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SBE 2020: Quantitative Convergence of Lifespan Development, Neuroimaging, and Genetic Epidemiology

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Abstract
This white paper discusses the potential benefits of the interdisciplinary convergence of three areas: lifespan developmental psychology; neuroimaging and neurophysiology; and genetic epidemiology. This three–discipline convergence is likely to occur within the next 10 years due to shared interests of the three areas each of which have come to understand that their own future progress is limited by the need for the other two. One main interface at which these disciplines are communicating is through recent developments in intensive time series which are needed in each area and which affect the rate of discovery in each. The benefits of convergence are large: for instance, improvements in diagnosis and delivery of personalized medicine hinge on advances that require the coordinated effort of these three areas. However, funding mechanisms for three–discipline projects and centers is very limited. This white paper proposes that the National Science Foundation create initiatives that will speed the synthesis of theory, methodology, and results from genetic epidemiology and functional neuroimaging over the course of the human lifespan. The proposed synthesis poses difficult challenges, but the rewards are great.

1 The Challenge

Many, if not most, of the challenges facing the social and behavioral sciences involve processes that unfold over time at multiple time scales. That is to say, humans interact with, adapt to, and affect their environment while they perceive, decide, learn, develop and age. Data from these adaptive processes provide a complex, multivariate, time–varying challenge to understanding problems in the social and behavioral sciences.

The heart of the problem is that an aggregation of cross–sectional measurements does not necessarily represent the adaptive process of any individual in a population (Molenaar, 2004). Thus, it is critical to perform repeated observations of individuals over the timescales in which processes of interest unfolds and perform analyses at the individual level prior to generalizing to the population.

This problem has been widely recognized and a substantial proportion of studies currently underway incorporate longitudinal designs or measurement bursts, i.e., repeated observations with short intervals between samples. These new data, intensively sampled in time, have spurred work on formulating and testing statistical process–oriented models, often

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referred to as dynamical systems analysis. Methods for estimating individual differences in dynamics so that general principles can be adduced at the population level remain largely unexplored territory. However, there are promising new candidate methods that address the problem of generalization when there are individual differences in the properties of adaptive processes.

Three major areas of science have been early in recognizing the challenge of individual differences in adaptive processes: Lifespan Development; Functional Neuroimaging / Neurophysiology; and Genetic Epidemiology. Each of these areas address problems that are easily recognized as involving adaptive process and have begun development of methods for addressing the resulting data.

Those who study functional neuroimaging and neurophysiology are confronted with large individual differences in brain structure, individual differences in the timing of responses, and non–stationary signals all in a multivariate environment. Some of the most innovative modern work in multivariate statistics for nonstationary time series is focused on solving problems posed by these data. If one is to understand and account for the observed differences both in structure and response of the brain, it is inevitable that answers will be needed for questions concerning human development, environment, genetic epidemiology, and gene by environment interactions.

Genetic epidemiology is confronted with the perplexing problem that Genome Wide Association Studies (GWAS) are finding many single nucleotide polymorphisms (SNPs) for each target heritable trait. It is beginning to appear that exactly which SNP is relevant at any one time may depend on the environmental context. Gene by environment interaction has become an extremely hot topic in this field. There are many indications that specific alleles may be associated with greater sensitivity to specific adverse or favorable environmental contexts. Again, a process–oriented view of the individual will be necessary in order to measure and model the complex adaptive relationships inherent in genetic epidemiology. Specific environment contexts may have greater or lesser impact depending on an individual's genetics, but it is also the case that people can choose aspects of their environmental context and/or adapt their environment to meet their needs. If one is to understand these mechanisms, it will become necessary to ask questions concerning development across the lifespan as well as questions about how adaptive decisions are made.

The field of lifespan development asks questions with timespans from milliseconds to decades, frequently mixing multiple timescales within the same study. For instance neurophysiological measurements may be acquired from children, young adults, and older adults with follow–up measurement occasions separated by years. Data from such an experiment must address short term dynamics, year to year within–person change in these short term dynamics, and group comparisons across a wide span of ages. Recent work in multilevel dynamical systems analysis has begun to address this synthesis of timescales into unified models. Many lifespan researchers are already using the tools of neuroimaging (Lindenberger, Li, & B□ackman, 2010) and it is also beginning to be recognized that answers to questions in genetic epidemiology will be needed in order to understand lifespan development as bundled concurrent processes rather than a sequence of stages.

We expect the need for convergence across the fields of neuroimaging/neurophysiology, genetic epidemiology, and lifespan development will increase over the next 10 years. We expect that advances in statistical modeling of adaptive processes at the level of the individual will help enable this convergence. The challenge is great since these three areas have separate traditions and language. The three areas are frequently in separate academic departments if not separate colleges. Furthermore, the three areas are most often funded from separate federal agencies or directorates/institutes within agencies. However, the successful integration of data, methods and theories from these three areas would positively transform how we go about the study of brain and behavior. We see the National Science Foundation as being ideally positioned to facilitate the cross–cutting cooperation required in

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order to meet the challenges posed by this interdisciplinary convergence.

