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CONCEPT
CONTINUING & PROFESSIONAL STUDIES

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Ketamine & Large-Scale Brain Networks

How Network-Level Changes Drive Therapeutic Effects

Sharon Niv, PhD

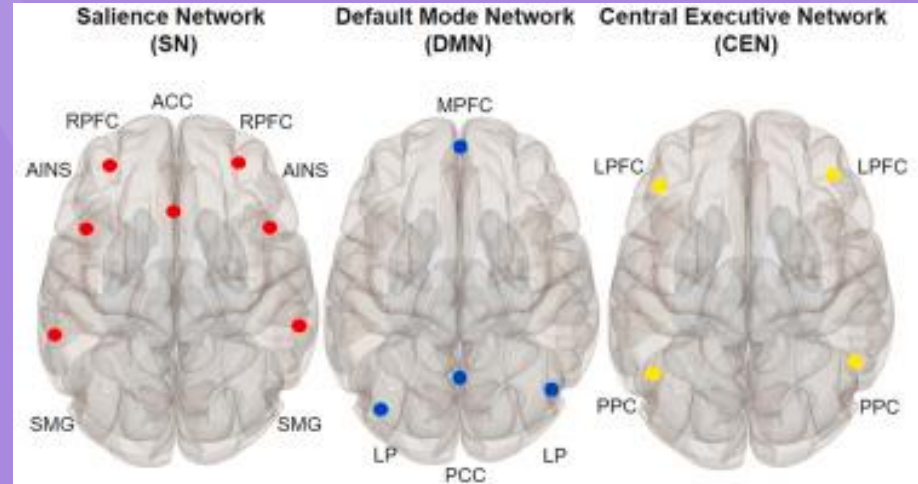
The Network Revolution in Neuroscience

The Network Revolution in Neuroscience

- *Old thinking: Specific brain regions = specific functions*
- *New understanding: Coordinated networks of connected areas govern experience and behavior*
- *Different networks active during different mental states*
- *Network dysfunction underlies mental health conditions*

Three Key Networks Affected by Ketamine: *The Critical Trio*

- Default Mode Network (DMN)
 - Active during rest, mind-wandering, self-focus
- Central Executive Network (CEN)
 - Active during focused, goal-oriented tasks
- Saliency Network (SN)
 - Acts as "switch" between internal and external focus

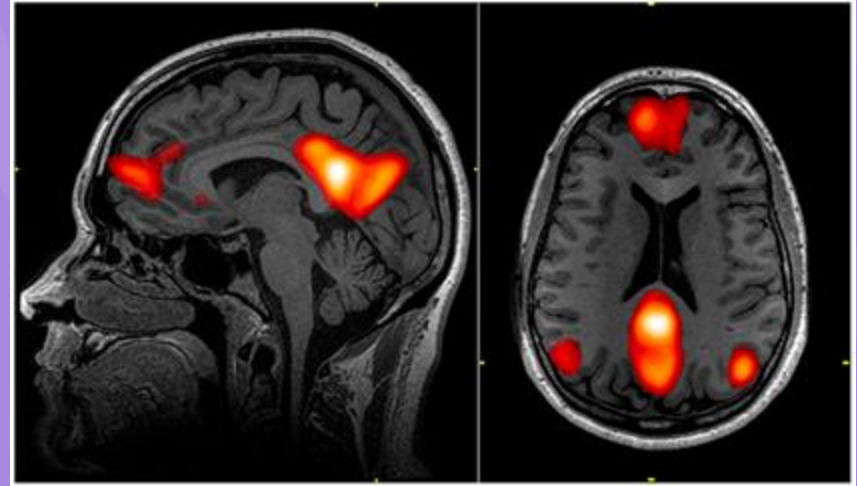


Krönke, K. M., Wolff, M., Shi, Y., Kräplin, A., Smolka, M. N., Bühringer, G., & Goschke, T. (2020). Functional connectivity in a triple-network saliency model is associated with real-life self-control. *Neuropsychologia*, 149, 107667.

Default Mode Network - The Frequent Culprit

When Self-focus goes wrong

- **Key Areas:** Medial prefrontal cortex, posterior cingulate cortex, precuneus
- **Normal Function:** Mind-wandering, self-referential thinking
- **When Overactive:**
 - Depressive rumination
 - Anxiety loops
 - Repetitive negative thinking
 - Associated with PTSD, ADHD, autism patterns



By John Graner, Neuroimaging Department, National Intrepid Center of Excellence, Walter Reed National Military Medical Center, 8901 Wisconsin Avenue, Bethesda, MD 20889, USA. - <http://www.frontiersin.org/Neurotrauma/10.3389/fneur.2013.00016/full>, Public Domain, <https://commons.wikimedia.org/w/index.php?curid=25872800>

Ketamine's DMN Reset

Breaking the Rumination Cycle

Ketamine's Action:

- Reduces DMN activity and connectivity
- Interrupts medial prefrontal ↔ posterior cingulate communication
- Breaks repetitive negative thought patterns

Therapeutic Result:

- Reduced rumination
- Enhanced cognitive flexibility
- Opens space for new perspectives

