to arrange a meeting for the Foundation's trustees with Dr. Lee Goldman, dean of Columbia University Medical Center. In the meantime, should you have any questions or suggestions, I can be reached at (212) 305–9194 or sas68@columbia.edu.

Thank you for your time and consideration.

Sincerely yours,

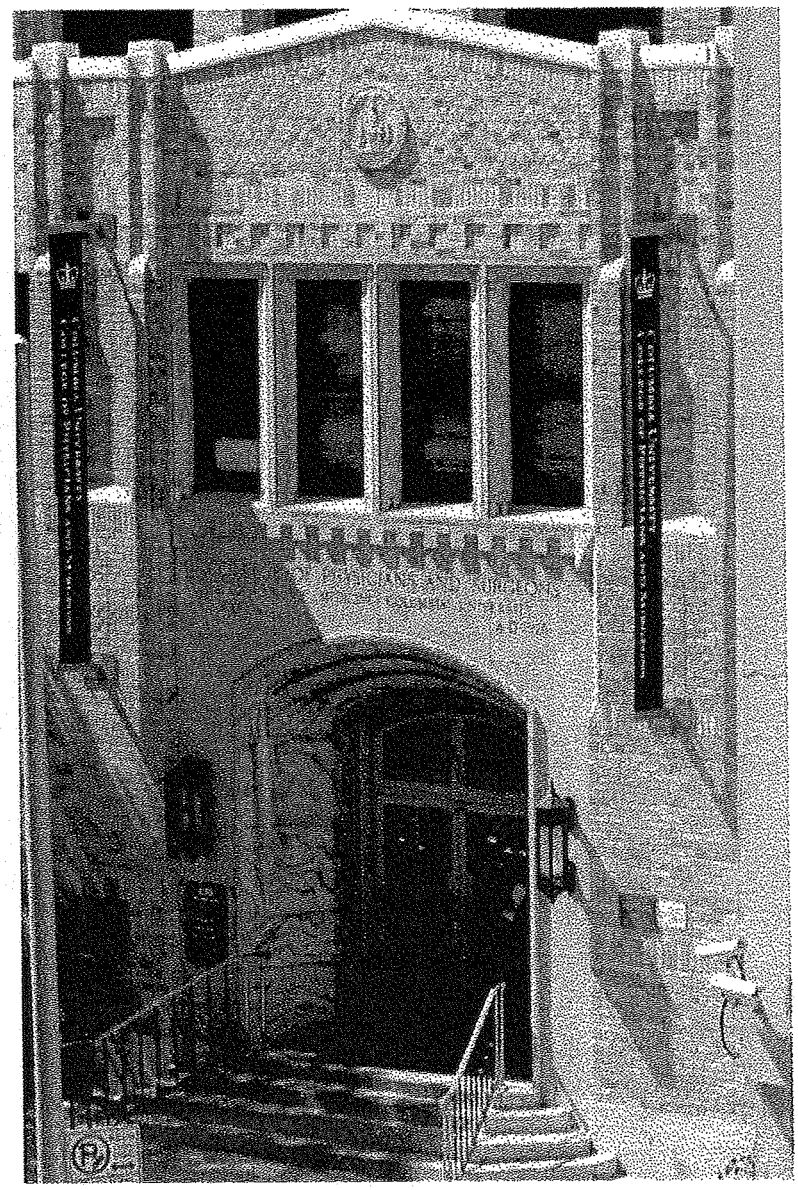
Scott A. Small, M.D.
Associate Professor of Neurology

cc: J. Lee Dockery

COLUMBIA UNIVERSITY MEDICAL CENTER

Evelyn F. McKnight Brain Center at Columbia University Medical Center

A Proposal Presented to The McKnight Brain Research Foundation



August 2010

Executive Summary

As a means of advancing the interests of The McKnight Brain Research Foundation in understanding and alleviating age-related memory loss, Columbia University Medical Center proposes to create the Evelyn F. McKnight Brain Center at CUMC. The Center would focus on translational research into cognitive aging and the memory decline it causes, with the ultimate aim of developing effective interventions. The Center would not focus on memory loss caused by Alzheimer's disease, which is a different pathology entirely, and a focus of investigations elsewhere at CUMC.

