Identifying Predictive Markers of Field Performance: The Potential Role of Individual Differences in Threat Sensitivity

Project Leads

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Statement of Problem

It is often critical for Department of Homeland Security (DHS) employees to be sensitive to the presence of a threat. Whether a threat presents itself at a personal level (such as in the one-on-one interactions that occur at border crossings and airports) or a more global level (such as in general monitoring for impending danger or disaster), the more sensitive employees are to the threat the more likely it can be averted. Due to natural predisposition or personal experiences, some individuals are more sensitive to the presence of a threat than others, and it would be immensely informative to quickly and affordably identify these individuals before they are charged with the duties of DHS positions that require high threat sensitivity.

This research brief examines the recent advances in neurogenetics research that are poised to address the challenge of how best to preselect individuals who will exhibit high levels of threat sensitivity. Recent research has highlighted how the integration of behavioral, neural,
and genetic markers can uniquely reveal the mechanisms that give rise to individual differences, and this brief explores the relevance of this work in establishing predictive markers of increased threat sensitivity.

The primary questions of interest are as follows:

1. How can behavioral, neural, and genetic markers be combined to identify specific biological pathways associated with aptitude for detecting threat?
2. Are there general biological pathways that are broadly associated with threat sensitivity, or are there specific, individual pathways that are each tied to specialized tasks requiring threat sensitivity?
3. Is there a panel of identifiable genetic markers that can accurately predict variability in these biological pathways (and moreover, in aptitude for threat detection) that can be used as a screening tool by DHS?

**Background**

All healthy adults share some basic abilities and traits, yet the immense variability among people makes certain individuals more capable than others to perform certain tasks. Efforts to identify the biological basis of a given individual’s superior abilities have been buoyed with significant progress made in the last 5 years in describing the contributions of multiple common genetic markers to individual differences in complex behaviors. Through a step-by-step process that encompasses genes, brain chemistry, brain function, behavior, and the environment, it is possible to identify effects of functional genetic markers on the brain circuits that mediate behavioral responses to challenges in our environments (Hariri, 2009). The vast potential of this integrated approach is highlighted by recent studies whose collective results demonstrate a cascade of causal relations wherein common functional markers in human genes that bias key components of brain chemistry result in predictable differences in brain circuit function. These differences in function, in turn, mediate individual differences in complex behaviors such as sensitivity to threat (see Figure 1 for a general framework of this relationship cascade).

Many aspects of our emotions, personality, and temperament remain relatively stable across time (Cloninger, Svrakic, & Przybeck, 1993; Costa & McCrae, 1997; Kagan, 1992; Kagan, Reznick, & Snidman, 1988). These enduring aspects play a critical role in shaping our complex behaviors and our ability to successfully navigate social interactions and overcome challenges from an ever-changing environment. Naturally occurring differences between individuals in such traits may serve as important predictors of aptitude for a variety of tasks that depend on these abilities. Accordingly, identifying the biological mechanisms that give rise to such individual differences affords a unique opportunity to develop a deeper understanding of human traits and the emergence of related variability in task aptitude and performance.
Note: Integration of complementary technologies can be used to reveal the neurobiology of individual differences in complex behavioral traits. (a) Individual differences in personality and temperament are critical in shaping complex human behaviors and may serve as important predictors of vulnerability to neuropsychiatric disorders. (b) Neuroimaging technologies, especially BOLD fMRI, can identify relationships between variability in brain circuit function and individual differences in personality and temperament. (c) Multimodal PET/fMRI (or pharmacological fMRI) can map individual differences in behaviorally relevant brain circuit function to variability in specific molecular signaling pathways. (d) Variability in specific molecular signaling pathways can be mapped to functional genetic polymorphisms that inform the pathways’ ultimate biological origins and can be used to efficiently model how such emergent variability impacts behaviorally relevant brain function. (e) Each level of analysis can potentially inform issues relevant for personnel selection to provide guiding principles for the development of more effective and accurate markers of task aptitude and performance.

An intriguing goal of this general research enterprise is to ultimately bypass the middle steps of Figure 1 and make the connection directly from genes to behavior. Making this connection rests upon being able to accurately and confidently move from one step to the next. Recent research has begun this process. First, human neuroimaging studies, especially those employing functional magnetic resonance imaging (fMRI), have begun to reveal the neural substrates of inter-individual variability in complex behavioral processes such as anxiety, neuroticism, rumination, and sensitivity to threat (Barrett & Armony, 2009; Bishop, Jenkins, & Lawrence, 2007; Drabant, McRae, Manuck, Hariri, & Gross, 2009; Etkin et al., 2004; Haas, Omura, Constable, & Canli, 2007; Killgore & Yurgelun-Todd, 2005; Most, Chun, Johnson, & Kiehl, 2006; Phan, Fitzgerald, Nathan, & Tancer, 2006; Ray et al., 2005; Schienle, Schafer, Stark, Walter, & Vaitl, 2005; van Reekum et al., 2007). Recent studies have established that fMRI measures represent temporally stable and reliable indices of brain function (Johnstone et al., 2005; Manuck, Brown, Forbes, & Hariri, 2007). Thus, much like their behavioral counterparts, patterns of brain activation represent enduring, trait-like phenomena, which in and of themselves may serve as important markers of individual differences. Moreover, our understanding of such measures of brain function may move us one step further along this chain of processes, since they may reveal important dispositional tendencies (and corresponding abilities) that may not be captured by overt behavioral measures that are vulnerable to biases associated with self-report and measurement error.

