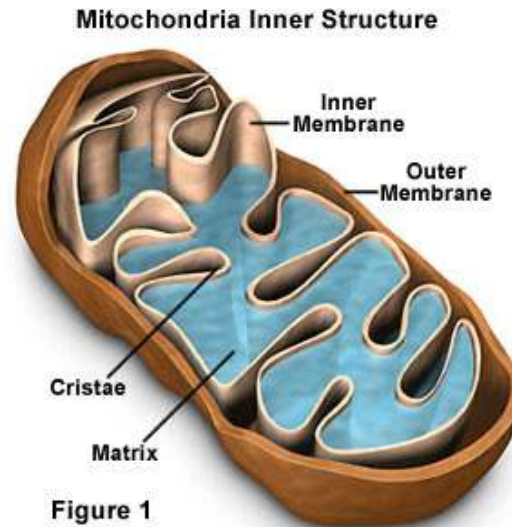


Mitochondria and Psychiatry



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Disclosure Statement

Employee Of	Massachusetts General Hospital
Consultant For	Abbott Laboratories, Astra Zeneca, Basilea, BrainCells Inc., Bristol-Myers Squibb, Cephalon, Clexio, Clintara, Corcept, Esai, Eli Lilly & Co., Forest, Genaissance, Genentech, Ginger/Headspace Health, GlaxoSmithKline, Innapharma, Janssen Pharmaceutica, Jazz Pharmaceuticals, Lundbeck, Medavante, Merck, Myriad, Neuronetics, NeuroRx, Novartis, Ostuka, PamLabs, PGx Health, Pfizer, Protogenics, Roche, Sepracor, Schering-Plough, Shire, Somerset, Sunovion, Takeda, Targacept, Teva
Stockholder In	4M Therapeutics, Alitmate, Flow, Unravel Biosciences
Grant Support From	AFSP, AHRQ, Bristol-Myers Squibb, Cederroth, Cyberonics, Forest Pharmaceuticals, GlaxoSmithKline, Janssen Pharmaceutica, Lichtwer Pharma, Eli Lilly, NARSAD, NIMH, PCORI, Pfizer, Shire, Stanley Foundation, Takeda, Wyeth-Ayerst
Honoraria From	MGH Psychiatry Academy in the past 3 years (Prior to 3 years ago, honoraria from Bristol-Myers Squibb, Cyberonics, Forest Pharmaceuticals, GlaxoSmithKline, Eli Lilly,, Shire, Wyeth-Ayerst), No speaker bureaus since 2003