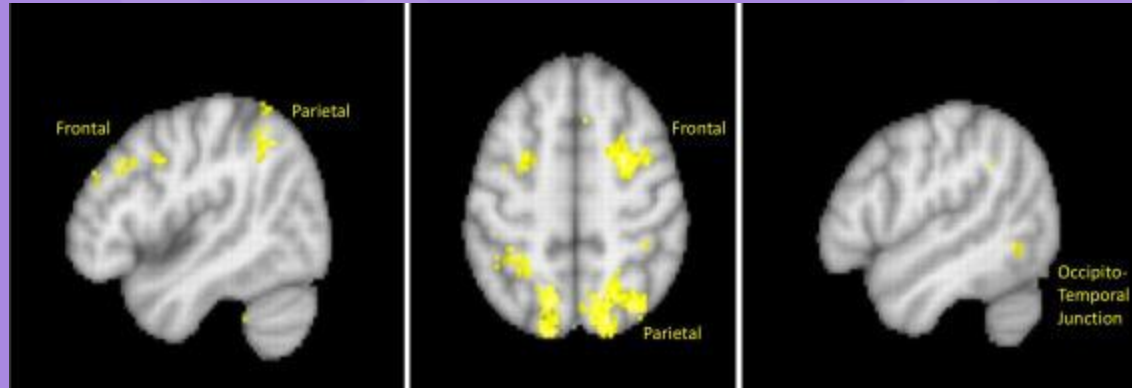
Central Executive Network - External Focus

The Task-Positive Network

Key Areas: Dorsolateral prefrontal cortex, parietal cortex

Functions:

- *Working memory*
- *Attention control*
- *Goal-oriented thinking*



Ketamine's Indirect Enhancement:

- *Reduced DMN dominance allows CEN to engage more effectively*
- *Shifts brain from internal rumination to external engagement*

Mulders, P. C., van Eijndhoven, P. F., Schene, A. H., Beckmann, C. F., & Tendolkar, I. (2015). Resting-state functional connectivity in major depressive disorder: a review. *Neuroscience & Biobehavioral Reviews*, 56, 330-344.

Saliience Network - The Traffic Controller

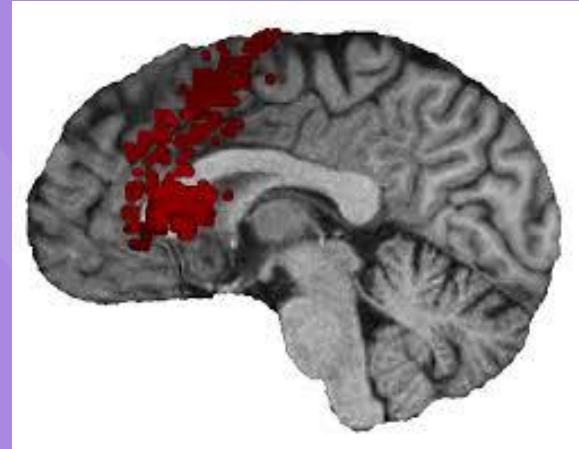
Managing Attention and Emotion

Key Areas: Anterior insula, anterior cingulate cortex

Critical Function: Switches brain between DMN and CEN based on what's important

In Mental Health Conditions:

- *Misinterprets emotional cues*
- *Over-responds to threats*
- *Poor switching between internal/external focus*



Ketamine's Salience Network Modulation

Improving Emotional Processing

Ketamine's Effects:

- Modulates SN activity for better emotional responsiveness
- Enhances ability to process difficult emotions
- Particularly important at psychedelic doses
- Creates openness to therapeutic exploration

The Network Dance - Before vs. After

Rebalancing Brain Activity

Typical Depression/Anxiety Pattern:

- DMN overactive (stuck in rumination)
- CEN underactive (poor external focus)
- SN dysregulated (poor switching)

After Ketamine:

- DMN activity reduced
- CEN engagement enhanced
- SN better regulated
- Result: Flexible switching between mental states

Dose-Dependent Network Effects

Different Doses, Different Network Impacts

Lower Psychedelic Doses:

- Gentle network rebalancing
- Access to difficult emotions
- Enhanced therapeutic openness
- Maintained sense of self

Higher Doses:

- More dramatic network disruption
- Dissociation from personal narratives
- Distance from intense emotions
- "Ego dissolution" effects

The Neuroplasticity Window

Network Reset Creates Therapeutic Opportunity

Ketamine's "Reset" Effect:

- Disrupts habitual network patterns
- Creates enhanced neuroplasticity window
- Breaks maladaptive thought cycles
- Opens brain to new therapeutic insights

Clinical Implication: Optimal time for therapeutic intervention

Clinical Applications & Future Directions

From Networks to Treatment

Treatment Optimization:

- Network activity as biomarkers for dosing
- Personalized protocols based on individual network patterns
- Timing therapy sessions with network effects

Research Directions:

- Real-time network monitoring during treatment
- Predicting treatment response from baseline network activity
- Combination therapies targeting specific networks

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PRACTICE LIFELONG EXCELLENCE