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**SUMMARY STATEMENT**  
( Privileged Communication )

**Release Date:** 07/31/2008

Samanez Larkin, Gregory R  
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**Application Number:** 1 F31 AG032804-01A1

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

**Meeting Date:** 07/21/2008

**Council:** OCT 2008

**PCC:** 2BCOGJK

**Requested Start:**

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

**Requested:** 2 years

**Sponsor:** KNUTSON, BRIAN D  
**Department:** PSYCHOLOGY & neuroscience  
**Organization:** STANFORD UNIVERSITY  
**City, State:** STANFORD CALIFORNIA

**SRG Action:** Priority Score: 142  
**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

**RESUME AND SUMMARY OF DISCUSSION:** This application proposes to examine the neural basis of age related differences in decision making through a research design that involves functional magnetic imaging. The letters of reference are laudatory and the applicant has an impressive publication record for a predoctoral student. During the discussion the reviewers disagreed on the strength of the training plan. While some reviewers stated that the training plan will help prepare the applicant for a research career, others felt that the number of activities and projects planned could actually hinder the applicant's progress. However the reviewers agreed that the sponsor is an ideal fit for the research proposal, and the training and research opportunities available at Stanford increase the training potential of the proposal. Overall the enthusiasm for this proposal is high.

**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. 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:** Gregory Samanez-Larkin has already shown considerable research productivity at a relatively early career stage. He has two high profile publications, one in Nature Neuroscience, three additional published papers, and is noted to be continuing this level of productivity. His undergraduate record from University of Michigan and graduate record at Stanford show good yet somewhat variable academic performance, but this is countered by the uniformly glowing praise of the referees and his demonstrated research aptitude and productivity. He is described as being on track for an outstanding career in cognitive and affective neuroscience.

**Sponsor and Training Environment:** The applicant will be co-mentored by Brian Knutson, who has published widely and is an expert in the areas of affective neuroscience and reward, and Laura Carstensen, who is an expert on cognitive aging. Both of the sponsors have an excellent history of mentorship, and there is a good fit between the sponsors and the applicant's goals as described in the application. The training environment at Stanford University is ideal, with ample opportunity for the applicant to expand his skills in cognitive and affective neuroscience, and state-of-the art neuroimaging resources. The revised application now clarifies that additional funding to support the proposed studies will be available from the co-mentor Dr. Carstensen.

**Research Training Plan:** In this revised application, the applicant has been relatively responsive to prior comments and has clarified, expanded and elaborated on the research training plan. Specific

collaborations, journal clubs, colloquia, and opportunities for presenting at scientific conferences are outlined. The applicant has already completed the required coursework, and it is argued that the individualized opportunities afforded by the interactions with collaborators, etc. go beyond what could be obtained from courses. However, it seems likely that the applicant would still benefit from an appropriate advanced seminar or similar course that would complement the individual training in the plan.

The proposed experiments have been revised slightly but remain essentially similar to the ones previously proposed. Briefly, the guiding rationale derives from work by Carstensen and others that has shown a positive bias (greater attentional and memorial bias towards positive affect) in aging, and also from more recent work in the lab of the sponsor that shows a related phenomenon where older adults show less sensitivity to anticipated losses but relatively preserved sensitivity to anticipated gains. The applicant will investigate this hypothesis in a series of three studies systematically examining incentive learning (Experiment 1), incentive learning in a task that additionally incorporates reversal learning (Experiment 2), and finally, learning in a more ecologically valid paradigm modeled after financial investing.

Each study will concurrently examine both learning performance and neural correlates associated with learning and the role of valence and individual differences including risk preference, trait affect, and cognitive ability. The rationale for each study and the anticipated results are well described and there is adequate consideration of alternative results and how they will be handled, both practically and theoretically. The revised application now clarifies some points such as the selection of a lower-field magnet to reduce artifacts when imaging specific brain regions; other minor revisions have also been made based on prior comments.

**Training Potential:** The training potential is high. The applicant is highly productive and talented, and there is a good match between the expertise of the co-mentors, the applicant's goals, and the research training plan.

**Summary and Recommendation:** The proposed series of studies is well grounded theoretically, interesting, and will provide training that will help prepare the applicant for a research career in affective neuroscience and aging. The combination of applicant, co-sponsors, training environment, and the specific training plan is excellent.

**Responsible Conduct of Research:** The proposed training is acceptable.

**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 are not included. This is scientifically justified because this is a study of cognitive aging and developmental changes occurring in subjects under this age would complicate the interpretation of the findings.

## **CRITIQUE 2:**

**Applicant:** The applicant received his BA from the University of Michigan in 2002 and began graduate study at Stanford University in 2005. He received an MA degree in 2008. At Michigan and Stanford he received many B's and A's. The GRE scores were 500, 650, and 5.0 in Verbal, Quantitative, and Analytical, respectively. The letters of reference are extremely positive and supportive. The applicant

has been first author of two articles (in Nature Neuroscience and Psychological Science), and an author of three other articles.

