Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is "None", please specify "None" as your response. "Not applicable" is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format.

1. **Grantee Institution:** The Pennsylvania State University

2. **Reporting Period (start and end date of grant award period):** 1/1/2010 - 12/31/2013

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** John Anthony, MPA

4. **Grant Contact Person's Telephone Number:** 814 935 1081

5. **Grant SAP Number:** 4100050904

6. **Project Number and Title of Research Project:** 37. Mechanisms of Excess Dietary Salt on Sympathetic-Cardiovascular Function

7. **Start and End Date of Research Project:** 7/26/2010 - 12/31/2011

8. **Name of Principal Investigator for the Research Project:** Sean D. Stocker, PhD

9. **Research Project Expenses**.

   9(A) Please provide the total amount of health research grant funds spent on this project for the entire duration of the grant, including indirect costs and any interest earned that was spent:

   $ 59,778

   9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name, First Name	Position Title	% of Effort on Project	Cost
Miller, Shane	Research Tech	100%	$15,986 (sal+fr)
Sauder, Charity	Research Suppt Asst	15%	$4,025 (sal+fr)
Luckett, Brittany	Graduate Student	100%	$4,313 (sal+fr)

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name, First Name	Position Title	% of Effort on Project
Cui, Jian	Research Associate Professor	5
Monahan, Kevin	Research Associate Professor	5
Stocker, Sean	PI	5

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost
NONE		

10. Co-funding of Research Project during Health Research Grant Award Period. Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes_____ No____X_____

If yes, please indicate the source and amount of other funds:

11. Leveraging of Additional Funds

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes___X_____ No_____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If

you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert "not funded" in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
Novel Neurogenic Actions of Dietary Sodium in Human Cardiovascular Regulation	■NIH ☐ Other federal (specify:_____) ☐ Nonfederal source (specify:_)	6/2011	$413,000	Not Funded
Neurogenic Actions of Dietary Sodium in Sympathetic-Cardiovascular Regulation	☐NIH ☐ Other federal (specify:_____) ■ Nonfederal source (specify: American Heart Association)	7/2011	$400,000	$400,000

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes___X_____ No_____

If yes, please describe your plans:

We are currently writing a multi-investigator project between multiple institutions to apply for a National Institutes of Health Investigator-Initiated Project (R01) in June 2014. The project will examine the impact of dietary sodium on sympathetic and cardiovascular reflexes in salt-resistant subjects. The project involves two major laboratories at Penn State College of Medicine and University of Delaware. Penn State College of Medicine will use "state-of-the-art" approaches in animals to understand how the ingestion of dietary salt intake alters cardiovascular regulation through actions in the brain. The research group at The University of Delaware will examine these same effects in humans. The data from this previously funded project formed the basis and protocols that are part of the new NIH application.

12. Future of Research Project. What are the future plans for this research project?

As outlined below, we encountered problems related to quantification or validation of the sodium content in the normal versus high NaCl diets. In other words, the amount of NaCl ingested in self-reports by the study subjects contradicted the amount of NaCl collected in the urine samples. Quantification of NaCl in urine is the "gold-standard" in the field. Unfortunately, these values reflected no differences in approximately 50% of the subjects on the high and low salt diets. This represents a major challenge to perform these studies.

We have already initiated collaboration with human physiologists at the University of Delaware. These investigators examine the impact of dietary sodium on blood vessel function and have published several papers illustrating that their experimental manipulations produce clear differences in urine NaCl excretion. The unique advantage of this research group is their access to nutritionists that prepare the food and alter NaCl content. With these resources and collaboration, we have already started collecting data in the past year. This has resulted in 2 new abstracts to be presented at the 2014 Experimental Biology Meeting and an anticipated NIH R01 application (anticipated requested budget: $3,060,000 over 5 years).

