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What Is a Representative Brain? Neuroscience Meets Population Science

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What Is a Representative Brain? Neuroscience Meets Population Science

Abstract

The last decades of neuroscience research have produced immense progress in the methods available to understand brain structure and function. Social, cognitive, clinical, affective, economic, communication, and developmental neurosciences have begun to map the relationships between neuro-psychological processes and behavioral outcomes, yielding a new understanding of human behavior and promising interventions. However, a limitation of this fast moving research is that most findings are based on small samples of convenience. Furthermore, our understanding of individual differences may be distorted by unrepresentative samples, undermining findings regarding brain–behavior mechanisms. These limitations are issues that social demographers, epidemiologists, and other population scientists have tackled, with solutions that can be applied to neuroscience. By contrast, nearly all social science disciplines, including social demography, sociology, political science, economics, communication science, and psychology, make assumptions about processes that involve the brain, but have incorporated neural measures to differing, and often limited, degrees; many still treat the brain as a black box. In this article, we describe and promote a perspective—population neuroscience—that leverages interdisciplinary expertise to (i) emphasize the importance of sampling to more clearly define the relevant populations and sampling strategies needed when using neuroscience methods to address such questions; and (ii) deepen understanding of mechanisms within population science by providing insight regarding underlying neural mechanisms. Doing so will increase our confidence in the generalizability of the findings. We provide examples to illustrate the population neuroscience approach for specific types of research questions and discuss the potential for theoretical and applied advances from this approach across areas.

Keywords

neuroimaging, life course, statistics, survey methodology, physics

Disciplines

Communication | Neuroscience and Neurobiology | Psychology

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What is a representative brain? Neuroscience meets population science

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The last decades of neuroscience research have produced immense progress in the methods available to understand brain structure and function. Social, cognitive, clinical, affective, economic, communication, and developmental neurosciences have begun to map the relationships between neuro-psychological processes and behavioral outcomes, yielding a new understanding of human behavior and promising interventions. However, a limitation of this fast moving research is that most findings are based on small samples of convenience. Furthermore, our understanding of individual differences may be distorted by unrepresentative samples, undermining findings regarding brain–behavior mechanisms. These limitations are issues that social demographers, epidemiologists, and other population scientists have tackled, with solutions that can be applied to neuroscience. By contrast, nearly all social science disciplines, including social demography, sociology, political science, economics, communication science, and psychology, make assumptions about processes that involve the brain, but have incorporated neural measures to differing, and often limited, degrees; many still treat the brain as a black box. In this article, we describe and promote a perspective—population neuroscience—that leverages interdisciplinary expertise to (i) emphasize the importance of sampling to more clearly define the relevant populations and sampling strategies needed when using neuroscience methods to address such questions; and (ii) deepen understanding of mechanisms within population science by providing insight regarding underlying neural mechanisms. Doing so will increase our confidence in the generalizability of the findings. We provide examples to illustrate the population neuroscience approach for specific types of research questions and discuss the potential for theoretical and applied advances from this approach across areas.

neuroimaging | life course | statistics | survey methodology | physics

Why Population Neuroscience?

How do biology, social situations, and the broader environmental context interact to guide behavior, health, and development? This question is fundamental to most, if not all, social and behavioral sciences. We argue that to effectively address the many topics that stem from this larger question across disciplines, it is necessary to (i) bring a “population perspective” to neuroscience and (ii) leverage neuroscience tools within population sciences, which are subdisciplines of many fields, areas, and departments focused on documenting and understanding the dynamics of human populations, including outcomes such as health, well-being, behavior, etc.

Although recent advances in neuroscience research, and neuroimaging in particular, speak to how social, cognitive, and emotional processes unfold (1–5), the extent to which existing knowledge in human neuroscience

applies to broader, theoretically relevant populations, and the ways that macrolevel structures (e.g., social structure, neighborhood safety, school quality, media exposure) influence neural processes is often unknown (6). Thus, in parallel with a broader social science focus on the limitations of nonrepresentative samples (7, 8), we are now at a critical juncture for social and biological science. What would a “representative group of brains” tell us about the generalizability of current samples and current findings regarding brain-behavior mechanisms? How do individual differences in brain structure and function affect cognitive, affective, and behavioral outcomes and how do social situations and broader environmental contexts interact with these processes? Current methods in much of neuroscience research and the absence of neural measures in most population-based research limit our ability to answer these questions (9).

