Cooperative Agreement No.: N66001-14-2-4032

P.R. No.: 1300418366

Effective Date: Date signed by Government

<u>CFDA No</u>.: 12.910 <u>AGO Code</u>: N62880

Payment Office Code: HQ0337

RESEARCH COOPERATIVE AGREEMENT MODIFICATION # P00009

Grantor: Space and Naval Warfare Systems Center, Pacific

Code 22530 53560 Hull Street

San Diego, CA 92152-5001

(Attn: Sammy Haji, (619) 553-4539, suhail.haji@navy.mil)

Recipient: The Trustees of the University of Pennsylvania

3451 Walnut Street

Philadelphia, PA 19104-6205

Recipient Identification Numbers/Codes:

DUNS: 042250712 CAGE: 7G665 TIN: 23-1352685

Authority: 10 U.S.C. 2358 as amended and 31 U.S.C. 6305

1. <u>PURPOSE</u>: This modification is to incorporate a revised Attachment 1, Statement of Work (SOW), of the Cooperative Agreement and to acknowledge a no-cost realignment of the Agreement budget. As a result, Schedule item 1. is revised to read:

1. <u>Purpose</u>:

The purpose of this Cooperative Agreement is to fund research in support of a DARPA sponsored program. This effort shall be carried out generally as set forth in the Government's Statement of Work Revision 2, Attachment 1, dated 24 August 2016, which has been based on the Recipient's proposal, "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)", and Data Matrix, Attachment 2, copies of which are in the possession of both parties.

2. ALL OTHER TERMS AND CONDITIONS REMAIN UNCHANGED.

FOR RECIPIENT:		FOR The United States of America, Space and Naval Warfare Systems Center, Pacific			
		(b)(6)			
		2016.1	1.04 11:19:27 -07'00'		
(Signature)		LYNN M. BIEDERMANN Grants Officer	(Date)		
, M.A., Ed., CRA	11/4/2016				
(Name/Title)	(Date)				

Cooperative Agreement No.: N66001-14-2-4032

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Effective Date: Date signed by Government

<u>CFDA No</u>.: 12.910 <u>AGO Code</u>: N62880

Payment Office Code: HQ0337

RESEARCH COOPERATIVE AGREEMENT MODIFICATION # P00010

Grantor: Space and Naval Warfare Systems Center, Pacific

Code 22530 53560 Hull Street

San Diego, CA 92152-5001

(Attn: Veronica Velarde, (619) 553-7734, veronica.velarde@navy.mil)

Recipient: The Trustees of the University of Pennsylvania

3451 Walnut Street

Philadelphia, PA 19104-6205

Recipient Identification Numbers/Codes:

DUNS: 042250712 CAGE: 7G665 TIN: 23-1352685

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Accounting and Appropriation Data:

ACRN: AG 97 17180400 1320 BQ61TT 2017 BT 01 CORE A DARPA 255 HR0011725535 02 000

20602115E00 012199 MIPR# HR0011725535

\$3,246,877.00

1. <u>PURPOSE</u>: This modification obligates an increment of funding for the Option 1 period. As a result, Cooperative Agreement Schedule item 8. is revised to read:

8. Cooperative Agreement Funding:

This Cooperative Agreement is incrementally funded in the amount of \$21,333,592.00. Of this amount, \$13,724,629.00 is for the Base Period and \$7,608,963.00 is for the Option 1 Period. The Government's obligation to make payments to the Recipient is limited to only those funds obligated by this Cooperative Agreement or by modification to this Cooperative Agreement. Subject to availability of funds and continued satisfactory progress on the Cooperative Agreement as determined by the Government, the Government may agree to provide additional funding. The unfunded balance is \$1,402,591.00.

The Recipient shall notify the AGO in writing promptly whenever the total Agreement amount is expected to exceed the needs of the Recipient for the project period by more than \$5,000 or 5% of the award, whichever is greater. This notification shall not be required if an application for additional funding is submitted for a continuation award.

2. ALL OTHER TERMS AND CONDITIONS REMAIN UNCHANGED.

FOR The United States of America, Space and Naval Warfare Systems Center, Pacific

(b)(6)

2016.11.23 09:34:07 -08'00'

LYNN M. BIEDERMANN Grants Officer

Date

STATEMENT OF WORK FOR UNIVERSITY OF PENNSYLVANIA

Title – Restoring Active Memory (RAM): "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)

1.0 SCOPE

This effort promises to use direct	brain recordings and stimula	ation in humans and	animals to creat	e a real-time			
system for enhancing encoding an	system for enhancing encoding and long-term retrieval of memories for specific types of information. The team						
consists of nine leading clinical c	enters for the surgical treatm	nent of epilepsy and r	novement disor	ders, each led			
by a clinician scientist with subst	antial experience in one or n	nore key areas of elec	ctrical brain stin	nulation, human			
cognition, computational electrop	hysiology, and realtime ada	ptive control systems	. The neurologi	cal and			
neurosurgical teams are aligned of	on the common goal of rapid	ly developing and tes	sting approaches	s to enhance			
and restore memory through a stu	idy of unprecedented scope:	more than 100 paties	nts each year in	a large array			
of experiments. Pending Investig	gational Device Exemption (IDE) approval, patiei	nts in Phase 2 of	f the project			
will be implanted with a complete	e memory neuromodulation	(b)(4)					
			to	our memory			
testing paradigms. This will be ac	complished through an acco	elerated U.S. Food at	nd Drug Admini	stration (FDA)			
submission of the technical area t	two (TA2) system at the end	of Phase 1. Through	application of a	ı			
computational model of human	(b)(4)		to the behavior	ral and			
electrophysiological data the reci	pient shall define biomarkers	s of memory	(b)(4)				
	These biomarke	ers will be used	(b)(4)				
	(b)(4)	(b)(4)					
(b)(4)							

1.1. BACKGROUND

The Defense Advanced Research Projects Agency (DARPA) seeks new methods for analysis and decoding of neural signals in order to understand how neural stimulation could be applied to facilitate recovery of memory encoding following brain injury. Ultimately, it is desired that a prototype implantable neural device that enables recovery of memory in a human clinical population be developed. Additionally, the program encompasses the development of quantitative models of complex, hierarchical memories and exploration of neurobiological and behavioral distinctions between memory function using the implantable device versus natural learning and training.

2.0 APPLICABLE DOCUMENTS

- (a) DARPA BAA-14-08.
- (b) UPENN Technical Proposal Titled "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)" dated January 23, 2014

3.0 PROJECT WORK DESCRIPTION AND REQUIREMENTS

The recipient shall provide the facilities necessary to develop the effort as described herein.

Human use **is** anticipated in this effort. The recipient shall obtain all necessary Institutional Review Board (IRB) approvals, show proper assurance documentation, and obtain proper approval from the Government officials prior to human use testing.

Animal use **is** anticipated in this effort. The recipient shall obtain all necessary Institutional Animal Care and Utilization Committee (IACUC) approval and demonstrate this approval to the Government prior to beginning experimentation with animals. If animal use is no longer anticipated, or changes significantly from the approved

IACUC then the PI must submit a letter stating the discontinuation of animal use for this effort and/or receive appropriate authorization for IACUC changes of previously specified protocols. Unless prior approval by DARPA is given IACUC documentation must be provided prior to contract award.

3.1 BASE PERIOD (PHASE I)

Technical Area 1

3.1.1.4 Build a

(b)(4)

model for

(b)(4)

memory:

(b)(4)

3.1.1 A computational model for describing behavior in declarative memory tasks.

3.1.1.1 Predicting moment-by-moment behavior in a variety of memory tasks. The recipient shall document a model of memory (b)(4)(b)(4)(b)(4)(a) The recipient shall document the code base for the (b)(4) (b)(4)[Month 3]. (b) The recipient shall extend the model (b)(4)[Month 6]. (c) The recipient shall document fully commented, optimized (b)(4)Code shall be able to execute model (b)(4)Month 6]. (d) The recipient shall document the code base for the (b)(4)[Month 9]. (e) The recipient shall fit the (b)(4)[Month 12] (f) The recipient shall document fully commented, optimized Code shall be able to execute model (b)(4)[Month 12]. 3.1.1.2 [DELETED] 3.1.1.3. Build a (b)(4)model of free recall: (b)(4)(a) Develop software that allows us to construct the (b)(4) model for an entire session of FR1 in 30 seconds or less [Month 15] (b) [DELETED] (c) [DELETED]

UPE	NN PI- KAHANA					
	(a) Develop a model prototype	(b)(4)		(b)(4)		[Month
21]	(a) Develop a model prototype			(b)(4)		[Woltin
-	(b) Deliver fully documented conth 24]	ode		(b)(4)		
3.1.2	Integrating neurophysiological	biomarke	ers into the co	mputational mod	lel of beha	vior.
3.1.2	.1 Characterize distribution of	(b)(4)	biomarker	S	(b)(4)	
		(=)(-)			(-)(-)	
	.1.1 A prototype for analyzing	(b)(4) r	neural	(b)(4)		shall be deployed and
evait	nated [Month 12].					
3.1.2	.1.2 The recipient shall document	the prototy	ype software		(b)(4)	
				[Month 12]		
2 1 2	1.2 Chamatania tha (1.)(4)	1, 1,	.1 41.	1-1 C C	11 1 (1	V(A)
3.1.2	1.1.3 Characterize the (b)(4) (a) Characterize the (b)(4)		_	e models of free re ients performing t		
	(a) Characterize the (b)(1)	o i o i i	arrers for pur	ents performing t	[Month 1	
	(b) Characterize the (b)(4)	biom	arkers for pat	ients performing t	he (b)(4) n	
		(b)(4)				[Month 24].
2 1 2	1.477		0			
3.1.2	.1.4 The recipient shall document		pe software (b)(4)		(b)(4)	
(1	b)(4) The recipient shall docum			(b)(4)		(b)(4)
ì			(b)(4)	,,,,		
	(b)(4) Month 24].					
313	Electrophysiological recording	s to define	hiomorkors		(b)(4)	
	(b)(4) memory.	s to define	Diviliai Kei S		(D)(4)	
	Objective: Define biomarkers			(b)(4)		memories, as
	measured in a broad array of t					<u> </u>
	(b)(4) free recall of (b)(4) (b)(4)	word list (b)(4		associate learning		tial navigation (b)(4)
3.1.3	.1 The recipient shall design, prog	ram, pilot,	execute, and	analyze data from	Experimen	FR1 on patients in the
epile	psy monitoring unit. Recording ne	ural activit	ty	(b)(4)		shall be
	to identify (b)(4) biomarkers (b)			•	. T	hese biomarkers will
serve	e a critical role in subsequent (b) (a) Design, program, and pilo			recipient shall:		
	(b) Write initial data analysis	_	-			
	(c) Analyze data on 13 patien	ts from exp	periment FR1			
	(d) Analyze data on 26 patien					
	(e) Analyze data on 39 patien		•			
	(f) Analyze data on 58 patient	ь пошехр	Jerment FKI	լւմանում Հ4յ.		

UPENN PI- KAHANA	anatata nationt data fu	one the allegate arm on	mant ta ba abau	mad swith improaction	otomo om d				
	nnotate patient data fro precisely localize elec	_		_					
program personner,	(b)(4)	ctrode contacts (neur	[Mont	•	cconstructions				
(h) Complete interio	m reports on data from	n the above experim		-	etings and with				
	ersonnel. Reports sha				(b)(4)				
Drift 11 program pe	Toomier. Teoports sha		•	es of the electrop	. , . ,				
correlates of (b)(4)	memory	, 43	(b)(4)	s of the electrop	nysiological				
	includity		(2)(.)	[Mon ¹	th 24].				
* /	ected in a deidentified	•	with the public	_	-				
•	code for experiment [-							
	analysis functions [M	_	DI 1516	1 0 43					
* /	structions of all patier		-	-	3.6 .4 0.43				
` '	reporting on analyze	•		-	-				
	ated data to the public				e I [Month 24].				
(o) Deliver report or	n (b)(4	4) b10	omarkers [Mo	nth 24].					
3.1.3.2 Design, program, pilo	ot execute and analy	ze data from Experi	ment CatFR1 (1	n=46) on natient	s in the				
epilepsy monitoring unit. In t	•	-		(b)(4)	s in the				
cpricepsy momenting unit. In t	(b)(4)	The recipi		(5)(4)					
(a) Design, program, a		•	ent shair.						
(b) Write initial data a									
(c) Analyze data on 1			th 81						
(d) Analyze data on 2		_	-						
•		-	-						
	Analyze data on 28 patients from experiment CatFR1 [Month 18]. (f) Analyze data on 33 patients from experiment CatFR1 [Month 24].								
	(s) Organize and annotate patient data from above experiment [Month 24].								
(0)) Complete interim reports on data from the above experiment [Month 24].								
(i) Post all data collec				ublic data portal	[Month 24]				
(j) Fully document co		-	ioie with the pi	ione data portar	[Month 24].				
(k) Fully document ar	-	-							
(1) Create 3D reconstr		-	nase 1 [Month	241					
(m) Provide interim re					nth 24].				
(n) Post fully annotate		•		-	-				
(o) Deliver report on	(b)(4)		narkers [Month		. ,				
(c) Benver report on	(0)(4)	01011	idikeis [ivioliti	. 2 .].					
3.1.3.3 Design, program, pilo	ot, execute, and analy	ze data from Experii	ment YC1 (n=4	14) on patients ir	the epilepsy				
monitoring unit. In this task t	•		(b)(4)	, ·)(4)				
		(b)(4)	(2)(1)	(4)					
	(b)(4)	(=)(-)	Tł	ne recipient shall	identify				
(b)(4) memory biomarkers,		(b)(4)		, as well as	(b)(4)				
memory biomarkers,		(b)(4)							
(b)(4) . The recipient sl	nall:								
	n, and pilot task [Mon	th 2].							
	a analysis scripts [Mo	_							
	11 patients from exp	_	h 8].						
· · · · · · · · · · · · · · · · · · ·	22 patients from exp	_	_						
	33 patients from exp								
	50 patients from expe								
	notate patient data from								
	m reports on data from	_		1.					
· · · · =	ected so far in a deide	_	_		al [Month 24].				
() = === 311 3311 3011		p		1					

(j) Fully document code for experiment [Month 2].

The recipient shall: (a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 4 patients from experiment DBS2 [Month 8]. (d)-(n) [DELETED] 3.1.4 Stimulation to (b)(4) memory 3.1.4.1 Design, program, pilot, execute, and analyze data from Experiment FR2 (n=18). The recipient shall test the hypothesis (b)(4) The recipient shall compare the degree to	UPENN	PI- KAHAN		functions [Month 3	1			
(m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24]. (n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (o) Deliver report on (6)(4) biomarkers [Month 24]. (a) Design, program, pilot, execute, and analyze data from Experiment PALI (n=30) on patients in the epilepsy monitoring unit. In this task the recipient shall identify biomarkers (a)(4) of (6)(4) associations and shall: (a) Design, program, and pilot task [Month 2], (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 7 patients from experiment PALI [Month 8]. (d) Analyze data on 7 patients from experiment PALI [Month 13]. (e) Analyze data on 22 patients from experiment PALI [Month 14]. (g) Organize and annotate patient data from the above experiment [Month 24]. (g) Organize and annotate patient data from the above experiment [Month 24]. (i) Fully document code for experiment [Month 2], (k) Fully document analysis functions [Month 3]. (l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24]. (n) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24]. (n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (n) Post fully annotated data to the public data from Experiment DBS2 (n=20) on patients undergoing DBs for movement disorders and Parkinson's Disease. In this task the recipient shall perform a patients undergoing DBs for movement disorders and Parkinson's Disease. In this task the recipient shall perform a patients undergoing DBs (b)(4) recall task (c)(4) [Policy report on (b)(4)		•	•	-	-	Phase 1 [Month 24	.].	
(a) Deliver report on (b)(4) biomarkers [Month 24]. 3.1.3.4 Design, program, pilot, execute, and analyze data from Experiment PAL1 (n=30) on patients in the epilepsy monitoring unit. In this task the recipient shall identify biomarkers (b)(4) of (b)(4) associations and shall: (a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 7 patients from experiment PAL1 [Month 8]. (d) Analyze data on 14 patients from experiment PAL1 [Month 13]. (e) Analyze data on 22 patients from experiment PAL1 [Month 13]. (g) Organize and annotate patient data from above experiment [Month 24]. (g) Organize and annotate patient data from above experiment [Month 24]. (i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24]. (j) Fully document ende for experiment [Month 2]. (k) Fully document analysis functions [Month 3]. (l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24]. (m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24]. (n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (a) Deliver report on (b)(4) biomarkers [Month 24]. (b) Collected and Parkinson's Disease. In this task the recipient shall perform a (b)(4) recall task (see (b)(4) Recall Task, above). (b)(4) The recipient shall: (a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 4 patients from experiment PR2 [Month 8]. (d)(n) [DELETED] 3.1.4 Stimulation to (b)(4) The recipient shall compare the degree to which The recipient shall: (a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 4 patients from experiment FR2 [Month 8]. (d) Analyze data on 4 patients from experiment FR2 [Month 8]. (e) Analyze data on 8 patients from experiment FR2 [Month 18]. (e) Analyze data on 8 patients from experim						-	_	onth 24].
3.1.3.4 Design, program, pilot, execute, and analyze data from Experiment PALI (n=30) on patients in the epilepsy monitoring unit. In this task the recipient shall identify biomarkers (b)(4) of (b)(4) associations and shall: (a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis serripts [Month 3]. (c) Analyze data on 7 patients from experiment PALI [Month 13]. (e) Analyze data on 12 patients from experiment PALI [Month 13]. (e) Analyze data on 22 patients from experiment PALI [Month 13]. (g) Organize and annotate patient data from above experiment [Month 24]. (h) Complete interim reports on data from the above experiment [Month 24]. (i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24]. (j) Fully document code for experiment [Month 2]. (k) Fully document analysis functions [Month 3]. (l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24]. (n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (n) Deliver report on (b)(4) biomarkers [Month 24]. (a) Design, program, pilot, execute and analyze data from Experiment DBS2 (n=20) on patients undergoing DBS for movement disorders and Parkinson's Disease. In this task the recipient shall perform a (b)(4) recall task (see (b)(4) Recall Task, above). (b)(4) The recipient shall compare the degree to which (a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 4 patients from experiment FR2 [Month 8]. (d) Analyze data on 4 patients from experiment FR2 [Month 13]. (e) Analyze data on 8 patients from experiment FR2 [Month 18]. (f) Analyze data on 13 patients from experiment FR2 [Month 18]. (g) Organize and annotate patient data		(n) Post fully	annotated data t	o the public data po	ortal for all	patients run in the t	ask in Phase	1 [Month 24].
monitoring unit. In this task the recipient shall identify biomarkers (b)(4) of (b)(4) associations and shall: (a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 7 patients from experiment PAL1 [Month 13]. (d) Analyze data on 14 patients from experiment PAL1 [Month 13]. (e) Analyze data on 22 patients from experiment PAL1 [Month 18]. (f) Analyze data on 22 patients from experiment PAL1 [Month 18]. (g) Organize and annotate patient data from above experiment [Month 24]. (h) Complete interim reports on data from the above experiment [Month 24]. (i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24]. (ii) Pully document code for experiment [Month 2]. (b) Fully document code for experiment [Month 2]. (c) Fully document analysis functions [Month 3]. (d) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24]. (iii) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (iv) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (iv) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (iv) Design, program, pilot, execute and analyze data from Experiment DBS2 (n=20) on patients undergoing DB for movement disorders and Parkinson's Disease. In this task the recipient shall perform a (b)(4) recall task (see (b)(4) Recall Task, above). (b)(4) Recall Task, above). (b)(4) Write initial data analysis scripts [Month 3]. (c) Analyze data on 4 patients from experiment DBS2 [Month 8]. (d)-(n) [DELETED] 3.1.4 Stimulation to (b)(4) memory 3.1.4.1 Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 8 patients from experiment FR2 [Month 8]. (d) Analyze data on 8 patients from experiment FR2 [Month 13]. (e) Analyze data on 8 patients from experiment FR2 [Month 18].		(o) Deliver re	port on	(b)(4)	bi	iomarkers [Month 2	24].	
(a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 7 patients from experiment PAL1 [Month 8]. (d) Analyze data on 14 patients from experiment PAL1 [Month 18]. (e) Analyze data on 22 patients from experiment PAL1 [Month 18]. (f) Analyze data on 25 patients from experiment PAL1 [Month 24]. (g) Organize and annotate patient data from above experiment [Month 24]. (h) Complete interim reports on data from the above experiment [Month 24]. (i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24]. (j) Fully document code for experiment [Month 2]. (k) Fully document analysis functions [Month 3]. (l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24]. (m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24]. (n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (o) Deliver report on [b)(4) biomarkers [Month 24]. 3.1.3.5 Design, program, pilot, execute and analyze data from Experiment DBS2 (m=20) on patients undergoing DB: for movement disorders and Parkinson's Disease. In this task the recipient shall perform a [b)(4) recall task (see [b)(4) Recall Task, above). (b)(4) Recall Task, above). (b)(4) The recipient shall: (a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 4 patients from experiment FR2 [Month 8]. (d)-(n) [DELETED] 3.1.4 Stimulation to [b)(4) memory 3.1.4.1 Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 3 patients from experiment FR2 [Month 8]. (d) Analyze data on 13 patients from experiment FR2 [Month 13]. (e) Analyze data on 4 patients from experiment FR2 [Month 13]. (f) Analyze data on 43 patients from experiment FR2 [Month 13]. (g) Organize and annotate patient data from the above experiment to be shared with investigato				•	-		_	
(b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 7 patients from experiment PAL1 [Month 8]. (d) Analyze data on 12 patients from experiment PAL1 [Month 13]. (e) Analyze data on 25 patients from experiment PAL1 [Month 18]. (f) Analyze data on 25 patients from experiment PAL1 [Month 24]. (g) Organize and annotate patient data from above experiment [Month 24]. (h) Complete interim reports on data from the above experiment [Month 24]. (i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24]. (j) Fully document code for experiment [Month 2]. (k) Fully document analysis functions [Month 3]. (l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24]. (m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24]. (n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (o) Deliver report on (b)(4) biomarkers [Month 24]. (3).3.1.3.5 Design, program, pilot, execute and analyze data from Experiment DBS2 (n=20) on patients undergoing DBS for movement disorders and Parkinson's Disease. In this task the recipient shall perform a (b)(4) recall task (see (b)(4) Recall Task, above). The recipient shall: (a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 4 patients from experiment DBS2 [Month 8]. (d)-(n) [DELETED] 3.1.4 Stimulation to (b)(4) The recipient shall compare the degree to which (b)(4) The recipient shall: (a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 4 patients from experiment FR2 [Month 8]. (d) Analyze data on 8 patients from experiment FR2 [Month 13]. (e) Analyze data on 13 patients from experiment FR2 [Month 13]. (f) Analyze data on 43 patients from experiment FR2 [Month 13]. (g) Organize and annotate patient data from the above experiment to be shared with investigators and prog	and shall	11:						
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 (a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 4 patients from experiment FR2 [Month 8]. (d) Analyze data on 8 patients from experiment FR2 [Month 13]. (e) Analyze data on 13 patients from experiment FR2 [Month 18]. (f) Analyze data on 43 patients from experiment FR2 [Month 24]. (g) Organize and annotate patient data from the above experiment to be shared with investigators and program personnel; precisely localize electrode contacts (b)(4) and carry out 3D reconstructions (b)(4) 	which			(b)(4)			
 (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 4 patients from experiment FR2 [Month 8]. (d) Analyze data on 8 patients from experiment FR2 [Month 13]. (e) Analyze data on 13 patients from experiment FR2[Month 18]. (f) Analyze data on 43 patients from experiment FR2 [Month 24]. (g) Organize and annotate patient data from the above experiment to be shared with investigators and program personnel; precisely localize electrode contacts (b)(4) and carry out 3D reconstructions (b)(4) 								
(c) Analyze data on 4 patients from experiment FR2 [Month 8]. (d) Analyze data on 8 patients from experiment FR2 [Month 13]. (e) Analyze data on 13 patients from experiment FR2 [Month 18]. (f) Analyze data on 43 patients from experiment FR2 [Month 24]. (g) Organize and annotate patient data from the above experiment to be shared with investigators and program personnel; precisely localize electrode contacts (b)(4) and carry out 3D reconstructions			-					
(d) Analyze data on 8 patients from experiment FR2 [Month 13]. (e) Analyze data on 13 patients from experiment FR2[Month 18]. (f) Analyze data on 43 patients from experiment FR2 [Month 24]. (g) Organize and annotate patient data from the above experiment to be shared with investigators and program personnel; precisely localize electrode contacts (b)(4) and carry out 3D reconstructions			-		7D2 [Month	01		
(e) Analyze data on 13 patients from experiment FR2[Month 18]. (f) Analyze data on 43 patients from experiment FR2 [Month 24]. (g) Organize and annotate patient data from the above experiment to be shared with investigators and program personnel; precisely localize electrode contacts (b)(4) and carry out 3D reconstructions (b)(4)								
(f) Analyze data on 43 patients from experiment FR2 [Month 24]. (g) Organize and annotate patient data from the above experiment to be shared with investigators and program personnel; precisely localize electrode contacts (b)(4) and carry out 3D reconstructions (b)(4)								
(g) Organize and annotate patient data from the above experiment to be shared with investigators and program personnel; precisely localize electrode contacts (b)(4) and carry out 3D reconstructions (b)(4)		•	-	-	-	-		
program personnel; precisely localize electrode contacts (b)(4) and carry out 3D reconstructions (b)(4)			_	_	_	_	with investiga	tors and
and carry out 3D reconstructions (b)(4)			_		_			wis und
		Program berse						
		[N				(5)(,	

UPENN	• •	eports on data from the aboves	-	•	
	DAKI A program per	(b)(4)		ell as analyses of the ele	
	correlates of (b)(4)	()()		(b)(4)	
					[Month 24].
	(j) Fully document c(k) Fully document a(l) Create 3D reconst(m) Provide final rep(n) Post fully annota	octed so far in a deidentified ode for experiment [Month analysis functions [Month 3 tructions of all patients run porting on analyzed data fro ted data to the public data p	2].]. in the task in P m all patients r	hase 1 [Month 24]. run in the task in Phase tients run in the task in I	1 [Month 24].
	(o) Expand analysis	Tunctions		(b)(4) Deliver updated and to	fully documented
	analysis code [Month	n 7].		. Denver apaated and i	uny documented
3.1.4.2		t, execute, and analyze data (b)(4)	from Experim	ent FR3 (n=18). The rec	cipient shall test
		l shall:			
		, and pilot task [Month 12].	1		
		analysis scripts [Month 13 4 patients from experiment		41	
	(d) [DELETED]	4 patients from experiment	rks [Monui 14	+].	
		10 patients from experimen	t FR3 [Month 2	241	
	•	18 patients from experimen	-	-	
	•	notate patient data from abo	_	_	
		eports on data from the above	-		
	(i) Post all data colle	ected so far in a deidentified	format compa	tible with the public dat	a portal [Month 30].
	(j) Fully document c	ode for experiment [Month	12].		
	•	analysis functions [Month 1	3].		
	(l) [DELETED]				
	(m) [DELETED]				
	(n) [DELETED]	functions		(b)(4)	
	(o) Expand analysis	iunctions		(b)(4) Deliver updated and to	fully documented
	analysis code [Month	1 13].		F	,

3.1.4.3 [DELETED]

3.1.4.4 Design, program, pilot, execute, and analyze data from Experiment CatFR2. (b)(4)

Further, the recipient (b)(4)

and shall:

- (a) Design, program, and pilot task [Month 2].
- (b) Write initial data analysis scripts [Month 3].
- (c) Analyze data on 4 patients from experiment CatFR2 [Month 8].
- (d) Analyze data on 8 patients from experiment CatFR2 [Month 13].
- (e) Analyze data on 13 patients from experiment CatFR2 [Month 18].
- (f) Analyze data on 18 patients from experiment CatFR2 [Month 24].
- (g) Organize and annotate patient data from above [Month 24].
- (h) Complete final reports on data from the above experiment [Month 24]
- (i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24]
- (j) Fully document code for experiment [Month 2].

OI LIVIV		fall patients run in the task in Ph nalyzed data from all patients ru	n in the task in Phase 1 [Month 24]. ents run in the task in Phase 1 [Month 24]. (b)(4)
	analysis code [Month 7].		Deliver updated and fully documented
3.1.4.5 ltest the a		and analyze data from Experime (b)(4)	ent CatFR3. In CatFR3 the recipient shall
iest the t		(b)(4)	. The
recipient	 (a) Design, program, and pilot to (b) Write initial data analysis so (c) Analyze data on 4 patients food (d) Analyze data on 8 patients food (e) [DELETE] (f) [DELETE] (g) [DELETE] (h) [DELETE] (i) Post all data collected so far (j) Fully document code for exp (k) Fully document analysis fur (l) [DELETE] (m) [DELETE] (n) [DELETE] 	eripts [Month 13]. from experiment CatFR3 [Month from experiment C	_
	(o) Expand analysis functions		(b)(4) Deliver updated and fully documented
	analysis code [Month 13].		
3.1.4.6 1	Design, program, pilot, execute, stimulation	, (k	ent YC2. The recipient shall apply (b)(4)
		•	all test the ability of stimulation to improve
memory		(b)(4)	
	(j) Fully document code for exp(k) Fully document analysis fur(l) Create 3D reconstructions of(m) Provide final reporting on a	ask [Month 2]. cripts [Month 3]. from experiment YC2 [Month 8] from experiment YC2 [Month 1] from experiment YC2 [Month 1] from experiment YC2 [Month 2] nt data from above experiment [Interpretate of the property of	3]. 8]. 8]. 4]. Month 24]. Month 24]. ble with the public data portal [Month 24]. ase 1 [Month 24]. n in the task in Phase 1 [Month 24] un in the task in Phase 1 [Month 24]. (b)(4)
			Deliver updated and fully documented

UPENN PI- KAHANA analysis code [Month 7].