Andrew A. Nierenberg, MD

Disclosure Statement

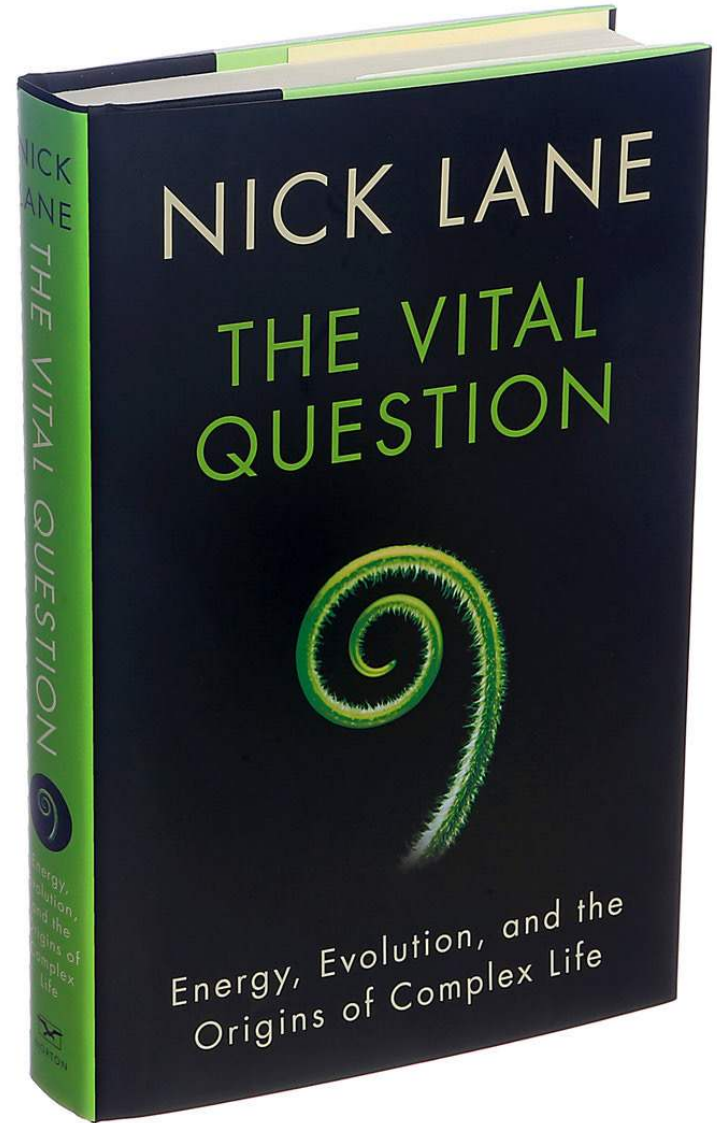
Other Income	MBL Publishing for past services as Editor-in-chief of CNS Spectrums; Slack Inc. for services as Associate Editor of Psychiatric Annals; Editorial Board, Mind Mood Memory, Belvior Publications
Patents and Copyrights	Copyright joint ownership with MGH for Structured Clinical Interview for MADRS and Clinical Positive Affect Scale
Additional Honoraria	ADURS, Brain and Behavior Foundation Colvin Prize, University of :Pisa, University of Wisconsin at Madison, University Texas Southwest at Dallas, Health New England and Harold Grinspoon Charitable Foundation and Eli Lilly and AstraZeneca, American Society for Clinical Psychopharmacology and Zucker Hillside Hospital and Forest and Janssen, Brandeis University, International Society for Bipolar Disorder

Outline

- **Mitochondria and the brain**
- **Psychiatric symptoms and diagnoses in Mito diseases**
- **Mito dysregulation in psychiatric disorders**

A vast field of stars in space, with a central cluster of bright blue and white stars. The background is a deep blue, filled with numerous small, distant stars. In the center, there is a prominent cluster of larger, brighter stars, many of which are blue and white, with some showing diffraction spikes. The overall scene is a rich, multi-colored stellar population.

