Recipient Information

1. Recipient Name
TRUSTEES OF BOSTON UNIVERSITY
1 SILBER WAY

BOSTON, 02215

2. Congressional District of Recipient
07

3. Payment System Identifier (ID)
1042103547A1

4. Employer Identification Number (EIN)
042103547

5. Data Universal Numbering System (DUNS)
049435266

6. Recipient's Unique Entity Identifier
THL6A6JLE1S7

7. Project Director or Principal Investigator
Helen Barbas, PHD
Professor
barbas@bu.edu
617-353-5036

8. Authorized Official
Diane Baldwin
ospera@bu.edu
617-353-4365

Federal Agency Information

9. Awarding Agency Contact Information
THOMAS JOSEPH Peters

NATIONAL INSTITUTE OF MENTAL HEALTH
tom.peters@nih.gov

10. Program Official Contact Information
Andrew Rossi
Health Scientist Administrator
NATIONAL INSTITUTE OF MENTAL HEALTH
rossia@mail.nih.gov
301-443-1576

Federal Award Information

11. Award Number
5R01MH117785-33

12. Unique Federal Award Identification Number (FAIN)
R01MH117785

13. Statutory Authority
42 USC 241 42 CFR 52

14. Federal Award Project Title
Prefrontal Anatomic Pathways in Executive Control

15. Assistance Listing Number
93.242

16. Assistance Listing Program Title
Mental Health Research Grants

17. Award Action Type
Non-Competing Continuation (REVISED)

18. Is the Award R&D?
Yes

Summary Federal Award Financial Information

19. Budget Period Start Date 02/01/2022 – **End Date** 01/31/2023	
20. Total Amount of Federal Funds Obligated by this Action	$65,504
20 a. Direct Cost Amount	$39,699
20 b. Indirect Cost Amount	$25,805
21. Authorized Carryover	$0
22. Offset	$0
23. Total Amount of Federal Funds Obligated this budget period	$655,038
24. Total Approved Cost Sharing or Matching, where applicable	$0
25. Total Federal and Non-Federal Approved this Budget Period	$655,038
26. Project Period Start Date 07/01/1987 – **End Date** 01/31/2025	
27. Total Amount of the Federal Award including Approved Cost Sharing or Matching this Project Period	$2,078,893

28. Authorized Treatment of Program Income
Additional Costs

29. Grants Management Officer - Signature
Theresa R. Jarosik

30. Remarks

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

RESEARCH
Department of Health and Human Services
National Institutes of Health

NATIONAL INSTITUTE OF MENTAL HEALTH

SECTION I – AWARD DATA – 5R01MH117785-33 REVISED

Principal Investigator(s):
Helen Barbas, PHD

Award e-mailed to: ospera@bu.edu

Dear Authorized Official:

The National Institutes of Health hereby revises this award to reflect an increase in the amount of $65,504 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to Trustees of Boston University in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Mental Health of the National Institutes of Health under Award Number R01MH117785. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please direct questions to the Federal Agency contacts.

Sincerely yours,

Theresa R. Jarosik
Grants Management Officer
NATIONAL INSTITUTE OF MENTAL HEALTH

Additional information follows

Cumulative Award Calculations for this Budget Period (U.S. Dollars)

Salaries and Wages	$271,231
Fringe Benefits	$57,487
Personnel Costs (Subtotal)	$328,718
Materials & Supplies	$57,763
Travel	$6,132
Publication Costs	$4,380
Federal Direct Costs	$396,993
Federal F&A Costs	$258,045
Approved Budget	$655,038
Total Amount of Federal Funds Authorized (Federal Share)	$655,038
TOTAL FEDERAL AWARD AMOUNT	$655,038
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$65,504

SUMMARY TOTALS FOR ALL YEARS (for this Document Number)		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
33	$655,038	$655,038
34	$641,523	$641,523
35	$627,604	$627,604

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

Payment System Identifier:	1042103547A1
Document Number:	RMH117785I
PMS Account Type:	P (Subaccount)
Fiscal Year:	2022

IC	CAN	2022	2023	2024
MH	8022557	$655,038	$641,523	$627,604

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: 72-NBX / **OC**: 41025 / **Released**: Jarosik, Theresa 05/15/2022
Award Processed: 05/16/2022 12:05:49 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R01MH117785-33 REVISED

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – STANDARD TERMS AND CONDITIONS – 5R01MH117785-33 REVISED

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final

progress report when applicable.

f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VII Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to obtain a unique entity identifier (UEI) and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a UEI requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01MH117785. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

This award is not subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:

Additional Costs

SECTION IV – MH SPECIFIC AWARD CONDITIONS – 5R01MH117785-33 REVISED

Clinical Trial Indicator: No

This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

REVISION #1

RESTORATION:

In keeping with NOT-OD-22-105, FY2022 appropriation, and NIMH Fiscal Policy, this grant is restored to reflect the FY2022 committed level indicated on the FY2021 Notice of Award. Outyear commitments remain unchanged.

THIS REVISED AWARD SUPERSEDES THE NOTICE OF AWARD ISSUED ON 02/22/2022. THE FOLLOWING TERMS & CONDITIONS REMAIN IN EFFECT.

AWARD NOTICE:

This award has been made in response to the application submitted under the Funding Opportunity Announcement PA19-056 which can be referenced at: https://grants.nih.gov/grants/guide/pa-files/PA-19-056.html.

INFORMATION:

This grant is awarded with the understanding that project delays and challenges may occur due to COVID-19. It is NIMH's intention to ensure the ultimate success of each project: to that end, we will work with recipients on a case-by-case basis to identify flexibilities and find solutions. You are encouraged to refer to the NIH Guide (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-086.html, and updates referenced therein) and to the regularly updated Frequently Asked Questions (https://grants.nih.gov/faqs#/covid-19.htm) for guidance on delays in research progress, delays in financial and RPPR reporting, costs, and other relevant issues, and contact your grants specialist and/or program officer with questions.

SPREADSHEET SUMMARY
AWARD NUMBER: 5R01MH117785-33 REVISED

INSTITUTION: Trustees of Boston University

Budget	Year 33	Year 34	Year 35
Salaries and Wages	$271,231	$269,479	$269,479
Fringe Benefits	$57,487	$57,487	$57,487
Personnel Costs (Subtotal)	$328,718	$326,966	$326,966
Materials & Supplies	$57,763	$51,324	$44,640
Travel	$6,132	$6,132	$4,380
Publication Costs	$4,380	$4,380	$4,380
TOTAL FEDERAL DC	$396,993	$388,802	$380,366
TOTAL FEDERAL F&A	$258,045	$252,721	$247,238
TOTAL COST	$655,038	$641,523	$627,604

Facilities and Administrative Costs	Year 33	Year 34	Year 35
F&A Cost Rate 1	65%	65%	65%
F&A Cost Base 1	$396,993	$388,802	$380,366
F&A Costs 1	$258,045	$252,721	$247,238

Recipient Information

1. Recipient Name
TRUSTEES OF BOSTON UNIVERSITY
1 SILBER WAY

BOSTON, MA 02215

2. Congressional District of Recipient
07

3. Payment System Identifier (ID)
1042103547A1

4. Employer Identification Number (EIN)
042103547

5. Data Universal Numbering System (DUNS)
049435266

6. Recipient's Unique Entity Identifier
THL6A6JLE1S7

7. Project Director or Principal Investigator
Helen Barbas, PHD
Professor
barbas@bu.edu
617-353-5036

8. Authorized Official
Diane Baldwin
ospera@bu.edu
617-353-4365

Federal Agency Information

9. Awarding Agency Contact Information
THOMAS JOSEPH Peters

NATIONAL INSTITUTE OF MENTAL HEALTH
tom.peters@nih.gov

10. Program Official Contact Information
Andrew Rossi
Health Scientist Administrator
NATIONAL INSTITUTE OF MENTAL HEALTH
rossia@mail.nih.gov
301-443-1576

Federal Award Information

11. Award Number
5R01MH117785-33

12. Unique Federal Award Identification Number (FAIN)
R01MH117785

13. Statutory Authority
42 USC 241 42 CFR 52

14. Federal Award Project Title
Prefrontal Anatomic Pathways in Executive Control

15. Assistance Listing Number
93.242

16. Assistance Listing Program Title
Mental Health Research Grants

17. Award Action Type
Non-Competing Continuation

18. Is the Award R&D?
Yes

Summary Federal Award Financial Information

19. Budget Period Start Date 02/01/2022 – **End Date** 01/31/2023	
20. Total Amount of Federal Funds Obligated by this Action	$589,534
20 a. Direct Cost Amount	$357,294
20 b. Indirect Cost Amount	$232,240
21. Authorized Carryover	$0
22. Offset	$0
23. Total Amount of Federal Funds Obligated this budget period	$589,534
24. Total Approved Cost Sharing or Matching, where applicable	$0
25. Total Federal and Non-Federal Approved this Budget Period	$589,534
26. Project Period Start Date 07/01/1987 – **End Date** 01/31/2025	
27. Total Amount of the Federal Award including Approved Cost Sharing or Matching this Project Period	$2,013,389

28. Authorized Treatment of Program Income
Additional Costs

29. Grants Management Officer - Signature
Heather Weiss

30. Remarks

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

RESEARCH
Department of Health and Human Services
National Institutes of Health

NATIONAL INSTITUTE OF MENTAL HEALTH

SECTION I – AWARD DATA – 5R01MH117785-33

Principal Investigator(s):
Helen Barbas, PHD

Award e-mailed to: ospera@bu.edu

Dear Authorized Official:

The National Institutes of Health hereby awards a grant in the amount of $589,534 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to Trustees of Boston University in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Mental Health of the National Institutes of Health under Award Number R01MH117785. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please direct questions to the Federal Agency contacts.

