



Published in final edited form as:

Obesity (Silver Spring). 2017 October ; 25(10): 1653–1659. doi:10.1002/oby.21924.

Behavioral and Psychological Phenotyping of Physical Activity and Sedentary Behavior: Implications for Weight Management

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Abstract

Objective—Risk for obesity is determined by a complex mix of genetics and lifetime exposures at multiple levels from the metabolic milieu to psychosocial and environmental influences. These phenotypic differences underlie the variability in risk for obesity and response to weight management interventions, including differences in physical activity and sedentary behavior.

Methods—As part of a broader effort focused on behavioral and psychological phenotyping in obesity research, the National Institutes of Health convened a multidisciplinary workshop to explore the state of the science in behavioral and psychological phenotyping in humans to explain individual differences in physical activity, both as a risk factor for obesity development and in response to activity-enhancing interventions.

Results—Understanding the behavioral and psychological phenotypes that contribute to differences in physical activity and sedentary behavior could allow for improved treatment matching and inform new targets for tailored, innovative, and effective weight management interventions.

Conclusions—This summary provides the rationale for identifying psychological and behavioral phenotypes relevant to physical activity and identifies opportunities for future research to better understand, define, measure, and validate putative phenotypic factors and characterize emerging phenotypes that are empirically associated with initiation of physical activity, response to intervention, and sustained changes in physical activity.

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DISCLOSURE: Dr. Bryan, Dr. Hunter, Dr. Evans, and Dr. Yanovski declared no conflicts of interest.

DISCLAIMER: The opinions expressed herein and the interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official recommendation, interpretation, or policy of the National Institutes of Health or the U.S. Government.

CLINICAL TRIAL REGISTRATION: Not Applicable

Keywords

physical activity; sedentary behavior; phenotype; obesity

Introduction

Risk for obesity varies by individual and is determined by a complex mix of genetics and lifetime exposures at multiple levels; from the metabolic milieu to psychosocial, behavioral, and environmental influences. Even within the same obesogenic environment, some individuals will gain excess weight, whereas others will remain lean. Physical activity and sedentary behavior are key contributors in weight control, both for prevention of weight gain and weight loss/maintenance, as well as overall health and risk for chronic disease. Despite these well-known benefits of physical activity, the prevalence of physical inactivity across the U.S. population remains high.(1) Moreover, individuals with overweight or obesity are even less likely to meet physical activity guidelines than those of normal weight.(2)

Many factors influence individual differences in both physical activity and sedentary behavior, including genetic variability,(3, 4) physiological responses,(5) built environment, (6) and social environment;(7) however, many others likely remain unidentified. Even among individuals living in the same built or social environments, there is considerable individual variability in physical activity and sedentary behavior.(8) Similarly, interventions to increase physical activity or reduce sedentary behavior in the general population produce considerable variability,(9, 10) and predictors for response to a given intervention remain elusive.(3, 11)

In the context of weight loss and weight control, most interventions focus both on reductions in energy intake and increases in energy expenditure (primarily an increase in moderate to vigorous physical activity as well as reduction in sedentary time), with considerable individual variation in trajectories of weight loss and weight loss maintenance. Several reviews and position statements have discussed the role of physical activity in weight loss and weight loss maintenance.(12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22) Within clinical trials, in general, after an initial period of successful weight loss and increased physical activity, most individuals return to their initial physical activity levels, with only a small proportion of individuals successfully maintaining high levels of physical activity.(23, 24, 25)

The *2008 Physical Activity Guidelines for Americans* (currently under revision) recognize that many adults seeking to lose weight may need to engage in higher levels of physical activity than recommended for the general population (150 min of moderately vigorous physical activity per week) to lose weight or keep it off. The *2013 American Heart Association/American College of Cardiology/The Obesity Society Guidelines* recommend 150 min per week of moderate to vigorous physical activity for individuals seeking to lose weight and 300 min per week for maintenance of weight loss.(18) This is consistent with earlier recommendations from professional organizations that recommended the need for high levels of physical activity to control body weight.(16, 26, 27, 28) As observed in the National Weight Control Registry, higher levels of physical activity (approximately 2600 kcal/week) are a key factor associated with successful weight loss maintenance,(29) and this

has been confirmed by others in response to weight loss interventions.(23, 24, 30, 31, 32) However, in practice, interventions to successfully achieve and maintain these higher levels of physical activity and reduced sedentary behavior remain an unmet challenge.