3.1.4.7 [DELETED]

.1.4.8 Design, program, pilot, ex	ecute, and analyze data from E	Experiment PAL2.	(b)(4	4)
	. The recipient (b)(4)	(b)	(4)	
	1 (7)	. ,	、	shall:
(a) Design, program, an				
(b) Write initial data and				
	atients from experiment PAL2	-		
	tients from experiment PAL2	_		
	atients from experiment PAL2			
	patients from experiment PAL2			
	te patient data from above exp			
	rts on data from the above expe			155 1 4
	l so far in a deidentified format	compatible with the	e public data	portal [Month 24
	for experiment [Month 2].			
	ysis functions [Month 3].		1.043	
	tions of all patients run in the t	_	_	2.5 1.043
-	ng on analyzed data from all p			
	data to the public data portal f	-	the task in Pl	hase 1 [Month 24
(o) Expand analysis fund	ctions	(b)(4)	adatad and fi	illy documented
analysis code [Month 7]		Denver uj	puateu anu ru	my documented
The recipient shall:				
. The recipient shall: (a) Design, program, and	nilot took [Month 12]			
(b) Write initial data anal				
(c) [DELETED]	ysis scripts [Month 15].			
(d) [DELETED]				
	ients from experiment PAL3 []	Month 241		
	ients from experiment PAL3 [N	-		
(g) [DELETED]	ients from experiment 1 AL3 [1	violitii 50j.		
(h) [DELETED]				
(i) [DELETED]				
	For experiment [Month 12].			
(k) Fully document analy		(b)(4)		
[Month 13].	sis functions,	(0)(4)		
(l) [DELETED]				
(m) [DELETED]				
(n) [DELETED]				
(o) Expand analysis funct	ions	(b)(4)		
(e) Empaira amaryons runes			lated and full	y documented
analysis code [Month 13]		Zon or spe		
1.4.10 Design, program, pilot,	·			
The recipient shall evaluate	(b)(4)	tor	(b)(4)	learning durin

UPENN	I PI−	KAHANA								
a	(b))(4)	task.			(b)	(4)			
				The recipient shall	l vary			(b)(4)		
paramet	ers.					(b)(4)				
				The recipient	shall index	x learning		(b)(4)		
		(b)(4)		The rec	cipient sha	all compare	e (b)(4)	across the five co	onditions	(b)(4)
				and	(2) ident	ify (b)	(4)	parameters	(b)(4)	
	and	shall:								
	(a)	Design, pro	gram,	and pilot task [Mon	nth 2].					
	(b)	Write initia	l data	analysis scripts [M	onth 3].					
	(c)	Analyze dat	ta on 1	0 patients from exp	periment I	DBS1 [Mo	nth 8].			
	(d) -	-(n)[DELE	TED]							
3.1.4.11	Des	sign, prograi	m, exe	cute, and analyze d	ata from l	Experimen	ts PS1, I	PS2 & PS3. The red	cipient sha	ll (b)(4)
				(b)(4)			identif	y (b)(4) stimulati	on parame	eters:
	(a)	Design and	progr	am tasks [Month 12	2].				•	
				4 patients each fro		nents PS1,	PS2, & 1	PS3 [Month 16].		
				29 patients each from						
	(d)	Post fully a	nnotat	ed data to the publi	c data noi	rtal for all 1	natients 1	run in the task in P	hase 1 [Me	onth 301.
	()				F					
3.1.5 D	evelo	op control al	gorith	ms		(b)(4)				
3.1.5.1	[DE]	LETED]								
3.1.5.2	Deve	lop algorith	ms			((b)(4)			
		The recipie								
	(a)	Complete in	nterim	report			(b)(4)			
					[Month	19].				
	(b)	Develop pro	ototyp				o)(4)			
				Cor			erim repo	ort on algorithms,	(b)	(4)
					. [Month	12].				
		[DELETED	_							
		[DELETED	_							
				interim report on			_	_		
	(f)	Provide 12-	month	interim report on	(b)(4)	algorit	hms [Mo	onth 12].		
	(g)	Document 1	12-mo	nth prototype (b)(4)	algorithms	[Month	12].		
	(h)	[DELETED)]							
	(i)	[DELETED]							
	(j)	[DELETED	1							
		DELETED	_							
	` /	-	-							
3.1.5.3	DEI	ETED1								
ا د.د.د.	LULL	LILD								

3.1.5.4 [DELETED]

3.1.6 Core project resources devoted to TA1.

- 3.1.6.1 The recipient shall perform electrophysiological experiment development and programming, data analysis, computational cluster effort towards data analysis and computational modeling from TA1.
- 3.1.6.2 The recipient shall provide project coordination, data sharing and data storage.

UPENN PI- KAHANA 3.1.7 Determine electrode requirements for (b)(4)	stimulation in Phase 2.	. The recipies	nt shall characterize
(b)(4)			for modulating and
restoring memory function.			
3.1.7.1 The recipient shall design and develop an electronic shall design and develop shall de	rode (b)(4)	capable	(b)(4) . The recipient
shall:			1
(a) Based on precise anatomical analyses	(b)(4)		
(b) (b) Working with Lawrence Livermore National Labs (materials that can be put into place by the beginning of		echnical draw	ving and list of
(c) Working with LLNL, complete ISO-10993 testing t design history file and associated ISO test results require (d) [DELETED]			
3.1.8 [DELETED]			
3.1.9 [DELETED]			
Technical Area 2			
3.1.10 Validate system architecture and individual c the high-level system design requirements against cu	•		nent and review
3.1.10.1 The recipient shall validate system level specified	fication with TA1 team [M	Ionths 1–6].	
3.1.10.2 [DELETED]			
3.1.10.3 The recipient shall refine the specifications for , continually refining a	electronics s needed [Months 4–9].	(b)(4)	
3.1.10.4 The recipient shall validate the specification for [Months 5–6].	or the Algorithm prototypin	ng system and	user interface
3.1.10.5 The recipient shall define the sub-chronic safe IDE approval [Month 6] and shall:	ty and performance data re	equired by the	FDA for 29-day
(a) Document definitions of the functional, op [Month 6].(b) Document definitions of the component-le	<u>-</u>	•	•
external packaging, and algorithm prototyping (c) Document definitions of the sub-chronic sa	system [Month 9].		
day IDE approval [Month 6]		required by ti	ic i DA for the 2)-
(d) Deliver definitions of stakeholder requirement	ients [Month 4]		
3.1.11 Design, fabrication, and characterization of the shall develop a (b)(4) electrodes. (*and any adaptations needed to ensure the shall develop a (b)(4)	caj	pable of mati	or. The recipient ng with (b)(4)
3.1.11.1 The recipient shall design and manufacture of e (b)(4) [Months 7–18].	electronics,	(b)(4)	

3.1.11.2 The recipient shall (b)(4) software (firmware) to control the electronics and provide (b)(4)

UPENN PI- KAHANA capability [Months 7–18].

	The recipient shall ical depth electrodes	•	_				(b)(4)	to interface	with
3.1.11.4	The recipient shall					ormance testir ystem deliver	-		hs 19_
241	***	пртерагано	11 101 1 1071	IDL Suomi	ssion and s	ystem den ver	y to cilinea	i sites [iviont	113 17
24].	(a) Design and bui	ild electroni	cs,			(b)(4)		[M	Ionths
	(b) Document the capability [Month	. , . ,	oftware tha	t controls	the electron	ics and docur	ment (b)(4	4) algorith	m
	(c) Modify the design verification	testing [Mo	onth18].		and build 22	2	(b)(4)	1	for
	(d) Test and docur IDE submission [M		and perforn	nance	(I	0)(4)	in pre	eparation for	FDA
recipiei	Connectorization a nt shall develop a conic (b)(4) neural	onnectoriza	tion metho			(b)(4) riety of clinic	,	stimulator le designs w	
3.1.12.1	The recipient shall	define spec	ifications f	or the conr	nector		(b)(4)		
	•	1				[Months			
3.1.12.2	2 [DELETED]								
3.1.12.3	[DELETED]								
	The recipient shall ce, mechanical integ (a) Define specific (b) [DELETED]	rity [Month	s 15–24].	Γhe recipie	nt shall:	al conductivit	y and reliab	oility, moistu	re
	(c) Document the	assembly pr	rocess			(b)(4)			
	[Month 15].								
	(d) Complete and (e) Design verification integrity [Month 24]	ation testing		<i>P</i> 1 L	-	and reliabilit	y, and mech	nanical	
3.1.13	Algorithm prototyp	oing system	. The reci	pient shall	develop a	n algorithm j	prototyping	g system (b)(4)
3.1.13.1	The recipient shall		(b)(4) ths 1–6].	interfac	ce		(b)(4)		
3.1.13.2	? The recipient shall	document t	he software		onths 1–12]	(b)(4)			
3.1.13.3	The recipient shall	develop so:	ftware	(b))(4)	[Months	s 7–18].		
	The recipient shall ipient shall	verify and	validate tes	ting and do	ocumentatio	on for IDE sul	bmission [N	Months 19–2	4].
	_	b)(4)	interface			(b)(4)			

UPENN PI- KAHANA (b)(4) [Month 6].
(b) Document the software used (b)(4)
(b)(4) [Month 12].
(c) Document the software (b)(4) [Month 18].
(d) Complete prototype software package [Month 18].
(e) Verify and validate testing and documentation for IDE submission [Month 24].
3.1.14 System verification and validation testing. The recipient shall evaluate and verify system lifetime, sterility and biocompatibility. The recipient shall also verify and validate the system functions and interfaces
(b)(4)
. Additionally, system verification and validation shall be performed.
3.1.14.1 [DELETED]
3.1.14.2 [DELETED]
3.1.14.3 [DELETED]
3.1.14.4 The recipient shall perform (b)(4) system verification testing for sub-chronic ($<$ 29-days) use as outlined in ANSI / AAMI / ISO 14971:2007/(R)2010 [Months 19–24].
3.1.14.5 The recipient shall validate the (b)(4) system [Month 19–24]. The recipient shall:
 (a) Fabricate and assemble fully-integrated systems for testing [Month 18]. (b) [DELETED] (c) [DELETED] (d) [DELETED] (e) Report on electronics testing for sub-chronic (< 29-days) use as outlined in ANSI / AAMI / ISO 14971:2007/(R)2010 [Month 24]. (f) [DELETED] (g) Validate and fully document a system that is ready for FDA IDE submission; deliver system verification and validation reports [Month 24].
3.1.15 [DELETED]
3.1.16 (b)(4) Electrode Design.
3.1.16.1 The recipient shall deliver development plans for a novel (b)(4) lead suitable for interfacing with the (b)(4) device. The recipient shall: (a) Identify at least one partner capable of delivering the electrode [Month 7] (b) Deliver a technical drawing, estimated development and manufacturing budget, and identify any cost
sharing activities [Month 7]
Technical Area 3 The recipient shall perform basic research findings. (b)(4)
The recipient shall perform basic research findings (b)(4) to inform the human stimulation studies in
TA1 and guide device development in TA2.
The recipient shall document the protocols for measuring monkey (b)(4) I memory (b)(4) and
shall train animals in the (b)(4) task. In parallel, the recipient shall conduct studies of the neurophysiology of
stimulation (b)(4)

_				the electrophysiology	(b)(4) i	n two monkeys. The
recipient	shall also p	erform a systema)(4)	
			. The recipient s	hall also probe the neur	rophysiology	(b)(4)
3.1.16 Id	dentifying n	euronal basis of	(b)(4) memory	y in NHPs and probin	g the role of	stimulation <mark>(</mark> b)(4)
		(b)(4)	. This p	hase of the work seek	s to characte	rize the patterns of
neuronal	l activity th	at underlie (b)(4	1) memory in n	on-human primates. T	The recipient	shall conduct (b)(4)
(b)(4)	recording	gs		(b)(4)		
3.1.16.1	The recipies	nt shall design, p	rogram, and test	experimental protocol	for measuring	monkey (b)(4) memo
performa	nce	(b)(4)		[Months 1-4].		
	(a) The reci	pient shall desig	n and program a	behavioral task for mea	asuring monke	ey (b)(4) memory
	[Month 4].					
3.1.16.2	The recipier	nt shall documen	t the hardware in	terface for the (b)(4)	task to inte	erface with recording
equipme		•	-			
	(a) The reci	pient shall docur	nent the hardwar	re/software interface for	r interfacing e	lectrophysiological
:	recordings,	eye tracker, and i	monkey behavior	al paradigm [Month 5]		
3.1.16.3	The recipier	nt shall train	(b)(4) to	(b)(4))	(b)(4)
(b)(4) m	emory task	[Months 5-24].				
	(a) The reci	pient shall obtain	n one monkey, co	omplete pre-training he	alth checks, pl	lace collars,
	complete qu	arantine and roo	m acclimation pr	ocedures [Month 8].		
	(b) The rec	ipient shall train	the monkey in ch	airing and handling pro	ocedures, accl	imate monkey to
	working in t	he laboratory, be	gin food delay p	rocedures, train monke	y on initial be	havioral tasks, (b)(4)
			hicl	h will be used in the ey	e-tracking cal	ibration procedure of
	(b)(4) mem	ory task [Month	10].			
	(c) The reci	pient shall train t	the animal in the	(b)(4) memory paradi	gm [Month 24	.].
3.1.16.4	The recipier	nt shall prepare n	nonkey for record	ding and stimulation st	udies, includir	ng MRIs, surgeries to
implant h	neadposts an	d recording chan	nbers, and cranio	tomies. The recipient s	hall conduct s	tudies of
neurophy	siological c	orrelates of monl	key (b)(4) behav	ior without stimulation	[Months 5-24	4] and shall:
			e monkey and pe	rform surgery to impla	nt headpost. C	omplete recovery
from surg	gery [Month	12].				
(b) Train	n one monke	y on initial joysti	ck task, includin	g eye calibration and fi	ixation trainin	g with head fixation
-	ost [Month	-				
	•		•	n surgery to implant rec	ording chamb	er [Month 18].
(d) The	recipient sh	all document all	findings in a fina	ıl report [Month 19]		
3.1.16.5	[DELETED	0]				
2.2		•				
3.1.17 C	Comprehens	ive examination	of the electroni	nysiology of stimulatio	on in non-hur	nan primates. (b)(4)
	_		_	The recipient shall per		_
ability fo	-	stimulation	(b)(4)	and ident		(4) parameter
	(~)(')	(b)(4)		The recipient shall cor		
		(5)(4)	•	ine recipient shan coi	iddet both st	(0)(4)

3.1.17.1	The recipient shall pro	epare untrained mor	nkeys for (b)(4) rec	ording and stin	nulation studies	(b)(4)
		The recipient sha	ll perform MRIs to	o guide electrod	le implantation,	surgeries to
implant	headposts and recording	_	•			
	(a) The recipient sha [Month 6].	ll perform monkey	surgeries to implai	nt electrodes	(b)(4)
3.1.17.2	2 The recipient shall de	monstrate that neuro	onal stimulation		(b)(4)	
	(a) The recipient shal		(b)(4) stim [Month 9].	ulation	(b)(4)	
	(b) The recipient shall				(b)(4)	
					[Month 11].	
	(c) The recipient shall	document all finding	ngs in a final repor	rt [Month 19]		
3.1.17.3	[DELETED]					
3.1.17.4	[DELETED]					
3.1.17.5	[DELETED]					
Technic	TION PERIOD (PHA cal Area 1 xtending computation		(b)(4)			
Technic 3.2.1 E	cal Area 1 xtending computation	al model				
Technic 3.2.1 E	cal Area 1 xtending computation Modeling the dynamic	al model	(b)(4)			
Technic 3.2.1 E	cal Area 1 xtending computation	al model				
Technic 3.2.1 E	xtending computation Modeling the dynamic (a)	al model	(b)(4) (b)(4)		. [Month	28]
Technic 3.2.1 E	cal Area 1 xtending computation Modeling the dynamic	al models s of brain activity	(b)(4)		. [Month	28]
Technic 3.2.1 E	xtending computation Modeling the dynamic (a)	al models s of brain activity	(b)(4) (b)(4)		. [Month	28]
Technic 3.2.1 E	xtending computation Modeling the dynamic (a)	al models s of brain activity	(b)(4) (b)(4) (4) (b)(4)		. [Month	28]
Technic 3.2.1 E	xtending computation Modeling the dynamic (a)	s of brain activity (b)((b)(4) (b)(4) (4) (b)(4)	130]		
Technic 3.2.1 E	xtending computation Modeling the dynamic (a) (b)	s of brain activity (b)((b)(4) (b)(4) (4) (b)(4)	a 30] ased to perform	these analyses.	
3.2.1 E	xtending computation Modeling the dynamic (a) (b)	s of brain activity (b)((b)(4) (b)(4) (b)(4) [Months including code u	a 30] ased to perform	these analyses.	[Month 36]
3.2.1 E	xtending computation Modeling the dynamic (a) (b) (c) Formal report on the	s of brain activity (b)((b)(4) (b)(4) (b)(4) [Months including code upodeling to impose to impose the control of the code upodeling to impose the code upodeling the code upod	a 30] ased to perform	these analyses.	[Month 36]
3.2.1 E	xtending computation Modeling the dynamic (a) (b) (c) Formal report on the	s of brain activity (b)((b)(4) (b)(4) (b)(4) [Months including code under the important of the i	a 30] ased to perform	these analyses.	[Month 36]
3.2.1 E	xtending computation Modeling the dynamic (a) (b) (c) Formal report on the	s of brain activity (b)((b)(4) (b)(4) (b)(4) [Months including code umodeling to im (b)(4)	a 30] ased to perform	these analyses.	[Month 36]
3.2.1 E. 3.2.1.1	cal Area 1 Extending computation Modeling the dynamic (a) (b) (c) Formal report on the computation Using (a)	s of brain activity (b)((b)(4) (b)(4) (b)(4) [Months including code under the important of the i	a 30] ased to perform	these analyses.	[Month 36]

UPENN PI-KAHANA (b)(4) . [Month 30] modeling to improve memory (b)(4) (c) Final report on the use of (b)(4)(b)(4)restoration. [Month 36] 3.2.1.3 Incorporate modeling into (b)(4) algorithms: (b)(4)(a) (b)(4) (b)(4) (b)(4) (b)(4). [Month 28] (b)(4) [Month 30]. (c) Deliver final report on the role (b)(4) across the various RAM tasks, and predicting which stimulation parameters (b)(4) (b)(4) are most likely to improve memory. [Month 34] 3.2.1.4 Using (b)(4) analysis to model (b)(4)memory: (a) (b)(4) [Month 28] (b)(4)(b) (b)(4)(b)(4) . [Month 30] (b)(4)(c) (b)(4). [Month 34] (d) Final report on (b)(4) (b)(4)(b)(4) [Month 36] 3.2.1.5 Build a revised control algorithm strategy (b)(4) (b)(4)(b)(4) [Month 30] (b) Complete a reanalysis of all parameter search (b)(4)

		(b)(4)		
		(b)(4)		
	(b)(4)		. 1	[Month 34].
(c) Complete algorithm for (b)(4) TH6 tasks to maximize memory per (d) Deliver a final report based on the	formance. [N	Month 38]		ring FR6, PAL6, CatFl
6 Collect high-resolution imaging and (b)(4) The recipien		(b)(4)	models	(b)(4)
(a) Collect high-resolution magnetic diffusion and resting state functions	c resonance		quences in 10 s	ubjects, including T1/7
(b) Collect high-resolution magnetic diffusion and resting state functions	al scans. [M	onth 42]		
(c) Collect high-resolution magneti diffusion and resting state functions	al scans. [M	onth 48]	quences in 100	•
(d) Deliver interim report on predicted to reliably	.,	selection (b)(4)	memory	(b)(4) (b)(4)
				[Month 38]
(e)	(b)(4)		[Month 38]
[Month 41]				
(f) Deliver interim report on the (b)(4) memory	(b)(4)	selection	(b)(4)	that reliably enhan
[Montl	h 441			
(g) Final report on the efficacy of s	_	arget selecti	on based upon	(b)(4)
(b)(4) biomarkers in	(b)(4)	memory	tasks. Report	will include data from
minimum of 20 (b)(4) memory test sessions (•	*	e.g. FR6, CatFF	R6, PAL6) and 10 (b)(4

- 3.2.1.7 The recipient shall complete data collection in experiment FR1 and shall:
 - (a) Analyze data on 60 patients from experiment FR1 [Month 30].
 - (b) Analyze data on 66 patients from experiment FR1 [Month 36].
 - (c) Analyze data on 72 patients from experiment FR1 [Month 42].

	PI- KAHANA d) Analyze data on 78 patients from experiment FR1 [Month 48].	
		-)/4)
(e) Complete final reports on data from the above experiment, (b)(4) [Month 48].	b)(4)
(f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48]	
(g) Post fully annotated data to the public data portal for all patients run in the tas	sk in Phase 2 [Month 48].
	the recipient shall complete data collection in experiment CatFR1 and shall: a) Analyze data on 36 patients from experiment CatFR1 [Month 30].	
	b) Analyze data on 38 patients from experiment CatFR1 [Month 36].	
	c) Analyze data on 41 patients from experiment CatFR1 [Month 42].	
,	d) Analyze data on 43 patients from experiment CatFR1 [Month 48].	
`		0)(4)
	(b)(4) [Month 48].)(-1)
(f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48]	
	g) Post fully annotated data to the public data portal for all patients run in the tas	
,	h) Expand analysis functions (b)(4)	
	[Month 30]	
22105		
3.2.1.9 De	esign, program, pilot, execute, and analyze data from Experiment TH1. The recipi (b)(4) (b)(4)	ent (b)(4) shall:
(a) Deliver fully documented code and analysis functions [Month 26].	
(b) Analyze data on 21 patients from experiment TH1 [Month 30].	
(c) Analyze data on 32 patients from experiment TH1 [Month 36].	
(d) Analyze data on 43 patients from experiment TH1 [Month 42].	
(e) Analyze data on 54 patients from experiment TH1 [Month 48].	
(f) Complete final reports on data from the above experiment, [Month 48].)(4)
(g) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48]	.
(h) Post fully annotated data to the public data portal for all patients run in the tas	sk in Phase 2 [Month 48].
	The recipient shall complete data collection and analysis in experiment PAL1 and a) Analyze data on 31 patients from experiment PAL1 [Month 30].	d shall:
	b) Analyze data on 36 patients from experiment PAL1 [Month 36].	
	c) Analyze data on 42 patients from experiment PAL1 [Month 42].	
	d) Analyze data on 47 patients from experiment PAL1 [Month 48].	
•		0)(4)
	[Month 48].	
`	f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48] g) Post fully annotated data to the public data portal for all patients run in the task	
3.2.2 Stir	nulation to enhance (b)(4)	memory
22216		

- 3.2.2.1 Continue to collect and analyze data from Experiment FR3. The recipient shall:
 - (a) Organize and annotate data from 19 patients [Month 36].
 - (b) Complete final reports on data from the above experiment, including a report on the anatomical specificity of target selection [Month 48].
 - (c) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
 - (d) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.2 Design, program, execute, and analyze data from Experiment PS4/FR5.	(b)(4)	
(b)(4)		
(b)(4)		
. The recipient shall:		

- (a) Deliver fully documented PS4/FR5 code and analysis functions [Month 32].
- (b) Organize and annotate data from 6 PS4/FR5 patients [Month 36].
- (c) Organize and annotate data from 9 PS4/FR5 patients [Month 42].
- (d) Organize and annotate data from 18 PS4/FR5 patients [Month 48].
- (e) Complete final reports on data from the PS4/FR5 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in FR3. [Month 48].
- (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.3 Design, program, execute, and analyze data from Experiment PS5/FR6.	(b)(4)	
		The
2. 2. 3. 4. 41		

recipient shall:

- (a) Deliver fully documented PS5/FR6 code and analysis functions [Month 38].
- (b) Organize and annotate data from 6 PS5/FR6 patients [Month 42].
- (c) Organize and annotate data from 14 PS5/FR6 patients [Month 48].
- (d) Complete final reports on data from the PS5/FR6 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in FR5. [Month 48].
- (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.4 [DELETED]

- 3.2.2.5 Continue to collect and analyze data from Experiment CatFR3. The recipient shall:
 - (a) Organize and annotate data from 10 patients [Month 36].
 - (b) Complete final reports on data from the above experiment, including a report on the anatomical specificity of target selection [Month 48].
 - (c) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
 - (d) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.6 Design, program, execute, and analyze data from Experiment PS4/CatFR5.	(b)(4)
(b)(4)	
	The

recipient shall:

- (a) Deliver fully documented PS4/CatFR5code and analysis functions [Month 32].
- (b) Organize and annotate data from 6 PS4/CatFR5 patients [Month 36].
- (c) Organize and annotate data from 9 PS4/CatFR5 patients [Month 42].
- (d) Organize and annotate data from 16 PS4/CatFR5 patients [Month 48].
- (e) Complete final reports on data from the PS4/CatFR5 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in CatFR3 [Month 48].
- (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

UPENN PI- KAHANA 3.2.2.7 Design, program, execute, and analyze data from Experiment PS5/CatFR6.	(b)(4)
(b)(4)	
The recipient shall: (a) Deliver fully documented PS5/CatFR6 code and analysis functions, [Month 38].	(b)(4)
(b) Organize and annotate data from 6 PS5/CatFR6 patients [Month 42]. (c) Organize and annotate data from 13 PS5/CatFR6 patients [Month 48].	
(d) Complete final reports on data from the PS5/CatFR6 experiment, including a specificity of target selection, and a comparison with stimulation efficacy in CatF	FR5 [Month 48].
(e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal fully annotated data to the public d	-
3.2.2.8 Design, program, execute, and analyze data from Experiment TH3.	(b)(4)
(b)(4)	
 The recipient shall: (a) Deliver fully documented code and analysis functions [Month 26]. (b) Organize and annotate data from 5 patients [Month 30]. (c) Organize and annotate data from 10 patients [Month 36]. (d) Complete final reports on data from the above experiment, including a report 	rt on the anatomical
specificity of target selection [Month 48].	
(e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 4 (f) Post fully annotated data to the public data portal for all patients run in the t	_
3.2.2.9 Design, program, execute, and analyze data from Experiment PS4/TH5.	(b)(4)
The recipient shall:	
 (a) Deliver fully documented PS4/TH5 code and analysis functions [Month 32] (b) Organize and annotate data from 5 PS4/TH5 patients [Month 36]. (c) Organize and annotate data from 8 PS4/TH5 patients [Month 42]. (d) Organize and annotate data from 10 PS4/TH5 patients [Month 48].].
(e) Complete final reports on data from the PS4/TH5 experiment, including a respecificity of target selection, and a comparison with stimulation efficacy in TH3	-

- (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.10	Design, program, execute, and analyze data from Experiment PS5/TH6.	(b)(4)	
		. The recipient shall:	

- (a) Deliver fully documented PS5/TH6code and analysis functions [Month 38].
- (b) Organize and annotate data from 5 PS5/TH6 patients [Month 42].
- (c) Organize and annotate data from 10 PS5/TH6 patients [Month 48].
- (d) Complete final reports on data from the PS5/TH6 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in TH5 [Month 48].
- (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].

(f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.11 Design, program, execute, and analyze data from Experiment PAL3.

(b)(4)

(b)(4)

The recipient shall:

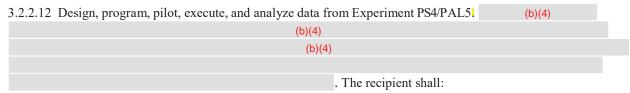
(a) Analyze data on 15 patients from the PAL3 experiment [Month 36].

(b) Analyze data on 18 patients from the PAL3 experiment [Month 42].

(c) Analyze data on 14 patients from the PAL3 experiment [Month 48].

(d) Complete final reports on data from the above experiment, including a report on the anatomical specificity of target selection [Month 48].

- (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].



- (a) Deliver fully documented PS4/PAL5 code and analysis functions [Month 32].
- (b) Analyze data on 6 patients from the PS4/PAL5 experiment [Month 36].
- (c) Analyze data on 9 patients from the PS4/PAL5 experiment [Month 42].
- (d) Analyze data on 14 patients from the PS4/PAL5 experiment [Month 48].
- (e) Complete final reports on data from the above experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in PAL3 [Month 48].
- (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.13	Design, program, execute, and analyze data from Experiment PS5/PAL6	(b)(4)	
		The recipient shall:	

- (a) Deliver fully documented PS5/PAL6 code and analysis functions [Month 38].
- (b) Organize and annotate data from 5 PS5/PAL6 patients [Month 42].
- (c) Organize and annotate data from 10 PS5/PAL6 patients [Month 48].
- (d) Complete final reports on data from the PS5/PAL6 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in PAL5 [Month 48].
- (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].
- 3.2.2.14 Continue to collect and analyze data from Experiments PS2. The recipient shall:
 - (a) Analyze data on 50 patients from experiments PS2 [Month 30].
 - (b) Analyze data on 71 patients from experiments PS2 [Month 36].
 - (c) Analyze data on 82 patients from experiments PS2 [Month 42].
 - (d) Analyze data on 93 patients from experiment PS2 [Month 48].
 - (e) Post fully annotated data to the public data portal for all patients run in the task [Month 48].

3.2.2.15. [DELETED]

3.2.2.17. Design, program, execute, and analyze data from Experiment REC1.	(b)(4)
(b)(4)	
(b)(4)	
(b)(4) The recipient shall:	
(a) Deliver fully documented code and analysis functions [Month 28	3].
(b) Organize and annotate data from 2 patients [Month 30].	
(c) Organize and annotate data from 4 patients [Month 36].	
(d) Organize and annotate data from 6 patients [Month 42].	
(e) Organize and annotate data from 8 patients [Month 48].	
(f) Complete final reports on data from the above experiment,	(b)(4)
Month 48].	

- (g) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (h) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

Technical Area 2

Phase 2 objectives in TA2 shall be to support FDA IDE approval and clinical site training, develop clinical systems, and (b)(4) Phase 1 algorithms.

- 3.2.4 Update system architecture and individual components based on TA1. The recipient shall review and, if necessary, redefine, document and review the high-level system design requirements for the (b)(4) system based on the discovery and feedback from TA1 in phase 1.
- 3.2.4.1 The recipient shall review and, if necessary, redefine system level specification with TA1 team based on the phase 1 results [Months 25–30].
- 3.2.4.2 The recipient shall review and, if necessary, redefine the specifications for neural interfaces [Months 25–30].
- 3.2.4.3 The recipient shall review and, if necessary, redefine the specifications for electronics including the stimulating and recording electronics [Months 25–30].
- 3.2.4.4 The recipient shall review and, if necessary, redefine the sub-chronic safety and performance data required by the FDA for 29-day IDE approval [Months 25–30].
- 3.2.4.5 The recipient shall produce a final set of documents detailing the specifications for the overall system and its components [Month 30].
- 3.2.5 Fabrication of the reusable (b)(4) stimulators for clinical studies. The recipient shall produce the balance of (b)(4) stimulator units for use at the clinical sites in early Phase 2. The recipient shall:
 - (a) Deliver ten tested and documented (b)(4) systems [Month 26].
 - (b) Deliver an additional thirty tested and documented (b)(4) systems [Month 30].
 - (c) Deliver an updated development plan, requirements, and design history file and limited verification and validation activities to cover the system integration with the(b)(4) Lead and (b)(4) splitter cable [Months 30].
 - (d) Utilize the (b)(4) to perform recording and closed-loop stimulation during memory testing in at least 50 patients [Month 48].
- 3.2.6 Evaluation of commercially available (b)(4) leads for memory enhancement. The recipient

shall.

