

Putting Basic Behavioral Science to Work: Bench-to-Bedside Examples

Developing New Treatments for Depression Based on Self-Regulation Theory

Basic behavioral research in the areas of self-perception and emotion regulation has uncovered the mechanisms that connect these two processes. This knowledge is the foundation for the development of more effective clinical therapies for depressed patients by integrating self-evaluation techniques.

There is a pressing need for cost-effective, scientifically-proven treatments for people who suffer from disorders such as anxiety and depression. Basic behavioral science research is meeting this need by producing the fundamental knowledge that is critical for the development of innovative clinical approaches. One of the most recent examples is self-system therapy, a brief course of psychotherapy for depression that is currently being tested in an NIMH-sponsored clinical trial. This therapy is an outgrowth of basic behavioral science studies relating to how people regulate their thoughts and moods. Specifically, basic research has shown that people often react with bouts of depression or anxiety to certain self-discrepancies, such as differences between their perceptions of who they are versus their "ideal" or "ought to be" selves. Further research finds that when these self-discrepancies are chronic, so too is the negative affect such as depression or anxiety (Higgins, 1987). This chronic condition, when combined with other risk factors, can also increase the individual's vulnerability to more serious emotional problems. Drawing on these basic research findings on the psychology of self-evaluation, Dr. Timothy Strauman, Duke University, developed a multidimensional model of depression that replicates the connections between self-perception and emotion regulation and incorporates related risk factors (Strauman, 1996). Using this theoretical model, Strauman and his colleagues identified which individuals would most benefit from interventions aimed at reducing their self-discrepancies. Further research has confirmed that Strauman's self-system therapy has proven to be beneficial for depressed patients (Strauman et al., 2006).

Higgins, E.T. (1987). Self-discrepancy: A theory relating self and affect. *Psychological Review*, 94, 319-340.

Strauman, T.J. (1996). Stability within the self: A longitudinal study of the structural implications of self-discrepancy theory. *Journal of Personality and Social Psychology*, 71, 1142-1153.

Strauman, T.J., Vieth, A.Z., Merrill, K.A., Woods, T.E., Kolden, G.G., Klein, M.H., Papadakis, A.A., Schneider, K.L., & Kwapil, L. (2006). Self-system therapy as an intervention for self-regulatory dysfunction in depression: A randomized comparison with cognitive therapy. *Journal of Consulting and Clinical Psychology*, 74, 367-376.

Uncovering the Differences in Message Framing that Lead to Proactive Health Care

Basic cognitive research into how people make decisions shows that different messages are needed for different kinds of health promotion. This finding has been the basis for a new generation of tailored health-related public service messages that advance the goal of encouraging people to protect their health.

Improving public health often boils down to the kind of decisions people make in avoiding health risks, consulting their health care providers, and complying with prevention and treatment regimens. Basic decision science research elucidates the cognitive, emotional, and social factors that influence judgment and choice, and how judgment and decision-making can be predicted and improved. This research plays a central role in health education by identifying the most effective ways to frame messages that will encourage behavior change. For example, fundamental cognitive research has shown that for certain kinds of prevention efforts, public health information is best conveyed in a gain-framed message (e.g., *If you regularly apply sunscreen you will help prevent skin cancer, versus If you don't apply sunscreen, you increase your risk for skin cancer*), whereas early detection strategies should be conveyed in a loss-framed way (e.g., *If you do not obtain a mammogram, tumors cannot be detected early, and the later the detection of cancer, the fewer the treatment options*) (Wilson et al., 1988). Additional research has shown that the influence of message framing on health behavior is also related to the type of behavior being promoted (Rothman & Salovey, 1997): People are risk-seeking when they consider losses and risk-averse when they consider gains, which is directly applicable to health-relevant decision-making. These findings originated in the cognitive psychology laboratory, and were then used in large-scale, field-based experiments designed to promote health behaviors in community-based interventions.

Rothman, A.J., & Salovey, P. (1997). Shaping perceptions to motivate healthy behavior: The role of message framing. *Psychological Bulletin*, 121, 3-19.