Although continued exploration of genetic, physiologic, and other biological variables will be important for understanding individual differences in physical activity behavior, it is also imperative to consider other factors that may explain differences and point to novel intervention approaches. A relatively new but potentially promising avenue for identifying novel targets for behavior change involves a focus on behavioral and psychological *phenotypes* that may differentiate active versus inactive individuals or those who initiate and maintain physical activity from those who do not. To be sure, there has been a tremendous amount of research on behavioral and psychological factors that predict physical activity. For example, an enormous body of research from the health psychology tradition has focused on the role of *motivation to engage in physical activity*. Self-determination Theory (33) characterizes motivation on a continuum from amotivation to extrinsic motivation to intrinsic motivation to be active, while the Theory of Planned Behavior (34) takes a multi-construct approach to characterize motivation (intentions to be active) as the combination of ones attitudes towards, normative support for, and self-efficacy for engage in physical activity. Related research on the Model of Action Phases (35) has focused on different phases of physical activity, from the *predecisional phase* in which motivation is developed, to the *preactional phase* involving the formation of implementation intentions (plans of action with “if-then” contingencies), to the *actional phase* in which implementation intentions are acted upon and behavior is enacted. Experience of the behavior (either positive or negative), then, recapitulates the model and leads back into the *post-actional phase* in which post-behavior evaluations of the outcomes feed back into future decisions to engage in the behavior. While these and other theoretical frameworks have amassed extensive empirical support, particularly in the area of physical activity,(36, 37, 38) the bulk of work in this area is targeted to the critical role of *intentions to be active*. As such, a complaint leveled against this area of research is the well-known “intention-behavior gap”,(39) such that intentions generally account for only a small to moderate amount of the variance in behavior. (40) Further, these models are extremely complex and multifaceted, and are thus ill-suited for developing profiles of meaningful individual differences that predict different approaches to behavior or to identify specific phenotypes.

A workshop led by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), “Behavioral and Psychological Phenotyping to Understand Differences in Physical Activity and Sedentary Behavior Affecting Weight Management,” was convened to bring together experts in human behavior, behavioral genetics, exercise science, psychology, and neuroscience as well as researchers focused on obesity-related physical activity interventions and environmental influences on activity. The purpose of the meeting was to explore the state of the science in behavioral and psychological phenotyping related to physical activity and sedentary behavior across the lifespan and to identify future directions for research.

This paper provides the rationale for identifying psychological and behavioral phenotypes relevant to physical activity and, as illustrative examples, discusses two promising

phenotypic factors related to individual differences in activity and sedentary behavior: reinforcing value and affective response. We also identify several opportunities for future research including the need to better understand, define, measure, and validate putative phenotypic factors and to discover and characterize emerging phenotypes that are empirically associated with initiation of physical activity, response to intervention, and sustained changes in physical activity over time.

What is behavioral and psychological phenotyping?

A phenotype refers to a set of observable characteristics that differentiate one person from another. In general, phenotypes are thought to result from an interaction between genotype and the environment, where they range from more static observable differences, such as eye color, to more dynamic behavioral differences, such as awareness/responsivity to internal cues or impulsivity. *Behavioral and psychological* phenotypes, on the other hand, are infrequently tied to a single gene and are rarely static; rather they are reliable characteristics that shape or influence an individual's behavioral tendencies and patterns. The ultimate expression of the psychological phenotype, characteristics which make each individual unique, is then influenced by a myriad of other internal and external exposures—from genes to the intrauterine environment to the broader social and built environment(s).(41) An individual's behavioral or psychological phenotype is thought to be a relatively stable characteristic of the person expressed with differential intensity based on learning and context (i.e., a trait), not a fleeting state.(42) Most psychological or behavioral constructs are multidimensional. However, the behavioral or psychological phenotype reflects a more generalized and enduring predisposition versus a situation-specific response. For example, an individual who is prone to anxiety (trait) will experience cognitive and emotional responses consistent with anxiety across many situations and to a more intense degree than those less prone to anxiety.(43) This is differentiated from an anxiety “state” which reflects a more transient and situation-specific emotional arousal such as low-to-moderate levels of arousal in advance of a competition or a high level of arousal in response to the threat of physical harm.

