

can be trialed in people with CKD for the prevention and treatment of CKD-MBD.

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### Metformin normalizes impaired renal and cardiac function in a rat model of transient undernutrition

Branka Stanic<sup>1</sup>, Aline M.A de Souza<sup>1</sup>, Hong Ji<sup>1</sup>, Kyle Korolowicz<sup>2</sup>, Kathryn Sandberg<sup>1</sup> and Carolyn M. Ecelbarger<sup>1</sup>

<sup>1</sup>Department of Medicine, Georgetown University and <sup>2</sup>Preclinical Imaging Research Laboratory, Georgetown University

**OBJECTIVES/GOALS:** In the U.S., over 4 million people including children experience transient periods of undernutrition annually. Cardio-metabolic and renal diseases are more prevalent in this population. We are investigating therapeutic strategies to reverse the long-term risk of these diseases in a rat model of transient undernutrition followed by refeeding. **METHODS/STUDY POPULATION:** Thirty six female Fischer rats (3-months of age) were initially divided into 2 groups. Half were fed regular chow (CT) while the other half were severely food restricted (sFR) by 60% from 0-2 weeks (wks) followed by refeeding from 2-14 wks (sFR-Refed). These 2 groups were then subdivided and treated  $\pm$  metformin (Met) from wk 7 to wk 12 (n=9/group). High precision ultrasound was conducted on live rats to assess heart and kidney function immediately after the sFR period ended (wk 2) and at the end of the study (wk 14). At the conclusion of the experiment, the rats were sacrificed and the histology of the kidney and heart tissues were analyzed in hematoxylin and eosin-stained sections. The protein to DNA ratio was also calculated in homogenates from these tissues. **RESULTS/ANTICIPATED RESULTS:** In sFR-Refed rats, cardiac output (CO), heart rate (HR) and renal artery blood flow (RBF) were decreased by  $11 \pm 1.5\%$ ,  $7.0 \pm 6.0\%$  and  $22 \pm 0.6\%$ , respectively, compared to control (CT) rats; #p<0.05. Mean glomerular diameter was reduced in the kidneys of sFR-refed rats compared to CT and this effect was attenuated by metformin treatment [( $\mu$ m): CT,  $406 \pm 31$ ; sFR-Refed,  $383 \pm 11$ , p<0.06; CT+Met,  $393 \pm 18$ ; sFR-Refed+Met,  $407 \pm 18^*$ ]. Furthermore, the mean cardiomyocyte thickness was reduced in sFR-Refed rats compared to controls while metformin treatment prevented this effect [( $\mu$ m): CT,  $16.4 \pm 3.6$ ; sFR-Refed,  $11.5 \pm 2.3\#$ ; CT+Met,  $16.4 \pm 3.6$ ; sFR-Refed+Met,  $15.9 \pm 3.2^*$ ]. #p<0.05 vs. CT, same treatment; \*p<0.05 vs. Met, same diet; two-way ANOVA. **DISCUSSION/SIGNIFICANCE:** These findings have promising implications for metformin use to mitigate long-term impairments in heart and kidney structure and function in individuals who have experienced bouts of undernutrition earlier in life for either voluntarily (e.g., very low calorie dieting) or involuntary (e.g., very low food security) reasons.

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### A Nationwide Pilot Study Testing a Remotely-Delivered Prolonged Nightly Fasting Intervention in Stressed Midlife Adults Living with Obesity and Memory Decline

Dara L. James<sup>1</sup>, Linda K. Larkey<sup>1</sup>, Molly Maxfield<sup>1</sup>, Edward Ofori<sup>1</sup>, Nanako A. Hawley<sup>2</sup>, Kate Alperin<sup>1</sup>, Peyton Osha<sup>1</sup>, Chung Jung Mun<sup>1</sup> and Dorothy D. Sears<sup>1</sup>

<sup>1</sup>Arizona State University and <sup>2</sup>University of South Alabama

**OBJECTIVES/GOALS:** Cognitive decline is associated with obesity, stress, poor sleep, and circadian rhythm misalignment, which are themselves functionally intertwined. Irregular food intake timing exacerbates these all. Prolonged nightly fasting (PNF) aligns food

intake with innate circadian rhythms. **METHODS/STUDY POPULATION:** A nationwide, remotely-delivered, 2-arm randomized controlled trial was conducted to assess feasibility and 8-week outcomes of cognition, stress, sleep, eating behaviors, and general eating habits, after a PNF intervention (14-hr nightly fast, 6 nights/week, no calories after 8pm) compared to a health education control (HEC) condition. Eligible participants were living with obesity, stress (Perceived stress scale-4 (PSS-4) total score  $\geq 5$ ), and memory “not as good as it used to be.” Data were collected via Zoom meetings with participants and trained staff and entered into REDCap. All participants had weekly staff check-in calls to report fasting times (PNF group only) and feedback. **RESULTS/ANTICIPATED RESULTS:** Eligible participants were enrolled from 37 of 50 US states; N=58, 86% women, 71% white, 93% non-Latinx, mean (SD) 50.1 (5.1) years of age, BMI 35.6 (3.6) kg/m<sup>2</sup>. No group differences existed at baseline. Linear mixed-effects models were used to compare group differences across all outcome changes. Compared to the HEC condition, the PNF intervention was associated with improved sleep quality (Pittsburgh Sleep Quality Index; B = -2.52; SE = 0.90; 95% CI -4.30 to -0.74; p=0.006). Stress, everyday cognition, and emotional eating behavior significantly changed over time (p<0.02), but there were no group differences. Analysis of feasibility outcomes are on-going. **DISCUSSION/SIGNIFICANCE:** Changing food intake timing 6 days per week, to exclude nighttime eating without mandating food quality/quantity change, may benefit many individuals living with obesity, stress and memory decline to improve their sleep. Improved sleep quality may lead to more health benefits over time.

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### Substance Abuse Research: Bench to Community (SARB2C) as a Model for Team Science

Tamara A Millay and Linda B Cottler

University of Florida

**OBJECTIVES/GOALS:** To present Substance Abuse Research: Bench to Community (SARB2C) as a model for team science both within and between institutions. Emerging from targeted efforts by the NIH to engage translational scientists in prominent public health issues, the initiative illustrates the benefits of bringing together researchers and trainees to share ideas. **METHODS/STUDY POPULATION:** In 2019 a group was formed at University of Florida to discuss ongoing translational research in the area of substance abuse, including faculty, staff, and trainees from across the campus. The group was expanded in February 2022 to include domestic colleagues at the University of Kentucky as well as international collaborators at Chulalongkorn University in Bangkok, Thailand. One-hour monthly meetings began in person but now take place virtually. Larger projects are discussed individually, focusing on opportunities for collaboration. Attendees also provide updates on their work, including proposals in development and manuscripts in process. This facilitates dialogue around the science, from the bench to the community, and connects people to advance team science. **RESULTS/ANTICIPATED RESULTS:** In light of the ongoing opioid epidemic and the public health threat of other emerging substances, collaboration among researchers in this area is essential to advance the science and explore real-world solutions. SARB2C demonstrates the benefit of connecting researchers across T0 to T4, and that of including trainees for invaluable experience. This environment fosters open discussion and creativity and helps break down the silos that impede science. A highlight from early in the