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The University of Chicago

Affiliate Lab Interview

Talma Hendler

Talma Hendler, M.D., Ph.D., an affiliate of the CCSN, is the founding director of the Functional Brain Center at Tel Aviv Sourasky Medical Center and associate professor of psychiatry and psychology at Tel-Aviv University. Hendler's work focuses on brain mechanisms mediating the dynamic nature of emotional experience and its regulation under stress and trauma.

ABOVE: The Sourasky Medical Center and Functional Brain Center in Tel-Aviv, Israel.

A LARGE PART OF THE UNIQUE EMOTIONAL EXPERIENCE EXISTS IN THE PATTERNS OF TRANSITION FROM ONE STATE TO ANOTHER.

TALMA HENDLER

THIS METHOD PROVIDES NEURAL FINGERPRINTS OF OUR SUBJECTIVE EMOTIONAL EXPERIENCE.

TALMA HENDLER

What is the focus of your research?

My work focuses on emotion processing in the brain: how we come to be aware of feelings, how life events change our emotional experience, and what constitutes our one-of-a-kind subjective experience. With regard to methodology, we utilize complementary methods to measure brain activity including functional magnetic resonance imaging (fMRI), diffusion tensor imaging (DTI) and electroencephalography (EEG). Together, these techniques provide information about the structure and function of the living brain with superb spatial and temporal resolutions. Where things are happening and how they are happening over time are both important in understanding how the brain works.

This is especially critical to emotion, because emotions are dynamic. A large part of the unique emotional experience exists in the patterns of transition from one state to another, and how an individual comes to a certain state of feeling. In the lab, we now have ways of measuring this change in emotional experience by observing how different parts of the brain connect during this process as well as by recording verbal reflections of individuals about their experiences.

How do you investigate the dynamic nature of emotions in individuals?

In one of our current research projects, we ask participants to watch different kinds of sad movies, and observe how their brains respond as the story unfolds. For example, one film may be a maternal melodrama, while another film might depict sadness and loss during war. When participants are asked to rate these films on emotional sadness, independent of one another, they rate them as similarly sad. However, this measurement does not reflect the complexity of their experience, for when we look at the brain, we see very different response patterns for different kinds of sad movies. We expect we will see differences in their verbal reflections and their autonomic responsivity in heart rate.

Over the course of the different movie sequences we see activity in many different areas of the brain: the limbic system, a relatively primitive part of the brain which serves as an emotional hub; the lateral prefrontal cortex, which mediates attention allocation and executive function; and the medial prefrontal cortex, which is involved in self awareness as well as empathy. We look for connections within and between these three clusters of regions during the process of watching sad video excerpts. Using fMRI technology to look at brain activity, we can see the number and strength of connections over time within these clusters, as well as the correlations of the activity among these clusters. While watching the films, we see the limbic system and medial prefrontal cortex are highly active and internally connected, and these connections correlate with the emotional rating of sadness. In addition, at times we see sustained connection between the limbic system and the prefrontal cortex. These high points seem to correspond to extreme dramatic moments in the films in which two characters hug or closely relate to each other. Intriguingly, the highs and lows of these neural connections vary among different movies. When sadness was accompanied by mercy and sympathy, these connections were mostly high. When sadness was accompanied by horror and anger, these connections were low.

What are some potential benefits of this research?

Altogether, our new method allows researchers to trace the dynamism of emotional processing in the brain, and portray the unique

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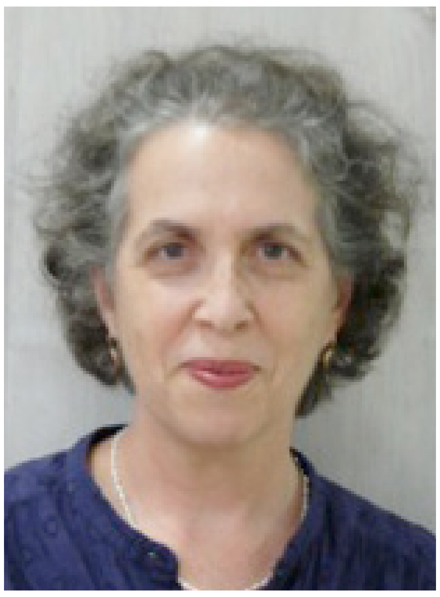

ABOVE: Talma Hendler, founding director of the Functional Brain Center at Tel Aviv Sourasky Medical Center and associate professor of psychiatry and psychology at Tel-Aviv University.

patterns of response at the level of an individual brain. This provides neural fingerprints of our subjective emotional experience and can be used in individually tailored treatments for specific psychiatric disorders.

For example, when patients with schizophrenia view a horror movie, we see less connectivity within and between these brain clusters. The schizophrenic participants' reactions are less pronounced, and modulate less with the action of the film, possibly reflecting on negative symptoms of schizophrenia (e.g., social withdrawal and affective bluntness).

