Making the case for psychophysiology during the era of molecular biology

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Abstract
The Office of Behavioral and Social Sciences Research (OBSSR) at the National Institutes of Health opened in 1995 to facilitate the advancement of research on social and behavioral influences on health. The establishment of the OBSSR coincided with the ascendancy of molecular biology, with its emphasis on more reductionistic influences on health. This greater emphasis on genetic aspects of health has the potential to produce a widening chasm between biomedical research and social, behavioral, and psychological research. We discuss the chasm between sociobehavioral and biomedical research during what might be considered the era of molecular biology and propose the concept of levels of analysis as a unifying framework for research in the health sciences, using research on hypertension in African Americans as a representative example. We also argue for the primacy of psychophysiological research in bridging the chasm and furthering a multilevel perspective and summarize some of the activities of the OBSSR that are relevant to this perspective.

Descriptors: Molecular biology, Psychophysiology, Social research, Behavioral research, Levels of analysis, Interdisciplinary

As a longtime member of the Society for Psychophysiological Research, it was indeed an honor for me (N.B.A.) to have been invited to give a keynote address at the 1997 annual meeting. The invitation provided me with the opportunity to share some insights gained over the last 2.5 years as the first director of the Office of Behavioral and Social Sciences Research (OBSSR) at the National Institutes of Health (NIH). In this article, my colleague and I summarize and expand on my presentation. Specifically, the main purpose of this article is to discuss what we perceive as a widening chasm between sociobehavioral and biomedical research at a time of unprecedented advances in molecular biology. To bridge this chasm, we propose the concept of levels of analysis as an organizing framework for health sciences research. To illustrate the use of this multilevel framework, research on the problem of hypertension in African Americans is examined from this perspective. Finally, we highlight the centrality of the field of psychophysiology to advancing a multilevel perspective and summarize some of the activities of the OBSSR that are congruent with it.

The Era of Molecular Biology
If one defines an era as a “time period marked by particular circumstances, events, or personages” (Webster’s II, 1994), then the recent accomplishments of the science of molecular biology and its visibility in popular culture suggest that this is indeed the era of molecular biology. Perhaps the best illustration of the ascendancy of molecular biology was the initiation of the Human Genome Project (HGP) in 1990. The HGP is a 15-year effort to map and sequence the approximately three billion base pairs that make up the human genome. The focus of this effort has been the National Center for Human Genome Research at NIH, which was recently elevated to the status of institute, The National Human Genome Research Institute (NHGRI). The elevation of the Genome Center to the Genome Institute is a reflection of the greater emphasis and importance placed on research in molecular biology. In addition, the budget for the Human Genome Center/Institute has grown substantially over the last decade. Starting with an initial budget of about $59.5 million in fiscal year (FY) 1990, the NHGRI received almost $218 million in FY 1998 and is budgeted to receive almost $265 million in FY 1999.

The return on the investment in the NHGRI and in genetics research in general has been impressive. Over the last decade, genetic predictors for neurological disorders such as Creutzfeldt–Jakob disease (Goldfarb, Korczyn, Brown, Chapman, & Gajdusek, 1990a; Goldfarb, Mitrova, Brown, Ton, & Gajdusek, 1990b), amyotrophic lateral sclerosis (Lou Gehrig disease) (Rosen et al., 1993), Huntington’s disease (Huntington’s Disease, 1993), and Parkinson’s disease (Polymeropoulos et al., 1996, 1997) have been identified. Genes have also been linked to many types of cancer,
including those of the breast (Miki et al., 1994; Wooster et al., 1994), uterus (Risinger et al., 1996), pancreas (Lancaster et al., 1996), prostate gland (Smith et al., 1996), colon (Pretlow, Brasitus, Fulton, Cheyer, & Kaplan, 1993), and skin (Hahn et al., 1996; Johnson et al., 1996). In addition, genes have been discovered that play a role in certain forms of Alzheimer’s disease (Levy-Lahad et al., 1995; Strittmatter et al., 1993), in systemic lupus erythematosus (Tsao et al., 1997), and in susceptibility to HIV-1 infection (Dean et al., 1996; Smith et al., 1997).

These discoveries and the ethical, legal, and social issues associated with them have received widespread coverage in the popular media. A search of the New York Times and Washington Post was done for stories on genetic topics for the years 1986–1996. For comparison purposes, a search was also done for stories on stress and health topics for the same years. For the genetic stories, the title of the article had to contain one of the following keywords: gene, genes, genetic, genetics, or DNA. For the stress and health stories, either the title or text of the article had to contain one of the following pairs of keywords: stress and health, stress and illness, stress and disease, stress and behavior, or stress and physiology. The search revealed a continual increase in the number of stories on genetic topics over this time period; these stories far outnumbered those on stress-related topics. Specifically, as shown in Figures 1 and 2, stories on genetics increased from 55 in 1986 to 106 in 1996 in the New York Times and from 15 to 66 in the Washington Post over the same time period. In contrast, the number of stories dealing with the effects of stress over the same period were much lower, averaging between 15 and 17 stories a year, and showed no consistent increase over time (see Figures 1 and 2). This difference between stress and genetics stories occurred even though the search used only the titles of articles for genetic stories but used both the titles and the text for stress stories. Thus, even using a conservative search strategy for genetic stories, they far outnumbered those on stress.