In animals, there are many examples of behavioral phenotypes, for example, a sheep dog's natural drive is to herd. Although sheep dogs have an instinct to herd, it is not the case that all sheep dogs are immediately able to herd perfectly. With training and the right environment, a sheep dog can become a highly effective herder. In contrast, a dog that did not have the herding phenotype (e.g., Labrador retriever) might be able to learn to herd but, since they lack the natural drive, they would likely need more extensive training (i.e., intervention). Like animal models, humans who are exposed to the same environment or learning opportunities may show different outcomes based on their inherent phenotypes; however, given the greater complexity of cognitive, social, and environmental influences for humans than dogs, identification of the underlying patterns resulting in a physically active or sedentary life style will clearly be harder to identify.

Within the context of energy intake or eating behavior, there are several examples of potential behavioral phenotypes under investigation, such as eating in the absence of hunger, (44, 45) satiety and food responsiveness,(46) and loss of control/binge eating.(47) While

continued refinement and study of these phenotypes is needed, the data, to varying degrees of confidence, show that they are predictive of increased susceptibility to obesity or diminished response to treatment.

Unlike eating behavior, research identifying psychological or behavioral phenotypes relevant to physical activity and sedentary behavior in humans, particularly as it relates to weight management, is limited. Identifying behavioral and/or psychological phenotypes that drive the propensity to be active or inactive for unique subtypes of individuals may result in identification of novel targets for more effective and tailored approaches to increase and sustain physical activity and reduce sedentary behavior.

Characterization and validation of phenotypes

Characterizing putative phenotypes in order to understand their distribution across the weight spectrum, including those with or at risk for overweight and obesity, is an important step in identifying who will benefit more from a given intervention and ultimately realize the goal of enhanced precision in behavioral medicine and public health interventions.(48, 49, 50) The process of characterizing phenotypes includes three components. First, there needs to be wide distribution of the phenotype across the population. For example, if the phenotype characterizes 90% of the population, it may not have enough variability to be useful in understanding the full range of obesity-related behaviors including physical activity and sedentary behavior. Second, to meaningfully inform intervention, the phenotype must be related to the target behavior (i.e., exercise). If the phenotype is a continuous variable, a strong relationship between the phenotype and objectively measured physical activity in the free-living environment would be expected. Third, to assure that a focus on the phenotype is likely to be relevant to behavior change and health outcomes, the phenotype should tap into unique sources of variance to understand the target behavior.(51)

After characterizing the phenotype, it must be validated as a target for behavior change interventions and, ultimately, a change in a health indicator such as weight status. The experimental medicine approach involves identifying a target for intervention (e.g., phenotype), manipulating the target through intervention, and testing whether engaging the target produces the hypothesized behavior change.(40, 52, 53) For example, applying interventions that address a psychological phenotype that is reliably related to physical activity (e.g., affective response to exercise) should produce improvement in physical activity. Lastly, an important goal of behavioral phenotyping is to understand the underlying psychological or biological mechanisms that underlie the individual differences that characterize specific phenotypes. Understanding these mechanisms may be particularly relevant for the development of tailored approaches to address the needs of individuals across the range of the phenotype to increase physical activity or reduce sedentary behavior.

Promising Psychological and Behavioral Phenotypes

The purpose of the workshop was to explore a variety of phenotypic factors that may relate to activity level; particularly in response to individual or population based approaches to preventing weight gain or improving weight loss across the lifespan. However, given the relative newness of the field and the complex concept of behavioral and psychological

phenotypes, this paper focuses on two illustrative examples of phenotypic constructs related to physical activity and sedentary behavior—relative reinforcing value and affective response—in an effort to highlight this area of research and its promise for informing future interventions. These examples are not intended to be representative of the full spectrum of potentially relevant behavioral and psychological phenotypes. Rather, they were chosen because they were highlighted at the NIDDK workshop as some of the most developed areas of research focused on understanding behavioral and psychological phenotypes that predict physical activity.