We are all made of stars.
Moby





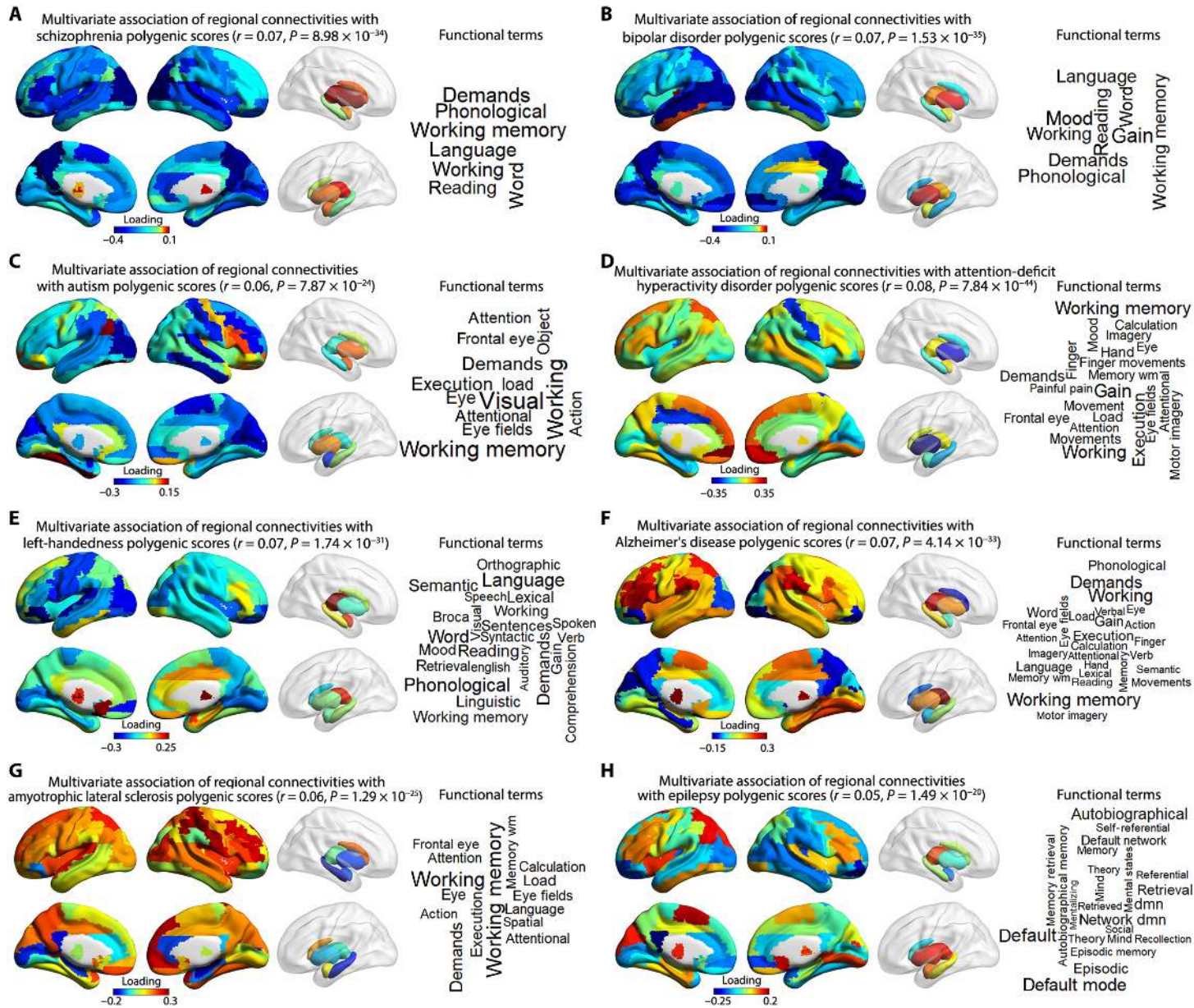
<https://medium.com/@joanathanrobbins/your-brain-mind-has-become-an-extension-of-the-internet-5ed2d653c47c>

Science Advances

17 FEBRUARY 2023



AAAS



A vast field of stars in space, with a central cluster of bright blue and white stars. The background is a deep blue, filled with numerous small, distant stars. In the center, there is a prominent cluster of larger, brighter stars, many of which are blue and white, with some showing diffraction spikes. The overall scene is a rich, multi-colored star field.