During the past few years, some of the leading news and science magazines such as Time, Newsweek, U.S. News and World Report, Discover, and Scientific American have run cover stories on topics related to genetics. Titles for these cover stories included “Genetics: The future is now” (Time, January 17, 1994), “Heredity: Can it be changed?” (U.S. News & World Report, August 22, 1994); “Violence, genes, and prejudice” (Discover, November 1994); “Why do we do what we do?” (Discover, October 1997); “The hunt for the breast cancer gene” (Newsweek, December 6, 1993); “Is it all in the genes?” (Commentary, September, 1997); and “Gene therapy: How it will work against cancer, AIDS, Alzheimer’s and more” (Scientific American, June 1997).

Perhaps one of the biggest scientific news stories of 1997 was the successful cloning of a sheep using DNA taken from adult mammary gland cells. The story appeared on the front pages of newspapers, was the lead story on evening television news programs, and was the subject of cover stories in several magazines. It was deemed the year’s top scientific breakthrough by Science magazine (Science, December 19, 1997) and came in fourth on CNN’s list of the year’s top news stories (CNN Website). This coverage touched off a national debate on the possibility of cloning humans.

In addition to newspaper and magazine articles, many popular books on genetic discoveries have been published recently. A search of the Books in Print/Books Out of Print databases for the years 1986–1996 using the keywords gene, genes, genetic, genetics, or DNA showed that the number of books published on genetic topics has grown steadily each year, from 92 in 1986 to 285 in 1996 (Figure 3). These books cover a wide range of topics, including the nature of DNA (Aldridge, 1996), the HGP (Cooper, 1994), cultural and social issues associated with genetic discoveries (Hubbard & Wald, 1997; Nelkin & Lindee, 1995; Teichler-Zallen, 1997; Wexler, 1995), and the use of DNA in the courtroom (Levy, 1996). Even Hollywood has begun to incorporate genetic themes into its films, with one recent major motion picture dealing with a futuristic society divided into genetic “valids” and “invalids” (Gattaca,
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A Growing Chasm Between Sociobehavioral
and Biomedical Research?
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prove our ability to prevent and treat serious illnesses. At the same
time, discoveries in molecular biology often lead, either implicitly or explicitly, to more reductionistic explanations for health and
behavior, with the accompanying unidirectional views of causation (i.e., “upward” from genes to physiology and behavior). This type of thinking necessarily leads to a conceptual divide or a chasm between molecular biology and fields concerned with behavioral
and social influences on health.
In the neurosciences, Miller (~1996) noted the frequent use of phrases such as “biological underpinnings,” “physiological foun-
dations,” or “neural substrates” of psychological phenomena, all suggesting that biology is somehow more fundamental than psy-
chology. The implication of these phrases is that psychological phenomena can be “explained” by biological factors. In the field of
genetics, one often encounters phases such as the “gene for,” the
“gene that causes,” or the “gene that determines” various health outcomes (e.g., breast cancer). The implication of this terminology is that genes exert their influence independently of other biological and environmental influences, which they do not. In one authori-
tative textbook in genetics (Suzuki, Griffiths, Miller, and Lewontin, 1989, p. 83), the authors stated that
A gene does not determine a phenotype [noticeable trait] by acting alone; it does so only in conjunction with other genes and with the envi-
ronment. Although geneticists do routinely ascribe a particular phenotype to an allele of a gene they have identified, we must remember that this is merely a convenient kind of jargon designed to facilitate genetic analysis. This jargon arises from the ability of geneticists to isolate individual com-
ponents of a biological process and to study them as part of genetic dis-
section. Although this logical isolation is an essential aspect of genetics, . . . a gene cannot act by itself.
Discoveries in molecular biology may also reinforce the belief that the identification of genetic risk factors necessitates biological intervention (e.g., drugs, gene therapy). Thus, as biomedical re-
search becomes more molecular, biomedical researchers, medical
practitioners, and the public may be less likely to see the relevance of behavioral avenues for treatment. Nelkin and Lindee (1995, p. 195) wrote that
The new molecular genetics is also appealing for its promise of medical ‘breakthroughs’ and wonder therapies—of biological rather than behav-
ioral or environmental control of disease . . . . In popular narratives, con-
trolling the body depends on understanding and manipulating DNA. Health depends on biological intervention rather than diet, exercise, emotional
resiliency, or other environmental and behavioral attributes. The future of medicine seems to lie in more aggressive biological manipulation rather than in social intervention to change behaviors that promote disease.
Similarly, Miller (1996) noted that the worst consequence of the divide between biology and psychology is the assumption that
dysfunctions conceptualized biologically necessitate biological in-
terventions and that problems conceptualized psychologically re-
quire psychological interventions. As Miller pointed out, this assumption is rampant in the popular press and common in prom-
inent scholarly works, but it is groundless.
The greater reliance on reductionistic explanations for health and behavior, which are unfortunate consequences of the era of
molecular biology, is perhaps the principal reason for what we perceive as a growing conceptual chasm between sociobehavioral and biomedical science. In other words, the nature–nurture pendu-
ulum has now swung over to and is resting comfortably on the
nature side. In addition to reductionism, the chasm between socio-
behavioral and biomedical research is also widened by other fac-
tors. These include different scientific languages, disciplinary
chauvinism, and disincentives for collaboration.
Different scientific languages. It is not surprising that biomedical and sociobehavioral researchers have different scientific lan-
guages or use different terminology in their work. After all, these are different fields. Yet, what is troubling vis-à-vis the chasm is that sometimes the same terminology means different things when used by biomedical and sociobehavioral researchers. For example, both groups of scientists may recognize the importance of preven-
tion research. Yet, to the behavioral scientist a term such as preven-
tion may mean approaches to modify diet, physical activity, smoking, and the like to forestall the occurrence of negative health outcomes. In contrast, to many biomedical researchers prevention means the use of pharmacological or chemical agents to accom-
plish the same objective. Similarly, both groups of researchers may agree that a better understanding of environmental influences on health is critical. Yet, the expression environmental influences could mean either the social and physical surroundings (for the sociobeh-
avioral scientist) or phenomena occurring immediately outside the nucleus of a cell (for the biomedical scientist).
It is not that one group is using the terms incorrectly, since there are in fact behavioral and biological approaches to prevention, and
there are extraorganism and extranucleus environments. What is troubling is that the biological meaning of such terms is becoming the only meaning. For example, a recent volume from the Annals of the New York Academy of Sciences on cancer prevention contained 53 articles, of which only 9–11 could be considered behav-
ioral or social (e.g., cancer screening), and none dealt with the reduction of behavioral risk factors for cancer as a preventative strategy (Bradlow, Osborne, & Veronesi, 1995).
Disciplinary chauvinism. The chasm may be further widened by the attitude that the most important scientific discoveries are occurring in whatever discipline in which one holds an advanced
degree. Although there is an understandable pride in the accomplishments of one’s own discipline, there is often a corresponding dismissal of the contributions from other fields. Although we have observed this phenomenon across the spectrum of behavioral, social, and biological sciences (e.g., sociologists criticizing psychological research as being too individualistic), we have been especially struck by the sometimes wholesale dismissal of behavioral and social research by some biomedical scientists. In essence, sociobehavioral science is sometimes viewed as inferior to biomedical approaches, with the former seen as having little potential to contribute to advancing health.

