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### Triglycerides cross the blood–brain barrier and induce central leptin and insulin receptor resistance

WA Banks, SA Farr, TS Salameh, et al (2017) Int J Obes [1]

*Objective:* Resistance at the brain receptors for leptin and insulin has been associated with increased feeding, obesity and cognitive impairments. The causal agent for central resistance is unknown but could be derived from the blood. Here we postulate whether hypertriglyceridemia, the major dyslipidemia of the metabolic syndrome, could underlie central leptin and insulin resistance.

*Design:* We used radioactively labeled triglycerides to measure blood–brain barrier (BBB) penetration, western blots to measure receptor activation, and feeding and cognitive tests to assess behavioral endpoints.

*Results:* Human CSF was determined to contain triglycerides, a finding previously unclear. The radioactive triglyceride triolein readily crossed the BBB and centrally administered triolein and peripherally administered lipids induced in vivo leptin and/or insulin resistance at hypothalamic receptors. Central triolein blocked the satiety effect of centrally administered leptin. Decreasing serum triglycerides with gemfibrozil improved both learning and memory inversely proportionate to triglyceride levels.

*Conclusions:* Triglycerides cross the blood–brain barrier rapidly, are found in human cerebrospinal fluid, and induce

central leptin and insulin receptor resistance, decreasing satiety and cognition.

*Commentaires :* Cette étude suggère une action inhibitrice des triglycérides sur la voie de signalisation de la leptine, non pas par phénomène de compétition au niveau du récepteur de la leptine, mais par un phénomène post-liaison au récepteur restant à détailler. L'hypertriglycéridémie du syndrome métabolique serait donc une cible thérapeutique potentielle dans la leptinorésistance.

### Later circadian timing of food intake is associated with increased body fat

AW McHill, AJ Phillips, CA Czeisler, et al (2017) Am J Clin Nutr [2]

*Background:* Weight gain and obesity have reached alarming levels. Eating at a later clock hour is a newly described risk factor for adverse metabolic health; yet, how eating at a later circadian time influences body composition is unknown. Using clock hour to document eating times may be misleading owing to individual differences in circadian timing relative to clock hour.

*Objective:* This study examined the relations between the timing of food consumption relative to clock hour and endogenous circadian time, content of food intake, and body composition.

*Design:* We enrolled 110 participants, aged 18–22 y, in a 30-d cross-sectional study to document sleep and circadian behaviors within their regular daily routines. We used a time-stamped-picture mobile phone application to record all food intake across 7 consecutive days during a participant's regular daily routines and assessed their body composition and timing of melatonin release during an in-laboratory assessment.

*Results:* Nonlean individuals (high body fat) consumed most of their calories 1.1 h closer to melatonin onset, which heralds the beginning of the biological night, than did lean individuals (low body fat) (log-rank  $P = 0.009$ ). In contrast, there were no differences between lean and nonlean individuals in the clock hour of food consumption ( $P = 0.72$ ). Multiple regression analysis showed that the timing of food

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intake relative to melatonin onset was significantly associated with the percentage of body fat and body mass index (both  $P < 0.05$ ) while controlling for sex, whereas no relations were found between the clock hour of food intake, caloric amount, meal macronutrient composition, activity or exercise level, or sleep duration and either of these body composition measures (all  $P > 0.72$ ).

*Conclusions:* These results provide evidence that the consumption of food during the circadian evening and/or night, independent of more traditional risk factors such as amount or content of food intake and activity level, plays an important role in body composition.

*Commentaires :* Cent dix participants ont renseigné pendant 30 jours leurs horaires de sommeil ainsi qu'un relevé alimentaire sous une forme photographique. Un dosage toutes les heures de mélatonine (hormone produite principalement lors du sommeil) salivaire était par ailleurs effectué entre 16 et 7 h, ainsi qu'un relevé de composition corporelle par impédancemétrie bioélectrique. Il est ainsi déterminé qu'il n'y a pas de relation significative entre la composition corporelle et l'heure du repas du soir, sa composition en macronutriments, ou encore la durée de sommeil lui succédant. Par contre, il est montré que les participants ayant davantage de masse grasse ont des repas du soir plus rapprochés de la sécrétion de mélatonine que les sujets minces. Ce constat suggère que les repas les plus rapprochés du « sommeil biologique » auraient un impact sur la composition corporelle.

### Body fat distribution is more predictive of all-cause mortality than overall adiposity

SW Lee, JY Son, JM Kim, et al (2018) Diabetes Obes Metab [3]

*Aims:* The relationship between directly measured body fat and all-cause mortality has been rarely studied. The aim of this study was to evaluate the predictive significance of computed tomography (CT)-measured body fat, including both visceral fat area (VFA) and subcutaneous fat area (SFA), for mortality.