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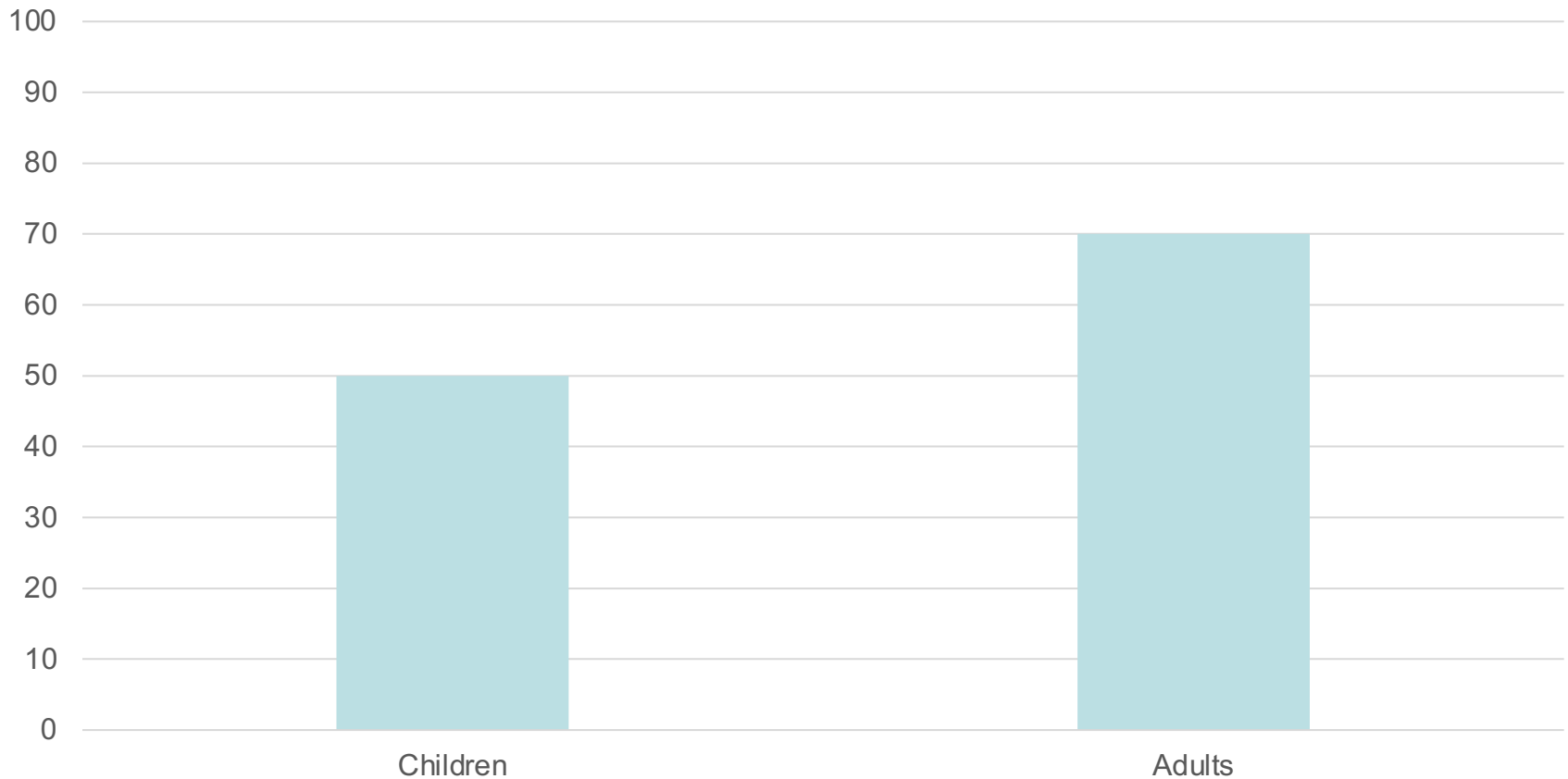
Lifetime Prevalence Psychiatric Disorders in Mito Disease

- **Onset of psychiatric disorders**
13 years before mito disease diagnosis
- **Psychiatric disorders resistant to medications**

Fattal O, et al. CNS Spectr 2007;12:429–438; Morava E, et al. Mitochondrion 2010; 10:528–533

Lifetime Prevalence Psychiatric Disorders in Mito Disease

Depression or Psychiatric Disorders



*Fattal O, et al. CNS Spectr 2007;12:429–438;
Morava E, et al. Mitochondrion 2010; 10:528–533*

Psychiatric Presentations

- **Major depressive disorder**
- **Bipolar disorder**
- **OCD**
- **Anorexia**
- **Bizarre hallucinations**
- **Anxiety disorders**
- **Substance abuse**
- **Borderline personality disorder**

Treatment

- **Coenzyme Q₁₀,**
- **Creatine monohydrate**
- **Alpha lipoic acid**
- **Vitamin E, vitamin C, and riboflavin**
- **Antioxidant idebenone**
- **Reduction or discontinuation of psychotropic drugs**

Anglin et al. The Journal of Neuropsychiatry and Clinical Neurosciences 2012; 24:394–409)

