SUMMARY STATEMENT

PROGRAM CONTACT:
Jonathan King
(301) 402-4156
kingjo@nia.nih.gov

(Privileged Communication) ***Release Date:*** **04/01/2008**

Application Number: **1 F31 AG032804-01**

Samanez Larkin, Gregory R
PO BOX 19779
STANFORD, CA 94309

Review Group: **ZRG1 F02A-H (20)**
Center for Scientific Review Special Emphasis Panel
Fellowships: Behavioral Neuroscience

Meeting Date: **03/17/2008**
Council: **MAY 2008** ***PCC:*** **2BCOGJK**
Requested Start:

Project Title: **Incentive learning and decision making in the aging brain**

Requested: **2 years 6 months**

Sponsor: **KNUTSON, BRIAN D**
Department: **psychology and neuroscience**
Organization: **STANFORD UNIVERSITY**
City, State: **STANFORD CALIFORNIA**

SRG Action: **Priority Score: 167**
Human Subjects: **30-Human subjects involved - Certified, no SRG concerns**
Animal Subjects: **10-No live vertebrate animals involved for competing appl.**
Gender: **1A-Both genders, scientifically acceptable**
Minority: **1A-Minorities and non-minorities, scientifically acceptable**
Children: **3A-No children included, scientifically acceptable**
Clinical Research - not NIH-defined Phase III Trial

ADMINISTRATIVE NOTE

RESUME AND SUMMARY OF DISCUSSION: This application proposes to examine age difference in incentive learning through an innovative research design that involves behavioral measures and functional magnetic imaging. Strengths of the proposal include the productivity of the applicant as well as the research environment at Stanford University. During the discussion the reviewers stated that the main concern with the proposal is the lack of detail in the training plan. In addition it does not appear that the applicant will be learning a sufficient amount of new techniques. There are also a number of small errors and typos in the proposal. Overall these concerns decrease the enthusiasm for this proposal.

DESCRIPTION (provided by applicant): As the proportion of older adults continues to grow at an unprecedented rate, aging adults may be required to make increasingly more independent health-related and financial decisions. Thus, it is increasingly imperative to better understand the impact of age-related changes in both cognitive and affective processing on decision making. Both behavioral and neural evidence suggests that younger and older adults differ in the processing of monetary incentives (e.g., older adults show attenuated anticipation of monetary losses), which could have specific consequences for financial decisions (e.g., older adults may be generally less sensitive to the warning signs of potential negative outcomes). Although these affective preferences may be healthy and adaptive for regulating emotional experience and optimizing well-being, they may have harmful effects on financial learning and decision making. The main objective of the proposed research is to examine age differences in incentive learning and incentive-based decision-making using both behavioral measures of performance and functional magnetic resonance imaging. The specific aims of this proposal are to (1) investigate the influence of reinforcement valence on incentive processing across the life span, (2) examine whether older adults show the same valence asymmetry in more cognitively demanding reversal learning, and (3) examine whether older adults differ from younger adults both in rational risky decision making and risk preference in a more applied investment decision paradigm. PUBLIC HEALTH RELEVANCE Findings from this line of basic research may have implications for scientists' understanding of how processes underlying decision making change with age, and might eventually also facilitate identification of markers for suboptimal decisions in older adults. The long-term goal of this line of research is to improve the financial and emotional health of older adults by improving decision making at the individual level.

CRITIQUE 1:

Applicant: Mr. Samanez-Larkin received his BA in Psychology from the University of Michigan in 2002, after which he served as a laboratory research assistant for a few years before joining the graduate program in psychology at Stanford. The applicant’s academic performance and GRE scores are generally good. His research productivity has been outstanding as indicated by a first author publication in “Nature Neuroscience” and two others in press or in preparation. In addition, he already has several co-author publications. He also has received numerous academic and research awards and served as a co-investigator on three small grants. His letters of recommendation are among the most positive and supportive I have seen. Overall, the applicant is outstanding.