Disincentives for collaboration. In many areas of investigation, the chasm is being bridged by interdisciplinary collaborations. However, despite the many successes of interdisciplinary research, there remain significant barriers to this approach. First, investigators from different disciplines may have a hard time deciding how to assign credit for the results of interdisciplinary research (Epstein, 1998). Traditionally, research credit has gone to the senior investigator, or to the first author, or to the principal investigator on a grant. Epstein (1998) noted, however, that in interdisciplinary research, these designations may not accurately reflect the relative contributions of the different members of a given collaborative effort. Accurate credit for research becomes a critical issue, for example, in decisions about tenure or promotion (Epstein, 1998). If investigators do not feel that they will receive adequate credit for interdisciplinary collaborations from departmental tenure or promotion committees, they may be less willing to collaborate outside of their discipline. Second, university departments, organized largely by disciplines, simply are not structured to encourage interdisciplinary communication and collaboration. For example, in many universities, the department receives a portion of the indirect costs associated with a particular grant (Epstein, 1998). In the case of interdisciplinary collaborations, this portion may be lower than normal, leading department heads to not encourage these types of collaborations. In addition, there may actually be disincentives to publishing in journals outside one’s home discipline, which often occurs with interdisciplinary collaborations. As with the issue of assignment of credit, the problem becomes most salient during tenure and promotion deliberations, where an investigator’s status within his/her discipline is often a criterion. Departmental review committees may be less familiar with journals outside their discipline and, as a consequence, may have difficulty evaluating the status and importance of these periodicals. Third, a frequent complaint is that interdisciplinary research proposals fare less well during the NIH grant review process. The reason often given is that collaborative research tends to be broader than research within a single discipline, and therefore the evaluation of such proposals requires broader knowledge of research areas than sometimes exists on review committees. The perception is that such proposals are disadvantaged as a consequence. There is no way of stating at this time if this problem is indeed pervasive (although OBSSR is examining this issue), but if true, it could certainly be a disincentive to interdisciplinary collaborations.