Wilson, D.K., Purdon, S.E., & Wallston, K.A. (1988). Compliance to health recommendations: A theoretical overview of message framing. *Health Education Research: Theory and Practice*, 3, 161-171.

Animal Research on Biological Clocks Leads to New Understanding and Treatment of Bipolar Affective Disorder

Circadian rhythms — our “biological clocks”— are the internal time-keepers that organize the ebbs and flows of an organism’s activities. These processes have been extensively studied in non-human species by basic behavioral scientists. Researchers have discovered a critical role played by 24-hour circadian rhythms in a form of mental illness, bipolar affective disorder. These findings have led to effective new treatments of this devastating disorder, for which pharmacologic treatments often are not effective and are poorly tolerated.

Circadian rhythms influence activities ranging from sleep to hormone production to pain tolerance. Extensive basic behavioral research shows that disruptions in circadian rhythms can worsen the symptoms of bipolar affective disorder (formerly called manic-depressive illness). Researchers have identified strong connections between circadian rhythms that regulate sleep-wake cycles and mood. Lack of sleep and disruptions in sleep-wake patterns can worsen symptoms in bipolar subjects (Barbini et al., 1998). Behavioral therapies aimed at repairing disrupted rhythms have shown great promise in treating this debilitating disorder. For example, a form of psychotherapy called IPSRT (interpersonal and social rhythm therapy) that is based on these findings is designed to regulate circadian rhythms, including sleeping and other behaviors. With training in a combination of behavioral strategies such as self-monitoring, realistic goal-setting, and monitored task assignments, patients are successfully stabilizing their patterns of eating, sleeping, and social stimulation. IPSRT, used in combination with traditional drug treatment, was found to reduce recurrence of bipolar episodes over a two-year period (Frank et al., 2005).

Barbini, B, Colombo, C., Benedetti, F., Campori, E., Bellodi, L., & Smeraldi, E. (1998). The unipolar-bipolar dichotomy and the response to sleep deprivation. *Psychiatry Research*, 79, 43. 50.

Frank, E., Kupfer, D J., Thase, M.E., Mallinger, A.G., Swartz, H.A., Eagiolini, A.M., Grochocinski, V., Houck, P., Scott, J., Thompson, W., & Monk, T. (2005). Two-Year Outcomes for Interpersonal and Social Rhythm Therapy in Individuals With Bipolar I Disorder. *Archives of General Psychiatry*, 62, 996-1004.

Revolutionizing PTSD Treatment with Virtual Reality Exposure Therapy

Basic behavioral research on intrusive memories of traumatic events has uncovered a link between incomplete mental and emotional processing of traumatic events and post-traumatic stress disorder (PTSD). This knowledge has furthered the development of exposure therapy methods for Iraq veterans suffering from PTSD, leading to a more effective treatment using virtual reality systems.

As the number of Iraq war veterans increases, so has the number of cases of post-combat post-traumatic stress disorder (PTSD), prompting an unprecedented demand for more effective treatments. Basic psychological research has suggested that PTSD results from an incomplete mental and emotional processing of a traumatic memory and that people can overcome this only by revisiting their traumatic experience in a controlled environment, such as a supervised clinic.¹ Further research by Jaycox and colleagues² examined various treatment styles and found that fear memories can be successfully modified only when the patient is emotionally engaged in the treatment. Traditional and widely used methods of exposure therapy, in which patients describe their traumatic experiences over and over, are rarely effective in alleviating PTSD symptoms because they are limited by the patient's avoidance of trauma reminders and emotional numbness. Drawing on this and subsequent basic research on exposure therapy, Difede and her colleagues³ have helped develop clinical trials using Virtual Iraq, a virtual reality therapy tool that features a scent machine, an audio player, and a version of the video game *Full Spectrum Warrior*. Patients in these trials are gradually and systematically exposed to the various sensory aspects of their traumatic experiences in order to jog their memories. Preliminary results from clinical trials indicate that patients with acute PTSD have significant reductions in symptoms of both major depression and PTSD.³ This ground-breaking development in PTSD therapy has the potential to help recent war veterans treat their disorder sooner and more effectively, preventing years of struggling with this condition and the associated disabilities.

