

October 7, 2008

Reviewers' Response to the Evaluation Report of the McKnight Endowment Fund for Neuroscience

We have carefully read the report, entitled "Evaluation of the McKnight Endowment Fund for Neuroscience", carried out by Dr. Susan Fitzpatrick and her colleagues and have discussed it among ourselves. The report comprises two parts. The first is a careful and detailed examination of the programs of the Endowment Fund for Neuroscience (ENF) that address a series of questions outlined in the letter from Kate Wolford (President, The McKnight Foundation) and Carla Shatz (President of the McKnight ENF) specifying the charge to the evaluation team. The programs are examined thoughtfully and seriously, leading to a series of specific observations and considerations. The second part of report, which goes beyond the original charge, is a section that is "primarily intended to be used prospectively for future planning" and contains lengthy discussions evaluating the reductionist vs. integrationist approach to neuroscience research, a comparative discussion of philanthropic approaches to funding scientific research, and a lengthy essay on dementia and Alzheimer's disease. Because the two parts of the report are so different in scope and intent, and, we believe, in their value to the Foundation, we address our comments to each in turn.

Programmatic Evaluation:

The McKnight Foundation established its awards program in neuroscience in 1976 "to support fundamental research in neuroscience, especially as it pertains to memory and its biological substrates". The original McKnight programs were, and continue to be, highly successful in carrying out this mission. In 1994, the Abt Associates Report proposed continuing the original program in basic neuroscience and building on it by establishing two new programs, one intended to accelerate progress in applying basic neuroscience knowledge to the understanding and amelioration of diseases of the brain and the other to the development of new technologies, in recognition of the importance of technology in driving science (e.g. recombinant DNA and magnetic resonance imaging, or MRI, as two examples).

The evaluation report addresses the strengths and weaknesses of each of the core areas of the McKnight ENF: the McKnight Scholars Award; the McKnight Neuroscience of Brain Disorders Award; the McKnight Technological Innovations in Neuroscience Award; and the Annual McKnight Neuroscience Conference and Workshop. In addition, as requested, there are comments about ENF Management and Award Selection.

Scholars Award: The report correctly acknowledges that the Scholars Awards program, because of its success and prestige, is the flagship program of the ENF and devotes much of its analysis to it. The report documents the extremely high quality of the Scholars in

terms of the quality of their research as Scholars and their subsequent scientific success. The prestige and impact of the McKnight Scholars Award program are widely recognized in the scientific community. The stellar record and the impact of the Scholars Award on the careers of young scientists, and thus on the field, is hard to overemphasize.

The most important conclusions that the Report makes with respect to the Scholars Award are:

- The Scholars Award program should continue to champion basic neuroscience. Moreover, it should consider broadening the scope of fundamental research on the nervous system to further emphasize higher functions of the nervous system. We believe the suggestion to expand the interests of the ENF is timely, and that the direction of the expansion should be based primarily on scientific opportunity, rather than on other considerations. Our own view is that opportunities for study of the biology of cognition and behavior are particularly promising and offer a potential area of expansion that is scientifically promising and also very much within the mandate of the McKnight Foundation with its interest in memory and learning. The coupling of new methods of brain imaging with sophisticated behavioral paradigms, for example, have opened new areas of investigation with direct relevance to the interests of the Foundation.
- Increasing the number of Scholar Awards would increase the impact of the program without sacrificing quality.
- Recruiting Science Board members and reviewers with more diverse scientific backgrounds and from a more diverse group of academic institutions, as well as extending membership to international neuroscientists, would broaden the collective experience of the advisory boards and decrease the perception of a “closed shop”. New areas for inclusion might include clinical scientists and cognitive scientists. As the program expands its scope, new members can be sought with appropriate expertise.

Several of the recommendations in the report suggest changes that we believe would not be wise.

- We believe that the award selection process should continue to use research excellence as the primary funding criteria and that the ENF should not try “to build a complementary network of Scholars whose research interests combine in a synergistic manner”. Scholars should be encouraged to follow their own imagination and curiosity, rather than fitting into a programmatically defined group or project. We also believe that funding decisions should not be “weighted” to achieve balance. Scientific excellence, as judged by a panel of distinguished scientists, has been the hallmark of the program, and should continue to be the dominant selection criterion.

