

## **Executive Summary of the Evaluation Report prepared by Susan Fitzpatrick, Ph.D.**

### **Overview**

The McKnight Endowment Fund for Neuroscience (EFN) supports excellent scientists carrying out important, highly-cited neuroscience research. The real challenge for the evaluation team was not documenting the quality of the science but rather determining the unique effectiveness of the EFN as one program of philanthropic support for scientific research. Doing so is complicated, particularly in the United States, because of the immense size of the research enterprise and the billions of dollars of research funding contributed by public and private sectors.

The field of neuroscience has grown rapidly over the past three decades. The Society for Neuroscience annual meetings began in the 1970's with less than a thousand attendees. It now attracts close to 35,000. Federal and private support for neuroscience research totals billions of dollars. Such facts do not negate the effectiveness of small philanthropic programs, but the facts do require that philanthropic funds be adaptive, flexible, and invested strategically if they are to yield a positive return.

A challenge for the evaluation team was judging the effectiveness of the EFN in light of the McKnight philanthropic goals. Assessing the impact of philanthropic investments in academic research is tricky, in part, because of long time gaps and lengthy causal chains separating basic discoveries from useful applications. Determining the impact of philanthropic investment in basic neuroscience research in the context of improving the understandings of and treatments for human neurological disorders is even trickier in light of the vast complexity of the brain and nervous system functions and the unique capacities and frailties of human cognition. There has been significant progress in studies of the brain and nervous system. The McKnight Endowment Fund for Neuroscience-supported research that has led to advances in the field of neuroscience.

From its inception, McKnight support for neuroscience was motivated by a desire to improve the lives of individuals suffering from memory impairments and cognitive decline. The EFN strategy is "... to select problems that, if solved at the basic level, would have immediate and significant impact on clinically relevant issues such as learning and memory." Tactically, the EFN awards three types of grants and hosts an annual meeting. The evaluation team's findings and recommendations for each of the three award programs, the annual meeting, and the administration of the EFN are summarized below.

The roster of individuals affiliated with the program, as either grantees or advisors (or both) is, unequivocally a who's who of neuroscience research. The funds awarded by the EFN support laboratories at leading US research universities and contribute to the ongoing efforts of both prominent (in the case of senior researchers) and promising (in the case of junior faculty) scientific programs. The quality of the science supported by the

EFN has been documented by prior evaluations and recently summarized in the book by Gabrielle Strobel. Against this backdrop of scientific success, the evaluation team examined the impact and outcomes of the EFN programs through the lens of the McKnight Foundation's philanthropic mission and strategic goals. Put simply, is the McKnight Foundation getting maximum return on its philanthropic investment? We believe only partially. A second and related question we considered concerns how well the strategy of supporting basic neuroscience research is achieving the McKnight goal of ameliorating the cognitive decline associated with human aging and neurological disease. A third asks how well the individualized awards of the EFN match the McKnight Foundation's emphasis on uniting individuals to solve problems cooperatively. Again, we found partial fulfillment. We offer some recommendations for changes that could align the McKnight Endowment Fund for Neuroscience with the McKnight Foundation's philanthropic goals.

### **Relatedness to Memory**

In our conversations with McKnight Foundation Board members the emphasis on supporting research related to understanding memory loss came across as of central importance. The publicly disseminated descriptions of the EFN support this emphasis. However, the EFN strategy is supporting neuroscience broadly. **Less than a quarter of EFN grants are related to memory.** Regardless of the scientific situation 30 years ago, there is today a robust and readily identified science of memory ranging from the molecular to human behavior and involving a large research community. There is also much unknown about general principles of neural system function and such studies also have large robust constituencies. We encourage the McKnight Foundation and the EFN to resolve the intent of the funding. Is the intent to advance neuroscience or to advance an understanding of human memory and its failings? Clarifying the importance of memory research *per se* will be important as the program moves into its next phase.

### **Administration**

Prominent academic scientists face increasing time-demands for research, research-administration, travel, and service to the scientific community. Meanwhile, the pace of discovery is rapid and the volume of scientific information is vast. It may be time for the McKnight Foundation to consider recruiting a program officer with training in neuroscience, specifically in learning and memory, to scan the field with an eye to the McKnight Foundation's interests. The program officer could work closely with (but not for) the EFN leadership, but have primary responsibility for linking the EFN programs with the Foundation's philanthropic vision. By continually monitoring the responsiveness of the funding, the program officer position eliminates the need for periodic, retrospective, external analysis of effective grantmaking. We would expect the program officer to initiate new efforts bringing together groups of investigators, both EFN and non-EFN supported, to cooperatively identify and work to solve important scientific questions.