¹ Foa, E.B., Steketee, G., & Rothbaum, B.O. (1989). Behavioral/cognitive conceptualizations of post-traumatic stress disorder. *Behavior Therapy*, 20(2), 155-176.

² Jaycox, L.H., Foa, E.B., & Morral, A.R. (1998). Influence of emotional engagement and habituation on exposure therapy for PTSD. *Journal of Consulting and Clinical Psychology*, 66(1), 185-192.

³ Difede, J. & Hoffman, H.G. (2002). Virtual reality exposure therapy for World Trade Center post-traumatic stress disorder: A case report. *CyberPsychology & Behavior*, 5 (6).

Animal Research Underscores Benefits of Cognitive Exercise

Research on the brain's responses to an enriched environment has demonstrated the plasticity of the brain. These and other research findings have led to the discovery that even a limited amount of cognitive exercise can lead to significant and long-lasting improvements in the daily lives of elderly people.

The surge in the nation's elderly population has increased the need for basic and applied research on aging. While it was once thought that neural structures were immutable past a certain age, basic behavioral research has demonstrated surprising levels of plasticity in the adult brain. Walsh and his colleagues¹ discovered differences in the volume of rats' brains depending on whether their environment was complex or isolated. These results refute the idea that brain structures are innately unchangeable and raise the possibility of using the environment to change cognitive functioning. Additional animal behavior research has shown that cognitive learning tasks improve learning behavior in adult rats, demonstrating that neural functioning can be altered by mentally stimulating tasks.² These insights into the workings of the adult brain have led researchers to develop new methods of reversing cognitive decline. NIH researchers recently developed the first controlled trial, called Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE), to explore long-term impacts of cognitive exercise on older individuals. Prior ACTIVE trials had shown specific short term cognitive improvements in each of several areas (memory, reasoning, and speed of processing). The most recent ACTIVE trial examined the long-term impacts of this kind of training, finding that even relatively brief training improves cognitive task completion for, remarkably, up to five years. Additionally, participants who received the cognitive training reported less difficulty with daily activities, further highlighting the importance of cognitive exercise in the maintenance of overall health.³

¹ Walsh, R.N., Budtz-Olsen, O.E., Torok, A., & Cummins, R.A. (1971). Environmentally induced changes in the dimensions of the rat cerebrum. *Developmental Psychobiology*, 4(2), 115-122.

² Gould, E., Beylin, A., Tanapat, P., Reeves, A., & Shors, T.J. (1999). Learning enhances adult neurogenesis in the hippocampal formation. *Nature Neuroscience*, 2, 260-265.

³ Willis, S.L., Tennstedt, S.L., Marsiske, M., et al. (2006). Long-term effects of cognitive training on everyday functional outcomes in older adults. *Journal of the American Medical Association*, 296(23), 2805-2814.

Overeating is Linked to Social Factors in Obesity

Basic behavioral research into the ways environmental factors influence eating patterns shows that social factors often play a larger role in eating behavior than actual hunger. Based on this finding, researchers have explored the social components of the nation's overwhelming obesity problem and are paving the way for a new clinical approach to obesity.

With two-thirds of the nation now considered overweight or obese, many scientists are devoted to understanding the genetic and behavioral roots of this problem. The surge in research on eating and obesity has led to the discovery of a person-to-person connection in the spread of obesity. Basic behavioral research conducted by Stalling and Friedman¹ examined how people's eating patterns were affected by cues other than hunger, and found that social cues significantly affected how much and how fast people eat. Later research twins raised in different environments found that social and environmental factors clearly influenced weight beyond the effects of genes.² Most recently, Christakis and Fowler completed a 32-year longitudinal study evaluating the Body Mass Indexes of an interconnected social network of over 12,000 people in order to examine whether weight gain in one person was related to that of those around him or her.³ They found that distinct groups of obese people formed most prominently when individuals were linked by close friendship, and not by genetics. If a person has a friend who becomes obese, his/her chances of becoming obese increases dramatically. These demonstrations of the impacts of social factors on obesity point to important new directions for public health approaches to and clinical treatments for obesity.