Not everyone would acknowledge the existence of a chasm between sociobehavioral and biomedical research, especially in light of some exciting research developments in fields such as behavioral cardiology, psychoneuroimmunology, cognitive neuroscience, and behavioral genetics. In addition, even if one accepts the premise that a chasm exists, this is not necessarily a cause for concern. That is, why do we in the social and behavioral sciences need to worry about a conceptual divide between us and the biomedical world? The chasm has always existed, it could be argued, and sociobehavioral research has thrived nevertheless. So why be concerned now? There are two answers to these questions. First, as shown in Figure 4, most health problems are due to an interaction of sociobehavioral and biological processes. Although basic research in each of the individual domains represented in Figure 4 is critical, failure to conduct research across domains will severely limit a full understanding of health problems because, ultimately, it is the interactions across domains that affect health, even though individual risk factors can be isolated within separate domains. Thus, failure to understand these interaction could hamper the development of effective multimodel interventions. Second, the chasm is a problem because it is our biomedical colleagues who are primarily in charge of funding agencies, medical school departments, and private and public research institutions that fund and employ sociobehavioral scientists. They also play a substantial role in shaping public opinion about what is important in health research. In a purely pragmatic sense, to the degree that they do not see the value of sociobehavioral research, our disciplines will be at a disadvantage both scientifically and in the public domain. Although the chasm may not have posed a threat to sociobehavioral research in the past, the Zeitgeist now is that the “real” solutions to health problems will be found on the molecular level. I am sometimes asked by biomedical scientists and members of the lay public, “Why does NIH fund behavioral research, and what is the relevance of behavioral research now that the genetic picture is becoming clearer?” Thus, the chasm must be bridged, to not only improve the understanding, prevention, and treatment of disease but possibly for the very viability of our science.

Bridging the Chasm: The Utility of the Concept of Level of Analysis

To bridge the chasm between sociobehavioral and biomedical research, we need a new way of talking about and conceptualizing health research. The concept of levels of analysis, although not new, provides a potentially useful heuristic framework for health research. This approach is already paying dividends in the neurosciences, with the development of multilevel theoretical models and new research paradigms (Churchland & Sejnowski, 1988; Fodor, 1968; Gottlieb, Wahlsten, & Lickliter, 1998; Koob & Bloom, 1988; Miller, 1996; Tobach, 1987). The success of multilevel models and research in the neurosciences suggests that this approach may have useful applications in other areas of the health sciences.

Anderson (1998) outlined one potentially useful way of categorizing the various levels of analysis in health research: the social/environmental, behavioral/psychological, organ systems, cell-
lular, and molecular levels. Each of these levels contains a large number of indices that have been used to study specific health outcomes or pathogenic sociobehavioral or biological processes. Some of these indices are shown in Figure 5 (see Anderson, 1998). The social/environmental level includes such variables as stressful life events, social support, economic resources, neighborhood characteristics, and environmental hazards. The behavioral/psychological level may include emotion, cognition, memory, dietary practices, stress coping styles, and tobacco use. The organ systems level of analysis includes the cardiovascular, endocrine, immune, and central nervous systems and their outputs. On the cellular level, variables include receptor number and sensitivity, dendritic branches, synapse number, and electrical conductance. Finally, the molecular or genetic level includes such variables as DNA structure, proteins, mRNA, and transcription factors. Other approaches to levels of analysis (or levels of organization, as it is sometimes called) have used categories such as environment, behavior, neural activity, and genetic activity (Gottlieb, 1992) or environment, organism, tissue, cytoplasm, nucleus, chromosome, and gene (Weiss, 1959).

As previously discussed (Anderson, 1998), the determination of the categories of the various levels of analysis and which indices fall within which levels is admittedly somewhat arbitrary (e.g., do stressful life events fall in the social/environmental or behavioral/psychological levels?). The point, however, is that the majority of research in the health sciences occurs within a single level of analysis, closely tied to specific disciplines (e.g., sociologists working at the social level; psychologists working at the behavioral level; and geneticists working at the molecular level). Even when interdisciplinary research occurs, where scientists from different disciplines are working together on the same problem, it is not always multilevel research. This type of interdisciplinary research focuses on a single level of analysis (e.g., organ systems), with no exploration of influences from “higher” or “lower” levels on the problem of interest. The single-level approach clearly has been successful, with important contributions made to our understanding of phenomena at each level. For example, geneticists working at the molecular level have greatly increased our knowledge of the genetic component of many major diseases. At the same time, knowledge produced at one level has not always been used to inform research at other levels. Moreover, the science in some areas has progressed to a point where a more integrated, multilevel approach to research design and analysis could pay substantial scientific and health dividends. For example, recent studies have begun to show that environmental and physiological influences such as stress, pain, activity, or touch can activate gene transcription factors, effectively up- or down-regulating gene expression (Autelitano, 1998; Hermanson & Blomqvist, 1997; Perhonen et al., 1997; Wang, Bartolome, & Schanberg, 1996). Thus, activity at the genetic level is not static or determined but rather is responsive to influences from higher levels: cellular, organ system, behavioral, or social. Only research that is multilevel and interdisciplinary in nature will be able to fully reveal these types of multilevel influences.