Sincerely yours,

Heather Weiss
Grants Management Officer
NATIONAL INSTITUTE OF MENTAL HEALTH

Additional information follows

Cumulative Award Calculations for this Budget Period (U.S. Dollars)

Salaries and Wages	$244,108
Fringe Benefits	$51,738
Personnel Costs (Subtotal)	$295,846
Materials & Supplies	$51,987
Travel	$5,519
Publication Costs	$3,942
Federal Direct Costs	$357,294
Federal F&A Costs	$232,240
Approved Budget	$589,534
Total Amount of Federal Funds Authorized (Federal Share)	$589,534
TOTAL FEDERAL AWARD AMOUNT	$589,534
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$589,534

SUMMARY TOTALS FOR ALL YEARS (for this Document Number)		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
33	$589,534	$589,534
34	$641,523	$641,523
35	$627,604	$627,604

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

Payment System Identifier:	1042103547A1
Document Number:	RMH117785I
PMS Account Type:	P (Subaccount)
Fiscal Year:	2022

IC	CAN	2022	2023	2024
MH	8022557	$589,534	$641,523	$627,604

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: 72-NBX / **OC**: 41025 / **Released**: Weiss, Heather 02/18/2022
Award Processed: 02/22/2022 12:24:30 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R01MH117785-33

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – STANDARD TERMS AND CONDITIONS – 5R01MH117785-33

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final

progress report when applicable.

f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VII Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01MH117785. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

This award is not subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:

Additional Costs

SECTION IV – MH SPECIFIC AWARD CONDITIONS – 5R01MH117785-33

Clinical Trial Indicator: No

This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

AWARD NOTICE:
This award has been made in response to the application submitted under the Funding Opportunity Announcement PA19-056 which can be referenced at: https://grants.nih.gov/grants/guide/pa-files/PA-19-056.html.

INFORMATION:
This grant is awarded with the understanding that project delays and challenges may occur due to COVID-19. It is NIMH's intention to ensure the ultimate success of each project: to that end, we will work with recipients on a case-by-case basis to identify flexibilities and find solutions. You are encouraged to refer to the NIH Guide (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-086.html, and updates referenced therein) and to the regularly updated Frequently Asked Questions (https://grants.nih.gov/faqs#/covid-19.htm) for guidance on delays in research progress, delays in financial and RPPR reporting, costs, and other relevant issues, and contact your grants specialist and/or program officer with questions.

CONTINUING RESOLUTION:
NIH is currently operating under a Continuing Resolution (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-22-045.html). Therefore, this noncompeting award has been made at 90% of the amount committed for FY2022 in the previous Notice of Award. If the final appropriation permits, adjustments may be made up to the FY2022 funding plan level.

SPREADSHEET SUMMARY
AWARD NUMBER: 5R01MH117785-33

INSTITUTION: Trustees of Boston University

Budget	Year 33	Year 34	Year 35
Salaries and Wages	$244,108	$269,479	$269,479
Fringe Benefits	$51,738	$57,487	$57,487
Personnel Costs (Subtotal)	$295,846	$326,966	$326,966
Materials & Supplies	$51,987	$51,324	$44,640
Travel	$5,519	$6,132	$4,380
Publication Costs	$3,942	$4,380	$4,380
TOTAL FEDERAL DC	$357,294	$388,802	$380,366
TOTAL FEDERAL F&A	$232,240	$252,721	$247,238
TOTAL COST	$589,534	$641,523	$627,604

Facilities and Administrative Costs	Year 33	Year 34	Year 35
F&A Cost Rate 1	65%	65%	65%
F&A Cost Base 1	$357,294	$388,802	$380,366
F&A Costs 1	$232,240	$252,721	$247,238

Recipient Information

1. Recipient Name
TRUSTEES OF BOSTON UNIVERSITY
1 SILBER WAY

BOSTON, MA 02215

2. Congressional District of Recipient
07

3. Payment System Identifier (ID)
1042103547A1

4. Employer Identification Number (EIN)
042103547

5. Data Universal Numbering System (DUNS)
049435266

6. Recipient's Unique Entity Identifier
THL6A6JLE1S7

7. Project Director or Principal Investigator
Helen Barbas, PHD
Professor
barbas@bu.edu
617-353-5036

8. Authorized Official
Diane Baldwin
ospera@bu.edu
(617) 353-4365

Federal Agency Information

9. Awarding Agency Contact Information
THOMAS JOSEPH Peters

NATIONAL INSTITUTE OF MENTAL HEALTH
tom.peters@nih.gov

10. Program Official Contact Information
Andrew Rossi
Health Scientist Administrator
NATIONAL INSTITUTE OF MENTAL HEALTH
rossia@mail.nih.gov
301-443-1576

Federal Award Information

11. Award Number
5R01MH117785-32

12. Unique Federal Award Identification Number (FAIN)
R01MH117785

13. Statutory Authority
42 USC 241 42 CFR 52

14. Federal Award Project Title
Prefrontal Anatomic Pathways in Executive Control

15. Assistance Listing Number
93.242

16. Assistance Listing Program Title
Mental Health Research Grants

17. Award Action Type
Non-Competing Continuation (REVISED)

18. Is the Award R&D?
Yes

Summary Federal Award Financial Information

19. Budget Period Start Date 03/26/2021 **– End Date** 01/31/2022	
20. Total Amount of Federal Funds Obligated by this Action	$84,389
20 a. Direct Cost Amount	$0
20 b. Indirect Cost Amount	$0
21. Authorized Carryover	$0
22. Offset	$-84,389
23. Total Amount of Federal Funds Obligated this budget period	$668,163
24. Total Approved Cost Sharing or Matching, where applicable	$0
25. Total Federal and Non-Federal Approved this Budget Period	$668,163
26. Project Period Start Date 07/01/1987 **– End Date** 01/31/2025	
27. Total Amount of the Federal Award including Approved Cost Sharing or Matching this Project Period	$1,423,855

28. Authorized Treatment of Program Income
Additional Costs

29. Grants Management Officer - Signature
Heather Weiss

30. Remarks

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

RESEARCH
Department of Health and Human Services
National Institutes of Health

NATIONAL INSTITUTE OF MENTAL HEALTH

SECTION I – AWARD DATA – 5R01MH117785-32 REVISED

Principal Investigator(s):
Helen Barbas, PHD

Award e-mailed to: ospera@bu.edu

Dear Authorized Official:

The National Institutes of Health hereby revises this award to reflect an increase in the amount of $84,389 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to Trustees of Boston University in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Mental Health of the National Institutes of Health under Award Number R01MH117785. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please direct questions to the Federal Agency contacts.

Sincerely yours,

Heather Weiss
Grants Management Officer
NATIONAL INSTITUTE OF MENTAL HEALTH

Additional information follows

Cumulative Award Calculations for this Budget Period (U.S. Dollars)

Salaries and Wages	$271,231
Fringe Benefits	$57,487
Personnel Costs (Subtotal)	$328,718
Materials & Supplies	$64,841
Travel	$6,132
Publication Costs	$5,256
Federal Direct Costs	$404,947
Federal F&A Costs	$263,216
Approved Budget	$668,163
Total Amount of Federal Funds Authorized (Federal Share)	$668,163
TOTAL FEDERAL AWARD AMOUNT	$668,163
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$84,389

SUMMARY TOTALS FOR ALL YEARS (for this Document Number)		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
32	$668,163	$668,163
33	$655,038	$655,038
34	$641,523	$641,523
35	$627,604	$627,604

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

Payment System Identifier:	1042103547A1
Document Number:	RMH117785I
PMS Account Type:	P (Subaccount)
Fiscal Year:	2021

IC	CAN	2021	2022	2023	2024
MH	8022557	$668,163	$655,038	$641,523	$627,604

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: 72-NBX / **OC**: 41025 / **Released**: Weiss, Heather 01/04/2022
Award Processed: 01/05/2022 12:02:32 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R01MH117785-32 REVISED

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

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SECTION III – STANDARD TERMS AND CONDITIONS – 5R01MH117785-32 REVISED

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.

e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VII Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01MH117785. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

This award is not subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:

Additional Costs

SECTION IV – MH SPECIFIC AWARD CONDITIONS – 5R01MH117785-32 REVISED

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

REVISION #1
UNOBLIGATED BALANCE:
This revised award removes the offset of the unobligated balance taken on the Notice of Grant Award issued 04/26/2021. The authorized direct and facilities & administrative costs award levels remain unchanged.

THIS REVISED AWARD SUPERSEDES THE NOTICE OF AWARD ISSUED ON 04/26/2021. THE FOLLOWING TERMS & CONDITIONS REMAIN IN EFFECT.

AWARD NOTICE:
This award has been made in response to the application submitted under the Funding Opportunity Announcement PA19-056 which can be referenced at: https://grants.nih.gov/grants/guide/pa-files/PA-19-056.html.

DELAYED AWARD:
The budget period start date of this award has been delayed due to the late submission of an acceptable FFR and IRPPR for the -30 budget period. Allowable pre-award costs may be charged in accordance with the conditions outlined in the NIH Grants Policy Statement (http://grants.nih.gov/grants/policy/nihgps/index.htm) and in accordance with recipient organizational requirements for prior approval.

ADMINISTRATIVE REDUCTION:
In order to meet Institute program objectives within Fiscal Year 2020 budget constraints, the recommended levels for this grant have been reduced by 8.4% in the initial budget period 01, and 12.4% in the outyears to eliminate the proposed studies of CTE brains in Aim 4, and the CTE comparisons proposed in Aims 2c and 3c.

INFORMATION:
This grant is awarded with the understanding that project delays and challenges may occur due to COVID-19. It is NIMH's intention to ensure the ultimate success of each project: to that end, we will work with recipients on a case-by-case basis to identify flexibilities and find solutions. You are encouraged to refer to the NIH Guide (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-086.html, and updates referenced therein) and to the regularly updated Frequently Asked Questions (https://grants.nih.gov/faqs#/covid-19.htm) for guidance on delays in research progress, delays in financial and RPPR reporting, costs, and other relevant issues, and contact your grants specialist and/or program officer with questions.