With CUMC's extensive research infrastructure, superior personnel for collaboration, and our influential status as an internationally leading academic medical center, we have the resources necessary to advance the Foundation's research agenda. The proposed director of the Center, Dr. Scott Small, is a pioneer in cognitive aging and age-related memory loss. Dr. Small has built upon the existing literature and his own novel research contributions to synthesize a full model of age-related memory decline. This model suggests specific interventions that have the potential to ameliorate cognitive aging, either alone or in combination. Testing these interventions will be the first priority of the Center.

With the benefit of Columbia's extensive resources and international standing in the medical community, and with Dr. Small's expertise and leadership, The Evelyn F. McKnight Brain Research Center at CUMC will be the crown jewel of The McKnight Brain Research Foundation's centers. Its establishment will take the cause of alleviating age-related memory loss to a new level of international awareness.

INTRODUCTION

Age-related memory loss has become an epidemic. Though the media, the public, and even the biomedical research community itself tend to focus on Alzheimer's disease as the cause of memory loss in the elderly, cognitive aging is, in fact, distinct from Alzheimer's disease. Recent studies have shown that age-related memory loss involves the degeneration of different regions of the brain from those involved in Alzheimer's, as well as different pathogenic mechanisms. We now have an unprecedented opportunity to gain greater understanding of so-called "normal" cognitive aging – as well as the potential to develop interventions that could conceivably slow, or even reverse, memory decline in the elderly.

The Evelyn F. McKnight Brain Center at Columbia University Medical Center would exist with the mission to investigate age-related memory decline, primarily with translational research. Under the directorship of Dr. Scott Small, the Center's work would focus on the identification of interventions that could be effective for humans, to ameliorate the memory loss that afflicts many of us as we age.

It is our hope that The McKnight Brain Research Foundation will partner with us in this effort, by providing a $5 million endowment gift to open the Center and sustain its annual operations in perpetuity, as well as a gift of $2.5 million to endow a professorship to support the Center's director.

CUMC'S BACKGROUND AND RESOURCES FOR THE ADVANCEMENT OF THE MCKNIGHT MISSION

CUMC is the optimal home for The McKnight Brain Research Foundation's next innovative center for the research of age-related memory loss. The opening of the Evelyn F. McKnight Brain Center at CUMC would focus great attention on the issue of cognitive aging, by virtue of Columbia's status as one of the world's leading academic medical centers. This would raise awareness for age-related memory loss as distinct from Alzheimer's disease, attracting new funding as well as new scientific talent.

Such talent – and the means for nurturing it – abounds at Columbia. We are especially strong in the neurosciences, with superior imaging facilities and research infrastructure already in place, which can be used for the investigation of age-related memory loss. Perhaps as important for innovation in the field of cognitive aging, there are myriad opportunities for the Center's researchers to develop rich, interdisciplinary collaborations with Columbia's other top scientists.

CUMC has been recognized as a world-class presence in the neurological sciences since the late 1920s, when the Neurological Institute of New York, America's only hospital for brain disorders, moved to the then-new Medical Center. Housing our Departments of Neurology and Neurological Surgery, the Neurological Institute comprises faculty members who are among the most renowned experts in neurology in the world; their focus on translational research brings patients the most innovative and up-to-date treatments, as soon as they become available. Many of these faculty members have joint appointments in basic science departments, such as Pharmacology, Pathology and Cell Biology, and Genetics and Development.

Moreover, as a leader in medical education, and with our focus on nurturing promising young researchers through fellowships and other opportunities, CUMC has the resources to attract and train

the next generation of top scientists in the field of cognitive aging. Our Department of Neurology also has a proud tradition of training academic leaders and practitioners of neurology, and graduates of its educational programs can be found in medical centers throughout North America and around the world. The Department is consistently ranked among the top neurology departments in the nation; it is one of the largest, with nearly 160 faculty members and 46 post-residency fellows, representing all subspecialties of neurology. The large size and extensive facilities of the Department allow for exceptional clinical versatility and expertise, as well as numerous research opportunities.