I believe that the enhanced connections between and within brain regions relate to the simulation of other's feelings, while the decreased connections relate to avoidance of feeling, similar to a state of disassociation. This function could be very protective while facing an acute life threatening situation that calls for an immediate and appropriate reaction. However, if this disassociation persists following the acute event, like in post-traumatic stress disorder (PTSD), a person may not be able to emotionally process and work through a trauma, and suffer from alexethemia (difficulty to experience emotions).

Why is it valuable to study brain activity spatially and over time?

Using fMRI technology to simply observe detailed distribution of brain activity has yielded great insights, and since the beginning of the 1990s, there has been an ongoing explosion of information provided by this measurement. FMRI technology coupled with structural measures of connections between brain regions allows neuroscientists to see the working brain, live, for the first time. It is likely that there are important structural differences between individual brains, such as the volume of different brain structures and fiber connectivity, which may be important for understanding the subjective emotional experience. But without an understanding of the spatial-temporal characteristics of brain activity through the combined use of fMRI and EEG, we could not probe the dynamic nature of emotional response in the brain. The most exciting part of this work is examining how the brain works and changes over time: how it responds to stimuli in the world, how it responds to interaction with people, and how it responds to certain life events which, in turn, may modify how the brain itself works.

We are learning that how well an individual's brain processes feelings in response to external stimuli may determine their experience of emotions and their vulnerability to develop psychopathology.

For example, we recently conducted a large-scale fMRI study in which we recorded brain activity for military personnel before they entered active duty and were exposed to intense stress. Using this baseline, we were able to determine which soldiers were more prone to exhibit combat-related stress symptoms after exposure to active duty. These symptoms can trigger PTSD or major depression. These early biological markers could be used to diagnose and treat these individuals immediately following their exposure to situational trauma and therefore prevent or ameliorate their long-term suffering.

In looking at the amygdala, we could predict an individual's potential to develop PTSD symptoms. Other brain activity in the hippocampus, a memory related region, was modified by the stress giving indications of brain plasticity. These research findings can inform methods of therapeutic treatment for stress and trauma .

What is your ultimate goal for this research?

Our aim is to eventually be able to use these types of measurements to teach an individual how to better regulate his or her brain. We believe the flexibility of connectivity is very critical to a person's ability to regulate his or her emotional state and avoid extreme, harmful reactions. This could be done through training or a conditioning process that would teach a person how to modulate the working brain.

For example, in another experiment currently underway, we first ask participants in a scanner to try to relax. We then measure activity in brain regions related to emotional processing, and inform the participant of the times when he or she is able to increase or decrease this activity. We call this procedure 'neurofeeback'. Over time, people can come back to the technique they were employing to modulate activity in this region, and they can use that knowledge to access specific emotional brain states with greater ease and speed.This could be very valuable, especially if we learn that a certain region or a system is critical to processing disturbing emotional situations, and is related to individual vulnerability to develop psychopathology related to trauma, or drug consumption. For many years, researchers have been using biofeedback techniques to measure and report heart rate, skin conductance, and blood pressure to help people in somatic therapeutic settings. This is like that work, except that we are honing in on very precise brain regions using very sophisticated imaging technology. It is not science fiction anymore.

What are future directions for your research?

Neuroscience is at a turning point. It gives us wonderful tools we can use to describe how the brain works to a greater degree than ever before, and this may help people live better lives. But we are also aware, and concerned, that people looking to benefit commercially will exploit this new knowledge. Another concern lies in the interpretation of this new information. We must be very careful in our research- go step-by-step, collect large amounts of data and analyze the results in a most robust way. It's nice to dream about the possibilities of a full understanding of the brain, but we also have to work hard to avoid short-cuts and misinterpreting this new information.

Right now, we are looking at ways to narrow the dimensions of our examination, very much like the early days of genetics research, when researchers started to build bioinformatics by focusing on increasingly small pieces and looking at the sequences and patterns in the data. In neuroscience, people are now looking toward neuroinformatics. When this knowledge crystallizes, neuroscience will move into a new era, where brain imaging will focus on the interactions between clusters and systems, and not just on active or inactive regions. The story is probably about how the dynamics work at a global and local neural level. To tell that story, we need to develop new computational approaches as well as to continue and improve the integration between measures obtained all the way from a single neuron activity to whole brain networking.

WE ARE HONING IN ON VERY PRECISE BRAIN REGIONS USING VERY SOPHISTICATED TECHNOLOGY.

TALMA HENDLER

Another future pursuit will be developing an understanding of the spontaneous activity of the brain. In relation to imaging, neuroscientists have mostly been concerned with the way the brain responds to stimuli. In the last few years, it has become increasingly clear that the brain is working the whole time, not just when stimuli are presented, and this spontaneous activation varies by individual inborn tendency and prior experiences, sometimes even more than when stimuli are presented. For brain training, it may be beneficial to focus on spontaneous activity. For example, before a test, if someone could create a certain mode of spontaneous activity closely connecting the prefrontal cortex to the parietal lobe, then that person may be able to perform better by more effectively recruiting this particular connection.

This understanding of the brain deeply connects to broader elements of the human experience- free will, consciousness, morality, and social relationships. The next phase of research will thus help us answer some very big questions of the mind. •

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