SPREADSHEET SUMMARY
AWARD NUMBER: 5R01MH117785-32 REVISED

INSTITUTION: Trustees of Boston University

Budget	Year 32	Year 33	Year 34	Year 35
Salaries and Wages	$271,231	$271,231	$269,479	$269,479
Fringe Benefits	$57,487	$57,487	$57,487	$57,487
Personnel Costs (Subtotal)	$328,718	$328,718	$326,966	$326,966
Materials & Supplies	$64,841	$57,763	$51,324	$44,640
Travel	$6,132	$6,132	$6,132	$4,380
Publication Costs	$5,256	$4,380	$4,380	$4,380
TOTAL FEDERAL DC	$404,947	$396,993	$388,802	$380,366
TOTAL FEDERAL F&A	$263,216	$258,045	$252,721	$247,238
TOTAL COST	$668,163	$655,038	$641,523	$627,604

Facilities and Administrative Costs	Year 32	Year 33	Year 34	Year 35
F&A Cost Rate 1	65%	65%	65%	65%
F&A Cost Base 1	$404,947	$396,993	$388,802	$380,366
F&A Costs 1	$263,216	$258,045	$252,721	$247,238

Recipient Information

1. Recipient Name
TRUSTEES OF BOSTON UNIVERSITY
1 SILBER WAY

BOSTON, MA 02215

2. Congressional District of Recipient
07

3. Payment System Identifier (ID)
1042103547A1

4. Employer Identification Number (EIN)
042103547

5. Data Universal Numbering System (DUNS)
049435266

6. Recipient's Unique Entity Identifier

7. Project Director or Principal Investigator
Helen Barbas, PHD
Professor
barbas@bu.edu
617-353-5036

8. Authorized Official
Diane Baldwin
ospera@bu.edu
(617) 353-4365

Federal Agency Information

9. Awarding Agency Contact Information
Heather Weiss

NATIONAL INSTITUTE OF MENTAL HEALTH
heather.weiss@nih.gov
301-443-4415

10. Program Official Contact Information
Andrew Rossi
Health Scientist Administrator
NATIONAL INSTITUTE OF MENTAL HEALTH
rossia@mail.nih.gov
301-443-1576

Federal Award Information

11. Award Number
5R01MH117785-32

12. Unique Federal Award Identification Number (FAIN)
R01MH117785

13. Statutory Authority
42 USC 241 42 CFR 52

14. Federal Award Project Title
Prefrontal Anatomic Pathways in Executive Control

15. Assistance Listing Number
93.242

16. Assistance Listing Program Title
Mental Health Research Grants

17. Award Action Type
Non-Competing Continuation

18. Is the Award R&D?
Yes

Summary Federal Award Financial Information

19. Budget Period Start Date 03/26/2021 **– End Date** 01/31/2022	
20. Total Amount of Federal Funds Obligated by this Action	$583,774
20 a. Direct Cost Amount	$404,947
20 b. Indirect Cost Amount	$263,216
21. Authorized Carryover	$0
22. Offset	$84,389
23. Total Amount of Federal Funds Obligated this budget period	$668,163
24. Total Approved Cost Sharing or Matching, where applicable	$0
25. Total Federal and Non-Federal Approved this Budget Period	$668,163
26. Project Period Start Date 07/01/1987 **– End Date** 01/31/2025	
27. Total Amount of the Federal Award including Approved Cost Sharing or Matching this Project Period	$1,339,466

28. Authorized Treatment of Program Income
Additional Costs

29. Grants Management Officer - Signature
Heather Weiss

30. Remarks

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

RESEARCH
Department of Health and Human Services
National Institutes of Health

NATIONAL INSTITUTE OF MENTAL HEALTH

SECTION I – AWARD DATA – 5R01MH117785-32

Principal Investigator(s):
Helen Barbas, PHD

Award e-mailed to: ospera@bu.edu

Dear Authorized Official:

The National Institutes of Health hereby awards a grant in the amount of $583,774 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to Trustees of Boston University in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Mental Health of the National Institutes of Health under Award Number R01MH117785. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please direct questions to the Federal Agency contacts.

Sincerely yours,

Heather Weiss
Grants Management Officer
NATIONAL INSTITUTE OF MENTAL HEALTH

Additional information follows

Cumulative Award Calculations for this Budget Period (U.S. Dollars)

Salaries and Wages	$271,231
Fringe Benefits	$57,487
Personnel Costs (Subtotal)	$328,718
Materials & Supplies	$64,841
Travel	$6,132
Publication Costs	$5,256

Federal Direct Costs	$404,947
Federal F&A Costs	$263,216
Approved Budget	$668,163
Total Amount of Federal Funds Authorized (Federal Share)	$668,163
Cumulative Authorized Carryover and Offset for this Budget Period	$84,389
TOTAL FEDERAL AWARD AMOUNT	$583,774

AMOUNT OF THIS ACTION (FEDERAL SHARE) $583,774

SUMMARY TOTALS FOR ALL YEARS (for this Document Number)		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
32	$583,774	$583,774
33	$655,038	$655,038
34	$641,523	$641,523
35	$627,604	$627,604

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

Payment System Identifier: 1042103547A1
Document Number: RMH117785I
PMS Account Type: P (Subaccount)
Fiscal Year: 2021

IC	CAN	2021	2022	2023	2024
MH	8022557	$583,774	$655,038	$641,523	$627,604

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: 72-NBX / **OC**: 41025 / **Released**: Weiss, Heather 04/23/2021
Award Processed: 04/26/2021 12:05:05 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R01MH117785-32

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – STANDARD TERMS AND CONDITIONS – 5R01MH117785-32

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.

e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VII Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01MH117785. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

This award is not subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:

Additional Costs

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

AWARD NOTICE:
This award has been made in response to the application submitted under the Funding Opportunity Announcement PA19-056 which can be referenced at: https://grants.nih.gov/grants/guide/pa-files/PA-19-056.html.

DELAYED AWARD:
The budget period start date of this award has been delayed due to the late submission of an acceptable FFR and IRPPR for the -30 budget period. Allowable pre-award costs may be charged in accordance with the conditions outlined in the NIH Grants Policy Statement (http://grants.nih.gov/grants/policy/nihgps/index.htm) and in accordance with recipient organizational requirements for prior approval.

UNOBLIGATED BALANCE:
Funds in the amount of $84,389 have been used as an offset on this award in accordance with the unobligated balance reported on the -30 year Federal Financial Report (FFR).

ADMINISTRATIVE REDUCTION:
In order to meet Institute program objectives within Fiscal Year 2020 budget constraints, the recommended levels for this grant have been reduced by 8.4% in the initial budget period 01, and 12.4% in the outyears to eliminate the proposed studies of CTE brains in Aim 4, and the CTE comparisons proposed in Aims 2c and 3c.

INFORMATION:
This grant is awarded with the understanding that project delays and challenges may occur due to COVID-19. It is NIMH's intention to ensure the ultimate success of each project: to that end, we will work with recipients on a case-by-case basis to identify flexibilities and find solutions. You are encouraged to refer to the NIH Guide (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-086.html, and updates referenced therein) and to the regularly updated Frequently Asked Questions (https://grants.nih.gov/faqs#/covid-19.htm) for guidance on delays in research progress, delays in financial and RPPR reporting, costs, and other relevant issues, and contact your grants specialist and/or program officer with questions.

SPREADSHEET SUMMARY
AWARD NUMBER: 5R01MH117785-32

INSTITUTION: Trustees of Boston University

Budget	Year 32	Year 33	Year 34	Year 35
Salaries and Wages	$271,231	$271,231	$269,479	$269,479
Fringe Benefits	$57,487	$57,487	$57,487	$57,487
Personnel Costs (Subtotal)	$328,718	$328,718	$326,966	$326,966
Materials & Supplies	$64,841	$57,763	$51,324	$44,640
Travel	$6,132	$6,132	$6,132	$4,380
Publication Costs	$5,256	$4,380	$4,380	$4,380
TOTAL FEDERAL DC	$404,947	$396,993	$388,802	$380,366
TOTAL FEDERAL F&A	$263,216	$258,045	$252,721	$247,238
TOTAL COST	$583,774	$655,038	$641,523	$627,604

Facilities and Administrative Costs	Year 32	Year 33	Year 34	Year 35
F&A Cost Rate 1	65%	65%	65%	65%

F&A Cost Base 1	$404,947	$396,993	$388,802	$380,366
F&A Costs 1	$263,216	$258,045	$252,721	$247,238

Notice of Award

RESEARCH
Department of Health and Human Services
National Institutes of Health

NATIONAL INSTITUTE OF MENTAL HEALTH

Federal Award Date: 03/27/2020

Grant Number: 2R01MH117785-31
FAIN: R01MH117785

Principal Investigator(s):
Helen Barbas, PHD

Project Title: Prefrontal Anatomic Pathways in Executive Control

Diane Baldwin
Associate Vice President, Sponsored Programs
25 Buick Street
Boston, MA 022151300

Award e-mailed to: ospera@bu.edu

Period Of Performance:
Budget Period: 04/01/2020 – 01/31/2021
Project Period: 07/01/1987 – 01/31/2025

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $755,692 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to Trustees of Boston University in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Mental Health of the National Institutes of Health under Award Number R01MH117785. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Jane Z. Lin
Grants Management Officer
NATIONAL INSTITUTE OF MENTAL HEALTH

Additional information follows

SECTION I – AWARD DATA – 2R01MH117785-31

Award Calculation (U.S. Dollars)

Salaries and Wages	$309,557
Fringe Benefits	$65,238
Personnel Costs (Subtotal)	$374,795
Materials & Supplies	$71,292
Travel	$6,412
Publication Costs	$5,496
Federal Direct Costs	$457,995
Federal F&A Costs	$297,697
Approved Budget	$755,692
Total Amount of Federal Funds Obligated (Federal Share)	$755,692
TOTAL FEDERAL AWARD AMOUNT	$755,692
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$755,692

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
31	$755,692	$755,692
32	$668,163	$668,163
33	$655,038	$655,038
34	$641,523	$641,523
35	$627,604	$627,604

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Mental Health Research Grants
CFDA Number:	93.242
EIN:	1042103547A1
Document Number:	RMH117785I
PMS Account Type:	P (Subaccount)
Fiscal Year:	2020

IC	CAN	2020	2021	2022	2023	2024
MH	8022557	$755,692	$668,163	$655,038	$641,523	$627,604

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: 72-NBX / **OC**: 41022 / **Released**: [redacted] 03/20/2020
Award Processed: 03/27/2020 12:06:37 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 2R01MH117785-31

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 2R01MH117785-31

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.

d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VI Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01MH117785. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

This award is not subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – MH Special Terms and Conditions – 2R01MH117785-31

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

AWARD NOTICE:
This award has been made in response to the application submitted under the Funding Opportunity Announcement PA19-056 which can be referenced at: https://grants.nih.gov/grants/guide/pa-files/PA-19-056.html.

UNOBLIGATED BALANCE RESTRICTION:
The unobligated balance from Years 27-30 will be restricted and may not be used for any purpose. These funds may be used as an offset for the Year 32 award and/or to be carried into Year 32 after NIMH reviews the Federal Financial Report.