Processes and Principles of Integrated, Multilevel Research

In their discussion of an integrated, multilevel approach to social, psychological, and neuroscience research, Cacioppo and Berntson (1992, p. 1021) stated that “analysis of a phenomenon at one level of organization can inform, refine, or constrain inferences based on observations at another level of analysis and, therefore, can foster comprehensive accounts and general theories of complex psychological phenomena.” That is, the interpretation of findings from single-level research might benefit from the consideration of relevant factors from other levels. Applied to health sciences research more generally, an integrated, multilevel approach involves two types of processes, as shown in Figure 6. The first, following from Cacioppo and Berntson, involves the use of findings from one level of analysis to inform, refine, and constrain inferences from observations at another level of analysis. This process might be thought of as multilevel model or hypothesis development. Here, the objective is a more complete conceptualization of the phenom-

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Figure 5. Some indices of various levels of analysis (adapted from Anderson, 1998).
enon of interest by developing multilevel models, theories, or hypotheses, which necessitates the incorporation of findings from other levels. The researcher is asking the question, “What are the variables at higher or lower levels of organization that might influence or be influenced by the phenomenon that I am studying?” The second process logically follows the first and involves the simultaneous study of a phenomenon across levels of analysis to foster a more comprehensive understanding of the determinants of health outcomes or pathogenic processes. This second process is epitomized by integrated, multilevel, cross-disciplinary research designed to test well-articulated multilevel models or hypotheses.

Several principles and a corollary of multilevel research have been proposed (Cacioppo & Berntson, 1992) that may be adapted for the broader domain of health research (Anderson, 1998). These include the principle of parallel causation, the principle of convergent causation, the principle of reciprocal causation, and the corollary of proximity.

The principle of parallel causation. The principle of parallel causation holds that each level of organization may contain risk factors for a single health outcome or pathogenic process (Figure 7). Each of these risk factors may be sufficient but not necessary for the prediction of outcomes or processes. For example, in the prediction of coronary heart disease (CHD), social level risk factors include socioeconomic status and social isolation; behavioral level risk factors include physical inactivity and smoking, and organ systems level risk factors include low-density lipoproteins and hypertension. Each level of analysis contains variables that alone are sufficient to account for a significant proportion of the variance in CHD, although no particular level is necessary for the prediction of CHD.

The principles of convergent and reciprocal causation. With convergent causation, a convergence or interaction of variables from at least two levels of analysis leads to a health outcome or pathogenic process (Figure 8). Thus, variables within a single level may be necessary but not sufficient to produce an outcome. Here, factors from one level of analysis affect factors at another level, and this cross-level causation ultimately influences outcomes. The principle of reciprocal causation (Figure 9) is similar to convergent causation but posits bidirectional influences across levels, involving negative and positive feedback loops. For example, the initiation of cigarette smoking (behavioral level) in adolescents may be strongly tied to such social and environmental factors as peer influences and advertising (an example of convergent causation).

Smoking behavior in turn could later affect biological processes leading to a biological addiction (convergent causation), and this biological addiction may contribute to the maintenance of smoking behavior (reciprocal causation). Thus, the behavior of smoking leads to biological changes that further serve to maintain this behavior. The principles of convergent and reciprocal causation are the foundations of integrated, multilevel research in that they highlight the critical importance of interactions across levels of analysis in fostering more complete accounts of health phenomena.

The corollary of proximity This corollary holds that the mapping of elements or variables across levels of organization increases in complexity as the number of intervening levels increases (Cacioppo & Berntson, 1992). That is, research aimed at exploring interactions between variables at adjacent levels of analysis will
typically be less complex than that examining variables at nonadjacent levels, because events at any level of analysis (e.g., the cellular level) can be influenced by events within the same or at adjacent levels (e.g., organ systems level), which in turn may be affected by events at the next level of organization (e.g., behavioral level). This added complexity does not preclude research across nonadjacent levels but suggests that an incremental approach may be the most useful one (Cacioppo & Berntson, 1992). Churchland and Sejnowski (1998, p. 242) voiced a similar perspective:

The ultimate goal of a unified account does not require that it be a single model that spans all levels of organization. Instead, the integration will probably consist of a chain of models linking adjacent levels. When one level is explained in terms of a lower level, this does not mean that the higher level theory is useless or that high-level phenomena no longer exist. On the contrary, explanations will coexist at all levels.

