Cognitive and Emotional Health: The Healthy Brain Workshop

Jointly sponsored by:
National Institute of Neurological Disorders and Stroke (NINDS)
National Institute of Mental Health (NIMH)
National Institute of Aging (NIA)

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Table of Contents

I. Introduction

The National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Mental Health (NIMH), and the National Institute on Aging (NIA) are embarking on a major new initiative to understand issues related to cognitive and emotional health in U.S. adult populations – particularly how cognitive and emotional/mental health can be maintained and enhanced as people grow older. The project will assess the state of epidemiological research on demographic, social, and biologic determinants of cognitive and emotional health in aging populations, and the pathways by which cognitive and emotional health may reciprocally influence each other. It will seek to answer questions such as: Can individuals optimize their cognitive function and emotional health? How do psychosocial variables influence cognitive outcomes? And, can new technology (e.g. imaging) be used to identify those with the "healthiest" brains?

As part of this initiative, the sponsoring institutes held a workshop with experts in large-scale epidemiological studies of cognitive and emotional functioning on July 9-10, 2001. The purpose of the workshop was to evaluate the state of existing knowledge, the potential value of secondary analyses of existing data, the need for further instrument development to facilitate future studies, and potential designs of any future large studies.

II. Background

The workshop included three major sections: 1) overview presentations on cognitive health, emotional health, and methodological issues, 2) three breakout sessions with experts in the areas of emotional health, cognitive health, and demographic and social

factors, and 3) three interdisciplinary breakout sessions. Each of the six breakout groups generated a list of recommendations (see appendix). Recommendations from the breakout groups were used to generate a summary list of recommendations for the three sponsoring institutes.

Prior to the workshop, participants received a bibliography of research literature concerning measures that have been (or could be) used in epidemiologic research for each of four domains: (1) cognitive health, (2) emotional/mental health, (3) demographic/social factors, and (4) biomedical/physiologic factors.

III. Discussion

Introductory speakers at the workshop noted the importance of this research area to the three sponsoring institutes and stated several overriding goals for the event. These goals included: identifying key concepts; evaluating strengths, weaknesses, and gaps in existing resources and research; discussing hypothesized pathways and potential methods of measurement; discussing a potential design for a new population-based study, and providing recommendations for future directions. They noted that prior work has focused largely on avoiding and predicting disease, rather than maximizing function.

Concepts and Predictors of Cognitive Health

Many studies related to cognitive health have been reported. However, one of the key questions is what the definition of cognitive health should be. It should not be defined simply as the absence of diseases such as Alzheimer's disease. While the study of cognitive health cannot ignore dementia, the definition of cognitive health should be multidimensional and focus on successful aging instead of normal aging. Previously identified subfactors for cognitive health include fluid intelligence, crystallized intelligence, general memory and learning, broad visual perception, broad auditory perception, broad retrieval ability, broad cognitive speediness, and processing speed. Some of these decline more with age than others.

There are a variety of conceptual and methodological issues important for research on cognitive health. Measuring cognitive change in studies is typically difficult due to poor reliability and other issues. Difference scores and residualized gain scores can lead to very different conclusions from the same data. Other approaches include latent growth models and dichotomized incident cases. However, there is no consensus about how best to measure change, and studies to date have used such a variety of methods that it is almost impossible to do a meta-analysis of the results. Small effect sizes also present a challenge, as the variation between usual and successful aging is much smaller than the variation between normal aging and dementia. Research in this area needs very large sample sizes and long follow-ups to maximize the change that is observed. Tools from cognitive neuroscience, such as functional MRI (fMRI), may also be useful.

Cognitive factors significant to the elderly population should be considered when determining what measures to use. These factors include social connectedness; an ongoing sense of purpose; the ability to carry out activities of daily living (which often require a capacity for good judgment); and other factors that affect functional recovery, such as the ability to return to work. The physiological ability to express emotions and the ability to recognize facial expressions are examples of measurable factors that affect these abilities. It also is important to include sensory and motor measures since changes in central pathways for vision and hearing, and in motor functioning, can affect cognitive function. Cognitive researchers may be able to adapt tests developed for other purposes to measure these factors. It is clear that conditions in the body affect the brain, and that conditions in the brain affect the body, and this interrelationship should be factored into study designs.

Other important issues for consideration include acculturation and cultural orientation, since associated vernacular and style issues can yield misleading results. Measuring low-level, relatively universal tasks such as handling money and taking medications may help to alleviate some cultural variability between studies. However, it is very difficult to find universally applicable tests that cover the upper range of cognitive functioning. Another important question in cognitive studies is at what age the studies should begin. Effects of various factors on cognition may begin very early in life. However, the differences may be too small to measure until the study subjects have reached adulthood.