ADMINISTRATIVE REDUCTION:
In order to meet Institute program objectives within Fiscal Year 2020 budget constraints, the recommended levels for this grant have been reduced by 8.4% in the initial budget period 01, and 12.4% in the outyears to eliminate the proposed studies of CTE brains in Aim 4, and the CTE comparisons proposed in Aims 2c and 3c..

BUDGET/PROJECT PERIOD ADJUSTMENT:
This grant has been selected under the NIMH plan to redistribute grant workloads more evenly throughout the year. Consequently, the initial budget period reflects a 01/31/2021 end date. Subsequent budget periods will begin on February 01 and will be for a 12-month duration. Although this grant will have a slightly shorter budget period this year, it is awarded the full 12-month level of funds for the budget period. If needed, additional time may be requested at the end of the project period for a first no-cost extension through eRA Commons.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Heather Weiss
Email: heather.weiss@nih.gov **Phone**: 301-443-4415 **Fax**: 301-480-1956

Program Official: Andrew Rossi
Email: rossia@mail.nih.gov **Phone**: 301-443-1576 **Fax**: 301-402-4740

SPREADSHEET SUMMARY
GRANT NUMBER: 2R01MH117785-31

INSTITUTION: Trustees of Boston University

Budget	Year 31	Year 32	Year 33	Year 34	Year 35
Salaries and Wages	$309,557	$271,231	$271,231	$269,479	$269,479
Fringe Benefits	$65,238	$57,487	$57,487	$57,487	$57,487
Personnel Costs (Subtotal)	$374,795	$328,718	$328,718	$326,966	$326,966
Materials & Supplies	$71,292	$64,841	$57,763	$51,324	$44,640

Travel	$6,412	$6,132	$6,132	$6,132	$4,380
Publication Costs	$5,496	$5,256	$4,380	$4,380	$4,380
TOTAL FEDERAL DC	$457,995	$404,947	$396,993	$388,802	$380,366
TOTAL FEDERAL F&A	$297,697	$263,216	$258,045	$252,721	$247,238
TOTAL COST	$755,692	$668,163	$655,038	$641,523	$627,604

Facilities and Administrative Costs	Year 31	Year 32	Year 33	Year 34	Year 35
F&A Cost Rate 1	65%	65%	65%	65%	65%
F&A Cost Base 1	$457,995	$404,947	$396,993	$388,802	$380,366
F&A Costs 1	$297,697	$263,216	$258,045	$252,721	$247,238

Notice of Award

RESEARCH
Department of Health and Human Services
National Institutes of Health

NATIONAL INSTITUTE OF MENTAL HEALTH

Federal Award Date: 03/12/2020

Grant Number: 5R01MH117785-30 REVISED
FAIN: R01MH117785

Principal Investigator(s):
Helen Barbas, PHD

Project Title: Prefrontal Anatomic Pathways in Executive Control

DIANE MARIE BALDWIN
BOSTON UNIVERSITY
25 Buick Street
Boston, MA 022151300

Award e-mailed to: ospera@bu.edu

Period Of Performance:
Budget Period: 03/01/2019 – 03/31/2020
Project Period: 07/01/1987 – 03/31/2020

Dear Business Official:

The National Institutes of Health hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to Trustees of Boston University in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Mental Health of the National Institutes of Health under Award Number R01MH117785. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Heather Weiss
Grants Management Officer
NATIONAL INSTITUTE OF MENTAL HEALTH

Additional information follows

SECTION I – AWARD DATA – 5R01MH117785-30 REVISED

Award Calculation (U.S. Dollars)

Salaries and Wages	$242,759
Fringe Benefits	$56,380
Personnel Costs (Subtotal)	$299,139
Materials & Supplies	$57,750
Travel	$6,600
Publication Costs	$3,300
Federal Direct Costs	$366,789
Federal F&A Costs	$238,413
Approved Budget	$605,202
Total Amount of Federal Funds Obligated (Federal Share)	$605,202
TOTAL FEDERAL AWARD AMOUNT	$605,202
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$0

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
30	$605,202	$605,202

Fiscal Information:

CFDA Name:	Extramural Research Programs in the Neurosciences and Neurological Disorders
CFDA Number:	93.853
EIN:	1042103547A1
Document Number:	RNS024760H
PMS Account Type:	P (Subaccount)
Fiscal Year:	2019

IC	CAN	2019
MH	8022557	$605,202

NIH Administrative Data:
PCC: 72-NBX / **OC**: 41025 / **Released**: [redacted] 03/11/2020
Award Processed: 03/12/2020 12:02:26 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R01MH117785-30 REVISED

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 5R01MH117785-30 REVISED

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VI Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01MH117785. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

This award is not subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

This award represents the final year of the competitive segment for this grant. See the NIH Grants Policy Statement Section 8.6 Closeout for complete closeout requirements at: http://grants.nih.gov/grants/policy/policy.htm#gps.

A final expenditure Federal Financial Report (FFR) (SF 425) must be submitted through the eRA Commons (Commons) within 120 days of the period of performance end date; see the NIH Grants Policy Statement Section 8.6.1 Financial Reports, http://grants.nih.gov/grants/policy/policy.htm#gps, for additional information on this submission requirement. The final FFR must indicate the exact balance of unobligated funds and may not reflect any unliquidated obligations. There must be no discrepancies between the final FFR expenditure data and the Payment Management System's (PMS) quarterly cash transaction data. A final quarterly federal cash transaction report is not required for awards in PMS B subaccounts (i.e., awards to foreign entities and to Federal agencies). NIH will close the awards using the last recorded cash drawdown level in PMS for awards that do not require a final FFR on expenditures or quarterly federal cash transaction reporting. It is important to note that for financial closeout, if a grantee fails to submit a required final expenditure FFR, NIH will close the grant using the last recorded cash drawdown level. If the grantee submits a final expenditure FFR but does not reconcile any discrepancies between expenditures reported on the final expenditure FFR and the

last cash report to PMS, NIH will close the award at the lower amount. This could be considered a debt or result in disallowed costs.

A Final Invention Statement and Certification form (HHS 568), (not applicable to training, construction, conference or cancer education grants) must be submitted within 120 days of the expiration date. The HHS 568 form may be downloaded at: http://grants.nih.gov/grants/forms.htm. This paragraph does not apply to Training grants, Fellowships, and certain other programs—i.e., activity codes C06, D42, D43, D71, DP7, G07, G08, G11, K12, K16, K30, P09, P40, P41, P51, R13, R25, R28, R30, R90, RL5, RL9, S10, S14, S15, U13, U14, U41, U42, U45, UC6, UC7, UR2, X01, X02.

Unless an application for competitive renewal is submitted, a Final Research Performance Progress Report (Final RPPR) must also be submitted within 120 days of the period of performance end date. If a competitive renewal application is submitted prior to that date, then an Interim RPPR must be submitted by that date as well. Instructions for preparing an Interim or Final RPPR are at: https://grants.nih.gov/grants/rppr/rppr_instruction_guide.pdf. Any other specific requirements set forth in the terms and conditions of the award must also be addressed in the Interim or Final RPPR. *Note that data reported within Section I of the Interim and Final RPPR forms will be made public and should be written for a lay person audience*.

NIH strongly encourages electronic submission of the final invention statement through the Closeout feature in the Commons, but will accept an email or hard copy submission as indicated below.

Email: The final invention statement may be e-mailed as PDF attachments to: NIHCloseoutCenter@mail.nih.gov.

Hard copy: Paper submissions of the final invention statement may be faxed to the NIH Division of Central Grants Processing, Grants Closeout Center, at 301-480-2304, or mailed to:

National Institutes of Health
Office of Extramural Research
Division of Central Grants Processing
Grants Closeout Center
6705 Rockledge Drive
Suite 5016, MSC 7986
Bethesda, MD 20892-7986 (for regular or U.S. Postal Service Express mail)
Bethesda, MD 20817 (for other courier/express deliveries only)

NOTE: If this is the final year of a competitive segment due to the transfer of the grant to another institution, then a Final RPPR is not required. However, a final expenditure FFR is required and should be submitted electronically as noted above. If not already submitted, the Final Invention Statement is required and should be sent directly to the assigned Grants Management Specialist.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – MH Special Terms and Conditions – 5R01MH117785-30 REVISED

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement

Section 1.2 for NIH definition of Clinical Trial.

REVISION #1
BUDGET AND PROJECT PERIOD END DATES:
This award is revised to adjust the current budget period and project period end dates due to the funding of the renewal grant application 2R01MH117785-31.

THIS REVISED AWARD SUPERSEDES THE NOTICE OF AWARD ISSUED ON 02/11/2019. THE FOLLOWING TERMS & CONDITIONS REMAIN IN EFFECT.

AWARD NOTICE:
This award has been made in response to the application submitted under the Funding Opportunity Announcement PA13-302 which can be referenced at: https://grants.nih.gov/grants/guide/pa-files/PA-13-302.html.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Heather Weiss
Email: heather.weiss@nih.gov **Phone**: 301-443-4415 **Fax**: 301-480-1956

Program Official: Andrew Rossi
Email: rossia@mail.nih.gov **Phone**: 301-443-1576 **Fax**: 301-402-4740

SPREADSHEET SUMMARY
GRANT NUMBER: 5R01MH117785-30 REVISED

INSTITUTION: Trustees of Boston University

Budget	Year 30
Salaries and Wages	$242,759
Fringe Benefits	$56,380
Personnel Costs (Subtotal)	$299,139
Materials & Supplies	$57,750
Travel	$6,600
Publication Costs	$3,300
TOTAL FEDERAL DC	$366,789
TOTAL FEDERAL F&A	$238,413
TOTAL COST	$605,202

Facilities and Administrative Costs	Year 30
F&A Cost Rate 1	65%
F&A Cost Base 1	$366,789
F&A Costs 1	$238,413