13. New Investigator Training and Development. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes____X_____ No_____

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male				
Female	1			
Unknown				
Total	**1**			

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic	1			
Unknown				
Total	**1**			

	Undergraduate	Masters	Pre-doc	Post-doc
White	1			
Black				
Asian				
Other				
Unknown				
Total	**1**			

14. Recruitment of Out-of–State Researchers. Did you bring researchers into Pennsylvania to carry out this research project?

Yes_____ No____X_____

If yes, please list the name and degree of each researcher and his/her previous affiliation:

15. Impact on Research Capacity and Quality. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes____X_____ No____ _____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

This project facilitated collaborations between investigators in basic science and clinical departments at Penn State Hershey and as summarized above, this is leading to plans for a new collaborative research study with colleagues at the University of Delaware.

16. Collaboration, business and community involvement.

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes___X_____ No_____

If yes, please describe the collaborations:

As described above in Section 11 and 12, we encountered challenges with the research project associated with clear manipulation of dietary NaCl in human subjects. At Penn State College of Medicine, we do not have immediate access to a nutrition center. Through discussions with other researchers during the course of this project, it became apparent that we should collaborate with individuals who have experience with this manipulation in humans and the proper resources. Through this insight, we have begun a collaboration with researchers at the University of Delaware. However, this collaboration started after this project had ended.

16(B) Did the research project result in commercial development of any research products?

Yes_____ No____X_____

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes_____ No____X_____

If yes, please describe involvement with community groups that resulted from the research project:

17. Progress in Achieving Research Goals, Objectives and Aims.

List the project goals, objectives and specific aims (as contained in the grant agreement). Summarize the progress made in achieving these goals, objectives and aims for the period that the project was funded (i.e., from project start date through end date). Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

Despite compelling evidence that the ingestion of excess dietary salt enhances sympathetic-cardiovascular reflexes and increases blood pressure variability in laboratory animals, there is currently no data available in humans to indicate whether dietary salt intake, by itself, alters

sympathetic-cardiovascular regulation. Therefore, the purpose of this project is to examine whether dietary salt intake alters sympathetic-cardiovascular function in humans. Our working hypothesis is that excess dietary salt intake sensitizes central sympathetic circuits to produce greater changes in sympathetic nerve activity (SNA) and more pronounced fluctuations in arterial blood pressure (ABP). Over time, these greater changes in SNA and ABP increase the probability to develop hypertension. Our rationale for this project is 2-fold: 1) preliminary data in healthy humans to indicate that dietary salt intake alters sympathetic-cardiovascular reflexes and blood pressure variability would provide new evidence of role that excess dietary salt intake plays in increasing the risk of CVD, and 2) such preliminary data would form the foundation for experimental and translational applications for a National Institutes of Health R01, American Heart Association Established Investigator Award, and a Program Project Grant focused on dietary factors and cardiovascular regulation.

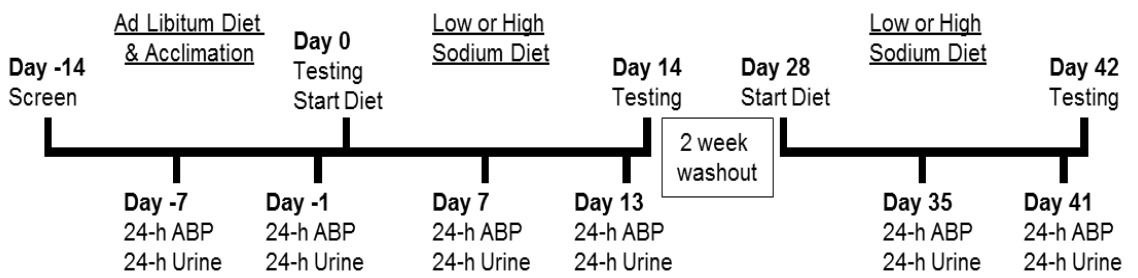

Figure 1. After a 2-week acclimation period, subjects will be randomly assigned to start on a low or high sodium diet and cross-over to the other condition after a 2 week washout. 24-h ABP, urine, and physiological tests are scheduled within each diet.