In more recent years, Columbia has developed additional resources and centers that foster basic neuroscience research, including the Mahoney-Keck Center for Brain & Behavior, the Kavli Institute for Brain Science, the Center for Theoretical Neuroscience, the Center for Motor Neuron Biology and Disease, the Taub Institute for Research on Alzheimer's Disease and the Aging Brain, the Sackler Institute for Developmental Psychobiology, and the Lieber Center for Schizophrenia Research.

With all of CUMC's resources at its disposal, the Evelyn F. McKnight Brain Center has the potential to become the crown jewel of the McKnight centers for research into cognitive aging. As the largest medical research institution in New York State, CUMC has the resources needed to advance all of the aspects of the Foundation's mission to understand and alleviate age-related memory decline. We plan to accomplish this under the exceptional leadership of Dr. Scott Small.

Dr. Scott Small, Proposed Director of the Center

Dr. Small is a leader in the field of cognitive aging research. He received his B.A. in psychology from New York University in 1986, graduating from the honors program *summa cum laude*; he also received the University Award for distinguished honors thesis, as well as the President's Award for academic excellence. In 1992, Dr. Small earned his M.D. from Columbia University, going on to complete his medical internship at UCLA and a neurology residency at CUMC. In 1996, he was selected as Chief Resident of the Department of Neurology. Upon completing a fellowship in Neurobehavior in 1998, he remained at CUMC as a faculty member. Dr. Small's honors at Columbia include the Herbert Irving award and the Paul Beeson Physician Faculty Scholar Award in aging research. Dr. Small is also a recipient of the prestigious McKnight Foundation award in clinical neuroscience.

Dr. Small's Research: A Path Toward the Amelioration of Cognitive Aging

Dr. Small's research into age-related memory loss has resulted in substantial insight into how the brain ages, and how this process is distinct from that of Alzheimer's disease. This new information, which Dr. Small has gleaned through his work with mouse models, is beginning to change the way medicine views neurological aging – not as natural and inevitable, but as a process in which we could potentially intervene, to improve the memory function and quality of life of aging people.

Background and Significance of Research in Cognitive Aging

It is well-documented that age-related memory decline is caused in part by dysfunction in the hippocampal formation, a brain structure vital for forming and storing memories. Hippocampal dysfunction observed in later life is caused by aging, but also by Alzheimer's disease (AD). In order

to develop and test effective interventions for memory loss caused by aging, it is first necessary to differentiate the pathogenic mechanisms of cognitive aging from those of AD, so as to hone in on the proper therapeutic target.

As documented more than a century ago, the hippocampal formation (HF) is made up of distinct subregions, which differ anatomically and morphologically: the entorhinal cortex (EC), the dentate gyrus (DG), the CA1 and CA3 subfields, and the subiculum (see Figure 1, below). Nevertheless, studies into the normal and abnormal function of the HF have historically investigated it as a singular structure. "Hippocampal-dependent" memory tests in humans and other mammals were originally developed to assess the HF globally, to contrast its function with other brain areas, or to implicate the HF in cognitively impaired patients. Indeed, because of its internal connectivity (as shown in the figure), the HF does function as an integrated circuit, and a lesion in any hippocampal subregion can manifest throughout, leading to overlapping cognitive problems.

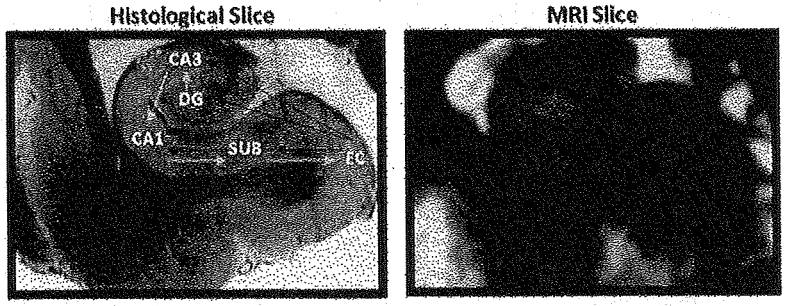


Figure 1.

