

Proposal for Level 1 Funding

1. Title of Proposal and name of PI:

To eat or not to eat: Effects of food availability on neural and subjective responses to food cues and monetary gains in restrained eaters; PI: Stephen Wilson, Ph.D.

2. 3-5 Descriptive Keywords

Food availability, restrained eating, reward, fMRI

3. Purpose:

The overarching goal of the proposed research is to provide preliminary data to support the feasibility of a larger study that examines the motivational processes as a function of food availability in individuals who have eating regulatory difficulties. To be specific, this study will use functional magnetic resonance imaging (fMRI) and computerized behavioral tasks to test the prediction that, for individuals who desire to reduce overeating but have difficulties in doing so, perceived availability of high-calorie, tasty foods will strengthen the salience and appeal of high-calorie food while weakening the attractiveness of alternative rewards. The objective of the current proposal for Level 1 funding is to conduct a pilot study using fMRI to explore how the anticipated availability of high-calorie foods alters the motivational and affective response to food and non-food stimuli. This pilot study will allow us to collect the preliminary data needed to apply for external funding to extend this line of research. We anticipate that what we learn from this research will help us characterize and identify individuals who might have a neurobiological susceptibility to overconsume in an obesogenic environment replete with energy-dense, highly palatable food. This new knowledge regarding the motivational processes elicited by perceived eating opportunity could identify novel targets for treatments aimed at moderating overconsumption in an environment where high-calorie, appetizing food is available.

4. Brief Background and Description of Activities:

The rising prevalence of obesity places an increasing burden on public health services and general economics in the United States (Dee et al., 2014; Spieker & Pyzocha, 2016). Dieters often fail, and the majority of people who lose weight through dieting gain it back, intensifying the growing challenge of obesity. In order to achieve or maintain a healthy weight, many resort to dietary restraint to control their eating. However, according to Dietary Restraint theory, restrained eating can often precipitate binge eating, particularly in an environment where there are numerous opportunities to eat tasty, high-calorie foods that may erode self-control mechanisms. This pattern of behavior—rigid restraint followed by binge episodes—often results in weight gain over time (Marcus, Wing, & Lamparski, 1985; Polivy & Herman, 1985). One cognitive account of this phenomenon lies in the restrained eaters' oversensitivity to external food cues and their increased food craving and appetite when faced with access to the foods that they are resisting to eat (Fedoroff, Polivy, & Herman, 2003; Herman & Polivy, 1984). This explanation corresponds to the emerging evidence of the association between substantial growths in availability of palatable, sweet/fat food combinations and increasing obesity prevalence over the past several decades (Carden & Carr, 2013). However, the motivational mechanisms through which the high-calorie food availability elicits poorly controlled eating in those motivated to regulate their intake but have difficulties doing so have not been sufficiently investigated.

The overarching hypothesis of this research is that the mere availability and opportunity to eat high-calorie, tempting food enhances the neural reactivity to and the subjective valuation of food

reward values, making high-calorie foods more salient and low-calorie foods and alternative reinforcers (e.g., money) less salient. Consistent with this hypothesis, a recent fMRI study found that available vs. unavailable food pictures were associated with increased activity in motivational/reward-related brain regions in healthy subjects (Blechert et al., 2016). Additional evidence in support of this hypothesis comes from the drug addiction literature, given the shared neurobiological pathways underlying eating dysregulation and drug addiction (Schulte, Grilo, & Gearhardt, 2016). For example, our prior study has suggested that the expectation of an opportunity to smoke cigarettes impairs motivational processing of monetary rewards in abstinent cigarette smokers, as manifested by blunted caudate reactivity (Wilson, Sayette, Delgado, & Fiez, 2008). To extend previous findings on the impact of reward availability on motivational processing, the proposed design will evaluate the neural and behavioral responses to food and alternative rewards in restrained eaters with overweight or obesity ($N = 10$). Specifically, brain activations elicited by high- and low-calorie food images in overweight restrained eaters between the ages of 18 and 45 will be compared between two experimental conditions: one where they are anticipating an opportunity to eat high-calorie food and one where they are not. Lastly, we expect that the changes in reward and valuation processing resulting from the perception of eating opportunity will predict the restrained eaters' success in refraining from eating to earn money.

This proposed Level 1 study will provide a valuable opportunity for us to refine the methodology in terms of subject screening, experimental design, and neuroimaging parameter settings. In addition, by allowing us to collect key preliminary data, the pilot study will provide a strong foundation to pursue funding for larger investigations on the motivational processing of food cues as a function of eating contexts in restrained eaters. The proposed investigators, Dr(s). Wilson and Keller, have demonstrated a successful interdisciplinary collaboration that has yielded both papers and external funding related to the neurocircuitry of overeating (English et al., 2016a; English et al., 2016b; Fearnbach et al., 2016). This research is a natural extension of this collaboration and will inform understanding of the motivational underpinnings of persistent diet failures that are prevalent in industrialized society. Further, the knowledge gained from this research will be instrumental in the development of targeted interventions to prevent/treat disordered eating and obesity.

5. Relevance to the mission of the sponsoring unit:

We are requesting Level 1 funds to support the development of a collaboration between Dr. Wilson from the Department of Psychology and Dr. Keller from the Department of Nutritional Sciences & Food Science. The goal of the proposed interdisciplinary research is to advance the understanding and treatment of poorly controlled eating and obesity. As obesity has become a significant public health problem and caused considerable economic costs, the objective of this proposed project fits well with the SSRI mission of promoting integrative research in the service of addressing complex societal problems and improving public health locally and nationally.