Sponsor and Training Environment: The sponsor, Dr. Brian Knutson is an Assistant Professor in the Psychology Department at Stanford. He has an outstanding publication record, with several manuscripts appearing in top tier journals, such as Neuron and Nature Neuroscience. One potential concern, though, is that the available funding listed expires in 2009, more than a year before the end of the projected end date for this proposal. Are there additional funding sources available to fund the applicant? The Psychology department at Stanford is outstanding and the trainee has abundant opportunities to interact with cognitive neuroscientists. Mr. Samanez-Larkin is in an environment that should put him on track for an outstanding academic and research career.

Research Training Plan: This three year training plan extends the earlier work by the applicant showing that aged individuals process positive cues (that predict gains) similarly to younger individuals, but show blunted behavioral and neural responses to negative cues (that predict losses). The first aim

will determine whether aged individuals show impaired learning in response to cues that signal high probability of monetary loss (but intact learning in response to cues that signal a gain). The second aim will determine if this age-dependent learning asymmetry diminishes as the cognitive demands of the learning task increase. The third aim will investigate aging differences in behavioral and neural responses in tasks that differ based on their perceived riskiness.

In general, these experiments are well-designed and should build considerably on the applicant's and the sponsor's previous work. But, has the applicant considered increasing the stakes for the "loss" trials to determine if aged individuals are capable of responding (behaviorally and neurally) at qualitatively and quantitatively similar levels compared to young adults? I raise this question because it's arguable whether the $5 loss in this task really carries the same value as a $5 gain (i.e. for the gain trials, the subjects win real money, but in the loss conditions, the subjects don't really lose their own money…it's like they're gambling with someone else's money).

Training Potential: The applicant is in an outstanding environment to study human cognition. However, the applicant has already completed all of his coursework, and it appears he is already quite adept at all the techniques and procedures used in these studies. As such, it would seem that the applicant has already "maxed-out" the training potential of this environment.

Summary and Recommendation: This application proposes interesting and important studies that will build on the applicant's previous work and contribute significantly to field of cognitive aging. Moreover, the practical appeal of these studies is quite high. The sponsor and the training environment are outstanding. The major concern is whether the proposed training plan will significantly enhance the applicant's experimental skill set and/or conceptual development.

Training in the Responsible Conduct of Research: The applicant has completed two research training components at Stanford, one of which involves an extensive online tutorial.

Protection of Human Subjects: The level of risks and protection of human subjects is acceptable.

Inclusion of Women Plan: There are adequate provisions for the inclusion of women.

Inclusion of Minorities Plan: There are adequate provisions for the inclusion of minorities.

Inclusion of Children Plan: Subjects under the age of 25 are not included as subjects.

CRITIQUE 2:

Applicant: The applicant Gregory Samanez-Larkin has a mostly excellent but somewhat mixed record, with a good academic record from his undergraduate institution, University of Michigan, with mostly As and Bs, but relatively low GRE scores. At his graduate institution, Stanford University, he continues a similar record but with some B grades in courses related to the topic of the application, such as a B+ in computational neuroimaging and a B in personality and psychopathology. On the other hand, his referees paint a glowing picture of his research potential and ability, and he has a very impressive publication record for a graduate student, with a first author publication in Nature Neuroscience, a top-tier journal, a first author on a paper in Psychological Science, a high impact psychology journal, co-author on three other publications, and co-pi on three small internal seed grants. He also has received an award for his undergraduate thesis, and several other accolades. Thus, there is ample evidence that despite some mixed grades and low test scores, the applicant is already a highly productive researcher who is highly regarded by some experts in the field.

Sponsor and Training Environment: The sponsor, Brian Knutson, is an expert in the field of affective neuroscience and incentive-based decision processes, fields which both are the focus on the training plan. He has a good record of past mentorship. The productive collaboration between the Knutson and

Carstensen laboratories is an ideal context in which to carry out the proposed research plan, and Stanford University is also ideal in terms of neuroimaging resources, and the scientific community in affective and cognitivie neuroscience. There is an excellent fit between applicant and sponsor, and it is noted that Dr. Carstensen will continue to advise the applicant through the collaboration.