Multilevel Health Research: The Example of Hypertension in Blacks

There are a number of excellent examples of multilevel research that have explored the influence of sociobehavioral factors on the organ systems (Coplan et al., 1996; Jiang et al., 1996; Kaplan, Manuck, Clarkson, Lusso, & Taub, 1982; Kiecolt-Glaser & Glaser, 1995), cellular (Greenough, Juraska, & Volkmar, 1979; Turner & Greenough, 1985; Yeh, Fricke, & Edwards, 1996), and molecular (Bank, LoTurco, & Alkon, 1989; Fordyce, Bhat, Baraban, & Wehner, 1994; Wang et al., 1996) levels. Likewise, research has also shown very clear biological influences on social and behavioral phenomena (Plomin, Owen, & McGuffin, 1994). Here, we highlight one area of health research, hypertension in African Americans, to illustrate how research on both the sociobehavioral and biological levels has resulted in the development of a multilevel model and new lines of psychophysiological investigation.

The prevalence of essential hypertension in the African American population rivals that of any group in the world (Burt et al., 1995). The prevalence of the disorder is more than twice that of White Americans. As a consequence, Blacks experience disproportionately higher rates of morbidity and mortality from heart disease, stroke, and renal disease (Mason, Fraumeni, Hover, & Blot, 1981). Although essential hypertension in both Blacks and Whites is idiopathic, that is, of unknown origin, it is clear that the disorder develops from multiple interacting mechanisms rather than from a single source. Among the contributors to the disorder are genetic and biological factors, nutritional factors, behavioral and psychological factors, and social and environmental factors (Anderson, Myers, Pickering, & Jackson, 1989b).

Attempts to understand the high rates of hypertension in Blacks have usually involved Black–White comparisons to determine if differences between these groups could be uncovered on factors that might predispose Blacks to hypertension. Both biological and psychosocial risk factors have been investigated (for reviews, see Anderson & McManus, in press; Anderson et al., 1989b; Fray & Douglas, 1993). Biological researchers have examined Black–White differences on the organ systems, cellular, and molecular levels. On the organ systems level, these studies have included variables such as catecholamines, plasma renin, blood volume, sodium sensitivity, sodium excretion and many other factors (Anderson & McManus, in press; Anderson et al., 1989b; Fray & Douglas, 1993). On the cellular level, variables have included intracellular sodium and calcium, sodium–lithium countertransport, and sodium–hydrogen exchange (Cooper & Borke, 1993). Although less work has been done on molecular level risk factors in Blacks and Whites, recently studies on these factors have also emerged (Kotanko et al., 1997; Svetkey et al., 1996; Watson et al., 1996).

One interesting finding in the biological literature on hypertension is the greater sodium retention observed in Blacks relative to Whites in many studies (Luft, Grim, Higgins, & Weinberger, 1977; Luft, Grim, & Weinberger, 1985). Using protocols involving the intravenous administration of fixed amounts of saline (sodium loading) to normotensive subjects, researchers have shown that Blacks excrete less sodium in urine and exhibit greater blood pressure increases than do their White counterparts. Greater sodium retention may increase the risk for hypertension in Blacks. In an attempt to interpret and explain this phenomenon, Wilson and Grim (1991; Grim & Wilson, 1989) proposed a Darwinian evolution hypothesis, whereby selection pressures occurring during the transport of slaves to this hemisphere favored those most able to retain sodium (Wilson & Grim, 1991). Thus, according to Wilson and Grim, African Americans today, who are in large part descendants of the middle passage survivors, may have an inherited tendency to retain sodium.

In a separate line of research, psychophysiologists have explored whether ethnic group differences in cardiovascular reactivity may be involved in the higher rates of hypertension in Blacks (Anderson, 1989; Anderson, McNeillly, & Myers, 1991). Studies in this area have included both children and adults and a wide variety of laboratory stressors, experimental designs, physiological measures, and population subgroups. Despite the diversity of approaches used, most studies have demonstrated that Blacks show greater blood pressure reactivity to laboratory stressors than do their White counterparts. Perhaps more important though is that the mechanisms responsible for blood pressure regulation during a reactivity task may be different in Blacks than in Whites. Despite wide within-group variability among Blacks and Whites, Blacks exhibit greater blood pressure reactivity mediated by increased peripheral vasoconstriction (e.g., increased total peripheral resistance), whereas the blood pressure response of Whites has shown greater cardiac involvement (e.g., increased heart rate and cardiac output). These results, particularly the heightened peripheral vaso-
constrictive responses in the Blacks, have been observed among children, adults, normotensives, and borderline hypertensives (Anderson, Lane, Taguchi, Williams, & Houseworth, 1989a; Arensman, Treiber et al., 1990; Light, Obrist, Sherwood, James, & Strogatz, 1987; Tischenkel et al., 1989). It has been most clearly seen in studies that used stressors that are specifically designed to produce a predominantly α-adrenergic pattern of reactivity, such as the forehead cold pressor procedure (e.g., Anderson, Lane, Muranaka, Williams, & Houseworth, 1988; Treiber et al., 1990).