,		ol amendment a		-	proval to in	nplant commerc	ially-av	ailable leads (b)
	(a) Develop protoco				f (1 2.47			
	(b)(4)		, ,	-	Months 34].			
	(b) Deliver interim	report on mem	ory	(b)(4)	performano	e in 10 subjects		(b)(4)
						[M	Ionths 4	1].
	(c) Develop protoco	ol amendment a	and obta	ain IRB ap	proval to in	_	ially-av	-
	(d) Deliver interim	report on stimu	ılation t	arget loca	lization in 1			(b)(4)
		Ionths 44].						
	(e) Final report on leads [M		(4)	performai	nce and targ	et localization in	n 40 sub	jects with (b)(4)
3.2.7 A	.lgorithm prototypi	ng system: (b)	(4) alg	orithm d	evelopment	from TA1, Pha	ase 1. T	he recipient sha
	ent the developmen	· ,			-		(b)(4)	•
	· · · · · · · · · · · · · · · · · · ·							
				iccessiui i			(=)(-)	
				eccssiui i	w- g		(=)(-)	
3 2 7 1	The recipient shall d	ocument the de						writhms from pl
	The recipient shall d	ocument the de	evelopm	nent of a	(b)(4) too			orithms from ph
3.2.7.1 1	The recipient shall d	ocument the de	evelopm		(b)(4) too			orithms from pl
1	(b)(4)		evelopm [Mont	nent of a hs 33–39]	(b)(4) too)	to translate exis	sting alg	orithms from ph
3.2.7.2	(b)(4) The recipient shall d		evelopm [Mont	nent of a hs 33–39]	(b)(4) too)		sting alg	orithms from ph
3.2.7.2	(b)(4)		evelopm [Mont	nent of a hs 33–39]	(b)(4) too)	to translate exis	sting alg	orithms from ph
3.2.7.2 Month 3.2.7.3	(b)(4) The recipient shall d	locument the de	evelopm [Mont	the same of a least of a to	(b)(4) too!	to translate exis	sting alg	
3.2.7.2 Month 3.2.7.3	(b)(4) The recipient shall des 33–39]. The recipient shall a	locument the de	evelopm [Monti	nent of a hs 33–39] nent of a to mode, clo	(b)(4) tool . ool sed-loop me	to translate existing to translate existing in	sting alg	
3.2.7.2 [Month 3.2.7.3	(b)(4) The recipient shall des 33–39]. The recipient shall a	locument the de dminister emb	[Monti	nent of a hs 33–39] nent of a to mode, clo	(b)(4) tool . cool sed-loop me	to translate existing in [Month 39].	sting alg	ilepsy Monitori
3.2.7.2 [Month 3.2.7.3	(b)(4) The recipient shall des 33–39]. The recipient shall a (a) Complete softv (b) Complete softv	locument the de dminister emb vare tool for loa vare tool for tra	evelopm [Mont] evelopm edded-1 ading nslating	the same of a length of a to length of a to length of a to length of a length	(b)(4) tool . col sed-loop mo b)(4) algorithm	(b)(4 emory testing in [Month 39].	the Ep	ilepsy Monitori [Month 39
3.2.7.2 Month 3.2.7.3	(b)(4) The recipient shall des 33–39]. The recipient shall a	locument the de dminister emb	evelopm [Mont] evelopm edded-1 ading nslating	ment of a hs 33–39] ment of a to mode, clo (g software bry task to	(b)(4) tool ool sed-loop mo b)(4) algorithm o five patier	(b)(4 emory testing in [Month 39].	sting alg	ilepsy Monitori [Month 39
3.2.7.2 Month 3.2.7.3	(b)(4) The recipient shall des 33–39]. The recipient shall a (a) Complete softv (b) Complete softv	locument the de dminister emb vare tool for loa vare tool for tra	evelopm [Mont] evelopm edded-1 ading nslating	ment of a hs 33–39] ment of a to mode, clo (g software bry task to	(b)(4) tool . col sed-loop mo b)(4) algorithm	(b)(4 emory testing in [Month 39].	the Ep	ilepsy Monitori [Month 39
3.2.7.2 [Month 3.2.7.3	(b)(4) The recipient shall des 33–39]. The recipient shall a (a) Complete softv (b) Complete softv	locument the de dminister emb vare tool for loa vare tool for tra	evelopm [Mont] evelopm edded-1 ading nslating	ment of a hs 33–39] ment of a to mode, clo (g software bry task to	(b)(4) tool ool sed-loop mo b)(4) algorithm o five patier	(b)(4 emory testing in [Month 39].	the Ep	ilepsy Monitori [Month 39
3.2.7.2 [Month 3.2.7.3 Unit:	(b)(4) The recipient shall des 33–39]. The recipient shall a (a) Complete softw (b) Complete softw (c) Administer	locument the de dminister emb vare tool for loa vare tool for tra	evelopm [Mont] evelopm edded-1 ading nslating	ment of a hs 33–39] ment of a to mode, clo (g software bry task to	(b)(4) tool ool sed-loop mo b)(4) algorithm o five patier	(b)(4 emory testing in [Month 39].	the Ep	ilepsy Monitori [Month 39
3.2.7.2 [Month 3.2.7.3 Unit:	(b)(4) The recipient shall des 33–39]. The recipient shall a (a) Complete softv (b) Complete softv	locument the de dminister emb vare tool for loa vare tool for tra	evelopm [Mont] evelopm edded-1 ading nslating	ment of a hs 33–39] ment of a to mode, clo (g software bry task to	(b)(4) tool ool sed-loop mo b)(4) algorithm o five patier	(b)(4 emory testing in [Month 39].	the Ep	ilepsy Monitori [Month 39
3.2.7.2 [Month 3.2.7.3 Unit:	(b)(4) The recipient shall des 33–39]. The recipient shall a (a) Complete softw (b) Complete softw (c) Administer	document the ded dminister emb ware tool for loa ware tool for tra (b)(4)	evelopm [Monti evelopm edded-rading nslating memo	ment of a hs 33–39] ment of a to mode, clo (g software bry task to	(b)(4) tool ool sed-loop mo b)(4) algorithm o five patier	(b)(4 emory testing in [Month 39]. (b)(4	the Ep (b)(4	ilepsy Monitori [Month 39

equipment and administration, integration between TA1, TA2, and TA3 modeling and electrophysiology shall be documented.

Technical Area 3 [DELETED]

3.3 PROGRAM MANAGEMENT AND REVIEW

The Government will actively monitor, review and approve the recipient's performance to ensure all the performers are in sync and matched with the Government's requirements. The Government will ensure that each of the performers share experimental data across the program and will further ensure that the performers develop techniques and capabilities that are compatible and integrate with each other. The recipient shall collaborate and cooperate with other performers in the program under the coordination of the Government team. At Government PI meetings, the recipient shall demonstrate technical capabilities and engage and/or challenge other performers in a cooperative and challenge environment. Along these lines, the Government will ensure that each performer shares technical information with the others to enable the testing/challenging of each other's capabilities. The Government will further oversee the program and will review, approve, and participate in the demonstrations.

3.3.1 Kick-off Meeting

The recipient shall hold a kick off meeting within 60 days of award of this agreement. In this meeting, the recipient shall present a program management plan and financial tracking plan.

3.3.2 Quarterly Financial Reports

The recipient shall provide quarterly financial progress reports to the Government Technical Representative (GTR) and DARPA Program Manager. The purpose of these reports is to provide a brief project progress and inform the GTR and Program Manager of any potential issues.

3.3.3 Quarterly Technical Reporting

The recipient shall provide quarterly progress reports to the Government Technical Representative (GTR) and DARPA Program Manager. The purpose of these reports is to present a summary of work completed by SOW tasking and milestones met, discuss any problems encountered, update the program schedule, present the program financial status, and discuss remaining work. Quarterly reports shall also include all technical data items generated including but not limited to experimental data, processed data along with methods of processing used, research reports and publications and software (source code and executables).

3.3.4 Monthly Status Reports

The recipient shall provide monthly status reports which will include all relevant project data including, but not limited to, raw and analyzed electrophysiological signals as well as any necessary annotations and interpretations of the data, such as time-stamped patient behaviors, necessary for appropriate analyses and interpretation of the data. Patient data shall be provided in a coded format that protects patient identities but will contain diagnosis (signs/symptoms), interventions including system modifications, technical observations, diagnostic tests/results, and patient outcomes. In addition, information about the device delivering therapy including device serial numbers, device model numbers, date of event, and country/state of event shall be annotated with the data and therapy. This data shall be made available on database accessible across the program and to Government personnel.

3.3.5 Final Agreement Review

The recipient shall host a final agreement review. The purpose of this review is to present a summary of all work completed and milestones accomplished and to discuss any relevant future efforts similar to the contract, which may be pursued. This report shall be provided to the Government Technical Representative (GTR) and DARPA Program Manager. A final summary report shall be provided at the end of the program.

3.3.6 System Development Plan (SDP)

The recipient shall describe the scope of the design and development effort, describe hardware, software architectures and experimental procedures (as applicable) in sufficient detail for review and replication, reference any applicable documents and provide a schedule. The recipient shall share the SDP with the other program performers and the Government.

3.3.7 System Documentation

The recipient shall provide system documentation documenting the source code, protocol and algorithm analysis, hardware description, format specifications, system diagrams, part numbers, and any other data necessary to replicate and test the designs.

4.0 INCIDENTAL HARDWARE AND SOFTWARE

Hardware and software incidental to this research shall be made available to the Government.

5.0 REPORTS AND PRESENTATION MATERIALS

The reports and presentation materials shall be delivered as described in the data matrix.

6.0 TRAVEL

Long distance domestic travel is estimated for Program Review meetings and Conferences.

7.0 PLACE OF PERFORMANCE

University of Pennsylvania 3401 Walnut St, Suite 302C Philadelphia, PA 19104

Ph: 215-746-3501, Fax: 215-746-6848

kahana@psych.upenn.edu

Cooperative Agreement No.: N66001-14-2-4032

P.R. No.: 1300418366

Effective Date: Date signed by Government

<u>CFDA No</u>.: 12.910 AGO Code: N62880

Payment Office Code: HQ0337

RESEARCH COOPERATIVE AGREEMENT MODIFICATION # P00011

Grantor: Space and Naval Warfare Systems Center, Pacific

Code 22530 53560 Hull Street

San Diego, CA 92152-5001

(Attn: Veronica Velarde, (619) 553-7734, veronica.velarde@navy.mil)

Recipient: The Trustees of the University of Pennsylvania

3451 Walnut Street

Philadelphia, PA 19104-6205

Recipient Identification Numbers/Codes:

DUNS: 042250712 CAGE: 7G665 TIN: 23-1352685

Authority: 10 U.S.C. 2358 as amended and 31 U.S.C. 6305

Accounting and Appropriation Data:

ACRN: AH 97 17180400 1320 BQ61TT 2017 BT 01 CORE A DARPA 255 HR0011728897 02 000 20602115E00 012199
MIPR# HR0011728897 \$559,209.60

- 1. <u>PURPOSE</u>: This modification increases the value of Option 1 and of the cooperative agreement, incorporates a revised Attachment 1, Statement of Work, dated 31 May 2017, and obligates an increment of funding for the Option 1 period. As a result, the following changes are made to the Cooperative Agreement document:
 - a. Total Cooerative Agreement Amount is revised:

FROM:

\$22,736,543

Base (Phase 1): \$13,724,629 Option (Phase 2): \$9,011,914

TO:

\$23,294,537

Base (Phase 1): \$13,724,629 Option (Phase 2): **\$9,569,908**

b. Schedule item 1. <u>Purpose</u> now reads:

The purpose of this Cooperative Agreement is to fund research in support of a DARPA sponsored program. This effort shall be carried out generally as set forth in the Government's Statement of Work, Attachment 1, dated 31 May 2017, which has been based on the Recipient's proposal, "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)", and Data Matrix, Attachment 2, copies of which are in the possession of both parties.

c. Schedule item 8. Cooperative Agreement Funding: now reads:

This Cooperative Agreement is incrementally funded in the amount of \$21,892,801.60. Of this amount, \$13,724,629.00 is for the Base Period and \$8,168,172.60 is for the Option 1 Period. The Government's obligation to make payments to the Recipient is limited to only those funds obligated by this Cooperative Agreement or by modification to this Cooperative Agreement. Subject to availability of funds and continued satisfactory progress on the Cooperative Agreement as determined by the Government, the Government may agree to provide additional funding. The unfunded balance is \$1,401,735.40.

The Recipient shall notify the AGO in writing promptly whenever the total Agreement amount is expected to exceed the needs of the Recipient for the project period by more than \$5,000 or 5% of the award, whichever is greater. This notification shall not be required if an application for additional funding is submitted for a continuation award.

2. ALL OTHER TERMS AND CONDITIONS REMAIN UNCHANGED.

FOR RECIPIENT:		FOR The United States of America, Space and Naval Warfare Systems Center, Pacific		
		(b)(6)		
(Signature) M.A., Ed., CRA		LYNN M. BIEDERMANN Grants Officer	(Date)	
Associate Director, Research Services	9/6/2017			
(Name/Title)	(Date)			

Cooperative Agreement No.: N66001-14-2-4032

P.R. No.: 1300418366

Effective Date: Date signed by Government

<u>CFDA No</u>.: 12.910 <u>AGO Code</u>: N62880

Payment Office Code: HQ0337

RESEARCH COOPERATIVE AGREEMENT MODIFICATION # P00012

Grantor: Space and Naval Warfare Systems Center, Pacific

Code 22530 53560 Hull Street

San Diego, CA 92152-5001

(Attn: Veronica Velarde, (619) 553-7734, veronica.velarde@navy.mil)

Recipient: The Trustees of the University of Pennsylvania

3451 Walnut Street

Philadelphia, PA 19104-6205

Recipient Identification Numbers/Codes:

DUNS: 042250712 CAGE: 7G665 TIN: 23-1352685

Authority: 10 U.S.C. 2358 as amended and 31 U.S.C. 6305

Accounting and Appropriation Data:

ACRN: AJ 97 18190400 1320 BQ61TT 2018 BT 01 CORE A DARPA 255 HR0011831162 02 000 20602115E00 012199
MIPR # HR0011831162 \$1,119,277.00

1. <u>PURPOSE</u>: This modification is to obligate an increment of funding for the Option 1 period. As a result, Cooperative Agreement Schedule item 8. is revised to read:

8. Cooperative Agreement Funding:

This Cooperative Agreement is incrementally funded in the amount of \$23,012,078.60. Of this amount, \$13,724,629.00 is for the Base Period and \$9,287,449.60 is for the Option 1 Period. The Government's obligation to make payments to the Recipient is limited to only those funds obligated by this Cooperative Agreement or by modification to this Cooperative Agreement. Subject to availability of funds and continued satisfactory progress on the Cooperative Agreement as determined by the Government, the Government may agree to provide additional funding. The unfunded balance is \$282,458.40.

The Recipient shall notify the AGO in writing promptly whenever the total Agreement amount is expected to exceed the needs of the Recipient for the project period by more than \$5,000 or 5% of the award, whichever is greater. This notification shall not be required if an application for additional funding is submitted for a continuation award.

2. ALL OTHER TERMS AND CONDITIONS REMAIN UNCHANGED.

FOR The United States of America, Space and

(b)(6)

2017.11.14 13:56:01 -08'00'

LYNN M. BIEDERMANN Grants Officer

(Date)

Cooperative Agreement No.: N66001-14-2-4032

P.R. No.: 1300418366

Effective Date: Date signed by Government

<u>CFDA No</u>.: 12.910 AGO Code: N62880

Payment Office Code: HQ0337

RESEARCH COOPERATIVE AGREEMENT MODIFICATION # P00013

Grantor: Space and Naval Warfare Systems Center, Pacific

Code 22530

53560 Hull Street

San Diego, CA 92152-5001

(Attn: Veronica Velarde, (619) 553-7734, veronica.velarde@navy.mil)

Recipient: The Trustees of the University of Pennsylvania

3451 Walnut Street

Philadelphia, PA 19104-6205

Recipient Identification Numbers/Codes:

DUNS: 042250712 CAGE: 7G665 TIN: 23-1352685

Authority: 10 U.S.C. 2358 as amended and 31 U.S.C. 6305

Accounting and Appropriation Data:

ACRN: AK 97 18190400 1320 BQ61TT 2018 BT 01 CORE A DARPA 255 HR0011832694 02 000

20602115E00 012199

MIPR # HR0011832694 \$282,458.40

ACRN: AL 97 18190400 1320 BQ61TT 2018 BT 01 CORE A DARPA 255 HR0011832726 02 000

20602115E00 012199

MIPR # HR0011832726 \$89,278.64

- 1. <u>PURPOSE</u>: This modification increases the value of the Option and overall value of the Cooperative Agreement, incorporates a revised Attachment 1, obligates an increment of funding for the Option period, and adds an additional subrecipient, Nia Therapeutics. As a result, the following changes are made to the Cooperative Agreement document:
 - a. Total Cooperative Agreement Amount is revised:

FROM: \$23,294,537.00

Base (Phase 1): \$13,724,629.00 Option (Phase 2): \$9,569,908.00

TO: \$23,383,815.64

Base (Phase 1): \$13,724,629 Option (Phase 2): **\$9,659,186.64**

b. Schedule Item 1. Purpose: now reads:

The purpose of this Cooperative Agreement is to fund research in support of a DARPA sponsored program. This effort shall be carried out generally as set forth in the Government's Statement of Work, Attachment 1, dated 18 January 2018, which has been based on the Recipient's proposal, "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)", and Data Matrix, Attachment 2, copies of which are in the possession of both parties.

Schedule item 8. Cooperative Agreement Funding: now reads:

This Cooperative Agreement is now fully funded in the amount of \$23,383,815.64. Of this amount, \$13,724,629.00 is for the Base Period and \$9,659,186.64 is for the Option Period.

The Recipient shall notify the AGO in writing promptly whenever the total Agreement amount is expected to exceed the needs of the Recipient for the project period by more than \$5,000 or 5% of the award, whichever is greater. This notification shall not be required if an application for additional funding is submitted for a continuation award.

d. Schedule item 10. Sub-Awards: now reads:

Sub-awards with the following organizations are hereby approved, as set forth in the Recipient's proposal, in accordance with the funding limitations described in Section 8. of this Schedule:

University of Washington, Clinical University of Washington, Primate **Emory University** Drexel University Thomas Jefferson University Dartmouth College **Boston University** Mavo Clinic Medtronic, Inc. NeuroPace, Inc. Swansea University University of Texas Columbia University **Nia Therapeutics**

2. ALL OTHER TERMS AND CONDITIONS REMAIN UNCHANGED.

FOR RECIPIENT:	FOR The United States of America, Space and Naval Warfare Systems Center, Pacific				
	(b)(6)	15.22.27 07'00'			
	2018.03.22	15:32:37 -07'00'			
(Signature)	LYNN M. BIEDERMANN Grants Officer	(Date)			
M.A., Ed., CRA Associate Director, Research Services					
(Name/Title) (Date) 3/22/2018					

STATEMENT OF WORK FOR UNIVERSITY OF PENNSYLVANIA

Title – Restoring Active Memory (RAM): "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)

1.0 SCOPE

This effort promises to use direct brain recordings and stimulation in humans and animals to create a real-time						
system for enhancing encoding and long-term retrieval of memories for specific types of information. The team						
consists of nine leading clinical centers for the surgical treatment of epilepsy and movement disorders, each led						
by a clinician scientist with substantial experience in one or more key areas of electrical brain stimulation, human						
cognition, computational electrophysiology, and realtime adaptive control systems. The neurological and						
neurosurgical teams are aligned on the common goal of rapidly developing and testing approaches to enhance						
and restore memory through a study of unprecedented scope: more than 100 patients each year in a large array						
of experiments. Pending Investigational Device Exemption (IDE) approval, patients in Phase 2 of the project						
will be implanted with a complete memory neuromodulation (b)(4)						
	(b)(4)		to	our memory		
testing paradigms. This will be accomplished through an accelerated U.S. Food and Drug Administration (FDA)						
submission of the technical area two (TA2) system at the end of Phase 1. Through application of a						
computational model of human	(b)(4)		to the behavioral and			
electrophysiological data the recipient shall define biomarkers of memory (b)(4)						
(b)(4)	These biomarkers	will be used	(b)(4)			
	(b)(4)					
(b)(4)						

1.1. BACKGROUND

The Defense Advanced Research Projects Agency (DARPA) seeks new methods for analysis and decoding of neural signals in order to understand how neural stimulation could be applied to facilitate recovery of memory encoding following brain injury. Ultimately, it is desired that a prototype implantable neural device that enables recovery of memory in a human clinical population be developed. Additionally, the program encompasses the development of quantitative models of complex, hierarchical memories and exploration of neurobiological and behavioral distinctions between memory function using the implantable device versus natural learning and training.

2.0 APPLICABLE DOCUMENTS

- (a) DARPA BAA-14-08.
- (b) UPENN Technical Proposal Titled "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)" dated January 23, 2014

3.0 PROJECT WORK DESCRIPTION AND REQUIREMENTS

The recipient shall provide the facilities necessary to develop the effort as described herein.

Human use **is** anticipated in this effort. The recipient shall obtain all necessary Institutional Review Board (IRB) approvals, show proper assurance documentation, and obtain proper approval from the Government officials prior to human use testing.

Animal use **is** anticipated in this effort. The recipient shall obtain all necessary Institutional Animal Care and Utilization Committee (IACUC) approval and demonstrate this approval to the Government prior to beginning experimentation with animals. If animal use is no longer anticipated, or changes significantly from the approved

IACUC then the PI must submit a letter stating the discontinuation of animal use for this effort and/or receive appropriate authorization for IACUC changes of previously specified protocols. Unless prior approval by DARPA is given IACUC documentation must be provided prior to contract award.

3.1 BASE PERIOD (PHASE I)

Technical Area 1

3.1.1 A computational model for describing behavior in declarative memory tasks.

3.1.1.1 Predicting moment-by-moment behavior in a variety of memory tasks. The recipient shall document a model of memory (b)(4)(a) The recipient shall document the code base for the (b)(4) (b)(4)[Month 3]. (b) The recipient shall extend the model (b)(4) [Month 6]. (b)(4)(c) The recipient shall document fully commented, optimized (b)(4)Code shall be able to execute model (b)(4)(b)(4)[Month 6]. (b)(4) (d) The recipient shall document the code base for the (b)(4)[Month 9]. (b)(4)(e) The recipient shall fit the (b)(4)[Month 12]. (b)(4)(f) The recipient shall document fully commented, optimized Code shall be able to execute model (b)(4)(b)(4)[Month 12]. (b)(4)3.1.1.2 [DELETED] 3.1.1.3. Build a (b)(4)model of free recall: (b)(4)(b)(4)(a) Develop software that allows us to construct the (b)(4) model for an entire session of FR1 in 30 seconds or less [Month 15] (b) [DELETED] (c) [DELETED] 3.1.1.4 Build a (b)(4)model for (b)(4)memory: (b)(4)

> (b)(4) (b)(4)

(b)(4)

UPE	NN PI- KAHANA	(1-) (4)							
	(a) Develop a model prototype	(b)(4)	(b)(4)	Month					
21]	(a) Develop a model prototype		(6)(4)	[Month					
[Mor	(b) Deliver fully documented counth 24]	le	(b)(4)						
3.1.2 Integrating neurophysiological biomarkers into the computational model of behavior.									
3.1.2	2.1 Characterize distribution of	(b)(4) biomarke	ers	(b)(4)					
		(b)(4)		(-/(-/					
		(b)(4)							
		(b)(4)	<u> </u>						
		(b)(4)							
	2.1.1 A prototype for analyzing (auted [Month 12].	b)(4) neural	(b)(4)	shall be deployed and					
3.1.2	2.1.2 The recipient shall document to	he prototype software	[Month 12].	(b)(4)					
	(b)(4)		[Wolldi 12].						
3.1.2	2.1.3 Characterize the (b)(4)	biomarkers using the	he models of free reca	all and (b)(4) navigation:					
	(a) Characterize the (b)(4)	biomarkers for pa	tients performing the						
	(b) Characterize the (b)(4)	hiomarkers for no		Month 18]. (b)(4) navigation task,					
	(b) Characterize the (b)(4)	(b)(4)	trients performing the	[Month 24].					
				-					
3.1.2	2.1.4 The recipient shall document th	ne prototype softwar	(i	0)(4)					
	TTI ' ' 4 1 11 1			4.740					
((b)(4) The recipient shall docume			(b)(4)					
	[Month 24].	(b)(4)							
	. ,								
	Electrophysiological recordings	to define biomarker	S	(b)(4)					
((b)(4) memory. Objective: Define biomarkers		(b)(4)	memories, as					
	measured in a broad array of tas	sks. The subtask list th							
	-	word lists (FR), (b		FR), spatial navigation (b)(4)					
212	.1 The recipient shall design, progra	um nilot avacuta and	l analyza data from Ex	eneriment ED1 on notionts in the					
	psy monitoring unit. Recording neu		(b)(4)	shall be					
	to identify (b)(4) biomarkers (b)		mory (b)(4)	. These biomarkers will					
serve	e a critical role in subsequent (b)(ne recipient shall:						
	(a) Design, program, and pilot								
(b) Write initial data analysis scripts [Month 3].(c) Analyze data on 13 patients from experiment FR1 [Month 8].									
(d) Analyze data on 26 patients from experiment FR1 [Month 13].									
	(e) Analyze data on 39 patients	from experiment FR	1 [Month 18].						
	(f) Analyze data on 58 patients	from experiment FR	[Month 24].	(f) Analyze data on 58 patients from experiment FR1 [Month 24].					

LIDENINI	DI IZATIAN								
		and ann	recisely local	data from the ab		radiology) a			
	(h) Complete	interim	. ,	ata from the abo	ve experimen	_	-	meeti	ngs and with
			•	orts shall include	•	•			b)(4)
	Driid Trprogr	am per	somiei. reep	or is shall merade		•	es of the elec		. / (/
	correlates of (b)(4) memory (b)(4)							Siological	
		(-)(-)		(b)(4)		(-)(-)	[]	Month	241.
	(j) Fully docu(k) Fully docu(l) Create 3D(m) Provide in	iment comment ar reconst nterim rannotat	ode for expernalysis functions of a reporting on a	lentified format of iment [Month 2] ons [Month 3]. Il patients run in analyzed data fro e public data por (b)(4)	the task in Pl om all patient tal for all pat	nase 1 [Monts run in the	nth 24]. task in Phas the task in I	se 1 [M	Ionth 24].
21221	Dagian nuagua	m nilat	t overute en	d analyze data fr	om Evnovima	ont CatED 1	(n=16) on no	tionts i	in the
		-		cipient shall defin	-		(n=40) on pa (b)(4)	tients i	ii uie
срперзу	momtoring un	(b)(orprent shan dem	The recipier		(D)(4)		
(c) (d) (e) (f) (g) (h) (i) (j) (k) (l) (n)	Analyze data Analyze data Analyze data Organize an Complete in Post all data Fully docum Fully docum Create 3D real	a on 11 ta on 23 ta on 28 ta on 33 d annotaterim recollected tent code tent ana teconstruction repeated	patients from a patients from ate patient date ed so far in a e for experimallysis function ctions of all porting on ana	in experiment Cat in experiment Cat in experiment Cat it a from above ex it a from the above deidentified form thent [Month 2].	atFR1 [MontlatFR1 [MontlatFR1 [MontlatFR1 [MontlatFR1 [MontlatFR1 [MontlatFR1 [Montlate]]] at compatible task in Phasall patients rull for all patie	h 13]. h 18]. 24]. Ionth 24]. Month 24]. le with the p	24]. k in Phase 1 ne task in Pha	[Mont	h 24].
3.1.3.3 I	Design, progra	m, pilot	t, execute, an	d analyze data fr	om Experime	ent YC1 (n=	44) on patier	nts in tl	he epilepsy
		-		all identify bion	-	(b)(4)	memory	(b)(4	
				(b)(4)					
						T	he recipient	shall ic	lentify
(b)(4) 1	nemory bioma	irkers,		(b)(4	!)		, as well a	s	(b)(4)
memory	biomarkers,				(b)(4)				
(b)(4)	. The recip	oient sha	all:						
	•	ial data lata on 1	analysis scri	_	-	-			

- (d) Analyze data on 22 patients from experiment YC1 [Month 13].
- (e) Analyze data on 33 patients from experiment YC1 [Month 18].
- (f) Analyze data on 50 patients from experiment YC1 [Month 24].
- (g) Organize and annotate patient data from above experiment [Month 24].
- (h) Complete interim reports on data from the above experiment [Month 24].
- (i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
- (j) Fully document code for experiment [Month 2].

UPENN	PI- KAHAN		sis functions [Mon	th 21				
			ons of all patients r		r in Dl	ase 1 [Month 2/1]		
						run in the task in P	hase 1 [M	onth 241.
		_	-	_		tients run in the task	_	_
	(o) Deliver re		(b)(4)	u portur for t		narkers [Month 24]		1 [1/1011411 2 1].
	(0) Deliver ic	port on	(b)(4)		UIUII	narkers [Woltin 24]		
			•	-		nt PAL1 (n=30) on	•	
	_	is task the rec	ipient shall identify	y biomarkers		(b)(4)	of (b)(4)	associations
and shal				_				
		-	pilot task [Month 2	_				
			ysis scripts [Month					
			ents from experime					
			atients from experi					
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		_	tients from experim	_		_		
	(0)		patient data from a					
	` /		orts on data from the					
	(i) Post all da	ata collected s	so far in a deidentif	ied format co	ompat	ible with the public	data porta	ıl [Month 24].
	(j) Fully doc	ument code f	or experiment [Mo	onth 2].				
	(k) Fully doc	ument analys	sis functions [Mont	h 3].				
	(l) Create 3D	reconstruction	ons of all patients r	un in the task	c in Pł	nase 1 [Month 24].		
	(m) Provide i	nterim report	ing on analyzed dat	ta from all pa	tients	run in the task in P	hase 1 [Mo	onth 24].
	(n) Post fully	annotated da	ata to the public dat	ta portal for a	all pat	ients run in the task	in Phase	1 [Month 24].
	(o) Deliver re	port on	(b)(4)		bion	narkers [Month 24]		
21251	ъ :		. 1 1 1	, C E		(DDC2 (20)	ı· ,	1 ' DD(
		_	-	_		nt DBS2 (n=20) on	_	
			son's Disease. In the	nis task the re	ecipie	•	(b)(4)	recall task
(see	(b)(4) Rec	all Task, abo				(b)(4)		Th
shall:			(b)(4)					The recipient
Silaii.	(a) Design n	rogram and	pilot task [Month 2	1				
			sis scripts [Month	_				
			ents from experime		onth S	21		
	(d)-(n) [DELI		ents from experime		OHIII (0].		
	(d)-(II) [DELI	נטטונ						
2 1 1 84	imulation to			/L- \		_		
3.1.4 51	imulation to			(b)(4)		ı	nemory	
31411	Design progra	m nilot evec	rute, and analyze da	ata from Exne	erime	nt FR2 (n=18). The	recinient	shall test the
hypothes		m, phot, exce	rate, and analyze at	(b)(4)	CI IIIIC	nt 11t2 (n 10). The	recipient	shan test the
пуроще	313	(h)(4)	(6)(4)		The recipient shall	compare t	the degree to
which		(0))(-1)	(b)(4)		The recipient shari	compare	ne degree to
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			pilot task [Month 2	1				
			sis scripts [Month					
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	•	-	tients from experim	_		-	. inv41.	t no suct
			-	_	erime	ent to be shared with	ı mvestiga	iors and
		_	ely localize electrod			(b)(4)		
	(b)(4)	and carry	out 3D reconstruct	IONS		(b)(4)		

(b)(4) [Month 24].

UPENN	PI-	KAHAN
	(h)	Complet
	DA	DD A

e final reports on data from the above experiment to be presented at team meetings and with DARPA program personnel. Reports shall include detailed analyses of behavioral data, , as well as analyses of the electrophysiological (b)(4)correlates of (b)(4) memory [Month 24]. (b)(4)(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24]. (j) Fully document code for experiment [Month 2]. (k) Fully document analysis functions [Month 3]. (1) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24]. (m) Provide final reporting on analyzed data from all patients run in the task in Phase 1 [Month 24]. (n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24]. (o) Expand analysis functions . Deliver updated and fully documented (b)(4)analysis code [Month 7]. 3.1.4.2 Design, program, pilot, execute, and analyze data from Experiment FR3 (n=18). The recipient shall test (b)(4)nd shall: (a) Design, program, and pilot task [Month 12]. (b) Write initial data analysis scripts [Month 13]. (c) Analyze data on 4 patients from experiment FR3 [Month 14]. (d) [DELETED] (e) Analyze data on 10 patients from experiment FR3 [Month 24]. (f) Analyze data on 18 patients from experiment FR3 [Month 30]. (g) Organize and annotate patient data from above experiment [Month 30]. (h) Complete final reports on data from the above experiment [Month 30]. (i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 30]. (j) Fully document code for experiment [Month 12]. (k) Fully document analysis functions [Month 13]. (l) [DELETED] (m) [DELETED] (n) [DELETED] (o) Expand analysis functions Deliver updated and fully documented analysis code [Month 13]. 3.1.4.3 [DELETED] 3.1.4.4 Design, program, pilot, execute, and analyze data from Experiment CatFR2. (b)(4)Further, the (b)(4)recipient (b)(4)and shall: (b)(4)(a) Design, program, and pilot task [Month 2]. (b) Write initial data analysis scripts [Month 3]. (c) Analyze data on 4 patients from experiment CatFR2 [Month 8]. (d) Analyze data on 8 patients from experiment CatFR2 [Month 13]. (e) Analyze data on 13 patients from experiment CatFR2 [Month 18]. (f) Analyze data on 18 patients from experiment CatFR2 [Month 24]. (g) Organize and annotate patient data from above [Month 24]. (h) Complete final reports on data from the above experiment [Month 24]

(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24]

(i) Fully document code for experiment [Month 2].