### **Scholar Awards**

The Scholar Awards, aimed at promising young investigators in the early stages of their academic careers, are prestigious and highly selective. The Scholars are all excellent

young scientists. Analysis of their career trajectories demonstrates that Scholars fulfill, or exceed, expectations of academic career success.

The Scholar Awards balance a high-risk strategy, that of investing in basic neuroscience research, much of it carried out in model organisms, as a route to important insights about human brain function and human neurological disease, with the lower-risk strategy of investing in career development of promising young faculty likely to assume leadership positions in the field of neuroscience. Funding broadly in basic neuroscience is a reasonable strategy for understanding neural structure as it is not clear which basic neuroscience findings will be important to the understanding of human cognition and human neurological disease. We encourage the EFN to maintain its support for fundamental neuroscience and to de-emphasize disease-related research.

In response to questions raised by the McKnight Foundation concerning the impact of the Scholar Awards, one analysis we carried out looked at a comparison of individuals selected to receive Scholar awards and those who were interviewed but not funded (finalists). Acknowledging that the small sample sizes rule out rigorous statistical analysis, **we found little difference between the two groups on a number of measures**. We found the lack of differences could be attributed, in part, to Scholars and finalists obtaining support from multiple sources to maintain their research programs.

In general, Scholars can be characterized as:

- Assistant professors recruited into tenure-track positions at elite research universities
- Likely to achieve promotion and tenure quickly, usually within 6 years post-hire
- Geographically stable; most Scholars remain at their original sponsoring institution
- Successful at garnering private and public (NIH, NSF) support for their research programs
- Contributing to the advancement of basic neuroscience as judged by publication records in high impact journals.
- Overwhelmingly male. The percentage of women receiving Scholar Awards remains small (no change since Abt Associates report) even though women are as likely to pursue careers in neuroscience as men.

The Scholar Awards are highly selective. During the decade evaluated 65% of Scholar Awardees were on the faculty of 8 elite research institutions (Harvard, Stanford, MIT, Salk Institute, UCSF, UCSD, Rockefeller University, and the University of Washington).

In terms of their neuroscience research interests, the Scholars tend toward projects:

- related to development rather than aging or neurodegeneration
- studying sensory and motor processes rather than memory
- biased towards molecular and cellular approaches rather than integrative systems-level projects

- focusing on experimental model organisms, especially invertebrates and rodents, rather than human subjects

In general, experimental approaches to neuroscience from neurochemistry, energetics, neuroanatomy, comparative evolution, and cognitive/behavioral studies are rarely represented by Scholar research programs.

### **Recommendations:**

The Scholar Awards program could be enhanced by diversifying Scholar selection with respect to topics within neuroscience and institutional affiliation. More effort should be made to identify promising candidates outside the small circle of elite institutions currently capturing the bulk of the awards. Without sacrificing quality, priority could be granted to candidates with research projects somewhat orthogonal to dominant theories or common experimental approaches. Such individuals will greatly benefit from the both the resources and the recognition bestowed by a Scholar Award. In return, such candidates will bring additional intellectual vibrancy to the EFN.

We suggest:

- Increasing the number of Scholar awards to allow for greater risk-taking.
- Diversifying the Science Board and Review Committee members with respect to neuroscience expertise and institutional affiliation (including international representation).
- Diversifying the Scholar awardees both with respect to the levels of organization at which they work within the field of neuroscience and their institutional affiliation. Internationalizing the awards should be considered if possible.
- Reconsidering the use of references to human neurological disease in the Scholar Award description.

### **Technological Innovation Awards**

The description of these awards provided in the letter describing the EFN evaluation states:

“In the first year of these awards, 1999, the committee received preliminary proposals from 130 research laboratories. Clearly, the existence of this award stimulated new thinking and brought together scientists from different areas. The McKnight Technological Innovation award has a unique mission to catalyze the invention and development of new ways of approaching brain function.”

The evaluation committee’s analysis suggests a different interpretation of the robust response of the research community to the initiation of the Technology awards.

- The continued development and refinement of tools and experimental methodologies is central to progress in neuroscience and is an active and ongoing aspect of neuroscience research.

- Technological advances ranging from single cell electrophysiology to human functional brain mapping have allowed researchers to access neural function and have been essential to progress.
- Neuroscience research is dependent on refining and expanding scientist's ability to monitor, influence, disrupt, and model neural activity and the inputs (stimuli) and the outputs (behavior) of neural activity.
- Neuroscientists have benefitted by attracting as collaborators physicists, chemists, engineers, computer scientists, and other specialists drawn to study the brain and nervous system for the same reason individuals are drawn directly into neuroscience – the challenge of understanding the brain and its wonderful complexity.