At the same time, most social scientists are interested in thoughts and behaviors (e.g., decision making, empathy, attitudes), which must have some relationship to the brain. As such, neural measures, especially neuroimaging, have become widely used in several specific social science disciplines (e.g., psychology, decision science) (1–5, 10–12).

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research questions is clear. Population neuroscience leverages well-known sampling techniques that are routinely used in other fields such as demography, epidemiology, and survey research (11, 12) to strengthen the link between sample and target population and enhance the generalizability of results. The extent to which neuroscience findings can inform and be informed by disciplines that focus on macro level structures (e.g., demography, sociology) rests on our ability to maximize generalizability to relevant populations. It should be noted that what constitutes a relevant population is often subjective and project specific. Researchers may target different populations (e.g., by disease status/risk, age, geographic region, or SES level) based on their research goals and substantive theoretical questions, but a key aspect of moving research forward is identifying and describing the relevant population the research is intended to characterize or address. Not explicating the population could lead to problems of comparability, replication, and inference.

This is not to say that all studies must use samples that represent entire nations or that treat variability across major cultural groups. In fact, collecting larger representative data without clear hypotheses or a target population to generalize to may not yield helpful conclusions either. Rather, the goal is for neuroscience studies to consider sampling as one critical component of the design, just as researchers would consider functional MRI (fMRI) pulse sequences, task, stimuli, and/or analysis strategy. In fact, many clinical studies and high-risk population studies are excellent examples where neuroimaging is used on a carefully selected and characterized sample that generalizes to a specific, relevant population (but see ref. 27). Ideally, in the study design phase, researchers should consider to whom their research question should ideally apply and then take steps to recruit participants who represent the target group and report information relevant to this process. Through a focus on theory-relevant sampling and interdisciplinary discussion between neuroscientists and population scientists, population neuroscience can improve the external validity, replicability, and generalizability of neuroscience findings to relevant populations and clarify to which population(s) the results can be generalized. In parallel, this creates opportunities to make the results more applicable to a wider range of social scientific fields and to test key theoretical questions of interest to population scientists. To achieve these goals, however, requires a cross-discipline emphasis on both the internal validity (a greater focus in neuroscience) and the external validity of studies (a greater focus within

population studies). It also requires multidisciplinary communication and collaboration (e.g., development of methodology and common language shared across areas), so that critical methods and findings across the disciplines that study these phenomena can inform each other.

Getting Inside the Black Box: Adding Neuroimaging and Other Neuroscience Methods to Broader Population Science

Over the last several years, there has been a rapid expansion of social and population researchers using biomarkers (e.g., cortisol response, cholesterol levels, epigenetics) to examine how the social environment gets under the skin (17, 35). Examining these biological mechanisms of social environment and health has produced important justifications for funding of continued work in the social and population sciences (5, 36). However, very little current population-focused work has examined the brain, which may be an optimal biomarker to examine the wide variety of variables typically found in population-based studies (e.g., health, decision-making, educational achievement, acceptance of new ideas). Thus, the current practice of many population researchers using large, omnibus studies is well suited to allow even a small group of population neuroscience experts to make immediate impacts on a wide variety of research areas. With the help of neuroscientists, population scientists can begin to open the black box of the brain that has long been assumed, but rarely examined, in most population-based models.

For example, one set of topics of interest to population scientists includes the effects of neighborhood and family poverty and social inequality on later outcomes such as family instability, educational attainment, health, employment, crime, and psychiatric disorders. Although population research has established robust effects of poverty and inequality on these outcomes (37–42), neural mechanisms of these effects have not been a primary focus in population approaches. However, within neuroscience and health psychology, research has begun to show that early life experiences such as parenting and SES have effects on brain areas such as the amygdala and prefrontal cortex (43–47), areas that have also been linked to a variety of relevant outcomes such as crime and violence (48, 49), depression (50), social cognition (51, 52), drug use (53, 54), and cognitive control (55). For example, a recent study demonstrated that early life stress predicted stress responses in the hypothalamic-pituitary-adrenal axis, which in turn predicted the connectivity between the amygdala and prefrontal cortex and later risk for depression (56).