6

UPENN	PI- KAHANA				
		ment analysis functions [-		
	* *	reconstructions of all patie			
			•	nts run in the task in Phase 1 [Mon	-
			lic data portal for al	ll patients run in the task in Phase 1	I [Month 24].
	(n) Expand an	alysis functions		(b)(4)	
		(b)(4)		. Deliver updated and fully do	ocumented
	analysis code	Month 7].			
3.1.4.5	Design, prograi	n, pilot, execute, and anal	lyze data from Expe	eriment CatFR3. In CatFR3 the rec	cipient shall
test the a			(b)(4)		
			(b)(4)		. The
recipien	t shall:				
		ogram, and pilot task [Mo			
	(b) Write initi	al data analysis scripts [M	Ionth 13].		
	(c) Analyze da	ata on 4 patients from exp	eriment CatFR3 [N	/Ionth 24].	
	(d) Analyze da	ta on 8 patients from expe	eriment CatFR3 [M	Ionth 30].	
	(e) [DELETE			•	
	(f) [DELETE]	•			
	(g) [DELETE				
	(h) [DELETE				
	` ' -	-	dentified format co.	mpatible with the public data porta	al [Month 30]
		ment code for experiment		inputiole with the public data porta	ii [ivioniii 50].
	•	ment analysis functions []			
			Monui 13].		
	(l) [DELETE]				
	(m) [DELETE	-			
	(n) [DELETE	-			
	(o) Expand an	alysis functions		(b)(4)	. 1
	amalyzaia aada	(b)(4)		. Deliver updated and fully do	ocumented
	analysis code	Monui 13].			
3146	Decian program	n nilot evecute and anal	lyze data from Evn	eriment YC2. The recipient shall a	annly (b)(4)
J.1.7.0	(b)(4)	stimulation	lyze data irom Expe	(b)(4)	(b)(4)
	(b)(4)		The reginie	ent shall test the ability of stimulati	ion to improve
		(b)(4)		shi shan test the ability of stillulati	ion to improve
memory			(b)(4)		
		771 · · · · · 1 11	(b)(4)		
	(b)(4)	The recipient shall			
		ogram, and pilot task [Mo	_		
		al data analysis scripts [M	_		
		ata on 5 patients from exp	_	_	
	(d) Analyze da	ata on 10 patients from ex	speriment YC2 [Mo	onth 13].	
	(e) Analyze da	ata on 16 patients from ex	periment YC2 [Mo	onth 18].	
	(f) Analyze da	ata on 33 patients from exp	periment YC2 [Mo	onth 24].	
	(g) Organize a	and annotate patient data f	from above experin	nent [Month 24].	
	(h) Complete	final reports on data from	the above experim	nent [Month 24].	
		=	_	mpatible with the public data portal	1 [Month 24]
		ment code for experiment			- [o 2 1].
		ment analysis functions [
		reconstructions of all patie	_	in Dhasa 1 [Month 24]	
	* *	*		in Phase 1 [Month 24]. nts run in the task in Phase 1 [Mon	th 241
	THE LEGYTOR III	THE RESERVE OF A LICENSE OF	viola ilvilli all palici	and run in the lask HLT Hase I HVIOH	LLL Z-T-L

(n) Post annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

(o) Expand analysis functions

(b)(4)

Deliver updated and fully documented

UPENN PI-KAHANA analysis code [Month 7].

3.1.4.7 [DELETED]

3.1.4.8 Design, program, pilot, execu	•	xperiment PAL2.	(b)(4)	
(b)(4)	(b)(4) The recipient shall	(b)(4)	
(b)(4)	. The recipient shan	(b)(4)	
(d) Analyze data on 6 patients (e) Analyze data on 9 patients (f) Analyze data on 11 patients (g) Organize and annotate (h) Complete final reports (i) Post all data collected so (j) Fully document code for (k) Fully document analysis (l) Create 3D reconstructions	sis scripts [Month 3]. ents from experiment PAL2 ents from experiment PAL2 ents from experiment PAL2 ents from experiment PAL2 patient data from above experiment data from the above experiment patient in a deidentified format rexperiment [Month 2].	Month 13]. [Month 18]. [Month 24]. eriment [Month 24]. riment [Month 24]. compatible with the	th 24].	
	ta to the public data portal for		_	_
(o) Expand analysis function		(b)(4)		.se i [ivisital 2 i].
· / -			dated and full	y documented
analysis code [Month 7].				
	(b)(4)			
he recipient shall:				
(a) Design, program, and pil (b) Write initial data analysis (c) [DELETED] (d) [DELETED] (e) Analyze data on 4 patien (f) Analyze data on 8 patient (g) [DELETED] (h) [DELETED] (i) [DELETED] (j) Fully document code for (k) Fully document analysis (b)(4) [Month 13]. (l) [DELETED] (m) [DELETED] (n) [DELETED] (o) Expand analysis function	ts from experiment PAL3 [Nots from experiment PAL3 [Nots from experiment PAL3 [Nots from experiment [Month 12].	(b)(4)	ated and fully	documented
analysis code [Month 13].		. Deliver upd	ated and fully	documented
		E 4 DDC1		
3.1.4.10 Design, program, pilot, exe	· ·	•	(b)(4)	learning during
THE LECTINE OF SHALL EVALUATE	IDWAL	1000	11111/41	- IEST OFFICE OFFI

a	I PI- KAHANA					
	(b)(4) task.			(b)(4)		
		. The recipient sha	ll vary		(b)(4)	
paramet	ters.		(b)(4)			
			shall index learnin	_	(b)(4)	
	(b)(4)		cipient shall comp	are (b)(across the five c	ondition (b)(4)
		, and	d (2) identify	(b)(4)	parameter	(b)(4)
	and shall:					
	(a) Design, program,	_	_			
	(b) Write initial data		_			
	(c) Analyze data on (d) – (n) [DELETED]		periment DBS1 [N	Ionth 8].		
2 1 4 1 1	ъ.:			, DG1	DG2 0 DG2 FI	
3.1.4.11	Design, program, exc	ecute, and analyze of (b)(4)	lata from Experim		ify (b)(4) stimulati	_
	(a) Design and progr	am tasks [Month 12	2].		_	
	(b) Analyze data on	14 patients each fro	m experiments PS	1, PS2, &	k PS3 [Month 16].	
	(c) Analyze data on 2	29 patients each from	m experiments PS	1, PS2, &	PS3 [Month 24].	
	(d) Post fully annota	ted data to the publ	ic data portal for a	ll patient	s run in the task in P	hase 1 [Month
3.1.5 D	evelop control algorith	nms	(b)(d	4)		
3.1.5.1	[DELETED]					
3.1.5.2 I	Develop algorithm			(b)(4)		
3.1.5.2 I		all:		(b)(4)		
3.1.5.2 I	The recipient sha				I)	
3.1.5.2 I			[Month 9].	(b)(4)	4)	
3.1.5.2 I	The recipient sha	report	[Month 9].	(b)(4	I)	
3.1.5.2 I	The recipient sha (a) Complete interim	report oe		(b)(4)		(b)(4)
3.1.5.2 I	The recipient sha (a) Complete interim	report oe Cor		(b)(4)	port on algorithms,	(b)(4)
3.1.5.2 I	The recipient sha (a) Complete interim (b) Develop prototyp	report oe Cor	mplete 12-month i	(b)(4)		(b)(4)
3.1.5.2 I	The recipient sha (a) Complete interim (b) Develop prototypy (b) (c) [DELETED] (d) [DELETED]	report ce Cor (4)	mplete 12-month in [Month 12].	(b)(4) (b)(4) nterim re	port on algorithms,	(b)(4)
3.1.5.2 I	The recipient sha (a) Complete interim (b) Develop prototyp (b) (c) [DELETED] (d) [DELETED] (e) Provide 9-month	ce Con (4)	mplete 12-month in [Month 12].	(b)(4) (begin the second secon	port on algorithms, [onth 9].	(b)(4)
3.1.5.2 I	The recipient sha (a) Complete interim (b) Develop prototyp (b) (c) [DELETED] (d) [DELETED] (e) Provide 9-month (f) Provide 12-month	ce Cor (4) interim report on a interim report on	mplete 12-month in [Month 12]. (b)(4) algor (b)(4) algor	(b)(4) (b)(4) nterim re ithms [M	port on algorithms, [onth 9]. Month 12].	(b)(4)
3.1.5.2 I	The recipient sha (a) Complete interim (b) Develop prototypy (b) (c) [DELETED] (d) [DELETED] (e) Provide 9-month (f) Provide 12-month (g) Document 12-month	ce Con (4) interim report on a interim report on	mplete 12-month in [Month 12].	(b)(4) (b)(4) nterim re ithms [M	port on algorithms, [onth 9]. Month 12].	(b)(4)
3.1.5.2 I	The recipient sha (a) Complete interim (b) Develop prototyp (b) (c) [DELETED] (d) [DELETED] (e) Provide 9-month (f) Provide 12-month (g) Document 12-month (h) [DELETED]	ce Con (4) interim report on a interim report on	mplete 12-month in [Month 12]. (b)(4) algor (b)(4) algor	(b)(4) (b)(4) nterim re ithms [M	port on algorithms, [onth 9]. Month 12].	(b)(4)
3.1.5.2 I	The recipient sha (a) Complete interim (b) Develop prototyp (b) (c) [DELETED] (d) [DELETED] (e) Provide 9-month (f) Provide 12-month (g) Document 12-month (h) [DELETED] (i) [DELETED]	ce Con (4) interim report on a interim report on	mplete 12-month in [Month 12]. (b)(4) algor (b)(4) algor	(b)(4) (b)(4) nterim re ithms [M	port on algorithms, [onth 9]. Month 12].	(b)(4)
3.1.5.2 I	The recipient sha (a) Complete interim (b) Develop prototyp (b) (c) [DELETED] (d) [DELETED] (e) Provide 9-month (f) Provide 12-month (g) Document 12-mo (h) [DELETED] (i) [DELETED] (j) [DELETED]	ce Con (4) interim report on a interim report on	mplete 12-month in [Month 12]. (b)(4) algor (b)(4) algor	(b)(4) (b)(4) nterim re ithms [M	port on algorithms, [onth 9]. Month 12].	(b)(4)
3.1.5.2 I	The recipient sha (a) Complete interim (b) Develop prototyp (b) (c) [DELETED] (d) [DELETED] (e) Provide 9-month (f) Provide 12-month (g) Document 12-month (h) [DELETED] (i) [DELETED]	ce Con (4) interim report on a interim report on	mplete 12-month in [Month 12]. (b)(4) algor (b)(4) algor	(b)(4) (b)(4) nterim re ithms [M	port on algorithms, [onth 9]. Month 12].	(b)(4)

3.1.5.4 [DELETED]

3.1.6 Core project resources devoted to TA1.

- 3.1.6.1 The recipient shall perform electrophysiological experiment development and programming, data analysis, computational cluster effort towards data analysis and computational modeling from TA1.
- 3.1.6.2 The recipient shall provide project coordination, data sharing and data storage.

•		n in Phase 2. T	he recipien	t shall characterize
restoring memory function.	4)			for modulating and
3.1.7.1 The recipient shall design and develop an (b)(4		(b)(4)	capable	(b)(4) . The recipient
shall: (a) Based on precise anatomical analyses (b)(4) [Month 12]. (b) Working with Lawrence Livermore National materials that can be put into place by the beginni (c) Working with LLNL, complete ISO-10993 tedesign history file and associated ISO test results red) [DELETED] 3.1.8 [DELETED]	Labs (LLNL), deliv ng of Phase 2 [Mor sting to verify lead	nth 18]. biocompatibilit	y and stabili	ing and list of
3.1.9 [DELETED]				
Technical Area 2 3.1.10 Validate system architecture and individe the high-level system design requirements againts 3.1.10.1 The recipient shall validate system level	nst current design	assumptions.		ent and review
3.1.10.2 [DELETED]				
3.1.10.3 The recipient shall refine the specification (b)(4) continually refined the specification continually refined the specification continually refined the specification (b)(4) continually refined the specification continually refined the specification (b)(4) continually refined the specification (c)(4) continually refined the sp	ons for electronics ning as needed [Mo	onths 4–9].	(b)(4)	
3.1.10.4 The recipient shall validate the specificate [Months 5–6].	tion for the Algorith	nm prototyping	system and	user interface
 3.1.10.5 The recipient shall define the sub-chroni IDE approval [Month 6] and shall: (a) Document definitions of the function [Month 6]. (b) Document definitions of the compon external packaging, and algorithm protot (c) Document definitions of the sub-chro day IDE approval [Month 6] (d) Deliver definitions of stakeholder required. 	ent-level specificat yping system [Mon nic safety and perfo	erformance requions for the neuth 9]. ormance data re	uirements o	f the overall system
3.1.11 Design, fabrication, and characterizatio shall develop a (b)(4) (b)(4) electrodes. (*and any adaptations needed to		capa	ble of matir	or. The recipient ng with (b)(4)
3.1.11.1 The recipient shall design and manufactu (b)(4) [Months 7–18].	re of electronics,		(b)(4)	

3.1.11.2 The recipient shall (b)(4) software (firmware) to control the electronics and provide (b)(4)

UPENN PI- KAHANA capability [Months 7–18].

	The recipient sha ical depth electrod	•	•				(b)(4)	to interface with
3.1.11.4	The recipient sha				•		_	ver (b)(4) l sites [Months 19–
24].	(6)(4)	in propurue	ion for T D7T	IDE saom	ission and s	ystem den ver	, to chimea	r sites [iviolities 17
۷۳].	(a) Design and b 7-18].	ouild electron	nics		(b)(4)		[Months
	(b) Document the capability [Month	. , . ,	software that	at controls	the electron	nics and docun	nent (b)((4) algorithm
	(c) Modify the d design verification	-		connector	and build 22	2	(b)(4)	for
	(d) Test and doc IDE submission		y and perform	nance	(1	b)(4)	in pre	eparation for FDA
2 1 12		17.			• 41	4340		
	Connectorization	_			-	(b)(4)		stimulator. The
-	onic (b)(4) neur			od and int	tegrate a va	riety of clinic	al electro	de designs with the
3.1.12.1	The recipient sha	all define sp	ecifications f	or the con	nector		(b)(4)	
		(b)(4)			[Months	1–6].	
3.1.12.2	2 [DELETED]							
3.1.12.3	[DELETED]							
	The recipient shace, mechanical into (a) Define specific (b) [DELETED]	egrity [Mon fications for	ths 15–24].	The recipi	ent shall:	al conductivity	and reliab	pility, moisture
	(c) Document th	e assembly	process			(b)(4)		
	[Month 15].		_					
	(d) Complete and (e) Design verification integrity [Month	cation testir		• • •	_	and reliability	, and mech	nanical
3.1.13	Algorithm protot	yping syste	m. The reci	pient shal	ll develop a	n algorithm p	rototyping	g system (b)(4)
3.1.13.1	The recipient sha (b)(4)		(b)(4) onths 1–6].	interfa	ace		(b)(4)	
2 1 12 2	The recipient sha	all documen	t the coftwor	a usad		(b)(4)		
3.1.13.2		(b)(4)	t tile softwar		onths 1–12]	(b)(4)		
3.1.13.3	The recipient sha	all develop s	oftware	(I	b)(4)	[Months	7–18].	
	The recipient sha	all verify and	d validate tes	sting and d	ocumentation	on for IDE sub	mission [N	Months 19–24].
	(a) Design	(b)(4)	interface			(b)(4)		

-		behavioral studies of t	the electrophysiology	(b)(4) in tw	o monkeys. The
recipient s	shall also perform a sy		•	b)(4)	
		The recipient s	hall also probe the net	ırophysiology	(b)(4)
(1.) (1.)			(b)(4)		
(b)(4)					
2 1 16 T.J.	ontifuina nouvonal ha	sis of (b)(4) momor	v in NIIDs and nuchi	na the velo of atim	ulation(h)(4)
3.1.10 1 u €	entifying neuronal ba	nsis of (b)(4) memory	_	_	
neuronal	activity that underlic	(b)(4) memory in n	hase of the work see		_
ncui onai a	recordings	(b)(4) memory in ii	_	The recipient sna	ii conduct (b)(4)
	- C	0)(4)	(b)(4)		
	(L)(+)			
3.1.16.1 T performan	_	gn, program, and test (b)(4)	experimental protocol [Months 1-4].	for measuring mor	nkey (b)(4) memory
`	a) The recipient shall Month 4].	design and program a	behavioral task for mo	easuring monkey (l	memory
3.1.16.2 T		ument the hardware in nths 3-5].	terface for the (b)(4	task to interfac	e with recording
(2	a) The recipient shall	document the hardwar and monkey behavior			ophysiological
3.1.16.3 T	The recipient shall train	n (b)(4) to	(b)(4)	(b)(4)
(b)(4) men	mory task [Months 5-2	24].			
(a	a) The recipient shall	obtain one monkey, co	omplete pre-training h	ealth checks, place	collars,
C	omplete quarantine an	d room acclimation pr	ocedures [Month 8].		
(t	b) The recipient shall	train the monkey in ch	airing and handling p	rocedures, acclimat	e monkey to
W	orking in the laborate	ry, begin food delay p	rocedures, train monk	ey on initial behavi	oral tasks, (b)(4)
	(b)(4)	which	h will be used in the e	ye-tracking calibrat	ion procedure of th
((b)(4) memory task [M	Ionth 10].			
(0	c) The recipient shall	train the animal in the	(b)(4) memory parad	igm [Month 24].	
		pare monkey for record	•	_	_
_		chambers, and cranio	_		
	-	monkey (b)(4) behav			
		on one monkey and pe	rform surgery to impla	ant headpost. Comp	lete recovery
_	ery [Month 12].		121 22 1	~ .· . · · ·	4.1. 1.6
	-	joystick task, includin	g eye calibration and	iixation training wi	ın nead fixation
_	ost [Month 15].	mamamy to als		aandina ahaashaa D	Month 101
		memory task, perform		cording chamber [I	vionui 18].
(u) The re	ecipiciii siiaii docume	nt all findings in a fina	n rebou [monu 19]		
3 1 16 5 🖽	DELETED]				
J.1.10.J					
3.1.17 Co	mprehensive examin	ation of the electropl	nysiology of stimulati	on in non-human	primates. (b)(4)
-		logy of stimulation. T		-	c study of the
ability for			and iden	-	parameters
	(b)(4)		The recipient shall co	nduct both studie	s (b)(4)
			(b)(4)		

3.1.17.1	The recipient shall pr	epare untrained monl	keys for (b)((4) recording and sti	mulation studie	(b)(4)
			_	RIs to guide electro	ode implantatio	n, surgeries to
implant	headposts and recording	-				
	(a) The recipient sha [Month 6].	ıll perform monkey sı	urgeries to i	mplant electrodes	(b)	0(4)
3.1.17.2	2 The recipient shall de	emonstrate that neuro	nal stimulat	ion	(b)(4)	
			(b)(4)			
	(a) The recipient shall	ll show that	b)(4)	stimulation	(b)(4)	
	(b)(4		Month 9].		(=)(-)	
	(b) The recipient shall		f data analys	ses	(b)(4)	
	() 7771	(b)(4)		F1.5 d 101	[Month 11].	
	(c) The recipient shall	I document all findin	gs in a final	report [Month 19]		
3.1.17.3	[DELETED]					
3.1.17.4	[DELETED]					
3.1.17.5	[DELETED]					
Technic	TION PERIOD (PHA					
3.2.1 E	xtending computation	nal model	(b)(4)			
3.2.1.1	Modeling the dynamic	es of brain activity		(b)(4)		
	(a)	·	(b)(4	4)		
					EN C	41. 201
	(b)		(b)(4)	Livion	th 28]
	(0)		(5)(7)		
			(b)(4)			
	(c) Formal report on t	he above milestones	_	Month 30] ode used to perform	n these analyse	s [Month 36]
	(c) I official report on t	ne above ninestones	merading c	ode used to periorn	ir tilese allaryse	s. [Worth 50]
3.2.1.2	Using	(b)(4)	modeling	to improve memory	(b)(4)	restoration:
((a)		(b)(4	1)		
	[Month 28]					
((b)		(b))(4)		

(b)(4)

(a)

(b) Complete a reanalysis of all parameter search

[Month 30]

	(b)(4)		
(c) Complete algorithm for (b)(4) select		on parameters d	uring FR6 and CatFR6 ta
maximize memory performance. [Month 4		[M4]. 40]	
(d) Deliver a final report based on the about	ve denverables.	. [Month 48]	
Collect high-resolution imaging and link	(b)(4)	models	(b)(4)
(b)(4) The recipient shall			
(a) Collect high-resolution magnetic reso		sequences in 10	subjects, including T1/T2
diffusion and resting state functional scar (b) Collect high-resolution magnetic reso		saguanaas in 50	subjects including T1/T
diffusion and resting state functional scar		sequences in 50	subjects, including 11/12
(c) Collect high-resolution magnetic reso		sequences in 10	0 subjects, including T1/7
diffusion and resting state functional scar		1	<i>y</i> ,
1	target selection		(b)(4)
predicted to reliably enhan	(b)(4)	memory	(b)(4)
	(b)(4) (b)(4)		
	(0)(4)		
	(b)(4)		
(a)			[Month 38]
(e)			
. [Month 41]			
(f) Deliver interim report on the (b)		(/(/	that reliably enhance
(b)(4) memory	•)(4)	
	(b)(4)		
		_	Month 46]
(g) Final report on the efficacy of stimular biomarkers in (b)(4) memory	- C		, , , ,
(b)(4) memory test sessions	•		
(b)(+) memory test sessions	(6.5. 110, 041	ito). [ivional to	.1
The recipient shall complete data collection	on in experiment	t FR1 and shall:	
(a) Analyze data on 60 patients from exp	eriment FR1 [N	Month 30].	
	periment FR1 [N	Month 36].	
(b) Analyze data on 66 patients from exp	Г-		
(b) Analyze data on 66 patients from exp(c) Analyze data on 72 patients from exp	_	Month 42].	
	periment FR1 [N	_	
(c) Analyze data on 72 patients from exp(d) Analyze data on 78 patients from exp(e) Complete final reports on data from the	periment FR1 [Noeriment FR1 [N	Month 48].	(b)(4)

f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48]

(g) Post fully annotated data to the public data portal f	or all patients run in the task in Phase 2 [Month 48].
3.2.1.8 The recipient shall complete data collection in experiment (a) Analyze data on 36 patients from experiment CatF (b) Analyze data on 38 patients from experiment CatF (c) Analyze data on 41 patients from experiment CatF (d) Analyze data on 43 patients from experiment CatF (e) Complete final reports on data from the above experiment CatF (f) Create 3D reconstructions of all patients run in the formula (g) Post fully annotated data to the public data portal formula (h) Expand analysis functions	R1 [Month 30]. R1 [Month 36]. R1 [Month 42]. R1 [Month 48]. riment, (b)(4) ask in Phase 2 [Month 48].
[Month 30]	
3.2.1.9 Design, program, pilot, execute, and analyze data from E (a) Deliver fully documented code and analysis functions (b) Analyze data or 21 potings from any prince THI	shall: ons [Month 26].
 (b) Analyze data on 21 patients from experiment TH1 (c) Analyze data on 32 patients from experiment TH1 (d) DELETED (e) DELETED (f) DELETED (g) DELETED (h) DELETED 	
3.2.1.10 The recipient shall complete data collection and analyst (a) Analyze data on 31 patients from experiment PAL (b) Analyze data on 36 patients from experiment PAL	1 [Month 30]. 1 [Month 36].
(c) Analyze data on 42 patients from experiment PAL(d) Analyze data on 47 patients from experiment PAL	
(e) Complete final reports on data from the above expe	
[Month 48]. (f) Create 3D reconstructions of all patients run in the to (g) Post fully annotated data to the public data portal for the public data portal	
3.2.2 Stimulation to enhance (b)(4)	memory
3.2.2.1 Continue to collect and analyze data from Experiment F (a) Organize and annotate data from 19 patients [Mon (b) Complete final reports on data from the above expe of target selection [Month 48]. (c) Create 3D reconstructions of all patients run in the	th 36]. riment, including a report on the anatomical specificity task in Phase 2 [Month 48].
(d) Post fully annotated data to the public data portal f3.2.2.2 Design, program, execute, and analyze data from Exper	
(b)(4) The recipient shall:	

- (a) Deliver fully documented PS4/FR5 code and analysis functions [Month 32].
- (b) Organize and annotate data from 6 PS4/FR5 patients [Month 36].
- (c) Organize and annotate data from 9 PS4/FR5 patients [Month 43].
- (d) Organize and annotate data from 29 PS4/FR5 patients [Month 48].
- (e) Complete final reports on data from the PS4/FR5 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in FR3. [Month 48].
- (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.3 Design, program, execute, and analyze data from Experiment PS5/FR6.	(b)(4)
(b)(4)	
	The
recipient shall.	

- recipient shall:
 - (a) Deliver fully documented PS5/FR6 code and analysis functions [Month 38].
 - (b) Organize and annotate data from 6 PS5/FR6 patients [Month 45].
 - (c) Organize and annotate data from 14 PS5/FR6 patients [Month 48].
 - (d) Complete final reports on data from the PS5/FR6 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in FR5. [Month 48].
 - (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
 - (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.4 [DELETED]

- 3.2.2.5 Continue to collect and analyze data from Experiment CatFR3. The recipient shall:
 - (a) Organize and annotate data from 10 patients [Month 36].

The recipient shall:

- (b) Complete final reports on data from the above experiment, including a report on the anatomical specificity of target selection [Month 48].
- (c) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (d) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.6	Design, program, execute, and analyze data from Experiment PS4/CatFR5.	(b)(4)
		The
recipien	t shall:	
	(a) Deliver fully documented PS4/CatFR5code and analysis functions [Month 32].	
	(b) Organize and annotate data from 6 PS4/CatFR5 patients [Month 42].	
	(c) Organize and annotate data from 9 PS4/CatFR5 patients [Month 43].	
	(d) Organize and annotate data from 37 PS4/CatFR5 patients [Month 48].	
	(e) Complete final reports on data from the PS4/CatFR5 experiment, including a report	on the anatomical
	specificity of target selection, and a comparison with stimulation efficacy in CatFR3 [Mon	nth 48].
	(f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].	
	(g) Post fully annotated data to the public data portal for all patients run in the task in P	hase 2 [Month 48]
3.2.2.7	Design, program, execute, and analyze data from Experiment PS5/CatFR6.	(b)(4)

(b)(4)

- (a) Deliver fully documented PS5/CatFR6 code and analysis functions, (b)(4)
 [Month 38].
- (b) Organize and annotate data from 6 PS5/CatFR6 patients [Month 45].
- (c) Organize and annotate data from 23 PS5/CatFR6 patients [Month 48].
- (d) Complete final reports on data from the PS5/CatFR6 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in CatFR5 [Month 48].
- (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].
- 3.2.2.8 Design, program, execute, and analyze data from Experiment TH3.

(b)(4)

(b)(4)

The recipient shall:

- (a) Deliver fully documented code and analysis functions [Month 26].
- (b) Organize and annotate data from 5 patients [Month 30].
- (c) Organize and annotate data from 8 patients [Month 36].
- (d) DELETED
- (e) DELETED
- (f) DELETED
- 3.2.2.9 DELETED
- 3.2.2.10 DELETED
- 3.2.2.11 Design, program, execute, and analyze data from Experiment PAL3.

(b)(4)

(b)(4)

(b)(4)

The recipient shall:

- (a) Analyze data on 14 patients from the PAL3 experiment [Month 36].
- (b) Analyze data on 14 patients from the PAL3 experiment [Month 42].
- (c) Analyze data on 14 patients from the PAL3 experiment [Month 48].
- (d) Complete final reports on data from the above experiment, including a report on the anatomical specificity of target selection [Month 48].
- (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].
- 3.2.2.12 Design, program, pilot, execute, and analyze data from Experiment PS4/PAL5.

(b)(4)

The recipient shall:

- (a) Deliver fully documented PS4/PAL5 code and analysis functions [Month 32].
- (b) Analyze data on 4 patients from the PS4/PAL5 experiment [Month 36].
- (c) DELETED
- (d) DELETED
- (e) DELETED
- (f) DELETED
- (g) DELETED
- 3.2.2.13 DELETED

- 3.2.2.14 Continue to collect and analyze data from Experiments PS2. The recipient shall:
 - (a) Analyze data on 50 patients from experiments PS2 [Month 30].
 - (b) Analyze data on 71 patients from experiments PS2 [Month 36].
 - (c) Analyze data on 82 patients from experiments PS2 [Month 42].
 - (d) Analyze data on 93 patients from experiment PS2 [Month 48].
 - (e) Post fully annotated data to the public data portal for all patients run in the task [Month 48].

3.2.2.15. [DELETED]

3.2.2.16. [DELETED]

3.2.2.17. Design, program, execute, and analyze data from Experiment RE	C1. (b)(4)
The recipient shall:	
(a) Deliver fully documented code and analysis functions [Mont	th 28].
(b) Organize and annotate data from 2 patients [Month 30].	
(c) Organize and annotate data from 4 patients [Month 36].	
(d) Organize and annotate data from 6 patients [Month 42].	
(e) Organize and annotate data from 8 patients [Month 48].	
(f) Complete final reports on data from the above experiment,	(b)(4)
[Month 48].	

