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ASK THE EXPERT
with Dr. Kim

FEATURED EXPERT

An Interview with Guido Frank, MD

Professor of Psychiatry,
University of California

Q: How did you become interested in translational research? And eating disorders specifically?

A: Eating disorders are among the most difficult-to-treat problems we have in psychiatry. There are many factors across the bio-psycho-social spectrum that contribute to development and maintenance of those illnesses and I think only a translational research approach that brings together those different directions will lead us to a better understanding and novel effective treatments. I was trained as a psychotherapist in a psychosomatic hospital after medical school. Later I trained in biological brain research and as a psychiatrist. That training experience led me to believe that translational research is key in our field.

Q: I notice you are currently recruiting for a study examining specific dietary interventions for anorexia nervosa. Tell us about that. How does the dietary intervention in your study fit into the "all foods fit" dogmatic approach used in most eating disorder care? How did you choose it?

A: We have no biological treatments approved for anorexia nervosa. While psychotherapy and meal support are effective in weight restoration, they often cannot resolve the cognitive-emotional aspects of anorexia nervosa. In fact, after weight restoration, the fear of weight gain and body image problems can be even worse compared to the underweight state. The underlying etiology of AN remains unclear, but it has been hypothesized that the underlying disease mechanisms include metabolic risk factors or that anorexia nervosa may be a "metabolic disorder of psychological origin."

During starvation, the body breaks down fats after depletion of sugar stores and derives its energy from ketone bodies, breakdown products from the released body fats and fatty acids.

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We believe that the brain in anorexia nervosa can utilize those ketones better than the glucose, which makes the starvation state so reinforcing in anorexia nervosa. The detrimental downside, of course, is emaciation and death. In this study, we are using a therapeutic ketogenic diet that maintains weight in individuals who are weight-recovered from anorexia nervosa, which will provide energy via ketone bodies and eliminate the need for self-starvation. We published a small study recently using the ketogenic diet in five individuals who were weight-recovered from anorexia nervosa but with ongoing severe psychopathology that supported our approach (Calabrese et al., 2020; https://link.springer.com/article/10.1007/s40519-022-01455-x).

Q: Do you think TMS has any potential in the treatment of anorexia, bulimia, or BED?

A: I think there is a very good chance for that. However, the caveat is that TMS is time consuming and in the study that we are conducting, participants are often worried that something is done to their brain that they cannot control, creating much anxiety and difficulties with recruitment.

Q: I notice you have a study looking at CBD for anorexia. What led you and your collaborators to investigating this for AN?

A: CBD is commonly used for anxiety, but OTC products are not regulated. We decided to use an FDA-approved product to test CBD for mealtime anxiety and fears around body weight and shape in a manner where we have a weight dependent dosing and assess blood levels for a rigorous study design.

Q: What 3 papers are you most proud of in your research career?

A: Association of Brain Reward Response with Body Mass Index and Ventral Striatal-Hypothalamic Circuitry Among Young Women with Eating Disorders. Frank GKW, Shott ME, Stoddard J, Swindle S, Pryor TL. JAMA Psychiatry. 2021 Oct 1;78(10):1123-1133. doi: 10.1001/jamapsychiatry.2021.1580.PMID: 34190963 Free PMC article.

Association of Elevated Reward Prediction Error Response with Weight Gain in Adolescent Anorexia Nervosa. DeGuzman M, Shott ME, Yang TT, Riederer J, Frank GKW. Am J Psychiatry. 2017 Jun 1;174(6):557-565. doi: 10.1176/appi.ajp.2016.16060671. Epub 2017 Feb 24.PMID: 28231717 Free PMC article.

Anorexia nervosa and obesity are associated with opposite brain reward response. Frank GK, Reynolds JR, Shott ME, Jappe L, Yang TT, Tregellas JR, O'Reilly RC. Neuropsychopharmacology. 2012 Aug;37(9):2031-46. doi: 10.1038/npp.2012.51. Epub 2012 May 2.PMID: 22549118 Free PMC article.

Q: Relatively little has been published in the literature about atypical anorexia. Putting weight status aside, is there any data that supports it being considered a distinct phenotype from AN?

A: I have been studying eating disorder subgroups from a transdiagnostic perspective and looking more at behavioral and neurobiological trajectories across groups than separating groups. It seems that many cognitive-emotional aspects are shared while brain biology differs, in part based on weight.

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Q: As a researcher clinician leader in the eating disorder field, what are you most concerned about in the field? What areas of clinical care are lacking most in research and treatment strategies?

A: I think it is most important that we design and conduct studies that have real world implications and that connect brain function and biology with real-world behavior. There is not an either/or but rather a complementary function of biological and behavioral studies. We have to advance and design treatments that are based on empirical data. We also have to train a workforce of mental health clinicians that integrate brain biology and behavior, just as in other areas of medicine. This will help build integrative disease models and bring those disorders from a black box or "difficult to understand" perspective to a transparent view where we can identify – and that is most important – with the patients and their families, treatment targets that we can work toward.