Applied Psycholinguistics **26** (2005), 129–135
Printed in the United States of America
DOI: 10.1017.S0142716405050101

Language and genetics: Needs and opportunities

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ABSTRACT
This paper describes the next steps for establishing detailed, useful behavioral phenotypes and for moving forward in the study of the relationships among genes, the environment, and language disorders. Key issues are recognizing the continuum of language behaviors to accurately describe disorders and the spectrum of typical development. A coordinated plan with foundational studies that address definition, measurement, design, and analytical methods is needed. Researcher capacity must be increased, and a greater focus on communication across disciplines to successfully accomplish interdisciplinary research is required. Language is not static, even in disorders; thus, we must study change over time. It is necessary to think about behavioral phenotypes in terms of developmental trajectories. Finally, data sharing and ethical and legal issues must be addressed.

A May 2002 Merrill Conference, "The Relationship of Genes, Environments, and Developmental Language Disorders: Research for the 21st Century," provided an important initial step in bringing together a small group of interdisciplinary scholars to discuss the current state of research in the genetics of language disorders. Broad research needs were identified. A follow-up workshop, cosponsored by the Merrill Advanced Studies Center of the University of Kansas and the National Institute of Child Health and Human Development, focused on the steps necessary to address those research needs and identified limitations to implementing future research.

The investigation of the genetic bases of language and language disorders will require clear delineation of behavioral phenotypes, identification of neurocognitive substrates, synthesis of emerging discoveries across different clinical diagnoses (e.g., Williams syndrome, fragile X, autism, specific language impairment), new

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https://doi.org/10.1017/S0142716405050101 Published online by Cambridge University Press

models of genetic mechanisms, new methods of gene discovery, and new quantitative techniques for estimation of genetic effects and effect sizes. Despite progress that continues to be made in this important area, there are factors that impede the research: distributed sources of funding, traditional disciplinary boundaries, and insufficient communication networks among scientists.

In the September 2003 workshop and McCardle and Cooper (2004), four major issues were outlined that are crucial to moving forward in the area of language and genetics.

THE FOUR ISSUES

There must be recognition of the continuum of language behaviors

We must not lose sight of the fact that language abilities fall along a continuum from typical language development, observable in monolingual and bilingual children and deaf children of deaf parents, through the spectrum of children with language impairments, whether related to specific syndromes or as-yet unknown etiologies. Although language impairments vary in timing and severity, for most groups of children they seem to fall along a developmental continuum, showing slowed, arrested, or regressed development, but not showing characteristics that are totally foreign to what we know of some period of typical language development. Thus, as we seek clues to the role of genetics in language development and its disorders we must be both "lumpers" and "splitters" as we seek to define narrow behavioral phenotypes and to develop and test interventions. That is, not only must we combine and look across groups to capture what is general or common, across disorders, but we must also look narrowly within our cohorts of children with specific disorders for more specific subtypes.

It is important to have a coordinated research plan for the field

Collaboratively and across disciplines, we must as a field clearly delineate a plan for investigation. It is necessary to study the genetics of language and language disorders in a coordinated way, gathering similar types of data in order to be able to compare across studies and pool data to make maximum use of data from each case in order to not overburden those with rare disorders. This will necessarily include plans for data archiving and data sharing to make the most of the valuable, detailed, well-documented data that we are already collecting and will continue to collect.

Foundational studies are needed

We must move beyond clinical "art" to science-based diagnoses, but this can only be done through foundational studies that address definition, measurement, design, and analytical methods. Clearly this must integrate with the second major aim: a plan of investigation. We need to coordinate across studies the key constructs that should be measured, the instruments to use, and the design and analytical methods.

Researcher capacity must be increased

We must work to attract and train the next generation of scientists from a variety of disciplines. Such training should include mentoring of trainees to be

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open and responsible collaborators, to work cooperatively to investigate these important issues in an integrated, multidisciplinary way. Opportunities for training across disciplines of genetics, molecular biology, linguistics, neuroscience, or developmental disabilities along with typical language development need to be established and encouraged.

THE SECOND WORKSHOP

To build on the momentum of the first workshop, and to more specifically outline how the field could proceed to accomplish these major aims, a second workshop was held. As the papers in this Special Issue have indicated, there are very concrete things that must be done if we are to progress in the study of the genetics of language and language disorders. The following key issues were agreed upon as the "big picture" areas that all studies should aim to address.

Behavioral phenotypes

First, we must understand the effects not only of the environment on the phenotype but also of the phenotype on the environment. This bidirectional approach to assessing the phenotype–environment interaction is particularly important when developmental processes are considered. As behavior changes with development, the environment responds to those changes and thus affects the phenotype differently over time. These complexities must be taken into account as well as the genetic contributions to the phenotype. This level of complexity requires that we carefully define the behavioral phenotypes and neurocognitive outcomes of different syndromes with different etiologies, in order to inform and support the cellular and molecular studies that will lead to the identification of the genes that contribute to the pathways to language development and language disorders. In addition, it will be important to examine how the behavioral phenotypes are manifested in family members of the probands.