Specific Aim #1 will determine whether excess dietary salt intake alters sympathetic-cardiovascular reflexes and blood pressure variability in humans. Normotensive, healthy humans will be placed on a low NaCl (2.5 g per day) or high NaCl (12.5 g per day) for 2 weeks. Then, sympathetic and blood pressure responses to the baroreflex, hypoxia, and isometric handgrip exercise will be determined. In addition, blood pressure variability will be measured through an ambulatory monitor for 24-h. After the experimental session, the subject will be placed on the opposite diet for 2 weeks, and the experimental session will be performed again.

Figure 1 illustrates the study protocol. There is an acclimation period in which subjects are introduced to the study protocol, experimental manipulations, and measurements. On Day 0, subjects are randomly assigned to a normal or high sodium diet followed by urine and 24-h ambulatory cuff measurements. The normal diet consists of "Healthy Choice Meals", cereal, milk, granola bars, protein bars, and unlimited fresh fruit and vegetables. The diets are then supplemented with 9 placebo (normal, cellulose) or 1 g NaCl (high) capsules per day. On Day 14 and 42 (Testing), subjects returned to the Clinical Research Center to measure sympathetic nerve activity, blood pressure, heart rate, and renal blood flow in response to handgrip exercise. At 1 day prior to the testing, subjects are fitted with an ambulatory blood pressure cuff (SpaceLabs) for blood pressure measurements every 15 min through the 24-h cycle. Subjects are also provided a urine collection jug for urine measurements.

We enrolled 14 subjects (13 male, 1 female) in the study. Of these, 3 subjects did not complete the study due to illness (n=2) or inability to complete dietary recommendations (n=1). Of the remaining 11 subjects (10 male, 1 female), ambulatory cuff measurements were performed to determine salt-sensitivity. Salt-sensitivity was defined as a difference in 24-h ambulatory blood pressure >4 mmHg between low and high NaCl diets on the final day. Approximately 18% (2/11) of the subjects were salt-sensitive.

At the beginning of the study, we collected data from 3 subjects with clear differences in urine sodium excretion (thereby reflecting a difference in sodium intake). In these subjects, analyses of urine sodium and plasma renin activity indicated a clear difference between the low versus high NaCl diets (Figure 2). As expected, the high NaCl diet significantly decreased plasma renin activity and increased urine sodium excretion. These measurements confirmed the experimental manipulation in our subjects.

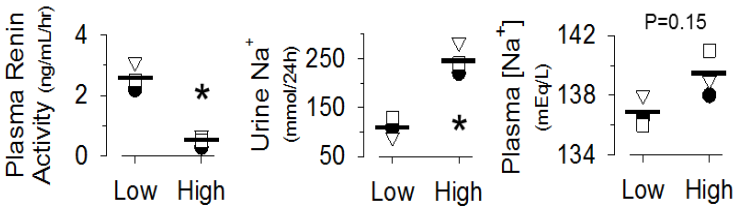

Figure 2. Plasma renin activity, urine sodium excretion, and plasma sodium concentration. A high NaCl diet significantly reduced plasma renin activity and significantly increased urine sodium concentration. Both indices suggest subjects were compliant to the dietary regimen. Mean, —; *P<0.05 versus low sodium (2-tailed)

Ambulatory cuff measurements of 24-h blood pressure indicated that measurements indicate that 1 of 3 subjects were salt-sensitive defined as a difference in blood pressure > 5 mmHg between the low and high salt diet conditions (Figure 3). Consequently, 2 subjects were salt-resistant. When blood pressure variability was analyzed, all 3 subjects had significantly higher blood pressure variability (as reflected by the standard deviation of systolic blood pressure) on a high versus low sodium diet. These findings are important as increased blood pressure variability has been reported as a major risk factor for the development of cardiovascular disease.