Relative Reinforcing Value—The first example of a promising phenotype which may be applicable to weight management involves the relative reinforcing value of physical activity or sedentary behavior. The core principle behind the relative reinforcing value of physical activity is the choice between being active or sedentary;(54, 55) specifically, how much work an individual will engage in to obtain access to a particular active or sedentary behavior.(55, 56) This paradigm is based on decades of behavioral research that uses progressive ratio schedules to establish reinforcing value.(57) This approach has been highly successful in the context of both eating behavior (58) and substance use treatment,(59) with reviews of hundreds of studies showing evidence for the importance of reinforcing value in behavior and behavior change. Emerging work in the exercise domain shows promising evidence that reinforcing value may be just as effective for changing physical activity and sedentary behavior.(60) From a broader perspective, providing a choice between two alternatives, rather than only working for one behavior has strong ecological validity, since people seldom only have one alternative available to them.

The first demonstration of the reinforcing value of activity compared physical activity versus sedentary behavior in children across non-overweight, overweight and obese categories.(61) When there were no constraints on behavior, all children chose to be sedentary, but as the cost to be sedentary increased (more button presses on a computerized task were required to earn the reinforcer), children who were lean and children with moderately overweight increased the value of being active, but heavier children remained sedentary even as the cost for being sedentary drastically increased; potentially revealing a meaningful phenotypic difference.

The theoretical underpinnings of the reinforcing value phenotype lie in the model of incentive salience, which describes different neurobiological systems for wanting (dopaminergic) versus liking (opioid) and can provide insight into the biological mechanism(s) that promote physical activity.(62, 63, 64) Research applying this model to physical activity suggests that reinforcing value (wanting) is a strong determinant of how much activity children get, but it interacts with liking, so that children who are motivated to be active enjoy engaging in the greatest moderate to vigorous physical activity.(65)

For people who find sedentary behavior to be more reinforcing than physical activity (a behavioral phenotype), it may be possible to use the reward of sedentary behavior as a reinforcer for physical activity.(66, 67, 68) This can be done in the laboratory, by making television or playing computer games contingent upon exercising,(66) and this same technology can be applied in the home where television watching is contingent upon riding

an exercise bicycle.(67) Thus, identifying the relative reinforcing value of physical activity or sedentary behavior for an individual or sub-group of individuals can inform approaches to tailor intervention contingencies to enhance the treatment effect. For example, in an intervention designed to reduce sedentary behavior in children who were obese, children who showed a higher reinforcing value for sedentary behavior were less likely to lose weight.(69) There is also evidence that adults who find physical activity more rewarding are more likely to meet physical activity guidelines,(60) suggesting that directly targeting changes in reinforcing value might lead to increases in physical activity.

Affective Response—The second illustrative phenotype is affective response to exercise. Affective response to exercise describes the pleasure or displeasure one experiences during a bout of physical activity.(70) Affective response to exercise is conceived broadly as the “global affective space” rather than the measurement of discrete emotions (e.g., happiness, sadness) or psychological states (e.g., anxiety, depression).(71) The global measure of the construct is reflected in its operationalization; affective response is most typically measured with a bipolar adjective scale known as the Feeling Scale that ranges from –5 (very bad) to 0 (neutral) to very good (+5).(72) Critically, affective response should be measured at multiple timepoints *during a bout of physical activity* as it may vary throughout the session.

