The Mind Matters: Psychology as an Overlooked Variable Within Physiology Studies

Data reproducibility has been a topic of intense discussion in recent years after the call from the National Institutes of Health (NIH) director Francis Collins (3). Scientists are being asked to be more cautious in study design and transparent in methods reporting as we collectively try to better understand the important variables that influence data reproducibility. In this editorial, we present the case for a role of psychological metrics as key overlooked variables in animal and human physiology studies.

The new NIH grant guidelines effective January 2016 list four categories for enhanced reproducibility in studies: scientific premise, scientific rigor, biological variables, and key biological/chemical resources. The category of biological variability addresses gender and “underlying health issues,” among other things (9). As one considers the whole organism, we must accept that psychology is a part of integrative physiology and is a quantifiable variable that we argue is part of overall “underlying health” for animals and humans. Herein, we present animal and human data in support of the notion that psychological metrics can dramatically influence physiological outcomes in a variety of body systems and settings.

Physiologists often have a limited familiarity with psychological literature; thus many overlook that some of the day-to-day activities and care of laboratory animals evoke varying levels of mental/psychological stress. The social hierarchy within group housing, number of animals per cage, frequency of cage cleanup, transportation of animals, noise exposure, variations in researchers handling the animal, restraint/immobilization for a procedure or recording, temperature in the animal facility and laboratory, and other daily activities are in fact models for acute mental stress within the psychology literature (2). When some of these models of stress are evoked experimentally, they provide valuable insight into the impact of mental stress on various physiological systems. For example, restraint stress increases sympathetic nerve activity and plasma catecholamines, and dirty cage switching results in heightened activity within key brain regions related to autonomic outflow (2). Unfortunately, these acute stressors can occur during normal animal care and are not intended to be part of the experimental approach; thus they become confounders and another plausible explanation for the lack of data reproducibility (3).

Pryce et al. (10) highlighted how variability of animal care can evoke mental stress that has an influence into adulthood. Specifically, maternal care of rodents varies widely based on species and laboratory setting, and this variation can be dramatically impacted by human-rodent interaction. Early life stress associated with maternal separation and differences in care (e.g., early human handling vs. nonhandling) can have profound effects on hypothalamic-pituitary-adrenocortical (HPA) reactivity. For example, early human handling appears to downregulate basal hypothalamic corticotropin-releasing factor mRNA levels and blunt adrenocorticotropic hormone (ACTH) stress responses during early postnatal days and at weaning, and reduces overall stress responsiveness to ACTH and glucocorticoids in adulthood (10). One suggested mediator for these apparent “resiliency” adaptations is that early handling pups receive more maternal care in the form of dam-pup grooming compared with nonhandling pups (10). Such findings underscore the importance of standardization of postnatal conditions to avoid unanticipated long-term effects of early life stress and to ensure that data collected on adult animals is tightly controlled for difference in hormonal and stress responsiveness. Moreover, while the practice of purchasing and shipping animals from a company, and/or the use of students and trainees for animal care, offers economical options in a time of fiscal constraint, it remains possible that the heterogeneity of postnatal and pre-experimental care have an important influence on experimental findings and “translational” physiology.

In humans, a case has been made for a holistic view, which defines women and men as a biopsychosocial entities (1). That is to say that, when studying humans, there are five realms of being: physical, chemical, biological, psychological, and sociological (1). Furthermore, there is a field of psycho-physiology dedicated to mind-body interactions; yet basic and clinical physiology research largely focus on the chemical and biological aspects, and do not often evaluate the role of psychology as a variable in its studies.

It is typical for well controlled human physiological research to include an objective assessment of the basal state. Moreover, it is common to record information such as physical activity levels, smoking status, nutritional habits, habitual sleep patterns, and/or menstrual cycle phase or postmenopausal status (if female). It is widely acknowledged that each of these can impact the outcomes of physiological studies, and as such they serve as screening tools to limit variability. However, it is far less common to objectively assess the psychological basal state and personality traits in the same manner. What this means is that for a 6- to 12-mo longitudinal study, we might be able to confirm that there have been no major alterations in physical activity, nutrition, sleep, and other key variables, but we often have no insight into potential changes in levels of anxiety, depression, anger, empathy, hostility, and other mental states. Experimental studies demonstrate that changes in mental state can elicit robust alterations in HPA, autonomic, and cardiovascular responsiveness in humans (2, 4, 5). Moreover, changes in social structure or social hierarchy (i.e., new job or change in social status) can dramatically impact cardiovascular health (7). Are physiologists not
interested in how these factors might be influencing their data, or does the lack of attention reflect time constraints and/or lack of understanding as to which psychological assessments are most appropriate and reliable? Either way, we strongly advocate for the use of objective assessment of psychological metrics as part of the normal study recruitment and screening process.

So where do we go from here? In animal studies, we posit that it is essential to monitor any changes to the environment and exposure to potential stressors surrounding data collection, and we encourage telemetric monitoring of heart rate and blood pressure to monitor stress reactivity and recovery. Furthermore, setting standards for avoiding stress within a time frame immediately preceding data collection or animal sacrifice seems essential to ensure that something like the stress of animal transport is not influencing study outcomes. In human studies, investigators need to include objective psychological assessments that provide insight into mental states (i.e., anxiety, depression, etc.) and account for the potential role of changes in mental state during longitudinal studies. Self-report surveys such as the State-Trait Anxiety Inventory (STAI), Beck Depression Inventory (BDI), Positive and Negative Affect Schedule Expanded Form (PANAS-X), and other validated surveys offer a cost- and time-efficient solution in human studies, but where does one start and are these self-report assessments enough? The National Institutes of Mental Health’s Research Domain Criteria (RDoC) initiative is attempting to integrate multiple assessments such as genomics, neuroimaging, physiological measurements, observed behavior, and self-report to provide a more reliable assessment of behavior and mental health (6, 8). Mental health clearly exists along a complex spectrum, and RDoC aims to provide new rigor and approaches to assessing mental health; we encourage physiologists to follow this ongoing initiative since it may represent the future of how we objectively assess psychological health in both humans and animals.

Given the compelling evidence summarized above, this editorial is a call to physiologists to be attentive to the role of state of mind, social and environmental stress, personality, and other psychological metrics as measurable experimental variables that can influence data outcomes and reproducibility of both animal and human studies. There is a clear need for better monitoring and reporting of objective psychological metrics in animal and human experiments, and doing so would address part of the complex interplay of variables in physiological studies that impact intra- and interpersonal data variability and reproducibility.

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References