Recently, however, the clinical and cognitive importance of individual hippocampal subregions has come to the fore. Most pathological processes that affect the HF typically do so by differentially targeting selective components of the circuit. Gene expression profiling has revealed distinct expression patterns across hippocampal subregions, and this "molecular map" provides a mechanism for discovering the distinct vulnerabilities of the different subregions, to determine which are involved in specific cognitive dysfunctions.

In all mammalian brains that have been examined, age-dependent decline in the function of the HF has been observed. Because most mammals do not develop AD, however, it can be assumed that aging can, in principle, target the HF independent of AD. At the same time, while it is true that the dominant form of AD occurs late in life, there is a rare early-onset form of AD – which shows that AD can and does occur independent of aging.

These observations suggest that AD and aging might be mechanistically distinct; informed by the molecular map, we can hypothesize that they might target different areas. Nevertheless, establishing with certainty the differentiation between AD and aging is not trivial. On the one hand, because AD typically occurs in late life, the pattern of dysfunction observed in patients represents a *combination* of aging and disease, which must be teased apart into its components. On the other, because of the difficulty in diagnosing AD in its earliest stages, there is often undetected disease; these subjects, thought to be "normal" (but who actually have early-onset Alzheimer's), confound the construction of a pattern of hippocampal dysfunction related to AD, with changes that have already begun in their brains. Additionally, imprecise attempts at early diagnosis of AD run the risk of mislabeling more

severe cases of normal aging as "disease." In any case, both AD and aging progress slowly, over the course of decades. So, even if lesions are confined to select hippocampal subregions, over time this will secondarily affect other areas of the HF – because of the phenomenon discussed above, in which the HF acts as an integrated circuit, with a complex interplay among parts.

Using fMRI to Elucidate the Differences Between Aging and Alzheimer's Disease

Aware of these challenges, and building on earlier work in the field, Dr. Small and his team were able to design an experimental protocol that shed crucial new light on the issue of cognitive aging versus Alzheimer's disease. They realized that, in order to map HF dysfunction in both AD and cognitive aging, they needed a variant of functional imaging that not only possessed sufficient spatial resolution with which to visualize hippocampal subregions, but also one that could generate high-resolution HF maps in humans and animal models.

Animal models are particularly useful, because in their "wildtype" state they develop HF dysfunction that is solely age-related (independent of AD, as described above), and because transgenic mice can be forced to produce AD-like changes at young ages (independent of advanced age). In other words, the animal models closely replicate the type of HF dysfunction seen in humans, but can be controlled to produce the single state desired by the researchers: they can either be allowed to develop naturally into only age-related HF dysfunction, or they can be experimentally manipulated to exhibit only AD.

Deciding to focus on functional magnetic resonance imaging (fMRI), Dr. Small and his colleagues dedicated a number of years to exploring different fMRI paradigms and different fMRI variables: deoxyhemoglobin ("BOLD"), cerebral blood flow (CBF), and cerebral blood volume (CBV). They ultimately found that a technique that generated basal CBV maps with intravenous injections of gadolinium provided the highest spatial resolution with the best signal-to-noise ratio, and was therefore ideally suited for their purposes.

For generating high-resolution maps in humans and non-human primates, the team was able to use conventional scanners, and simply optimized acquisition parameters of a previously developed technique. For mouse fMRI, however, the techniques available at the time had significant limitations. To overcome these limitations, Dr. Small and his team constructed a dedicated mouse fMRI laboratory, on the 10th floor of the William Black Building at CUMC, which houses a small-bore 9.4 Tesla magnet and various monitoring devices. More importantly, they were able to develop a modified CBV approach, designed to generate high-resolution, functional HF maps of mice, longitudinally over time. With these fMRI techniques in hand, Dr. Small used them to map HF dysfunction in human subjects both with and without AD, aging rhesus monkeys, and mouse models of aging and AD.