Research Training Plan: The training plan notes that the applicant has already taken all the required courses but that additional courses related to the training plan will be available; greater specificity regarding additional coursework, including what specific courses the applicant will take, would be helpful in evaluating this aspect of the plan. The description of resources available in terms of seminars, talks, and lab meetings is adequate but a minor concern is that it is described rather generically in terms of what is available and what is required, rather than connecting each piece systematically into a coordinated plan for the goals of this specific applicant.

The research plan is an extension of previous research in the sponsor's lab that with aging, older adults show a relative insensitivity to anticipated losses and a relatively preserved sensitivity to anticipated gains, which fits with work, much of it from the Carstensen lab, that shows a positivity bias in older adults relative to younger adults in processing of emotional stimuli and in memory for those stimuli. The hypotheses are well motivated and follow logically from the background that is discussed. The specific aims fit together well and will provide considerable additional research training for the applicant as well as having the potential for revealing important age-related differences in incentive learning and risky decision making.

In the research plan's preliminary data section, the applicant should be careful to consistently describe results; Figure 2's caption states that "older adults were slower to learn to avoid losses", but the accompanying text states that the older adults were not statistically impaired, although they were numerically lower than the young controls. This is also important because whether the older adults are impaired is important for the interpretation of some of the results. The rest of the plan is consistent with the text and the experiments will be interesting regardless of whether there is or is not a deficit, so this is not a major problem. Hypothesis number 2 is interesting as it posits that an individual difference in cognitive ability will interact with the reversal learning. This is a plausible hypothesis and even if it is not observed the experiment is worthwhile. Specific aim #3 is perhaps the most interesting, as it deals with a quasi-realistic investment task and has a nice complementary hypothesis to specific aim #2, namely, that in the investment (risky decision) task, it will be affective traits including trait affect, rather than cognitive traits, that will influence risk preference. Regarding neuroimaging parameters, it is unclear why only a 1.5 Tesla magnet will be used, when the proposed studies will clearly benefit from a high-field scanner (the 3.0 T GE scanner mentioned in the environment section), and a higher-resolution scan protocol should be used. However, given the sponsor's expertise, it is likely that these issues will be corrected quickly, and even at 1.5 T the studies would provide some useful data.

Training Potential: The training potential is quite high, with the combination of a talented applicant with an impressive research record, interesting and important experiments, and an excellent research environment and collaboration with a lab that will contribute substantially to ongoing training. Some minor issues were noted with the scholastic record and the research plan.

Summary and Recommendation: This is an excellent proposal with an exciting set of hypotheses that build systematically on what the applicant and sponsor have been investigating in prior studies. The excellent match between applicant, sponsor, research plan, and environment bode well for the success of the proposed studies and should provide excellent training to prepare the applicant for a future career in affective neuroscience and aging.

Training in the Responsible Conduct of Research: The training is appropriate.

Protection of Human Subjects from Research Risks: The level of risks and protection of human subjects is acceptable.

Inclusion of Women Plan: There are adequate provisions for the inclusion of women.

Inclusion of Minorities Plan: There are adequate provisions for the inclusion of minorities.

Inclusion of Children Plan: Subjects under the age of 25 will not be studied, because this is primarily a study of cognitive aging and maturational effects under this age would complicate interpretation.

CRITIQUE 3:

Applicant: The applicant received a BA in 2002 at University of Michigan. His grades are very good at the graduate and undergraduate levels. He has completed formal coursework at Stanford. He has 5 journal articles in good to excellent journals with 1 more in preparation, and 19 conference presentations. He has consistently excellent to outstanding letters of recommendation.

Sponsor and Training Environment: Dr. Knutson is an Assistant Professor at Stanford and has a strong publication record in the area of the research plan. He has relevant funding for this kind of work, but has only trained one previous graduate student. The environment is excellent for this work.