**Sponsor and Training Environment:** The sponsor has previously trained one three postdoctoral fellows, one predoctoral fellow, and one clinical fellow. The predoctoral fellow, and two of the postdoctoral now have faculty positions at major research universities; the other postdoctoral fellow is an Extramural Grants Administrator and the National Institute of Aging (NIH).

The sponsor is a leading researcher in affective neuroscience, and eminently well qualified to supervise this research and training. He currently will supervise three other PhD candidates and one post-doctoral fellow during the applicant's fellowship. The facilities at Stanford available to the applicant are outstanding, and well-described in the application. Funds are available for the research costs.

**Research Training Plan:** In the first year of the fellowship, the applicant will spend about 70% time on research, and 30% as a graduate teaching assistant for courses on longevity and statistics; in the second (final) year, he will spend 100% on research and complete the PhD.

A detailed training plan is provided. It includes the following activities: He will work with his sponsors (Knutson and Carstensen) on a series of book chapters and journal reviews to begin to develop a comprehensive theory of aging and economic decision-making. He will get management and mentoring experience by being the primary supervisor of two research students. He will regularly attend events sponsored by three Centers (Longevity, Advancing Decision Making in Aging, and Demography and Economics of Health and Aging), and present annually to each of the three Centers. And he will regularly attend weekly lab meetings of the Symbiotic Project on Affective Neuroscience lab, and the Life-span Development lab, and present quarterly at each of them.

In addition, he will have quarterly meetings with his dissertation committee (Knutson, Carstensen, Wagner, McClure, and Garber). Specifically Knutson and Carstensen will deal with analysis of age-related effects, McClure with computational models for behavioral and neuroimaging data, and Garber and Kuhnen on Bayesian rational actor models to characterize single trial behavior.

One concern is that, although each of these activities would be valuable, too many of them may interfere with each other and, more importantly, interfere with concentrated achievement associated with the PhD research.

The proposed research concerns age differences in performance in tasks involving monetary gains and losses, and functional magnetic resonance imaging. It relies heavily upon data suggesting that 12 older participants (65-81 years old) responded differently than 12 younger participants. The difference was an interaction--they responded similarly for gains, but the older participants were less affected by the losses. Because of the time and expense of fMRI research, this cannot be readily extended to large samples, but large sample behavioral tests could easily be done. If the behavioral results are general, the obtained correlation between the brain and behavioral measures provides some plausible causal mechanisms, But early critics might speculate about alternatives. For example, if the younger participants were on a tighter budget than the older participants, they might be more affected by the loss of \$5.00.

**Training Potential:** The applicant will be better prepared for a research faculty position by having this fellowship.

**Summary and Recommendation:** The research and training environment is outstanding for the analysis of the relationship between incentives, decision, and brain processes. The proposed research and training plan may be overambitious, but provides a good framework for a two-year fellowship.

**Responsible Conduct of Research:** The training has been done in an acceptable manner.

**Protection of Human Subjects from Research Risks:** The behavioral tasks are standard ones that have no unusual risks; the fMRI requires careful procedures that are clearly described.

**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 will NOT be included as subjects, and this is appropriate.

### **CRITIQUE 3:**

**Summary and recommendation:** The applicant has a very productive graduate career with two first authored publications in top-tiered journals. His recommendation letters rate him extremely high on all dimensions. Although his grades in both his undergraduate and graduate course have been good to excellent, they are somewhat lower than what might be expected. In this re-submission, the applicant responded to comments regarding the lack of novel training experiences in the proposed projects by outlining the guidance he will be receiving from the project's sponsor and co-sponsor (added because of concerns about laboratory funding). The projects have an interesting theoretical foundation and a good case was laid out for its translational relevance. This study is an interesting investigation of the relationship between the decision making patterns in the elderly and their neural correlates. This correlations raise some theoretical issues that were only briefly addressed. What is the likely direction of causality in the behavioral and neural observations? Why would aging affect the integrity of certain neural systems but not others? Addressing such issues could provide for a richer interpretive context.

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

**PROTECTION OF HUMAN SUBJECTS (Resume): ACCEPTABLE**

**INCLUSION OF WOMEN PLAN (Resume): ACCEPTABLE**

**INCLUSION OF MINORITIES PLAN (Resume): ACCEPTABLE**

**INCLUSION OF CHILDREN PLAN (Resume): ACCEPTABLE**

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

**TRAINING IN RESPONSIBLE CONDUCT OF RESEARCH:** The proposed training is acceptable.

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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-X (20) L  
July 21, 2008 - July 22, 2008**

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