It is important to find a way to distinguish cognitive aging from Alzheimer's disease. The known risk factors for dementia are also risk factors for cognitive decline. Hypothetically, there may be factors that affect normal successful aging but not the risk of dementia. It is crucial to have long follow-up times in studies, in order to better distinguish people who are developing Alzheimer's disease (before their symptoms become apparent) from those who will not develop this disease. However, a problem with long follow-up times when studying the elderly population is that those who do not score as well on cognitive measures often tend to die sooner than others in the study population. This can confound longitudinal studies.

Studies of cognitive health have looked at the effects of demographic and social factors such as socioeconomic status, education, social connectedness, occupational environment, race and ethnicity; emotional health factors such as depression and self-efficacy; and a variety of biomedical/physical factors such as use of estrogen, use of non-steroidal anti-inflammatory drugs (NSAIDS), hypertension, homocysteine, cholesterol, "syndrome X", cortisol, DHEA-S, brain structure, physical activity, antioxidants and insulin resistance. Studies have also examined the effect of "allostatic load", or the cumulative physiological burden of attempts to respond to life's demands, on cognitive health. Many other potential factors, such as acculturation and assimilation, religion and spirituality, discrimination, and optimism and self-esteem, have not been studied much in relation to cognitive health. Education, ApoE genotype, use of estrogen, specific MRI changes, and hypertension look promising as factors that influence cognitive health. However, these factors are also implicated in dementia, and researchers still do not have enough evidence for any factor to be certain any of them are important. Collaborative re-

analysis of longitudinal data from existing studies may help to fill some of the gaps. Many results from studies are never reported because of inconclusive or negative results. It is also important to carefully define the goals of future studies, and to include data-sharing plans in the study designs to ensure that the data will eventually be available to the research community.

There are three possible mechanisms by which emotional health may interact with cognitive health. These include glucocorticoid secretion (linked to stress); brain-derived neurotrophic factor (BDNF) regulation of synaptic activity (also linked to stress), and cerebrovascular disease, a known cause of cognitive impairment which also may lead to a syndrome of "vascular depression" due to subcortical and frontal brain lesions. Demographic and social factors may affect all three of these mechanisms. Curiously, theories of emotion and cognition have all focused on negative emotions – the effects of positive emotions seem to have been completely ignored as a possible factor in cognitive health.

Concepts and Predictors of Emotional Health

Participants noted that a true consideration of emotional health separately from cognitive health is impossible because emotion is always involved in cognitive processes. Therefore, the two concepts are separated only for heuristic purposes of discussion. Emotional health is generally considered a component of well-being and quality of life. It can be considered as a predictor, as an outcome, or as a mediator for other types of health. However, emotional and mental health are very important outcomes by themselves. An understanding of emotional health in the population and how it affects other aspects of health will likely require an integrative approach that includes the fields of psychology, epidemiology, sociology, and other social, biomedical, and behavioral sciences. Such linking of facts and fact-based theories across disciplines to create a common groundwork for explanation is known as consilience. Bringing together perspectives from different areas often leads to new and exciting results.

What is emotional health?
Emotional health is not simply the lack of emotional dysregulation, anxiety, depression, anger, hostility, type A behavior, or psychiatric disorders, although in general these factors are negatively correlated with emotional health. Also, emotional health is not just the absence of negative emotions - some negative emotions can be constructive (for example, fear can motivate people to get out of dangerous situations), and low levels of anxiety/other problems don't necessarily mean happiness. Under normal circumstances, emotions are functionally appropriate processes that motivate individuals to respond to the environment, communicate social information, and allow adaptive flexibility. However, emotions may have dysfunctional consequences when the system is taxed or if they are chronically evoked. Some people may try to cope with emotion by smoking, drinking, or other negative behaviors. Many people believe emotions run on a continuum from normal to pathological. Any emotion, positive or negative, in the extreme is probably detrimental. This suggests that a definition of emotional health should say

something about the ability of the emotional system to help individuals regulate and negotiate their environment in an adaptive way. Emotional health may equate to emotion regulation and/or emotional intelligence. Emotion regulation is defined as individuals influencing which emotions they have, when they have them, and how much they experience and express those emotions. Emotional intelligence is the ability to perceive and express emotions, understand affect-laden information, use emotional knowledge, and regulate conditions to foster intellectual growth and well-being.