New technologies can have a broad and powerful effect on fields of research and we commend the EFN for its bold effort to seed technological innovation. New techniques open up entirely new avenues of research. That said, the McKnight Technology Awards are too small in number and provide funds too limited in both amount and duration to have a unique impact on methods and/or tool development in neuroscience. Technique development is expensive and risky and deserves support, but such support may be better awarded as an explicit component of a research program.

The evaluation team findings include:

- ~50% of the awards supported just 4 institutions (Stanford, NYU, MIT, and Harvard)
- Many of the projects were focused at improving molecular and cellular approaches
- The research programs of the principal investigators on the awards emphasize technological approaches as a primary research interest

### **Recommendations:**

We suggest that the EFN revisit its motivation for initiating the Technology Innovations Awards. Some of the intended goals can be achieved through the Scholar Awards and some may be better achieved through support of cooperative, collaborative efforts.

### **Brain Disorder Awards**

The Brain Disorders Award were initiated in response to the original interests of William McKnight as stated in the charge letter "...the founders looked forward to a time when basic neuroscience research could be applied to the diagnosis, prevention, and treatment of brain disorders, especially those that affect cognition and memory in old age." The program description goes on to state:

"...also extends to other disorders that can be illuminated by basic neuroscience discoveries—such as spinal cord injury, stroke, drug addiction,

schizophrenia, and mood disorders. With modern tools of genetics, molecular biology, physiology, and functional imaging in hand, it is now possible to systematically dissect and understand brain disorders and elucidate causes. The Neuroscience of Brain Disorders Awards will encourage many of the best neuroscientists, as well as scientists from other disciplines, to turn their attention to diseases and disorders of the brain.”

The Brain Disorder Awards shares funding goals with NIH and disease-interested private funders. The size of the program relative to the capacity of the field is captured by noting that the overall funding rate is less than 5% of applications. We applaud the willingness of the EFN to launch a bold experiment in funding translational research through a competitive proposal process but the scope and difficulty of the problem may require a more innovative funding mechanism.

We find:

- ~30% of the awards went to just 3 institutions (Columbia, Harvard Medical School, and Cal Tech). One of the institutions, Cal Tech, does not have a medical school and is not noted for clinically-relevant research.
- Grantees are commonly Ph.D.s with appointments in basic science departments.
- Only one project involved human subjects.
- ~10% of the projects involve assessments of memory or other cognitive functions.
- Few if any projects involved pragmatic contributions to human disorders in the near-term.

### **Recommendations:**

We acknowledge that the current slant of the program towards basic science may result from the newness of the Awards and the attempt to depart from the traditional EFN focus on fundamental neuroscience. Driving translational neuroscience has proved difficult, even for the National Institute of Neurological Diseases and Stroke, the federal agency charged with this responsibility. Translational neuroscience may be best achieved via alternative funding mechanisms such as multi-disciplinary networks integrating across multiple levels of nervous system organization. Collaborative groups also provide a way to focus on a particular type of brain disorder, for example, age-related executive dysfunction.

### **Annual Meeting**

The annual meeting is characterized by high quality research presentations in a relaxed, informal environment. The use of the traditional symposium format does not extract the most value from the wealth of talent gathered. We suggest:

- Shifting the Scholar's component of the annual meeting away from retrospective reporting (what was done) to prospective, shared problem-solving.
- Using the meeting as a forum for identifying knowledge gaps, prioritizing problems, discussing controversies, comparing methodological approaches, and other questions important to advancing the current state of knowledge.

**Summary of Overall Recommendations:**

- Clarify the role of memory research and understanding memory disorders.
- Encourage collaborative efforts designed to advance knowledge through cooperative rather than competitive funding mechanisms.
- Recruit a neuroscience program officer, experienced with learning and memory, with primary reporting responsibility to the McKnight Foundation and its philanthropic vision.
- Shift the emphasis of the annual meeting from retrospective to prospective.
- Enhance the Scholar Awards program by increasing the number of awards and bringing diversity to the selection process.
- Diversify the institutional affiliations and expertise of the EFN leadership.
- Consider re-deploying the funds currently allocated for the Technology Awards and the Brain Disorders awards. Funds could initiate non-institutional, collaborative, cooperative research networks focused on solving difficult problems pertinent to human brain/cognitive function and ameliorating related disorders.