Therefore, emerging research showing that early experience can affect the function, structure, and connections within and between key brain areas may help explain why experiences such as poverty lead to deleterious health and behavioral outcomes and also why some individuals are more susceptible to these experiences.

Although this research is beginning to elucidate biological embedding of experience at the neural level, it has not yet addressed a second related key process linking experience and behavior: the effect of culture in developing cognitive maps that allow us to understand and navigate the world (57). For example, our brains help us to acquire and then use complex information specific to our culture(s), such as knowing the difference between breakfast and snack foods, how to respond to authority, whether smoking is bad, etc., but the content of these cognitive maps is not currently accessible through neuroimaging, suggesting the importance of interdisciplinary partnerships (58–60). Furthermore, additional work linking such processes with macrolevel variables (e.g., social network structure) and biological variables (e.g., neural responses to cognitive tasks) also stands to advance both population and neuroscientific theory.

Overall, by partnering with neuroscientists, population scientists can specify new biological processes such as brain structure and function, which would shape cognition and perception of experiences thereby influencing behavior. This process leads to an interaction through which experience and biology shape each other over time (61, 62). Although neuroscience cannot capture experience at all levels, it can help to specify how some experience is biologically embedded and how experience and biology interact over time to explain questions of interest to population scientists.

Integrative Framework

How can these goals become reality? How can we link multiple levels of analysis (i.e., move from synapse to cell to brain to individual to groups to regions to nations)? Below, we outline six concrete steps toward the big picture goal of promoting generalizability in neuroscience investigations and harnessing neuroscience tools to understand processes of interest to population scientists.

Goal 1: Integrate Brain Imaging into Existing Representative (Sub)samples. By using techniques such as sample stratification, cluster sampling, subsampling, and “planned missingness” (63), neuroscience methods can be integrated with ongoing and large-scale population-level studies without needing to collect neural data on every sample

participant. This strategy can afford greater generalizability of brain processes and insights about underlying mechanisms that contribute to macro level processes (10). Larger-scale studies of the type typically conducted by survey researchers and demographers often contain rich longitudinal measures of behavior and experience. Presently, it is rare for these types of data to be examined in dialogue with neuroimaging data [although a growing number of studies have scanned subsamples of participants within specific existing longitudinal or archival studies (64–66)]. One large-scale example that might be considered a model for integration of brain imaging into existing representative samples is the National Institutes of Health Pediatric MRI Database (NIH-PD) (6, 67), which used population-based sampling at six sites, based on the 2000 census data. This study includes information about social and environmental variables (e.g., socioeconomic position, prenatal exposure to risk factors such as alcohol), cognitive tests, and behavioral measures, including laboratory-based tests of executive function and academic skills, and a range of structural brain images. The key to this point is that using these sampling techniques, along with “piggybacking” on another study, means that neuroimaging studies need not necessarily be of large magnitude to yield large findings if sampled thoughtfully within the context of a larger study. Moreover, when piggybacked on another study, the neuroimaging data are enhanced through more precise (and often longitudinal) behavioral phenotypes at both the individual and macro level of behavioral analysis (6, 64). Substantially more work is needed to broaden this understanding and to more fully integrate what is known about large-scale social phenomena with the individual level processes that yield these larger-scale phenomena.

Goal 2: Development of Methods to Scale Up Neuroimaging Studies to Larger and More Representative Samples with Methods Allowing for Cross-Study, Cross-Age, and Cross-Culture Comparisons. Recently, several large-scale neuroimaging studies have emerged by expertly piecing together smaller convenience samples (68, 69), scanning larger and larger samples of individuals (6, 70, 71), using data sharing and open access data (68, 72–74), consortium models (75–77), and neuroimaging meta-analysis (78, 79). These models emphasize that neuroimaging approaches can be done on a larger scale and across research teams. However, these studies also highlight many of the current methodological challenges to going big with neuroimaging studies (68, 75, 78). For example,