6. Indicate if SSRI services will be used:

The proposed project will use the SLEIC. Dr. Wilson, will cover fMRI costs of fMRI scanning using scan hours that he was provided as a part of his start-up package.

7. Budget and Justification:

We are requesting funds for the following:

Advertisements to recruit participants (radio/newspaper ads, fliers)	\$1500
Payment for participants ($N = 10$, \$300/participant)	\$3000
Costs of food purchase ($N = 10$, \$50)	\$500
	TOTAL: \$5,000

Name and phone number of your department's budget coordinator: Micki Bower, 865-1815

Budget and fund number: budget 221-55 UP, fund 10010

Administrative area number: 021

8. Timeline:

We expect to complete data collection and analysis for this Level 1 research by October, 2018. The data will be used as preliminary data in an NIH application (R21 or R01) to extend this line of research, with a targeted submission of February, 2019.

9. Investigator Information:

Identify the lead investigator, collaborating investigators, and the departments or units they represent. Contact information should be included for all investigators. Please follow the format below for each investigator.

Lead Investigator:

Stephen Wilson, PhD
Associate Professor
Psychology
Liberal Arts / University Park
814-865-6219
sjw42@psu.edu
Tenure Track – Yes (Psychology)

Collaborating Investigator:

Name: Kathleen L. Keller, PhD
Title: Associate Professor
Department/Organization: Nutritional Sciences & Food Science
College/Campus: Health and Human Development / Agricultural Sciences
Phone: 814-863-2915
Email: klk37@psu.edu
Tenure Track – Yes, Nutritional Sciences

[Please include complete contact information for additional investigators here.]

10. Letters of Support from All Collaborators

See attached

Collaborating investigators should indicate their support of the project by writing letters of support; these letters should be emailed to the Lead Investigator, and be attached to this proposal.

11. Attach NIH or NSF biosketches

See attached

Literature Cited

- Blechert, J., Klackl, J., Miedl, S. F., & Wilhelm, F. H. (2016). To eat or not to eat: Effects of food availability on reward system activity during food picture viewing. *Appetite, 99*, 254-261.
- Carden, T. J., Carr, T. P. (2013). Food availability of glucose and fat, but not fructose, increased in the US between 1970 and 2009: Analysis of the USDA food availability data system. *Nutrition Journal, 12*(130), 1-8.
- Dee, A., Kearns, K., O'Neil, C., Sharp, L., Staines, A., O'Dwyer, V., ... & Perry, I. J. (2014). The direct and indirect costs of both overweight and obesity: A systematic review. *BMC Research Notes, 7*, 242.
- English, L. K., Fearnbach, S. N., Lasschuijt, M., Schlegel, A., Harris, S., Wilson, S. J., ... & Keller, K. L. (2016a). Brain regions implicated in inhibitory control and appetite regulation are activated in response to food portion size and energy density in children. *International Journal of Obesity, 40*, 1515-1522.
- English, L. K., Fearnbach, S. N., Wilson, S. J., Fisher, J. O., Savage, J. S., Rolls, B. J., Keller, K. L. (2016b). Food portion size and energy density evoked different patterns of brain activation in children. *American Journal of Clinical Nutrition, 105*(2), 295-305.
- Fearnbach, S. N., English, L. K., Lasschuijt, M., Wilson, S. J., Savage, J. S., Fisher, J. O., ... Keller, K. L. (2016). Brain response to images of food varying in energy density is associated with body composition in 7- and 10-year-old children: Results of an exploratory study. *Physiology & Behavior, 162*, 3-9.
- Fedoroff, I., Polivy, J., & Herman, C. P. (2003). The specificity of restrained versus unrestrained eaters' responses to food cues: General desire to eat, or craving for the cued food? *Appetite, 41*, 7-13.
- Herman, C. P., & Polivy, J. (1983). A boundary model for the regulation of eating. In A. J. Stunkard, & E. Stellar (Eds.), *Eating and its disorders* (pp. 141-156). New York: Raven.
- Marcus, M. D., Wing, R. R., Lamparski, D. M. (1985). Binge eating and dietary restraint in obese patients. *Addictive Behaviors, 10*, 163-168.
- Polivy, J., Herman, C. P. (1985). *American Psychologist, 40*(2), 193-201.
- Spieker, E. A., & Pyzocha, N. (2016). Economic impact of obesity. *Primary Care, 43*(1), 83-95.
- Schulte, E. M., Grilo, C. M., & Gearhardt, A. N. (2016). Shared and unique mechanisms underlying binge eating disorder and addictive disorders. *Clinical Psychology Review, 44*, 125-139.
- Wilson, S. J., Sayette, M. A., Delgado, M. R., & Fiez, J. A. (2008). Effect of smoking opportunity on responses to monetary gain and loss in the caudate nucleus. *Journal of Abnormal Psychology, 117*(2), 428-434.

PENNSTATE



Kathleen L. Keller, Ph.D.