- (g) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (h) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.18 Enhance (b)(4) decoding capabilities

(a) Assess (b)(4) de	ecoding perform	nance within in	dividual	patients. For	all patien	ts who part	icipated	in the
CatFR1 task, report						-	termine	
regions contributing to		performance.		•		,		
(b) Assess differences	3	(b)(4)		_	within in	dividual pa	itients. A	Assess
(b)(4) to d	etermine brain	regions involve	ed	(b)(4)	_	(i.e.,	
significant regions). []	Month 44]							
(c) Develop a model t	o align neural	features across	patients		(b)(4)		Evaluat	e the
ability of the model to	predict brain	activity from he	eld-out p	atients. [Mont	th 45]			
(d) Using neural featu	res aligned acr	oss patients,		(b)(4)		(b)(4)		
			(b)(4)					
					[Month	46]		
(e) Develop joint mod	lels			(b)(4)				
			(b)(4)					
		(b)(4)				[Month 47]	
(f) Final report on	(b)(4)	apability	. Develo	p final report		(b)(4)		
	(b)(4)			Future re	search and	develop	ment
opportunities will also	be identified.	[Month 48]						

3.2.3 Technology commercialization.

3.2.3.1 Develop implantable device concepts. Determine key risks and unknowns related to hardware development and identify strategies to reduce these risks. The recipient shall:

Establish preliminary requirements and specifications for the mechanical assembly of the implant, document the design intent and design the initial device concepts. Define the lead geometry and develop surgical placement guidance based on patient data collected as part of the RAM project. Complete an early feasibility analysis and cost

analysis of the identified device concept and a detailed project plan for subsequent development phases. [Month 44]

2 Develop device programmer prototype.	(b)(4)
	The recipient shall:
(a) Develop implantable device simulator and API	. (b)(4)
	[Month 45]
(b) Develop a graphical user interface	(b)(4)
	(b)(4)
[Month 46]	
(c) Develop the patient testing module	(b)(4)
	(b)(4)
[Month 47]	(~)(~)
[101011111 7 / [

- 3.2.3.3 Hold informational meeting with the FDA. The purpose of this meeting is to review Nia's product development roadmap with the FDA and obtain informal feedback from the FDA that can be used to guide future development efforts. Topics to be reviewed with the FDA include: Nia's concept of operations for the use of the technology in the home and the clinic, its mechanism of action, the patient populations that could benefit from our technology, and the outcome measures we propose to use to evaluate its therapeutic effect. The recipient shall:
 - (a) Submit an informational meeting request to the FDA [Month 46]
 - (b) Meet with the FDA to review Nia's development plans [Month 48]
- 3.2.3.4 Final report on technology commercialization activities. This report shall summarize progress on all of the commercialization activities, including the implantable device concepts, the programmer prototype and the informational meeting with the FDA. [Month 48]

Technical Area 2

Phase 2 objectives in TA2 shall be to support FDA IDE approval and clinical site training, develop clinical systems, and (b)(4) Phase 1 algorithms.

- 3.2.4 Update system architecture and individual components based on TA1. The recipient shall review and, if necessary, redefine, document and review the high-level system design requirements for the (b)(4) system based on the discovery and feedback from TA1 in phase 1.
- 3.2.4.1 The recipient shall review and, if necessary, redefine system level specification with TA1 team based on the phase 1 results [Months 25–30].
- 3.2.4.2 The recipient shall review and, if necessary, redefine the specifications for neural interfaces [Months 25–30].
- 3.2.4.3 The recipient shall review and, if necessary, redefine the specifications for electronics including the stimulating and recording electronics [Months 25–30].
- 3.2.4.4 The recipient shall review and, if necessary, redefine the sub-chronic safety and performance data required by the FDA for 29-day IDE approval [Months 25–30].
- 3.2.4.5 The recipient shall produce a final set of documents detailing the specifications for the overall system and its components [Month 30].
- 3.2.5 Fabrication of the reusable (b)(4) stimulators for clinical studies. The recipient shall produce

	PI- KAHA							
the bala	ance of	(b)(4)	timulator	units for use	at the clinical site	es in early Phas	e 2.The re	ecipient
shall:								
					ems [Month 26].			
	\ /		-		nented (b)(4) system			
	\ /		1	1 / 1	ements, and desig ion with the(b)(4)I	,		
	(d) Utilize t patients [Me		perform red	cording and clo	osed-loop stimula	tion during mem	nory testing	g in at least 50
3.2.6 E	valuation of	commerc	ially availa	ble (b)(4)	leads for men	nory enhancem	ent. The r	recinient
shall:	, w.			(5)(1)	100005 101 111011			ou-promo
	(a) Develop	protocol a	mendment a	and obtain IRE	approval to impl	ant commercial	lv-availabl	e leads (b)(4)
		1		study patients			,	(-)(-)
	(b) Deliver i	interim rep		ory (b)(4)	performance i	n 10 subjects	(b)(4)	
		1)(4)	,	()()	
				`	, ,	[Mon	ths 41].	
	(c) Develop	protocol a	mendment a	and obtain IRE	approval to impl	-	-	e leads (b)(4)
		1	(b)(4		11	[Months 40].	•	
	(d) Deliver i	interim rep	ort on stimi	ılation target l	ocalization in 10 s		ed (b)	(4)
		•				, ,	,	
		Mon	ths 44].					
	(e) Final rep	ort on mer	mory (b h 48].)(4) perform	nance and target l	localization in 40	0 subjects	with (b)(4)
							4	
					n development fr			cipient shall
docume	ent the devel	opment of	a tool to	b)(4) successi	ul TA1 algorithm	IS (I	b)(4)	
2271	The mainian	+ ahall daay	umant tha de	violenment of	a (b)(4) taal ta	tuonaloto aviatin	م ماممسندامه	na fuam mhaga
	-		iment the de		a (b)(4) tool to	translate existin	g aigorimi	ns from phase
1		(b)(4)		[Months 33-4	1 2].			
2272	The medianism	+ ahall daar	umant tha da	avalammant of	o to o1	(h.)(4)		
	s 33–42].	t Shan doct	illelli tile de	evelopment of	a 1001	(b)(4)		
[Monus	8 33–42].							
2272	The medianion	مساء المامة	iniatan anah	addad mada	closed-loop memo	ami taatina in th	o Emilanar	· Manitanina
Unit:	The recipien	i Silali aulii	illister ellio	edded-mode,	riosed-toop memo	ory testing in th	e Ephepsy	Monitoring
Omi.	(a) Comple	te software	tool for los	nding	(b)(4)	[Month 42].		
	. ,			nslating softwa		(b)(4)		[Month 42].
	(c) Admini		(b)(4)	_	k to five patients	(b)(4)	(b)(4)	[WORTH 42].
	(c) Admini	StCI	(D)(4)	memory tas	(b)(4)		(b)(4)	
				(b)(4)	(2)(.)		Month	48]
								•
3.2.8 [D	ELETED							
	,							
3.2.9 C	ore project	resources	devoted to	TA2:	(b)(4)	algorithm	ıs, compu	tational cluster
					A1, TA2, and TA			
	imented.		, 8		,, ****** 11:			J ~~~~ 8J ~~~
Technic	al Area 3							
[DELET								

3.3 PROGRAM MANAGEMENT AND REVIEW

The Government will actively monitor, review and approve the recipient's performance to ensure all the performers are in sync and matched with the Government's requirements. The Government will ensure that each of the performers share experimental data across the program and will further ensure that the performers develop techniques and capabilities that are compatible and integrate with each other. The recipient shall collaborate and cooperate with other performers in the program under the coordination of the Government team. At Government PI meetings, the recipient shall demonstrate technical capabilities and engage and/or challenge other performers in a cooperative and challenge environment. Along these lines, the Government will ensure that each performer shares technical information with the others to enable the testing/challenging of each other's capabilities. The Government will further oversee the program and will review, approve, and participate in the demonstrations.

3.3.1 Kick-off Meeting

The recipient shall hold a kick off meeting within 60 days of award of this agreement. In this meeting, the recipient shall present a program management plan and financial tracking plan.

3.3.2 Quarterly Financial Reports

The recipient shall provide quarterly financial progress reports to the Government Technical Representative (GTR) and DARPA Program Manager. The purpose of these reports is to provide a brief project progress and inform the GTR and Program Manager of any potential issues.

3.3.3 Quarterly Technical Reporting

The recipient shall provide quarterly progress reports to the Government Technical Representative (GTR) and DARPA Program Manager. The purpose of these reports is to present a summary of work completed by SOW tasking and milestones met, discuss any problems encountered, update the program schedule, present the program financial status, and discuss remaining work. Quarterly reports shall also include all technical data items generated including but not limited to experimental data, processed data along with methods of processing used, research reports and publications and software (source code and executables).

3.3.4 Monthly Status Reports

The recipient shall provide monthly status reports which will include all relevant project data including, but not limited to, raw and analyzed electrophysiological signals as well as any necessary annotations and interpretations of the data, such as time-stamped patient behaviors, necessary for appropriate analyses and interpretation of the data. Patient data shall be provided in a coded format that protects patient identities but will contain diagnosis (signs/symptoms), interventions including system modifications, technical observations, diagnostic tests/results, and patient outcomes. In addition, information about the device delivering therapy including device serial numbers, device model numbers, date of event, and country/state of event shall be annotated with the data and therapy. This data shall be made available on database accessible across the program and to Government personnel.

3.3.5 Final Agreement Review

The recipient shall host a final agreement review. The purpose of this review is to present a summary of all work completed and milestones accomplished and to discuss any relevant future efforts similar to the contract, which may be pursued. This report shall be provided to the Government Technical Representative (GTR) and DARPA Program Manager. A final summary report shall be provided at the end of the program.

3.3.6 System Development Plan (SDP)

The recipient shall describe the scope of the design and development effort, describe hardware, software architectures and experimental procedures (as applicable) in sufficient detail for review and replication, reference any applicable documents and provide a schedule. The recipient shall share the SDP with the other program performers and the Government.

3.3.7 System Documentation

The recipient shall provide system documentation documenting the source code, protocol and algorithm analysis, hardware description, format specifications, system diagrams, part numbers, and any other data necessary to

replicate and test the designs.

4.0 INCIDENTAL HARDWARE AND SOFTWARE

Hardware and software incidental to this research shall be made available to the Government.

5.0 REPORTS AND PRESENTATION MATERIALS

The reports and presentation materials shall be delivered as described in the data matrix.

6.0 TRAVEL

Long distance domestic travel is estimated for Program Review meetings and Conferences.

7.0 PLACE OF PERFORMANCE

University of Pennsylvania 3401 Walnut St, Suite 302C Philadelphia, PA 19104

Ph: 215-746-3501, Fax: 215-746-6848

kahana@psych.upenn.edu

P.R. No.: 1300418366

Effective Date: Date signed by Government

<u>CFDA No</u>.: 12.910 AGO Code: N62880

Payment Office Code: HQ0337

RESEARCH COOPERATIVE AGREEMENT MODIFICATION # P00014

Grantor:	Space and Naval	Warfare Systems	Center, Pacific

Code 22530

53560 Hull Street

San Diego, CA 92152-5001

(Attn: Megan Ashley, (619) 553-2244, megan.ashley@navy.mil)

Recipient: The Trustees of the University of Pennsylvania

3451 Walnut Street

Philadelphia, PA 19104-6205

Recipient Identification Numbers/Codes:

DUNS: 042250712 CAGE: 7G665 TIN: 23-1352685

Authority: 10 U.S.C. 2358 as amended and 31 U.S.C. 6305

1. <u>PURPOSE</u>: This modification extends the period of performance for Option 1. As a result, the following change is made to schedule item 2. <u>Term</u> of the Cooperative Agreement:

FROM: The term for the Option 1 Period of this Cooperative Agreement commences on the effective date of award and continues through 22 July 2018.

TO: The term for the Option 1 Period of this Cooperative Agreement commences on the effective date of award and continues through 18 November 2018.

2. ALL OTHER TERMS AND CONDITIONS REMAIN UNCHANGED.

FOR RECIPIENT:	Naval Warfare Systems Center, P	· •
	(b)(6)	
(Signature) M.A., Ed., CRA	LYNN M. BIEDERMANN Grants Officer	(Date)
Associate Director, Research Services 6/28/2018		
(Name/Title) (Date)		

P.R. No.: 1300418366

Effective Date: 16 November 2018

<u>CFDA No</u>.: 12.910 AGO Code: N62880

Payment Office Code: HQ0337

RESEARCH COOPERATIVE AGREEMENT MODIFICATION # P00015

Grantor: Space and Naval Warfare Systems Center, Pacific

Code 22720

53560 Hull Street

San Diego, CA 92152-5001

(Attn: Veronica Velarde, (619) 553-7734, veronica.velarde@navy.mil)

Recipient: The Trustees of the University of Pennsylvania

3451 Walnut Street

Philadelphia, PA 19104-6205

Recipient Identification Numbers/Codes:

DUNS: 042250712 CAGE: 7G665 TIN: 23-1352685

Authority: 10 U.S.C. 2358 as amended and 31 U.S.C. 6305

1. <u>PURPOSE</u>: This modification extends the period of performance for Option 1. As a result, the following change is made to schedule item 2. <u>Term</u> of the Cooperative Agreement:

FROM: The term for the Option 1 Period of this Cooperative Agreement commences on the effective date of award and continues through 18 November 2018.

TO: The term for the Option 1 Period of this Cooperative Agreement commences on the effective date of award and continues through 31 December 2018.

2. ALL OTHER TERMS AND CONDITIONS REMAIN UNCHANGED.

FOR RECIPIENT:		FOR The United States of America, Space and Naval Warfare Systems Center, Pacific		
		(b)(6)	.01110	
		2018.1	1.27 12:08:27 -08'00'	
(Signature)		LYNN M. BIEDERMANN Grants Officer	(Date)	
Associate Director Research Services	11/27/2018			
(Name/Title)	(Date)			

P.R. No.: 1300418366

Effective Date: 31 December 2018

<u>CFDA No</u>.: 12.910 AGO Code: N62880

Payment Office Code: HQ0337

RESEARCH COOPERATIVE AGREEMENT MODIFICATION # P00016

Grantor: Space and Naval Warfare Systems Center, Pacific

Code 22720

53560 Hull Street

San Diego, CA 92152-5001

(Attn: Veronica Velarde, (619) 553-7734, veronica.velarde@navy.mil)

Recipient: The Trustees of the University of Pennsylvania

3451 Walnut Street

Philadelphia, PA 19104-6205

Recipient Identification Numbers/Codes:

DUNS: 042250712 CAGE: 7G665 TIN: 23-1352685

Authority: 10 U.S.C. 2358 as amended and 31 U.S.C. 6305

Accounting and Appropriation Data:

ACRN: AM 97 19200400 1300 BTBIAA 2019 MED 01 CONGTBI A DARPA 255 HR0011938593 01

000000 10601 012199 MIPR # HR0011938593

\$964,227.00

- 1. <u>PURPOSE</u>: This modification increases the value of the Option and overall value of the Cooperative Agreement, incorporates a revised Attachment 1, revises the term of the cooperative agreement, and obligates an increment of funding for the Option period. As a result, the following changes are made to the Cooperative Agreement document:
- a. Total Agreement Amount is revised:

FROM:

\$23,383,815.64

Base (Phase 1): \$13,724,629.00 Option (Phase 2): \$9,659,186.64

TO:

\$24,348,042.64

Base (Phase 1): \$13,724,629.00 Option (Phase 2): **\$10,623,413.64**

b. Schedule item 1. Purpose now reads:

The purpose of this Cooperative Agreement is to fund research in support of a DARPA sponsored program. This effort shall be carried out generally as set forth in the Government's Statement of Work Revision 4, Attachment 1, dated 30 November 2018, which has been based on the Recipient's proposal, "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)", and Data Matrix, Attachment 2, copies of which are in the possession of both parties.

c. Schedule item 2: Term now reads:

FROM: The term for the Option 1 Period of this Cooperative Agreement commences on the effective date of award and continues through 31 December 2018.

TO: The term for the Option 1 Period of this Cooperative Agreement commences on the effective date of award and continues through 31 October 2019.

d. Schedule item 8. Cooperative Agreement Funding now reads:

This Cooperative Agreement is now fully funded in the amount of \$24,348,042.64. Of this amount, \$13,724,629.00 is for the Base Period and \$10,623,413.64 is for the Option 1 Period.

The Recipient shall notify the AGO in writing promptly whenever the total Agreement amount is expected to exceed the needs of the Recipient for the project period by more than \$5,000 or 5% of the award, whichever is greater. This notification shall not be required if an application for additional funding is submitted for a continuation award.

2. ALL OTHER TERMS AND CONDITIONS REMAIN UNCHANGED.

FOR RECIPIENT:		FOR The United States of America, Space and Naval Warfare Systems Center, Pacific		
		(b)(6)		
		2019.0	02.10 20:45:46 -08'00'	
(Signature)		LYNN M. BIEDERMANN Grants Officer	(Date)	
ssociate Director-Research Services	2/8/2019			
(Name/Title)	(Date)			

P.R. No.: 1300418366

Effective Date: Date Signed By Government

<u>CFDA No</u>.: 12.910 AGO Code: N62880

Payment Office Code: HQ0337

RESEARCH COOPERATIVE AGREEMENT MODIFICATION # P00017

Grantor:	Naval	Informati	ion Sys	stems Cent	er, Pacific

Code 22530

53560 Hull Street

San Diego, CA 92152-5001

(Attn: Sabina Sabedra, (619) 553-4522, sabina.sabedra@navy.mil)

Recipient: The Trustees of the University of Pennsylvania

3451 Walnut Street

Philadelphia, PA 19104-6205

Recipient Identification Numbers/Codes:

DUNS: 042250712 CAGE: 7G665 TIN: 23-1352685

Authority: 10 U.S.C. 2358 as amended and 31 U.S.C. 6305

1. <u>PURPOSE</u>: This modification extends the period of performance for Option 1. As a result, the following change is made to schedule item 2. <u>Term</u> of the Cooperative Agreement:

FROM: The term for the Option 1 Period of this Cooperative Agreement commences on the effective date of award and continues through 31 October 2019.

TO: The term for the Option 1 Period of this Cooperative Agreement commences on the effective date of award and continues through 31 January 2020.

2. ALL OTHER TERMS AND CONDITIONS REMAIN UNCHANGED.

FOR RECIPIENT:	FOR The United States of America, Space and Naval Warfare Systems Center, Pacific
	(b)(6)
	2019.10.01 09:17:39 -07'00'
(Signature)	LYNN M. BIEDERMANN (Date) Grants Officer
Associate Director-Research Services 10/0	1/2019
(Name/Title) (Da	te)

STATEMENT OF WORK FOR UNIVERSITY OF PENNSYLVANIA

Title – Restoring Active Memory (RAM): "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)

1.0 SCOPE

This effort promises to use direct brain recor	dings and stimulation in humans	s and animals to crea	te a real-time					
system for enhancing encoding and long-term retrieval of memories for specific types of information. The team								
consists of nine leading clinical centers for the surgical treatment of epilepsy and movement disorders, each led								
by a clinician scientist with substantial exper	rience in one or more key areas of	of electrical brain stir	nulation, human					
cognition, computational electrophysiology,	and realtime adaptive control sy	stems. The neurolog	ical and					
neurosurgical teams are aligned on the comm	non goal of rapidly developing a	nd testing approache	s to enhance					
and restore memory through a study of unpre	ecedented scope: more than 100	patients each year in	a large array					
of experiments. Pending Investigational Dev	vice Exemption (IDE) approval,	patients in Phase 2 o	f the project					
will be implanted with a complete memory n	euromodulation	(b)(4)						
		to	our memory					
testing paradigms. This will be accomplished	d through an accelerated U.S. Fo	ood and Drug Admin	istration (FDA)					
submission of the technical area two (TA2) s	system at the end of Phase 1. Th	rough application of	a					
computational model of human	(b)(4)	to the behavio	oral and					
electrophysiological data the recipient shall of	define biomarkers of memory	(b)(4)						
	These biomarkers will be used	(b)(4)						
	(b)(4)							

1.1. BACKGROUND

The Defense Advanced Research Projects Agency (DARPA) seeks new methods for analysis and decoding of neural signals in order to understand how neural stimulation could be applied to facilitate recovery of memory encoding following brain injury. Ultimately, it is desired that a prototype implantable neural device that enables recovery of memory in a human clinical population be developed. Additionally, the program encompasses the development of quantitative models of complex, hierarchical memories and exploration of neurobiological and behavioral distinctions between memory function using the implantable device versus natural learning and training.

2.0 APPLICABLE DOCUMENTS

- (a) DARPA BAA-14-08.
- (b) UPENN Technical Proposal Titled "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)" dated January 23, 2014

3.0 PROJECT WORK DESCRIPTION AND REQUIREMENTS

The recipient shall provide the facilities necessary to develop the effort as described herein.

Human use **is** anticipated in this effort. The recipient shall obtain all necessary Institutional Review Board (IRB) approvals, show proper assurance documentation, and obtain proper approval from the Government officials prior to human use testing.

Animal use **is** anticipated in this effort. The recipient shall obtain all necessary Institutional Animal Care and Utilization Committee (IACUC) approval and demonstrate this approval to the Government prior to beginning experimentation with animals. If animal use is no longer anticipated, or changes significantly from the approved

IACUC then the PI must submit a letter stating the discontinuation of animal use for this effort and/or receive appropriate authorization for IACUC changes of previously specified protocols. Unless prior approval by DARPA is given IACUC documentation must be provided prior to contract award.

3.1 BASE PERIOD (PHASE I)

Technical Area 1

3.1.1 A computational model for describing behavior in declarative memory tasks.

3.1.1.1	Predicting n	noment-by	-moment behav	ior in a var	iety of memo	ry tasks.		
The reci	pient shall d	locument a	model of mem	ory		(b)(4)		
	(-) Th	_::	11 4 44		C 41			
	(a) The re	ecipieni sna	ll document the	code base	for the	(b)(4)		
	[Month 3].							
		cipient sha	ll extend the mo	del		(b)(4)		
		1				[Month 6]		
	(c) The red	cipient shal	l document full	y commen	ted, optimize)(4)	
		C	ode shall be ab	e to execut	e model	(b)((4)	
		_	nth 6].					
	(d) The red	-	ll document the					
	() TI	(b)(4)	11 (% 41	[Month 9].		(1) (4)		
	(e) The red	cipient snai	ii fit the			(b)(4)	ГМ	Ionth 12].
	(f) The rec	cinient shal	l document full	v comment	ed ontimized	d (b)(4)	10IIII 12].
	(i) The rec	orprent shar	r document run		-	e able to execute mo		(b)(4)
								(-)(-)
				[Month	12].			
3.1.1.2	[DELETE]	D]						
3.1.1.3.	Build a	(b)(4)	model of free	recall:		(b)(4)		
	a) Davalan	anfricana tl	nat allows us to	oonstmiet t	ho (b)(4)	model for an entire	gaggian a	fED1 in 20
•	or less [Mo		iat allows us to	construct t	he (b)(4)	moder for all entire	session o	1 FK1 III 30
	b) [DELET:	_						
•	c) [DELET]	_						
,	<i>,</i> L	,						
3.1.1.4 E	Build a	(b)(4)	model for	(b)(4)	memory:	(b)(4)	

UPE	NN PI- KAHANA					
	() D. 1	(b)(4)				D. (
21]	(a) Develop a model prototype			(b)(4)		[Month
[Mor	(b) Deliver fully documented conth 24]	ode		(b)(4)		
3.1.2	Integrating neurophysiological	biomark	ers into the co	mputational mo	del of beh	avior.
3.1.2	2.1 Characterize distribution of	(b)(4)	biomarker	S	(b)(4)
	2.1.1 A prototype for analyzing lated [Month 12].	(b)(4)	neural	(b)(4)		shall be deployed and
3.1.2	2.1.2 The recipient shall document	the protot	ype software		(b)(4)	
				[Month 12].	
3 1 2	2.1.3 Characterize the (b)(4)	hioma	rkers using the	e models of free i	ecall and	(b)(4) navigation:
3.1.2	(a) Characterize the (b)(4)		_	ents performing		
			1	1 2	[Month	
	(b) Characterize the (b)(4)		-	ients performing	the (b)(4)	navigation task,
		(b)(4)			[Month 24].
		_				
3.1.2	2.1.4 The recipient shall document	•			(b)(4)	
	The recipient shall docum		(b)(4) oftware used	(b)(4)		(b)(4)
	The recipient shair decan	ioni ino se	it water asset	(5)(1)		(8)(1)
	[Month 24].					
3.1.3	B Electrophysiological recording	s to define	e biomarkers		(b)(4	
	memory. Objective: Define biomarkers			(b)(4)		memories, as
	measured in a broad array of ta	asks. The	subtask list tha		ces the fol	
	(b)(4) free recall of (b)(4)	word list		4) free recall (associate learning		patial navigation (b)(4)
3 1 3	3.1 The recipient shall design, progr	ram pilot	execute and	analyze data from	Experime	ent FR1 on patients in the
	epsy monitoring unit. Recording ne	_		(b)(4)		shall be
	to identify (b)(4) biomarkers (b)		-			These biomarkers will
serve				recipient shall:		
	(a) Design, program, and pilo	_	-			
	(b) Write initial data analysis(c) Analyze data on 13 patien		_	[Month 8]		
	(d) Analyze data on 26 patien		•			
	(e) Analyze data on 39 patien					
	(f) Analyze data on 58 patient	s from ex	periment FR1	[Month 24].		

UPENN PI- KAHANA (g) Organize and annota program personnel; prec	-	_		arry out 3D i		
(b) (a) [Month 24]. (b) Complete interim reports on data from the above experiment to be presented at team meetings an						
DARPA program person	=	_	_		(b)(4)	
DAKI A program persor	iner. Reports shan me		l as analyses of		() ()	
correlates of (b)(4) m	nemory	as wel	•	i ille electrop	niysiologicai	
correlates of (b)(4) m	leffior y		(b)(4)	ſΜon	th 24].	
(i) Post all data collecte (j) Fully document code (k) Fully document anal (l) Create 3D reconstruc (m) Provide interim rep (n) Post fully annotated (o) Deliver report on	e for experiment [Mon ysis functions [Month ctions of all patients ru orting on analyzed dat	th 2]. 3]. In in the task in Phata from all patients a portal for all patie	ase 1 [Month 2 run in the task	tta portal [Mo 4]. c in Phase 1 task in Phase	onth 24]. [Month 24].	
3.1.3.2 Design, program, pilot, e epilepsy monitoring unit. In this	•	•	of (6) on patient b)(4)	s in the	
(a) Design, program, and (b) Write initial data analy (c) Analyze data on 11 pa (d) Analyze data on 23 p (e) Analyze data on 28 p (f) Analyze data on 33 pa (g) Organize and annotate (h) Complete interim repo (i) Post all data collected (j) Fully document code f (k) Fully document analy (l) Create 3D reconstructi (m) Provide interim report (n) Post fully annotated da (o) Deliver report on 3.1.3.3 Design, program, pilot, e monitoring unit. In this task the r	ysis scripts [Month 3]. Itients from experiment atients from experiment atients from experiment atients from experiment experiment data from about so far in a deidentified for experiment [Month 3] ons of all patients runting on analyzed data from the public data public	t CatFR1 [Month 8 nt CatFR1 [Month nt CatFR1 [Month t CatFR1 [Month 2 ve experiment [Motove experiment [Moto	13]. 18]. 4]. onth 24]. Month 24]. e with the public et 1 [Month 24]. in the task in the t	Phase 1 [Mo sk in Phase 1]. on patients in	nth 24]. [Month 24].	
momenting unit. In this task the i	cerprent shan rachtrry	olomarkers on	(b)(4) IIIC	oniory (b)	/(*)	
				ecipient shall	-	
(b)(4) memory biomarkers,		(b)(4)		as well as	(b)(4)	
memory biomarkers,		(b)(4)				
(b)(4) The recipient shall:						
(a) Design, program, an(b) Write initial data an(c) Analyze data on 11(d) Analyze data on 22(e) Analyze data on 33	alysis scripts [Month 3 patients from experim patients from experim	3] ent YC1 [Month 8] ent YC1 [Month 13	3].			

(f) Analyze data on 50 patients from experiment YC1 [Month 24].

(j) Fully document code for experiment [Month 2].

(g) Organize and annotate patient data from above experiment [Month 24].(h) Complete interim reports on data from the above experiment [Month 24].

(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].

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			-	ions [Month 3]		· 101	1.53.6	2.47		
	· /			l patients run ir nalyzed data fro			-	_	so 1 FMa	onth 241
			-	public data po	_				_	_
		er report on	d data to the	(b)(4)	11tai 101 a		arkers [Mon		II I Hase	1 [Month 24].
	· /	1					·			
	ring unit.	-		analyze data fi	_		(b)(4)			the epilepsy associations
	(b) Write (c) Anal (d) Anal (e) Anal (f) Anal (g) Orga (h) Com (i) Post (j) Fully (k) Fully (l) Crea (m) Proven (n) Post (n) Post (n)	lyze data on 1 lyze data on 2 lyze data on 25 mize and announced and data collect document coly document and te 3D reconstruide interim refully annotate	patients from 4 patients from 2 patients from 5 patients from	_	t PAL1 [int Pal1	Month Month Into 1 Month Month Into 1 Month	n 13]. n 18]. 24]. Month 24]. t [(Month 24] ble with the p ase 1 [Month run in the tas ents run in th	public da n 24]. sk in Pha ne task in	use 1 [Mo	onth 24].
		ver report on		(b)(4)		-	arkers [Mon			
2 1 2 5	ъ :		. 1	1 1	Б		4 DDG2 (- 2	-	.· .	1 ' DD(
				analyze data fi	_					
(see	(b)(4)	Recall Task,		sease. In this to	ask the re	ecipien	_	ппа	(b)(4)	recall task
(See	(b)(4)	Recall Lask,	abovej.				(b)(4)			The recipient
shall:										The recipient
ondi.	(a) Desi	gn, program, a	and pilot task	(Month 21.						
		e initial data a	-	_						
				n experiment D	BS2 [Mo	onth 8].			
	(d)-(n) [I	DELETED]	•	•			-			
3.1.4 S	timulatio	n to		(b)(4)	1			me	emory	
3.1.4.1	Design, pr	ogram, pilot,	execute, and	analyze data fi	om Expe	erimen	nt FR2 (n=18)). The re	ecipient s	shall test the
hypothe	esis				(b)(4)					
							The recipien	t shall co	ompare t	he degree to
which				(b)(4)					
	The recip	oient shall:								
		gn, program, a								
		e initial data a								
				n experiment F						
				n experiment F						
		•	-	om experiment	_		-			
		-	_	m experiment	_		_			
			_	data from the a	_	perime			nvestiga	tors and
	program		-	ize electrode co				(b)(4)		
			-	reconstructions			((b)(4)		
	(b)(4)	[Month 24].							E

UPENN	PI- KAHANA				
		m personnel. Re	_	eriment to be presented at to iled analyses of behavioral	data, (b)(4)
		(b)(4)		, as well as analyses of the	ne electrophysiological
	correlates of	(b)(4) memory		(b)(4)	D 6 1 0 47
	(j) Fully documents (k) Fully documents (l) Create 3D running (m) Provide für (n) Post fully at (o) Expand analysis	ment code for expendent analysis fur econstructions of the post of the constructions of the constructions of the constructions of the code	periment [Month 2]. nctions [Month 3]. f all patients run in the analyzed data from all 1	task in Phase 1 [Month 24]. task in Phase 1 [Month 24]. task in Phase 1 in the task in Phase all patients run in the task in Phase all patients run in the task (b)(4) Deliver updated	nase 1 [Month 24].
	analysis code [Month 7].			
3.1.4.2	(b)(4) (a) Design, program (b) Write initia (c) Analyze da (d) [DELETEI (e) Analyze da (f) Analyze da (g) Organize a (h) Complete f (i) Post all data (j) Fully docum (k) Fully docum (l) [DELETED (m) [DELETEI (n) [DELETEI	and shall: ogram, and pilot ogram, and pilot of data analysis so ta on 4 patients ta on 10 patients ta on 18 patients and annotate patie inal reports on d of collected so far ment code for exp ment analysis fun of D of	(b)(4) task [Month 12]. cripts [Month 13]. from experiment FR3 [If from experiment FR3 from experiment FR3 ent data from above expent from the abov	[Month 24]. [Month 30]. Periment [Month 30]. Periment [Month 30]. Periment to the public to the publ	
	(o) Expand ana	lysis functions		(b)(4) Deliver undated	and fully documented
	analysis code	Month 131.		Deliver updated	and fully documented
3.1.4.3 [DELETED]				
3.1.4.4	Design, progra	m, pilot, execute	, and analyze data fron	Experiment CatFR2.	(b)(4)
				X	Further, the
recipien		11	(b)(4		
	nd sh	iall: oram and nilot:	to als [Month 2]		
	Tal Design hro	TOUR DIOL MILE	ZASK LIVIOHIH 7 I		

- (a) Design, program, and pilot task [Month 2].
- (b) Write initial data analysis scripts [Month 3].
- (c) Analyze data on 4 patients from experiment CatFR2 [Month 8].
- (d) Analyze data on 8 patients from experiment CatFR2 [Month 13].
- (e) Analyze data on 13 patients from experiment CatFR2 [Month 18].
- (f) Analyze data on 18 patients from experiment CatFR2 [Month 24].
- (g) Organize and annotate patient data from above [Month 24].
- (h) Complete final reports on data from the above experiment [Month 24]
- (i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24]
- (j) Fully document code for experiment [Month 2].