¹ Stalling, R.B. & Friedman, L. (1981). External social cues and obesity: The influence of others' food evaluations on eating. *Journal of Obesity & Weight Regulation*, 1(2), 111-118.

² Stunkard, A.J., Harris, J.R., Pedersen, N.L., & McClearn, G.E. (1990). The body mass index of twins who have been reared apart. *New England Journal of Medicine*, 322, 1483-1487.

³ Christakis, N.A. & Fowler, J.H. (2007). The spread of obesity in a large social network over 32 years. *New England Journal of Medicine*, 357(4), 370-379.

Neurobehavioral Therapy: A New Frontier in Treating Depression

Basic behavioral research, capitalizing on advancements in neuroscience, has uncovered a link between symptoms of major depression and specific areas of brain activity. Using this knowledge as a foundation, researchers are developing complementary therapies combining behavioral and neurologic methods to improve treatments for severe depression.

Innovative, scientifically-based treatments for depression are in increasingly high demand as many severely depressed patients do not respond well to traditional pharmacological and psychological treatments. Basic behavioral science research is providing the foundation needed to link the observable symptoms of depression to its biological bases, enabling scientists to understand the disorder more completely. Neurobehavioral therapy, one of the most recent advancements in the clinical approach to depression, combines aspects of neuroscience and cognitive behavioral therapy (CBT) to create a systematic behavioral intervention targeting the specific brain regions affected by depression. This therapy stems from years of behavioral research in conjunction with neuroscience applications examining biological links to behavior. For example, basic research has demonstrated that people with depressive symptoms also tend to have decreased functioning in the prefrontal cortex, a brain region involved in self-regulation and personality expression.¹ Building upon this and other neuroscience-based theories, Siegle and his colleagues have developed Cognitive Control Training+, which is a neurobehavioral intervention comprised of behavioral tasks designed to increase prefrontal cortex functioning in severely depressed patients.² Siegle has found that Cognitive Control Training, when combined with medication and psychotherapy, produces a significantly greater improvement in depressive symptoms and neural function than do the traditional methods alone. These preliminary results provide a solid foundation for further research into how psychopathology is related to particular aspects of brain functioning and to innovative neurobehavioral treatments that are based on these relationships.

¹ Baxter, L.R., Schwartz, J.M., Phelps, M.E., Mazziotta, J.C., et al. (1989). Reduction of prefrontal cortex glucose metabolism common to three types of depression. *Archives of General Psychiatry*, 46(3), 243-250.

² Siegle, G.J., Ghinassi, F., & Thase, M.E. (2007). Neurobehavioral therapies in the 21st century: Summary of an emerging field and an extended example of cognitive control training for depression. *Cognitive Therapy and Research*, 31(2), 235-262.

Eyewitness Protection: Legal Reforms to Decrease Unjust Convictions

Basic behavioral research on memory recall has revealed that even our clearest memories may not be as accurate as we would like to think. This information is enabling the implementation of legislative reform in judicial proceedings, many of which rely on eyewitness testimony as evidence.

In 2003, Calvin Willis of Louisiana was released from prison after serving time for a rape he was convicted of in 1982. DNA testing conducted in 1998 proved that he could not have been the perpetrator. Due to eyewitness misidentification, Willis had served 21 years for a crime he did not commit. Cases like Willis are unnecessarily common: It has been recently shown that eyewitness misidentification is the single greatest cause of wrongful convictions around the world, accounting for 75% of cases overturned by DNA testing¹. Legislators have been responding to these astonishing numbers by applying reforms to key judicial procedures in order to reduce the likelihood of wrongful conviction². Though human error can never be fully eradicated, systematic reforms can strengthen judicial fairness by improving policies on jury instruction, witness questioning, and police information. Much of what we now know about the potential for inaccuracy in eyewitness testimony stems from basic behavioral research on the malleability of memory and the potential for misremembering. Though legal experts have been questioning the accuracy of eyewitness testimony since the early 1900s, it wasn't until recently that scientists began to see true behavioral evidence of people's certainty of events that never transpired or people they never truly saw. In 1975, Elizabeth Loftus and Guido Zanni conducted experiments on eyewitness testimony, which uncovered that something as simple as the wording of a question can cause memory reconstruction, so that people may remember events that never really occurred³. More recently, Loftus demonstrated that interfering with a person's narration of an experience can inhibit the ability to provide open and accurate recollections⁴. These behavioral studies, along with the many others, have brought scientific clarity to a question that people unknowingly encounter every day: Am I remembering correctly? Additionally, thanks to this field of behavioral research, legal procedures eventually will be altered to the point at which systematic eyewitness error no longer occurs.