Associate Professor Department of Nutritional Sciences & Department of Food Science

321 Chandlee Laboratory

University Park, PA 16802

Phone: 814-863-2915

Email: klk37@psu.edu

March 22, 2018

To Whom it May Concern:

I am writing this letter in support of the Level I SSRI pilot grant from PI Stephen J. Wilson, PhD, "*To eat or not to eat: effects of food availability on neural and subjective responses to food cues and monetary gains in restrained eaters.*" I am excited to serve as a co-Investigator on this compelling project aimed at gathering insight about the neurobiological characteristics that contribute to dieting successes and failures in restrained eaters. As a Nutritional Scientist who specializes in the neurobiology of overeating in children, I will contribute expertise to the design, execution, and interpretation of data obtained from this project.

Obesity continues to be a critical public health challenge, and behavioral approaches for weight loss often lead to disordered eating and a pattern of "yo-yo" dieting. Currently, there are limited therapies to successfully treat obesity, and there is a need to understand why some individuals are particularly vulnerable to overeating in the current environment. There are known overlaps in the neurobiological pathways contributing to addiction and overeating, and there is a need to apply theories and concepts from the field of addiction to understanding why people overeat. Thus, I am particularly excited to collaborate with Dr. Wilson on this project. He will be able to apply his expertise in neuroimaging and addiction to test the effect of food availability on neural and behavioral responses to food cues in frequent dieters. This question has real-world relevance because we live in an environment where tasty, high-calorie foods are ubiquitous. The research questions proposed in this project could lead to improved treatments for behavioral weight loss programs.

Dr. Wilson and I have collaborated for the past 6 years on several projects on the neurobiology of feeding and overeating in both adults in children. I look forward to continuing this collaboration on this exciting new project!

Sincerely,

A handwritten signature in cursive script that reads "Kathleen Keller". The ink is dark and the signature is fluid and legible.

Kathleen L. Keller

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Stephen J. Wilson, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): SJWILSON

POSITION TITLE: Associate Professor of Psychology

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Univ. of Pittsburgh-Johnstown, Johnstown, PA	B.S.	12/1999	Psychology
Univ. of Pittsburgh, Pittsburgh, PA	M.S.	07/2004	Clinical and Biological/Health Psychology
Center for the Neural Basis of Cognition, Pittsburgh, PA	n/a	08/2008	Cognitive Neuroscience
Univ. of Pittsburgh, Pittsburgh, PA	Ph.D.	08/2008	Clinical and Biological/Health Psychology

A. Personal Statement

I study behaviors that have a negative impact on health, with a particular interest in cigarette smoking and maladaptive eating patterns. My research uses an interdisciplinary approach that integrates theory and methods from affective, cognitive and social neuroscience. I have extensive experience using functional magnetic resonance imaging (fMRI) to investigate cue-reactivity and reward processing in smokers. I am serving (or have served) as the principal investigator on funded projects that incorporate fMRI to examine affective/motivational processing in smokers (R01DA041438, R21CA190093, R03DA035929, and R03DA029675). In addition, I have collaborated extensively with Dr. Keller (co-investigator on the proposed project) on a series of fMRI studies designed to characterize the mechanisms of eating behavior in 6-10 year-old children. This collaboration has resulted in several co-authored publications (listed below), as well as additional manuscripts that are currently under review. Given my research background and expertise and my history of productive collaboration with Dr. Keller, I believe that I am well-suited to serve as principal investigator on the proposed project.

- English, L.K., Fearnbach, S.N., Lasschuijt, M., Schlegel, A., Anderson, K., Harris, S., Wilson, S.J., Fisher, J.O., Savage, J.S., Rolls, B.J., Keller, K.L. (2016). Brain regions implicated in inhibitory control and reward are activated in response to food portion size and energy density in children. *International Journal of Obesity*, 40(10), 1515-1522.
- English, L.K., Fearnbach, S.N., Wilson, S.J., Fisher, J.O., Savage, J.S., Rolls, B.J., & Keller, K.L. (2017). Food portion size and energy density evoke different patterns of brain activation in children. *American Journal of Clinical Nutrition*, 105(2), 295-305.
- Fearnbach S.N., English, L.K., Wilson, S.J., Lasschuijt, M., Savage, J.S., Fisher, J.O., Rolls, B.J., Keller, K.L. (2016). Neural response to images of food varying in energy density is associated with body composition in 7-10 year-old children. *Physiology & Behavior*, 162, 3-9.

- Keller, K.L., English, L.K., Fearnbach, S.N., Lasschuijt, M., Anderson, K., Bermudez, M., Fisher, J.O., Rolls, B.J., Wilson, S.J. (in press). Brain response to food cues varying in portion size is associated with individual differences in the portion size effect in children. *Appetite*.