neuroscience methods have lagged in terms of addressing the use of multiple scanners (69, 80, 81), standardizing tasks used for functional (and resting-state: ref. 82) MRI studies, understanding the effect of different pulse sequences on findings (83, 84), standardization of single data processing streams (85, 86), and statistical approaches for issues such as multiple comparisons (68). Understanding the extent to which different laboratories, scanners, and methods can reliably collect data (80) is also vital to population-based studies because most large studies rely on cluster sampling, which is conducive to using multiple laboratories for imaging. Cross-team data sharing also highlights the need for better methods for secure data sharing and computation across sites. Moreover, research is needed to examine factors that affect MRI results (e.g., head motion, ability to attend to a task) that covary with health factors and behaviors (e.g., chronic hypertension, smoking), which may be linked to environmental factors being studied (e.g., SES, geography). We also need designs and analytic tools that allow us to combine variables and processes at different time scales and levels of analysis. Finally, research that examines translation from neuroimaging to neural methods or proxies including self-report measures that are cost-effective and can be implemented at a population level are also critical in the translation of this research from smaller samples to larger samples and to wide-scale clinical relevance.

Ultimately, methodological advances (including sampling approaches) will be inherently intertwined with theory and the hypotheses being tested in these studies. Although sampling for large-scale representativeness may not be appropriate for all research questions, goal 2 emphasizes the need for methods in cases where the scientific question calls for this type of generalizability and/or where theoretical questions cannot be adequately addressed using data from one level of analysis alone.

Goal 3: Use Strategic Sampling When Recruiting for Stand-Alone fMRI Studies. Statisticians, survey methodologists, and demographers can partner with neuroscientists to improve the inferential and statistical quality of smaller studies by helping neuroscientists clarify to whom it is important for their results to generalize and then to sample accordingly. Population scientists have extensive experience using a variety of methods to reduce bias, increase power, and improve causal inference in smaller sample studies (87). These methods include knowledge of matching sampling frames and target populations to reduce coverage error, reducing sampling costs by using

cluster samples and subsampling within clusters, and improving representativeness through stratified sampling (23, 88–91). For example, developmental scientists interested in the role of psychological resources on limbic system reactivity during adolescence might benefit from input from population scientists in selecting specific subgroups of adolescents who represent the demographic profile of high- and low-risk adolescents within the United States. The process of more precisely specifying the target population can help clarify theoretical predictions and advance understanding of boundary conditions for effects observed. In considering the demographic profile of teens, developmental neuroscientists and population scientists might both benefit from selecting adolescents who vary along some key dimension (e.g., SES, risk-taking status) and examining the interplay between the target macro level processes and the brain.

Further, there may be great interest in examining the predictors of participation and nonresponse in brain imaging studies with the goal of improving and adjusting for non-response bias in our statistical models. Combined with goal 1 of scanning existing participants of current population-based studies, a particularly useful concept may be using a large population-based study as the control for several smaller case-control neuroimaging studies. This way the controls can be used to provide generalizability, whereas the case studies provide the necessary power for disease or behavior conditions that may be too rare to power a study from a standard population-based study (e.g., see the Welcome Trust Case Control Consortium in genetic research as an exemplar; ref. 92).

Goal 4: Explore Moderators of Brain-Behavior Links and Neural Predictors of Relevant Outcomes. A growing body of research has demonstrated that environmental factors influence brain development. For example, childhood SES predicts brain structure (46) and function (45). Likewise, the size of our social networks relates to brain structure (93, 94). Given that the social environment is known to affect a wide array of biological responses (5, 17, 19, 95), a next important goal for neuroscience will be to further understand how experience at multiple levels (e.g., culture, family, social networks, SES) affects neural structure and function (46, 96–101). In parallel, it is certain that social and environmental variables moderate the link between brain and behavior (12), but further research is needed to examine such interactions. For example a recent study has demonstrated that level of perceived social support moderates the previously much replicated relationship between

amygdala reactivity and trait anxiety, indicating that many brain–behavior relationships may vary by environment and experience (102). However, if research does not explore these moderators, then these relationships may be assumed to be invariant across people and environments.