The fields of psychology and epidemiology have different focuses concerning emotional health. Psychologists generally focus on theoretical perspectives for how emotional dysregulation occurs, whereas epidemiologists tend to focus on the prevalence or incidence of emotional problems in the population. Psychosocial factors such as mastery and self-efficacy, self-esteem, and optimism are known to be related to emotions and are probably related to emotional health as well. Researchers also need to understand the biology that underlies positive and negative emotions.

One important question raised at the workshop is whether people need emotional exercise. The "use it or lose it" hypothesis is commonly applied to cognitive aging, but not to emotional aging, and it is not clear why that is the case.

How can emotional health be measured?
Most currently available measures for emotional health pertain to emotional dysregulation. For example, researchers have developed structured interviews for mood and anxiety disorders that can be used to assess mental health in a population. These measures have been used in a number of large-scale epidemiological studies. Non-clinical levels of emotional dysregulation, such as anxiety and depression, are usually diagnosed through self-report measures. These measures are well-characterized, but do not address overall emotional health, only aspects of it. Researchers need to define the utility of measures of dysfunction in measuring emotional health. Measures related to positive emotional health are also primarily self-reports and include measures for emotional vitality, optimism, and disclosure. Measures of emotional regulation and emotional intelligence are new and untried in an epidemiological health context.

Challenges in developing measures for emotional health include the need for explicit conceptualization and operationalization. Researchers need to decide whether to tightly constrain the measures to the emotional domain or to include other positive psychological factors such as control and self-efficacy. Another question is whether measures of specific emotions such as happiness are more appropriate than measures of generalized positive or negative affect. Researchers need to devise an approach practical for large-scale studies. In addition, they need to examine Emotional Health in context – some affects are short-term (i.e. anger) while others are long-term (i.e. hostility). These affective processes have been lumped together in most conventional studies. Temporary states of a particular emotion may be very different from the chronic experience of particular moods. Temperament/personality, social resources, social patterning of emotions, and other individual factors may influence affective states. Factors such as genes and cultural norms also may influence which emotions are displayed. More

persisting behavioral dispositions such as temperament and personality must be distinguished from the individual's state at a particular point in time.

Other important questions to be addressed include how frequently different emotional traits need to be measured over time and how culturally sensitive different measures are. Some existing measures have been tested in different cultures, but others have not and may not be as sensitive across cultures as they are in one population. Another challenge is to integrate efforts across disciplines. Researchers should re-examine what is known about emotion and expand the framework to obtain a more comprehensive picture.

Emotional health affects cognitive and physiological health in both direct and indirect ways. Direct effects include physiological and biological effects, such as the effects of emotion on immune function. Indirect effects include emotion's influence in behavioral changes, coping resources, and interpersonal relationships, all of which may be linked to cognitive function. One important question when studying proposed effects of emotion is what is the direction of effect – for example, depression is linked to cognitive impairment in the elderly, but it may be that the cognitive loss is causing the depression instead of the other way around. Research has shown that negative emotions such as anger and anxiety increase the risk for poor health outcomes such as cardiovascular disease, while optimism reduces the risk of coronary heart disease. Factors related to positive emotions, such as self-efficacy and control beliefs, are associated with higher levels of cognitive function, while cortisol levels (linked to stress) have been linked to impaired memory.

As with cognitive health, the epidemiology of emotional health in the past has largely addressed rates of mortality and morbidity in humans, rather than rates of emotional wellness. Researchers need to overcome any barriers that may prevent shifting the focus to emotional health. Other barriers to progress in this area include the typically disease-focused structure of funding opportunities and the lack of clear existing measures of emotional health that would help with secondary data analyses. Researchers also need to integrate work across disciplines and consider complex models that allow consideration of emotional health not only as an outcome or a predictor of other types of health but also as a potential mediator or moderator. Finally, researchers need to be sure to relate the abstract concepts of emotion and cognition and behavior to the underlying neurobiology.

Methodologic Issues

One of the challenges in understanding cognitive and emotional health is to develop mathematical/statistical methods to longitudinally assess health in these domains. There are issues with integration across psychosocial and biological domains and issues with the integration of evidence over time.