	(m) Provide final reporting on a	f all patients run in the task in Ph nalyzed data from all patients rur the public data portal for all pation	ase 1 [Month 24]. In in the task in Phase 1 [Month 24]. The ents run in the task in Phase 1 [Month 24]. (b)(4) Deliver updated and fully documented	
	analysis code [Month 7].		Deriver updated and fully documented	
		•	nt CatFR3. In CatFR3 the recipient shall	
test the a	bility	(b)(4)	. The	
recipient	shall:	(6)(4)	, The	
	(d) Analyze data on 8 patients five [DELETE] (f) [DELETE] (g) [DELETE] (h) [DELETE] (i) Post all data collected so far (j) Fully document code for exp (k) Fully document analysis fun (l) [DELETE] (m) [DELETE] (n) [DELETE]	cripts [Month 13]. From experiment CatFR3 [Month com experiment CatFR3 [Month in a deidentified format compatiberiment [Month 12].	30]. ble with the public data portal [Month 30].	
	(o) Expand analysis functions		(b)(4)	
	analysis code [Month 13].		Deliver updated and fully documented	
3.1.4.6 1		(b	nt YC2. The recipient shall apply (b)(4) (a)(4) (b)(4) (b)(4) (c)(4)	
memory		(b)(4)		
	(d) Analyze data on 10 patients (e) Analyze data on 16 patients (f) Analyze data on 33 patients (g) Organize and annotate patie (h) Complete final reports on d (i) Post all data collected so far (j) Fully document code for exp (k) Fully document analysis fur (l) Create 3D reconstructions of (m) Provide final reporting on a	task [Month 2]. cripts [Month 3]. from experiment YC2 [Month 8]. from experiment YC2 [Month 1] cent data from above experiment [II ata from the above experiment [II in a deidentified format compatible periment [Month 2]. actions [Month 3]. fall patients run in the task in Phanalyzed data from all patients run	3]. 8]. 8]. 4]. Month 24]. Month 24]. ble with the public data portal [Month 24]. ase 1 [Month 24]. a in the task in Phase 1 [Month 24] an in the task in Phase 1 [Month 24]. (b)(4)	
			Deliver updated and fully documented	

UPENN PI- KAHANA analysis code [Month 7].

3.1.4.7 [DELETED]

.1.4.8 Design, program, pilot, exec	cute, and analyze data from Ex	periment PAL2.	(b)	(4)
	The recipient shall	(b)	(4)	
(d) Analyze data on 6 pati (e) Analyze data on 9 pati (f) Analyze data on 11 pa (g) Organize and annotate (h) Complete final reports (i) Post all data collected s (j) Fully document code f (k) Fully document analys (l) Create 3D reconstruction	pilot task [Month 2]. ysis scripts [Month 3]. ients from experiment PAL2 [I ients from experiment [I	Month 8]. Month 13]. Month 18]. [Month 24]. riment [Month 24]. riment [Month 24]. compatible with the	e public data th 24]. k in Phase 1	[Month 24].
(o) Expand analysis funct	ion \$ b)(4)	(b)(4)	adatad amd f	ully documented
analysis code [Month 7].		Denver up	odated and i	uny documented
The recipient shall:				
 (a) Design, program, and p (b) Write initial data analys (c) [DELETED] (d) [DELETED] 				
(f) Analyze data on 8 paties(g) [DELETED](h) [DELETED]	nts from experiment PAL3 [M nts from experiment PAL3 [M	_		
(i) [DELETED](j) Fully document code for	r experiment [Month 12]			
(k) Fully document analysi [Month 13]. (l) [DELETED] (m) [DELETED]		(b)(4)		
(n) [DELETED]				
(o) Expand analysis function	ons	(b)(4)	lated and fu	lly documented
analysis code [Month 13].		Benver upc	anca ana tu	ii, documented
1.4.10 Design, program, pilot, ex	secute and analyze data from F	Experiment DRS1		
he recipient shall evaluate	(b)(4)	-	(b)(4)	learning durir

	N PI- KAHA	11 17 1									
a	(b)(4)	task.				(b)(4)					
	(b)(4)		The recipi	ent shall var	y			(b)(4)			
parame	ters.				(b)(4)						
			The rec	cipient shall	index learning	g			(b)(4)		
				The recipier	nt shall compa	are	(b)(4)	cross the	e five c	onditions	(b)(4)
		(b)(4)		and (2) i	dentify ((b)(4)	par	ameters		(b)(4)	
	and shall:										
			_	sk [Month 2]							
	` '		•	ipts [Month :	-						
	• •		0 patients fi	rom experim	ent DBS1 [M	Ionth :	8].				
	(d)-(n)[D	ELETED									
.1.4.11	l Design, pro	ogram, exe		ialyze data fi	rom Experime					_	
	() D :	1	(b)(4)	1.107		1d0	entify	(b)(4) st	ımulatı	on param	eters:
			am tasks [M		· DO:	1 DC2	0 DG2) F) (1	1.67		
			•		periments PS		2, & PS:	iviontn	_		
	(c) Anaiyz		0		DC 1			FN / 41-			
					periments PS1		, & PS3			1 1 1 1	1.00
					periments PS1 a portal for al		, & PS3			hase 1 [M	Ionth 30
.1.5 D		lly annotat	ed data to th			l patio	, & PS3			hase 1 [M	Ionth 30
	(d) Post fu	lly annotat	ed data to th		a portal for al	l patio	, & PS3			hase 1 [M	Ionth 30
.1.5.1	(d) Post fu Develop control [DELETED	lly annotatrol algorith	ed data to th		a portal for al	ll patio	ents run			hase 1 [M	Ionth 30
3.1.5.1	(d) Post fu	lly annotatrol algorith	ed data to th		a portal for al	l patio	ents run			hase 1 [M	Ionth 30
.1.5.1	(d) Post fu Develop contr [DELETED Develop algo	lly annotat rol algorith] prithms	ed data to the		a portal for al	ll patio	ents run			hase 1 [M	Ionth 30
.1.5.1	(d) Post fu Develop control [DELETED Develop algo The re	lly annotat rol algorith] prithms cipient sha	ed data to the		a portal for al	(b)(4	, & PS3			hase 1 [M	Ionth 30
.1.5.1	(d) Post fu Develop contr [DELETED Develop algo	lly annotat rol algorith] prithms cipient sha	ed data to the	ne public dat	a portal for al	(b)(4	ents run			hase 1 [M	Ionth 30
.1.5.1	(d) Post fu Develop contr [DELETED Develop algo The re (a) Comple	lly annotated algorithms cipient sha	ed data to the ms	ne public dat	a portal for al	(b)(4	, & PS3 ents run (a)			hase 1 [M	Ionth 30
.1.5.1	(d) Post fu Develop control [DELETED Develop algo The re	lly annotated algorithms cipient sha	ed data to the ms	ne public dat	a portal for al	(b)(4)	, & PS3 ents run b)	in the ta	sk in P		
.1.5.1	(d) Post fu Develop contr [DELETED Develop algo The re (a) Comple	lly annotated algorithms cipient sha	ed data to the ms ll: report	ne public dat	a portal for al	(b)(4)	, & PS3 ents run b)	in the ta	sk in P		Jonth 30
.1.5.1	(d) Post fu Develop contr [DELETED Develop algo The re (a) Comple	lly annotated algorithms cipient shate ete interim p prototyp (b)(ed data to the ms ll: report	ne public dat	a portal for al (b)(4 fonth 9].	(b)(4)	, & PS3 ents run b)	in the ta	sk in P		
.1.5.1	(d) Post fu Develop contr [DELETED Develop algo The re (a) Comple (b) Develor	lly annotated algorithms cipient shatete interim p prototyp (b)(TED]	ed data to the ms ll: report	[M	a portal for al (b)(4 fonth 9]. e 12-month ir Ionth 12].	(b)(4) (b)(4) (b)nterim	ents run (a)	on algori	sk in P		
.1.5.1	(d) Post fu Develop control [DELETED Develop algo The re (a) Comple (b) Develop (c) [DELE (d) [DELE	lly annotated algorithms cipient shate the interiment of the prototype (b)(TED] TED]	ed data to the ms ll: report	[M	a portal for al (b)(4 fonth 9].	(b)(4) (b)(4) (b)nterim	ents run (a)	on algori	sk in P		
.1.5.1	(d) Post fur Develop control [DELETED Develop algorithm of the region of	lly annotated algorithms cipient shapete interim p prototyp (b)(TED] TED] g 9-month	ed data to the ms	[Magnet on Section Content on Complete Complete Content on Content	fonth 9]. e 12-month in Jonth 12].	(b)(4) (b)(4) (b)terim	ents run (a)	on algori	sk in P		
.1.5.1	(d) Post fur Develop control [DELETED Develop algored The real (a) Complete (b) Develop (c) [DELE (d) [DELE (e) Provide (f) Pr	lly annotated algorithms cipient shadete interim p prototyp (b)(TED] TED] e 9-month is 12-month	ed data to the ms ll: report e	Complete . [M	fonth 9]. e 12-month in Jonth 12].	(b)(4) (b)(4) (b)(thms	(, & PS3 ents run () () () () () () () () () () () () ()	on algori	sk in P		
.1.5.1	(d) Post fur Develop control [DELETED Develop algored The real (a) Complete (b) Develop (c) [DELE (d) [DELE (e) Provide (f) Pr	lly annotated algorithms cipient shate the interimed prototype (b)(TED] TED] 2 9-month to the interior in t	ed data to the ms III: report e interim report interim report	Complete . [Mort on (b) ort on (b)	fonth 9]. e 12-month in Ionth 12]. (4) algorian (4) alg	(b)(4) (b)(4) (b)(thms	(, & PS3 ents run () () () () () () () () () () () () ()	on algori	sk in P		
.1.5.1	(d) Post fur Develop control [DELETED Develop algored The re (a) Complete (b) Develop (c) [DELE (d) [DELE (e) Provide (f) Provide (g) Documents (g) Documents (g) Documents (g) Developments (g) Provide (g) Documents (g) Documen	lly annotated algorithms cipient shapete interim p prototyp (b)(TED] TED] te 9-month is 12-monthment 12	ed data to the ms III: report e interim report interim report	Complete . [Mort on (b) ort on (b)	fonth 9]. e 12-month in Ionth 12]. (4) algorian (4) alg	(b)(4) (b)(4) (b)(thms	(, & PS3 ents run () () () () () () () () () () () () ()	on algori	sk in P		
3.1.5.1	(d) Post fur Develop control [DELETED Develop algorithms of the region o	lly annotated algorithms cipient shapete interim p prototyp (b)(TED] TED] e 9-month is 12-month itent 12-mo TED]	ed data to the ms III: report e interim report interim report	Complete . [Mort on (b) ort on (b)	fonth 9]. e 12-month in fonth 12]. (b)(4) algorian algo	(b)(4) (b)(4) (b)(thms	(, & PS3 ents run () () () () () () () () () () () () ()	on algori	sk in P		

- 3.1.5.4 [DELETED]

3.1.6 Core project resources devoted to TA1.

- 3.1.6.1 The recipient shall perform electrophysiological experiment development and programming, data analysis, computational cluster effort towards data analysis and computational modeling from TA1.
- 3.1.6.2 The recipient shall provide project coordination, data sharing and data storage.

UPENN PI- KAHANA 3.1.7 Determine electrode requirements for (b)(4) s	timulation in Phas	se 2. The recinien	nt shall characterize
(b)(4)		c 2. The recipien	for modulating and
restoring memory function.			
3.1.7.1 The recipient shall design and develop an electrod (b)(4)	e (b)(4) (b)(4)	capable	(b)(4) . The recipient
shall:			. The recipient
(a) Based on precise anatomical analyses	(b)(4)		
(b)(4) [Month 12].			
(b) Working with Lawrence Livermore National Labs (LL materials that can be put into place by the beginning of Pha	* *	nal technical draw	ing and list of
(c) Working with LLNL, complete ISO-10993 testing to v design history file and associated ISO test results required for(d) [DELETED]			
3.1.8 [DELETED]			
3.1.9 [DELETED]			
Technical Area 2			
3.1.10 Validate system architecture and individual com the high-level system design requirements against curre			nent and review
3.1.10.1 The recipient shall validate system level specifical	tion with TA1 team	[Months 1–6].	
3.1.10.2 [DELETED]			
3.1.10.3 The recipient shall refine the specifications for elements (b)(4), continually refining as n		(b)(4)	
3.1.10.4 The recipient shall validate the specification for the [Months 5–6].	ne Algorithm protot	yping system and	user interface
3.1.10.5 The recipient shall define the sub-chronic safety a IDE approval [Month 6] and shall:	nd performance dat	a required by the	FDA for 29-day
(a) Document definitions of the functional, operation [Month 6].	ion, and performan	ce requirements o	f the overall system
(b) Document definitions of the component-level external packaging, and algorithm prototyping sys	•	ne neural interface	e, electronics,
(c) Document definitions of the sub-chronic safety		lata required by th	ne FDA for the 29-
day IDE approval [Month 6] (d) Deliver definitions of stakeholder requirement	s [Month 4]		
3.1.11 Design, fabrication, and characterization of the			_
shall develop a (b)(4) (b)(4)electrodes. (*and any adaptations needed to ensure		capable of matin care.)	ng with (b)(4)
3.1.11.1 The recipient shall design and manufacture of elec	tronics,	(b)(4)	
Months 7–18].			

3.1.11.2 The recipient shall (b)(4) software (firmware) to control the electronics and provide (b)(4) (b)(4)

UPENN PI- KAHANA capability [Months 7–18].

	The recipient shall modify cal depth electrodes and con	-			(b)(4) o interfa	ace with
	The recipient shall manufa in prepar			rformance testing, I system delivery to		0 <mark>(4)</mark> onths 19–
24].	(a) Design and build elect 7-18].	ronics,		(b)(4)		[Months
	(b) Document the (b)(4) capability [Month 18].			onics and docume	n (b)(4) algor	rithm
	(c) Modify the design of the design verification testing	[Month18].		22	(b)(4)	for
	(d) Test and document saf IDE submission [Month 24]		nce	(b)(4)	in preparation	for FDA
recipien	Connectorization and Intent shall develop a connecton (b)(4) neural stimul	rization method		(b)(4) variety of clinical		tor. The s with the
3.1.12.1	The recipient shall define	specifications for	the connector	[Months 1-	b)(4) -6].	
3.1.12.2	[DELETED]					
3.1.12.3	[DELETED]					
	The recipient shall design the mechanical integrity [Moreover, mechanical integrity [Moreover, and the mechanical integrity [M	onths 15–24]. Th	e recipient shall:	ical conductivity a	nd reliability, moi	sture
	(c) Document the assemble	y process		(b)(4)		
	[Month 15].					
	(d) Complete and docume (e) Design verification tes integrity [Month 24].				and mechanical	
3.1.13	Algorithm prototyping sys	tem. The recipi	ent shall develop	an algorithm pro	ototypin (b)(4)	(b)(4)
3.1.13.1	The recipient shall design	(b)(4) Months 1–6].	interface	(t	0)(4)	
3.1.13.2	The recipient shall docum	ent the software i	Months 1–1	(b)(4) 2].		
3.1.13.3	The recipient shall develop	software	(b)(4)	[Months 7-	-18].	
	The recipient shall verify a pient shall:	and validate testing	ng and documenta	tion for IDE subm	ission [Months 19	-24].
	(a) Design (b)(4)	interface t				

(b)(4) Month 6].
(b) Document the software used (b)(4)
[Month 12].
(c) Document the software (b)(4) [Month 18].
(d) Complete prototype software package [Month 18].
(e) Verify and validate testing and documentation for IDE submission [Month 24].
3.1.14 System verification and validation testing. The recipient shall evaluate and verify system lifetime, sterility and biocompatibility. The recipient shall also verify and validate the system functions and interfaces
(b)(4) (b)(4)
(b)(4) Additionally, system verification and validation shall be performed.
3.1.14.1 [DELETED]
3.1.14.2 [DELETED]
3.1.14.3 [DELETED]
3.1.14.4 The recipient shall perform (b)(4) system verification testing for sub-chronic (< 29-days) use as outlined in ANSI / AAMI / ISO 14971:2007/(R)2010 [Months 19–24].
3.1.14.5 The recipient shall validate the (b)(4) system [Month 19–24]. The recipient shall:
 (a) Fabricate and assemble fully-integrated systems for testing [Month 18]. (b) [DELETED] (c) [DELETED] (d) [DELETED] (e) Report on electronics testing for sub-chronic (< 29-days) use as outlined in ANSI / AAMI / ISO 14971:2007/(R)2010 [Month 24]. (f) [DELETED] (g) Validate and fully document a system that is ready for FDA IDE submission; deliver system verification and validation reports [Month 24].
3.1.15 [DELETED]
3.1.16 (b)(4) Electrode Design.
3.1.16.1 The recipient shall deliver development plans for a novel (b)(4) lead suitable for interfacing with the (b)(4) device. The recipient shall: (a) Identify at least one partner capable of delivering the electrode [Month 7] (b) Deliver a technical drawing, estimated development and manufacturing budget, and identify any cost sharing activities [Month 7]
Technical Area 3
The recipient shall perform basic research findings (b)(4)
to inform the human stimulation studies in
TA1 and guide device development in TA2.
The recipient shall document the protocols for measuring monkey (b)(4) memory (b)(4) and shall train animals in the (b)(4) task. In parallel, the recipient shall conduct studies of the neurophysiology of stimulation (b)(4)

The recipient shall then conduct behave				nonkeys. The
recipient shall also perform a systema		(b)(4) also probe the neurop		(b)(4)
	The recipient shan	also probe the hearof	niysiology	(b)(4)
3.1.16 Identifying neuronal basis of	(b)(4) memory in	NHPs and probing t	the role of stimula	ation(b)(4)
(b)(4)	. This phas	se of the work seeks t	o characterize the	patterns of
neuronal activity that underlie (b)(4	memory in non-	human primates. Th	e recipient shall c	onduct (b)(4)
recordings		(b)(4)		
3.1.16.1 The recipient shall design, pr performance (b)(4) (a) The recipient shall design [Month 4].		[Months 1-4].		
. ,				
3.1.16.2 The recipient shall document equipment (b)(4) [Months 3-(a) The recipient shall docum	-5].		task to interface w	
recordings, eye tracker, and n	nonkey behavioral p	paradigm [Month 5].		
3.1.16.3 The recipient shall train	b)(4) to	/h\/.4\		perform the
(b)(4) memory task [Months 5-24].	5)(4) 10	(b)(4)		perioriii tile
(a) The recipient shall obtain	one monkey comr	olete pre-training healt	h checks inlace col	lars
complete quarantine and room	-	-	ii cheeks, place coi	1415,
(b) The recipient shall train t	_		edures acclimate n	nonkey to
working in the laboratory, be	gin food delay proc	edures, train monkey	on initial behaviora	al tasks, (b)(4)
(1)(A) - A 1-FM (1):		ill be used in the eye-t	racking calibration	procedure of th
(b)(4) memory task [Month]	_	1.	FM 41 241	
(c) The recipient shall train the	ne animal in the (b)	(4) memory paradigm	[Month 24].	
3.1.16.4 The recipient shall prepare mimplant headposts and recording chamneurophysiological correlates of monk (a) Perform pre-surgical MRIs on one	bers, and cranioton (b)(4) behavior	nies. The recipient sha without stimulation [N	ll conduct studies of Months 5-24] and s	of hall:
from surgery [Month 12].	, ,			•
(b) Train one monkey on initial joystivia headpost [Month 15].	ok task, including e	ye canbradon and fixa	uion training with i	iead iixatioii
(c) Train monkey on the (b)(4) memory	orv task nerform su	rgery to implant recor	ding chamber [Mo	nth 181
(d) The recipient shall document all f			unig chamoer [wo	am 10j.
3.1.16.5 [DELETED]				
3.1.17 Comprehensive examination			-	
(b)(4) study of the electrophysiology of	of stimulation. The		-	-
ability for (b)(4) stimulation	(b)(4)	and identify		parameters
(b)(4)		recipient shall cond	uct both studies	(b)(4)
	(b)(d	4)		

3.1.17.1	1.17.1 The recipient shall prepare untrained monkeys for (b)(4) recording and stimulation studies (b)(4)						
		. The recipient s	(b)(4) hall perform M	IRIs to guide elec	trode implantation	n, surgeries to	
implant	headposts and recor	ding chambers, and	craniotomies.	_			
	(a) The recipient s [Month 6].	shall perform monke	y surgeries to i	mplant electrodes	(b))(4)	
3.1.17.2	2 The recipient shall	demonstrate that ne	uronal stimulat	tion	(b)(4)		
	(a) The recipient s	hall show that	(b)(4) [Month 9].	stimulation	(b)(4)		
	(b) The recipient s	hall document result	s of data analy	ses	(b)(4)		
	(c) The recipient sh	nall document all fin	dings in a final	report [Month 19	[Month 11].		
3.1.17.3	[DELETED]						
3.1.17.4	[DELETED]						
3.1.17.5	[DELETED]						
Technic	TION PERIOD (P) cal Area 1 extending computat	· 	(b)(4)				
3.2.1.1	Modeling the dynar	nics of brain activity		(b)(4)			
	(a)		(b)(4	4)			
			(b)(4)		[Mor	nth 28]	
	(b)		(b)(4)			
	(c) Formal report o	n the above mileston	-	Month 30] code used to perfo	orm these analyse	es. [Month 36]	
3.2.1.2		(b)(4)		to improve memo	ory (b)(4)	restoration:	
	(a)		(b)(4	+)			
	[Month 28]						
((b)		(b)(4)			

UPENN PI-KAHANA . [Month 30] (b)(4) (c) Final report on the use of modeling to improve memory (b)(4) (b)(4)(b)(4)restoration. [Month 36] 3.2.1.3 Incorporate modeling into (b)(4) algorithms: (b)(4)(a) (b)(4) (b)(4)[Month 28] (b) (b)(4) [Month 30]. (c) Deliver final report on the role (b)(4)across the various RAM tasks, and predicting which stimulation parameters are most likely to improve memory. [Month 34] 3.2.1.4 Using (b)(4) analysis to model memory: (a) [Month 28] (b) [Month 30] (c) [Month 34] (d) Final repor [Month 36] 3.2.1.5 Build a revised control algorithm strategy (b)(4) (b)(4)[Month 30] (b) Complete a reanalysis of all parameter search (b)(4)

	1771		(b)(4)				
(a) Commista	algorithm for (b)(4)	aalaatian a	f atimovlatica		_	Month 34].	tos
•	e algorithm for (b)(4) emory performance. [N		i stiiilulation	paramete	rs during Fi	Xo and Cairko	tas
	final report based on t	_	liverables. [Month 48			
(4) 2 311 (31 4	Time Top of Coupen of C						
Collect high-	resolution imaging and	d link	(b)(4)	models		(b)(4)	
	The recipies	nt shall:					
	high-resolution magnet			quences in	10 subjects	s, including T1	/T2
	nd resting state function	_	_				
	high-resolution magnet			quences in	50 subject	s, including T1	/T2
	nd resting state function	_	_		100 11	=	. /
* *	high-resolution magnet			quences in	100 subjec	ts, including T	1/T
	nd resting state function				(1.) (4.)	\	
(d) Deliver	interim report on (b) predicted to reliably		selection	*** ***	(b)(4		
	predicted to remain	ennance	(b)(4)	memor	. y (t	0)(4)	
					[Mon	th 38]	
(e)			(b)(4)		[IVIOII	iti 50]	
			()()				
[Mon							
	interim report on the	(b)(4)	selection	(b)	(4) th	at reliably enh	anc
(b)(4) mem	ory		(b)(4))			
					Dr. d. 4	61	
() F: 1		1	1		[Month 40	-	
	port on the efficacy of		_		-	(b)(4)	15
(b)(4)	biomarkers in (b)(4)	-	_			ı 111111111111111111111111111111111111	IJ
(b)(4)	memory test se	ssions (e.g.	r Ko, Cair Ko	o <i>)</i> . Livionu	1 +0]		
The recipien	nt shall complete data co	allection in e	vneriment F	R1 and she	.11·		
	e data on 60 patients fro				111.		
	=	_	_	_			
	e data on 66 patients fro	_	_	_			
	e data on 72 patients fro	_	_	_			
· · ·	e data on 78 patients fro	_	_	_			
(e) Comple	te final reports on data	from the about 14 from the about 15 from the abo	-	ent,	(t	0)(4)	
(f) Create 2	D reconstructions of all		_	in Phace ?	[Month 191		

UPENN PI- KAHANA (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].
3.2.1.8 The recipient shall complete data collection in experiment CatFR1 and shall: (a) Analyze data on 36 patients from experiment CatFR1 [Month 30]. (b) Analyze data on 38 patients from experiment CatFR1 [Month 36]. (c) Analyze data on 41 patients from experiment CatFR1 [Month 42]. (d) Analyze data on 43 patients from experiment CatFR1 [Month 48]. (e) Complete final reports on data from the above experiment, (b)(4)
[Month 48]. (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48]. (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48]. (h) Expand analysis functions (b)(4)
[Month 30]
3.2.1.9 Design, program, pilot, execute, and analyze data from Experiment TH1. The recipient (b)(4) and shall: (a) Deliver fully documented code and analysis functions [Month 26]. (b) Analyze data on 21 patients from experiment TH1 [Month 30]. (c) Analyze data on 32 patients from experiment TH1 [Month 36]. (d) DELETED (e) DELETED (f) DELETED (g) DELETED (h) DELETED
3.2.1.10 The recipient shall complete data collection and analysis in experiment PAL1 and shall: (a) Analyze data on 31 patients from experiment PAL1 [Month 30].
(b) Analyze data on 36 patients from experiment PAL1 [Month 36].
(c) Analyze data on 42 patients from experiment PAL1 [Month 42].
(d) Analyze data on 47 patients from experiment PAL1 [Month 48].
(e) Complete final reports on data from the above experiment, (b)(4) (b)(4) [Month 48].
(f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48]. (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].
3.2.2 Stimulation to enhance (b)(4) memory
 3.2.2.1 Continue to collect and analyze data from Experiment FR3. The recipient shall: (a) Organize and annotate data from 19 patients [Month 36]. (b) Complete final reports on data from the above experiment, including a report on the anatomical specific of target selection [Month 48]. (c) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(d) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].
3.2.2.2 Design, program, execute, and analyze data from Experiment PS4/FR5. (b)(4)
The recipient shall:

- (a) Deliver fully documented PS4/FR5 code and analysis functions [Month 32].
- (b) Organize and annotate data from 6 PS4/FR5 patients [Month 36].
- (c) Organize and annotate data from 9 PS4/FR5 patients [Month 43].
- (d) Organize and annotate data from 29 PS4/FR5 patients [Month 48].
- (e) Complete final reports on data from the PS4/FR5 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in FR3. [Month 48].
- (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.3 Design, program, execute, and analyze data from Experiment PS5/FR6.	(b)(4)	
	The	
recipient shall:		

- (a) Deliver fully documented PS5/FR6 code and analysis functions [Month 38].
- (b) Organize and annotate data from 6 PS5/FR6 patients [Month 45].
- (c) Organize and annotate data from 14 PS5/FR6 patients [Month 48].
- (d) Complete final reports on data from the PS5/FR6 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in FR5. [Month 48].
- (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.4 [DELETED]

- 3.2.2.5 Continue to collect and analyze data from Experiment CatFR3. The recipient shall:
 - (a) Organize and annotate data from 10 patients [Month 36].

The recipient shall:

- (b) Complete final reports on data from the above experiment, including a report on the anatomical specificity of target selection [Month 48].
- (c) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (d) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.6 Design, program, execute, and analyze data from Experiment PS4/CatFR5.	(b)(4)
	The
recipient shall:	
(a) Deliver fully documented PS4/CatFR5code and analysis functions [M	Ionth 32].
(b) Organize and annotate data from 6 PS4/CatFR5 patients [Month 42].	
(c) Organize and annotate data from 9 PS4/CatFR5 patients [Month 43].	
(d) Organize and annotate data from 37 PS4/CatFR5 patients [Month 48].	
(e) Complete final reports on data from the PS4/CatFR5 experiment, inclu specificity of target selection, and a comparison with stimulation efficacy in	-
(f) Create 3D reconstructions of all patients run in the task in Phase 2 [Mo	nth 48].
(g) Post fully annotated data to the public data portal for all patients run in	-
3.2.2.7 Design, program, execute, and analyze data from Experiment PS5/CatFR6.	(b)(4)

- (a) Deliver fully documented PS5/CatFR6 code and analysis functions, (b)(4)
 [Month 38].
- (b) Organize and annotate data from 6 PS5/CatFR6 patients [Month 45].
- (c) Organize and annotate data from 23 PS5/CatFR6 patients [Month 48].
- (d) Complete final reports on data from the PS5/CatFR6 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in CatFR5 [Month 48].
- (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.8 Design, program, execute, and analyze data from Experiment TH3. (b)(4)

(b)(4) . The recipient shall:

- (a) Deliver fully documented code and analysis functions [Month 26].
- (b) Organize and annotate data from 5 patients [Month 30].
- (c) Organize and annotate data from 8 patients [Month 36].
- (d) DELETED
- (e) DELETED
- (f) DELETED
- 3.2.2.9 DELETED
- 3.2.2.10 DELETED

3.2.2.11 Design, program, execute, and analyze data from Experiment PAL3.

(b)(4)

The recipient shall:

- (a) Analyze data on 14 patients from the PAL3 experiment [Month 36].
- (b) Analyze data on 14 patients from the PAL3 experiment [Month 42].
- (c) Analyze data on 14 patients from the PAL3 experiment [Month 48].
- (d) Complete final reports on data from the above experiment, including a report on the anatomical specificity of target selection [Month 48].
- (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.12 Design, program, pilot, execute, and analyze data from Experiment PS4/PAL5. (b)(4

The recipient shall:

- (a) Deliver fully documented PS4/PAL5 code and analysis functions [Month 32].
- (b) Analyze data on 4 patients from the PS4/PAL5 experiment [Month 36].
- (c) DELETED
- (d) DELETED
- (e) DELETED
- (f) DELETED
- (g) DELETED
- 3.2.2.13 DELETED

- 3.2.2.14 Continue to collect and analyze data from Experiments PS2. The recipient shall:
 - (a) Analyze data on 50 patients from experiments PS2 [Month 30].
 - (b) Analyze data on 71 patients from experiments PS2 [Month 36].
 - (c) Analyze data on 82 patients from experiments PS2 [Month 42].
 - (d) Analyze data on 93 patients from experiment PS2 [Month 48].
 - (e) Post fully annotated data to the public data portal for all patients run in the task [Month 48].