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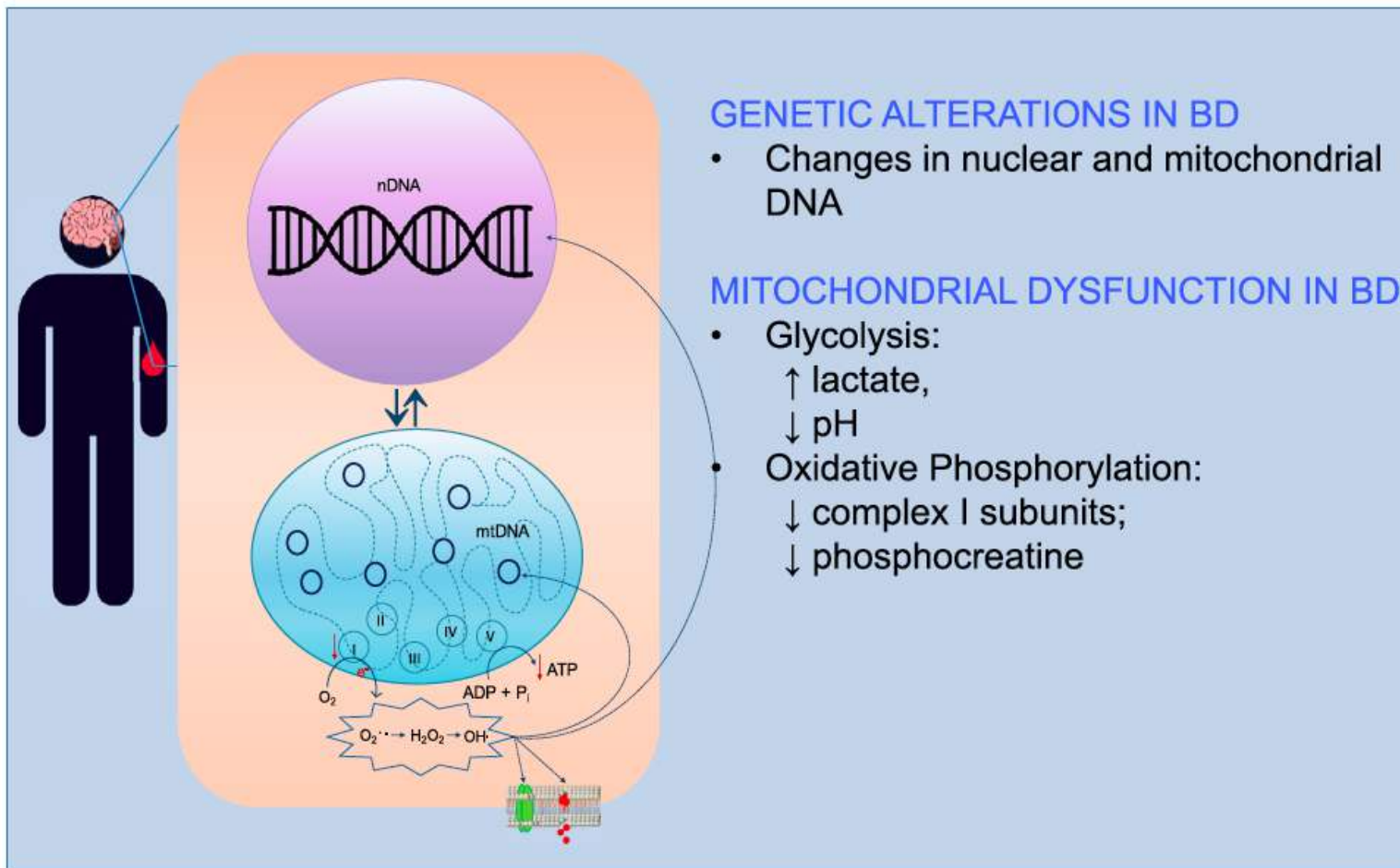
Commentary