Language behaviors

Second, we must determine the levels of development at which specific language functions or specific aspects of language disorders manifest themselves, examine their co-occurrence with neurocortical function, and track these trajectories over time. Given that language ability is basic to so many adaptive functions, we must investigate the role of language impairments in shaping the behavioral phenotype and how language behavior constrains other areas of development.

Impact of intervention

Third, we must study not only how interventions are implemented and whether they are effective in improving function but also how interventions impact the trajectories of growth in various domains. The long-term adaptation of individuals with language impairments is an important area of study that will have implications for the application of findings on intervention design, as well as informing the study of the interactive effects of behavioral phenotype and environment.

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Measurement

Fourth, because researchers often use multiple measures of the same construct to examine different aspects of it, or to gain convergent data, agreement on key constructs of the genetics of particular language disorders is important to advancing the field. These constructs will lay the foundation for greater systematicity in developing the science of the genetics of language and language disorders. However, few measures exist that can be used to measure these constructs. Thus, the area of measurement was identified as the top priority for research attention, which is foundational to broader research in the field.

There is a known problem in the measurement of various domains of child development from preschool through school age, because few measures (and in some domains, none) exist that can be used across these ages: few exist that reliably measure the same constructs across the developmental trajectory. To develop the behavioral phenotypes that will be required, we must be able to study aspects of children's development, particularly language, in much greater detail than has been done in the past. In addition, not only the effects of intervention but also the implementation of those interventions must be carefully measured. New measures will need to be developed. Even where measures exist, we cannot continue to use measures that have not been normed on today's racially and culturally diverse population of children; thus, existing measures, if they are to continue to be used, will need to be renormed.

WORKSHOP PRIORITIES

September workshop participants were asked what they thought were the impediments to being able to research the genetics of language and language disorders and to prioritize the research needs in this area. They identified the development, refinement, and revision of measurement tools as one of the highest priorities. These scholars of various disciplines (molecular, cellular and behavioral genetics, developmental psychology, linguistics, mental retardation, developmental disorders and other syndromes, and research methods), noted that, although a great deal more research is needed, research faces a major and primary limitation in the area of measurement. This area was judged to be the highest priority because without new and better measures, future research will be inhibited and delayed. For example, without measures that accurately capture details of specific aspects of language behavior, identification of commonalities across language disorders will not be possible. Determining the onset of a particular behavior and tracking the timing of when language behaviors manifest aberrances would be difficult if not impossible. Further, the identification of subtypes within language disorders, which is so critical to a phenotype for genetic studies, would be seriously limited. All of these rely heavily on appropriate, sensitive, and accurate measurements of language and language related behaviors.

There are a number of problems with available measures. There are few if any measures available for particular age ranges or for particular areas of development. Measures are needed that will provide detailed information, are normed on today's children, are culturally and linguistically appropriate, and can be used across

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age ranges or can interface adequately to allow for continuous measurement of constructs over time. Extant measures generally do not fully assess behavior. That is, the measures are limited in range and scope. For certain impaired children, available measures may mask or insufficiently tap the child's true level of abilities, thereby underestimating the child's capability; this can have a significant impact on intervention recommendations and expectations.

Specifically, there is a need for the development or improvement of measures for focal areas of language. Improved measures of expressive vocabulary are needed, as well as measures that will examine relational language abilities (the ability to understand and use concepts, and the individual's flexibility of understanding and using vocabulary). In addition, measures are needed that will accurately document the developmental trajectory of language, which will measure the onset of words and phrases. Language has traditionally been assessed and reported as expressive versus receptive; this may not be the most informative approach to assessment or reporting of language behaviors, and the use of omnibus measures is often less informative than finer grained measures that offer greater dimensionality.

Systems should be developed for pairing observation with informant report for the assessment of pragmatics. There are few instruments available to assess oromotor abilities in children who are seemingly neurologically intact (i.e., not dysarthric) yet are unable to pronounce or sequence sounds. Measures of imitation are also needed, including imitation in gross motor, fine motor, speech sounds, and other behaviors that are foundational to the development of language. Measures are needed for the identification of language impairment in adults and in children who do not speak English and English language learners. There are also nonlanguage areas where additional or improved measures are needed. These areas include adaptive behavior, temperament, parent–child interaction, and motivation.

In addition to the development of new measures, for extant measures it will be important to reevaluate the specific behaviors being assessed and the available norming in commonly used measures; are the norms outdated and valid for today's population of children? Currently available measures may need to be normed to lower levels, to additional standard deviations, in order to allow for better, more detailed assessment of lower functioning children.

Generally, currently available measures tend to make a "has it or does not have it" judgment. As a result, valuable information about the child's behavior is lost. Unscorable responses on many measures are underutilized, although such information could provide insight into how a child responds when tasks are too difficult or incomprehensible to a child. Thus, measures are needed that will tap processes and strategies. In addition, computer-based measures should be explored, because these have the potential for efficient assessment that may be appealing to children.