B. Positions and Honors

Positions and Employment

1998-99	Research Assistant, Dept. of Psychology, U. Pittsburgh-Johnstown, Johnstown, PA
2000-01	Research Assistant, Dept. of Psychology, U. of Pittsburgh, Pittsburgh, PA
2001-08	Graduate Student Researcher, Dept. of Psychology, U. of Pittsburgh, Pittsburgh, PA
2007-08	Clinical Psychology Intern, VA Pittsburgh Healthcare System, Pittsburgh, PA
2008-09	Research Associate, Dept. of Psychology, Penn State U., University Park, PA
2009-15	Assistant Professor, Dept. of Psychology, Penn State U., University Park, PA
2015-	Associate Professor, Dept. of Psychology, Penn State u., University Park, PA
2010-	Affiliated Faculty, Child Study Center, Penn State U., University Park, PA
2011-	Affiliated Faculty, Center for Health Aging, Penn State U., University Park, PA

Honors

1995	Senior Thesis Excellence Award, U. of Pittsburgh-Johnstown
1995-96	Rhea Louise Smith Scholarship for Academic Excellence, U. of Pittsburgh-Johnstown
2000	Natural Sciences Division Travel Grant, U. of Pittsburgh-Johnstown
2000	College Scholar Award in Psychology, U. of Pittsburgh-Johnstown
2000	Outstanding Graduate Student Award, U. of Pittsburgh-Johnstown
2001	Honorable Mention, American Psychological Association Minority Fellowship Program
2001	Ford Foundation Predoctoral Fellowship for Minorities
2002	K. Leroy Irvis Fellowship (academic excellence), U. of Pittsburgh
2002-03	African American Summer Graduate Research Award, U. of Pittsburgh
2004	National Institute on Drug Abuse Frontiers in Addiction Research Travel Award
2004-07	Bassell Student Publication Award (best paper), U. of Pittsburgh
2007	Bassell Award for Excellence in the Clinical Psychology Program, U. of Pittsburgh
2009-11	National Institutes of Health Clinical Research Loan Repayment Program
2010	SRNT Tobacco-Related Health Disparities Travel Award

C. Contribution to Science

1. Smokers who are trying to quit are particularly vulnerable to relapse (a return to regular smoking) when they encounter cigarette-related cues, in part because such cues often elicit a strong urge or craving to smoke. One objective of my program of research has been to provide insight into the links between cue-elicited craving and smoking relapse using functional magnetic resonance imaging (fMRI). fMRI offers an attractive approach to the assessment of craving because it measures patterns of neurophysiological activity related to emotional and cognitive processes as they unfold over time. As a result, fMRI makes it possible to obtain information that can be very difficult to capture using other methods (e.g., verbal report). One of our key observations has been that cigarette cue exposure evokes stronger activation of and coordinated activity (connectivity) among areas of the brain linked to reward and motivation when cigarettes are perceived to be available in the near future (i.e., when cigarette use is not impeded by external/situational or internal/motivational barriers), relative to when cigarettes are perceived to be unavailable for an extended time. This pattern suggests that the motivational properties of smoking cues are enhanced when such stimuli are encountered in the context of an impending opportunity to engage in cigarette use, an effect that is likely to contribute to the difficulty that smokers experience when they try to quit smoking.
 - a. Wilson, S. J., Creswell, K. G., Sayette, M. A., & Fiez, J. A. (2013). Ambivalence about smoking and cue-elicited neural activity in quitting-motivated smokers faced with an opportunity to smoke. *Addictive Behaviors*, 38(2), 1541-1549. doi:http://dx.doi.org/10.1016/j.addbeh.2012.03.020

- b. Wilson, S. J., Sayette, M. A., & Fiez, J. A. (2012). Quitting-unmotivated and quitting-motivated cigarette smokers exhibit different patterns of cue-elicited brain activation when anticipating an opportunity to smoke. *Journal of Abnormal Psychology, 121*(1), 198-211. doi:10.1037/a0025112
 - c. Wilson, S. J., Sayette, M. A., & Fiez, J. A. (2013). Neural correlates of self-focused and other-focused strategies for coping with cigarette cue exposure. *Psychology of Addictive Behaviors, 27*(2), 466-476. doi:10.1037/a0027055
 - d. Zelle, S. L., Gates, K. M., Fiez, J. A., Sayette, M. A., & Wilson, S. J. (2017). The first day is always the hardest: Functional connectivity during cue exposure and the ability to resist smoking in the initial hours of a quit attempt. *NeuroImage, 151*, 24-32. doi:10.1016/j.neuroimage.2016.03.015
2. Whereas the incentive value of cigarette-related cues appears to be amplified in the context of perceived cigarette availability, results from our work suggest that non-drug rewards lose their motivational potency under such conditions. Specifically, my colleagues and I have found that smokers who anticipated having a chance to smoke soon exhibited weaker responses to monetary gains (a proxy for non-drug rewards, more generally) in a reward-related brain areas compared to those who anticipated having to wait several hours before being able to use cigarettes. One interpretation of our initial findings is that monetary gains were “less rewarding” for smokers who were anticipating the chance to smoke soon, relative to those who did not expect to smoke in the near future. We speculated that this effect is likely to play a significant role in smoking relapse. That is, in addition to the heightened salience of cigarette-related cues, a second reason why smokers abandon quit attempts may be because alternative, non-drug sources of reinforcement (e.g., the prospect of saving money and improving health) seem less appealing in the face of an opportunity to smoke in the near future. This prediction was supported by follow up work, in which we found that smokers who exhibited the weakest neural response to monetary rewards when expecting to have access to cigarettes in the near future were least willing to delay smoking for monetary reinforcement outside of the scanner. Recently, my colleagues and I have extended our initial studies by examining the effects of cue signaling cigarette availability on responses to food rewards and the valuation of personal health.
- a. MacLean, R. R., Martino, S., Carroll, K. M., Smyth, J. M., Pincus, A. L., & Wilson, S. J. (2017). Momentary associations between reported craving and valuing health in daily smokers. *Nicotine & Tobacco Research, 19*(6), 716-722. doi:10.1093/ntr/ntw253
 - b. Manghani, H. R., Lewis, A. H., Wilson, S. J., & Delgado, M. R. (2017). Pavlovian-to-instrumental transfer of nicotine and food cues in deprived cigarette smokers. *Nicotine & Tobacco Research, 19*(6), 670-676. doi:10.1093/ntr/ntx007
 - c. Wilson, S. J., Delgado, M. R., McKee, S. A., Grigson, P. S., MacLean, R. R., Nichols, T. T., & Henry, S. L. (2014). Weak ventral striatal responses to monetary outcomes predict an unwillingness to resist cigarette smoking. *Cognitive, Affective, & Behavioral Neuroscience, 14*(4), 1196-1207. doi:10.3758/s13415-014-0285-8
 - d. Wilson, S. J., Sayette, M. A., Delgado, M. R., & Fiez, J. A. (2008). Effect of smoking opportunity on responses to monetary gain and loss in the caudate nucleus. *Journal of Abnormal Psychology, 117*(2), 428-434. doi:10.1037/0021-843X.117.2.428
3. In addition to our empirical work, my colleagues and I have conducted quantitative and conceptual reviews of the literature, with an emphasis on significant theoretical and methodological issues facing the field. This includes reviews highlighting the importance of treatment-seeking status and urge intensity as factors to consider when designing and interpreting neuroimaging craving studies. My colleagues and I have also conducted reviews aimed at fostering innovative strategies for advancing research in the field, such as through combining the unique and complementary strengths of functional magnetic resonance imaging and ecological momentary assessment methods.
- a. Lydon, D. M., Wilson, S. J., Child, A., & Geier, C. F. (2014). Adolescent brain maturation and smoking: What we know and where we're headed. *Neuroscience & Biobehavioral Reviews, 45*, 323-342. doi:https://doi.org/10.1016/j.neubiorev.2014.07.003
 - b. Wilson, S. J., & Sayette, M. A. (2015). Neuroimaging craving: urge intensity matters. *Addiction, 110*(2), 195-203. doi:10.1111/add.12676
 - c. Wilson, S. J., Sayette, M. A., & Fiez, J. A. (2004). Prefrontal responses to drug cues: a neurocognitive analysis. *Nat Neurosci, 7*(3), 211-214.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Keller, Kathleen L