Research Training Plan: The applicant proposes a well designed series of studies that address issues of incentive learning, risk, anticipation, and cognitive flexibility during aging. The experiments are nicely hypothesis driven and well motivated by the existing literature. The hypotheses and aims lack an explicit overall integration.

The applicant has completed formal course requirements but there is a vague discussion of additional courses to be taken and opportunities to conduct research with other PIs. There are weekly lab meetings and departmental seminars. He will also be participating as a teaching assistant.

Summary and Recommendation: The project is well designed and nicely hypothesis driven. Aspects of the training plan lack specificity. The proposed mentor is relatively inexperienced with graduate students, but has a very good research track record. The environment and applicant are outstanding.

Training in the Responsible Conduct of Research: The training is acceptable.

Protection of Human Subjects: The level of risks and protection of human subjects is acceptable.

Inclusion of Women Plan: There are adequate provisions for the inclusion of women.

Inclusion of Minorities Plan: There are adequate provisions for the inclusion of minorities.

Inclusion of Children Plan: Children are not included as subjects.

THE FOLLOWING RESUME SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW ADMINISTRATOR TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE ON THE FOLLOWING ISSUES:

COMMITTEE BUDGET RECOMMENDATIONS: The proposed duration of training was recommended as requested.

PROTECTION OF HUMAN SUBJECTS (Resume): ACCEPTABLE

INCLUSION OF WOMEN PLAN (Resume): ACCEPTABLE

INCLUSION OF MINORITIES PLAN (Resume): ACCEPTABLE

INCLUSION OF CHILDREN PLAN (Resume): ACCEPTABLE

Administrative Note: The plan for training in the responsible conduct of research is acceptable.

NOTICE: The NIH has modified its policy regarding the receipt of amended applications. Detailed information can be found by accessing the following URL address: http://grants.nih.gov/grants/policy/amendedapps.htm

MEETING ROSTER

Center for Scientific Review Special Emphasis Panel
CENTER FOR SCIENTIFIC REVIEW
FELLOWSHIPS: BEHAVIORAL NEUROSCIENCE
ZRG1 F02A-H (20) L
March 17, 2008 - March 18, 2008

CHAIRPERSON

SIMANSKY, KENNY J, PHD
PROFESSOR
DEPARTMENT OF PHARMACOLOGY
AND PHYSIOLOGY
DREXEL UNIVERSITY
PHILADELPHIA, PA 19102

MEMBERS

ALBERINI, CRISTINA M, PHD
ASSOCIATE PROFESSOR
DEPARTMENT OF NEUROSCIENCE
MOUNT SINAI SCHOOL OF MEDICINE
NEW YORK, NY 10029

AMICO, JANET A, PHD
PROFESSOR
MEDICINE AND PHARMACEUTICAL SCIENCES
UNIVERSITY OF PITTSBURGH
PITTSBURGH, PA 15261

BARRIONUEVO, GERMAN , PHD
PROFESSOR
DEPARTMENT OF NEUROSCIENCE
AND PSYCHIATRY
UNIVERSITY OF PITTSBURGH
PITTSBURGH, PA 15260

COHEN, ROCHELLE S., PHD
PROFESSOR
DEPARTMENT OF ANATOMY
UNIVERSITY OF ILLINOIS MEDICAL SCHOOL
CHICAGO, IL 60612

CONRAD, CHERYL D, PHD
ASSOCIATE PROFESSOR
DEPARTMENT OF PSYCHOLOGY
ARIZONA STATE UNIVERSITY
TEMPE, AZ 852871104

DE VRIES, GEERT J, PHD
PROFESSOR
DEPARTMENT OF PSYCHOLOGY
UNIVERSITY OF MASSACHUSETTS
AMHERST, MA 01003

DEVOOGD, TIMOTHY J, PHD
PROFESSOR
DEPARTMENT OF PSYCHOLOGY AND
NEUROBIOLOGY AND BEHAVIOR
CORNELL UNIVERSITY
ITHACA, NY 14853