The Contribution of Glucose Dysregulation to Cognitive Aging

Studies have relied on the patterns of HF dysfunction, and on cross-species fMRI, to identify an etiological contributor to cognitive aging – a sort of trigger that touches off the aging process. Previous studies have suggested that age-related changes in glucose, insulin, or cerebral vascular disease can affect brain function. Any factor might be considered an etiological contributor of cognitive aging if it is shown to differentially target the dentate gyrus (DG), tracking the spatial

pattern of cognitive aging. Additionally, the factor should worsen progressively across the adult life span, tracking the temporal pattern of cognitive aging.

By imaging humans with elevations in blood glucose, shown in Figure 2, rhesus monkeys, and the streptozotocin mouse model, studies have found that glucose dysregulation differentially targets the DG.

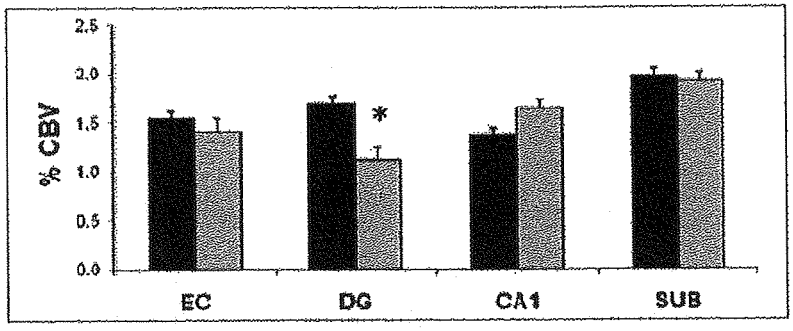


Figure 2.

A separate series of cross-species studies have shown that age-related changes in glucose regulation begin in the third decade of life and worsen with advancing age. Taken together, age-related glucose regulation worsens progressively across the adult life span and targets the DG, suggesting that glucose dysregulation is at least one etiologic contributor underlying cognitive aging.

In a recent study, Dr. Small and his team further found that elevations in glucose differentially affect a standardized neuropsychological task called the Benton Facial Recognition Test, which is heavily dependent on pattern separation (a task closely interrelated with memory). This observation is important for two reasons. First, because pattern separation is a task that is mediated by the DG, this finding further supports the link between glucose dysregulation and the DG. Second, at a practical level, this finding shows that the Benton Facial Recognition Test is a standardized neuropsychological test that can be used to measure DG dysfunction when testing interventions for cognitive aging in human studies.

Dr. Small combined this new finding with previous studies in the field, which show that cognitive aging and glucose dysregulation are associated with a deficiency in RbAp48 – a molecule that has been previously found to regulate histone acetylation, by interacting with the CREB-binding protein. Most recently he has worked with other investigators at Columbia to develop a novel transgenic mouse, expressing a dominant-negative inhibitor of RbAp48. The extensive study of these mice has linked RbAp48 deficiency to "downstream" features characteristic of cognitive aging: decreased histone acetylation, dentate gyrus selective dysfunction, and defects in pattern separation.

Summary of Findings: A Workable Model for Experimental Interventions in Cognitive Aging

Taken together, the composite findings of a series of fMRI, cognitive, and post-mortem studies identified a pattern of dysfunction in the hippocampal formation (HF) that distinguishes cognitive aging from Alzheimer's disease (AD). Specifically, the composite of findings suggest that the entorhinal cortex (EC) is differentially affected by AD, while the dentate gyrus (DG) is differentially linked to cognitive aging. This is illustrated in Figure 3 below: in contrast to AD, cognitive aging is

characterized by differential dysfunction in the dentate gyrus (DG, indicated in red in the figure), with relative preserved function in the entorhinal cortex (EC, indicated in blue in the figure).