*Methods:* The study included 36,656 participants who underwent abdominal CT as part of a health check-up at a single university-affiliated healthcare center in 2007 to 2015. Of those, 32,593 participants with data regarding vital status as of May 2016 were included in the final analysis. The main factors evaluated were VFA, SFA and visceral-to-subcutaneous fat area ratio (VSR), and the primary outcome was all-cause mortality.

*Results:* There were 253 deaths during a mean follow-up of 5.7 years. Increased SFA was associated with decreased

all-cause mortality, whereas an increased VFA and VSR were related to increased all-cause mortality. Compared with the predictive power of body mass index (BMI), SFA and VSR showed a larger area under the curve than did BMI. In Kaplan–Meier survival curve analysis, increased SFA and VSR were associated with decreased and increased hazard of all-cause death, respectively. However, in multivariate Cox proportional hazard regression analysis, only VSR was independently associated with all-cause mortality. Moreover, this relationship was paralleled by the harmful impact of increased VSR on metabolic profiles.

*Conclusion:* Increased VSR was an independent predictor of all-cause mortality. This suggests that the location of fat deposits may be more important than the actual amount of body fat.

*Commentaires :* Il est maintenant bien connu que la graisse périviscérale est un facteur de risque indépendant de maladies métaboliques alors que le tissu adipeux sous-cutané a, quant à lui, un impact bénéfique sur ces mêmes pathologies. Les données anthropométriques (comme le tour de taille) ne permettent pas de distinguer correctement cette répartition grasseuse, alors que des examens d'imagerie (dans cette étude le CT-scan) le font parfaitement. Dans cette très large cohorte rétrospective coréenne de 36 656 individus ayant bénéficié d'un scanner abdominal, les auteurs ont étudié la mortalité, toutes causes confondues, en fonction de la répartition sous-cutanée ou périviscérale du tissu adipeux (notamment avec le calcul d'un ratio). Parmi les 253 décès survenus sur les huit ans d'analyse, il est observé davantage d'hommes, plus âgés, avec un IMC plus important, mais surtout une masse adipeuse totale plus importante. Par ailleurs, la répartition périviscérale apparaît être un facteur de risque de mortalité toutes causes confondues, en lien probable avec l'impact métabolique négatif de cette localisation adipeuse, alors que la répartition sous-cutanée est associée à une diminution de ce risque. Tout cela reste à confirmer par des données prospectives apportant un niveau de preuve plus important.

### Deep Brain Stimulation – Possible Treatment Strategy for Pathologically Altered Body Weight

P Prinz, A Stengel (2017) Brain Sci [4]

The treatment of obesity and eating disorders such as binge-eating disorder or anorexia nervosa is challenging. Besides lifestyle changes and pharmacological options, bariatric surgery represents a well-established and effective-albeit invasive-treatment of obesity, whereas for binge-eating disorder and anorexia nervosa mostly psychotherapy options exist. Deep brain stimulation (DBS),

a method that influences the neuronal network, is by now known for its safe and effective applicability in patients with Parkinson's disease. However, the use does not seem to be restricted to these patients. Recent preclinical and first clinical evidence points towards the use of DBS in patients with obesity and eating disorders as well. Depending on the targeted area in the brain, DBS can either inhibit food intake and body weight or stimulate energy intake and subsequently body weight. The current review focuses on preclinical and clinical evidence of DBS to modulate food intake and body weight and highlight the different brain areas targeted, stimulation protocols applied and downstream signaling modulated. Lastly, this review will also critically discuss potential safety issues and gaps in knowledge to promote further studies.

*Commentaires : La stimulation cérébrale profonde est aujourd'hui de plus en plus largement utilisée dans le traitement de la maladie de Parkinson. Les effets de ce procédé de stimulation cérébrale font actuellement l'objet de nombreuses recherches concernant la douleur chronique ou l'épilepsie. Étant donné les dysfonctionnements possibles du circuit de la récompense en jeu chez les patients présentant des problèmes pondéraux, il paraissait logique de questionner l'application de cette méthode à ces problématiques. Cette revue de la littérature s'intéresse aux études animales et humaines conduites jusqu'alors dans le champ de l'anorexie mentale, de l'obésité et du Binge Eating Disorder (zones stimulées, durée de stimulation, puissance délivrée, efficacité et effets secondaires potentiels) et à l'implication clinique de ces résultats. Les résultats apparaissant prometteurs, mais mitigés, les auteurs insistent sur la nécessité de mener des études de plus grande ampleur à l'échelle animale et humaine et notamment d'études en double insu. Malgré tout, étant donné la résistance de certains patients en situation d'obésité aux prises en charge médicales, psychothérapeutiques et même chirurgicales, la stimulation cérébrale profonde semble dans ce cadre une perspective novatrice à creuser.*