- We do not believe that a programmatic focus on memory research is the best course at this time. We believe that the balance between “memory research” and more broadly-based research has been appropriate and is the best long-term strategy for understanding and treating disorders of memory. Molecular, cellular and systems neuroscience all have a part to play and involvement of clinical expertise would also be valuable.

Neuroscience of Brain Disorders

Because the Neuroscience of Brain Disorders Program has been in existence for a shorter period of time, its long-term impact on the field is more difficult to determine. The report does not explicitly address the quality of the work supported by the ENF, but suggests in several places that the projects as a whole are too much directed toward laboratory work and to work with animal models of disease. In particular, the report suggests that more work on human subjects be funded; also that only diseases affecting a large number of individuals be studied. We do not believe that these would be wise decisions. The ENF Program from its beginning has been committed to the study of disease mechanism as the surest path to long-term success in developing therapies for brain disorders. The use of genetics and model organisms has been one of the most powerful tools for studying human disease and we believe that the projects so far supported by the ENF Program appropriately take advantage of this scientific opportunity. New methods make it also possible to extend some of these studies to human subjects and we believe that the ENF can profitably look for opportunities to do so. Such studies should be firmly grounded in the biology of the brain, however, and should continue the mechanistic commitment indicated in the title of the program. In our opinion, the repeated suggestion that the ENF program be extended to clinical outcomes research would distract the ENF program from the goals it is achieving so successfully. To be rigorous, research focused on clinical outcomes must be done on large populations of human subjects over long periods of time, usually requiring multiple centers and large sums of money. This is precisely the kind of work that the NIH or the private sector is best suited to carry out. We also believe that it would be a serious mistake to focus only on diseases that affect a large number of people. As the report itself points out, private foundations and the NIH spend large amounts of money on diseases such as stroke, Alzheimer’s disease and other brain disorders. The ENF should not base its funding decisions on disease incidence, but look for opportunities in which research can illuminate the causes of disease and thus suggest new therapeutic approaches. Such opportunities may involve either common or rare diseases. Dr. Huda Zoghbi’s pioneering work on Rett’s syndrome with a very small patient base, for example, offers important insights into autism and other much more common mental disorders.

We support two of the suggestions made by the report:

- Consider waiving the requirement that applicants have a tenured or tenure-track position. Many outstanding scientists, particularly in clinical departments, do not have tenured positions and the removal of this barrier would increase the pool of talented applicants with disease interests.

- Consider funding focused workshops that would bring together those doing research on human subjects and those working on disease models to help bridge the laboratory/clinical divide. In addition, the annual meeting could be used to promote synergy among scientists with different backgrounds by including panels focused on particular topics of interest.

Technological Innovation Awards:

The report recognizes the importance of technological innovation in advancing a field and that those involved in this research often do not receive support from conventional sources. There is a suggestion that there be a more explicit attempt to engage engineers and physical scientists, which we support. In particular, imaging the human brain has been a powerful tool for investigating higher functions of the nervous system and we believe that there are fruitful opportunities for technological innovation that would enhance the value and applications of such techniques as magnetic resonance imaging (MRI), magnetoencephalography (MEG) and event-related potentials (ERP). Again, workshops at the annual meeting or elsewhere could be used to foster interdisciplinarity.

Annual Meeting

The value of the annual meeting is recognized in the report as crucial for developing a sense of community between junior and senior scientists as well as promoting informal discussion. We believe that overlap with other meetings is not an issue, because of the unique nature of the McKnight meeting and its value to the participants. The idea of including focused panels on particular topics that extend across disciplines or diseases, as mentioned above, seems well worth exploring.

Scientific Board and Reviewers

The report commends the quality of the scientists who comprise the scientific review board and committees and their excellent track record in selecting and encouraging young scientists. We wholeheartedly agree with that assessment. We support the recommendation of the report that broadening the expertise and institutional representation of the Board and the reviewers would strengthen it. In particular, such an extension would serve to counter any impression of a “closed shop”. The Board includes Dr. Larry Squire, an individual who is a widely recognized leader in memory research, but additional expertise in cognitive neuroscience would strengthen the Board if a decision is made to extend awards in this direction