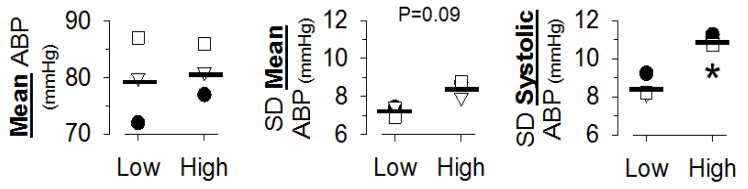

Figure 3. Mean ABP and ABP variability of 3 subjects (▽,□,●) provided a low (2.5g) or high (6.5g) sodium diet for 2 weeks. Note that mean ABP increased in 1 subject (salt-sensitive) yet ABP variability as indicated by the standard deviation of mean or systolic ABP increased in all subjects. Mean, ▬; *P<0.05 versus low sodium (2-tailed)

The overall hypothesis is that increased dietary NaCl intake would sensitize blood pressure circuits within the brain to result in exaggerated cardiovascular responses to different stressors. To test this possibility, these individuals were instrumented with an IV line for administration of drugs, Finapres and blood pressure cuff for blood pressure measurements, and tungsten microelectrode in a sympathetic nerve bundle to measure sympathetic nerve activity. The first challenge was isometric handgrip exercise which consists of the subject squeezing a device with he/her hand at a constant tension for several minutes. Figure 4 shows a representative experiment from a subject. As the subject begins the isometric handgrip exercise, blood pressure, heart rate, and muscle sympathetic nerve activity (SNA) progressively increase. This same manipulation is repeated under low and high NaCl diets. Figure 5 illustrates summary data from the 3 subjects above. Handgrip exercise produced greater increases in mean blood pressure, heart rate, and muscle SNA. In addition,

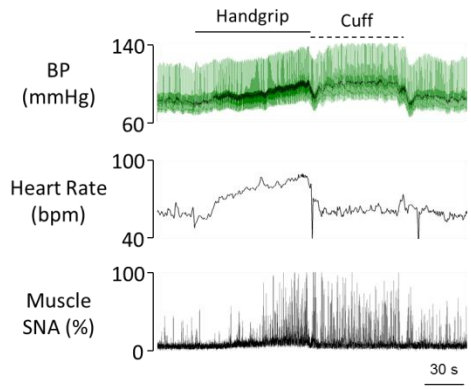

Figure 4. Blood pressure (BP), heart rate, and muscle sympathetic nerve activity (SNA) in a subject on a low NaCl diet performing an isometric handgrip exercise. Note the increase in BP, heart rate, and muscle SNA during handgrip.

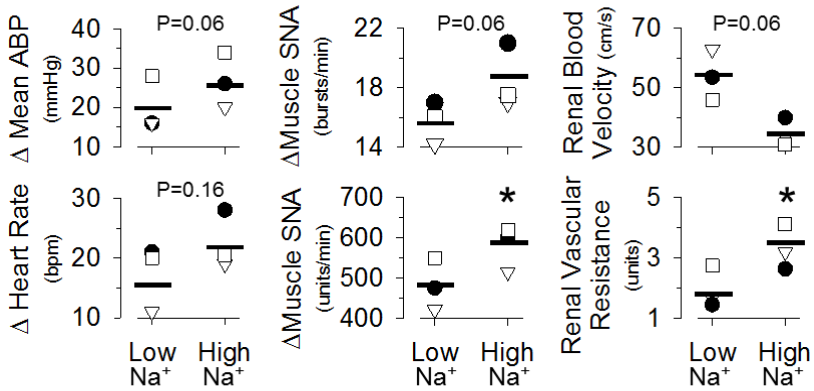

Figure 5. Sympathetic and cardiovascular responses to handgrip (30% max to fatigue) in 3 healthy subjects (▽,□,●) provided a low (2.5g) or high (6.5g) sodium diet for 2 weeks. **(LEFT)** Δmean ABP and heart rate, **(MIDDLE)** Δmuscle SNA, and **(RIGHT)** Renal blood velocity and vascular resistance. Note that a high sodium diet was associated with greater changes in mean ABP and heart rate. Analysis of muscle SNA and renal blood flow suggests this greater effect was mediated by the sympathetic nervous system and increased vascular resistance. Mean, ▬; *P<0.05 vs low sodium (2-tailed)