A. COVER PAGE

Project Title: Prefrontal Anatomic Pathways in Executive Control	
Grant Number: 5R01MH117785-32	**Project/Grant Period:** 07/01/1987 - 01/31/2025
Reporting Period: 04/01/2020 - 01/31/2021	**Requested Budget Period:** 02/01/2021 - 01/31/2022
Report Term Frequency: Annual	**Date Submitted:** 12/14/2020
Program Director/Principal Investigator Information: HELEN BARBAS , BA MS PHD **Phone Number:** 617-353-5036 **Email:** barbas@bu.edu	**Recipient Organization:** BOSTON UNIVERSITY (CHARLES RIVER CAMPUS) BOSTON UNIVERSITY 881 COMMONWEALTH AVENUE BOSTON, MA 022151390 **DUNS:** 049435266 **EIN:** 1042103547A1 **RECIPIENT ID:**
Change of Contact PD/PI: NA	
Administrative Official: DIANE MARIE BALDWIN 25 Buick Street Boston, MA 02215 **Phone number:** 6173534365 **Email:** ospera@bu.edu	**Signing Official:** DIANE MARIE BALDWIN 25 Buick Street Boston, MA 02215 **Phone number:** 6173534365 **Email:** ospera@bu.edu
Human Subjects: No	**Vertebrate Animals:** Yes
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Goal-directed behavior requires selection of external and internal signals, weighed in context with memory of prior experience for action. These processes engage the prefrontal cortex (PFC) and medial temporal lobe (MTL) cortices, which are often disrupted in psychiatric diseases. Our goal is to study in rhesus monkeys a pathway from medial frontal area 25 (A25) to MTL, and intrinsic connections within MTL, in the context of the excitatory-inhibitory make-up in both regions in monkeys and humans. These studies are rooted in our Structural Model, which predicts the laminar pattern and strength of connections, the sequence of information flow between areas, the plasticity-stability continuum of areas, and predilection of some areas to psychiatric diseases. Depression is associated with disruption of A25 and MTL with marked hyperactivity in A25, affecting the integrative processes of interoception, emotion and memory. The above goals are identical to those originally proposed. The goals were modified to focus on the normal monkey and human cortex. Our goals were expanded to also study features in the sequence of pathways from lateral PFC to ACC A32 and then to A25 based on our predictive Structural Model, to help understand nodes that may be vulnerable to disruption in depression in humans.

Specific Aim 1: The synaptic targets of A25 within the excitatory-inhibitory environment of MTL A28
Since the excitatory and inhibitory make-up of A28 is critical for communication with the hippocampus and high-order association areas, in pathways that process in context memory and emotions, we will test:
1a: the hypothesis that the ratio of excitatory to inhibitory neurons labeled for parvalbumin (PV), calbindin (CB) and calretinin (CR) varies in parallel across layers of A28 in rhesus monkeys and humans.
1b: if a predominant pathway from A25 to the deep layers of A28 forms synapses with PV and CR neurons.

Specific Aim 2: Parallels in laminar connections within MTL in monkeys
Based on evidence that cortical laminar structure varies systematically, we will test these hypotheses:
2a: Laminar connections of A28 with other MTL areas vary by the relational rules of the Structural Model.
2b: Laminar specific connections within MTL interface preferentially with distinct inhibitory neurons labeled with PV, CB or CR in monkeys.

Specific Aim 3: Comparison of neurons, NMDA receptors, and glia in A25 in monkeys and humans
Based on evidence that excitatory and inhibitory neurons regulate function, and excitation mediated by NMDA receptors in A25 increases in depression, and is antagonized by ketamine, we will test these hypotheses:
3a: The ratio of excitatory to inhibitory neurons labeled for PV, CB and CR varies in parallel across layers in A25 in rhesus monkeys and humans.
3b: In primate A25 NMDA receptors are denser on CR neurons, which are disinhibitory to excitatory neurons, suggesting that NMDA antagonism can curb run-away excitation in A25 in depression.
3c: Pathways from lateral PFC to ACC A32 and then to A25 follow the rules of the Structural Model and interface with distinct classes of inhibitory neurons in monkeys.

Neural pathways in rhesus monkeys will be labeled with distinct neural tracers, combined with multiple labeling for the neurochemical classes of PV, CB, and CR inhibitory neurons for laminar-specific comparison with human cortex. Quantitative data will be collected using correlated light, confocal and electron microscopy (EM), and analyzed using statistical analyses and synthesized via modeling. Findings will establish the circuit basis for key frontal and MTL cortices associated with interoception, emotion and memory, in processes that are disrupted in depression.

Innovation: This is the first study that is driven by a predictive model of connections established in non-human primates and applied to study the human prefrontal cortex. The studies in non-human primates and human brains will employ an unprecedented range of levels from the system to the synapse. The studies will proceed in the context of the excitatory and inhibitory environments of the MTL and A25 regions.

B.1.a Have the major goals changed since the initial competing award or previous report?

Yes

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File Uploaded : Y1nimh31forDec20StudiesAndResults.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File Uploaded : B4ProfessionalDevY31oneOf54MKateR.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The paper below was chosen by the Journal of Neuroscience for press release, and was picked up and discussed by US and foreign news organizations. The findings were also highlighted in This Week in the Journal of Neuroscience, and featured on the cover. The findings were also discussed in a story at a central research weekly of Boston University (the Brink, slated for publication this Fall).

Joyce, M.K.P., García-Cabezas, M.A. and John, Y.J. and Barbas, H. J Neurosci. 2020, 40(43):8306-8328. Serial Prefrontal Pathways Are Positioned to Balance Cognition and Emotion in Primates. PMID: 32989097 PMCID: PMC7577604

The following links are of news media that have covered our findings:

https://scitechdaily.com/area-32-how-the-brain-balances-emotion-and-reason/

https://www.sciencedaily.com/releases/2020/09/200928133155.htm

https://es.paperblog.com/el-dificil-pero-imprescindible-equilibrio-entre-razon-y-emocion-en-plena-pandemia-6303050/

https://www.laprensagrafica.com/salud/El-dificil-pero-imprescindible-equilibrio-entre-razon-y-emocion-en-plena-pandemia-20201116-0071.html

https://theconversation.com/el-dificil-pero-imprescindible-equilibrio-entre-razon-y-emocion-en-plena-pandemia-147863

http://ct.moreover.com/?a=43237973695&p=1pl&v=1&x=0fdHQqj7XmpIvzSVCANUtQ

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

In year 2 of the 5 year of support we plan to study the inhibitory make-up of the three neurochemical classes of inhibitory neurons in A25 in the human cortex. This information is needed to establish whether there are parallels between monkeys and humans in the inhibitory microenvironment in A25, which is prerequisite to understanding how neural pathways to A25 may affect neural dynamics for normal function and in depression.
We will also begin to investigate the inhibitory microenvironment in medial temporal A28 (the entorhinal cortex, Specific Aim 1a) in rhesus monkey and normal human cortex, as a prelude to study the pattern of innervation of a robust pathway from

A25 to entorhinal (A28) cortex in rhesus monkeys.

B.2 (Y1nimh31forDec20StudiesAndResults.pdf)

Studies and Results

The neurochemical inhibitory environment of subgenual area 25 (A25)

One of our goals was to study the inhibitory microenvironment in A25, which is essential to understand disruption in depression. We thus compared the density of neurons labeled for parvalbumin (PV), calbindin (CB), and calretinin (CR) in A25 in rhesus monkeys, and compared it with nearby A32, and lateral prefrontal A46 (expanded Aim 3a for monkey brain). The CB antibody also labels some pyramidal neurons in cortex, and we studied cellular features to differentiate them from inhibitory neurons. CB+ pyramidal (excitatory) neurons could be reliably distinguished from inhibitory neurons by labeling intensity and morphology. CB+ pyramidal neurons were lightly labeled in the cytoplasm but not in the nucleus. In contrast, CB+ inhibitory neurons appeared uniformly dark, and were non-pyramidal but multipolar. Multiple-labeling for GAD-67 (a synthetic enzyme for GABA), GABA and CB supported distinction of CB+ neurons into excitatory and inhibitory classes. Stereological analysis revealed that the density of CB+ pyramidal neurons was higher in superficial than in deep layers, and was highest in A25 among the three prefrontal cortices studied.

We found that PV neuron density in the middle to deep layers of A46 was almost double that of A32 and A25, while CB and CR neuron densities were comparable across areas (one-way ANOVA, $F(2,6) = 22.997$, $p=0.002$]. PV neurons were localized mostly in the middle to deep layers in all areas, while CR and darkly stained (inhibitory) CB neurons were localized preferentially in the superficial layers. These findings depict a changing laminar population of inhibitory neurons at each node, and demonstrate that limbic prefrontal areas A32 and A25 are comparatively impoverished in middle-layer PV inhibitory neurons as compared to A46. These findings suggest differences in inhibitory dynamics among prefrontal cortices.

Selectivity of NMDA glutamate receptors on excitatory and distinct inhibitory neurons

We then examined in A25 the distribution of NMDAR on inhibitory neurons by their label of calcium binding proteins (PV, CB, CR) and pyramidal-shaped excitatory neurons using double immunofluorescence labeling for the calcium binding proteins and NR1, the obligatory subunit present in NMDARs (Specific Aim 3b for monkey brain). The rationale is based on evidence that NMDA receptors may mediate excitatory effects in A25 and increased excitation in depression. We found that pyramidal neurons in all layers were enriched in NMDARs. We also found a moderate level of NR1 labeling around the cytoplasm of the inhibitory neurons.

How serial pathways from lateral PFC to ACC A32 to A25 may affect circuit dynamics

We found that feedforward pathways from lateral A46 innervated ACC A32, which in turn innervated all layers of A25, in a pattern that is consistent with our Structural Model. In the pathway from A32 to A25 we found that about a quarter of the synapses were on presumed inhibitory neurons, as labeled using PV, CB and CR, using confocal and electron microscopy. Among these, A32 axon boutons preferentially targeted CR postsynaptic sites in the upper layers of A25, and were more likely to target PV postsynaptic sites in the deep layers than in the superficial layers.

One of the most striking features of the A32 pathway termination in A25 was its robust density, evident even at very high resolution at the synaptic level. We next investigated whether the A32 pathway was similar or different from unlabeled terminations forming asymmetric (presumed excitatory) synapses in the neuropil of A25. We found that A32 boutons were significantly larger than those in the neuropil.

Other factors also affect synaptic efficacy, such as the presence of mitochondria in presynaptic terminations, the postsynaptic density (PSD) surface area, and the presence of a perforated PSD. The PSD surface area increases when synapses are perforated, and is correlated with the magnitude of response in the postsynaptic neuron. Compared with excitatory synapses in the surrounding neuropil, we found that almost double the number of A32 synapses in A25 contained mitochondria ($p=0.014$) and significantly more formed perforated synapses ($p=0.003$).