There is now some evidence that the greater blood pressure reactivity seen in Blacks may have a genetic component (Kotanko et al., 1997). In that study, a strong association was found between a variant of the β2-adrenoceptor gene and hypertension in African Caribbeans. Specifically, this gene variant encodes for glycine rather than arginine at position 16, leading to enhanced agonist-mediated receptor downregulation. This enhanced receptor downregulation may lead to an attenuated vasodilator response, thereby predisposing this population to hypertension. In the presence of sufficient psychosocial or behavior stressors, these types of genetic predispositions may lead to actual phenotypic differences, such as increased vasoconstriction or increased blood pressure.

The contribution of psychosocial and behavioral factors to hypertension in Blacks has also been an active area of investigation. Topics include the effects of socioeconomic status, social support, dietary factors, John Henryism, racial discrimination, physical activity, and perceived stress on blood pressure (for reviews, see Anderson et al., 1989a; Anderson & McManus, in press; Macera, Armstead, & Anderson, in press; Myers & McClure, 1993). Socioeconomic status (SES) is perhaps the social variable that has received the most research attention over the years. Although measured by a variety of indices (e.g., income, occupation, or educational level), SES is consistently and inversely related to blood pressure levels among both Blacks and Whites (Hypertension Group, 1977). For example, the Hypertension Detection and Follow-up Program Cooperative Group (1977) examined the relation between education and racial differences in hypertension prevalence among individuals 18–74 years of age in 14 U.S. communities. Although the overall hypertension rate among Blacks was almost twice that of Whites, education was inversely related to hypertension in both race and gender groups; that is, the lower the education level achieved, the more likely a subject was to be diagnosed hypertensive. However, although controlling for education level reduced the discrepancy between Blacks and Whites in hypertension prevalence, Blacks at the highest educational level (college graduates) were still twice as likely as Whites to be diagnosed as hypertensive.

An Integrated, Multilevel Approach to Hypertension in Blacks

Recently, a multilevel model for hypertension in Blacks was proposed in an attempt to integrate some of the biological and socio-behavioral research in this field and to guide biobehavioral studies (Anderson, McNeilly, & Myers, 1991, 1992). The model, illustrated in Figure 10, proposes that exposure to chronic and acute stressors and environmental demands may lead to increased sympathetic activity, increased sodium retention and vascular reactivity, and hypertension. The connections among stress, sympathetic activity, and enhanced sodium retention have been amply demonstrated in animal studies (for reviews, see Anderson et al., 1991, 1992). In addition, there is some indication that sodium may augment acute vascular reactivity (Dimsdale, Graham, Ziegler, Ziman, & Berry, 1987; Rankin, Luft, Henry, Gibbs, & Weinberger, 1981).

Although research has shown greater vascular reactivity and sodium retention among African Americans relative to Whites, few published studies have examined the basis for these differences. The model predicts that ethnic group differences in biological functioning are due principally to differences in social and environmental factors, especially greater exposure to psychosocial stressors (residential stressors, racial discrimination) and lower SES in Blacks. Many of these chronic social and environmental stressors have been associated with hypertension among Blacks (Harburg et al., 1973; James and Kleinbaum, 1976; Kreiger, 1990; Krieger and Sidney, 1996; Strogatz et al., 1997). The model further predicts that the effects of stress on biological functioning may be augmented or reduced by other psychosocial and behavioral factors. For example, behavioral and psychological factors such as John Henryism (James, Hartnett, & Kalsbeek, 1983) and anger suppression (Johnson, Schork, & Spielberger, 1987) may interact with stress to increase potentially pathophysiological processes, whereas others, such as physical exercise or stress management (Schneider et al., 1995), may reduce psychological and physiological risk. In addition, coping resources such as increased social support and/or religious participation may decrease the untoward effects of stress on blood pressure (Strogatz et al., 1997). Research has revealed that religious participation may serve to buffer the effects of stress exposure in older Blacks (Krause & Van Tran, 1989). The model predicts that the effects of chronic stress are potentially modified by “constitutional” factors such as age, gender, obesity, and parental history of hypertension.2

Some preliminary support for this model is available. Matthews, Gump, Block, and Allen (1997) discovered that various forms of chronic or background stressors (major life events, daily hassles, etc.) may augment cardiovascular reactivity to acute stress in children. In a study involving 40 Black female participants (ages

2 Many of the studies cited did not involve an experimental manipulation but rather compared groups that already differed on variables such as level of social support, SES, or amount of religious activity. Although these types of studies are important, one important strategy for fostering the integrative, multilevel approach we are proposing would be through studies in which these types of variables or the hypothesized mechanisms by which they operate are manipulated experimentally when feasible.
In the fall of 1996, the OBSSR and the National Institute of Dental Research (NIDR) cosponsored an interdisciplinary teleconference entitled *OBSSR/NIDR Collaborative Science Conference.*
Creating New Paradigms for Collaboration in Biology, Oral Clinical Research and the Sociobehavioral Sciences. This conference linked speakers at NIH with biomedical and sociobehavioral participants at 17 dental schools across the nation for a discussion of interdisciplinary research opportunities in dental research. Because of the success of the conference, plans are now underway to issue a Request for Applications (RFA) for competing supplements in interdisciplinary, biobehavioral oral health research.