To fully leverage the fruits of the methodological goals outlined above, neuroscientists and population scientists might also reconsider the ways that neural variables are conceptualized (103). Traditional neuroimaging research has focused on the brain as a dependent measure (e.g., Where do certain processes take place in the brain? What structures support those processes?). Decades of neuroimaging literature have now characterized several processes that may be able to predict outcomes of interest to population scientists [e.g., neural activity in response to health communications predicts large-scale effects of media campaigns (104)]. With this in mind, neural variables (e.g., structure, function, connectivity) can be hypothesized in advance and treated as predictor variables of relevant population level outcomes (103). This use of neuroimaging methods may contribute explanatory power that is not readily available from other sources and may be a source of convergent validity for identifying the best measures of behavior (103–105). Moreover, increasingly, there has been a shift from the assumption that the brain is only a dependent or independent variable but also can be a moderator and mediator of paths from experience to behavior or between genes, brain,

and behavior (56, 61, 102, 103, 106). Moreover, evidence is mounting that that brain–behavior links may be powerfully moderated by experience, context, and culture (102, 107).

Goal 5: Changing of the Cultures in Neuroscience and Population Research.

As population research has recently begun to acknowledge the usefulness and importance of including genetic and other biomarker data (108–113), scholars note a lack of brain research in the examination of the influence of macrolevel processes on health and behavior (111, 114). Moreover, we argue that even though most population researchers may not use MRI data, a better general understanding of the behaviorally relevant elements of basic brain research will be important for the progress of the field, especially as cross-discipline studies are becoming the norm rather than exception. Likewise, for many neuroscience questions, smaller targeted samples make sense, and many findings within the social, affective, and cognitive neurosciences have replicated well across laboratories, across geographical locations, and across time. However, neuroscience has compelling insight to add to population level investigations and will benefit from increased focus on who the relevant sample is. Both goals will be advanced with minimal burden by researchers providing more basic data on the sample and how the sample relates to larger populations that might be of interest in both publications and grant applications. Building on the excellent checklist

developed by Poldrack and colleagues (115), we propose the addition of some basic sampling strategy information, as well as the facts that would typically be included in a Consolidated Standards of Reporting Trials (CONSORT) flow diagram (www.consort-statement.org/consort-statement/) to the checklist (Table 1).

Funding for interdisciplinary training and interaction, support for interdisciplinary working groups, and consultation across disciplines will promote true cross-pollination. For example, conferences that bring together scientists across these disciplines can lead to more explicit collaboration and a better understanding of methods and the benefits of each discipline's area of expertise. Funding that focuses explicitly on these specific aims may yield studies that have big impacts, not only on the study's specific question but more broadly on how we interpret and understand neuroimaging and population science. Although these studies may seem risky to funding agencies, these are the types of studies that can have big rewards.

Goal 6: Emphasis on Development and Ecological and Interactional Models.

One other major theme population science brings to a population neuroscience approach is an appreciation of development and multilevel ecological models (18, 19). Many fundamental neuroscience questions require longitudinal data and a developmental perspective (17, 61, 79). Social ecological models of development and life course will be fundamental to the

Table 1. Guidelines for presentation of neuroimaging studies with a focus on population neuroscience areas of emphasis

Specific subject and recruitment details to report	Advantages of reporting this information regularly
Target population: Author note about who the sample may generalize to in the larger population	Draws attention to the author specified relevant population and draws attention to when samples may be limited in generalizing to other populations
Sample design: Sampling strategy used to select potential participants from a larger population pool	Allows readers to understand the strengths of the strategy used, as well as possible sampling error and bias within the study, and what methods will be needed to appropriately account for the strategy
Recruitment strategy and response rate: Techniques used to find, contact and encourage study participation	Allows for assessment of selectivity of sample by learning the extent to which nonresponse bias may influence the findings
Analysis exclusion criteria: Measures used to distinguish analysis sample	Delimits the sample and population of who and who is not included
Attrition bias: (longitudinal studies) Rates of continued participation	Allows for the assessment of selectivity of a longitudinal sample due various types of attrition
Demographics: age, race, and ethnicity, SES at each step from recruitment to scanning to those with usable data	Draws attention to the diversity of characteristics of the sample and potential bias in who is retained at any step along the way
Efforts to standardize across multiple scanners if the study includes such data: If multiple scanners or scan sites were used in data collection, what specific steps were taken to standardize pulse sequences, protocols, and other factors that might affect the imaging data? What steps were taken to adjust for scanner variability without removing variability that is due to differing demographics or participant characteristics across sites?	Draws attention to portions of the protocol that are standard across sites, and elements that may introduce variability