The Dual Mode Theory elucidates the underlying evolutionary, neurocognitive, and physiological underpinnings of the affective response to exercise.(71) This theory suggests that the affective response to exercise results from the interplay of two systems: one that is cognitive in nature involving appraisals, motivations, and goals relevant to activity versus a second system that is physiological in nature resulting from interoceptive cues experienced as the body responds to an exercise bout.(73) Empirical work has documented that there is considerable individual variability in affective response to physical activity, particularly during exercise at an intensity that is near but below the ventilatory threshold. Ventilatory threshold is associated with the point during exercise when lactate begins to accumulate in the blood and causes an increase in ventilation.(74) The assessment of ventilatory threshold involves a graded maximal exercise test, where an individual completes exercise at increasing levels of grade/intensity until they can no longer sustain the effort. A number of assessments, including expired carbon dioxide, are taken during the maximal exercise bout, and the ventilatory threshold is the inflection point at which there is an excess production of carbon dioxide relative to oxygen. Though the exact assessment of ventilatory threshold is complex,(75) subjectively it is the intensity of exercise at which breathing becomes labored, exercise becomes more difficult, and it is no longer possible to sustain a conversation. At this level of intensity, the variability lies more in the cognitive side of the affective response process.(76) At intensities above the ventilatory threshold, the interoceptive/physical cues “take over” and there is considerably less individual variability since exercising at very high intensity is almost universally unpleasant. For this reason, assessment of affective response to exercise is conducted at or below an individual’s ventilatory threshold.

Multiple studies have shown that there are genetic factors associated with affective response to physical activity,(77, 78) and while affective appraisals of physical activity are considered a near fundamental aspect of the exercise experience,(79) individual differences in physiologic response (fitness/maximal oxygen consumption, respiratory rate, muscular

strength, etc.) to a given intensity of exercise also contribute to affective response. Rhodes, Fiala and Conner (57) included a total of 102 studies of affective response to exercise in their metaanalysis of the association between affective judgments and physical activity and found a moderate association between the two. Further, Rhodes and Kates (58) used rigorous inclusion criteria to identify 24 longitudinal studies of the association between affective response and future exercise behavior, concluding that individuals who have a more positive affective response to a bout of physical activity at or below the ventilatory threshold are more likely to exercise in the future.(80) This association is found in youth as well as adults; Nasuti and Rhodes (81) identified 56 correlational studies and 14 intervention studies for inclusion in a meta-analysis on the association between affective response to exercise and physical activity among young people between the ages of 5 and 18 and showed a moderate effect size for the association. A more positive affective response to a bout of exercise is also associated with a more favorable response to an exercise intervention(82) and is thus predictive of more favorable cognitive appraisal and motivation to engage in physical activity.(80, 83) Although there are certainly contextual factors that influence affective response to exercise, most notably intensity of activity,(76) there are also good reasons to believe that affective response to physical activity is a reliable individual difference. As such, identifying affective phenotypes in response to exercise initiation and maintenance can inform novel approaches to interventions that better address the individual experience of exercise.

Discussion

Although the scientific premise of identifying behavioral and psychological phenotypes of physical activity and sedentary behavior to inform interventions is compelling, the field is very new and there are several research gaps that require attention to realize this potential. A clear gap exists in understanding individual-level drivers of both sedentary behavior and physical activity as meaningful contributors to weight trajectory and maintenance of weight loss.(84, 85) There is also a need for more research to better understand, define, measure, and validate putative phenotypic factors and to discover and characterize how these emerging phenotypes are empirically associated with change in physical activity, from initiation to maintenance of increased physical activity and reduced sedentary behavior as well as response to interventions to change these behaviors. Such research should lead to better, more targeted interventions and thus improved obesity outcomes over time. A more systematic focus on behavioral intervention development is also required,(86) including the use of an experimental medicine approach to testing mechanisms of change.(52) Towards this end, a few challenges and priorities for advancing the field are outlined below.

Taxonomy and measurement of phenotypes

Consistent taxonomy including reliable and meaningful measurement is the foundation of good science and fundamental to identifying behavioral and psychological phenotypes. Although the behavioral and social sciences have a rich history in theory-driven measurement and psychometrics, there is a need for greater precision and application of new data science methods and technology to accelerate and transform the field to advance precision behavioral medicine.(87) In psychiatric and neurological diseases, behavioral