3.2.2.15. [DELETED]

3.2.2.16. [DELETED]

3.2.2.17. Design, program, execute, and analyze data from Experiment REC1.	(b)(4)
The recipient shall:	
(a) Deliver fully documented code and analysis functions [Month 28].	
(b) Organize and annotate data from 2 patients [Month 30].	
(c) Organize and annotate data from 4 patients [Month 36].	
(d) Organize and annotate data from 6 patients [Month 42].	
(e) Organize and annotate data from 8 patients [Month 48].	
(f) Complete final reports on data from the above experiment,	(b)(4)
[Month 48].	

- (g) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (h) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.18 Enhance (b)(4) decoding capabilities

(a) Assess (b)(4)	dec	oding pert	ormance within inc	lividual patients. For	all patients wh	no participated in the
CatFR1 task, repor	t	(b)(4)	accuracy and signi	ficance, and analyze	(b)(4)	to determine brain
regions contributir	g to	(b)(4)	performance. [Month 43]		
(b) Assess differen	ces		(b)(4)		within individ	dual patients. Assess
(b)(4)	o det	ermine bra	ain regions involve	d ((b)(4)	(i.e.,
significant regions). [M	onth 44]				
(c) Develop a mod	el to	align neur	al features across p	atients	(b)(4)	. Evaluate the
ability of the mode	el to p	redict bra	in activity from hel	d-out patients. [Mon	th 45]	
(d) Using neural fe	ature	s aligned	across patients,		(b)(4)	v
					. [Month 46]	
(e) Develop joint r	node	s		(b)(4)		
					. [Mo	nth 47]
(f) Final report on		(b)(4)	capability.	Develop final report	(b)(4)
					. Future researd	ch and development
opportunities will a	also l	oe identifie	ed. [Month 48]			

3.2.3 Technology commercialization.

3.2.3.1 Develop implantable device concepts. Determine key risks and unknowns related to hardware development and identify strategies to reduce these risks. The recipient shall:

Establish preliminary requirements and specifications for the mechanical assembly of the implant, document the design intent and design the initial device concepts. Define the lead geometry and develop surgical placement guidance based on patient data collected as part of the RAM project. Complete an early feasibility analysis and cost

UPENN PI-KAHANA analysis of the identified device concept and a detailed project plan for subsequent development phases. [Month 44]

·				
3.2.3.2 I	Develop device programmer prototype.	(b)(4)		
			recipient shall:	
	(a) Develop implantable device simulator as	nd API.	(b)(4)	
		[Month 45]		
	(b) Develop a graphical user interface	(b)((4)	
	(b) Develop a grapmear user interface	(b)(4)	
	Month 46]			
	(c) Develop the patient testing module	(b)(4)	
	D. (1. 471)			
	[Month 47]			
developi developi technolo	Hold informational meeting with the FDA. T ment roadmap with the FDA and obtain info ment efforts. Topics to be reviewed with the gy in the home and the clinic, its mechanism gy, and the outcome measures we propose to (a) Submit an informational meeting request (b) Meet with the FDA to review Nia's devi	rmal feedback from the FDA FDA include: Nia's concept of action, the patient populate use to evaluate its therapeut to the FDA [Month 46]	that can be use of operations for ations that could	d to guide future or the use of the d benefit from our
commer	Final report on technology commercialization cialization activities, including the implantational meeting with the FDA. [Month 48]			
3.2.4 Ev	aluate (b)(4) stimulation in patient of	cohort with a history of trau	ımatic brain in	njury (TBI)
implanta Each sub cognitive at least of	ition of intracranial electrodes, with a focus object will undergo testing for at least five (5) e testing sessions to characterize biomarkers one (1) session to search the parameter space	sessions across three (3) task (b)(4)	of traumatic brack phases: 1) at 1 for (b)	east three (3) (4) stimulation; 2) and 3) at least one
	on to evaluate (b)(4) stimulation	(b)(4)		tive enhancement.
	will undergo high-resolution DTI scans and			
a charac biomark	terization of the anatomical correlates of the ers, (b)(4) and data qua	ir TBI. For each subject, behality shall be characterized.	avioral perforn	nance, EEG
<u>(a)</u>	Collect and analyze record-only (b)(4) free traumatic brain injury Test and report on 3 additional subjects wit recall task. [Month 57] Test and report on 6 additional subjects wit	h a prior history of traumatic	brain injury on	a record-only free
(5)	recall task. [Month 61]			with the same and
<u>(a)</u>	Collect and analyze high-resolution diffusion Collect high-resolution diffusion imaging d detailing imaging analyses characterizing ex	ata for 3 subjects with prior hach patient's history of traum	istory of TBI. atic brain injur	Deliver interim report y. [Month 57]
<u>(b)</u>	Collect high-resolution diffusion imaging d detailing imaging analyses characterizing ea			
	Collect and analyze (b)(4) epilepsy and history of traumatic brain injur			_
(a)	Test 3 additional subjects with a prior history	ry of traumatic brain injury o	n a (b)(4)	stimulation free

	PI- KAHA							
	ecall stimula Month 57]	ation task			(b)(4)			
	Deliver inter	im report o	n (b)(4) stin	nulation.	The report will include id	entificatio	n of biomarkers	
<u>i</u>	ndicative of	memory pe			on of the TBI cohorts with			
_				tory of tra	umatic brain injury on a	(b)(4)	stimulation free	
r	ecall stimula		is with a prior mo	tory or tru	(b)(4)	(2)(1)		
	Month 61] Deli	iver final re	port on (b)(4)	stimule	tion in the TBI cohort, in	cluding da	ta from the historical	
· / / · /	RAM dataset			Deminara	international desirence, in	ordanig da		
Technic	al Area 2							
Phase 2			be to support FDA	A IDE app	roval and clinical site trai	ning, deve	lop clinical systems,	
3.2.4 Uı	ndate syster	n architect	ure and individu	al compo	nents based on TA1. The	recipient	shall review and, if	
_	-			_	system design requirem	_		
based or	n the discov	ery and fee	edback from TA1	in phase	1.			
	The recipien results [Mon			ry, redefin	e system level specification	on with TA	al team based on the	
22127	The reginien	t shall ravid	wand if nagassa	ry radafin	e the specifications for ne	ural interfe	aces [Months 25	
30].	The recipien	t shan revie	w and, ii necessa.	ry, redeim	e the specifications for he	urai interio	ices [Wolfins 25–	
	_		ew and, if necessar onics [Months 25-	-	e the specifications for ele	ectronics ir	ncluding the	
			ew and, if necessar roval [Months 25-		e the sub-chronic safety a	nd perforn	nance data required	
	The recipien onents [Mor	-	uce a final set of o	locuments	detailing the specification	ns for the o	overall system and	
3.2.5 Fa	abrication o	f the reusa	ble (b)(4)	stimula	ntors for clinical studies.	The recin	ient shall produce	
the bala		(b)(4)			the clinical sites in early	_	-	
shall:	(a) Dalizzam	ton toatad .	and documented (b)/4) arvatam	og [Month 26]			
	` '					301		
	(b) Deliver an additional thirty tested and documented (b)(4) systems [Month 30].(c) Deliver an updated development plan, requirements, and design history file and limited verification and							
	validation activities to cover the system integration with the(b)(4)Lead and (b)(4) splitter cable [Months 30].							
	(d) Utilize t patients [M		perform recording	g and clos	ed-loop stimulation durin	g memory	testing in at least 50	
3.2.6 Ev	valuation of	commerci	ally available	(b)(4)	leads for memory enha	ancement.	The recipient	
shall:								
	(a) Develop				approval to implant comm	nercially-a	vailable leads (b)(4)	
	(b) Dolivian	(b)(4)	ort on memory		Months 34]. performance in 10 subje	acta	(b)(4)	
	(b) Deliver	пистии тер	ore on memory	(b)(4)	performance in 10 subje	CCIS	(b)(4)	
						[Months	41].	
	(c) Develop	protocol a		tain IRB a	approval to implant comm	•	vailable leads (b)(4)	
			(b)(4)		[Months	40].		

UPENN	PI- KAHANA (d) Deliver interim repo	ort on stimula	ation target localiz	ration in 10 s	ubjects implanted	(b)(4)
	[Mont (e) Final report on mem leads [Month) performance	and target lo	ocalization in 40 sub	pjects with (b)(4)
	lgorithm prototyping sent the development of a			•		he recipient shall
3.2.7.1	The recipient shall docu: (b)(4)		elopment of a (b) Months 33–42].	(4) tool to	translate existing alg	gorithms from phase
	The recipient shall documes 33–42].	ment the deve	elopment of a tool		(b)(4)	
3.2.7.3 Unit:	The recipient shall admi	nister embed	lded-mode, closed	l-loop memo	ory testing in the Ep	ilepsy Monitoring
	(a) Complete software	tool for loadi	ng (b)(4)	[Month 42].	
	(b) Complete software	tool for trans	lating software al	gorithm	(b)(4)	[Month 42].
	(c) Administer	(b)(4)	memory task to f	ve patients	(b)(4)
					. [N	In [48]
3.2.8 [D	DELETED					
3.2.9 C	ore project resources d	levoted to TA	A2:	(b)(4)	algorithms, co	mputational cluster
	ent and administration mented.	ı, integration	between TA1, T	'A2, and TA	3 modeling and ele	ctrophysiology shall

Technical Area 3 [DELETED]

3.3 PROGRAM MANAGEMENT AND REVIEW

The Government will actively monitor, review and approve the recipient's performance to ensure all the performers are in sync and matched with the Government's requirements. The Government will ensure that each of the performers share experimental data across the program and will further ensure that the performers develop techniques and capabilities that are compatible and integrate with each other. The recipient shall collaborate and cooperate with other performers in the program under the coordination of the Government team. At Government PI meetings, the recipient shall demonstrate technical capabilities and engage and/or challenge other performers in a cooperative and challenge environment. Along these lines, the Government will ensure that each performer shares technical information with the others to enable the testing/challenging of each other's capabilities. The Government will further oversee the program and will review, approve, and participate in the demonstrations.

3.3.1 Kick-off Meeting

The recipient shall hold a kick off meeting within 60 days of award of this agreement. In this meeting, the recipient shall present a program management plan and financial tracking plan.

3.3.2 Quarterly Financial Reports

The recipient shall provide quarterly financial progress reports to the Government Technical Representative (GTR) and DARPA Program Manager. The purpose of these reports is to provide a brief project progress and inform the GTR and Program Manager of any potential issues.

3.3.3 Quarterly Technical Reporting

The recipient shall provide quarterly progress reports to the Government Technical Representative (GTR) and DARPA Program Manager. The purpose of these reports is to present a summary of work completed by SOW tasking and milestones met, discuss any problems encountered, update the program schedule, present the program financial status, and discuss remaining work. Quarterly reports shall also include all technical data items generated including but not limited to experimental data, processed data along with methods of processing used, research reports and publications and software (source code and executables).

3.3.4 Monthly Status Reports

The recipient shall provide monthly status reports which will include all relevant project data including, but not limited to, raw and analyzed electrophysiological signals as well as any necessary annotations and interpretations of the data, such as time-stamped patient behaviors, necessary for appropriate analyses and interpretation of the data. Patient data shall be provided in a coded format that protects patient identities but will contain diagnosis (signs/symptoms), interventions including system modifications, technical observations, diagnostic tests/results, and patient outcomes. In addition, information about the device delivering therapy including device serial numbers, device model numbers, date of event, and country/state of event shall be annotated with the data and therapy. This data shall be made available on database accessible across the program and to Government personnel.

3.3.5 Final Agreement Review

The recipient shall host a final agreement review. The purpose of this review is to present a summary of all work completed and milestones accomplished and to discuss any relevant future efforts similar to the contract, which may be pursued. This report shall be provided to the Government Technical Representative (GTR) and DARPA Program Manager. A final summary report shall be provided at the end of the program.

3.3.6 System Development Plan (SDP)

The recipient shall describe the scope of the design and development effort, describe hardware, software architectures and experimental procedures (as applicable) in sufficient detail for review and replication, reference any applicable documents and provide a schedule. The recipient shall share the SDP with the other program performers and the Government.

3.3.7 System Documentation

The recipient shall provide system documentation documenting the source code, protocol and algorithm analysis, hardware description, format specifications, system diagrams, part numbers, and any other data necessary to replicate and test the designs.

4.0 INCIDENTAL HARDWARE AND SOFTWARE

Hardware and software incidental to this research shall be made available to the Government.

5.0 REPORTS AND PRESENTATION MATERIALS

The reports and presentation materials shall be delivered as described in the data matrix.

6.0 TRAVEL

Long distance domestic travel is estimated for Program Review meetings and Conferences.

7.0 PLACE OF PERFORMANCE

University of Pennsylvania 3401 Walnut St, Suite 302C Philadelphia, PA 19104

Ph: 215-746-3501, Fax: 215-746-6848

kahana@psych.upenn.edu

STATEMENT OF WORK FOR UNIVERSITY OF PENNSYLVANIA

Title – Restoring Active Memory (RAM): "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)

1.0 SCOPE

This effort promises to use direct brain recordings and stimulation in humans and animals to create a real-time								
system for enhancing encoding and long-term retrieval of memories for specific types of information. The team								
consists of nine leading clinical centers for the surgical trea	atment of epilepsy and movemen	nt disorders, each led						
by a clinician scientist with substantial experience in one o	r more key areas of electrical br	ain stimulation, human						
cognition, computational electrophysiology, and realtime a	daptive control systems. The ne	urological and						
neurosurgical teams are aligned on the common goal of rap	oidly developing and testing app	roaches to enhance						
and restore memory through a study of unprecedented scop	e: more than 100 patients each	year in a large array						
of experiments. Pending Investigational Device Exemptio	of experiments. Pending Investigational Device Exemption (IDE) approval, patients in Phase 2 of the project							
will be implanted with a complete memory neuromodulation	on (b)(4)							
		to our memory						
testing paradigms. This will be accomplished through an a	ccelerated U.S. Food and Drug	Administration (FDA)						
submission of the technical area two (TA2) system at the e	nd of Phase 1. Through applicat	ion of a						
computational model of human (b)(4	to the b	ehavioral and						
electrophysiological data the recipient shall define biomark	cers of memory (b))(4)						
These bioma	rkers will be used	(b)(4)						
(b)(4)	(b)(4)	(b)(4)						
(b)(4) .								

1.1. BACKGROUND

The Defense Advanced Research Projects Agency (DARPA) seeks new methods for analysis and decoding of neural signals in order to understand how neural stimulation could be applied to facilitate recovery of memory encoding following brain injury. Ultimately, it is desired that a prototype implantable neural device that enables recovery of memory in a human clinical population be developed. Additionally, the program encompasses the development of quantitative models of complex, hierarchical memories and exploration of neurobiological and behavioral distinctions between memory function using the implantable device versus natural learning and training.

2.0 APPLICABLE DOCUMENTS

- (a) DARPA BAA-14-08.
- (b) UPENN Technical Proposal Titled "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)" dated January 23, 2014

3.0 PROJECT WORK DESCRIPTION AND REQUIREMENTS

The recipient shall provide the facilities necessary to develop the effort as described herein.

Human use **is** anticipated in this effort. The recipient shall obtain all necessary Institutional Review Board (IRB) approvals, show proper assurance documentation, and obtain proper approval from the Government officials prior to human use testing.

Animal use **is** anticipated in this effort. The recipient shall obtain all necessary Institutional Animal Care and Utilization Committee (IACUC) approval and demonstrate this approval to the Government prior to beginning experimentation with animals. If animal use is no longer anticipated, or changes significantly from the approved

IACUC then the PI must submit a letter stating the discontinuation of animal use for this effort and/or receive appropriate authorization for IACUC changes of previously specified protocols. Unless prior approval by DARPA is given IACUC documentation must be provided prior to contract award.

3.1 BASE PERIOD (PHASE I)

Technical Area 1

3.1.1 A computational model for describing behavior in declarative memory tasks.

3.1.1.1 Predicting moment-by-moment behavior in a variety of memory	y tasks.
The recipient shall document a model of memory	(b)(4)
(b)(4)	
(a) The recipient shall document the code base for the	(b)(4)
[Month 3].	
(b) The recipient shall extend the model	(b)(4)
	[Month 6].
(c) The recipient shall document fully commented, optimized	(b)(4)
Code shall be able to execute model	(b)(4)
[Month 6]	
[Month 6]. (d) The recipient shall document the code base for the	(b)(4)
[Month 9].	(0)(4)
	(b)(4)
	[Month 12].
(f) The recipient shall document fully commented, optimized	(b)(4)
Code shall be	able to execute model (b)(4)
[Month 12].	
[wonth 12].	
3.1.1.2 [DELETED]	
3.1.1.3. Build a (b)(4) model of free recall:	(b)(4)
(a) Davidon coftware that allows us to construct the (b)(4)	model for an entire session of FR1 in 30
(a) Develop software that allows us to construct the (b)(4) seconds or less [Month 15]	model for an entire session of FRT in 30
(b) [DELETED]	
(c) [DELETED]	
3.1.1.4 Build a (b)(4) model for (b)(4) memory:	(b)(4)

UPEN	NN PI- KAHANA					
	(a) Develop a model prototype	(b)(4)		(b)(4)		[Month
21]	(a) Develop a model prototype			(b)(4)		[Wilditii
_	(b) Deliver fully documented co th 24]	ode		(b)(4)		
3.1.2	Integrating neurophysiological	biomarke	ers into the com	putational mode	l of behavi	ior.
3.1.2.	1 Characterize distribution of	(b)(4)	biomarkers		(b)(4)	
		(2)(.)			(=)(:)	
2 1 2	1 1 1 1	(1-)(4)	1	(1. \ / 4 \)		-1-111 4144
	1.1 A prototype for analyzing ated [Month 12].	(b)(4) 1	neural	(b)(4)		shall be deployed and
3.1.2.	1.2 The recipient shall document	the protot	ype software		(b)(4)	
				[Month 12].		
2 1 2	1.3 Characterize the (b)(4)	hioma	rkers using the m	nodels of free rec	all and (b)	(A) navigation:
3.1.2.	(a) Characterize the (b)(4)		_	ts performing the		
			1		[Month 18	
	(b) Characterize the (b)(4)			ts performing the	e (b)(4) na	
		(b)(4)				[Month 24].
2 1 2	1.4771	.1	C		4.7.40	
3.1.2.	1.4 The recipient shall document	the prototy	ype software		(b)(4)	
	The recipient shall docum	nent the so	ftware	(b)(4)		(b)(4)
	·					
	[Month 24].					
313	Electrophysiological recording	s to dofine	hiomorkors of		(b)(4)	
3.1.3	memory.	s to define	bioinal Kers of		(D)(4)	
	Objective: Define biomarkers	of		(b)(4)		memories, as
	measured in a broad array of to					• .
	(b)(4) free recall of (b)(4) (b)(4)			sociate learning (al navigation (b)(4)
	1 The recipient shall design, progr				xperiment	
	osy monitoring unit. Recording ne to identify (b)(4) biomarkers (b)			(b)(4)	Th	shall be ese biomarkers will
	•		eriments. The re		. 111	ese diomarkers will
	(a) Design, program, and pilo					
	(b) Write initial data analysis		-			
	(c) Analyze data on 13 patien					
	(d) Analyze data on 26 patien(e) Analyze data on 39 patien					
	(f) Analyze data on 58 patient		-	-		

UPENN PI- I		nnotate natient data	from the above e	vneriment to be	shared with investig	rators and
	-	_		_	y) and carry out 3D i	-
prog	rum personner,	(b)(4)	rectione contacts	` .	Month 24].	.cconstructions
(h) (Complete interi		rom the above exp	-	oresented at team me	etings and with
		ersonnel. Reports s				(b)(4)
				, as well as ana	alyses of the electrop	physiological
corre	elates of (b)(4)	memory		(b)(4)		
					[Mon	nth 24].
(i) P	ost all data coll	lected in a deidentif	fied format compa	tible with the p	ublic data portal [Mo	onth 24].
• /	•	code for experimen				
		analysis functions [
		structions of all pat		_	-	
` ′				•	the task in Phase 1	
	-	_		_	n in the task in Phas	e 1 [Month 24]
(o) D	Deliver report of	n (t	o)(4)	biomarkers	[Month 24].	
2 1 2 2 Dogia	n nearon nil	at avacuta and an	lyza data fram Ex	znarimant CatE	R1 (n=46) on patient	ta in the
_		this task the recipies	-	_	(b)(4)	.s iii tile
(b)(4)	(b)(4)	(b)(4)		recipient shall:	(b)(4)	
	. , . ,	and pilot task [Mor		recipient shair.		
		analysis scripts [Mo	_			
1 1		1 patients from exp	-	Month 81		
	•	23 patients from ex		_		
` '	•	28 patients from ex	•	-		
	-	3 patients from exp	_			
	-	otate patient data fr	_	_	1.	
	_	reports on data from	•	-	-	
					he public data portal	[Month 24].
* /		de for experiment [•		
• ,	•	nalysis functions [N	-			
(l) Cre	eate 3D reconstr	ructions of all paties	nts run in the task	in Phase 1 [Mo	onth 24].	
(m) Pro	ovide interim re	porting on analyze	d data from all pa	tients run in the	task in Phase 1 [Mo	nth 24].
(n) Pos	st fully annotate	ed data to the public	e data portal for a	ll patients run i	n the task in Phase	[Month 24].
(o) Del	iver report on	(b)(4	1)	biomarkers [M	[onth 24].	
_			-	_	(n=44) on patients in	
monitoring un	nit. In this task t	the recipient shall id	-	s of (b)(4)	memory (b)(4) .(b)(4)
		# N/ 6N	(b)(4)		TT1 1 11	1:1 ::0
(1.)(4)	1: 1	(b)(4)	(1) (4)		. The recipient shall	-
	ory biomarkers,		(b)(4)	(4)	, as well as	(b)(4)
memory biom		hall.	(D)	(4)		
	The recipient sl	nan: n, and pilot task [M	onth 21			
* *		a analysis scripts [N	-			
		a analysis scripts [1 11 patients from e	_	Month 81		
	-	n 22 patients from e	-	_		
		1 33 patients from e				
		50 patients from ex				
		nnotate patient data			241	
	_	m reports on data fi	_	_	_	
					n the public data por	tal [Month 241
		code for experimen		1	1	[

	Fully docume	•	ctions [Month 3].		· N 154	1 0 43		
(m)	Provide inter	im reporting on	analyzed data fro	om all pat	in Phase 1 [Montients run in the ta ll patients run in	ask in Ph	_	_
(o)	Deliver repor	t on	(b)(4)		biomarkers [Mo	nth 24].		
-			nd analyze data fr shall identify bio	-	riment PAL1 (n=			the epilepsy associations
(b) (c) (d) (e) (f) (g) (h)	Write initial of Analyze data Analyze data Analyze data Analyze data Organize and Complete into	on 14 patients on 22 patients on 25 patients f annotate patien erim reports on	ipts [Month 3]. om experiment P. from experiment from experiment from experiment I t data from above data from the above	t PAL1 [1 t PAL1 [1 PAL1 [M e experin	Month 13]. Month 18]. Jonth 24].	_	ata portal	[Month 24].
(j) (k) (l) (m) (n)	Fully docume Fully docume Create 3D rec Provide inter-	ent code for expent analysis func- constructions of im reporting on notated data to the	eriment [Month 2 ctions [Month 3]. all patients run in analyzed data fro	2]. n the task om all pat	in Phase 1 [Montients run in the ta ll patients run in biomarkers [Mo	th 24]. ask in Pha the task i	ase 1 [Mo	onth 24].
	nt disorders an		-	_	riment DBS2 (n= cipient shall perfo (b)(4)		atients un (b)(4)	dergoing DBS recall task
	.,	,			(=)(-)			The recipient
(b) (c)	Write initial of	*		DBS2 [Mo	onth 8].			
3.1.4 Stimu	lation to		(b)(4)			m	emory	
3.1.4.1 Desig	gn, program, p	vilot, execute, an	d analyze data fr	om Expe	riment FR2 (n=1		•	
which			(b)(4)	, The recipie	iii siiaii c	ompare u	ie degree to
The (a) (b) (c) (d) (e) (f) (g)	Write initial of Analyze data Analyze data Analyze data Analyze data Organize and	ram, and pilot ta data analysis ser on 4 patients fron 8 patients fron 13 patients fron 43 patients fron 43 patients for 43 pa	sk [Month 2]. ipts [Month 3]. om experiment Flom experiment Florm experiment I	R2 [Mon R2 [Mon FR2[Mon FR2 [Mon bove exp	th 13]. nth 18].	red with:	investigat	ors and
1 (and carry out 3I) reconstructions			(b)(4)		
	Mon	th 24].						-

(final rep		ta from the above	detailed analy	ses of behaviora	team meetings and with al data, (b)(4)
	1 4 0	(1.) (4)			as we	•	the electrophysiological
(correlates of	(D)(4)	memory			(b)(4)	[Month 24].
((((j) Fully docu(k) Fully docu(l) Create 3D(m) Provide fi	ment co ament an reconstr inal repo	ode for expensive fundations of orting on a	eriment [Month 2 ctions [Month 3]. all patients run ir nalyzed data fron]. n the task in Ph n all patients ru	nase 1 [Month 24 in in the task in I	lic data portal [Month 24].
	(o) Expand an			ne paone data po	rui ioi uii puti	(b)(4)	isk in i nase i [wonth 2 i].
	O) Expand an	ary 515 To	directions				d and fully documented
8	analysis code	Month	7].				,
3.1.4.2 D	esign, prograi		, execute, a shall:	nd analyze data f (b)(4)	rom Experime	nt FR3 (n=18). T	Γhe recipient shall test
	(c) Analyze da (d) [DELETE (e) Analyze da (f) Analyze da (g) Organize a (h) Complete (i) Post all dat (j) Fully docu	rogram, ial data a ata on 4 D] ata on 1 ata on 1 ata on 1 ata collection collection ata and annotation ata	and pilot ta analysis sca patients fr 0 patients for 8 patients for otate patients ports on da oted so far in orde for expense.	ripts [Month 12]. ripts [Month 13]. ripts [Month 13]. rom experiment F from experiment I from experiment I nt data from above ta from the above in a deidentified f eriment [Month 1]	FR3 [Month 24 FR3 [Month 30 e experiment [Normat compation 2].	4]. 0]. Month 30]. Month 30].	olic data portal [Month 30].
((o) Expand an	alysis fi	unctions			(b)(4)	
			1.07			Deliver updated	d and fully documented
8	analysis code	[Month	13].				

3.1.4.3 [DELETED]

3.1.4.4 Design, program, pilot, execute, and analyze data from Experiment CatFR2. (b)(4)

Further, the recipient (b)(4)

and shall:

- (a) Design, program, and pilot task [Month 2].
- (b) Write initial data analysis scripts [Month 3].
- (c) Analyze data on 4 patients from experiment CatFR2 [Month 8].
- (d) Analyze data on 8 patients from experiment CatFR2 [Month 13].
- (e) Analyze data on 13 patients from experiment CatFR2 [Month 18].
- (f) Analyze data on 18 patients from experiment CatFR2 [Month 24].
- (g) Organize and annotate patient data from above [Month 24].
- (h) Complete final reports on data from the above experiment [Month 24]
- (i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24]
- (j) Fully document code for experiment [Month 2].

UPENN PI- KAHANA	unctions [Month 2]	
(k) Fully document analysis fu	of all patients run in the task in Phase 1 [Month 24].	
(m) Provide final reporting on a	analyzed data from all patients run in the task in Phase 1 [Moreover the public data portal for all patients run in the task in Phase (b)(4)	-
(ii) Expand unarysis functions	Deliver updated and fully of	documented
analysis code [Month 7].	ı	
3.1.4.5 Design, program, pilot, execute,	and analyze data from Experiment CatFR3. In CatFR3 the re	ecipient shall
test the ability of	(b)(4)	
	(b)(4)	The
recipient shall:		
(a) Design, program, and pilot	task [Month 12].	
(b) Write initial data analysis s	scripts [Month 13].	
(c) Analyze data on 4 patients	from experiment CatFR3 [Month 24].	
(d) Analyze data on 8 patients f	from experiment CatFR3 [Month 30].	
(e) [DELETE]		
(f) [DELETE]		
(g) [DELETE]		
(h) [DELETE]		
	r in a deidentified format compatible with the public data port	tal [Month 30].
(j) Fully document code for ex		
(k) Fully document analysis fu	nctions [Month 13].	
(l) [DELETE]		
(m) [DELETE]		
(n) [DELETE]		
(o) Expand analysis functions	(b)(4)	1
analysis code [Month 13].	Deliver updated and fully of	Jocumented
anarysis code [Worth 13].		
3.1.4.6 Design, program, pilot, execute,	and analyze data from Experiment YC2. The recipient shall	apply (b)(4)
stimulation	(b)(4)	
	. The recipient shall test the ability of stimula	ition to improve
memory	(b)(4)	Î
. The recip	ient shall:	
(a) Design, program, and pilot	task [Month 2].	
(b) Write initial data analysis s	scripts [Month 3].	
(c) Analyze data on 5 patients	from experiment YC2 [Month 8].	
(d) Analyze data on 10 patients	s from experiment YC2 [Month 13].	
(e) Analyze data on 16 patients	s from experiment YC2 [Month 18].	
(f) Analyze data on 33 patients	s from experiment YC2 [Month 24].	
(g) Organize and annotate patie	ent data from above experiment [Month 24].	
(h) Complete final reports on d	lata from the above experiment [Month 24].	
(i) Post all data collected so far	in a deidentified format compatible with the public data porta	al [Month 24].
(j) Fully document code for ex	periment [Month 2].	
(k) Fully document analysis fu	nctions [Month 3].	
	f all patients run in the task in Phase 1 [Month 24].	
(m) Provide final reporting on a	analyzed data from all patients run in the task in Phase 1 [Mor	nth 24]
(n) Post annotated data to the p	ublic data portal for all patients run in the task in Phase 1 [Mo	onth 24].
(o) Expand analysis functions	(b)(4)	
	Deliver updated and fully of	documented

UPENN PI- KAHANA analysis code [Month 7].