we measured renal blood velocity and calculated flow through a Doppler ultrasound. These measurements indicate that renal blood velocity and renal vascular resistance increased during handgrip. However, the increase in renal blood velocity was much smaller when subjects ingested high versus low NaCl diets. As a result, renal vascular resistance was much higher in subjects ingesting high versus low NaCl diet. These findings are consistent with the hypothesis that a high NaCl diet enhances sympathetic and cardiovascular responses to handgrip exercise.

We also examined how dietary NaCl would alter the baroreflex and sympathetic and cardiovascular responses to hypoxia. Baroreflex function has been assessed in all subjects using the modified Oxford technique (intravenous bolus of sodium nitroprusside followed by intravenous bolus of phenylephrine hydrochloride). We are separately considering baroreflex control of cardiac period (cardiovagal baroreflex sensitivity) and peripheral sympathetic outflow (sympathetic baroreflex sensitivity; using microneurography). Cardiovagal baroreflex sensitivity (BRS) is being assessed as the slope of the R-R interval-systolic blood pressure regression during pharmacologically induced changes in blood pressure. Cardiovagal BRS is similar during low NaCl (25.2±2.9 ms/mmHg) and high NaCl (27.6±2.7). Sympathetic BRS is being assessed as the slope of the muscle sympathetic nerve activity-diastolic blood pressure regression during pharmacologically induced changes in blood pressure. Sympathetic BRS is -5.0±0.9 au/beat/mmHg during low NaCl and -4.1±0.5 au/beat/mmHg during high NaCl (P=0.35). Inhalation of a hypoxic gas did not significantly alter muscle SNA or ABP in our subjects.

The results presented above represent data from 3 subjects. However, as noted above, 11 subjects completed the study. The reason that we have separated these 3 subjects out of the 11 subjects is that these individuals reflected clear differences in urine sodium excretion whereas the remaining 8 subjects did not, despite dietary log books. Urine sodium excretion is the "gold-standard" measurement for dietary sodium intakes. These other 8 subjects displayed similar urine sodium excretions between the low versus high NaCl conditions (105±15 versus 115±20 mmol/24h). As a result, this data would suggest our dietary NaCl manipulation did not produce differences in sodium intake. The sympathetic and cardiovascular responses to handgrip exercise also did not reflect significant differences in blood pressure, muscle SNA, or renal blood flow. It is unclear whether this reflects noncompliance of subjects to the dietary NaCl manipulation or some other factor. For this reason, we have initiated a collaboration with researchers who have access to nutritionists that directly prepare food with the NaCl manipulated directly rather than supplemented with capsules.

18. Extent of Clinical Activities Initiated and Completed. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be "No."

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes

___X___No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
__X____No

If "Yes" to either 18(A) or 18(B), items 18(C) – (F) must also be completed. (Do NOT complete 18(C-F) if 18(A) and 18(B) are both "No.")

18(C) How many hospital and health care professionals were involved in the research project?

_____Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

_____Number of subjects originally targeted to be included in the study
_____Number of subjects enrolled in the study

Note: Studies that fall dramatically short on recruitment are encouraged to provide the details of their recruitment efforts in Item 17, Progress in Achieving Research Goals, Objectives and Aims. For example, the number of eligible subjects approached, the number that refused to participate and the reasons for refusal. Without this information it is difficult to discern whether eligibility criteria were too restrictive or the study simply did not appeal to subjects.