A complement to the guidelines suggested by Poldrack et al. (115), which include suggestions for reporting design specification, task specification, planned comparisons, details of the subject sample (e.g., inclusions/exclusion criteria), ethics approval, behavioral performance, image properties, preprocessing, first level modeling, group level modeling, inferences related to statistical images, ROI analysis, and figures/tables.

organization of population neuroscience through their emphasis on the multiple layers of influence on behavior and cognition. Life course and development frameworks imply that the relationships between social context and the brain may not be constant across an individual's life, may vary as a function of the context in which individuals operate, and may not be constant over cohorts or historical periods (116). Developmental theory has as its primary focus the interaction of person, process, and context, as studied with regard to age and age-graded transitions in processes and relationships (20, 62, 117). Life course theories focus on context as well (cohort, period, and historical contexts) and will be relevant here. Thus, these theories highlight the (individual, societal, and historical) timing of transitions and adaptation to various transitions, which are likely to influence and qualify brain-behavior relationships in powerful ways that are yet to be examined. Beyond thinking of these contexts as predictors and moderators of brain processes, ecological models emphasize that brain processes are nested and embedded within larger social contexts at multiple levels and are likely to be influenced by and influence these contexts (Fig. 1). Thus, partnerships across these disciplines may bring a more complex and interactional framework to our understanding of neuroscience (20, 61, 62).

Benefits to Neuroscience, Population Science, and Broader Social Sciences

Implementation of the six steps outlined above would promote advances in the integration of

knowledge across levels of analysis (Table 2). In turn, neuroscience, population sciences, and related social and biological sciences all stand to benefit: Population neuroscience complements other movements toward larger team-based science (118–121), which have accomplished goals that could not be achieved with a single principal investigator (e.g., recent work in high energy physics on the Higgs Boson; the human genome project). Recent advances in handling “Big Data” (e.g., new methods for secure data sharing) should also inform this work. Most centrally, neuroscience and population science will benefit from knowing how brain structure and function varies across groups and what can be generalized, and population-based social sciences like demography and sociology will benefit by looking into the black box that has previously been a stand-in for the brain.

In addition, the mechanisms uncovered by neuroscience research can be incorporated within larger-scale models of human behavior. For example, longitudinal neuroimaging of representative samples, with repeat scans starting early and continuing across development, will advance developmental science, as well as our broad understanding of brain plasticity and relationship to experience (12, 18, 61, 122). Sociologists and social psychologists will also have a major stake in this research and will be particularly important in helping to formulate the possible chronic influences on brain structure and function, such as discrimination, poverty, SES, and social support (5, 17, 43, 44). As well, these influences

of brain function and structure may act as moderators of brain-behavior relationships, thus leading to a more dynamic model of social context, brain function, and behavior. Communication scholars are also increasingly interested in how neuroscience methods may inform our understanding of media effects (e.g., effects of violent media), as well as ways to predict individual differences in response to health communication, political communication, and inform media campaigns (123). However, a full understanding of how larger-scale mediated variables interact with individual level processes requires a more sophisticated set of methods for linking micro and macro level processes. Similarly, neuroimaging tools can be more efficiently applied within psychiatry, medicine, and clinical psychology with advances that allow tighter linkage between the samples under study and the broader populations that require treatment.

It should be noted that several relevant fields already have models for success: research in demography has transitioned from relatively coarse measures from the census to an emphasis on mechanisms and processes, statistical methods, and recent integration of biomarkers to the field (90, 110, 111). Methods from demography might also be harnessed as best practices for cross-cultural/cross-national analysis and work across broader sets of multilevel problems (i.e., international, national, regional). Likewise, in human genetics, genetic information is used as a predictor of behavior and moderator of the social environment. As illustrated by imaging genetics approaches, one