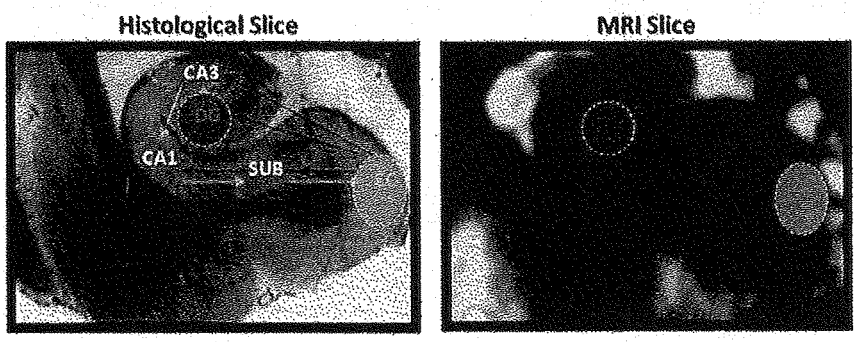


Figure 3.

Isolating this pattern of HF dysfunction with fMRI is important for a number of reasons. First, the pattern of HF dysfunction can be as used as an experimental handle, with which to indentify pathogenic mechanisms underlying cognitive aging, distinct from those that cause AD. Indeed, this pattern of HF dysfunction has been used in subsequent studies to identify age-related glucose dysregulation as one causative contributor to cognitive aging; additionally, this pattern can be used to identify molecular mechanisms. Second, the pattern of HF dysfunction – and the ability to visualize it with fMRI in humans and other aging animals – provides a method for assessing the effectiveness of therapeutic interventions, in translational studies designed to ameliorate cognitive aging.

Building upon his own work and the other literature in the field, Dr. Small has found it possible to propose a model of cognitive aging that links aging to memory decline, from contributing etiologies (glucose dysregulation), through molecular mediators (decreased histone acetylation), to cognitive consequences (defects in pattern separation).

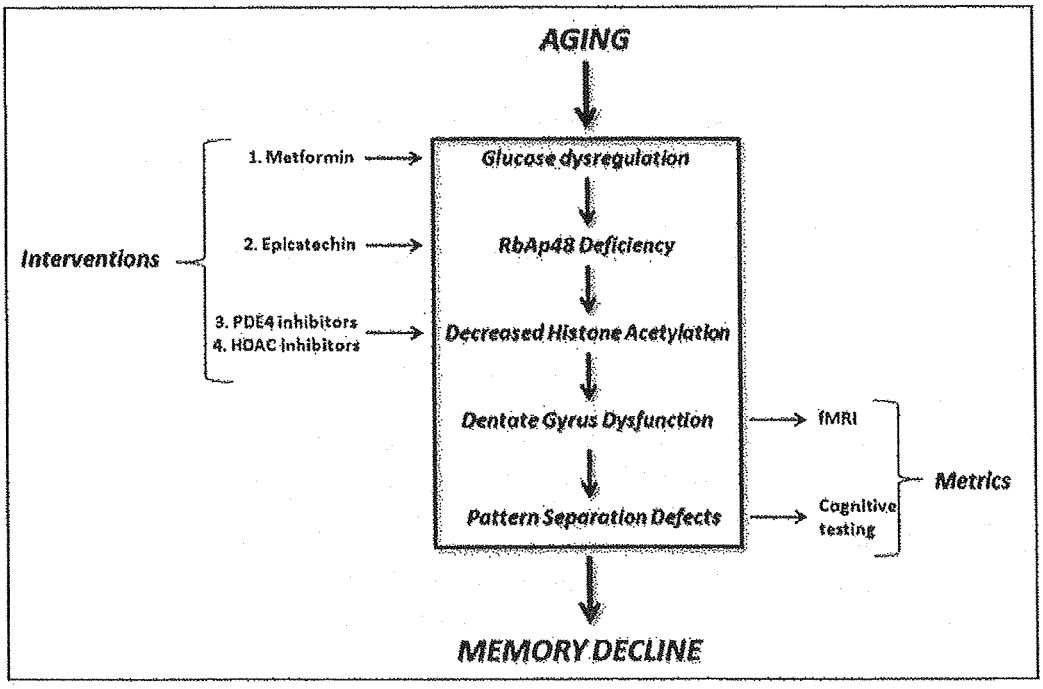


Figure 4. Model of cognitive aging leading to memory decline.