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:
_____Males
_____Females
_____Unknown

Ethnicity:
_____Latinos or Hispanics
____Not Latinos or Hispanics
_____Unknown

Race:
_____American Indian or Alaska Native
_____Asian
_____Blacks or African American
_____Native Hawaiian or Other Pacific Islander
_____White
_____Other, specify:_____
_____Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

19. Human Embryonic Stem Cell Research. Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?
_____Yes
__X____ No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?
_____Yes
_____ No

19(C) Please describe how this project involved human embryonic stem cells:

20. Articles Submitted to Peer-Reviewed Publications.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication or paper submitted for publication, listed in the table, in a PDF version 5.0.5 (or greater) format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, and an abbreviated title of the publication. For example, if you submit two publications for Smith (PI for Project 01), one publication for Zhang (PI for Project 03), and one publication for Bates (PI for Project 04), the filenames would be:

Project 01 – Smith – Three cases of isolated
Project 01 – Smith – Investigation of NEB1 deletions
Project 03 – Zhang – Molecular profiling of aromatase
Project 04 – Bates – Neonatal intensive care

If the publication is not available electronically, provide 5 paper copies of the publication.

Note: The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed

acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1. None*				☐Submitted ☐Accepted ☐Published

* Comment: No peer-review publications were submitted. The objective of this proposal was to collect preliminary data that would be used in subsequent grant applications. This was accomplished as outlined in the original proposal. Second, we submitted subsequent grant applications, and one of these was funded through 2017 (American Heart Association).

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes_____ No____X_____

If yes, please describe your plans:

21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project. Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

The object of this proposal was to collect preliminary data for subsequent grant applications to investigate the impact of dietary NaCl intake on sympathetic and cardiovascular reflexes in salt-resistant humans. The data collected thus far accomplished this goal when there were clear differences in urine sodium excretion. These data suggest that increased dietary NaCl exaggerates sympathetic and cardiovascular responses to handgrip exercise and also increases blood pressure variability. This indicates that dietary NaCl intake can have adverse health effects on the cardiovascular system in individuals with a normal resting blood pressure. This could indicate that individuals regardless of health status (normotensive versus hypertensive) should be concerned about the level of dietary NaCl intake.

22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment. Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were

no major discoveries, drugs or approaches, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None.

23. Inventions, Patents and Commercial Development Opportunities.

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes_____ No___X_____

If "Yes" to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is "No.")

a. Title of Invention:

b. Name of Inventor(s):

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____

If yes, indicate date patent was filed:

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ No____

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes___ No____

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes_____ No____X_____

If yes, please describe your plans:

24. Key Investigator Qualifications. Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Stocker, Sean D.	Associate Professor of Cellular & Molecular Physiology
eRA COMMONS USER NAME (credential, e.g., agency login) **Stocker**	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Allegheny College, Meadville, PA	BS	05/97	Biology, Psychology
University of Pittsburgh, Pittsburgh, PA	PhD	01/02	Neuroscience
University of Texas HSC, San Antonio, TX	Postdoc	08/05	Physiology

A. Personal Statement

My research career has an established track record to investigate the neural circuits and cellular mechanisms that regulate sympathetic nerve activity and blood pressure regulation under physiological challenges and pathological disease states (hypertension). My laboratory utilizes multiple approaches including simultaneous sympathetic nerve recordings, brain microinjections, in vivo single-unit recordings and juxtacellular labeling, functional neuroanatomy, chronic sympathetic nerve and blood pressure recordings using Data Sciences Telemetry system, and in vitro patch-clamp recordings. In the past 2 years at Penn State College of Medicine, we have initiated microneurography and renal blood flow measurements in humans through collaboration with Drs. Sinoway and Leuenberger in the Heart and Vascular Institute.