The spine apparatus is a specialized endoplasmic reticulum compartment in the spine head that is associated with plasticity, calcium dynamics, and second messenger systems. We found that the A32 pathway formed synapses on more spines containing a spine apparatus than terminations in the surrounding neuropil ($p=0.006$]. Collectively, these findings indicate that A32 has a major influence on A25, and the structural features of the pathway suggest high efficacy to propagate signals.

a. Significance:

Differences in inhibitory neuron composition within the cortical column and across cortical areas shown here may significantly contribute to the remarkable behavioral flexibility in primates, and contribute to transient

changes in synchrony. Variations in inhibitory neuron density may help explain functional specializations across prefrontal areas.

The feedforward pathway from lateral PFC to ACC A32, and then A32 innervation of A25 has a special significance based on the inverse relationship in activity between lateral PFC and A25 in humans. This relationship can be best explained through interaction with excitatory as well as inhibitory neurons in the sequential pathway. A32 is an intermediary in the circuit, because direct connections between lateral PFC and A25 are sparse. A32 is a hub that links functionally disparate prefrontal areas, as shown in our previous studies, and participates in cognitive, attentional, affective, and default mode networks. It is thus positioned to balance diverse cortical processes as an intermediary between lateral PFC and A25.

A32 terminations in the deep layers of A25 interacted more heavily with PV inhibitory neurons, where they are more abundant. PV neurons exercise strong perisomatic inhibition of nearby pyramidal neurons. Notably, the deep layer neurons in A25 project to other prefrontal areas, as the ultimate feedback system (Joyce & Barbas, 2018). The powerful inhibitory system that A32 engages in the deep layers of A25 likely has direct impact on this feedback system, which also innervates the amygdala, hypothalamus, and ventral striatum, supporting a role in homeostasis. Thus, A32 terminations in the deep layers of A25 may be a circuit mechanism to dampen affect-associated A25 activity within prefrontal networks and downstream autonomic projections, to allow a switch to cognitive tasks based on context.

The functional implications of the pathway from A32 to A25 are strengthened by its synaptic features. First, compared to unlabeled synapses in the neuropil, A32 boutons were larger, suggesting a higher input weight on local neurons. Second, A32 terminations were more likely to contain mitochondria, which are characteristic of active synapses. And third, A32 boutons formed more perforated synapses in A25, which increase the surface area and number of postsynaptic excitatory receptors. Together, these findings suggest that the A32 hub has a pronounced input weight in A25.

We recently showed that the Structural Model has been validated to predict the connectional pathology of complex psychiatric disorders in humans (Zikopoulos *et al.*, 2018). Mood disorders involve network dysfunction among many distributed brain areas, but the prefrontal areas studied here are consistently implicated. Inverse functional correlation has been associated between the metabolic activity of lateral PFC and subgenual A25 in depression. Significantly, many studies have cited pretreatment metabolism of A32 as a predictor of remission. This evidence implies that the reliability of the serial pathway is crucial for emotional equilibrium. Our findings suggest that when lateral PFC activity is attenuated, the serial pathway cannot dampen A25 activity in depression. Runaway activity in A25 may lead to iterative drive of the default mode network in depression, a state correlated with rumination and excessive negatively-valenced self-directed processes. The output of A25 is heavily weighted toward other prefrontal areas involved in emotion and internal states (Joyce & Barbas, 2018). A robust serial pathway from lateral PFC may dampen excessive activity in A25 and prevent perseverative cycling within the network. There is evidence that rTMS in lateral PFC modulates connectivity of the subgenual cingulate with the default mode network, and produces antidepressant effects. Unsuccessful rTMS attempts may reflect a weakened serial pathway.

The rich populations of NMDARs we found on pyramidal neurons in A25 in monkeys, are also densest among prefrontal areas in humans. One way to dampen A25 hyperactivity in depression may be through NMDAR antagonism, which may contribute to ketamine's rapid antidepressant effects in humans. In addition, while NMDARs were expressed on all inhibitory neurons in A25, CR neurons were the most numerous. In humans CR populations have expanded in number and architectonic detail. Because of their disinhibitory nature in the upper layers, we speculate that the superficial layer CR system could be one intriguing possibility for the ultra-rapid effects of intranasal ketamine, which is thought to target A25. A driving force of ketamine's effect in A25 may thus reflect reduction in activity of pyramidal neurons and the numerous superficial layer CR neurons. The binding of NMDAR antagonists on pyramidal neurons and superficial layer CR neurons in patients with depression may mimic the regulatory effects of the neurotypical serial pathway revealed here.

The following papers associated with our progress or broader goals were linked to this grant:

Joyce, M.K.P., García-Cabezas, M.A. and John, Y.J. and Barbas, H. J Neurosci. 2020, 40(43):8306-8328. Serial Prefrontal Pathways Are Positioned to Balance Cognition and Emotion in Primates. PMID: 32989097 PMCID: PMC7577604

Wells AM, García-Cabezas MÁ, Barbas H. Topological atlas of the hypothalamus in adult rhesus monkey. Topological atlas of the hypothalamus in adult rhesus monkey. Brain Struct Funct. 2020, 225(6):1777-1803. PMID: 32556476 PMCID: PMC7321918

B.4 (B4ProfessionalDevY31oneOf54MKateR.pdf)

One graduate student, Mary Kate Joyce, successfully defended her dissertation in our cross-university Graduate Program in Neuroscience (GPN), having conducted her research in my Neural Systems Lab. Mary Kate stayed on as a postdoctoral student to complete some studies in progress, while she also applied and secured a postdoctoral position at Yale. She will continue to work in our lab during the pandemic until she can be hired safely when the vaccine becomes available. Last Spring she participated in teaching some of the labs in a human neuroanatomy course to gain teaching experience for her future career. She will attend the Annual meeting of the Society for Neuroscience and present her latest findings on line in January, 2021 (abstract below). Mary Kate recently gave an invited talk for the Autonomous University of Madrid, Spain. A major paper from her research was published recently and was highlighted in This Week in the Journal (of Neuroscience), and featured on the cover. The article was received with considerable interest, including discussions in the US and foreign press. The article was also recently chosen by the Editorial Board of the Journal of Neuroscience in a group of 8 Spotlights for 2020, selected for articles that receive the strongest reviews.

Joyce MKP, Barbas H. Specialized projections of the primate subgenual cingulate area 25 to the amygdala. Neurosci. Abstr., Jan. 2021.

Joyce, M.K.P., García-Cabezas, M.A. and John, Y.J. and Barbas, H. J Neurosci. 2020, 40(43):8306-8328. Serial Prefrontal Pathways Are Positioned to Balance Cognition and Emotion in Primates. PMID: 32989097 PMCID: PMC7577604.

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
Complete	García-Cabezas MÁ, Zikopoulos B, Barbas H. The Structural Model: a theory linking connections, plasticity, pathology, development and evolution of the cerebral cortex. Brain structure & function. 2019 April;224(3):985-1008. PubMed PMID: 30739157; PubMed Central PMCID: PMC6500485; DOI: 10.1007/s00429-019-01841-9.
Complete	Timbie C, García-Cabezas MÁ, Zikopoulos B, Barbas H. Organization of primate amygdalar-thalamic pathways for emotions. PLoS biology. 2020 February;18(2):e3000639. PubMed PMID: 32106269; PubMed Central PMCID: PMC7064256; DOI: 10.1371/journal.pbio.3000639.
Complete	Wells AM, García-Cabezas MÁ, Barbas H. Topological atlas of the hypothalamus in adult rhesus monkey. Brain structure & function. 2020 July;225(6):1777-1803. PubMed PMID: 32556476; PubMed Central PMCID: PMC7321918; DOI: 10.1007/s00429-020-02093-8.
Complete	Joyce MKP, García-Cabezas MÁ, John YJ, Barbas H. Serial Prefrontal Pathways Are Positioned to Balance Cognition and Emotion in Primates. The Journal of neuroscience : the official journal of the Society for Neuroscience. 2020 October 21;40(43):8306-8328. PubMed PMID: 32989097; PubMed Central PMCID: PMC7577604; DOI: 10.1523/JNEUROSCI.0860-20.2020.
PMC Journal - In process	Wang J, John Y, Barbas H. Pathways for Contextual Memory: The Primate Hippocampal Pathway to Anterior Cingulate Cortex. Cerebral cortex (New York, N.Y. : 1991). 2020 November 18. PubMed PMID: 33207365; DOI: 10.1093/cercor/bhaa333.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
username	Y	Barbas, Helen	BA,MS,PHD	PD/PI	percent effort					NA
	N	Medalla, Maria	BS,PHD	Co-Investigator						NA
	N	Zikopoulos, Vasileios	BS,MS,PHD	Co-Investigator						NA
	N	Marshall, Laura		Research Assistant						NA
	N	Holz, Jess		Technician						NA
	N	Mark, Abigail		Technician						NA
	N	Banik, Shirmani		Consultant						NA
	N	John, Yohan		Co-Investigator						NA
	N	Joyce, MaryKate		Staff scientist (Doctoral level)						NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

No

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

Yes

G.8 PROJECT/PERFORMANCE SITES

Organization Name	DUNS	Congressional District	Address
Primary: BOSTON UNIVERSITY (CHARLES RIVER CAMPUS)	049435266	MA-007	BOSTON UNIVERSITY
BOSTON UNIVERSITY CHARLES RIVER CAMPUS	049435266		BOSTON UNIVERSITY 881 COMMONWEALTH AVENUE BOSTON, MA 022151390

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

Yes

Estimated unobligated balance: $256,067

G.10.b Provide an explanation for unobligated balance:
The amount left is equal to about 7% over the allowed carryover of 25%. The amount left is due to delay in hiring additional technical personnel for this project due to the pandemic.

G.10.c If authorized to carryover the balance, provide a general description of how it is anticipated that the funds will be spent
We will use about the remaining funds to support in part new research personnel, either at the postdoctoral level or graduate student level to work directly on the projects for this grant, as well as for supplies for assays that we were not able to conduct during the early months of the pandemic.