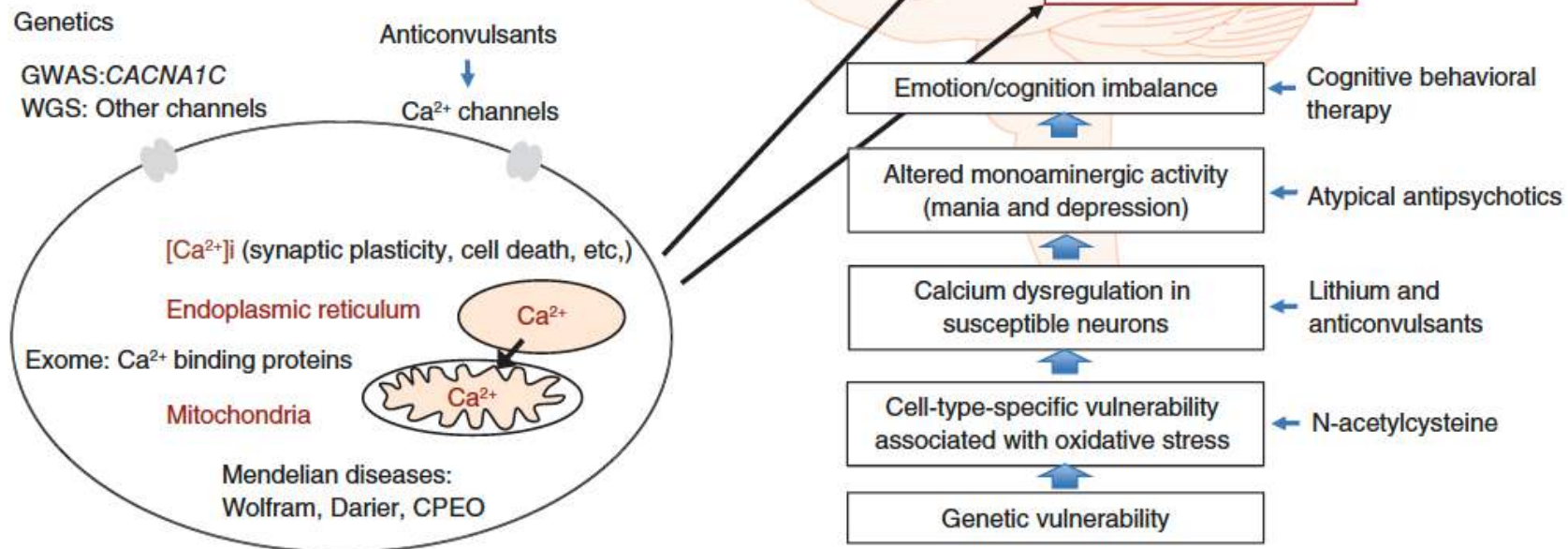
Mitochondrial Dysfunction: At the Core of Psychiatric Disorders?

Ana C. Andreazza and Andrew A. Nierenberg

Bipolar Disorder as a Mitochondrial Disease

Ana C. Andreazza, Angela Duong, and L. Trevor Young





The Role of Mitochondria in Mood Disorders: From Physiology to Pathophysiology and to Treatment

Anna Giménez-Palomo¹, Seetal Dodd^{2,3}, Gerard Anmella¹, Andre F. Carvalho^{4,5}, Giselli Scaini⁶, Joao Quevedo^{6,7,8,9}, Isabella Pacchiarotti¹, Eduard Vieta¹ and Michael Berk^{10,11,12}*

Mitochondrial Abnormalities in Bipolar Disorder

- Altered mitochondrial gene expression
- Decreased brain energy metabolism
- Markers of oxidative stress
- Bipolar calcium channel genes
- Decreased oxidative stress with lithium and valproate