In effect, the above neuroimaging studies illustrate the predictive relationship between regional brain activation and trait-like behaviors. For example, increased amygdala reactivity predicts sensitivity to threats in our environment. Further, it has been revealed that the amygdala plays a role in mediating awareness of, and attention to, a broad category of stimuli and is not solely related to explicit or implicit threat (e.g., Ousdal et al., 2008). The amygdala is not simply responsive to “innate” threats but is also critical both in driving arousal to any stimuli that are task-relevant and in mediating learning of stimulus-reward contingencies, regardless of valence (e.g., Davis & Whalen, 2001; Gallagher & Holland, 1994). Thus, individual difference measures related to amygdala activity may provide an effective means to identify variance in threat sensitivity.

The second wave of research that helps bring us closer to our goal of directly linking genes to behavior has focused on the relationships between brain function and brain chemistry. Recent neuroimaging studies employing pharmacological challenge paradigms, principally targeting monoamine neurotransmission, have revealed that even subtle alterations in dopaminergic, noradrenergic, and serotonergic signaling can have profound impact on the functional response of brain circuitries supporting emotion, personality, and temperament (Bigos et al., 2008; Hariri, Mattay, Tessitore, Fera, et al., 2002; Mattay et al., 2003; Tessitore et al., 2002). That is, targeted changes in brain chemistry have predictable and reliable effects on brain function, which, in turn, have predictable and reliable effects on behavior. Similarly, multimodal neuroimaging approaches collecting both positron emission tomography (PET) and...
fMRI data from the same subjects have revealed that naturally occurring differences in specific aspects of brain chemistry map onto variability in behaviorally relevant brain functions (Fisher et al., 2009; Fisher et al., 2006; Rhodes et al., 2007). Collectively, these approaches are revealing how individual differences in behaviorally relevant brain activation emerge as a function of underlying variability in key brain signaling pathways (e.g., increased serotonin signaling predicting increased amygdala reactivity). One logical next step is to identify the sources of inter-individual variability in these key signaling pathways.

As the final step in the chain of processes, we can turn to the relationships between brain chemistry and natural variability in the human genetic code. In the current era of genetics, it is possible to identify common variation in the genes that influence the functioning or availability of chemical components in brain signaling pathways. For example, a number of common genetic polymorphisms (i.e., variation that is frequent and present in all humans) have been indentified that predict variability in key steps of the serotonin signaling pathway (Brown et al., 2005; Buckholtz et al., 2008; Fakra et al., 2009; Hariri, Mattay, Tessitore, Kolachana, et al., 2002). These same variants have been used in fMRI studies to predict variability in brain function that, in turn, predicts individual differences in sensitivity to threat; for example, differences in amygdala reactivity can predict differences in trait anxiety (e.g., Fakra et al., 2009).

**Synthesis**

Recent research has provided promise that the existence of a predictable cascade of effects between related variables can provide a means to ultimately use genetic markers to predict behavioral performance in a given environment. In this line of research, observable behavior—such as performance on a cognitive task in response to environmental pressures such as stress, performance evaluation, or time limits—is predicted by self-report personality measures, which in turn are predicted by brain function differences, which in turn are predicted by changes in brain chemistry, which in turn are predicted by common genetic polymorphisms (Figure 1; Hariri, 2009). Given the research advancements described above that have illuminated the various steps along this process chain, a fruitful avenue of pursuit will be focusing on the impact of genetic polymorphisms that shape individual differences in brain chemistry, brain circuitry, and behavior. When a precise cascade of related neurobiological and behavioral effects is clearly established, such common polymorphisms can represent incredibly powerful predictive markers that are readily accessible (e.g., samples can be collected at nearly any office or jobsite without complicated equipment), applicable (e.g., even newborns can be genotyped), and economical (e.g., costing tens of dollars per sample compared to the hundreds and even thousands required for fMRI and related techniques).
Future Directions

The exciting and unique promise of this research enterprise is that by utilizing the integrative contributions of measures tapping into behavior, brain circuit function, brain chemistry, and genetics, it may be possible to ultimately devise simple and effective screening tools that predict variability in a number of domains, including task aptitude and performance. Of course, arriving at this ultimate reduction requires intensive and expansive efforts wherein all these technologies are first brought to bear on explicating the detailed biological mechanisms mediating individual differences. In the context of the unique goals of the DHS to thwart attempts at destabilizing our nation’s infrastructure and endangering the lives and well-being of our citizens, such research holds the promise of generating an effective and economical strategy for identifying personnel with the greatest sensitivity to threat and, consequently, the greatest aptitude for many critical DHS operations and positions.

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References