eRA COMMONS USER NAME (credential, e.g., agency login): KLKELLER

POSITION TITLE: Associate Professor

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Marquette University, Milwaukee, WI	B.S.	05/1995	Biology
Rutgers University, New Brunswick, NJ	PhD	05/2002	Nutritional Sciences
New York Nutrition Obesity Research Center, New York, NY	Post-Doc	06/2005	Pediatric Obesity

A. Personal Statement

I have a doctorate in Nutritional Sciences from Rutgers University and I am presently an Associate Professor at The Pennsylvania State University, Department(s) of Nutritional Sciences and Food Science. My research is focused on determining the factors, both environmental and biological, that influence eating behaviors and their relationship to the development of obesity in children. For the past 6 years, I have also received training in neuroimaging to investigate the mechanisms that drive overeating in children. I have over 17 years of experience conducting interdisciplinary feeding studies with children that has generated 56 peer-reviewed publications, over half of which are senior or first author. Since 2005, I have directed the completion of 13 experimental studies and have collected data from over 600 children and parents. In January 2012, I moved to Penn State to direct a Neuroimaging and Ingestive Behavior laboratory to further study the mechanisms of eating behavior in children. Through this position, I am also the Director of the Metabolic Kitchen and Children's Eating Behavior Laboratory. This facility serves as a state-of-the art testing site for the design, collection, implementation, and analysis of feeding studies with children. Over the past 6 years at Penn State, we have successfully completed functional neuroimaging scans with 167 children to better understand the mechanisms of eating behavior in 6-10 year-olds. These data will fill a critical gap in knowledge regarding our understanding of the neurobiological mechanisms of overeating and food intake decisions in pre-adolescent children. Dr. Wilson has been a collaborator on many of our studies and is a co-Investigator on my NIH/NIDDK R01 "Brain mechanisms of overeating in children." The publications below are representative of my recent research direction:

- English LK, Lasschuijt M, Keller KL. Mechanisms of the portion size effect: What is known and where do we go from here? *Appetite*. 2015. 88:39-49. PMID: 25447010
- Keller KL, English LK, Fearnbach SN, Lasschuijt M, Anderson K, Bermudez M, Fisher JO, Rolls BJ, & Wilson SJ. Brain response to food cues varying in portion size is associated with individual differences in the portion size effect in children. *Appetite*. In press.

