2022 James Wake Memorial Lecture



James Wake

I have learned through chaplaincy to honor the spiritual journey of each person, as it unfolds moment by moment, breath by breath, heartbeat by heartbeat.

Each person's journey is valid; each moment of the journey is sacred.

You are a person of goodness, unconditionally loved by God. I honor your journey; I honor you.





MARY-FRANCES O'CONNOR, PhD

Grieving BRAIN

The Surprising Science of How We Learn from Love and Loss

GRIEF AND GRIEVING THROUGH A MULTI-DISCIPLINARY LENS

MARY-FRANCES O'CONNOR, PHD

Associate Professor

Director Of The Grief, Loss, And Social Stress (GLASS) Lab

Psychology Department, University Of Arizona



THERE YOU ARE

"WHEN A LOVED ONE HAS BEEN WIPED OFF THE MAP, YET THE NEURONS KEEP FIRING DESPITE THEIR TARGET BEING ABSENT—THAT IS GRIEF."



TODAY'S TALK

- COGNITIVE NEUROSCIENCE AS A LENS ON GRIEF AND GRIEVING
- UNDERSTANDING GRIEF MEANS UNDERSTANDING LOVE AND BONDING
- GRIEVING IS A FORM OF LEARNING
- GRIEF IS DIFFERENT FROM GRIEVING (AND PROLONGED GRIEF)

UNDERSTANDING GRIEF MEANS UNDERSTANDING BONDING AND ATTACHMENT

PAIR BONDING IN VOLES

- Monogamous pair bonds in voles causes changes to the epigenetics in the nucleus accumbens
- Separation from the mate causes decreased oxytocin binding in this same brain region





Bosch et al, 2016

SPECIFIC NEURONS FIRE FOR REUNION WITH MATE

- Distinct ensembles of neurons in the nucleus accumbens are recruited during approach to their pair-bonded mate.
- The partner-approach neuronal ensemble increased in size following bond formation.
- The size of approach ensembles for partner predict bond strength.





Scribner et al, PNAS, 2020

HUMAN ATTACHMENT BONDS

- The brain uses dopamine, opioids, and oxytocin to teach us to stay with our loved ones
- Reward learning for attachment behavior uses these neurochemicals in specific basal ganglia regions, including nucleus accumbens





IFG/ alns

Paternal love

Wittfoth-Schardt et al, 2012



Romantic love Aron et al, 2005

BONDING IS ENCODED IN THE BRAIN

These discoveries shed light on how pair bonds may be encoded within the brain, what changes as bonds mature, and what must be updated after the death of a loved one.

FMRI STUDY OF GRIEF

•Human fMRI studies found activation in the nucleus accumbens in those with greater difficulty adjusting after the death of a loved one.

•The level of activation in the nucleus accumbens was correlated with the self-reported level of yearning for the deceased, and not correlated with time since death or other negative feelings.

O'Connor et al, Neuroimage, 2008





REWARD PROCESSING BRAIN NETWORK DYSFUNCTION IN LATE-LIFE GRIEF

- 65 bereaved older adults within 13 months post-loss.
- Those with higher grief showed higher ventral caudate connectivity in the medial prefrontal, orbitofrontal and subgenual cingulate cortices.
- Nucleus accumbens connectivity with the right insula/striatal cluster positively correlated with yearning (r=0.59, p<0.001).

Blair et al., Biological Psychiatry, 2022

NUCLEUS ACCUMBENS AND CAUDATE VOLUME ASSOCIATED WITH LOSS

- In 196 healthy young adults, structural MRI probed association between volume and loss across the life span.
- Loss (bereavement and breakup) was associated with larger right nucleus accumbens volumes in men.
- Bereavement loss was associated with increased caudate volumes irrespective of sex.



Acosta et al., J Neurosci Res. 2021

GRIEVING IS A FORM OF LEARNING

WHY DOES GRIEVING TAKE SO LONG?

FOR THE BRAIN, OUR LOVED ONE IS GONE AND EVERLASTING AT THE SAME TIME



TWO CONFLICTING STREAMS OF INFORMATION

Memory
of the death or funeral

 Attachment belief through bonding

O'Connor & Seeley, *Current Opinion in Psychology*, 2022

GRIEF IS DIFFERENT FROM GRIEVING

PROLONGED GRIEF DISORDER

- Grief never ends at a year, but grieving shows change over time
- At 1 year, trained clinicians can see that for some people, the intensity and frequency of grieving has not changed
- Research shows that psychotherapy can get them back on a healing trajectory



Djelantik, Robinaugh & Boelen, 2022

COMPLICATED GRIEF VS. PROLONGED GRIEF DISORDER

- Complicated grief only affects about 1 in 10 people who are bereaved.
- Prolonged grief disorder added to DSM 5 TR, following ICD-11.
- Complications analogy to healing a broken bone.



Fig. 1 Relationships between all grief, complicated grief and prolonged grief disorder in the Yale Bereavement Study (YBS) sample.

RUMINATION MAY INHIBIT LEARNING

- Rumination: repetitive and recurrent, self-focused negative thinking about past negative events and/or negative mood
- There are several forms of grief-related rumination, including would've/should've/could've thoughts
- Rumination as Avoidance Hypothesis (RAH) holds that rumination may serve to avoid painful aspects of the loss, thereby hampering adjustment to bereavement.
- In an eye-tracking study, bereaved high ruminators looked at photos of the deceased than low ruminators, demonstrating that avoidance may be an automatic process.

Eisma & Stroebe, Bereavement Care, 2017

GRIEF DURING RESTING STATE





Functional connectivity between default_{core} (IC27) and cingulo-opercular_{dACC} (IC26) network components

Seeley, Andrews-Hanna, Allen & O'Connor, Hum Brain Mapp, 2022

FUNCTIONAL CONNECTIVITY OF NETWORK COMPONENTS



- Each state represents a recurrent pattern of functional connectivity among selected network components (default_{retrospenial}, default_{Core}, cingulo-opercular_{dACC}, frontoparietal_R).
- On average, participants transitioned between states approximately eight times (SD = 3.4) over the course of the six-minute resting state scan.
- Participants with complicated grief spent more time in State 2 than the noncomplicated grief group.

Seeley, Andrews-Hanna, Allen & O'Connor, Hum Brain Mapp, 2022

THE QUESTION

If we take seriously the perspective of the brain, Then the question we ask those who are grieving might change. Perhaps instead of, "How are you doing?"… We might ask… "What has changed since your loss, what are you learning?"

THANK YOU

- National Institutes of Aging (NIA)
- DANA Foundation
- California Breast Cancer Program
- Retirement Research Foundation
- Institute for Mental Health Research

<u>Trainees</u> Austin Grinberg Brian Arizmendi Lindsey Knowles Mairead McConnell Saren Seeley Eva-Maria Stelzer Sebastian Karl Roman Palitsky Deanna Kaplan Christian Schultze-Florey Monica Fallon Da'Mere Wilson Jiah Yoo Sydney Friedman Colin Tidwell



Thank you for joining us.

In 1 – 2 days, you will receive an email

- brief program evaluation survey and certificate of attendance
- link to the Lecture recording

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