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period? No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

A. COVER PAGE

Project Title: Prefrontal Anatomic Pathways in Executive Control	
Grant Number: 5R01MH117785-33	**Project/Grant Period:** 07/01/1987 - 01/31/2025
Reporting Period: 03/26/2021 - 01/31/2022	**Requested Budget Period:** 02/01/2022 - 01/31/2023
Report Term Frequency: Annual	**Date Submitted:** 12/07/2021
Program Director/Principal Investigator Information: HELEN BARBAS , BA MS PHD **Phone Number:** 617-353-5036 **Email:** barbas@bu.edu	**Recipient Organization:** BOSTON UNIVERSITY (CHARLES RIVER CAMPUS) BOSTON UNIVERSITY 881 COMMONWEALTH AVENUE BOSTON, MA 022151390 **DUNS:** 049435266 **EIN:** 1042103547A1 **RECIPIENT ID:**
Change of Contact PD/PI: NA	
Administrative Official: DIANE MARIE BALDWIN 25 Buick Street Boston, MA 02215 **Phone number:** 6173534365 **Email:** ospera@bu.edu	**Signing Official:** DIANE MARIE BALDWIN 25 Buick Street Boston, MA 02215 **Phone number:** 6173534365 **Email:** ospera@bu.edu
Human Subjects: No	**Vertebrate Animals:** Yes
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Goal-directed behavior requires selection of external and internal signals, weighed in context with memory of prior experience for action. These processes engage the prefrontal cortex (PFC) and medial temporal lobe (MTL) cortices, which are often disrupted in psychiatric diseases. Our goal is to study in rhesus monkeys a pathway from medial frontal area 25 (A25) to MTL, and intrinsic connections within MTL, in the context of the excitatory-inhibitory make-up in both regions in monkeys and humans. These studies are rooted in our Structural Model, which predicts the laminar pattern and strength of connections, the sequence of information flow between areas, the plasticity-stability continuum of areas, and predilection of some areas to psychiatric diseases. Depression is associated with disruption of A25 and MTL with marked hyperactivity in A25, affecting the integrative processes of interoception, emotion and memory. The above goals are identical to those originally proposed. The goals were modified to focus on the normal monkey and human cortex. Our goals were expanded to also study features in the sequence of pathways from lateral PFC to ACC A32 and then to A25 based on our predictive Structural Model, to help understand nodes that may be vulnerable to disruption in depression in humans.

Specific Aim 1: The synaptic targets of A25 within the excitatory-inhibitory environment of MTL A28
Since the excitatory and inhibitory make-up of A28 is critical for communication with the hippocampus and high-order association areas, in pathways that process in context memory and emotions, we will test:
1a: the hypothesis that the ratio of excitatory to inhibitory neurons labeled for parvalbumin (PV), calbindin (CB) and calretinin (CR) varies in parallel across layers of A28 in rhesus monkeys and humans.
1b: if a predominant pathway from A25 to the deep layers of A28 forms synapses with PV and CR neurons.

Specific Aim 2: Parallels in laminar connections within MTL in monkeys
Based on evidence that cortical laminar structure varies systematically, we will test these hypotheses:
2a: Laminar connections of A28 with other MTL areas vary by the relational rules of the Structural Model.
2b: Laminar specific connections within MTL interface preferentially with distinct inhibitory neurons labeled with PV, CB or CR in monkeys.

Specific Aim 3: Comparison of neurons, NMDA receptors, and glia in A25 in monkeys and humans
Based on evidence that excitatory and inhibitory neurons regulate function, and excitation mediated by NMDA receptors in A25 increases in depression, and is antagonized by ketamine, we will test these hypotheses:
3a: The ratio of excitatory to inhibitory neurons labeled for PV, CB and CR varies in parallel across layers in A25 in rhesus monkeys and humans.
3b: In primate A25 NMDA receptors are denser on CR neurons, which are disinhibitory to excitatory neurons, suggesting that NMDA antagonism can curb run-away excitation in A25 in depression.
3c: Pathways from lateral PFC to ACC A32 and then to A25 follow the rules of the Structural Model and interface with distinct classes of inhibitory neurons in monkeys.

Neural pathways in rhesus monkeys will be labeled with distinct neural tracers, combined with multiple labeling for the neurochemical classes of PV, CB, and CR inhibitory neurons for laminar-specific comparison with human cortex. Quantitative data will be collected using correlated light, confocal and electron microscopy (EM), and analyzed using statistical analyses and synthesized via modeling. Findings will establish the circuit basis for key frontal and MTL cortices associated with interoception, emotion and memory, in processes that are disrupted in depression.

Innovation: This is the first study that is driven by a predictive model of connections established in non-human primates and applied to study the human prefrontal cortex. The studies in non-human primates and human brains will employ an unprecedented range of levels from the system to the synapse. The studies will proceed in the context of the excitatory and inhibitory environments of the MTL and A25 regions.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File Uploaded : Y2nimh32forDec21StudiesAndResultsOnly.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

My student, Mary Kate Joyce, who completed her doctoral studies in my laboratory, was invited to develop a video of her work here, to feature during the Society for Neuroscience meeting in November 2021. A link to the video she prepared can be obtained from the Society for Neuroscience website.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

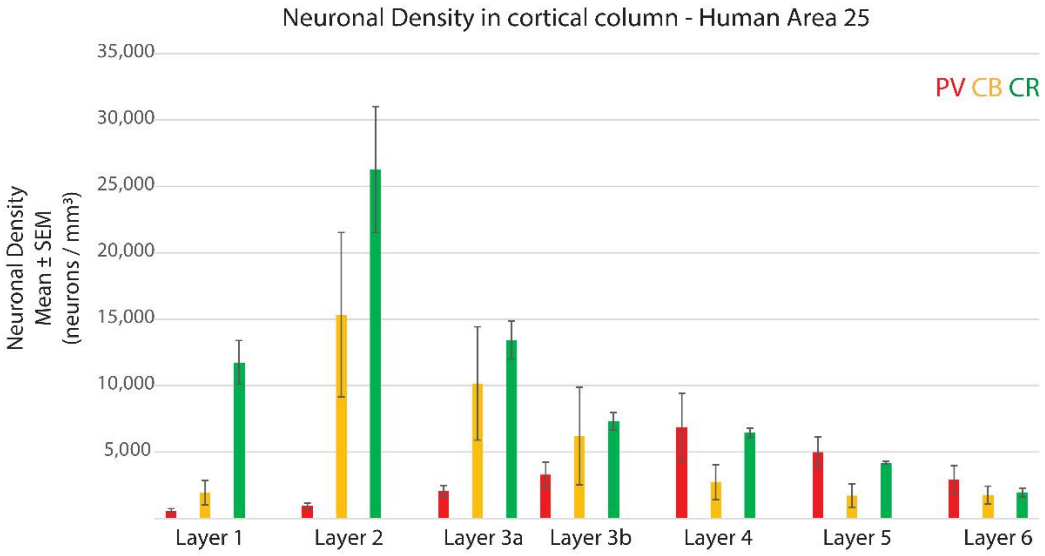
In year 3 we plan to expand our study of the composition of A25 in the human cortex by unbiased estimate of all neurons in A25 and all types of glia. This will make it possible to get for the first time this type of quantitative data for human A25.
We will also continue our study on the inhibitory microenvironment in medial temporal A28 (the entorhinal cortex, Specific Aim 1a) in rhesus monkey and normal human cortex. This study is needed for our goal to investigate a strong pathway from A25 to entorhinal (A28) cortex in rhesus monkeys in subsequent years.

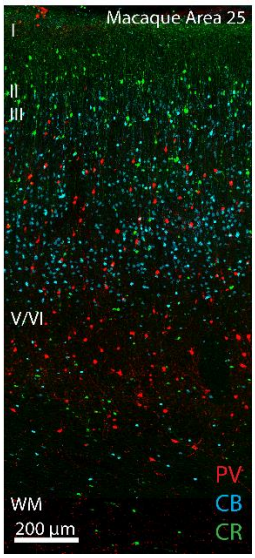
Studies and Results

The subgenual area 25 (A25) inhibitory microenvironment in human matches the rhesus monkey

In our study of the inhibitory microenvironment in subgenual A25 in primates, we initiated a study on the human brain, in order to compare with the rhesus monkey. To map the inhibitory microenvironment of A25 in humans we investigated the density of neurons labeled for parvalbumin (PV), calbindin (CB), and calretinin (CR) in the human cortex (expanded Aim 3a). We had previously established that the CB antibody also labels some pyramidal neurons in the rhesus monkey cortex, and here we found that the same applies for A25 in the human cortex. Briefly, as in the monkey, CB pyramidal neurons are lightly labeled and have a distinct pyramidal shape. By contrast, CB+ inhibitory neurons appeared uniformly dark, and were non-pyramidal in shape. Multiple-labeling for GABA, GAD-67 (a synthetic enzyme for GABA), and CB supported distinction of CB+ neurons into excitatory and inhibitory groups.

We used unbiased stereologic methods to estimate the laminar density of PV, CB, and CR neurons in A25 of *post-mortem* neurotypical human brains for comparison with data in the rhesus macaque. We found that CR neurons are denser in A25 than PV or CB. CR neurons were concentrated most densely in superficial layers I-IIIa of A25. Conversely, PV neurons were predominantly found in mid-deep layers (III-VI), while CB dark-labeled neurons had a more even distribution among layers, with somewhat higher density in the mid-superficial layers II and IIIa. As shown in Figure 1 below, these findings in human A25 show a striking resemblance to the rhesus macaque.





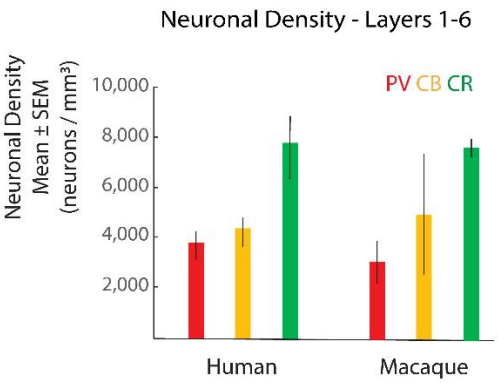


Figure 1. Comparison of the inhibitory microenvironment in A25 in humans and rhesus macaques

A25 receives the strongest connections from the hippocampus within the anterior cingulate cortices (ACC)

One of the key features of A25 is its association with goal directed actions within an emotional context, influenced by input from the hippocampus. We investigated the hippocampal pathway to A25, which is one of only a few prefrontal areas that receives direct hippocampal pathways. Within the ACC (A24a, A25 and A32), the densest hippocampal terminations innervated posterior A25, a region involved in affective processing and autonomic regulation. The hippocampal pathway innervated mostly excitatory neurons (~90%), an unusual high fraction by comparison with other prefrontal cortices, which innervate about 20-30% of postsynaptic sites that belong to inhibitory neurons. Among the small fraction of inhibitory targets, hippocampal terminations in A25 preferentially innervated calretinin neurons, a pattern that differs markedly from rodents. We also found that hippocampal terminations innervated spines with D1 receptors, particularly in the deep layers of A25, where D1 receptors were denser than in the upper layers. Our findings suggest that these hippocampal pathways may enable dopamine to enhance information transfer from the hippocampus to A25 and contribute to dopaminergic influence downstream on goal-directed action and emotional control by prefrontal cortices; these processes may be disrupted by excessive dopamine release during uncontrollable stress.