phenotyping is more established (88, 89) but the application of these principles to health behavior such as physical activity and sedentary behavior is relatively new. As noted above, there are phenotypes relevant to physical activity where the measurement work is detailed, well-developed, and generally agreed upon, such as the measurement of affective response to exercise. In contrast, for new, emerging hypotheses, it will be necessary to conduct basic behavioral research with a focus on understanding the circumstances in which a phenotype is important to understanding activity behavior both in the lab and in free-living circumstances. For some potentially promising behavioral or psychological phenotypes, it may also be that researchers from different disciplines or traditions are conducting research on what is ultimately the same phenotype, but are measuring it in different ways, as is likely the case with the research on relative reinforcing value and reward. Exercise is associated with increases in dopamine (90, 91) and opioids (92) and activation of the mesolimbic reward pathway,(93) which strengthens the behavior that led to these changes, including exercise behavior. These neurobiological changes should lead to people who find exercise more rewarding, working harder for exercise than those who experience less reward from engaging in exercise. Studies reporting physical activity, healthy eating, or adherence are examples where lack of precision in reporting the measured variable stunts scientific advancement.(94) These constructs are measured in a variety of ways and, although self-reported outcomes are often poorly correlated with the objectively measured outcomes, the same label is used to describe the construct (e.g.; self-reported physical activity and physical activity measured through accelerometry are reported as “physical activity”). Developing a clear and consistent ontology (vocabulary) for reporting outcomes and relationships between measured variables across behavioral and social science disciplines, will more rapidly advance knowledge discovery and hypothesis testing.(94)

Engagement of multi-disciplinary research teams

The complexity of behavioral phenotypes and the underlying mechanisms for these individual differences requires both a broad and deep understanding of multiple scientific areas, which demands a multidisciplinary approach to research. Focusing on only one dimension of a behavioral phenotype, at one level of analysis, provides a limited approach to the science of behavioral phenotyping. Understanding how to incorporate multiple constructs will require collaborations between scientists of many different perspectives and team science is therefore an important goal for future research on behavioral phenotyping of physical activity. A significant gap in scientific capacity is the ability to bridge the basic behavioral science/biomedical divide. To fill this gap, there is a need to form teams of scientists that can effectively work to integrate behavioral and biomedical data, with a focus on studying phenotypes of behaviors such as physical activity and sedentary behavior.

The paradigms associated with identification and validation of behavioral phenotypes for physical activity will also require working across levels of analysis, and using observational and experimental methods. It is important to consider training modalities that will produce scientists who thrive in a team science environment. This includes identifying optimal early training experiences that promote best practices to minimize insularity.

Conclusion

By identifying and experimentally testing behavioral and psychological phenotypes, we can improve our understanding of variation in individual response to treatment and inform the development and testing of subsequent more personalized/targeted approaches designed to help people become more active, help prevent obesity or help maintain weight loss in those who are in treatment for obesity. Although the focus of this paper was on behavioral and psychological phenotypes for physical activity and sedentary behavior, the research gaps and opportunities identified in the activity domain have implications for obesity prevention and control and these same needs and methods are also relevant to characterizing eating-related phenotypes.

Acknowledgments

Manuscript is based on a meeting sponsored by NIH/NIDDK, “Behavioral and Psychological Phenotyping to Understand Differences in Physical Activity and Sedentary Behavior Affecting Weight Management” held December 1–2, 2015, NIH Campus, Rockville, MD.

FUNDING: None

Dr. Jakicic reports grants from Weight Watchers International, personal fees from Weight Watchers International, grants from HumanScale. Dr. Epstein reports that he is a consultant and has equity in Kurbo.

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What is already known about this subject

- Physical activity and sedentary behavior are key contributors in weight control, both for prevention of weight gain and weight loss/maintenance, as well as overall health and risk for chronic disease.
- Despite these well-known benefits of physical activity, the prevalence of physical inactivity across the U.S. population remains high, with individuals who are obese or overweight being even less likely to meet physical activity guidelines than individuals of normal weight.

What this study adds

- This summary of a recent NIH/NIDDK meeting outlines evidence and gaps in understanding behavioral and psychological phenotypes that may contribute to differences in physical activity and sedentary behavior. Such phenotyping could allow for improved treatment matching and inform new targets for tailored, innovative, and effective weight management interventions.