B. Positions and HonorsHonors & Awards:

1996	Bunting-Cobb Graduate Fellowship for Women in Math and Science
1998	Association for Chemoreception Travel Award
2000	Society for the Study of Ingestive Behavior Young Investigator Award
2000	National Science Foundation K-12 Teaching Fellowship

2001 Gerber Foods Fellowship in Pediatric Nutrition
2001 Association for Chemoreception Travel Award
2001 NIH Extramural Loan Repayment Grant in Pediatric Nutrition
2004 Invited Keynote speaker for Science Research Night at JFK High School
2007 Science Unbound Foundation, Best Paper Award in Obesity Related Research
2010 NIH Funded Training Fellowship in Clinical Nutrition
2012 Roy C. Buck Faculty Award
2013 Mark T. Greenberg Early Career Professorship in Children's Health and Development
2014 Norman C. Kretchmer Memorial Award

Academic and Professional Positions:

1996 –1999 Teaching Assistant, Rutgers University Dept. of Nutritional Sciences, New Brunswick, NJ
1999 - 2000 Graduate Fellowship, Rutgers University Dept. of Nutritional Sciences, New Brunswick, NJ
2000 – 2001 National Science Foundation K-12 middle school teacher, New Brunswick, NJ
2004 – 2013 Research Associate, New York Obesity Nutrition Research Center, New York, NY
2005 – 2010 Adjunct Lecturer at Brooklyn College, Health and Nutritional Sciences Dept., Brooklyn, NY
2006 – 2012 Assistant Professor, Columbia University College of Physicians and Surgeons
2012 – 2017 Assistant Professor, The Pennsylvania State University, Departments of Nutritional Sciences and Food Science, University Park, PA
2017 – pres. Associate Professor, The Pennsylvania State University, Departments of Nutritional Sciences and Food Science, University Park, PA

Other Relevant Professional Positions:

2003 – 2011 Rapporteur for Columbia University's Seminar on Appetitive Behavior, New York, NY
2006 – 2008 General Editor, "The Encyclopedia of Obesity" Sage Reference Publishing
2011 – 2013 The Obesity Society Membership Committee
2013 – 2016 Editorial Board, International Journal of Obesity
2013 – pres. American Society for Nutrition, FASEB Science Research Conference Advisory Committee
2014 – pres. Society for the Study of Ingestive Behavior, Program Committee
2014 – pres. Co-Executive Editor, Appetite
2015 – pres. Editorial Board, International Journal of Behavioral Nutrition and Physical Activity

C. Contribution to Science

My research is focused on understanding the role of individual variation in the development of children's eating and weight-related behaviors. We use a number of methodologies to study eating behaviors, including genetics, characterization of the built environment, sensory phenotyping, laboratory test-meals, and most recently, functional magnetic resonance imaging.

* An asterisk to the left of the citation represents papers where students were involved as first and/or co-authors.

1. My early contributions to science helped to characterize the relationship between genetic variation in the ability to taste bitter thiourea compounds and eating behaviors and weight status in preschool children. Prior to these studies, the majority of research had focused on characterizing the relationship between taste phenotypes and eating behaviors in adults. Our research group was the first to report a relationship between genetic variation in the ability to taste 6-n-propylthiouracil (PROP) and weight status in children. Our follow-up studies characterized the relationship between the PROP taster phenotype, genetic variation at the *TAS2R38* gene, and children's eating behaviors. We were the first research group to assess the interaction between genetic taste variation and the built environment on children's taste preferences and weight status. In this study, we determined that the interaction between taste genetics and the food environment plays a greater role in determining children's food preferences than either factor alone. Example publications from this research are listed below:

- Keller KL, Steinmann L, Nurse RJ, Tepper BJ. Genetic taste sensitivity to 6-n-propylthiouracil influences food preferences and reported intake in preschool children. *Appetite*. 2002;38(1):3-12. PMID: 11883912.

- Keller KL, Tepper BJ. A possible role for taste sensitivity to 6-n-propylthiouracil (PROP) in dietary patterns and body weight differences in young children. *Obesity Res.* 2004;12:904-12. PMID: 15229328.
- * Keller KL, Reid A, MacDougall MC, Cassano H, Song JL, Deng L, Lanzano P, Chung WK, Kissileff HR. Sex differences in the effects of inherited bitter thiourea sensitivity on body weight in 4-6 year-old children. *Obesity.* 2010;18(6):1194-1200. PMID: PMC2877149.
- * Burd C, Senerat A, Chambers E, Keller KL. PROP taster status interacts with the built environment to influence children's food acceptance and body weight status. *Obesity.* 2013;21:786-94. PMID: PMC3661723.

2. A second line of research in my laboratory is understanding the role of oral fatty acid sensors in dietary intake of high-fat foods and chronic disease. Historically, dietary fat was thought to be perceived by texture, but not taste mechanisms. Work from other laboratories in animals and humans, however, demonstrated that it was possible to detect oral fatty acids even when olfactory and texture cues were masked, which suggests a putative role for basic taste in fat perception. However, no taste receptor for fatty acids had been identified. In animals, the fatty acid translocase CD36 was reported to be necessary for oral fat detection and preference. Our laboratory was the first to report a relationship between common variation at the *CD36* gene and reported acceptance of high-fat foods in African-American adults. Furthermore, we developed a quick screening procedure to phenotype adults based on their ability to discriminate oral fat concentrations in salad dressings. Based on this methodology, we were able to identify a relationship between poor oral fat discrimination and usual intake patterns for dietary fat. Example publications from this line of research are included below.

- * Keller KL, Liang L, Sakimura-McLean J, May D, van Belle C, Breen C, Driggin E, Tepper BJ, Lanzano P, Deng L, Chung WK. Common variants in the *CD36* gene are associated with reported fat preferences and obesity in African-Americans. *Obesity.* PMID: PMC3743670.
- * Liang L, Sakimura-McLean J, May D, Breen C, Driggin E, Tepper BJ, Chung WK, Keller KL. Fat Discrimination: A phenotype with potential implications for studying fat intake behaviors and obesity. *Physiol Behav.* 2012;105(2):470-5. PMID: PMC3743656.