What is positive health and how can it be operationalized on a psychosocial and biological level?
Positive health is defined as complete well-being, not just the absence of infirmity. Most reports have dealt with disease and infirmity and relatively little has been done to

operationalize positive health. One proposed set of criteria for positive health includes four key criteria: leading a life of purpose, having quality connections to other, possessing self-regard, and experiencing mastery over one's surroundings. These criteria have been operationalized in a set of well-being scales that have been used in many surveys. However, these are all psychosocial criteria and researchers also need to understand the biological foundations of these factors. Ideally, the biological parameters and the psychosocial parameters would be measured simultaneously and in a prospective way. However, such data does not currently exist.

What are the pathways to positive health?
One way to begin to understand the biological factors underlying cognitive and emotional health is to review the literature from affective neuroscience. One factor that appears to be correlated with positive and negative emotions is the amount of "cerebral activation asymmetry", or left/right asymmetry in the frontal cortex as seen on an electroencephalogram (EEG). The asymmetry seems to be linked to a person's manner of responding to situations. People who are left-side-activated in the absence of stimulation or other mental activity (resting asymmetry) tend to have positive affect in response to various emotional challenges. Right-side-activated adults tend to have negative affect in response to emotional challenges. This asymmetry seems to be stable after age 18. Individuals who are left-side-activated at baseline tend to score higher than others on the four criteria for well-being described above. Results from the Wisconsin Longitudinal Study showed that people with mostly negative experiences but good mental health tended to be strongly left-side activated. People who had early positive experiences but many problems in adult life tended to be more right-side-activated.

Other biological parameters related to cognitive and emotional health that may be worth measuring in future studies include factors associated with allostatic load, such as cortisol as a measure of HPA Axis Activity. Other biomarkers that might be related to positive health and overall well-being include cholesterol levels, blood pressure, which is a biomarker for cardiovascular health; oxytocin, serotonin, and dopaminergic neurotransmitters. These biomarkers have been compared to the psychosocial criteria for well-being and show a correlation. However, there are gender differences with some factors. For example, increases in cortisol level correlate with decreases in cognitive performance in women, but create virtually no change in men. These gender differences need explanation.

Methods for analyzing complex survey data
One problem in studying how different variables relate to positive health and life experiences is how to make sense of large amounts of aggregate data from survey analyses of multiple individuals. There may be a tremendous number of variables in the data set. One strategy to analyze this type of data is:

1. Develop a narrative life history for each of a small number of the respondents, perhaps 25 or 30 people. Ideally there would be more than one person doing the narratives to eliminate a sole investigator's personal biases.
2. Look for commonalities or conjunctions of conditions across the histories, and strong sources of differentiation.
3. Go back to the full sample and score the survey results on specific indicators identified in the small sample, such as mental health, physical health, family background, early life experiences, etc. Scoring can be broken into different numerical values, for example, positive experiences = +2, somewhat positive = +1, neutral = 0, somewhat negative = -1, and very negative = -2.

Another method for analyzing complex data, after the initial steps of producing the narratives and aggregating to obtain more abstract levels of variables, is recursive partitioning, a non-linear approach that groups the results into ranges of variables. With this method, researchers must decide what type of outcome they are trying to predict, such as mortality, cognitive function, or etc. The next step is to define cutpoints for different variables that correspond to high, moderate, or low risk for that outcome. Sometimes the data points are intervals.

A third method involves someone writing up a narrative for each individual, then five raters weight the narratives on different dimensions that they are interested in. The interviewers then suggest descriptions for the situations from each narrative. This generates a list of terms for analyzing the data. This method has been very successful in predicting depression and some physical outcomes.

A fourth method is graded membership analysis, which asks where each set of data sits in terms of ideal profiles of conditions, and classifies everyone in terms of the degree to which they share conditions. However, this method may lose much of the nuance in the data.

IV. Conclusions/recommendations

Each of the six breakout groups developed lists of recommendations based on specific discussion questions. The discussion questions and recommendations from these groups are presented in the Appendix to this report. Overall summary recommendations and conclusions from the two-day session were as follows:

1. Review of existing data
- Complete the bibliography
- Complete the catalogue of NIH-supported studies and explore the feasibility of adding information about non-NIH-supported and international studies. This information should be available to all investigators through a web site.

2. Determine the feasibility of obtaining similar information from all types of clinical trials, prevention trials, and population studies.

3. Create a panel to conduct a critical analysis of existing studies, with a goal of identifying opportunities for secondary analysis, add-on studies, and identifying weaknesses and gaps in existing data and proposing additional focused multisite analyses.

4. Encourage formation of a consortium of studies for collaborative analysis and reanalysis of existing data.

5. Create trans-institute RFA focused on cognitive and psychosocial health in adults. Psychosocial health must include the full range of functioning, including the high end.