3.1.4.7 [DELETED]

3.1.4.8 Design, program, pilot, ex	ecute, and analyze data from E	xperiment PAL2.	(b)((4)
	The recipient (b)(4)	(b	0)(4)	
	1	,	,,,	shall:
(d) Analyze data on 6 par (e) Analyze data on 9 par (f) Analyze data on 11 par (g) Organize and annota (h) Complete final report (i) Post all data collected (j) Fully document code (k) Fully document anal (l) Create 3D reconstruct (m) Provide final reporti		Month 13]. [Month 18]. [Month 24]. eriment [Month 24]. compatible with the sk in Phase 1 [Month 24].	l. ne public data nth 24]. sk in Phase 1	portal [Month 24]. [Month 24].
(o) Expand analysis fun		(b)(4)		
analysis code [Month 7] 3.1.4.9 Design, program, pilot, ex				ully documented
(f) Analyze data on 8 pate(g) [DELETED](h) [DELETED](i) [DELETED]	ysis scripts [Month 13]. ients from experiment PAL3 [Nients from experiment PAL3 [Nients from experiment PAL3 [Nients from experiment [Month 12].	(b)(4)	odated and ful	ly documented
analysis code [Month 13]		. Deliver up	odated and ful	iy documented
3.1.4.10 Design, program, pilot,	execute and analyze data from	Experiment DBS1.		
The recipient shall evaluate	(b)(4)	for	(b)(4)	learning during

UPENN	PI- K	CAHANA						
a	(b)(4	task.			(b)(4)			
			The recipient sha	ll vary		(b)(4)		
paramete	ers.			(b)(4)				
			The recipient	shall index learr	ning	(b)(4)		
		(b)(4)	The re	cipient shall cor	npare (b)(4)	across the five co	onditions (b)(4)
		(b)(4)	and	l (2) identif	(b)(4)	arameters	(b)(4)	
	and sh	nall:						
			and pilot task [Mo					
	(b) W	Vrite initial data	analysis scripts [M	onth 3].				
	(c) A	nalyze data on 1	0 patients from ex	periment DBS1	[Month 8].			
	(d) - (d)	(n) [DELETED]						
3.1.4.11	Desig	gn, program, exe	cute, and analyze o	lata from Exper	iments PS1, F	S2 & PS3. The rec	ipient shall	(b)(4)
			(b)(4)		identif	y (b)(4) stimulation	on paramet	ers:
	(a) D	esign and progra	am tasks [Month 12	2].				
	(b) A	analyze data on 1	4 patients each fro	m experiments l	PS1, PS2, & I	PS3 [Month 16].		
	(c) A	nalyze data on 2	9 patients each from	m experiments I	PS1, PS2, & F	PS3 [Month 24].		
	(d) P	ost fully annotat	ed data to the publ	ic data portal for	all patients r	run in the task in Pl	nase 1 [Moi	nth 30]
		-	_	-	_			,
3.1.5 De	evelop	control algorith	ms	(b)(4)			
	. D.E.I.							
3.1.5.1	DELE	ETEDJ						
3.1.5.2 L	J evelo	p algorithms			(b)(4)			
		D1 1	11					
		The recipient sha			(1.)(4)			
	(a) C	complete interim	report	F) 4 . 1 . 0.7	(b)(4)			
	(1) D			[Month 9].				
	(b) D	Develop prototyp				(b)(4)		
			. Co1		n interim repo	ort on algorithms,	(b)(4	!)
	() ET	DELETEDI		. [Month 12].				
		DELETED]						
	=	DELETED]		(1) (4) 1	'41 FM	41.01		
			interim report on	_	_	_		
			interim report on		gorithms [Mo	-		
		Ocument 12-mo	nth prototype	(b)(4) algori	thms [Month	12].		
	–	DELETED]						
	(i) [D	DELETED]						
		DELETED]						
	(k) [I	DELETED]						
3.1.5.3	DELE	TED]						
_								

3.1.5.4 [DELETED]

3.1.6 Core project resources devoted to TA1.

- 3.1.6.1 The recipient shall perform electrophysiological experiment development and programming, data analysis, computational cluster effort towards data analysis and computational modeling from TA1.
- 3.1.6.2 The recipient shall provide project coordination, data sharing and data storage.

UPENN PI- KAHANA 3.1.7 Determine electrode requirements for	(b)(4) stimulation	in Dhasa 7 Th	o vociniont	shall characterize
•	(b)(4) Stillulation	i iii fiiase 2. Tii		for modulating and
restoring memory function.	, ,			8
3.1.7.1 The recipient shall design and develop		(b)(4)	capable	(b)(4) The recipient
shall:	(b)(4)			The recipient
(a) Based on precise anatomical analyses (b)(4) [Month 12].		(b)(4)		
(b) Working with Lawrence Livermore Nation materials that can be put into place by the begi	*		nical drawi	ng and list of
(c) Working with LLNL, complete ISO-10993 design history file and associated ISO test result (d) [DELETED]				
3.1.8 [DELETED]				
3.1.9 [DELETED]				
Technical Area 2				
3.1.10 Validate system architecture and ind the high-level system design requirements a	•	-	all docume	ent and review
3.1.10.1 The recipient shall validate system le	vel specification with T	`A1 team [Montl	hs 1–6].	
3.1.10.2 [DELETED]				
3.1.10.3 The recipient shall refine the specific (b)(4) , continually	ations for electronics refining as needed [Mo		b)(4)	
3.1.10.4 The recipient shall validate the specif [Months 5–6].	fication for the Algorith	m prototyping s	ystem and ι	ser interface
3.1.10.5 The recipient shall define the sub-chr IDE approval [Month 6] and shall:	onic safety and perforn	nance data requir	red by the F	DA for 29-day
(a) Document definitions of the function [Month 6].	tional, operation, and pe	erformance requi	irements of	the overall system
(b) Document definitions of the compexternal packaging, and algorithm pro	ototyping system [Mont	h 9].		
(c) Document definitions of the sub-c day IDE approval [Month 6](d) Deliver definitions of stakeholder		_	uired by the	FDA for the 29-
3.1.11 Design, fabrication, and characteriza	ation of the external ne			_
shall develop a (b)(4)electrodes. (*and any adaptations neede	o)(4) ed to ensure adequate	_	e of mating	g with (b)(4)
3.1.11.1 The recipient shall design and manufa (b)(4) [Months 7–18].	acture of electronics,		(b)(4)	
3.1.11.2 The recipient shall (b)(4) software (fi	irmware) to control the	electronics and p	provide (b)(4) (b)(4)

UPENN PI- KAHANA capability [Months 7–18].

	The recipient sical depth electr	•	_				(b)(4) t	o interface with
3.1.11.4	The recipient s					_		er (b)(4) sites [Months 19–
24].		[[
۷٠٠].	(a) Design and 7-18].	d build electro	nics,		(b)	(4)		[Months
	(b) Document capability [Mo		software that	at controls	he electronic	s and document	(b)(4)	algorithm
	(c) Modify the design verification	_		connector a	and build 22	(t	0)(4)	for
	(d) Test and d IDE submission		_	mance	(b)((4)	in prep	aration for FDA
2.1.12	a							
	Connectorizati	_			-	(b)(4)		stimulator. The
_	nt shall develop onic (b)(4) ne			od and into	egrate a vari	ety of clinical e	electrode	designs with the
3.1.12.1	The recipient	shall define sp	ecifications t	for the conr	ector	(b)(4)	
	•	•				[Months 1-	6].	
3.1.12.2	2 [DELETED]							
3.1.12.3	[DELETED]							
	The recipient ce, mechanical in (a) Define specific (b) [DELETE	integrity [Monecifications for	ths 15–24].	The recipie	nt shall:	conductivity an	d reliabil	ity, moisture
	(c) Document	-	process			(b)(4)		
	[Month 15].	,	1					
	(d) Complete	rification testii		* * -	-	nd reliability, ar	nd mechai	nical
3.1.13	Algorithm prot	totyning syste	m. The reci	nient shall	develon an	algorithm nrot	otyning	system (b)(4)
5.1.15	angorium prod	iotyping syste	iii. The reel	piene snan	ucvelop an	argorithm prot	otyping .	(b)(4)
3.1.13.1	The recipient (b)(4)		(b)(4) onths 1–6].	interfa	ce	(b)	(4)	
3.1.13.2	2 The recipient	shall documen	t the softwar		onths 1–12].	(b)(4)		
3.1.13.3	The recipient	shall develop s	software	(b)	(4)	[Months 7–	18].	
	The recipient sipient shall:	shall verify an	d validate tes	sting and do	ocumentation	for IDE submis	ssion [Mo	onths 19–24].
1110 100	(a) Design	(b)(4)	interface			(b)(4)		
	(=) 201511	(~)(.)				(~)(')		

LIDENIN					
OI LIVIN	PI- KAHANA	FM41- /	(1		
	(b) (4) (b) Document the	[Month of	oj.	(b)(4)	
	1 1	(4)	[Month 12].	(0)(4)	
	(c) Document the		(b)(4)	[Month 18].	
	* *		package [Month 18].	. ,	
	(e) Verify and va	lidate testing and	d documentation for IDI	E submission [Month 24].	
3.1.14 \$	System verificatio	n and validatio	n testing. The recipien	nt shall evaluate and verify system lifetime	,
sterility	and biocompatib	ility. The recipi	ent shall also verify an	nd validate the system functions and inter	faces
			(b)(4)		
		. Additionally	, system verification a	nd validation shall be performed.	
3 1 14 1	[DELETED]				
J.1.17.1	[DECETED]				
3.1.14.2	[DELETED]				
	. ,				
3.1.14.3	[DELETED]				
2114	TDI	11 6			
			system verification 17/(R)2010 [Months 19–	testing for sub-chronic (< 29-days) use as	
ouimea	in ANSI / AAWII .	/ 180 149/1:200	7//(K)2010 [Months 19–	-24].	
3.1.14.5	The recipient sha	ll validate the (b)(4) system [Month 19–2	24]. The recipient shall:	
	1	V.	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	, 1	
	(a) Fabricate and	assemble fully-	integrated systems for to	esting [Month 18].	
	(b) [DELETED]				
	(c) [DELETED]				
	(d) [DELETED]				
		_	for sub-chronic (< 29-da	ays) use as outlined in ANSI / AAMI / ISO	
	14971:2007/(R)2 (f) [DELETED]	010 [Month 24].			
	() [fully document a	system that is ready fo	r FDA IDE submission; deliver system veri	ficatio
	and validation rej			1 1 DA IDE submission, denver system veri	IIcatio
				history file, fabrication data, and ANSI $\!\!/$	
AAMI/	ISO data for sub	-chronic (< 29 o	days) FDA IDE applica	ation.	
2 1 15 1	Th	11 1	DE4::41. 41 EI	DA 4	
	_		_	DA to establish the system requirements, and for the preparation and submission of IDE	
	ion [Months 26].	data, and addition	onai information require	a for the preparation and submission of IDE	
аррпсан	ion [wonths 20].				
3.1.15.2	The recipient sha	ll compile and w	rite the master file for t	he FDA [Months 28–29].	
	•	•			
3.1.15.3	The recipient sha	ll produce the m	aster file for FDA and the	he submit an IDE application for < 29-day h	uman
	ation of the system				
implanta		[Month 29].			
implanta 3.1.16	(b)(4) Elect	[Month 29].			
3.1.16		trode Design.	nment plans for a navel	(b)(4) lead quitable for interfecing	vith
3.1.16 3.1.16.1	The recipient sha	t rode Design. Il deliver develo	pment plans for a nove	l (b)(4) lead suitable for interfacing v	vith
3.1.16 3.1.16.1 the (b)(4)	The recipient sha device. The recip	trode Design. Il deliver develo ient shall:	pment plans for a novel		vith

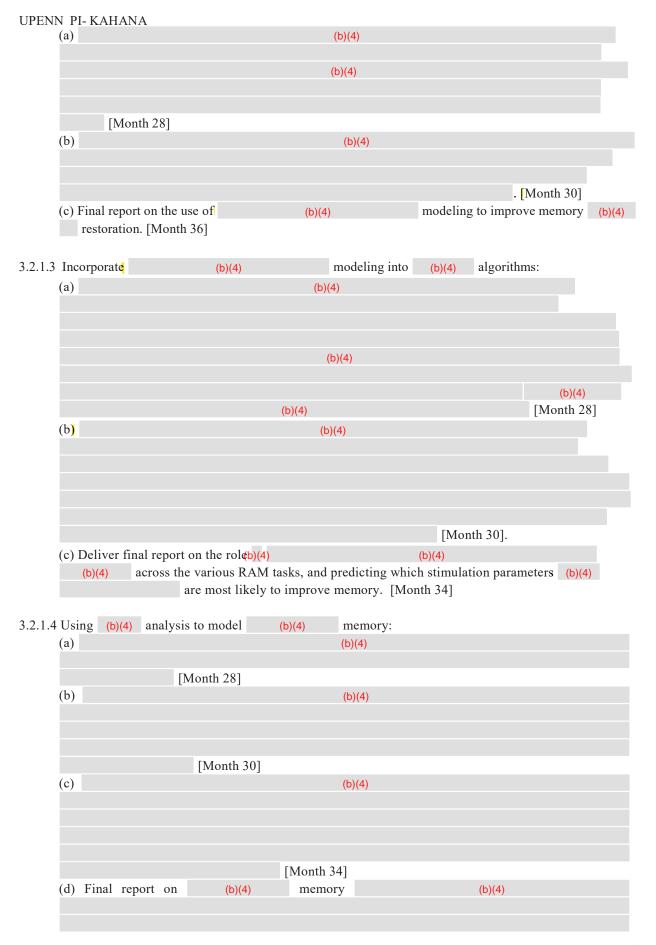
sharing activities [Month 7]

Technical Area 3 The recipient shall perform basic research findings (b)(4)to inform the human stimulation studies in TA1 and guide device development in TA2. The recipient shall document the protocols for measuring monkey (b)(4) memory (b)(4)and shall train animals in the (b)(4) task. In parallel, the recipient shall conduct studies of the neurophysiology of stimulation (b)(4)The recipient shall then conduct behavioral studies of the electrophysiology (b)(4)in two monkeys. The recipient shall also perform a systematic study (b)(4). The recipient shall also probe the neurophysiology (b)(4) (b)(4)(b)(4)3.1.16 Identifying neuronal basis of (b)(4) memory in NHPs and probing the role of stimulation(b)(4) . This phase of the work seeks to characterize the patterns of neuronal activity that underlie (b)(4) memory in non-human primates. The recipient shall conduct high (b)(4) recordings (b)(4)3.1.16.1 The recipient shall design, program, and test experimental protocol for measuring monkey (b)(4) memory performance [Months 1-4]. (a) The recipient shall design and program a behavioral task for measuring monkey (b)(4) memory [Month 4]. 3.1.16.2 The recipient shall document the hardware interface for the (b)(4) task to interface with recording (b)(4) Months 3-5]. equipment (a) The recipient shall document the hardware/software interface for interfacing electrophysiological recordings, eye tracker, and monkey behavioral paradigm [Month 5]. 3.1.16.3 The recipient shall train (b)(4) (b)(4)(b)(4)memory task [Months 5-24]. (a) The recipient shall obtain one monkey, complete pre-training health checks, place collars, complete quarantine and room acclimation procedures [Month 8]. (b) The recipient shall train the monkey in chairing and handling procedures, acclimate monkey to working in the laboratory, begin food delay procedures, train monkey on initial behavioral tasks, (b)(4) which will be used in the eye-tracking calibration procedure of the (b)(4)(b)(4) memory task [Month 10]. (c) The recipient shall train the animal in the (b)(4) memory paradigm [Month 24].

- 3.1.16.4 The recipient shall prepare monkey for recording and stimulation studies, including MRIs, surgeries to implant headposts and recording chambers, and craniotomies. The recipient shall conduct studies of neurophysiological correlates of monkey (b)(4) behavior without stimulation [Months 5-24] and shall:
- (a) Perform pre-surgical MRIs on one monkey and perform surgery to implant headpost. Complete recovery from surgery [Month 12].
- (b) Train one monkey on initial joystick task, including eye calibration and fixation training with head fixation via headpost [Month 15].
- (c) Train monkey on the (b)(4) memory task, perform surgery to implant recording chamber [Month 18].
- (d) The recipient shall document all findings in a final report [Month 19]

3.1.16.5 [DELETED]

	-	ive examination of the electrectrophysiology of stimulation			-	
ability f	-	stimulation (b)	_	and identify	(b)(4)	parameters
		(b)(4)		oient shall conduct	both studies	(b)(4)
			(b)(4)			
		•				
2 1 17 1	TD1	. 1 11	1 6 7 1			
3.1.17.1	The recipier	nt shall prepare untrained mon		4) recording and stin	nulation studies	(b)(4)
		The recipient shall	(b)(4)	RIs to guide electro	de implentation s	urgeries to
implant l	headposts and	d recording chambers, and cra		icis to guide electron	ic implantation, s	surgeries to
p.10111	-	ripient shall perform monkey s		mplant electrodes	(b)(4)	
	[Month 6].		J	1		
3.1.17.2	The recipier	nt shall demonstrate that neuro	onal stimulati	ion	(b)(4)	
	(a) The reci	ipient shall show that	(b)(4)	stimulation	(b)(4)	
	(a) The reci	•	(b)(4) Month 9].	Stillulation	(b)(4)	
	(b) The reci	ipient shall document results o	-	ses	(b)(4)	
		1			[Month 11].	
	(c) The recip	pient shall document all findin	igs in a final	report [Month 19]		
		_				
3.1.17.3	[DELETED]				
2 1 17 4	[DELETED]	1				
3.1.1/.4	[DELETED]					
3 1 17 5	[DELETED	1				
3.1.17.3	[DEEETED	1				
3.2 OP	TION PERIO	OD (PHASE II)				
Technic	al Area 1					
221 F						
3.2.1 Ex	xtending con	mputational model	(b)(4)			
3.2.1.1	Modeling the	e dynamics of brain activity		(b)(4)		
	(a)		(b)(4			
				,		
					[Month	28]
	(b)		(b)(4)			
			ГХ	Month 30]		
	(c) Formal re	eport on the above milestones	_	-	these analyses	Month 361
	(-) 1 0111141 10	To a control of the c	oraaning o	car asea to perioriii	inese anaryses.	
3.2.1.2 U	Jsing	(b)(4)	modeling	to improve memory	(b)(4) re	storation:



(b)(4) . [Month 36]

3.2.1.5 Build a revised control algorithm strategy

(a)

(b)(4)

[Month 30]

(b) Complete a reanalysis of all parameter search

(b)(4)

(b)(4)

(b)(4)

(b)(4)) [Month 34]. (c) Complete algorithm for (b)(4) selection of stimulation parameters during FR6, PAL6, CatFR6 and TH6 tasks to maximize memory performance. [Month 38]

(d) Deliver a final report based on the above deliverables. [Month 42]

3.2.1.6 [DELETED]

- 3.2.1.7 The recipient shall complete data collection in experiment FR1 and shall:
 - (a) Analyze data on 60 patients from experiment FR1 [Month 30].
 - (b) Analyze data on 66 patients from experiment FR1 [Month 36].
 - (c) Analyze data on 72 patients from experiment FR1 [Month 42].
 - (d) Analyze data on 78 patients from experiment FR1 [Month 48].
 - (e) Complete final reports on data from the above experiment [Month 48].
 - (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
 - (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].
- 3.2.1.8 The recipient shall complete data collection in experiment CatFR1 and shall:
 - (a) Analyze data on 36 patients from experiment CatFR1 [Month 30].
 - (b) Analyze data on 38 patients from experiment CatFR1 [Month 36].
 - (c) Analyze data on 41 patients from experiment CatFR1 [Month 42].
 - (d) Analyze data on 43 patients from experiment CatFR1 [Month 48].
 - (e) Complete final reports on data from the above experiment [Month 48].
 - (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
 - (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

(h) Expand analysis function(b)(4) (b)(4)

(b)(4) [Month 30]

- 3.2.1.9 Design, program, pilot, execute, and analyze data from Experiment TH1. The recipient (b)(4) and shall:
 - (a) Deliver fully documented code and analysis functions [Month 26].
 - (b) Analyze data on 21 patients from experiment TH1 [Month 30].
 - (c) Analyze data on 32 patients from experiment TH1 [Month 36].
 - (d) Analyze data on 43 patients from experiment TH1 [Month 42].
 - (e) Analyze data on 54 patients from experiment TH1 [Month 48].

- (f) Complete final reports on data from the above experiment [Month 48].
- (g) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (h) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].
- 3.2.1.10 The recipient shall complete data collection and analysis in experiment PAL1 and shall:
 - (a) Analyze data on 31 patients from experiment PAL1 [Month 30].
 - (b) Analyze data on 36 patients from experiment PAL1 [Month 36].
 - (c) Analyze data on 42 patients from experiment PAL1 [Month 42].
 - (d) Analyze data on 47 patients from experiment PAL1 [Month 48].
 - (e) Complete final reports on data from the above experiment [Month 48].
 - (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
 - (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2 Stimulation to enhance

(b)(4)

memory

- 3.2.2.1 Continue to collect and analyze data from Experiment FR3. The recipient shall:
 - (a) Organize and annotate data from 22 patients [Month 36].
 - (b) Complete final reports on data from the above experiment [Month 48].
 - (c) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
 - (d) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].
- 3.2.2.2 Design, program, execute, and analyze data from Experiment FR5.

(b)(4)

. The recipient shall:

- (a) Deliver fully documented code and analysis functions [Month 32].
- (b) Organize and annotate data from 6 patients [Month 36].
- (c) Organize and annotate data from 9 patients [Month 42].
- (d) Organize and annotate data from 12 patients [Month 48].
- (e) Complete final reports on data from the above experiment [Month 48].
- (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].
- 3.2.2.3 Design, program, execute, and analyze data from Experiment FR6.

(b)(4)

. The recipient shall:

- (a) Deliver fully documented code and analysis functions [Month 32].
- (b) Organize and annotate data from 6 patients [Month 36].
- (c) Organize and annotate data from 12 patients [Month 42].
- (d) Complete final reports on data from the above experiment [Month 48].
- (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].
- 3.2.2.5 Continue to collect and analyze data from Experiment CatFR3. The recipient shall:
 - (a) Organize and annotate data from 12 patients [Month 36].
 - (b) Complete final reports on data from the above experiment [Month 48].
 - (c) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
 - (d) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].
- 3.2.2.6 Design, program, execute, and analyze data from Experiment CatFR5.

(b)(4)

- (a) Deliver fully documented code and analysis functions [Month 32].
- (b) Organize and annotate data from 5 patients [Month 36].
- (c) Organize and annotate data from 8 patients [Month 42].
- (d) Organize and annotate data from 10 patients [Month 48].
- (e) Complete final reports on data from the above experiment [Month 48].
- (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.10 Design, program, execute, and analyze data from Experiment TH6l

(b)(4)

The recipient shall:

- (a) Deliver fully documented code and analysis functions [Month 38].
- (b) Organize and annotate data from 5 patients [Month 42].
- (c) Organize and annotate data from 10 patients [Month 48].
- (d) Complete final reports on data from the above experiment [Month 48].
- (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.11 Design, program, execute, and analyze data from Experiment PAL3. (b)(4)(b)(4)The recipient shall: (a) Analyze data on 15 patients from the PAL3 experiment [Month 36]. (b) Analyze data on 18 patients from the PAL3 experiment [Month 42]. (c) Analyze data on 22 patients from the PAL3 experiment [Month 48]. (d) Complete final reports on data from the above experiment [Month 48]. (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48]. (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48]. 3.2.2.12 Design, program, pilot, execute, and analyze data from Experiment PAL5. (b)(4). The recipient shall: (a) Deliver fully documented code and analysis functions [Month 32]. (b) Analyze data on 6 patients from the PAL5 experiment [Month 36]. (c) Analyze data on 9 patients from the PAL5 experiment [Month 42]. (d) Analyze data on 12 patients from the PAL5 experiment [Month 48]. (e) Complete final reports on data from the above experiment [Month 48]. (f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48]. (g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48]. 3.2.2.13 Design, program, execute, and analyze data from Experiment PAL6. (b)(4)(b)(4). The recipient shall: (a) Deliver fully documented code and analysis functions [Month 38]. (b) Organize and annotate data from 5 patients [Month 42]. (c) Organize and annotate data from 12 patients [Month 48]. (d) Complete final reports on data from the above experiment [Month 48]. (e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48]. (f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48]. 3.2.2.14 Continue to collect and analyze data from Experiments PS2. The recipient shall: (a) Analyze data on 50 patients from experiments PS2 [Month 30]. (b) Analyze data on 71 patients from experiments PS2 [Month 36]. (c) Analyze data on 82 patients from experiments PS2 [Month 42]. (d) Analyze data on 93 patients from experiment PS2 [Month 48]. (e) Post fully annotated data to the public data portal for all patients run in the task [Month 48]. 3.2.2.15. Design, program, execute, and analyze data from Experiments PS4. (b)(4)(b)(4)(a) Deliver fully documented code and analysis functions [Month 27]. (b) Analyze data on 10 patients from experiments PS4 [Month 30]. (c) Analyze data on 21 patients from experiments PS4 [Month 36]. (d) Analyze data on 26 patients from experiments PS4 [Month 42]. (e) Analyze data on 31 patients from experiment PS4 [Month 48]. (f) Post fully annotated data to the public data portal for all patients run in the task [Month 48].

3.2.2.16. Design, program, execute, and analyze data from Experiments PS5.

(b)(4)

(b)(4)

- (a) Deliver fully documented code and analysis functions [Month 32].
- (b) Analyze data on 10 patients from experiments PS5 [Month 36].
- (c) Analyze data on 20 patients from experiment PS5 [Month 42].
- (d) Analyze data on 31 patients from experiment PS5 [Month 48].
- (e) Post fully annotated data to the public data portal for all patients run in the task [Month 48].

3.2.2.17. Design, program, execute, and analyze data from Experiment REC1.

(b)(4)

The recipient shall:

- (a) Deliver fully documented code and analysis functions [Month 28].
- (b) Organize and annotate data from 2 patients [Month 30].
- (c) Organize and annotate data from 4 patients [Month 36].
- (d) Organize and annotate data from 6 patients [Month 42].
- (e) Organize and annotate data from 8 patients [Month 48].
- (f) Complete final reports on data from the above experiment [Month 48].
- (g) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
- (h) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

Technical Area 2

Phase 2 objectives in TA2 shall be to support FDA IDE approval and clinical site training, develop clinical systems, and (b)(4) Phase 1 algorithms.

- 3.2.4 Update system architecture and individual components based on TA1. The recipient shall review and, if necessary, redefine, document and review the high-level system design requirements for the (b)(4) system based on the discovery and feedback from TA1 in phase 1.
- 3.2.4.1 The recipient shall review and, if necessary, redefine system level specification with TA1 team based on the phase 1 results [Months 25–30].
- 3.2.4.2 The recipient shall review and, if necessary, redefine the specifications for neural interfaces [Months 25–30].
- 3.2.4.3 The recipient shall review and, if necessary, redefine the specifications for electronics including the stimulating and recording electronics [Months 25–30].
- 3.2.4.4 The recipient shall review and, if necessary, redefine the sub-chronic safety and performance data required by the FDA for 29-day IDE approval [Months 25–30].
- 3.2.4.5 The recipient shall produce a final set of documents detailing the specifications for the overall system and its components [Month 30].
- 3.2.5 Fabrication of the reusable (b)(4) stimulators for clinical studies. The recipient shall produce the balance of (b)(4) stimulator units for use at the clinical sites in early Phase 2.The recipient shall:
 - (a) Deliver ten tested and documented (b)(4) systems [Month 26].
 - (b) Deliver an additional thirty tested and documented (b)(4) systems [Month 30].

- (c) Deliver an updated development plan, requirements, and design history file and limited verification and validation activities to cover the system integration with the(b)(4)Lead and (b)(4) splitter cable [Months 30].
- (d) Utilize the (b)(4) to perform recording and closed-loop stimulation during memory testing in at least 50 patients [Month 48].

3.2.6 N	Manufacture and testing of human implantable system. The recipient shall build one h	undred (b)(4)
(b)(4)	leads for implantation in human patients. The recipient shall:		

- 3.2.6.1 Assemble one hundred human quality (b)(4) leads for sub-chronic use in patients in an epilepsy monitoring unit [Months 25–36].
- 3.2.6.2 Provide manufacturing documentation [Month 36].
- 3.2.6.3 Implant the (b)(4) leads and perform (b)(4) stimulation during memory testing (b)(4) (b)(4) in at least 15 patients under IDE approval from the FDA [Month 48].

3.2.7 Algorithm prototyping system: (b)(4) algorithm development from TA1, Phase 1. The recipient shall document the development of a tool to (b)(4) successful TA1 algorithms (b)(4)

- 3.2.7.1 The recipient shall document the development of a (b)(4) tool to translate existing algorithms from phase 1 (b)(4) [Months 33–39].
- 3.2.7.2 The recipient shall document the development of a tool (b)(4) [Months 33–39].
- 3.2.7.3 The recipient shall ensure verification and validation testing and documentation for IDE submission [Months 37–39]. The recipient shall:
 - (a) Complete software tool for loading (b)(4) [Month 39].
 - (b) Complete software tool for translating software algorithm (b)(4) [Month 39].
 - (c) Submit an updated Design History File to the FDA covering the firmware updates [Month 39].
- 3.2.8 IDE submission for the (b)(4) algorithm from TA1. The recipient shall seek approval of update to FDA IDE for adding (b)(4) algorithm in the (b)(4) .
- 3.2.8.1 The recipient shall submit the IDE to the FDA [Month 39].
- 3.2.8.2 The recipient shall obtain approval of IDE [Month 43].
- 3.2.9 Core project resources devoted to TA2: (b)(4) algorithms, computational cluster equipment and administration, integration between TA1, TA2, and TA3 modeling and electrophysiology shall be documented.

Technical Area 3
[DELETED]

3.3 PROGRAM MANAGEMENT AND REVIEW

The Government will actively monitor, review and approve the recipient's performance to ensure all the performers are in sync and matched with the Government's requirements. The Government will ensure that each of the performers share experimental data across the program and will further ensure that the performers develop techniques and capabilities that are compatible and integrate with each other. The recipient shall collaborate and cooperate with other performers in the program under the coordination of the Government team. At Government PI

meetings, the recipient shall demonstrate technical capabilities and engage and/or challenge other performers in a cooperative and challenge environment. Along these lines, the Government will ensure that each performer shares technical information with the others to enable the testing/challenging of each other's capabilities. The Government will further oversee the program and will review, approve, and participate in the demonstrations.

3.3.1 Kick-off Meeting

The recipient shall hold a kick off meeting within 60 days of award of this agreement. In this meeting, the recipient shall present a program management plan and financial tracking plan.

3.3.2 Quarterly Financial Reports

The recipient shall provide quarterly financial progress reports to the Government Technical Representative (GTR) and DARPA Program Manager. The purpose of these reports is to provide a brief project progress and inform the GTR and Program Manager of any potential issues.

3.3.3 Quarterly Technical Reporting

The recipient shall provide quarterly progress reports to the Government Technical Representative (GTR) and DARPA Program Manager. The purpose of these reports is to present a summary of work completed by SOW tasking and milestones met, discuss any problems encountered, update the program schedule, present the program financial status, and discuss remaining work. Quarterly reports shall also include all technical data items generated including but not limited to experimental data, processed data along with methods of processing used, research reports and publications and software (source code and executables).

3.3.4 Monthly Status Reports

The recipient shall provide monthly status reports which will include all relevant project data including, but not limited to, raw and analyzed electrophysiological signals as well as any necessary annotations and interpretations of the data, such as time-stamped patient behaviors, necessary for appropriate analyses and interpretation of the data. Patient data shall be provided in a coded format that protects patient identities but will contain diagnosis (signs/symptoms), interventions including system modifications, technical observations, diagnostic tests/results, and patient outcomes. In addition, information about the device delivering therapy including device serial numbers, device model numbers, date of event, and country/state of event shall be annotated with the data and therapy. This data shall be made available on database accessible across the program and to Government personnel.

3.3.5 Final Agreement Review

The recipient shall host a final agreement review. The purpose of this review is to present a summary of all work completed and milestones accomplished and to discuss any relevant future efforts similar to the contract, which may be pursued. This report shall be provided to the Government Technical Representative (GTR) and DARPA Program Manager. A final summary report shall be provided at the end of the program.

3.3.6 System Development Plan (SDP)

The recipient shall describe the scope of the design and development effort, describe hardware, software architectures and experimental procedures (as applicable) in sufficient detail for review and replication, reference any applicable documents and provide a schedule. The recipient shall share the SDP with the other program performers and the Government.

3.3.7 System Documentation

The recipient shall provide system documentation documenting the source code, protocol and algorithm analysis, hardware description, format specifications, system diagrams, part numbers, and any other data necessary to replicate and test the designs.

4.0 INCIDENTAL HARDWARE AND SOFTWARE

Hardware and software incidental to this research shall be made available to the Government.

5.0 REPORTS AND PRESENTATION MATERIALS

The reports and presentation materials shall be delivered as described in the data matrix.

6.0 TRAVEL

Long distance domestic travel is estimated for Program Review meetings and Conferences.

7.0 PLACE OF PERFORMANCE

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