3. In 2006, my laboratory began a series of studies to determine the impact of food marketing on children's eating behaviors. The impetus for these studies was historical work from Stanley Schachter who hypothesized that obesity was in part due to an increased responsiveness to external environmental cues. By the 1980s, this hypothesis had largely been discounted, however, more recent evidence from our laboratory and others suggested that overweight children might be more responsive to environmental cues like food marketing. Our initial studies in this area supported the hypothesis that overweight children were more responsive to external food cues than non-overweight children. In addition to continuing laboratory studies to understand the mechanisms underlying these differences, we have also started a line of research to apply these strategies to developing more effective feeding practices for parents. We recently completed a randomized controlled trial to teach parents to apply food marketing strategies and default options to increase children's intake of vegetables in the home. Publications included within this line of research are below.

- * Forman J, Halford JC, Summe H, MacDougall MC, Keller KL. Food branding influences ad libitum intake differently in children depending on weight status: results of a pilot study. *Appetite.* 2009;53:76-83. PMID: 19481125.
- * Keller KL, Kuilema LG, Lee N, Yoon J, Mascaro B, Combes A-L, Deutsch B, Sorte K, Halford JCG. The impact of food branding on children's eating behavior and obesity. *Physiol Behav.* 2012;106(3):379-86. PMID: 22450261.
- Keller KL. The use of repeated exposure and associative conditioning to increase vegetable intake in children: explaining the variability across studies. *J Acad Nutr Diet.* 2014; 114:1169-1173. PMID: 24928778.
- * Cravener TL, Schlechter H, Loeb KL, Radnitz C, Schwartz M, Zucker N, Finkelstein S, Wang YC, Rolls BJ, Keller KL. Feeding strategies derived from behavioral economics and psychology can increase vegetable intake in children as part of a home-based intervention: results of a pilot study. *J Acad Nutr Diet.* 2015; doi: 10.1016/j.jand.2015.03.024. PMID: 26014476

4. Our most recent studies have been focused on understanding the neural mechanisms of overeating in children. Brain imaging methodologies like functional magnetic resonance imaging (fMRI) have become the gold standard for understanding neural function in complex traits like eating behavior and obesity. Studies primarily done in adults showed the importance of reward processing, decision making, and inhibitory control in food intake and the development of obesity. However, few laboratories have successfully conducted these studies in children. We are presently conducting a study in 7-10 year-old children to characterize the neural mechanisms of children's response to portion size and energy density. In addition, we have an ongoing study in this age group to investigate the role of self-control in dietary decisions. These studies will be some of the first to combine neuroimaging with measures of ingestive behavior assessed in the laboratory. We have presented preliminary data from these studies at scientific meetings (i.e., Obesity Week, Society for the Study of Ingestive Behavior, and Society for International Behavioral Nutrition and Physical Activity) and are in the process of preparing to submit full manuscripts for publication. Example publications from this line of research are included below:

- * English LK, Lasschuijt M, Keller KL. Mechanisms of the portion size effect: What is known and where do we go from here? *Appetite*. 2015. 88:39-49. PMID: 25447010
- * English LK, Fearnbach SN, Lasschuijt M, Schlegel A, Anderson K, Harris S, Wilson SJ, Fisher JO, Savage JS, Rolls BJ, & **Keller KL**. Brain regions implicated in inhibitory control and appetite regulation are activated in response to food portion size and energy density in children. *International Journal of Obesity*. 2016;40:1515-22.
- * Fearnbach SN, English LK, Lasschuijt M, Wilson SJ, Savage JS, Fisher JO, Rolls BJ, Keller KL. Brain response to images of food varying in energy density is associated with body composition in 7- to 10-year-old children: Results of an exploratory study. *Physiol Behav*. 2016;162:3-9.
- * English LK, Fearnbach SN, Wilson SJ, Fisher JO, Williams JS, Rolls BJ, **Keller KL**. Food portion size and energy density evoke different patterns of brain activation in children. *Am J Clin Nutr*. 2017;105:295-305.

Completed list of my published work can be found in My Bibliography:

<https://www.ncbi.nlm.nih.gov/sites/myncbi/kathleen.keller.1/bibliography/47657865/public/?sort=date&direction=ascending>

D. Research Support

NIH/NIDDK R01 DK082580-06

Rolls (PI)

07/01/15 – 06/30/20

“Strategies to moderate energy intake for the prevention of obesity in children”

The goal of this study is to test the effectiveness of multiple strategies, including variety and portion size, to reduce energy intake in children over a sustained period of time.

Role: Co-I

McCormick Science Institute

Keller (PI)

01/15/15 – 12/31/18

“Using herbs and spices to increase children's acceptance and intake of school lunches”

The goal of this project is to teach school food service workers to prepare vegetables with herbs and spices to increase intake among middle and high school students in Central, PA.

Role: PI

2011-67001-30117

Rolls, B. (Director)

2/15/11-2/14/18

USDA National Institute of Food and Agriculture

The Pennsylvania State University Childhood Obesity Prevention Graduate Training Program

This grant will establish a sustainable comprehensive, problem-based graduate PhD training program in child obesity prevention (COP) that meets the goals of Agriculture and Food Research Initiative (AFRI) to “improve nutrition and end childhood obesity.”