Methodology

A final important issue in the area of behavioral measurement is that of methodology. There is a need for innovative methods for use in longitudinal research. A major issue is how to move from one measure to another, which purports to measure the same construct, or how to deal with data from overlapping measures at the age breaks where one measure ends and another begins. In addition, there

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is a need for test batteries that gather data on the key constructs that need to be measured yet are usable without overburdening research participants. Finally, measurement development and refinement must be coordinated carefully with analysis methods.

The neurocognitive area is one in which the field can benefit from methods and approaches other researchers are currently developing. This is an area that serves to emphasize the value of collaboration with researchers who may not be actively involved at present in genetics studies, and one that can serve as an example for the development of collaborative efforts more generally. Neuroimaging is already an area of interest to behavioral geneticists. In neuroimaging, structural and connectivity measures are important. They should be hypothesis driven. Early studies could simply look for areas of activation, but the field has progressed sufficiently that functional neuroimaging studies require strong hypotheses with good rationale and theoretical foundations. We are able with newer technologies to obtain functional neuroimaging data even with young children. However, it is important to plan for attrition, and to develop new ways to minimize attrition, which tends to be high among 5- to 6-year-old children. Collaborative studies represent one approach for obtaining larger numbers of subjects if attrition cannot be minimized or if a rare syndrome or very specific phenotype is being studied.

The use of a common, standard protocol across studies can maximize the value of the data obtained. Although there are likely others, two examples seem especially relevant here. The trans-NIH (NICHD, NIMH, NINDS, NIDA) consortium for the Pediatric MRI Study of Normal Brain Development has developed a model for a multisite study of brain development. Four hundred typically developing children between the ages of 5 and 18 years and 100 ages 0–5 years were recruited from six sites across the United States. The researchers developed a standardized protocol using different imaging machines, utilizing both a structural and a living phantom to calibrate the machines. The researchers will create a database of these scans with a fairly complete behavioral battery of tests on these children, including standardized tests of language development. Data will be available to researchers with the software to analyze the images. Children will be assessed and scanned again twice more at 2-year intervals. The protocols and behavioral tasks that have been and are being developed should be useful to those studying the genetics of language development and disorders.

In addition, the Collaborative Programs of Excellence in Autism (CPEA), a collaborative research network jointly funded by the NICHD and the National Institute on Deafness and Communicative Disorders (NIDCD), has developed a network that is examining the genetics of autism as part of its goals. Established in 1997, the NICHD/NIDCD Network on the Neurobiology and Genetics of Autism currently consists of 10 CPEAs that link together 129 researchers at 23 universities and more than 2,000 families of people with autism. This network conducts research on the possible genetic, immunological, neurobiological, and environmental causes of autism. The network also investigates the development of brain structures and their functions as they relate to autism as well as the developmental course of autism. These undertakings require each CPEA to implement a cohesive, site-specific, multidisciplinary research program as well as participate in trans-network, collaborative studies.

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Because of the number of autistic individuals enrolled in the research programs of the CPEA, the network continues to undertake studies that would be difficult or impossible to do at a single research site. A set of common measures has been agreed upon and is utilized across the network to allow pooling of data across sites. As a result of efforts of the CPEA centers, the network is now studying the world's largest group of well-diagnosed individuals with autism, for whom both genotypic and extensive phenotypic data will be available.

Many of the researchers involved in investigating the genetics of language development and disorders are also involved in large research consortia addressing other issues. These individuals can share which methods work, in what types of studies, and under what conditions. What kinds of database and informatics do we need to develop to have collections of data from many sources usable in one place? There are resources that can defray both time and costs of the research, and those involved in behavioral genetics will provide valuable information and insights to those out of their field; the give and take should enhance the work of all members.

There is a clear need for the development of databases of phenotypes, family histories, and results of behavioral measures. The existence of such databases linked to tissue samples would be extremely helpful to cellular and molecular geneticists, because it could enable them to link genetic findings more closely to behavioral patterns. Even when the specific genetic studies are not yet designed or even planned, these data will be important to moving the field forward. Clearly, ethical and legal issues must be considered and plans made for them, and consent forms need to be developed that will protect the participants but provide for research that can benefit future generations. All of this must be addressed in systematic, coordinated ways with clear communication among individual researchers across disciplines, in addition to across projects and across consortia.

Much remains to be done to identify, remedy, and resolve the roadblocks to understanding the genetic bases of language and language disorders. Contributors to this thematic Special Issue of *Applied Psycholinguistics* have addressed crucial issues related to design, behavioral measures, neurocognition, and etiology. Awareness of the limitations of our knowledge and available approaches to identification and treatment is the first step in the journey to the discovery of new strategies and new information. This issue, and the workshop from which it grew, provide a critical and important first step.

NOTE

The opinions and assertions contained herein are the private opinions of the authors and are not to be construed as official or reflecting the views of the US Department of Health and Human Services of the National Institutes of Health.

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