Effects of Lithium on Mito Genes

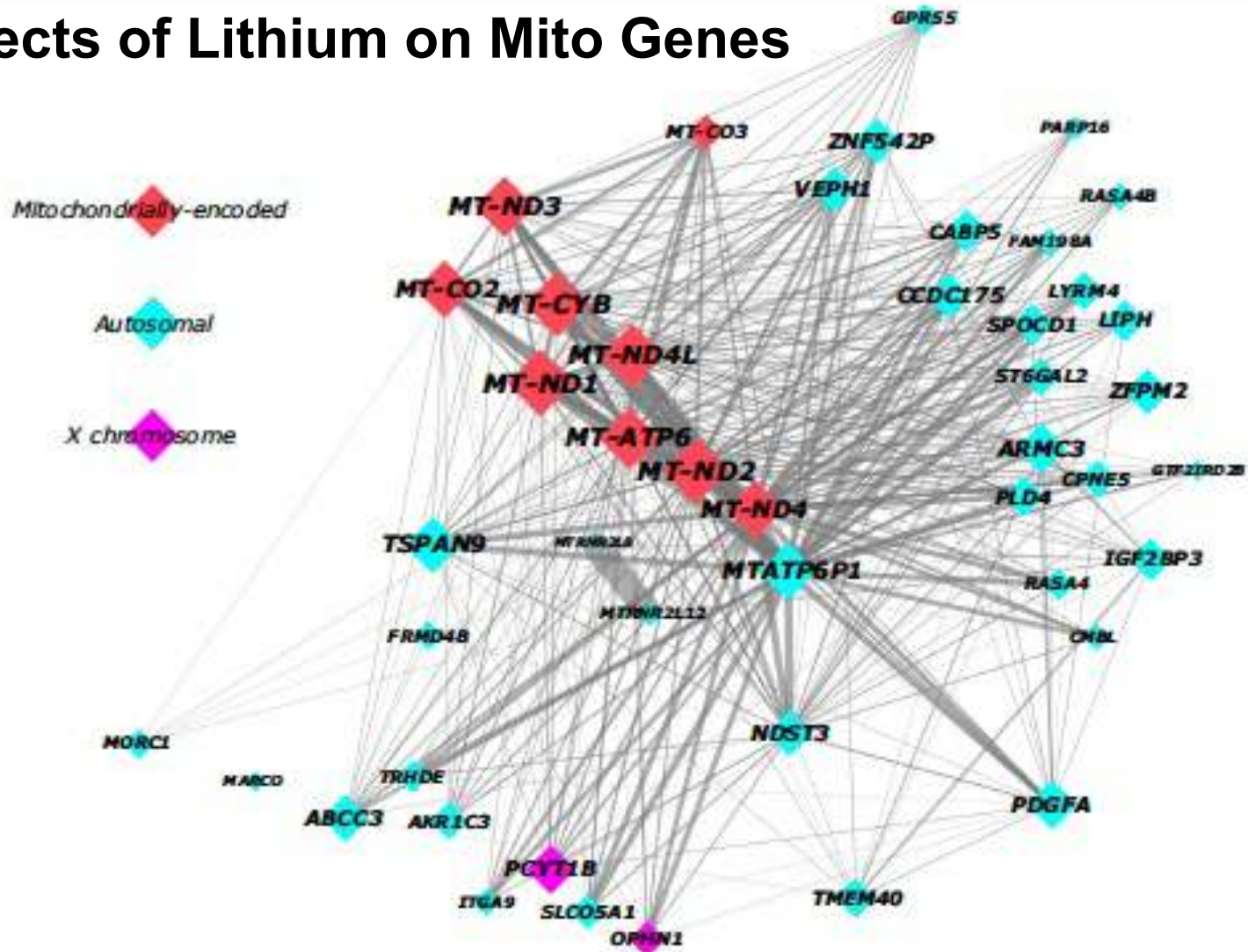


Fig. 2 Network graph summarising the royalblue co-expression module. The royalblue module was visualised according to a prefuse force-directed layout based on weighted correlations between genes. Minor manual changes to node placement were made to maximise clarity. The size of each node (and node label) reflects absolute module membership (MM) values, with larger nodes corresponding to higher MM values. Node colour indicates whether royalblue genes were encoded by autosomal (azure), X chromosome (purple), or mitochondrial (red) DNA. Edge width reflects the weighting of connections between nodes, with thicker edges corresponding to stronger connections.

Review

Biological
Psychiatry

Peroxisome Proliferator-Activated Receptor Gamma Coactivator-1 Alpha as a Novel Target for Bipolar Disorder and Other Neuropsychiatric Disorders

Andrew A. Nierenberg, Shamin A. Ghaznavi, Isadora Sande Mathias, Kristen K. Ellard,
Jessica A. Janos, and Louisa G. Sylvia

Biological Psychiatry May 1, 2018; 83:761–769

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