Table 2. Areas of emphasis within a population neuroscience framework

Areas of emphasis	Why?	How?
Increase the representativeness of samples using neuroimaging approaches	<ul style="list-style-type: none"> • Neuroimaging studies based on convenience samples may not optimally address target research questions or may come to erroneous conclusions • All brains are not the same 	<ul style="list-style-type: none"> • Increased emphasis on sampling approaches (goal 5) • Use of sophisticated sampling and analytic techniques to decrease <i>N</i> needed in samples (goal 3)
Increased collection of larger, well-characterized neuroimaging samples at multiple points across the life span	<ul style="list-style-type: none"> • Understand developmental trajectories of brain development • Increase replicability and generalizability of results 	<ul style="list-style-type: none"> • Merging existing data sets and meta-analysis (goal 2) • Large-scale collaborative studies • Piggybacking neuroimaging on existing behavioral studies • Increased work on cross-site imaging and standardization of protocols to allow for combining samples (goal 1) • Longitudinal imaging (goal 6)
Increase the emphasis on larger social context and experience as a predictor and moderator of brain-behavior links	<ul style="list-style-type: none"> • Evidence in social sciences emphasizes the importance of broader context and culture on behavior • Ignoring these variables assumes uniform brain-behavior relationships which is unlikely 	<ul style="list-style-type: none"> • Examination of moderators and collection of data from diverse groups (both cross- and within-culture) (goal 4) • Examination of ecological and interactional models (goal 6)
Increased training and collaboration between neural and social scientists	<ul style="list-style-type: none"> • Neural science can gain from increased focus on samples and on contextual effects • Population science can gain from increased understanding of the brain as a mediator of context-behavior links 	<ul style="list-style-type: none"> • Funding focused on this “high-risk, high-reward,” large-scale collaboration • Conferences and national meetings for collaboration and learning • Emphasis on making each discipline's methods accessible (goal 5)

meeting place of genetics and society is in the brain (61, 124). Therefore, neuroscience (e.g., MRI, psychophysiology) data could easily be seen as an outcome of great interest to population sciences, a moderator of environmental influences, a mediator of gene \times environment interactions (61), or at least, an important confounder to account for in their models.

Conclusion

We outlined a framework to better understand influences and mechanisms of behavior from culture to experience to brain structure and function, which would also improve confidence in the generalizability of neuroimaging findings. To take action on this framework, collaboration is needed between neuroscientists, survey methodologists, biophysicists, biostatisticians, and representatives from across social sciences, and population-based sciences in particular. These stakeholders include members of multiple social and behavioral sciences (psychology, sociology, economics, epidemiology, medicine, education, communication). Research across each of these disciplines will benefit from the resulting knowledge. However, our point is not simply that researchers should collaborate more across disciplines, rather it is more pressing: social and neural sciences are building huge literatures that could be more efficient and informative; however, at the present, “we don’t know what we don’t know”: human neuroimaging studies are limited in the extent to which results might generalize based on relatively less sophisticated sampling methods, whereas social science disciplines that ignore brain science may be missing a critical piece to understanding behavior phenomena even at macro levels. Thus, this is a critical moment for these disciplines. Collaboration can and should happen through funding opportunities, summer institutes, cross-disciplinary training of future scientists, graduate and postdoctoral training opportunities across areas, and with each area making their methods accessible to others. This framework is meant to be dynamic and will be refined as members of each of these groups agree on principles for the collection and analysis of representative brain imaging data. Although this goal is ambitious, the groundwork is in place, and several large-scale neuroimaging studies and existing nationally representative surveys with interest in adding neuroscience data provide jumping off points (6). Accomplishment of this overarching goal will provide deeper insights about how biology, social situations, and broader environmental context interact to guide behavior and development. In turn, this will advance basic science and provide concrete insight for the design of better interventions and policies.

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to bring together researchers across the social sciences and neuroscience to discuss the state of this research and ways to improve and validate findings. One of outcome of this conference was that investigators across the University began to meet and identify important synergies across broad areas of social and neural sciences. With support from the Institute for Social Research, the senior authors began hosting monthly meetings for these discussions. The group continues to grow and represent multiple disciplines and career stages, often with junior members contributing “cutting edge” new approaches. (ii) This manuscript was the result of discussions that the group has had from 2012–2013 and emerged as a way to organize our collective vision. Key to the production of the paper was that the three first authors were junior investigators with three very different backgrounds (e.g., demography, social neuroscience, and developmental neurogenetics) interested in collaborating and synthesizing interests from across our fields. As the three first authors were somewhat representative of the larger group, we were able to structure a paper and receive feedback from the larger group, especially in parts of the manuscript core to each member’s expertise. We also received excellent feedback from two reviewers: their thoughtful input significantly strengthened the manuscript.

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