¹ Eyewitness misidentification. (2008). *The Innocence Project*. Retrieved from <http://www.innocenceproject.org/understand/Eyewitness-Misidentification.php>

² Tulsy, F.N. (2006). Panel backs altering use of eyewitnesses. *Mercury News*. Retrieved from http://www.mercurynews.com/taintedtrials/ci_5168936?nclick_check=1&forced=true

³ Loftus, E.F. and Zanni, G. (1975). Eyewitness testimony: The influence of the wording of a question. *Bulletin of the Psychonomic Society*, 5(1), 86-88.

⁴ Wright, D.B., Loftus, E.F., & Hall, M. (2001). Now you see it, now you don't: Inhibiting recall and recognition of scenes. *Applied Cognitive Psychology*, 15(5), 471-482.

New Test to Predict Risk of Major Depression

Extensive research on the behavioral underpinnings of major depression has led to advancements in many aspects of treatment and prevention of the disorder. Researchers at the University College of London have taken this research to new levels with a new online test, which identifies individuals at risk for developing depression.

Depression is one of the most common psychological disorders worldwide. Through behavioral and medical research, scientists have developed multiple methods of treating the disorder, from medications to various types of counseling to combinations of the two. However, relatively less research has been conducted on the prediction and subsequent prevention of depression. A recent study at the University College of London headed by Professors Michael King and Irwin Nazareth, has made great leaps in filling this gap in research. Their risk algorithm, which can be found at <http://www.ucl.ac.uk/predict-depression/>, was modeled on risk indices for heart disease. These indices show risk as a percentage estimate over a period of time. The study tested the algorithm on 6,000 people in six European countries, as well as 3,000 people in Chile¹. It was shown to be highly accurate in predicting depression, and was published in the Archives of General Psychiatry². Many of the questions focused on behaviors that correlated with depression. Basic behavioral research has provided these professors a great deal of information on the types of behaviors associated with the onset of depression.

In 1986, Brown et al. examined the social and behavioral factors influencing the onset and course of depression in over 300 single mothers, finding low self-esteem and severe life events to be particularly important³. The discovery of these vulnerabilities has led to further examination of this connection. In 1991, Patten revisited these vulnerability factors and investigated their predictive value for depression. He found that of these factors (which include unemployment and early maternal loss), the lack of a confiding relationship was the most predictive of future onset of depression⁴. The establishment of the predictive value of behavioral components of depression has allowed researchers to focus on detecting warning signs and develop the testing algorithm mentioned above. With further behavioral research into similar mechanisms, physicians may be able to diagnose individuals before the onset of depression, hastening their recovery and lessening the numbers of those who suffer from depression around the world.

¹New test for depression. (2008). *Medical News Today*, 02 December. Retrieved 11 December, 2008. <http://www.medicalnewstoday.com/articles/131477.php>

²King, M. et al. (2008). Development and validation of an international risk prediction algorithm for episodes of major depression in general practice attendees. *Arch Gen Psychiatry*, 65(12), 1368-1376.

³Brown, G.W., Bifulco, A., Harris, T., & Bridge, L. (1986). Life stress, chronic subclinical symptoms and vulnerability to clinical depression. *Journal of Affective Disorders*, 11(1), 1-19.

⁴Patten, Scott B. (1991). Are the Brown and Harris vulnerability factors risk factors for depression? *Psychiatric Journal of the University of Ottawa*, 16(5), 267-271.