### **Paying people to lose weight: the effectiveness of financial incentives provided by health insurers for the prevention and management of overweight and obesity – A systematic review**

J Ananthapavan, A Peeterson, G Sacks (2017) *Obesity Rev* [5]

Curbing the obesity epidemic is likely to require a suite of interventions targeting the obesogenic environment as well as individual behaviour. Evidence suggests that the effectiveness of behaviour modification programmes can be enhanced by financial incentives that immediately reward

weight loss behaviour. This systematic review investigated the effectiveness of incentives with a focus on assessing the relative effectiveness of incentives that target different behaviours as well as factors of importance when implementing these programmes in real-world settings (health insurer settings). A narrative review of the academic and grey literature including a variety of study designs was undertaken. Twenty studies met inclusion criteria and were assessed using the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies. Results suggest that incentivizing weight loss is effective in the short term while the incentives are in place. There are various incentive designs, and although the relative effectiveness of each of these on weight loss is not clear, it appears that positive incentives increase the uptake into programmes and may reduce dropouts. As with other weight loss initiatives, there is a need to explore ways to maintain weight loss in the longer term – incentives for weight maintenance could play a role.

*Commentaires : Si le dessein de cette étude peut paraître surprenant (payer les gens pour maigrir est-il efficace ?), celle-ci a le mérite de dresser un état des lieux approfondi de cette tendance de plus en plus répandue qui consiste à inciter financièrement à mettre en place des changements afin de perdre du poids. La plupart des études de cette revue mettent en évidence que si la valorisation financière semble être efficace sur le court terme dès lors que l'incitation financière cesse, l'engagement dans les mesures ayant permis la perte de poids cesse lui aussi et que si cette incitation financière pouvait favoriser l'inclusion dans les programmes de perte de poids et réduire le nombre de drop-outs, ces méthodes doivent être pensées sur le long terme : payer à vie les gens pour maintenir un changement de santé ? Assister les sujets dans un changement qui leur convient et qui leur permet de développer des objectifs permettant un maintien sur le long terme ? [6].*

### **Attribution of weight regain to emotional reasons amongst European adults with overweight and obesity who regained weight following a weight loss attempt**

K Sainsbury, EH Evans, S Pedersen, et al (2017) *Eating and Weight disorders* [7]

*Purpose:* Despite the wide availability of effective weight loss programmes, maintenance of weight loss remains challenging. Difficulties in emotion regulation are associated with binge eating and may represent one barrier to long-term intervention effectiveness in obesity. The purpose of this study was to determine the relationship between

emotion regulation difficulties and the extent of weight regain in a sample of adults who had lost, and then regained, weight, and to examine the characteristics associated with emotional difficulties.

*Methods:* 2,000 adults from three European countries (UK, Portugal, and Denmark) completed an online survey assessing self-reported weight loss and regain following their most recent weight loss attempt. They also completed a binge eating disorder screening questionnaire and, if they had regained weight, were asked if they attributed it to any emotional factors (a proxy for emotion regulation difficulties). Spearman's correlations and logistic regression were used to assess the associations between emotion regulation, weight regain, and strategy use.

*Results:* Emotion regulation difficulties were associated with greater weight regain ( $n = 1,594$  who lost and regained weight). Attribution to emotional reasons was associated with younger age, female gender, loss of control and binge eating, lower perceptions of success at maintenance, using more dietary and self-regulatory strategies in weight loss, and fewer dietary strategies in maintenance.

*Conclusions:* Weight-related emotion regulation difficulties are common amongst regainers and are associated with regaining more weight. Affected individuals are already making frequent use of behavioural strategies during weight loss, but do not apply these consistently beyond active attempts. Simply encouraging the use of more numerous strategies, without concurrently teaching emotion regulation skills, may not be an effective means to improving weight outcomes in this group.

*Commentaires :* Cette étude à grande échelle conduite dans trois pays européens vient confirmer l'influence bidirectionnelle des difficultés de régulation émotionnelle chez

les patients en surpoids tentant d'infléchir leur courbe pondérale : en lien direct, car prédisposant à reprendre du poids à court terme, et indirectement sur le long terme en chronicisant le recours à des stratégies inadaptées, en diminuant le sentiment d'efficacité et en aggravant chez ces patients fragiles les effets délétères de la restriction cognitive. Ces résultats viennent soutenir la nécessité de prendre en charge au plus tôt les émotions de nos patients dans la mesure où celles-ci semblent être un médiateur central dans le développement et le maintien du surpoids.

## Références

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