2 Broader Impact of Successful Convergence

Forging a successful convergence of lifespan development, neuroimaging/neurophysiology, and genetic epidemiology promises to raise substantially the quality of human existence in many ways. Here are four examples.

1. Personalized Medicine — The most recent issue of Perspectives in Psychological Science (Reiss, 2010) was a special issue devoted to the potential contributions of genetic epidemiology to personalized medicine. Several of the articles emphasized that a lifespan developmental perspective was required in order to make sense of gene by environment interactions. Reiss states that we can expect four main benefits from epigenetic studies: better targeted interventions, better understanding of the mechanism of interventions, better understanding of individual differences in response to interventions, and better timing of interventions.

2. Eating Disorders and Emotion Regulation — There is evidence that day to day variation in disordered eating are related to emotion regulation and each of these appear to have within person cycles. The dynamics of these two variables appear to also be related to hormone regulation, particularly to ovarian hormones in younger women. There is also evidence that emotion regulation changes as an individual ages. Eating disorders such as anorexia can have long term negative health risks. In order to design effective interventions for eating disorders it is important to understand how the dynamics of emotion regulation are related to decision making and to understand how this changes over the lifespan. For instance, reducing negative emotional reactivity in young women may lead to lower incidence of disordered eating, which would over the lifespan result in better health and mobility in late life. Understanding who to target with which behavioral intervention and understanding how to adapt the intervention to an individual's emotional regulation cycle will require the convergence of neurophysiological, epigenetic, and lifespan data along with dynamical models of these individual–level data.

3. Childhood Learning / Cognitive Decline — A variety of studies report that education and environmental complexity during childhood and adolescence have association with a variety of effects in older age including obesity, smoking, and rates and age of onset of cognitive decline. These effects are plausible because neural plasticity has been demonstrated in response to a wide range of environmental stimuli. But these effects have a variety of confounds that reduce the ability to draw cause and effect conclusions from these correlational associations. Selection effects include that children with higher parental income, higher parental education, and/or higher ability tend to be exposed to better educational environments. In addition, decisions throughout life such as career, family, and social engagement can have profound effects on an individual's on–going environmental complexity and available resources for health maintenance. Conti & Heckman propose that analysis of twin data can help account for shared environment and shared genetic components. But there is much to be done before policy recommendations could be made about learning environments that would increase long term benefits given genetic and early childhood environmental heterogeneity. The integration of theory and methods from genetic epidemiology and neural structure and function studies will lead to better understanding of the dynamics of neural plasticity across the lifespan and thus to better recognition of the parameters which education policy makers could use in order to provide a spectrum of learning environments meeting the needs of individual students from a heterogeneous population.

4. Psychopathology

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Deviations in subjective experience are the core phenomenon to be explained by research on psychiatric disorders. Subjective experience refers to a first–person perspective, which is best captured by person–specific, “private” time–space coordinates. However, deviant behavior and its neuronal correlates are often described from a third–person perspective that can be more easily communicated and projected onto “public” time–space coordinates. Unfortunately, the systems and tools that are commonly used to diagnose psychiatric disorders consist of descriptive, atheoretical taxonomies of symptoms and syndromes, and generally have escaped any attempt at causal explanation so far. Specifically, psychiatric disorders are currently classified on the basis of surface similarities derived from a third–person perspective. The resulting disorder catagories are standardized and objective in the sense that they follow reproducible procedures. However, individuals grouped together in these categories differ widely in etiology, prognosis, and therapeutic options. Therefore, attempts need to be made to move away from categorical to dimensional diagnoses, identify biomarkers and genetic variants that increase the validity of diagnostic attributions, and include the patients’ subjective experience in the diagnostic process. Longitudinal data integrating behavioral neuroscience with systems and molecular biology and genetics will inform the formulation of testable neurocomputational theories about the development of psychiatric disorders, offering the promise to yield personalized and successful intervention schedules.

Although it is important to continue to develop these three domains in their own right, it is not enough. If we are to capitalize on the knowledge each provides to raise the quality of life in the 21st century, leaders in these fields must integrate them into coherent proposals for action. NSF can catalyze these leaders by encouraging scientific work that not only uses the knowledge provided by each but also builds and elaborates the interfaces between them.

3 Recommended NSF Funding Priorities

We propose four mechanisms that could be employed in order to facilitate the proposed convergence of disciplines. Science is becoming more and more a global endeavor. When it is feasible and promising, these initiatives should be implemented in ways that encourage active participation by international casts.

• Cross–Cutting Project Grants — A specific mechanism for collaborative project grants that span the three areas should be created. Review and funding would need to come from at least two directorates, one of which would be SBE.

• Center Grants — A call for proposals for centers along the lines of Science of Teaching and Learning Centers should be initiated. The call should require that scientists from each of these three disciplines be involved and clear goals for convergence would need to be established.

• Methodology Project Grants — Methodology is one of the prime facilitators for the proposed convergence. A call for proposals for methodology projects in multi time–scale dynamical systems analysis should be instituted.

• Interdisciplinary Graduate Training — Graduate training is frequently insulated within a discipline. The next generation of scientists in these three areas needs exposure to each others’ disciplines in order to more easily forge the collaborative teams that will be required in 2020.

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