Significance:

Figure 1 shows striking parallels in the distribution of distinct classes of inhibitory neurons in the rhesus monkey and human A25. This evidence lends significant support to use the rhesus monkey as a primate model system to study the human cortex. In humans, the activity of A25 increases in emotional arousal. A25 has strong connections with ACC A32, which, in turn, is connected widely within the prefrontal cortex, including lateral prefrontal areas associated with cognition and action. Our recent studies have provided critical information about the relationship of these pathways with excitatory as well as with inhibitory neurons, which can modulate the activity of neurons at the site of termination in A25 (Joyce and Barbas, J. Neuroscience, 2020). A32 innervates preferentially the powerful PV neurons in the deep layers of A25, which project to central autonomic structures. Activity in A25 is upregulated in clinical depression, upregulating also autonomic structures. The inhibitory microenvironment in A25, and its interaction with pathways in monkeys provides strong insights about circuit mechanisms that contribute to run-away activity in clinical depression.

Our recent study of a strong hippocampal pathway to A25 has significant implications as to how context can influence a cortical region associated with emotional processing and central autonomic functions. The hippocampal pathway innervated both the upper and deep layers of A25, suggesting a combination of ‘feedback’ and ‘feedforward’ patterns, by analogy with cortical sensory systems. The feedback component, which innervates the upper layers of A25, contacts the distal and mid-apical dendrites of pyramidal neurons, suggesting a modulatory role. The feedforward component of the projection, which innervates the deep layers of posterior A25, may drive neurons that send broad feedback type projections to cortex (Joyce and Barbas, 2018). The deep layers of A25 also project robustly to the amygdala in primates, and other subcortical limbic structures that have key roles in emotion and motivation.

Consistent with upregulation of A25 in depression, is our finding of a high density of D1 dopamine receptors in the deep layers of A25. This evidence provides another mechanism for elevating activity in A25 during stress, when dopamine levels are high, leading to upregulation of autonomic structures. High activity in A25 has been linked to de-motivating and anhedonic effects in both rodents and primates (e.g., Alexander et al., 2019), and may contribute to low motivation and anhedonia seen in patients with major depression, who also show high functional connectivity between hippocampus and prefrontal cortex (see discussion in Wang et al., 2021). Normal levels of dopamine may allow action initiation, but excessive dopamine may interfere with action and motivation, reminiscent of an “inverted U” curve relating motivation with dopamine, analogous to the performance curves observed in attention deficit disorders in primates [reviewed in (Arnsten et al., 2015)].

The hippocampal pathway to A25, and the possible dopaminergic modulation of this projection suggest a mechanism that links hippocampal processing of context, uncertainty and novelty with cortical modulation of motivation. These effects appear to be similar across species, but our findings suggest a distinct pattern of hippocampal signaling in prefrontal cortex in primates compared to rats or mice.

The following papers associated with our progress were linked to this grant.

Wang, J., John, Y. and Barbas, H. Pathways for contextual memory: the primate hippocampal pathway to anterior cingulate cortex. Cerebral Cortex, 2021 Feb 5;31(3):1807-1826. doi: 10.1093/cercor/bhaa333. PMID: 33207365 PMCID: PMC7869091 (available on 2021-11-18)

Kenwood, M.M., Kalin, N.H. and Barbas, H. The prefrontal cortex, pathological anxiety, and anxiety disorders. Neuropsychopharmacology, 2021, in press. (PMID: 34400783; in process citation)

One of my recent doctoral graduate students, Mary Kate Joyce, received her PhD from our cross-university Graduate Program in Neuroscience (GPN), having conducted her research in my Neural Systems Lab. Mary Kate stayed on as a postdoctoral student to complete some studies in progress, while she also applied and secured a postdoctoral position at Yale. She has since moved to Yale University, New Haven, to conduct postdoctoral research. Her work continues to excel. She was invited to develop a video of her work in my lab, for featuring in the Society for Neuroscience meeting in November 2021. She was also on two presentations emerging from her work in our lab, including one related to the present grant on the inhibitory microenvironment of subgenual area 25.

Another recent doctoral student, Jingyi Wang, who conducted her research in my lab, moved to a postdoctoral position at the Univ. CA, Santa Barbara a year ago. While in the lab she conducted several studies, including one that is related to the projects for this award to the P.I. The completed work revealed that the strongest pathway from hippocampus to medial prefrontal cortex was directed to subgenual area 25, which is at the center of our focus for this award. I elaborate on the key findings in this year's Progress Report.

Other students:
Anne Wells completed an MS degree while conducting research in my lab and was able to complete a conceptually difficult project on a new way of looking at the primate hypothalamus from a developmental perspective. Anne completed a full-length paper that was published in 2020. The paper was voted as the best for the journal that year, and Anne received an award at the Cajal Club meeting during the Society for Neuroscience meeting in 2021. Anne was accepted to an MD/PhD program in UT, San Antonio, where she is now pursuing her studies for the dual degree.

Recent papers and presentations by trainees (associated with the present award)

Papers:

Wang, J., John, Y. and Barbas, H. Pathways for contextual memory: the primate hippocampal pathway to anterior cingulate cortex. Cerebral Cortex, 2021 Feb 5;31(3):1807-1826. doi: 10.1093/cercor/bhaa333. PMID: 33207365 PMCID: PMC7869091 (available on 2021-11-18).

Wells AM, García-Cabezas MÁ, Barbas H. Topological atlas of the hypothalamus in adult rhesus monkey. Topological atlas of the hypothalamus in adult rhesus monkey. Brain Struct Funct. 2020 Jul;225(6):1777-1803. doi: 10.1007/s00429-020-02093-8. Epub 2020 Jun 16. PMID: 32556476. PMID: 32556476 PMCID: PMC7321918. Award winner as the best article in the journal in 2020.

Abstracts presented at professional meetings:

Joyce, MK and Barbas H. Specialized projections of the primate subgenual cingulate area 25 to the amygdala. Society for Neuroscience, Connectome conference, January, 2021.

Rakoczy M, Joyce MKP, Zikopoulos B, and Barbas H. Density of parvalbumin, calbindin, and calretinin inhibitory neurons in subgenual cingulate area 25 of the neurotypical human. Neurosci. Abstr., 2021.

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
Complete	García-Cabezas MÁ, Joyce MKP, John YJ, Zikopoulos B, Barbas H. Mirror trends of plasticity and stability indicators in primate prefrontal cortex. The European journal of neuroscience. 2017 October;46(8):2392-2405. PubMed PMID: 28921934; PubMed Central PMCID: PMC5656436; DOI: 10.1111/ejn.13706.
Complete	Zikopoulos B, García-Cabezas MÁ, Barbas H. Parallel trends in cortical gray and white matter architecture and connections in primates allow fine study of pathways in humans and reveal network disruptions in autism. PLoS biology. 2018 February;16(2):e2004559. PubMed PMID: 29401206; PubMed Central PMCID: PMC5814101; DOI: 10.1371/journal.pbio.2004559.
Complete	Barbas H, Wang J, Joyce MKP, García-Cabezas MÁ. Pathway mechanism for excitatory and inhibitory control in working memory. Journal of neurophysiology. 2018 November 1;120(5):2659-2678. PubMed PMID: 30256740; PubMed Central PMCID: PMC6295541; DOI: 10.1152/jn.00936.2017.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
username [redacted]	Y	Barbas, Helen	BA,MS,PHD	PD/PI	percent effort [redacted]					NA
	N	Zikopoulos, Vasileios	BS,MS,PHD	Co-Investigator						NA
	N	Medalla, Maria	BS,PHD	Co-Investigator						NA
	N	Mark, Abigail		Technician						NA
	N	Banik, Shirmani		Consultant						NA
	N	Alvarez, Julied		Research Assistant						NA
	N	Holz, Jess		Technician						NA
	Y	Marshall, Laura		Research Assistant						NA
	N	John, Yohan		Co-Investigator						NA
	N	Joyce, MaryKate		Staff scientist (Doctoral level)						NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support **Has there been a change in the active other support of senior/key personnel since the last reporting period?** No
D.2.d New Other Significant Contributors **Are there, or will there be, new other significant contributors?** No
D.2.e Multi-PI (MPI) Leadership Plan **Will there be a change in the MPI Leadership Plan for the next budget period?** NA

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

Yes

G.8 PROJECT/PERFORMANCE SITES

Organization Name	DUNS	Congressional District	Address
Primary: BOSTON UNIVERSITY (CHARLES RIVER CAMPUS)	049435266	MA-007	BOSTON UNIVERSITY

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

Yes

Estimated unobligated balance: $200,500

G.10.b Provide an explanation for unobligated balance:
Personnel: A half-time technician left, and we have not replaced her yet. A former graduate student, who remained as a postdoctoral fellow during the pandemic was able to go to her planned postdoctoral position at Yale. There are several possible postdoctoral fellows interested in working in my lab, but due to travel restrictions and the continued pandemic we have not filled the postdoctoral slot yet. In addition, we could not hire several undergraduate students who would have participated in the experiments, because the university has strict rules about social distancing and the number of people who can be in a room at any one time. Travel: Because of the travel restrictions all planned m

G.10.c If authorized to carryover the balance, provide a general description of how it is anticipated that the funds will be spent
We will use the remaining funds to: Hire personnel: A new postdoctoral fellow. A new technician to replace the one who left for industry. Undergraduate students to participate in the experiments and analysis, as we will be able to do now that students are vaccinated and tested weekly. Travel to help disseminate our findings. Finally, during the pandemic we concentrated in the extensive analyses that contributed to our progress and publications. It is now imperative that we do more lab bench experiments, which require supplies for assays, reagents and software.

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period? No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No