B. Positions and Honors

Positions and Employment

2005-2009 **Assistant Professor**, Department of Physiology, University of Kentucky
Gill Heart Institute Research Faculty, Cardiovascular Research Faculty
Director, Rodent Telemetry Core Facility

2009-Present **Associate Professor**, Department of Cellular & Molecular Physiology
Pennsylvania State College of Medicine, Hershey, PA

2010-Present Director, American Heart Association Summer Undergraduate Program

2013-Present Director, Rodent Telemetry and Physiology Core Facility

Other Experience / Professional Membership

2006-Present AHA Peer Review, Vascular Biology/Blood Pressure Regulation
2007-Present American Physiological Society CNS Steering Committee
2011-Present American Physiology Society Joint Program Committee
2011-Present Program Committee, AHA Council for High Blood Pressure Research

2009-Present Editorial Board Member, Hypertension

2013-Present	Editorial Board Member, Physiological Reports
2013-Present	Editorial Board Member, Am J Physiol Regul Integr Comp Physiol
2013-Present	Section Editor, Brain and Hypertension, Current Hypertension Reports
2014-Present	Associate Editor, Journal of Neurophysiology
2013-Present	Chair, Central Nervous System Section, American Physiological Society
2013-Present	Co-Chair, American Heart Vascular Biology/Integrative Blood Pressure
2014	NIH Hypertension and Microcirculation Study Section

C. Selected Peer-Reviewed Publications (38 peer-review publications):

Most relevant to current application

1. **STOCKER SD,** Simmons JR, Stornetta RL, Toney GM, Guyenet PG. Water deprivation activates a glutamatergic projection from the hypothalamic paraventricular nucleus to the rostral ventrolateral medulla. *J Comp Neurol* 494: 673-685, 2006. PMCID: PMC2861548.
2. **STOCKER SD D,** Toney GM. Vagal afferent input alters the discharge of osmotic and ANG II-responsive median preoptic neurons projecting to the hypothalamic paraventricular nucleus. *Brain Res* 1131: 118-128, 2007. PMCID: PMC1847371.
3. **STOCKER SD**, Meador R, Adams JM. Neurons of the rostral ventrolateral medulla contribute to obesity-induced hypertension in rats. *Hypertension* 49: 640-646, 2007.
4. Adams JM, Madden CJ, Sved AF, **STOCKER SD.** Increased dietary salt enhances sympathoexcitatory and sympathoinhibitory responses from the rostral ventrolateral medulla. *Hypertension* 50: 354-359, 2007. PMID: 17592069.
5. Adams JM, McCarthy JJ, **STOCKER SD.** Excess dietary salt alters angiotensinergic regulation of neurons in the rostral ventrolateral medulla. *Hypertension* 52: 932-937, 2008. PMCID: PMC2635570.
6. Adams JM, Bardgett ME, **STOCKER SD**. Ventral lamina terminalis mediates enhanced cardiovascular responses of rostral ventrolateral medulla neurons during increased dietary salt. *Hypertension* 54: 308-314, 2009. PMCID: PMC3024146.
7. Bardgett ME, McCarthy JJ, **STOCKER SD.** Glutamatergic receptor activation in the rostral ventrolateral medulla mediates the sympathoexcitatory response to hyperinsulinemia. *Hypertension* 55: 284-290, 2010. PMCID: PMC2861553.
8. Ward KR, Bardgett JF, Wolfgang L, **STOCKER SD.** Sympathetic response to insulin is mediated by melanocortin 3/4 receptors in the hypothalamic paraventricular nucleus. *Hypertension* 57: 435-441, 2011. PMCID: PMC1035263.
9. Luckett BS, Frielle J, Wolfgang L, **STOCKER SD**. Arcuate injection of the anti-insulin affibody prevents the sympathetic response to insulin. *AJP Heart Circ Physiol* 304: H1538-H1546.
10. **STOCKER SD** and Muntzel MS. Chronic recording of sympathetic nerve activity in rats: surgical techniques, assessment of nerve activity, and quantification. *AJP Heart Circ Physiol* 305: H1407-1416.