Role: Co-Director

NIH/NIDDK R01
"Brain mechanisms of overeating in children"
The goal of this 5-year longitudinal study is to determine the relationship between laboratory measures of overeating and brain response to portion size and energy density cues in healthy-weight 7-8 year-old children at high risk for obesity.
Role: PI

Keller (PI)

01/07/17 – 01/06/22

USDA AFRI
"Healthy Bodies Project: Modifying family and preschool environments to prevent obesity"
The goal of this project is to test the effectiveness of self-regulation training, repeated exposure and tasting, parent education, and physical activity on childhood obesity prevention at Head Start. The candidate is supervising the development and administration of lessons designed to assess self-regulation in children.
Role: Co-I

Francis/Belue (PIs) 04/01/15 – 03/31/20

Completed Research Support (past 3 years)

Clinical Translational Science Institute Pilot Award
"Developing novel methodologies to teach children to eat in response to hunger and fullness"
The goal of this project was to use virtual reality and behavioral teaching tools to develop effective methods to teach children how to eat in response to hunger and fullness cues. The candidate wrote the grant proposal and will manage all aspects of data collection, analysis, and presentation.
Role: PI

Keller (PI)

02/15/14 – 02/14/17

SSRI Level 2 Pilot Grant
"Neural mechanisms underlying child responses to food energy density and portion size"
The goal of this research was to elucidate the neural mechanisms involved with responsiveness of food portion size and energy density in obese and non-obese children.
Role: PI

Keller (PI)

03/01/13 – 02/28/15

Clinical Translational Science Institute Pilot Award (BENI)
The goal of this research was to use virtual simulation technology to co-design software with children that will improve eating behaviors and other health-related decisions.
Role: Co-I

Poole (PI)

03/15/13 – 03/14/15

NIH/NIDDK R01 DK082580
"Strategies to moderate energy intake for the prevention of obesity in children"
The goal of this study was to test the effectiveness of multiple strategies, including variety and portion size, to reduce energy intake in children.
Role: Co-I

Rolls (PI)

07/01/09 – 06/30/14

The goal this grant is to test random, non-contingent nicotine delivery as a novel alternative to the steady-state delivery of nicotine for the treatment of cigarette addiction. Specifically, the aims of the project are to test hypotheses that the random delivery of nicotine, rather than steady-state delivery, will: (1) be highly effective in reducing drug-induced devaluation of natural rewards in humans, (2) facilitate the ability to resist smoking by choosing money over a cigarette, and importantly, (3) bolster abstinence over a 6 week test period.

Role: Co-PI

Completed research support in past 3 years

R21 CA190093 Wilson (PI) 09/16/2014-08/31/2017

(PQA1) fMRI neurofeedback and decision-making in habitual cigarette smokers

The goal of this project was to test the prediction that increasing brain responses to nondrug rewards may be an effective way to enhance the influence that such stimuli have on behavior in smokers. The project examined this idea using a technique called real-time functional magnetic resonance imaging (fMRI) neurofeedback. The study tested the following specific hypotheses: (1) only smokers provided with valid neurofeedback would learn to reliably and voluntarily increase activation in reward-related brain regions using cognitive strategies; (2) this learning would be durable, such that smokers would be able to continue using cognitive strategies to increase reward-related brain activity after neurofeedback was removed; and (3) this learning would be functional, such that clinically-relevant decision making (the willingness to choose a nondrug reward over smoking) was influenced when smokers use the same strategies outside of the scanner.

Role: PI

R03 DA035929 Wilson (PI) 04/01/2014-03/31/2016

Nicotine dependence, reward sensitivity, and lapse behavior in light smoker

The goal of this grant was to test the hypothesis that sensitivity to non-drug rewards serves as an important marker for nicotine dependence severity in light-smoking emerging adults. The specific aims of the project were: (1) to examine the relationship between level of nicotine dependence and reward sensitivity; and (2) to examine the relationship between level of nicotine dependence and the ability to refrain from smoking in order to obtain non-drug incentives.

Role: PI

R21 MH099617 Berenbaum (PI) 12/13/2012-10/31/2015

Prenatal androgen effects on sex-related neural processing of reward and threat

The goal of this project was to examine gender development in early adolescence, with a particular focus on (a) gender-typing in relation to prenatal androgen exposure and social experiences, and (b) the links between gender development and psychological health.

Role: Co-I

K12 HD055882 Weisman (PI) 01/01/2013-06/30/2015

Career Development Program in Women's Health Research at Penn State

This award supported mentored research aimed at allowing me to expand my existing program of research to incorporate work investigating the associations between sex differences in brain structure, brain function and smoking behavior, with an emphasis on identifying the mechanisms that contribute to distinctive smoking-related cancer risk among women.

Role: Selected Scholar

Pennsylvania Department of Health, CURE program 01/01/2013-02/31/2014

Enhancing smokers' control over brain reward circuitry using fMRI neurofeedback

This project had two goals: (1) to set up the software (Turbo-BrainVoyager) and hardware required to implement real-time fMRI neurofeedback with cigarette smokers through consultation with Dr. Stephen Johnston from the UK; and (2) to conduct a small pilot study to demonstrate the feasibility of reliably isolating reward-related brain regions and using real-time fMRI neurofeedback to train smokers to upregulate neural responses to non-drug rewards in brain reward circuitry.

Role: PI