In a nutshell: cognitive aging is associated with glucose dysregulation, which leads to RbAp48 deficiency, which causes decreases in histone acetylation, which – within the HF – differentially causes dentate gyrus dysfunction, which manifests as cognitive defects in pattern separation, i.e., memory decline.

This model provides a framework for developing and testing promising interventions designed to ameliorate cognitive aging: the ultimate goal for research at the Evelyn F. McKnight Brain Center.

Evelyn F. McKnight Brain Center at Columbia University Medical Center

It is our hope now to establish the Evelyn F. McKnight Brain Center, with the generous partnership of The McKnight Brain Research Foundation, in order to use this model of cognitive aging to predict and test candidate therapies to fight age-related memory loss.

Under the strong leadership and expertise of Dr. Small, who will act as Director, the Center would consist of a laboratory occupying dedicated space at CUMC. This would house all of the resources required to perform translational research in age-related memory loss, including the mouse fMRI lab and equipment, animal behavior lab space, and space for personnel. The Center would potentially collaborate with the Department of Radiology to share imaging infrastructure, depending on the needs of the research.

Immediate Goal: Testing Four Promising Therapies for Age-Related Memory Loss

Through the Foundation's generosity, Dr. Small and his staff will be able to bring his research to the next level: testing the following interventions – born from Dr. Small's model of cognitive aging – for their potential to ameliorate age-related memory loss.

> **Intervention 1:** Test whether **improving glucose regulation with metformin** ameliorates cognitive aging.
>
> **Intervention 2:** Test whether **increasing hippocampal RbAp48 expression with epicatechin** ameliorates cognitive aging.
>
> **Intervention 3:** Test whether **enhancing histone acetylation with phosphodiesterase-4 (PDE4) inhibitors or with histone-deacetylase (HDAC)-inhibitors** ameliorates cognitive aging.
>
> **Intervention 4:** Test which **combination of interventions** best ameliorates cognitive aging.

These four interventions were chosen because: a) they manipulate different steps of the model (as shown in the figure); and b) they have been approved for human studies, and fit with the ultimate translational goal of the Center's research. The model also shows metrics that will be used to test the efficacy of these interventions: fMRI and cognitive testing. These metrics were chosen because, as discussed above, they can generate similar readouts of dentate gyrus dysfunction in mice and humans. The novel-object recognition task in mice and the Benton Facial Recognition Test in humans

provide a unified behavioral metric of pattern separation. With such unifying readouts, these metrics will allow a direct translation from mouse to human studies.

Given the translational aims of this research, the initial approach will be to test these interventions in aging mice, and then move to aging humans. During the first cycle of this proposal we will focus on aging mice, identifying which intervention or combination of interventions is able to affect cognitive aging. All studies will have the same general design. Two groups of twelve-month-old mice will be imaged at baseline; one group will receive an intervention, and the other will receive vehicle control. Mice will be imaged once a month, until they reach 16 months of age. At the end of the study they will be assessed cognitively, using a novel-object recognition task. By analysis-of-variance, interventions that ameliorate cognitive aging will be determined.

By confirming that the specific interventions have their hypothesized effects, the studies in this proposal will achieve two overlapping goals. First, these studies will confirm the general model, thereby enhancing our general understanding of cognitive aging. Second, and more importantly, these studies will identify interventions designed to ameliorate the memory decline that afflicts many of us as we age. This exciting work could potentially revolutionize the way our brains function as we age, and substantially improve quality of life for aging people – helping to preserve a lifetime of memories, or enhancing the storage and clarity of new memories, as we spend time with valued family and friends.