RFA on interdisciplinary training. In early 1997, the OBSSR organized an RFA to support educational workshops that would facilitate interdisciplinary research. Specifically, proposals were sought for workshops that would provide training for junior investigators interested in the integration of different fields of social and behavioral sciences research and/or the integration of these areas with more biological levels of analyses. The short-term goal of this initiative was to encourage social, behavioral, and biomedical scientists at an early stage of their careers to learn each other’s methods, procedures, and/or theoretical perspectives. In other words, the short term goal was to address “language differences” between scientists of different disciplines. The long-term goal of this RFA is to enable researchers to develop cross-disciplinary collaborations and to submit high-quality biobehavioral grant applications. Ten workshops were funded under this RFA, and it is anticipated that this initiative will be reissued in the near future.

Models of successful interdisciplinary research. In collaboration with the Social Science Research Council, the OBSSR is planning to organize a working group to understand and document the factors and circumstances that foster successful collaborations between biomedical researchers and researchers from the social and behavioral sciences. The working group will examine barriers to such collaboration (e.g., scientific language differences; disincentives for collaboration) and ways in which these difficulties can be overcome. This process will be informed by in-depth case studies of successful interdisciplinary collaborations.

Training needs in biobehavioral research. The OBSSR is also interested in developing more permanent methods for the training of biobehavioral investigators. Currently, there are few formal programs outside of traditional psychophysiology and health psychology that address this need. The Institute of Medicine (IOM) of the National Academy of Sciences has been asked to investigate the needs and strategies for interdisciplinary research training in the brain and behavioral sciences. The potential IOM study would result in a set of recommendations that address the type and extent of training and funding necessary to create scientists who are broadly trained to conduct research at the nexus of the behavioral and neurosciences. The study would also make recommendations to overcome barriers to the development and support of interdisciplinary education, programs, and research. Collaborating on this IOM study with OBSSR are The National Institute of Mental Health, The National Institute on Aging, and the National Institute of Nursing Research.

Working group on behavioral assessment of transgenic mice. In recent years, there has been increased interest among molecular biologists in examining behavioral phenotypes in knockout and transgenic animal models. In respond to this interest, the OBSSR formed a working group of behavioral scientists to assist it in developing a comprehensive, standardized battery of behavioral assessment procedures for examining transgenic mice. This battery will consist of diagnostic screening procedures to assess for general sensory deficits and physical limitations and a set of specialized tests to assess specific behavioral features. For example, tests may be outlined for animal models of depression, anxiety, cognitive functioning, and regulatory behavior. It is hoped that the development of such a standardized test battery will help foster multilevel research in the field of behavior genetics.

Biobehavioral research seminar series. The OBSSR has organized a seminar series at NIH that focuses on biobehavioral research. Each seminar has a specific theme and consists of an interdisciplinary researcher as the main speaker and two discussants. One discussant provides a biological perspective, and the other provides a behavioral or social science perspective. A major goal of the seminar series is to highlight successful examples of multilevel biobehavioral research for the NIH community, thereby demonstrating the value of a multilevel interdisciplinary approach to health research.

Peer review issues. The appropriate review of sociobehavioral research in general and biobehavioral research in particular is critical to the advancement of this field. At this time, the NIH is reviewing all study sections that evaluate social and behavioral grant applications to determine the most effective structure for such committees. The evaluation is being conducted under the auspices of the Center for Scientific Review (formerly the Division of Research Grants). The task of making recommendations about behavioral and social science review structure falls to a NIH committee chaired by Dr. Virginia Cain, Special Assistant to the Director of OBSSR. One important objective for this committee is to ensure that there are review committees in place with appropriate expertise and competence to evaluate multilevel research that cuts across sociobehavioral and biomedical fields. Input on the structure of such committees is being sought from the behavioral and social science research community.

Without question, the era of molecular biology poses substantial challenges to the relevance of behavioral and social sciences research to the health science agenda. At the same time, this challenge presents us with an unprecedented opportunity to not only demonstrate our relevance and highlight our successes, but to craft a new way of thinking and talking about health research. The concept of multilevel analysis may indeed represent a heuristic framework that will narrow the chasm between sociobehavioral and biomedical research and facilitate more integrative research approaches. For many reasons, psychophysiologists are perhaps uniquely suited to advance this framework through the development of multilevel models and research.

REFERENCES


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