FEIFEL, DAVID , PHD
PROFESSOR
DEPARTMENT OF PSYCHIATRY
UNIVERSITY OF CALIFORNIA, SAN DIEGO
SAN DIEGO , CA 921038218

FRENCH, JEFFREY A, PHD
PROFESSOR
DEPARTMENT OF PSYCHOLOGY
UNIVERSITY OF NEBRASKA AT OMAHA
OMAHA, NE 68182

FUDGE, JULIE L, PHD
ASSOCIATE PROFESSOR
DEPARTMENT OF PSYCHIATRY,
NEUROBIOLOGY AND ANATOMY
UNIVERSITY OF ROCHESTER MEDICAL CENTER
ROCHESTER, NY 14642

GITTIS, ALAN G, PHD
PROFESSOR
PSYCHOLOGY DEPARTMENT
WESTMINSTER COLLEGE
NEW WILMINGTON, PA 16172

HAMANN, STEPHAN B, PHD
ASSOCIATE PROFESSOR
DEPARTMENT OF PSYCHOLOGY
UNIVERSITY OF EMORY
ATLANTA, GA 30322

HELLER, H CRAIG, PHD
PROFESSOR AND CHAIR
DEPARTMENT OF BIOLOGICAL SCIENCES
STANFORD UNIVERSITY
STANFORD, CA 94305

HENNESSY, MICHAEL B PHD
PROFESSOR
DEPARTMENT OF PSYCHOLOGY
COLLEGE OF SCIENCE AND MATHEMATICS
WRIGHT STATE UNIVERSITY
DAYTON, OH 45435

KESNER, RAYMOND P, PHD
PROFESSOR
DEPARTMENT OF PSYCHOLOGY
COLLEGE OF SOCIAL AND BEHAVIORAL SCIENCE
UNIVERSITY OF UTAH
SALT LAKE CITY, UT 84112

MARKUS, ETAN J
ASSOCIATE PROFESSOR
DEPARTMENT OF PSYCHOLOGY
UNIVERSITY OF CONNECTICUT
STORRS, CT 062691020

MCGINTY, DENNIS J, PHD
ADJUNCT PROFESSOR
DEPARTMENT OF NEUROPHYSIOLOGY RESEARCH
UNIVERSITY OF CALIFORNIA-LOS ANGELES
V.A. SEPULVEDA
SEPULVEDA, CA 91343

NORRIS, CHRISTOPHER M, PHD
PROFESSOR
SANDERS-BROWN CTR ON AGING
UNIVERSITY OF KENTUCKY-COM
LEXINGTON, KY 40536

QUIRK, GREGORY J., PHD
ASSOCIATE PROFESSOR
DEPARTMENT OF PHYSIOLOGY
PONCE SCHOOL OF MEDICINE
PONCE, PR 00732

SHIROMANI, PRIYATTAM J, PHD
ASSOCIATE PROFESSOR
DEPARTMENT OF NEUROLOGY
BRIGHAM AND WOMEN'S HOSPITAL
VA BOSTON HEALTH CARE SYSTEM
HARVARD MEDICAL SCHOOL
WEST ROXBURY, MA 02132

SUTHERLAND, ROBERT JAMES, PHD
PROFESSOR
ALBERTA HERIAGE MEDICAL SCIENTIST
DEPARTMENT OF PSYCHOLOGY AND NEUROSCIENCE
UNIVERSITY OF LETHBRIDGE
LETHBRIDGE CANADA, T1K 3M4
CANADA

SCIENTIFIC REVIEW ADMINISTRATOR

HOSHAW, BRIAN , PHD
SCIENTIFIC REVIEW OFFICER
CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MD 20892

GRANTS TECHNICAL ASSISTANT

WAITERS, WYKENA B
EXTRAMURAL SUPPORT ASSISTANT
CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MD 20814

Consultants are required to absent themselves from the room during the review of any application if their presence would constitute or appear to constitute a conflict of interest.