Funding Request

Based upon the enormous potential of Dr. Small's research, we respectfully request that The McKnight Foundation consider partnering with us to create the Evelyn F. McKnight Brain Center at Columbia University Medical Center, with a contribution of $7.5 million. This would comprise:

1. a foundational endowment gift of $5 million, to be paid in equal installments over five years, for the establishment of the Center and its sustained operations in perpetuity; and

2. a gift of $2.5 million to endow the Evelyn F. McKnight Professorship in Neurology, for the perpetual support of the Director of the Evelyn F. McKnight Brain Center.

These two gifts are essential to the success of the Center: the endowment will generate interest income to cover the annual operations costs of the Center, while the endowed professorship will provide the director of the Center with the resources to advance its mission, without the burden of annual fundraising. Both of these components are crucial for sustaining the Center's research into age-related memory decline. Although the final decision on the incumbent of any endowed professorship rests with the Trustees of the University, it is our intention to recommend Dr. Small for director of the Center and beneficiary of the professorship, so that he may continue his groundbreaking research in cognitive aging.

It is also our understanding that The McKnight Brain Research Foundation, as a condition of partnership, will expect to see matching funds raised by CUMC toward the Evelyn F. McKnight Brain Center. CUMC is completely amenable to meeting these requirements, from sources such as NIH funding, other public grants, and private philanthropy, among others.

Should the Foundation choose to partner with CUMC in this Center, its generosity will be recognized in several ways. First, there will be a reception for the opening of the Center, featuring the Dean, Dr. Small, Foundation representatives, and invited guests from within and outside the University. The founding gift will be the subject of a press release, and will be acknowledged prominently in the Medical Center's Annual Report, website, and newsletter, *To Date*. There will also be a celebratory reception to formally announce the creation of the Evelyn F. McKnight Professorship in Neurology, and Dr. Small (and future Center directors) will use the professorship title on all peer-reviewed research publications and educational literature emanating from the Center, as well as on letterhead and other printed materials.

Conclusion

With the innovative research and stewardship of Dr. Small, and the outstanding resources and name recognition of CUMC, the Evelyn F. McKnight Brain Center has the potential to emerge as the high-profile leader in cognitive aging research. The addition of Columbia to the McKnight family of brain research centers will foster new collaborations in the area, new communication between the McKnight centers, and greater awareness among the public of age-related memory loss – and its distinction from Alzheimer's disease – than ever before.

The Evelyn F. McKnight Brain Center at Columbia will bring medicine closer to effective interventions for age-related memory decline. The seeds for this translational research are already present in Dr. Small's model of cognitive aging, which sets out a clear framework for the Center to get to immediate work, with testing of four promising interventions. We are very grateful for your consideration of this proposal to partner with Columbia University Medical Center, as we work together toward the improvement of quality of life, sharpness of mind, and vitality for aging people, of current and future generations.

Scott A. Small, MD

After graduating from NYU with a B.A. in experimental psychology, Dr. Small began the MD/PhD program at Columbia University in Eric Kandel's laboratory. Discovering that he enjoyed patient care more than he anticipated, he decided to focus exclusively on his medical training. After completing a medical internship at UCLA, a neurology residency and chief residency at Columbia, and a fellowship with Richard Mayeux, Dr. Small 'returned' to research. Informed by his prior experience studying neuronal physiology and pathophysiology he began a research program at Columbia dedicated to investigating intractable 'complex' disorders of the brain. Taking a decidedly top-down approach, he optimized brain imaging tools designed to pinpoint brain dysfunction in human patients and mouse models of disease. More recently, Dr. Small has combined brain imaging with gene-expression technologies to uncover novel molecular defects underlying Alzheimer's disease and cognitive aging. Dr. Small is the recipient of numerous awards, including the Beeson Scholar Award in Aging Research from the American Federation on Aging, the McKnight Neuroscience of Brain Disorders Award, the Derek Denny-Brown Young Neurological Scholar Award from the American Neurological Association, and the Lamport Award for Excellence in Clinical Science Research from Columbia University.